ECONOMIC BURDEN OF END-STAGE RENAL DISEASE IN CANADA

THE ECONOMIC BURDEN OF END-STAGE RENAL DISEASE IN CANADA: PRESENT AND FUTURE

By

JENNIFER ZELMER, B.Sc. M.A.

A Thesis

Submitted to the School of Graduate Studies

in Partial Fulfillment of the Requirements

for the Degree

Doctor of Philosophy

McMaster University

DOCTOR OF PHILOSOPHY (2005)
(Economics)

McMaster University
Hamilton, Ontario

TITLE: The Economic Burden of End-stage Renal Disease in Canada: Present and Future

AUTHOR: Jennifer Zelmer, M.A. (McMaster University), B.Sc. (University of Victoria)

SUPERVISOR: Professor Byron G. Spencer

NUMBER OF PAGES: xiii, 204

Abstract

End-stage renal disease (ESRD), or kidney failure, is a serious illness with significant health consequences and high-cost treatment options. Since the early 1980s, the number of Canadians with ESRD has more than quadrupled (CIHI, 2001), leading to questions about the current and future impact of the disease on public health, quality of life, health spending, and patients' productivity.

Using an economic burden of illness approach, this thesis estimates ESRD's "direct" health care costs and "indirect" costs, such as productivity losses due to premature death and short- and long-term disability. It also projects future results under various alternative assumptions using a multi-state discrete time Markov model.

The analysis suggests that, although less than 0.1% of Canadians have ESRD, it generated direct health care costs of $1.3 billion in 2000 or $51,099 per person with ESRD. That compares to $3,183 per capita for Canadians overall (CIHI, 2002b). Adding indirect morbidity and mortality costs brings the total to $1.9 billion.

Rising ESRD numbers suggest higher costs in the future. Further analysis explored the effect of various assumptions about drivers of past trends, such as population growth, changes in the age structure, and the prevalence of conditions known to cause ESRD (e.g. diabetes). Projections were most sensitive to assumptions about the rate at which new cases are diagnosed. If current trends continue, the total economic burden of the disease can be expected to reach $7.9 billion by 2015 (year 2000 dollars). On the other hand, if the rate of new cases in 2000 were maintained, the economic burden of illness would be $5.7 billion in 2015.

Nevertheless, under this and many other assumptions, there is likely to be a significant gap between available organs for transplant and the demand for transplantation. The likely effects of various options for addressing this gap are also explored.

Acknowledgements

While only one name appears on the title page, the completion of this thesis would not have been possible without the help of dozens of individuals and several organizations. Particular thanks are due to my supervisor, Byron Spencer, and the other members of my thesis committee, Frank Denton and Jerry Hurley. Their advice and mentorship shaped my understanding of both the questions explored in this thesis and the research process more broadly.

Data and time are also essential ingredients for this type of work. My thanks go to all those at the Canadian Institute for Health Information (CIHI), Health Canada, and Statistics Canada who helped me to obtain the former and to CIHI, particularly Richard Alvarez, for the precious gift of the latter.

Last, but not least, I owe a tremendous debt of gratitude to my friend and fellow thesis-writer Rebeccah Marsh and to my family who listened to progress reports over several years and provided essential advice and limitless support throughout. Thanks for caring; my life is infinitely richer because of you.

Please note that parts of the material presented in this thesis are based on data and information provided by CIHI through the Graduate Student Data Access Program. However, the analyses, conclusions, opinions, and statements expressed herein are those of the author, and not necessarily those of CIHI.

Table of Contents

List of Illustrations, Charts, and Diagrams

List of Tables

List of Figures

Chapter 1: Introduction

Canada's health care bill surpassed $100 billion for the first time in 2001 (Canadian Institute for Health Information, 2003b).[1] Large as this number seems, research suggests that what is spent directly on treatment, care, and rehabilitation is less than half of the total economic burden of illness facing the country (Policy Research Division of the Strategic Policy Directorate in the Population and Public Health Branch of Health Canada (subsequently referred to as Health Canada), 2002). The rest consists of a broad range of "indirect" costs, such as productivity losses due to premature death and short- or long-term disability.

Questions about the sustainability of current funding levels have been at the core of lively health care debates taking place from coast to coast.[2] Governments, health care providers, public commissions, and individual Canadians are struggling with difficult decisions about what services to fund and how health care should be delivered. A better understanding of the potential impact that alternative answers would have for the economic burden of illness would help to inform this debate.

This thesis models the current and future direct and indirect costs associated with the thousands of Canadians who have end-stage renal disease (ESRD),[3] a group that continues to grow year after year. It also explores the potential impact of various policy alternatives on the economic burden of this illness. This study was approved by the McMaster University Research Ethics Board (REB # 2002 059).

---

[1] This total includes any type of public or private sector spending for which the primary objective is to improve or prevent the deterioration of health status.

[2] See for example the Commission reports from across the country (Commision d'étude sur les services de santé et les services sociaux, 2000; Cuff, 2001; Fyke, 2001; Government of British Columbia, 2001; Premier's Advisory Council on Health, 2001; Commission on the Future of Health Care in Canada, 2002; Government of New Brunswick, 2002; Standing Senate Committee on Social Affairs, Science, and Technology, 2002), as well as the results of a recent pan-Canadian consultation on priorities for health services and policy research (Dault, et al., 2004).

[3] These costs are borne by a variety of groups, including governments, insurance plans, and individuals and their families.

Chapter 2 provides an overview of the disease, its treatment, and the current situation in Canada. Chapter 3 examines and attempts to understand the causes of the rapid growth in the number of new cases diagnosed each year over the past decade. For today's ESRD population, Chapter 5 estimates the economic burden of end stage renal disease from a societal perspective based on methods described in Chapter 4.

Building on this foundation, Chapter 6 provides a broad exploration of the dynamics of the disease and treatment process. This chapter introduces a mathematical model of ESRD care that has been designed to facilitate the projections of incidence and prevalence that are required to estimate the future economic burden of the disease.

Subsequent chapters apply this underlying model to project the annual incidence and prevalence of ESRD by type of treatment (Chapter 7) and to explore the potential effects of changes in demographics, disease incidence, and practice patterns (Chapter 8). These chapters also include associated estimates of the economic burden of illness in 2015. Chapter 9 extends this analysis with a focus on the potential impact of alternate transplant policy options.

This work builds on a body of literature related to projections of the incidence (number of new cases), prevalence (number of cases at a given point in time), treatment, and economic burden of chronic diseases. New contributions to the literature include:

- The empirical estimation of the relative contribution of population growth, demographic shifts, and the increase in diabetes to the rise in new ESRD cases in Chapter 3;
- Estimation of the current economic burden of ESRD in Canada (Chapter 5);
- The formal specification of a systems model of ESRD and its care in Chapter 6;
- Long-term projections of ESRD, as described in Chapters 7 and 8;
- Improved understanding of the sensitivity of projection results and estimates of the economic burden of illness to a range of assumptions regarding population demographics, the rate of new cases of ESRD, practice patterns and patient survival, productivity loss, and other factors (Chapters 5 and 8); and

- An evaluation of the potential impact of various policy alternatives that might affect the supply of kidneys for transplant, including a game theory representation of the trade-offs that individuals would face in deciding whether or not to register for a mutual insurance pool for organs (Chapter 9).

Chapter 2:
End-Stage Renal Disease in Canada ~ An Overview

A person's kidneys perform crucial functions that affect all parts and processes of the body. Healthy kidneys regulate the amount of water in the body, filter excess minerals and wastes from the blood, and produce hormones that help to regulate blood pressure and to support the production of red blood cells. Without treatment, a person will die within a short time when both of his/her kidneys fail.

End-Stage Renal Disease (ESRD) exists when a person's original kidneys "are permanently impaired and can no longer function normally to maintain life", often defined as functioning at less than 10% of their normal rate (Canadian Institute for Health Information (CIHI), 2001). By definition, untreated ESRD is universally fatal. Even with treatment, it is a serious disease that often leads to poorer than average health status and quality of life, significant financial consequences for patients and their families, and high costs for the health care system (Molzahn and Kikuchi, 1998; Wight, et al., 1998; Nissenson and Rettig, 1999; Belasco and Sesso, 2002; Van Manen, et al., 2002).

2.1 Leading Causes of ESRD

Many different diseases can lead to ESRD. The leading and increasingly common cause in most developed countries is diabetes (Reikes, 2000; Krishnan, et al., 2002). In 1999, it was the primary factor causing renal failure for 31% of new ESRD patients in Canada, up from 15% in 1981 (CIHI, 2001).[4] Renal vascular disease, including hypertension, accounted for a further 21% of new cases. The rich blood supply to the kidneys (about one fifth of the heart's output each minute) makes them vulnerable when disease processes affect blood vessels

[4] Unless otherwise specified, all data on end-stage renal disease incidence, prevalence, treatment, and outcomes in Canada are derived from the Canadian Organ Replacement Register (CORR). Appendix A includes a brief description of CORR. Appendix B provides a summary of trends in key ESRD parameters for Canada drawn from CORR.

(Smith, 1987). Glomerular diseases[5] are also an important cause of ESRD, although they have declined in relative importance in recent years. In 1999, glomerulonephritis was the primary factor causing renal disease for 15% of new patients.

The prevalence of these diseases and their underlying risk factors, as well as many other phenomena, influence the rate of ESRD in a population. For example, the availability and effectiveness of secondary prevention strategies that affect whether or not (or when) a person with diabetes, hypertension, or other conditions develops kidney disease can have an impact on ESRD rates (Klefter and Nielsen, 2002). In addition, patient, family, societal, and clinical preferences, practices, and resources may affect the likelihood that a person with ESRD is referred to, or chooses to, accept treatment (Port, 1995).

2.2 Treatment Options

ESRD cannot currently be cured, but there are several treatment options. Patients with ESRD generally either receive dialysis or have a kidney transplant. In both cases, survival rates have improved in recent years (Nissenson and Rettig, 1999; Schaubel, et al., 1999; Harris, et al., 2000). Nevertheless, some patients choose to refuse or withdraw from treatment, leading to death within days or weeks.

Over time, people move into and out of the dialysis, transplant, and potential organ donor populations. Chapter 6 describes the dynamics of the disease and treatment processes, including a mathematical model of the transitions between different treatment and survival states.

Dialysis

Dialysis removes toxic materials from a patient's blood stream and maintains fluid, electrolyte, and acid-base balance when his/her kidneys have failed (Gutch, et al., 1999). There are two major types of dialysis: hemodialysis and peritoneal dialysis.

Hemodialysis uses an external machine to filter blood through a semipermeable membrane, and a special dialysis fluid carries away wastes (Gutch, et al., 1999). Most commonly performed with the support of health professionals in a hospital or dialysis centre, hemodialysis can also be undertaken at home with appropriate training and assistance. A typical patient receives this

[5] The glomerulus is a network of capillaries in the kidney surrounded by an epithelial membrane that is involved in blood filtration (Gutch, et al., 1999).

type of dialysis three times a week for three or more hours each session (CIHI, 2001). Individuals with additional chronic conditions are more likely to receive hemodialysis than other types of care (Fenton, et al., 1993).

Peritoneal dialysis filters blood internally using the patient's peritoneal membrane. There are several types of peritoneal dialysis. Patients and/or their families are usually trained to perform the procedure at home, although hospital or clinic-based services may also be required. The frequency and duration of treatment varies depending on the form of peritoneal dialysis and the patient's needs. Most Canadian patients were on four dialysis exchanges per day in 1999, although there has been a trend towards increasing dialysis prescription in recent years (CIHI, 2001).

In spite of a wide range of sometimes contradictory studies, a number of recent reviews have concluded that no one type of dialysis offers a significant survival advantage across all patient groups, after adjusting for patient and clinical characteristics (Schaubel, et al., 1998b; Gokal, et al., 1999; Murphy, et al., 2000; Mehrotra and Nolph, 2001; Keshaviah, et al., 2002). In terms of health-related quality of life, home-based therapies generally perform better than centre-based dialysis (Gokal, et al., 1999; Starzomski and Hilton, 2000). The choice between types of dialysis may therefore depend on factors such as patients' personal preferences or lifestyle, clinical characteristics, and socioeconomic circumstances (Becker and Stone, 1997; Lameire and Van Biesen, 1999).

An international review found relatively similar cost differentials between types of dialysis among a range of countries, although the levels of spending differed from place to place (de Vecchi, et al., 1999). Specifically, centre-based hemodialysis was more costly than limited care hemodialysis (where patients care for themselves with some assistance from allied health professionals). Both types of dialysis had higher total treatment costs than hemodialysis or peritoneal dialysis performed at home by patients and their families. Similar results have been found in other studies (Martin, 1996; Peeters, et al., 2000).[6]

Some authors have suggested that the substantial variation in therapy choice within and among countries implies that differences in the organization of care and/or financial incentives also influence therapy selection (de Vecchi, et al., 1999; Hörl, et al., 1999). For example, the cost structures for the different types of dialysis vary considerably. Centre-based hemodialysis has higher fixed costs (mostly personnel and capital). Peritoneal dialysis tends to have higher variable costs (mostly for supplies), although lower total costs on average. As a result, where there is already excess capacity for centre-based hemodialysis or strong

[6] Cost estimates generally reflect direct treatment costs and may not include related patient/family costs and time.

incentives for investment in physical capital, there may be a tendency to select this type of therapy over peritoneal dialysis.[7]

Kidney Transplantation

Organ transplantation is one of the miracles of modern medicine. Its success reflects important advances in surgical knowledge and skill, as well as in post-surgical care. Better understanding of the immune system and of how to prevent the recipient's body from rejecting the transplanted organ has also been critical. This includes appropriate matching of donors and recipients based on blood groups, human leucocyte antigens (HLA),[8] and other factors, as well as new medications that reduce the risk of graft rejection (Smith, 1987; Gutch, et al., 1999).

Compared to dialysis, kidney transplantation generally offers ESRD patients improved quality of life and better long-term survival chances (Schaubel, et al., 1995; Wight, et al., 1998; Pascual, et al., 2002). For example, Rabbat (2000) found that while Ontario patients had a higher relative risk of dying in the first thirty days after a transplant than their counterparts on the waiting list had, at one year the situation reversed. Transplanted patients had lower death rates ($p<0.05$), after adjusting for gender, race, age, primary cause of renal failure, and time from first ESRD treatment to being placed on the waiting list. Transplants are typically also, at least after the first year, a more cost-effective treatment option (Goeree, et al., 1995; Lysaght and O'Loughlin, 2000; Manns, et al., 2000; Kaminota, 2001). A recent meta-analysis found that centre-based hemodialysis had a cost-effectiveness ratio of $55,000-$80,000 US per life year saved, compared to $33,000 to $50,000 for home hemodialysis and about $10,000 for kidney transplants (Winkelmayer, et al., 2002).[9] Accordingly, they have become the preferred form of care for many ESRD patients (Mendelssohn for the Professional and Public Policy Committee of the Canadian Society of Nephrology, 1997; National Coordinating Committee for Organ and Tissue Donation Distribution and Transplantation, 1999).

Although organs for transplant can come from living or cadaveric donors, the demand for kidney transplants continues to outstrip the supply of organs

[7] Depending on local policy and clinical practice, the distribution of costs among different payors (e.g. government health insurance programs, private insurers, and patients or their families) may also differ among treatment modalities. This may also influence care decisions.

[8] This is a group of genes on the sixth chromosome that has been found to have an important influence on the body's recognition of foreign tissue.

[9] All figures are in 2000 U.S. dollars per life year saved.

available. This imbalance is the result of a slower increase in the number of donors than in the number of patients waiting for transplants. For example, although cadaveric donor numbers rose 42% between 1992 and 2000, the kidney transplant waiting list grew by 66% (CORR/CIHI, 2002). Many factors affect the supply of cadaveric organs, including:

- the criteria for determining potential candidates for cadaveric organ donation;
- the number of deaths in circumstances that may make individuals candidates for donation (which can be affected by personal behaviours and risk factors, as well as a wide variety of policy decisions, including many, such as road safety legislation, that are outside the direct control of the health care system);
- the probability that candidate donors and/or their families are asked about and consent to organ donation (possibly affected by personal preferences and attitudes, as well as a variety of clinical and policy initiatives, such as the development of specialized organizations charged with coordinating the procurement and equitable distribution of cadaveric organs);
- the likelihood that organs are successfully harvested from candidate donors who have consented (which may be affected by factors as diverse as characteristics of the potential donor, the availability of necessary facilities and staff, and financial reimbursement mechanisms); and
- many other factors (Martin, 1996; Campbell and Sutherland, 1999; Holt, et al., 1999; Alberta Advisory Committee on Organ and Tissue Donation and Transplantation, 2000; Baxter, 2001).

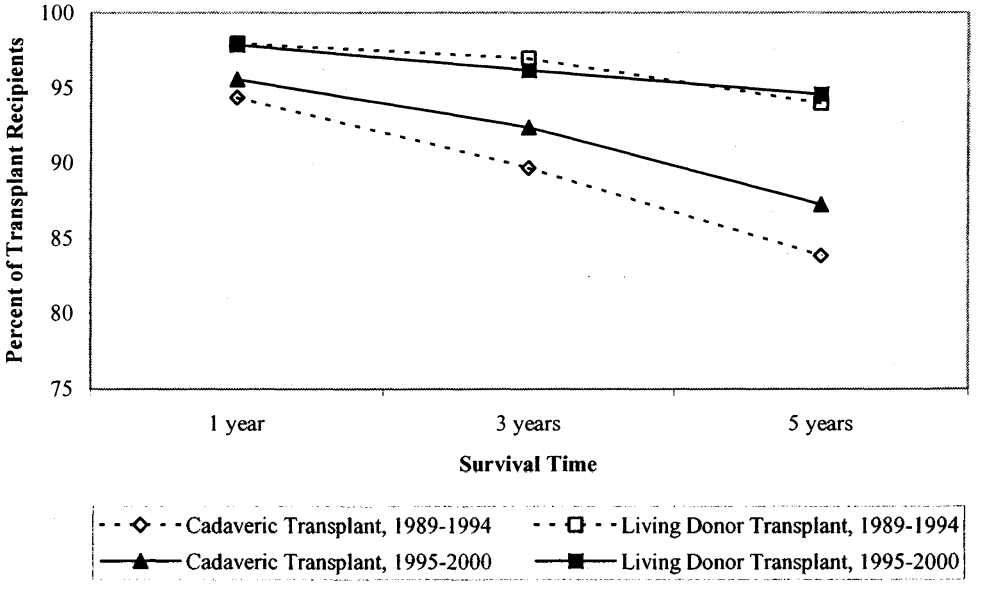
In spite of the growing waiting list for transplants, only a fraction of potential cadaveric organs are transplanted each year. Between 1992 and 1997, organs were retrieved from about 8 out of every 100 potential donors in Canada (CIHI and Clarica, 2001).[10] Only a relatively small portion of the gap between actual and potential organ donors is caused by non-acceptance or non-retrieval of organs for which consent was obtained. In 2000, in 84% of cases where patients were declared brain dead and their organs were offered, at least one organ was used for transplantation (CORR/CIHI, 2002).

Living donors are currently the only other source of kidneys for transplantation. They represent a growing, but still a minority share, of the total

[10] Following Holt, et al. (1999) "potential" donors are defined as patients in hospital aged zero to sixty-nine who are clinically brain dead and for whom there is no general contra-indication to donation. Most often, these patients have experienced a head injury or cerebrovascular accident.

donor pool. From 20% in 1992, kidneys from living donors grew to 34% of total transplanted organs in 2000 (CORR/CIHI, 2002). On average, recipients of organs from living donors continue to have better survival chances than their counterparts who receive cadaveric organs, although the gap has narrowed in recent years (see Figure 1).

Figure 1: One, Three, and Five Year Survival Rates for Patients who Received Cadaveric or Living Donor Kidney Transplants, Canada, 1989-1994 and 1995-2000[11]



As with cadaveric organ donations, a number of factors affect the supply of organs from living human donors. These include:

- clinical, ethical, and legal practices or policies (e.g. whether or not living donors who are not related to the transplant recipient are permitted to donate organs);

- the availability of alternatives to live donation (e.g. the length of the cadaveric waiting list and possibly xenotransplantation in the future[12]);

[11] Source: Canadian Organ Replacement Register (CORR/CIHI, 2002).

[12] Xenotransplantation involves transplanting animal organs into human hosts. To date, there have been no kidney transplants of this type in Canada, even as part of research programs, although patients have received pig-to-human skin grafts and pig heart valve transplants for many years (Bigam, et al., 1999). Solid organ xenotransplantation is a highly controversial practice with proponents pointing to

- the socio-demographic characteristics of patients requiring transplants (e.g. children are more likely to receive living donations than are adults);
- the availability of an open market for organs in Canada or internationally;[13] and
- the cost of care for organ donors and transplant recipients (Minister's Task Force on Kidney Donation, 1985; Baltzan, et al., 1997; Barrett, et al., 1997; Alberta Advisory Committee on Organ and Tissue Donation and Transplantation, 2000; Steiner and Gert, 2000; CORR/CIHI, 2002; Friedlaender, 2002).

2.3 ESRD in Canada

In 1947, Dr. Gordon Murray performed the first dialysis in Canada at a hospital in Toronto (McGill University Health Centre, 1998). Ten years later, the country's first kidney transplant took place at the Royal Victoria Hospital in Montreal. Since then, ESRD treatment has moved rapidly from experimental therapies to established standards of care.

By the end of 2000, an estimated 24,921 Canadians (810 per million population) were living with end-stage renal disease (CORR/CIHI, 2002). During that year, renal centres cared for approximately 4,515 new (incident) ESRD cases[14] and there were about 2,675 deaths.[15] This represents a significant health issue for the country, with about the same number of new cases each year as for

---

xenotransplantation as a potential solution to the current organ shortage and opponents pointing to the ethical, cost, and potential disease risks of the practice (National Forum on Xenotransplantation, 1999). A 2001 public consultation on animal-to-human transplantation recommended to the Federal Minister of Health that "Canada not proceed with xenotransplantation involving humans at this time as there are critical issues that first need to be resolved" (Public Advisory Group on Xenotransplantation, 2001).

[13] All Canadian provinces and territories have legislation prohibiting the sale of organs and tissues for profit (Health Canada, n.d.).

[14] Figures based on preliminary data and include CORR's estimate of 129 patients not yet reported by renal centres. For more information, please see Appendix A.

[15] Facility profile questionnaires for three Quebec centres had not been returned at the time that preliminary estimates were reported. CORR did not impute data for these centres and so they are not included in these figures.

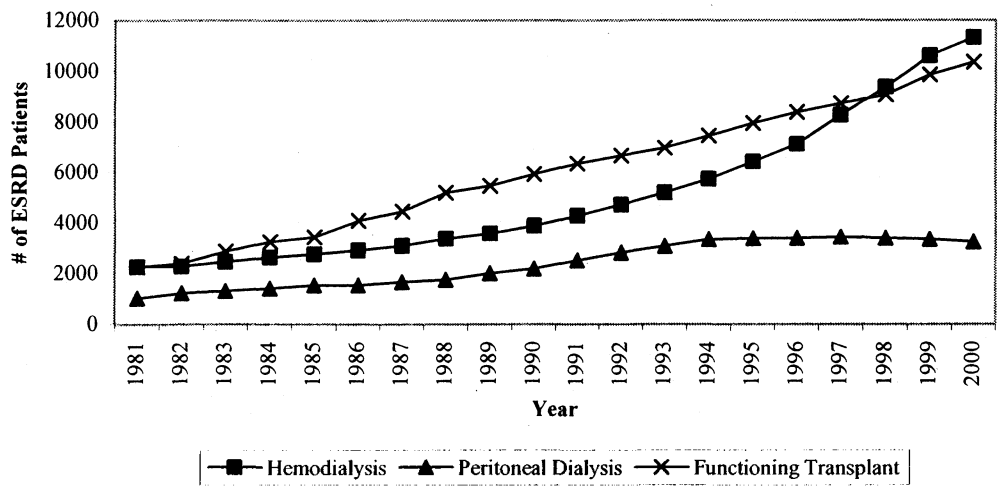
bladder cancer (4,700 forecast in 2001) and HIV infections (4,190 in 1999).[16] In comparison, the incidence of lung, breast, and prostate cancer is much higher. The National Cancer Institute of Canada (NCIC) forecast 21,200, 19,500, and 17,800 new cases respectively for 2001. Other diseases are more rare. For instance, there are fewer new cases of ovarian, thyroid, and cervical cancer each year (estimated at 2,500, 1,900, and 1,450 cases respectively in 2001).

Trends in ESRD Treatment in Canada

Over time, the mix of treatments provided to ESRD patients has evolved. Since the mid-1990s, there has been relatively rapid increase in the number of patients receiving hemodialysis, accompanied by a decline in peritoneal dialysis use. The number of patients alive with functioning kidney transplants has climbed steadily over the past two decades. Despite this increase, most Canadian ESRD patients (58.5%) received some type of dialysis in 2000, according to CORR data. Figure 2 shows the stock of patients on each type of treatment as of December 31st for each year between 1981 and 2000.

Figure 3 shows which treatments new patients received over the same period.

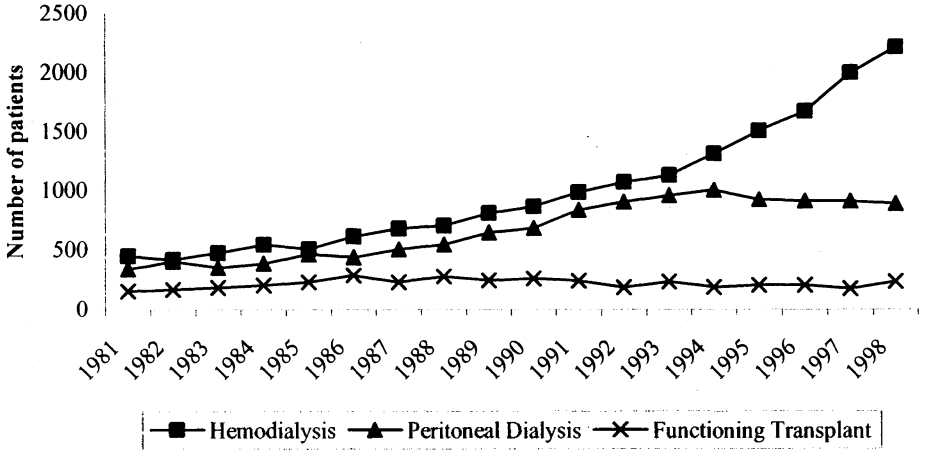
Figure 2: Number of ESRD Patients by Treatment Type on December 31st, 1981 to 2000, Canada[17]



[16] All cancer incidence estimates are based on NCIC forecasts (NCIC, 2001). HIV infection incidence rates are based on Health Canada statistics (Centre for Infectious Disease Prevention and Control, 2001).

[17] Source: Canadian Organ Replacement Register (CORR/CIHI, 2002).

Figure 3: Number of New ESRD Patients by Treatment Type One Year After Initiation of First Treatment, 1981 to 1998, Canada[18]



ESRD Policy in Canada

The relatively rapid growth in ESRD incidence and prevalence has led to concerns about the current and future impact of the disease on public health and quality of life, as well as on the long-term financial and clinical sustainability of treatment programs. These concerns have generated considerable clinical research and policy interest – a situation that will likely continue for the foreseeable future. For example, several jurisdictions across the country have evaluated and/or developed plans for future dialysis and transplant requirements (for example Minister's Task Force on Kidney Donation, 1985; Manitoba Health, 1998; Alberta Advisory Committee on Organ and Tissue Donation and Transplantation, 2000; Provincial Health Council, 2000). Studies have also been conducted at the national level (for example National Coordinating Committee for Organ and Tissue Donation Distribution and Transplantation, 1999; National Forum on Xenotransplantation, 1999).

Decisions made today – such as where to establish dialysis and transplant programs or whether to allow xenotransplantation research – may have far-reaching effects. The following chapters aim to support the establishment of sound health policy in this important area by enabling a better understanding of

[18] Source: Canadian Organ Replacement Register (CIHI/CORR, 2001). Excludes patients who recovered kidney function, died, or were lost-to-follow-up one year after initiation of first treatment.

the potential impact of various demographic, policy, care, and other factors on the direct and indirect economic burden of illness now and in the future.

Chapter 3: End-Stage Renal Disease ~ A Growing Policy Issue

In Canada and around the world, end-stage renal disease (ESRD) numbers have been climbing steadily for several decades (Reikes, 2000; Klefter and Nielsen, 2002; Krishnan, et al., 2002). Worldwide, researchers estimate that approximately 1.1 million people have ESRD (Lysaght, 2002). These patients account for a disproportionate share of health care resources. For example, a 1999 study of 6 European countries found that the 0.022%-0.06% of the population who were on dialysis accounted for 0.7%-1.8% of total health expenditure (de Vecchi, et al., 1999).

Although the rate of newly diagnosed cases varies considerably among developed countries, all have experienced rapid growth in the incidence and prevalence of ESRD in recent years. Lysaght (2002) estimates that the worldwide ESRD population has been growing by about 7% per year.[19]

There has been considerable speculation in the literature about the reasons behind this increase (for example Port, 1993; Choudhry and Naylor, 1995; Port, 1995; McKenzie, et al., 1998). Hypotheses range from a pure increase in the rate at which people develop kidney disease to demographic shifts, changes in practice patterns, and shifts in other relevant factors.

In order to project future trends, it is important to understand key drivers of past experience. Ultimately, this is an empirical question, although there have been few attempts to quantify the relative contributions of various factors to the rise in ESRD incidence. This chapter assesses the relative importance of three factors in Canada: population growth, changes in the age structure of the population, and the increasing prevalence of diabetes, a leading cause of ESRD.[20]

---

[19] This is significantly higher than the United Nations' estimate of annual population growth between 1995 and 2000: 1.3% (Population Division of the Department of Economic and Social Affairs at the United Nations Secretariat, 1999).

[20] Other health conditions (e.g. hypertension) were not studied due to limitations imposed by the sample size of available surveys.

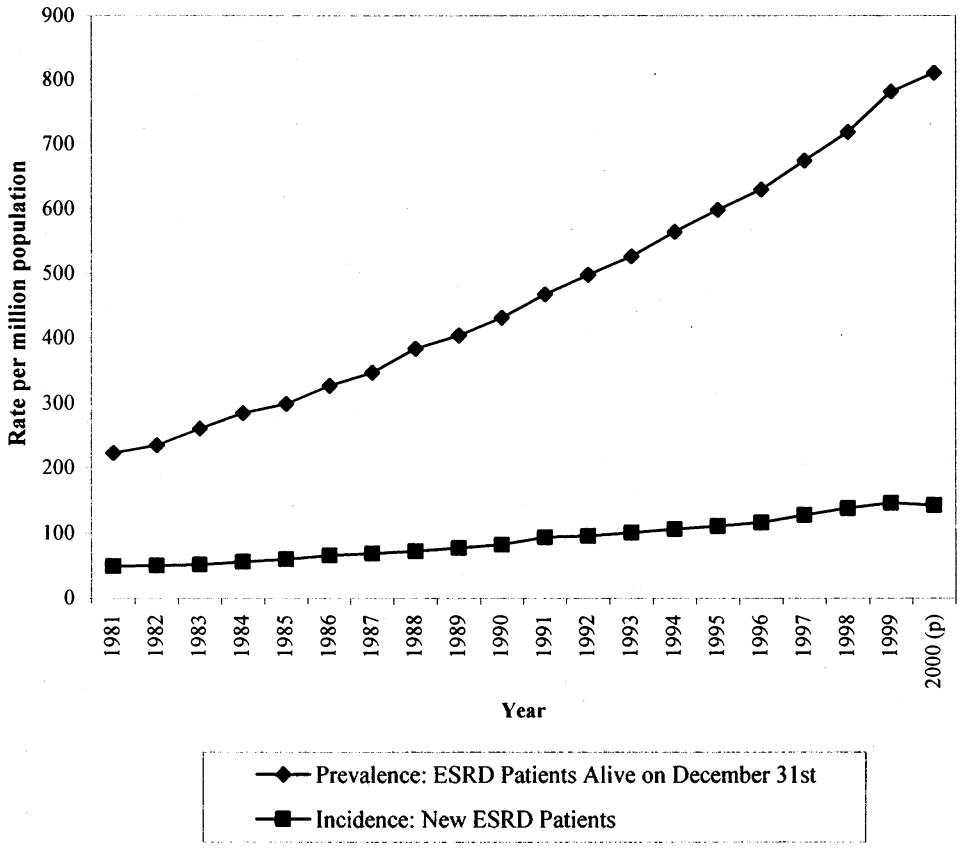
3.1 ESRD Trends in Canada

Like most developed countries, Canada has seen an upward trend in ESRD incidence (new cases of the disease) and prevalence (total cases at a given point in time) since at least the 1980s. As Figure 4 illustrates, more than four times as many people lived with ESRD in 2000 than in 1981 (CIHI, 2001).

In recent years, ESRD incidence has grown faster among older Canadians than their younger counterparts. Growth was particularly strong among older seniors (aged 75 and older). From just over 10% of those diagnosed with ESRD in 1990, they accounted for almost a quarter of new cases a decade later. Looking further back, average annual growth in incidence rates from 1981 to 1999 was 8.3% for those aged 65-74 and 12.7% for those 75 and over. In contrast, growth rates for those aged 15 to 44 and 45 to 64 were 2.4% and 3.8% respectively.

At 142.9 per million population in 1999, Canada's ESRD incidence rate falls in the middle of the range for developed countries (CIHI, 2001). For example, Australia (88.4 per million population) and Sweden (116.6) had lower rates, but Japan (248.5) and the United States (351.5) were at the other end of the spectrum.

Figure 4: Annual Incidence and Prevalence of ESRD on December 31st, Rate per Million Population, Canada, 1981-2000[21]



3.2 Understanding the Increase in ESRD Cases in Canada

In part, the growth in ESRD prevalence is due to improved survival for those diagnosed with the condition, but the number of *new* cases each year also continues to rise. For example, about 44% more patients were diagnosed with ESRD in Canada in 2000 than in 1994 (CORR/CIHI, 2002). The analysis that follows estimates the marginal effect of changes in population size, age structure, and diabetes prevalence on ESRD incidence over this period.

[21] Source: Canadian Organ Replacement Register (CORR/CIHI, 2002). 2000 figures based on preliminary data and include CORR's estimate of 129 new patients not yet reported by renal centres.

Methods

The marginal impact of various factors on the increase in ESRD incidence was estimated using direct standardization, a special case of predictive margin analysis (Inskip, et al., 1983; Korn and Graubard, 1999). In this type of analysis, one estimates the predictive margin (PM) for a standard population[22] where the distribution of the covariates is known using the following approach:

$$PM(r) = \sum_{s=1}^{S} \pi_s g(r, X_s, \theta) \qquad \textbf{Eq. 1}$$

where:

- r is the set of risk factors or treatment groups (not varied in direct age standardization);
- π_s is the probability that $X = X_s$ in the standard population where $\sum_{s=1}^{S} \pi_s = 1$ which in the case of direct age standardization is the proportion of individuals in the s^{th} age group in the standard or reference population (the group's weight);
- $g(r, x, \theta)$ is the quantity for which one wishes to predict the margin (i.e. the ESRD incidence rate observed in the s^{th} age group in a particular year); and
- X is a vector of covariates which takes on S distinct values $(X_1, \ldots, X_S)$, or in this case the four age categories used in this study (0-14, 15-44, 45-64, and 65+).[23]

Thus, age standardized rates were calculated according to the following formula:

$$StdRate = \sum_{s=0-14}^{65+} (c_s / p_s)\pi_s \qquad \textbf{Eq. 2}$$

where for age group s, c_s is the age-specific number of new cases, p_s is the age-specific population size, and π_s is the weight for that group from the standard population (Dever, 1984). To calculate a rate per million population, the result is multiplied by 1,000,000.

---

[22] In the case of direct age standardization, the PM is the estimated standardized incidence rate.

[23] A smaller number of age groups than are often used for standardized rates was employed because of the relatively small number of ESRD cases in some age groups, particularly when stratified by diabetes status in the next stage of the analysis.

Age standardized rates were compared with crude rates to estimate the marginal effect of changes in the age structure of the population on trends in ESRD incidence.

Direct age/diabetes-status standardization was also conducted. In this case, eight categories were used: each of the four age groups was subdivided into diabetic and non-diabetic sub-groups. Accordingly, standardized rates were calculated according to the following formula:

$$StdRate = \sum_{s=0-14}^{65+} \sum_{d=1}^{2} (c_{sd} / p_{sd})\pi_{sd} \qquad \textbf{Eq. 3}$$

where for age group s and diabetes status d (presence or absence of self-reported diabetes), c_{sd} is the age/diabetes status-specific number of new cases, p_{sd} is the age-diabetes status-specific population size, and π_{sd} is the weight for that group from the standard population.

Data Sources

Several different sources of data were required for this analysis. A brief outline is included below. More detailed descriptions, including information on the coverage and comprehensiveness of each data source, are provided in Appendix A.

Data on **ESRD incidence** come from the Canadian Organ Replacement Register. Custom tabulations subdivided the number of new ESRD cases reported for 1994 and 2000 by age group and primary renal disease (diabetes or other).[24] These tabulations were obtained in July 2002. At this time, 4,479 incident cases had been reported for 2000, an increase from the 4,386 available at the time of preliminary reporting (CORR/CIHI, 2002). Based on CORR's estimates at that time, a small proportion of cases (estimated at less than 0.8%) may still be outstanding.

Population estimates come from Statistics Canada. National population estimates by age group for July 1, 1994 and July 1, 2000 were obtained through Statistics Canada's CANSIM service.[25] For consistency, these population estimates were used throughout the analysis. As a result, there may be minor

[24] In some cases, ESRD patients have several co-existing conditions, such as diabetes and hypertension. For the purposes of this analysis, only the primary renal disease (as reported to CORR) was considered.

[25] The following series were downloaded from CANSIM on July 15, 2002: C892538, C892553, C892574, and C892577.

variations between crude rates presented here and those previously published. In this study, rates and case numbers for 2000 were standardized using parameters from the 1994 population to facilitate comparisons between the two years.

Data on **diabetes** were also required. Although federal, provincial, and territorial governments are collaborating on a National Diabetes Surveillance System, which aims to develop more comprehensive data based on administrative data sources, robust measures of long-term trends in diabetes incidence in Canada were not available at the time that this analysis was undertaken (Health Canada, 1999a; Health Canada, 1999b; Health Canada, 2002a).

There is, however, a recent cross-sectional time series for self-reported diabetes prevalence. These data come from Statistics Canada's 1994/95, 1996/97, and 1998/99 National Population Health Surveys, as well as the 2000/01 Canadian Community Health Survey. In each survey, a random sample of the household population aged 12 and older was asked whether they had ever been diagnosed with diabetes (as well as several other chronic conditions) by a health professional (Statistics Canada, 2002a).

Given the nature of the survey data, assumptions were required to estimate the size of the diabetic population by age group. These include:

- Survey results for 1994/95 and 2000/01 were used with calendar year 1994 and 2000 ESRD data respectively and with July 1st population estimates for 1994 and 2000 respectively.

- As with all surveys, there is the potential for sampling error. The significantly larger sample size in 2000/01 means that estimates for that year are more precise than those for 1994/95. In addition, the sampling frames changed somewhat between the two surveys (see Appendix A for details). Nevertheless, survey-based point estimates of diabetes prevalence by age group were used in this analysis for both years.

- National estimates of diabetes prevalence for children under the age of 12 are not available from the surveys. Accordingly, the age-specific prevalence for children aged 12 to 14 was assumed to apply to all those aged 15 and under. This approach slightly overestimates diabetes prevalence in younger age groups compared to other sources (for example Manitoba Health, 1998). Nevertheless, the impact on standardized rates is minor because very few new ESRD patients

under the age of 15 had a primary renal diagnosis[26] of diabetes and because the prevalence of diabetes in this age group is very low. Approximately 99.7% of Canadians aged 12 to 14 in 2000/01 were non-diabetic (Statistics Canada, 2002c).

- Canadians not covered by the survey sample frames (see Appendix A for details) or for whom diabetes status was reported as "not stated" were assumed to have the same diabetes-status distribution as those whose status was reported on the survey. As a result, the size of the diabetic population reported here will not exactly match that reported elsewhere and should be interpreted strictly as an estimate for the purpose of calculating standardized rates. For example, given that the survey is not conducted on reserves and that the prevalence of diabetes is higher for aboriginal peoples than for the Canadian population in general (Health Canada Medical Services Branch, 1997), survey results likely somewhat underestimate the true diabetes rate.

- 1991 diabetes prevalence estimates were not available so the 1994/95 estimates were applied to the standard population.

Reporting issues related to the relatively small sample size of the 1994/95 survey also imposed restrictions on the analysis that could be conducted. For example:

- In epidemiological analysis, age/sex standardization is often used. In this case, however, sex differences were not considered separately. This is consistent with other research on kidney failure (for example CORR/CIHI, 2002). It facilitates differentiation among significant risk factors, such as age and primary renal disease, in spite of the relatively small number of patients with ESRD and the limitations of diabetes prevalence estimates from surveys.

- The effect of changes in the prevalence of health conditions other than diabetes (e.g. hypertension) could not be explored because the survey sample sizes, particularly in 1994/95, were not large enough to provide robust prevalence estimates for multiple conditions by age group.

- In some cases, there was extreme sampling variability in the younger age groups (coefficient of variation greater than 33.3% for the proportion of the population with diabetes). Where this occurred, the inverse of the non-diabetic population proportion was used to estimate the diabetic population share. These estimates are likely to be less

[26] The Canadian Organ Replacement Register defines the primary renal diagnosis as the primary cause of kidney failure at the time of the patient's first treatment (CORR/CIHI, 1997).

reliable than others, as is perhaps reflected by the fluctuations between 1994/95 and 2000/01 for these age groups.

Based on these assumptions, Table 1 shows estimates of parameters derived from the data sources described above.

Table 1: Parameters Underlying Standardized Rates

Age Group	Diabetic	Standard Pop. ('000)	1994 Pop. ('000)	1994 New ESRD	2000 Pop. ('000)	2000 New ESRD
0-14	Yes	6	6	0	18	*
15-44	Yes	137	137	164	166	*
45-64	Yes	223	245	403	431	603
65+	Yes	360	385	300	490	641
Total	Yes	725	773	867	1,104	1,441
0-14	No	5,819	5,957	43	5,861	56
15-44	No	13,515	13,527	485	13,704	457
45-64	No	5,216	5,726	703	6,739	862
65+	No	2,849	3,052	1,017	3,362	1,663
Total	No	27,399	28,263	2,248	29,665	3,038

Results

Between 1994 and 2000, the absolute number of new ESRD patients grew by over 1,350, or about 43.8% (see Table 1). Several possible explanations for this increase have been proposed. For example, some authors have suggested that the increase may partly reflect the rising prevalence of diabetes (for example Nissenson and Rettig, 1999; Reikes, 2000; Yang, et al., 2001), but its impact has not previously been empirically estimated in Canada (Schaubel, et al., 1999). Ideally, this question would be evaluated longitudinally since patients may develop ESRD long after they are first diagnosed with diabetes. However, as

* To preserve confidentiality, this value is suppressed due to small numbers (n<5 in the 0-14 age group category), but actual counts were used in the rate calculations.

previously noted, only prevalence data from national surveys are currently available.

Based on the survey results, about 4.1% of Canadians aged 12 and older reported having diabetes in 2000/01, up from 3.0% in 1994/95 (Statistics Canada, 2002c; Statistics Canada, 2002b). In part, this growth may reflect an increasing prevalence of obesity, one of the risk factors for diabetes. Over the same period, the proportion of those aged 20 to 64 who were obese (defined as a body mass index of 30 or greater) grew from 13% to 15% (Statistics Canada, 2002a). In 2000/01, Statistics Canada estimates that 2.8 million Canadians aged 20 to 64 were obese, an increase of more than 500,000 people from 1994/95.

These changes in age-specific diabetes prevalence partly explain the rise in ESRD incidence between 1994 and 2000 since diabetics are much more likely than others to be diagnosed with kidney failure. To estimate the extent to which they contributed, the actual number of new ESRD cases observed in 2000 (4,479) was compared to the number that would have occurred had 1994 age-specific diabetes rates continued to 2000, *ceteris paribus*. This diabetes-standardized number of cases was 4,226. Thus increases in age-specific diabetes prevalence accounted for approximately 253/1,364 or 18.5% of the additional ESRD cases.

Population aging has also contributed to the rise in the number of new ESRD cases. To identify the impact of this on-going demographic transition, diabetes-standardized case numbers (4,226) were compared to age/diabetes standardized case numbers (3,983). The difference was 243 cases. Thus, changes in the age structure of the population explain an additional 17.8% of the growth in new ESRD cases over this period.

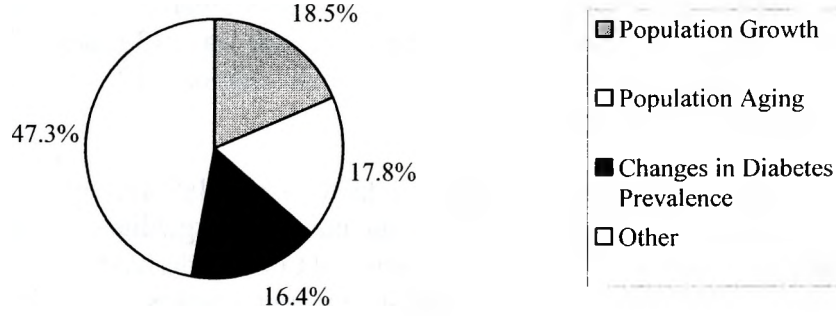
The effect of another demographic factor – population growth – was also explored. To estimate its contribution, the number of age/diabetes standardized incident cases for 2000 (3,983) was compared to those derived from a true age/diabetes standardized rate, taking into account changes in population size (3,759). Thus, population growth alone explains about 16.4% (224/1364) of the rise in new ESRD cases over this period.

Together, population growth, changes in the population's overall age structure, and the increase in the prevalence of diabetes explain over half (52.7%) of the rise in the number of new cases of ESRD between 1994 and 2000. Even after adjusting for all three factors, however, the number of new cases rose by more than 20% over this period (see Table 2 and Figure 5).

Table 2: Estimated ESRD Incidence in Canada in 2000 Under Various Scenarios

	# Incident Cases
Actual # Incident Cases of ESRD in 2000[27]	4479
Adjusted Based on 1994 Diabetes Rates	4226
Adjusted Based on 1994 Diabetes Rates and Age Distribution	3983
Adjusted Based on 1994 Diabetes Rates, Age Distribution, and Population Size	3759

Figure 5: Marginal Effect of Various Factors on the Growth in ESRD Incidence between 1994 and 2000, Canada



[27] This compares to just over 3,100 incident cases in 1994.

The residual growth is due to an increase in the age group- and diabetes-status specific incidence of ESRD. A variety of possible explanations for this rise have been proposed. For example, kidney disease may be becoming more common for a variety of reasons (Port, 1993; Port, 1995; Young, 1997; McKenzie, et al., 1998; Nissenson and Rettig, 1999; Reikes, 2000; Xue, et al., 2001; Klefter and Nielsen, 2002; Krishnan, et al., 2002; Lowance, 2002; Rao, 2002). Potential explanations include:

- demographic shifts not related to age (e.g. faster growth for population groups which tend to have higher rates of ESRD than for Canadians as a whole);
- changes in the prevalence of related conditions other than diabetes (e.g. hypertension);[28]
- a reduction in mortality from "competing diseases", such as cardiac conditions, so that there is a longer risk period for developing ESRD;
- environmental factors that may contribute to kidney disease (e.g. exposure to lead, silica, or organic solvents); or
- iatrogenisis related to the use of analgesics or other medication.

Changing practice patterns are another possible explanation. For example, the Canadian Society of Nephrology now recommends that "all competent patients who wish to undergo dialysis and who might benefit should be offered therapy for ESRD regardless of age, gender, employment status, race, co-morbid condition, or physical or mental handicap" (Mendelssohn for the Professional and Public Policy Committee of the Canadian Society of Nephrology, 1997). In the past, however, physicians were reported to be less likely to refer the elderly and those with certain serious co-existing illnesses for care (Wilson, et al., 2001). For instance, a 1999 survey found that 12% of Canadian family physicians and 4% of nephrologists felt that there was an age beyond which dialysis should not be offered (Sekkarie, et al., 2001). Some respondents also reported withholding dialysis in cases with significant chronic conditions or other impairments. In addition, in a survey by McKenzie (1998), 10% of Canadian nephrologists said that they had at least once withheld dialysis because there was insufficient funding to cover its costs.

[28] As noted above, it would theoretically be possible to differentiate the marginal effect of changes in the prevalence of hypertension on the incidence of ESRD from other contributing factors. Unfortunately, survey sample sizes were not sufficient to conduct this analysis since it would have required estimating potential interaction effects with diabetes.

3.3 Implications for Projections

The quality and utility of future projections depend heavily on the assumptions made. Based on recent experience, over half of the change in ESRD incidence in Canada can be explained by only three factors: population growth, changes in the age structure of the population, and the prevalence of diabetes. Thus, incorporating explicit assumptions regarding these factors should help to develop realistic projections of ESRD incidence for future years. That said, this analysis suggests that we continue to experience changes in age/diabetes-specific ESRD incidence rates. Accordingly, this is considered as part of the sensitivity analyses for the projections in subsequent chapters.

Chapter 4: Measuring the Economic Burden of Illness ~ An Overview

4.1 Introduction

Illness and disability have profound consequences for individuals, their families, and society as a whole. Many methods have been developed to summarize these effects. They are used for a wide range of purposes, including comparing health in different populations or for the same population over time; quantifying health inequalities; balancing attention on fatal and non-fatal health outcomes; informing priorities for health policy, health services management and delivery, and health research; and capturing the benefits of health interventions as part of cost-effectiveness analyses (Murray, et al.).

This chapter begins with an overview of some of the most common summary measures used in the economics and health policy literature. The remainder of the chapter focuses on one method – the economic burden of illness.[29] This methodology is used to estimate the economic burden of end-stage renal disease in Chapters 5, 7, and 8.

4.2 An Overview of Common Summary Measures

Until relatively recently, communicable diseases, deaths in childbirth, and trauma were leading causes of death, and policies to improve health often focused on preventing the spread of disease. Summary measures that were derived from vital statistics records, such as mortality rates and life expectancy, helped to inform these decisions (Committee on Summary Measures of Population Health of the Institute of Medicine, 1998). As the average life expectancy has lengthened, however, interest in promoting health throughout the life span (sometimes referred to as 'adding life to years'), rather than just adding years to life, has increased. As a result, economists, epidemiologists, and others have

[29] When the term 'economic burden of illness' is used in this and subsequent chapters, it refers to the specific methodological approach described below.

developed a wide range of measures that take into account disability, functioning, pain and suffering, health care costs, and other outcomes.

These measures have been described extensively elsewhere (see, for example, Torrance, 1986; Gafni and Birch, 1997; Committee on Summary Measures of Population Health of the Institute of Medicine, 1998; Murray, et al.). Different approaches attempt to capture different aspects of the consequences of illness, from the impact on mortality rates to broadly-defined welfare losses. They also use a variety of measurement approaches, each of which has strengths and weaknesses in terms of measuring the range of consequences of illness that its users intend to capture. Table 3 provides an overview of the outcomes captured by selected commonly used summary measures based on a categorization of costs and consequences suggested in the literature (Department of Clinical Epidemiology and Biostatistics at the McMaster University Health Sciences Centre, 1998).

Which of the different types of summary measures is most appropriate in a particular circumstance depends on the purpose for which it will be used. For example, some approaches place a relative value on different health states (e.g. disability adjusted life years, health utility index, self-reported health, and economic burden of illness[30] methodologies). Others – such as life expectancy, mortality rates, and person years of life lost – do not.

Likewise, the economic burden of illness methodology is the only approach that explicitly combines both health care costs and consequences. In contrast, other methodologies may be more suitable if quality of life considerations (e.g. pain and suffering) are of central importance for the research and/or policy question at hand. These factors may be significant but are not captured in an economic burden of illness approach, except as they result in productivity losses. Thus, this approach captures only a portion of the broadly-defined welfare losses resulting from a disease.

[30] This effect is measured through lost earnings and reductions in the imputed value of unpaid work.

Table 3: Elements Captured by Selected Commonly Used Summary Measures

Summary Measure	Mortality	Activity Limitation	Other Quality of Life	Direct Care Costs	Costs for Informal Caregivers	Other Costs[31]
Mortality rates (rate of death from all or selected causes)	✓					
Life expectancy (the number of years that a person would be expected to live based on age-specific mortality statistics for a given period)	✓					
Person years of life lost (the number of years of life "lost" when a person dies prematurely from all or selected causes, often defined as deaths before age 70 or 75)	✓					
Disability-free life expectancy (number of years that a person would be expected to live free of a disability based on age-specific mortality and activity limitation statistics for a given period)	✓	✓				
Disability-adjusted life expectancy (a measure that integrates data on mortality, activity limitation, and long-term institutionalization, assigning weights to yield a measure that reflects the quality and length of life)	✓	✓	~[32]		~[32]	
Disability-adjusted life years ("lost" years of healthy life due to disability or premature death)	✓	✓	~[32]		~[32]	
Health utility index (a measure of overall functional health with weights based on eight dimensions of functioning: vision, hearing, speech, mobility, dexterity, feelings, cognition, and pain)		✓	✓		~[32]	
Self-reported health (subjective assessments of overall health)	~[33]	✓	✓			
Economic burden of illness (summary in dollar terms of direct health care costs and the indirect economic burden of illness resulting from morbidity and mortality)	✓	✓	~[34]	✓	~[34]	~[34]

[31] These may include, for example, direct costs for other public programs (e.g. social services).
[32] May be implicitly reflected in subjective assessments of individual life states.
[33] May indirectly reflect perceived risks of mortality.
[34] While not included in the majority of studies, some researchers have attempted to quantify these costs.

The choice of measures is not strictly a methodological decision; it may also involve ethical and political considerations (Committee on Summary Measures of Population Health of the Institute of Medicine, 1998). For example, different methods differentially value the lives of the young and the old, those with physical versus mental disabilities, or those who have more or less earning power in the workforce. For instance, using foregone labour earnings as a measure of productivity loss places more weight on illnesses experienced by those in their prime earning years, an effect partially offset if the imputed value of lost productivity related to unpaid work is included in the calculations.

4.3 Research on Measuring the Economic Burden of Illness

Studies on the economic burden of illness (also sometimes referred to as cost of illness studies) attempt to summarize the direct health care costs and indirect costs associated with health consequences in terms of morbidity and mortality for one or more health conditions. A wide range of studies has been carried out over several decades. Some have attempted to calculate the economic burden of all illnesses for a nation and then to partition the results by disease (for example Rice, 1966; Cooper and Rice, 1976; Rice, et al., 1985; Wigle, et al., 1991; Moore, et al., 1997b; Health Canada, 2002). In contrast, most studies have focused on particular health conditions and/or populations. See Table 4 for a brief description of a selection of recent Canadian cost of illness studies.

Results have been used to inform policy and research priorities and decisions, estimate the relative societal impact of different health conditions, provide a framework for program evaluation, and other purposes (Rice, 2000). Nevertheless, cost of illness studies are not without controversy. At a global level, some argue, for instance, that decisions regarding policy or program trade-offs might be better informed by analyses that evaluate the relative marginal impact and costs of specific interventions (Donaldson and Narayan, 1998; Williams, 1999). On the other hand, as the analysis presented later in this thesis demonstrates, information based on a cost of illness framework can be used to understand the relative impact of such trade-offs on productivity losses, as well as direct health care costs.

Methodological debates also exist. For example, researchers must decide from whose perspective the analysis will be conducted; which types of costs to capture; what approach to take in estimating costs; and whether to consider costs for all patients with the condition at a given point in time or costs for a specific group of patients over time. Each of these choices is described in further detail below.

Perspective of the Analysis

One of the first decisions that a researcher conducting an economic burden of illness study must make is from whose perspective the analysis will be conducted. Some studies capture only costs borne by patients and their families. Alternatively, they may take the point of view of an employer or insurer. Analysis conducted from this perspective may, for instance, provide useful information to support decisions about insurance coverage or risk management. Most studies, however, take the perspective of society as a whole (Riegelman, 2000). This approach aims to quantify the consequences of illness in monetary terms, regardless of where they fall.

Range of Consequences Captured

The researcher's choice of perspective helps to determine what should be included and excluded in measuring the consequences of illness. At the core of most economic burden of illness studies is the concept of opportunity costs, the value of resources that are directed away from alternative uses because of the illness in question (Pindyck and Rubinfeld, 1992; Szava-Kovats and Johnson, 1997). The specific range of costs captured varies from study to study, but often includes:

- *Direct costs of health care services*: The value of goods and services used to prevent and/or treat the illness in question, from primary health care to palliative care, that cannot, as a result, be put to other uses. These costs are often calculated based on administrative data sources, surveys of patients, 'standard' average costs established for different types of care (for example Institute of Health Economics, 2000), and/or cost estimates published in the literature.

- *Direct costs of non-health care services*: In some cases, researchers also attempt to capture social services, legal/justice,[35] and/or other direct costs associated with the illness in question (e.g. Miller, 1995; Goeree, et al., 1999b).

- *Other care costs*: In rare cases, studies may also capture the costs and time incurred by the patient to access care and/or by informal caregivers who are providing care or assisting the patient to access services (Riegelman, 2000).

- *Premature mortality costs*: For health conditions that cause significant mortality, researchers often attempt to capture the value of productive

[35] For example, some researchers have assessed the costs of juvenile detention and other justice processes for persons with certain types of mental illness.

services that are foregone because of the illness in question. There are several options for measuring lost productivity due to premature mortality (see below).

- *Morbidity costs*: Researchers also typically include measures of lost productivity due to illness and disability. For example, they may attempt to capture the value of time lost from work or other activities. As for mortality, there are several options for measuring this lost productivity. A few studies also attempt to include lost productivity for informal caregivers and/or to quantify the 'cost' of quality of life reductions (e.g. pain and suffering).

Protocols developed by a Task Force of the U.S. Public Health Service have strongly influenced the design of economic burden of illness studies (Rice, 1966; Rice, et al., 1985). This approach estimates direct costs of health care and indirect costs of lost productivity due to premature mortality and morbidity. Similar methods have been used in broad-based national studies in Canada (Wigle, et al., 1991; Moore, et al., 1997a; Health Canada, 2002). Many studies of the economic burden of specific illnesses also reflect this approach, but others cover a broader or narrower range of costs (see for example Table 4).

Table 4: Selected Canadian Cost of Illness Studies

Study	Health condition(s)	Data year	Includes direct costs	Includes morbidity costs	Includes mortality costs	Incidence/ Prevalence
(Asche, et al., 1997)	Multiple sclerosis	1994	✓	✓	✓	P
(Bentkover, et al., 1999)	Irritable bowel syndrome	1996	✓	✓		P
(Birmingham, et al., 1999)	Obesity	1997	✓			P
(Canadian Burden of Illness Study Group, 1998a; 1998b)	Multiple sclerosis	1995	✓	✓		I/P
(Carabin, et al., 1999)	Common infections in toddlers attending day care centres in Quebec	1996-97	✓	✓		P
(Chan, et al., 1996)	Cardiovascular disease	1994	✓	✓	✓	P
(Chapman, et al., 2003)	Chronic obstructive pulmonary disease	n/a	✓	✓		P
(Choi and Pak, 1996)	Tobacco use in Ontario	1979 & 1988	✓	✓	✓	P
(Choi and Pak, 2002)	Cardiovascular disease	2000	✓	✓	✓	P

Study	Health condition(s)	Data year	Includes direct costs	Includes morbidity costs	Includes mortality costs	Incidence/ Prevalence
(Clarke, et al., 1997)	Rheumatoid arthritis (selected locations)	1980s and 1990s	✓	✓		I
(Clayton and Barcel, 1999)	Suicide in New Brunswick	1996	✓		✓	P
(Coyte, et al., 1998)	Musculoskeletal disorders	1994	✓	✓	✓	P
(Coyte, et al., 1999)	Otitis media	1994	✓	✓	✓	P
(Dawson, et al., 2002)	Diabetes	1998	✓		✓	P
(Goeree, et al., 1999b)	Schizophrenia	1996	✓	✓	✓	P
(Goeree, et al., 1999a)	Schizophrenia	1996			✓	P
(Grover, et al., 2000)	Prostate cancer	1997	✓			I
(Guttman, et al., 2003)	Parkinson's disease	1993/1994 inception cohort	✓			I
(Hanvelt, et al., 1994)	HIV/AIDS	1987-91			✓	P
(Health Canada, 2002)	Comprehensive	1998	✓	✓	✓	P
(Kaiserman, 1997)	Smoking	1991	✓	✓	✓	P
(Katzmarzyk and Janssen, 2004)	Physical inactivity and obesity	2001	✓	✓	✓	P
(Katzmarzyk, et al., 2000)	Physical inactivity	1999	✓		✓	P
(Krahn, et al., 1996)	Asthma	1990	✓	✓	✓	P
(Law, et al., 1999b) & (Law, et al., 1999a)	Chicken pox	mid 1990s	✓	✓		P/I
(Locker, et al., 2003)	Agricultural machinery injuries	1985-1996	✓	✓	✓	I
(Longobardi, et al., 2003)	Inflammatory bowel disease	1998/99		✓		P
(Maetzel, et al., 2004)	Rheumatoid arthritis, osteoarthritis, hypertension	1999/2000	✓	✓		P
(Miller, 1995)	Gunshot wounds	1991	✓	✓	✓	I
(Moore, et al., 1997b)	Comprehensive	1993	✓	✓	✓	P
(Muir and Zegarac, 2001)	Diabetes, Parkinson's Disease, neurodevelopmental effects and hypothyroidism, & deficits in intelligence quotient in Canada and the US	1998-98	✓	✓		P

Study	Health condition(s)	Data year	Includes direct costs	Includes morbidity costs	Includes mortality costs	Incidence/ Prevalence
(O'Brien, et al., 2001)	Diabetes	1996	✓			P
(Ostbye and Crosse, 1994)	Dementia	1991	✓			P
(Rockwood, et al., 2002)	Vascular cognitive impairment in older adults	1991-92, 1998	✓			P
(Single, et al., 1998)	Alcohol, tobacco, and illicit drugs	1992	✓	✓	✓	P
(SmartRisk, 2001)	Unintentional injury in British Columbia	1998	✓	✓	✓	I
(SmartRisk, 2003)	Unintentional injury in Atlantic Canada	1999	✓	✓	✓	I
(Stephens and Joubert, 2001)	Mental health problems	1996/97 - 2000	✓	✓	✓	P
(Taylor, et al., 2002)	Liver transplantation	1991/92	✓			I
(To and Wu, 1995)	Migraine in Ontario	1996	✓	✓		P
(Wall, et al., 2000)	Untreated opioid dependence in Toronto	1996/1997	✓	✓	✓	P
(Wiebe, et al., 1999)	Epilepsy in Ontario	1990	✓	✓		P
(Wigle, et al., 1991)	Comprehensive	1986	✓	✓	✓	P
(Xie, et al., 1998b)	Illicit drug use in Ontario	1992	✓	✓	✓	P
(Xie, et al., 1998a)	Alcohol abuse in Ontario	1992	✓	✓	✓	P
(Xie, et al., 1999)	Smoking in Ontario	1992	✓	✓	✓	P
(Zabinski, et al., 2001)	Arthritis	1998	✓			I

Methods for Estimating Costs

Decisions on how to measure both direct and indirect costs can significantly affect burden of illness calculations. For example, some studies only capture costs where the disease in question was the leading cause of the expenditure (e.g. hospitalizations where the condition was the most responsible cause of the hospital stay or consequences of disability that are directly attributable to the disease in question). Using this method, the sum of the costs attributed to individual diseases plus non-attributable costs equals the total burden of illness. As a result, it is the approach most commonly used in broad-based burden of illness research. Other studies attempt to capture a broader range of comorbidity costs. For instance, a study on diabetes might include some dialysis costs since

patients with diabetes are more likely than the general population to be diagnosed with kidney disease. This approach is typically used to calculate the cost of a single disease because determining attributable fractions of costs across a broad range of diseases and/or risk factors is very complex. As a result, the sum of the costs attributed to individual diseases using this method typically exceeds the total burden of illness.

Another key issue in this type of research is how to measure indirect costs. Several methods have been proposed to estimate the value of lost output or earnings related to morbidity and premature mortality, including willingness-to-pay, human capital, and friction cost approaches. Although used for similar ends, the underlying approaches are fundamentally different. The former, for example, focuses on the value that individuals place on different disease states while the others focus on the costs that diseases generate.

The *willingness to pay* method values human life based on how much people would be willing to spend to reduce the probability of having the consequences associated with a particular disease (e.g. symptoms, disability, or death) (Rice, 1994; Lang and Secic, 1997). Willingness to pay values may be derived using population-based surveys, surveys of patients and/or their care providers, indirect sources (e.g. the value of insurance settlements for a lost limb), or other methods. This method typically produces the largest estimates of the indirect costs of illness. Critics of this approach point to significant variations in willingness-to-pay values among groups (e.g. it may depend on the income distribution of the group), over time, and depending on the estimation method used. In addition, it has proven difficult in practice to place a value on small reductions in the probability of death (Health Canada, 2002).

The *human capital* approach is the most common method used in burden of illness studies to estimate indirect costs. It attempts to capture the value of lost productivity attributable to premature death and disability (Lang and Secic, 1997). Typically, this approach sees individuals as producing a stream of output over the years that is valued at their earnings. Morbidity and mortality reduce or eliminate this production (Rice, 2000).

Accordingly, the present value of lost earnings based on average wages, often disaggregated by age and sex, is typically used as a proxy for the impact of premature death and disability (Szava-Kovats and Johnson, 1997). The lost value of unpaid work (e.g. housework or informal care) is also captured in some studies (for example, Andersson, et al., 2002; Health Canada, 2002). Researchers using the human capital approach often interpret these production losses as a conservative estimate of the total societal welfare loss resulting from a given illness.

Critics of the human capital approach point to the failure to measure intangibles (e.g. pain and suffering), the difficulty of projecting earning potential over long periods of time (e.g. in the case of long-term disability incurred by children), the inherent bias towards diseases that tend to affect higher income earners,[36] the extent to which absenteeism or death reduces economic production, whether lost actual and imputed earnings are the best measure of production and/or welfare loss, and other challenges (National Health Strategy of the Department for Health Housing and Community Services 1993; Drummond, et al., 1997; Donaldson and Narayan, 1998; Rice, 2000). In addition, it does not take into account the fact that lower consumption might partially or completely offset lost productivity.

The *friction cost* method makes different assumptions regarding labour markets. Specifically, it takes into account the fact that adjustments in the labour market may reduce production losses arising from illness and death (Koopmanschap, et al., 1995). For example, unemployed workers can be recruited to replace those who are disabled or die without a loss elsewhere in the economy. Productivity costs are therefore limited to losses in output during a defined friction period while a new worker is sought (often 3 months), recruitment and training costs, and any medium-term macroeconomic impact resulting from labour market adjustments. As a result, it produces considerably lower estimates of indirect costs than other methods (Borghouts, et al., 1999; Hutubessy, et al., 1999). Critics argue that, as a measure of the full economic burden, this estimate is low because it does not consider full societal costs (e.g. someone who was fully employed and then becomes permanently unable to work would be counted the same way as someone who was temporarily off work for three months),[37] that it depends heavily on the economy's unemployment level, that it does not take into account the lost value of the recruited employee's leisure time or intangibles (e.g. pain and suffering), that it is based on implausible

[36] The human capital approach undervalues groups whose earnings and/or imputed value of unpaid work relative to other groups do not reflect their contribution to overall productivity because of market imperfections or other factors. In addition, it does not take account of other characteristics of individuals that may affect the value that society would place on their health gains or losses. For example, children earn little income. The human capital approach therefore estimates low or no costs for short-term disability in this group. Depending on the discount rate applied to lost future production, relatively low monetary values may also be applied to longer-term disability and death. This is, however, inconsistent with survey and other research that shows that health gains experienced by the young are often valued more highly than those for adults (Mooney and Jan, 1997).

[37] That said, the friction cost method was designed to capture production losses, not full societal welfare costs.

assumptions not supported by neoclassical economic theory, and that it uses inconsistent methods to value direct and indirect costs (Johannesson and Karlsson, 1997; Pritchard and Schulper, 2002).

Time Horizon

The time horizon is the follow-up period that determines which outcomes are included in the cost analysis (Riegelman, 2000). Some analyses use an 'incidence' approach, prospectively estimating costs over time for patients who acquire a disease in a given period. They typically calculate the present value of the lifetime direct and indirect costs associated with this group of patients. For diseases with long-term health consequences, incidence-based studies require sophisticated assumptions about the likely course and consequences of a disease over time. Results can be highly dependent on these assumptions (Moore, et al., 1997a).

More commonly, a 'prevalence' approach is used (Szava-Kovats and Johnson, 1997). These studies measure the economic burden (value of resources used or lost productivity) incurred during a given period of time for patients who have the disease(s) in question, regardless of the time of disease onset.

In both cases, a choice about how to discount future costs must be made. The discount rate selected can have an important effect on total and relative costs of different diseases, particularly for diseases that frequently result in early death (Lang and Secic, 1997). Sensitivity analysis is often employed since no definitive discount rate exists (Szava-Kovats and Johnson, 1997).

Chapter 5: Estimating the Economic Burden of End-Stage Renal Disease

End-stage renal disease (ESRD) exerts a significant toll on the health and the lives of those who have the condition. It also represents a substantial burden for society as a whole. This chapter presents estimates of the economic burden of end-stage renal disease in 2000, including baseline and sensitivity analyses. Projections to 2015 follow in Chapters 7 and 8.

Both the baseline and sensitivity estimates take a societal perspective and include direct costs, as well as estimates of the indirect production losses related to morbidity and mortality. In order to facilitate comparison with other diseases, the methods used parallel those employed for a recent broad-based national burden of illness study (Health Canada, 2002). Specifically, a prevalence-based approach is used to estimate all direct costs and indirect morbidity costs related to cases of ESRD in the period in question. Mortality cost estimates are based on the discounted value of current and future costs of premature deaths occurring in the year in question, calculated based on production losses using an incidence-based human capital approach.

5.1 Measuring Direct Costs

Direct health care costs are an important part of the economic burden of end-stage renal disease.[38] Although less than 0.1% of the population has end-stage renal disease, the condition accounts for a much larger share of health budgets in developed countries (Lysaght, 2002). In the short-term, transplant patients tend to have higher health care costs than those on dialysis, but their long-term costs are typically lower (Laupacis, et al., 1996). For example, a 1997 Canadian study suggests that the crossover point in average per capita costs occurs at 10-13 months for hemodialysis and 18 months for peritoneal dialysis (Prichard, 1997).

This study captures direct costs for ESRD patients in 2000 regardless of the type of care that they received. Total costs are divided into four components: the

[38] For the purposes of this study, direct health care costs are defined as "health care expenditures for which the primary objective is to improve and prevent the deterioration of health status" (Canadian Institute for Health Information, 2002b).

cost of organ retrieval for transplant; transplant surgery and aftercare; the organ donation/ transplantation system; and dialysis care.

As with most studies of the economic burden of illness, to the extent possible, costs directly related to the condition are captured, rather than the full spectrum of health care received by patients with ESRD. For example, dialysis costs are captured; care for a broken leg is not. Nevertheless, persons with ESRD tend to have other chronic health problems, such as diabetes and cardiovascular disease. They may receive care for these conditions while being treated for ESRD or may get help for their renal disease while receiving services primarily for another reason. A deduction for this cost is not made in the first case; costs for the latter are not included. These costs may be significant. For example, a recent study estimated that average annual medical costs for hospitalization and medications not related to kidney failure for persons with ESRD were about $9,560 for a 40-year-old and $11,561 for a 60-year-old in 1999 Canadian dollars (Manns, et al., 2003).

Other key assumptions underlying data used to estimate the total direct health care costs of end-stage renal disease include:

- In many cases, data on the cost of treating ESRD patients could not be obtained from national sources. Accordingly, this study relies on data from specific provinces and/or research studies as a proxy for costs of care across the country.

- The diverse sources of cost data have been inflation-adjusted to 2000 dollars, but the underlying source data come from the mid-1990s to the early 2000s. It is assumed that the processes and patterns of care reflected by these cost estimates are a reasonable representation of those in place across the country in 2000. In some cases, however, care processes are changing. For example, the use of a costly drug, erythropoietin, has been increasing across the country. In 1994, 66% of patients on hemodialysis and 51% of those on peritoneal dialysis were receiving erythropoietin (Canadian Organ Replacement Register/Canadian Institute for Health Information, 2002). By 2000, this had risen to 76% and 75% respectively. Because of changing practice patterns, cost data prior to the mid-1990s have not been used in this study.

- To convert cost estimates to 2000 dollars (to be consistent with data on the number of ESRD cases), a total health care implicit price index was used (CIHI 2002b). This index takes into account both government and private sector health care expenditure, as is appropriate in this case since outpatient costs include those borne by the provincial health insurance plan (e.g. physician visits) and those

borne by patients, their families, and/or their insurance plans (e.g. pain medication). Previous research has shown that health prices have increased more rapidly than overall prices in recent years, although the public sector component of CIHI's health care price index correlates well with Statistics Canada's overall index for government spending and the two indices tend to move together (Hicks, et al., 2001).

- Included costs primarily represent those borne by the health care system. Additional costs may also be borne by patients, their families, and their insurers. For example, medical transportation costs, costs of renovations to accommodate home dialysis, and other similar costs related to ESRD are not captured in this study.

- Acute care hospital costs have been included in the cost estimates, but costs for other institutional care (e.g. nursing home care) have not been included because it was not possible to identify whether patients were receiving this care specifically because of kidney failure or for other reasons.

- Payments to living kidney donors to recompense them for the donation of their kidney were not included since there is no market for organs in Canada. However, payments to donors have been documented in some countries, such as India and Iraq (Friedlaender, 2002). Some Canadians may choose to travel to those countries for a transplant. The extent to which this practice occurs is not known and any associated costs are not included in the estimates of the economic burden of disease in this study.

Organ Retrieval

Each year, hundreds of kidneys are retrieved for transplantation across the country from living and cadaveric donors. Significant costs are incurred as a result of this process by hospitals and others.

Data from the Canadian Institute for Health Information (CIHI) were used to estimate acute care hospital costs related to organ retrieval. Each year, CIHI produces cost weights that are designed to reflect the relative resource allocation for inpatient hospital care for different types of patients. These weights (called Resource Intensity Weights™) are derived using costing data primarily from hospitals in Ontario and Alberta, combined with length of stay data from across the country. They take into account hospitals' fixed and variable operating costs, such as wages and salaries for staff on the hospital payroll; laboratory, radiology,

™ Registered trademark of the Canadian Institute for Health Information.

and other diagnostic tests; drugs and medical supplies when provided in hospital; accommodation and meals for patients; and the operation and maintenance of hospitals' acute care facilities. A hypothetical average case has a weight of 1.0. The average cost per weighted case in 2000/01 was $3,001[39] (CIHI 2003a).

Resource Intensity Weights are calculated for each Case Mix Group (CMG). Patients are assigned to a CMG based on their diagnoses and the interventions that they receive in hospital. Beginning in 2001/02, provinces and territories began to introduce a new set of classification standards for health conditions (ICD-10-CA) and interventions (the Canadian Classification of Health Interventions or CCI). For the first time, these classifications include distinct codes for removal of kidneys for organ donation:

- 1.PC.58.LB-XX-J: Procurement, kidney from living donor using open abdominal approach
- 1.PC.58.PF-XX-J: Procurement, kidney from living donor using open lumbar [flank] approach
- 1.PC.58.QP-XX-J Procurement, kidney from living donor using open subcostal transperitoneal approach
- 1.PC.58.DA-XX-J Procurement, kidney from living donor using endoscopic (laparoscopic) approach
- 1.PC.58.LB-XX-K Procurement, kidney from cadaver using open abdominal approach
- 1.PC.58.PF-XX-K Procurement, kidney from cadaver using open lumbar [flank] approach
- 1.PC.58.QP-XX-K Procurement, kidney from cadaver using open subcostal transperitoneal approach.

Removal of a kidney from a living donor, regardless of the surgical approach used, most often fell into Case Mix Group 504 (Major Urinary Tract Procedures) with a Resource Intensity Weight of 1.6606 in 2002/03 (CIHI 2002a).[40] Accordingly, the average cost of a hospital stay for this purpose was

[39] This cost per weighted case represents a national average value. Since this period overlaps with the period of interest for the study (year 2000), no inflation adjustments were applied to this value.

[40] The 2002/03 weights were used because data based on ICD-10-CA/CCI was used in their calculation. The weights shown above represent a weighted average

$4983.46.[41] Retrievals of organs from a cadaveric donor were split among several Case Mix Groups because persons may become organ donors for multiple reasons. Because the marginal cost of cadaveric kidney donation was not available, the hospital cost for a living donor was used as a proxy.[42]

The hospital costs described above do not include fees paid to physicians in private practice for professional services. Typical surgeon and anaesthetist fees for a nephrectomy using an open procedure ($785.76 in 2000 dollars) were obtained from a recent Ontario study. (Pace, et al., 2003a).[43,44] Outpatient costs for living donors for the first four weeks after leaving hospital ($120.80) were obtained from the same source.[45] For cadaveric donors, physician fees were approximately $866.88 (Ontario Ministry of Health and Long-Term Care, 2003).[46]

---

of weights based on the distribution of patients by age group and complexity level in the Case Mix Group.

[41] In some cases, living donors experience complications of their surgery that require readmission to hospital or further care (Matas, et al., 2003). Fortunately, these situations are rare. Costs associated with readmissions or further care could not be identified from national sources and so are not included in the estimates.

[42] This choice would not include costs of maintaining a donor on life support prior to transplantation, but this underestimation would be offset by the inclusion of recovery costs for living donors that would not be incurred in the case of cadaveric donors.

[43] Average costs in the study were expressed in 2001 Canadian dollars. Using CIHI's total health care implicit price index, $1.012 in 2001 was equivalent to $1.00 in 2000 (see section 5.1 for details).

[44] Kidneys can be removed from living donors using either an open or a laparoscopic procedure. The former was more common during the time period for which the economic burden estimates are being calculated (and the procedure type was not available in the data obtained from the Canadian Organ Replacement Register) so costs for open procedures were used in this study. According to Pace and colleagues (2003a), less than $400 separated the average cost of these two procedures in 2001, so changing this assumption would not have had a material impact on the overall economic burden estimates since the physician's fee represents a relatively small portion of the total.

[45] This value represents a weighted average of cost estimates provided for patients with and without pain at 4 weeks post-surgery. The weights were based on the probability of pain for donors who underwent open surgical procedures.

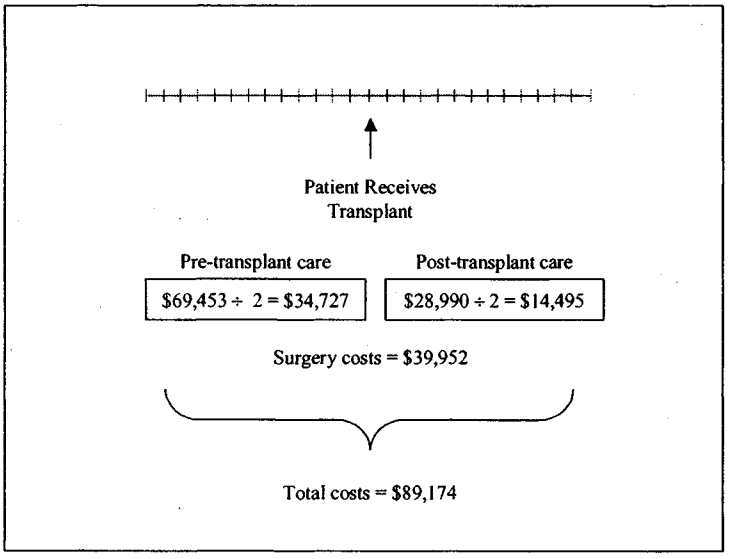
[46] This estimate is based on the September 1, 2003 Ontario fee-for-service physician payment schedule. (Ontario was selected for consistency with the source of other physician cost estimates). Under this schedule, physicians can charge the provincial health insurance plan $188.35 for a set of services related to "nephrological management of donor procurement," $94.45 for renal preservation

Transplant Surgery and Aftercare

Transplantation costs were derived from a 1994 study by Laupacis and colleagues (1996). They estimated that costs in the year prior to transplantation (while on dialysis) were $69,453, in the first year after transplantation were $68,942, and in subsequent years were $28,990.[47] Patients with a functioning transplant were assigned 'subsequent year' costs.

Since transplants occur throughout the year, direct health care costs for patients who received a transplant were assumed to be a blended average of pre-transplant and post-transplant maintenance costs, plus the cost of surgery (see Figure 6). Thus for half of the year, they were assumed to have experienced costs as a pre-transplant patient ($69453÷2 = $34,727). Transplant surgery costs of $39,952 (the difference between the transplant year and the post-transplant year costs) were added to this total, as were a half-year of post-transplant maintenance costs ($14,495), for a total of $89,174.

Figure 6: Calculation of Direct Costs for Transplant Patients



---

for transplantation (assuming not performed by the surgeon), and $640.40 for removing cadaveric kidneys. These fees were deflated using CIHI's total health care implicit price index ($1.065 in 2003 was equivalent to $1.00 in 2000; see section 5.1 for details). Surgical assistants' benefits have not been included in the cost calculations.

[47] All costs have been converted from 1994 to 2000 Canadian dollars using the same price index as described above ($0.929 in 1994 was equivalent to $1.00 in 2000). See section 5.1 for details.

Cost of the Organ Donation and Transplantation System

There are significant fixed costs associated with running an organ donation and transplantation system. These include the infrastructure to develop policies and procedures and legislation related to organ donation; to conduct public awareness campaigns on the benefits of organ donation; to recruit and screen organ donors; to match available organs with a candidate from those waiting for a transplant; to train health care workers involved in the process; to fund research related to transplantation; and much more.

These costs can be considerable. Comprehensive estimates are not available, but examples of related spending include:

- The 2002 national campaign for Organ Donor Awareness Week alone had a budget of $2.1 million (Health Canada, 2002b);
- The new Canadian Council for Donation and Transplantation received $4 million annually in federal funding beginning in 2001 (Health Canada, 2002b);
- Health Canada announced in 2001 that they would provide almost $2 million to the Canadian Standards Association to develop and maintain management standards to improve organ and tissue donation practices in Canada; and
- Ontario's Trillium Gift of Life Network, the organization which plans, promotes, coordinates, and supports organ and tissue donation across the province, spent $6.9 million in 2002-2003 (this includes reimbursing hospitals for the costs of maintaining potential donors on life support) (Trillium Gift of Life Network, 2003).

Nevertheless, these costs have not been included in the estimates for the economic burden of end-stage renal disease. This decision was made because these costs are relatively insensitive to the number of patients with end stage renal disease, because many of the costs are not specific to kidney transplantation,[48] because information on many of the costs (e.g. value of time spent by members of the Canadian Council for Organ Donation and Transplantation) is not available, and for consistency with other studies on the economic burden of illness.

[48] According to the Canadian Organ Replacement Register, approximately 58% of the solid organ transplants in 2003 were kidney transplants. Many more patients receive tissue transplants each year.

Dialysis Patients

A number of different types of dialysis are in use across the country and around the world. Each has different clinical characteristics and impacts on patients and their families, as described in section 2.2. Costs for the various types of dialysis also differ. Various international studies have found a surprising degree of consistency in the relative cost ranking of different treatment modalities, at least outside of the United States and Japan (de Vecchi, et al., 1999; Peeters, et al., 2000; Klefter and Nielsen, 2002). Hospital-based hemodialysis is typically the most costly, followed by self-care hemodialysis and peritoneal dialysis.

Canadian research reflects these overall findings from the international literature (see Table 5). Unfortunately, however, relatively few recent costing studies exist, and variations exist between studies in the types of costs captured, as well as the nature and size of the patient population. As for transplants, studies prior to the mid-1990s were excluded because of potential changes in practice patterns, therapeutic technologies, and costs. Four more recent studies were also not used:

- Coyte (1996) because it included only the pediatric population;
- Blake (1996) because researchers captured only the costs of dialysis supplies (excluding physician, staff, facility, and other significant costs);
- Baltzan (1997) because it did not differentiate between the costs of different types of dialysis; and
- Prichard (1997) because it focused on the first 18 months of therapy and research suggests that switching to a new type of dialysis is more costly than maintaining an existing treatment approach (de Wit, et al., 1998; Lysaght and O'Loughlin, 2000).

Table 5: Overview of Published Canadian Dialysis Costing Studies

Reference	Patients' Location	Year	Reported Costs (Annual Except Where Noted)
(Rae, et al., 1972)	B.C.	1969/70	• $8747 start-up for home hemodialysis (HD) • $3728 annual maintenance cost, for those who stay on home HD • $5854 annual maintenance cost, return to hospital HD

Reference	Patients' Location	Year	Reported Costs (Annual Except Where Noted)
(Hornberger, et al., 1997)	Manitoba	1983-1989 (Manitoba, Canada)	• Physician: $174/month • Outpatient: $2,151/month • Inpatient: $753/month • Total: $3,079/month
(Prichard, 1996; Prichard, 1997)	Montreal	1988	• Peritoneal dialysis (CAPD) 1st year: $58,173 • Self-care HD 1st year: $61,863 • Centre HD 1st year: $67,084 • CAPD switching cost: $10,022 • Self-care HD switching: $6,924 • Centre HD switching: $8,032 • CAPD subsequent years: $21,717 • Self-care HD subsequent years: $26,850 • Centre HD subsequent years: $29,210
		1994	• Transplant 1st 18 months: $42,000 • CAPD 1st 18 months: $42,500 • Self-care HD 1st 18 months: $48,500 • Centre HD 1st 18 months: $54,000
(Jassal, et al., 1998)	Toronto	1991	• HD at hospital $157,822 • HD at specialized chronic care facility $120,800
(Goeree, et al., 1995)	Southwestern Ontario	1993	• Centre HD: $67,951 US (1993) per life year gained • Self-care HD: $43,774 per life year gained • Home HD: $25,645 per life year gained • PD: $35,267 per life year gained
(Coyte, et al., 1996)	Toronto (pediatric patients only)	1993/94	• PD: $47,569-$50,438 • HD: $76,023-$78,568
(Baltzan, et al., 1997)	Saskatoon	1994	• Dialysis annual cost (averaged over all types of dialysis): $40,000
(BC Renal Council, 1994 as reported in de Vecchi, et al., 1999)	British Columbia	1994	• Centre HD: $59,038 • Limited Care HD: $42,312 • CAPD: $33,451 • APD: $42,154
(Blake, et al., 1996)	London, Ontario	1995	• $14,393 for typical PD patient • $2,323 per patient additional for increased PD dose
(McFarlane, et al., 2002)	Toronto (2 centres)	January 1, 2000 to March 1, 2001	• Centre HD: $68,935 • Home Nocturnal HD: $56,394

Two studies remained (BC Renal Data Council, 1994 as reported in de Vecchi, et al., 1999; McFarlane, et al., 2002). Cost estimates from these studies were converted to year 2000 dollars, using CIHI's implicit price index for health care (see section 5.1 for details). Resultant average costs used in this study are shown in Table 6.

Table 6: Estimates from Selected Canadian Studies of Annual Dialysis Costs and Average Costs Across the Studies (Year 2000 Dollars)

Reference	Centre-Based Hemo-dialysis	Limited Care Hemodialysis and/or Home Hemodialysis	Peritoneal Dialysis	Costs included
(BC Renal Council, 1994 as reported in de Vecchi, et al., 1999)	$63,584	$45,570	$45,400	• Treatment costs, including additional costs for laboratory, catetheter treatment, etc.
(McFarlane, et al., 2002)	$68,935	$56,394[49]	n/a	• Hemodialysis materials • Clinical and administrative staff related to dialysis care • Overhead and support • Outpatient medications • Hospital admission and procedures • Laboratory tests and medical imaging • Physician fees • Depreciation/capital costs
Average Costs	$66,259	$50,982	$45,400	

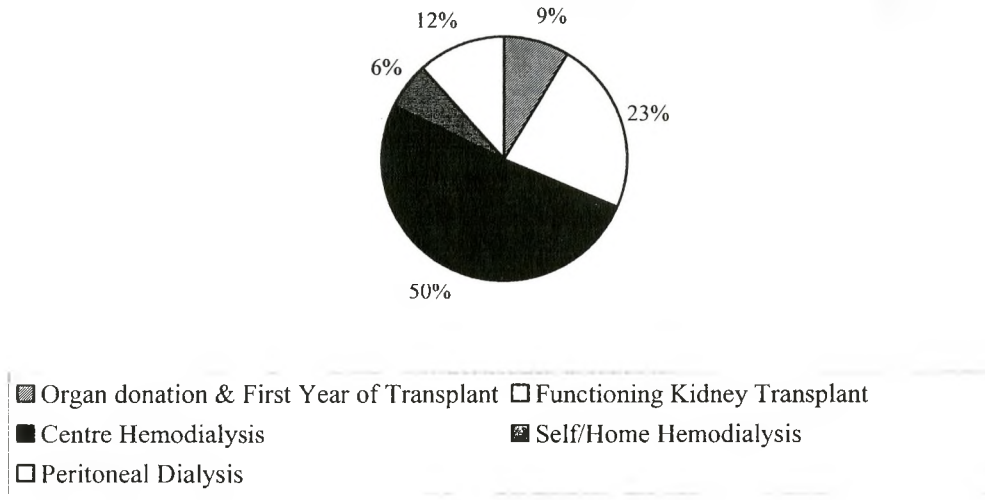
Summary of Direct Health Care Costs

In Canada, end-stage renal disease generated direct health care expenditures of about $1.27 billion in 2000 (see Table 7). That represents about 1.3% of total health care spending or just over 2% of what provincial and territorial governments spent on health services during the year. On a per capita basis, about $51,099 was spent on ESRD care for each person with the disease, significantly more than the $3,183 that was spent on average per Canadian to care for all health conditions (CIHI 2002b).

[49] Represents costs of nocturnal home hemodialysis.

The vast majority of the costs are attributed to maintenance therapy for persons with ESRD[50] (see Figure 7). More than two-thirds of direct health care expenditures (68.6%) were for persons on dialysis, although they accounted for 58% of persons with ESRD. Centre-based hemodialysis is particularly costly (see Figure 8). Health care costs for patients on this type of therapy were more than double those for someone with a functioning transplant. Centre-based hemodialysis alone accounts for half of all ESRD health care costs.

Figure 7: Distribution of Direct Health Care Costs for ESRD in 2000



[50] Medication provided in hospital is included in hospital costs. Medication consumed in the community is included in aftercare costs for living transplant donors, as well as in the annual costs for patients with a functioning transplant or on dialysis.

Table 7: Summary of Direct Annual Health Care Costs by Treatment Category in 2000 (Baseline Assumptions)[51,52]

Category (data year)	Original per capita cost	Inflation-adjusted cost per capita in 2000 $	Number in category in 2000[53]	Total direct cost in 2000 $
Living kidney donors - hospital costs (2000/2001) - physician surgery fees (2001) - aftercare (2001)	 $4,983 $795 $122	 $4,983 $786 $121	389	$2.29 million
Cadaveric kidney retrieval - hospital costs (2000/2001) - physician fees (2003)	 $4,983 $923	 $4,983 $867	470[54]	$2.75 million
Kidney transplant care in year of transplant (1994)	$89,174	$96,040	1,105	$106.1 million
Functioning kidney transplant care in subsequent years (1994)	$28,990	$31,222	9,249[55]	$288.8 million
Centre hemodialysis	n/a	$66,259	9,752	$646.2 million
Self/home hemodialysis	n/a	$50,982	1,568	$79.9 million
Peritoneal dialysis (1994)	$33,451	$45,400	3,247	$147.4 million
TOTAL	n/a	n/a	n/a	$1.27 billion

[51] Amounts rounded to nearest dollar for ease of presentation.

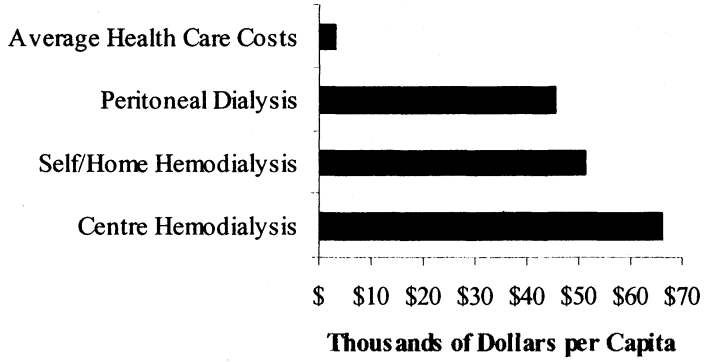
[52] The sources for these estimates are described in detail earlier in this chapter. See the *organ retrieval* section for sources of living kidney donor and cadaveric organ retrieval costs; the *transplant surgery and aftercare* section for transplantation care costs in the year of transplant and subsequent years; and the *dialysis patients* section (particularly Table 6) for dialysis care costs.

[53] These figures are as of December 31, 2000 (Canadian Organ Replacement Register/Canadian Institute for Health Information, 2002).

[54] This is the number of cadaveric kidney donors. In many cases, both kidneys were retrieved from a single donor. Cost estimates for organ retrieval are not affected by this practice.

[55] Calculated as the number of patients alive with functioning transplants as of December 31, 2000 minus the number who received transplants during that year. This assumption may slightly underestimate the number of patients who received care for a transplant at some point during the year.

Figure 8: Per Capita Annual Costs by Type of Dialysis Compared to the Overall Average Per Capita Health Care Costs for Canada, 2000



5.2 Indirect Costs – Mortality

End-stage renal disease reduces a person's life expectancy. This section describes how the economic burden of the resulting loss of productivity was estimated and what the results were for Canada in 1998. (All currency values in this section are in 1998 dollars to facilitate comparisons with other diseases from the latest overall national estimates of the economic burden of illness. In the summary in section 5.4, these figures are converted into 2000 dollars to facilitate integration with estimates of the direct costs of treatment and for consistency with the data year for the ESRD population used in the analysis.)

Methodology

Premature mortality costs (the discounted present value of lost future production) are estimated using the human capital approach. Specifically, these costs (V) were calculated as the sum of the discounted present value of remaining potential lifetime production lost as a result of each death in the year in question:

$$V = \sum_{n=a}^{85+} \left[\left(Y_{ns} W_{ns} P_{as}^{n} + H_{nsw} W_{ns} P_{as}^{n} \right) + \left(H_{nsh} K_{ns} P_{as}^{n} \right) \right] \left[\frac{(1+g)^{n}}{(1+i)^{n}} \right]$$

where[56]:

a = initial age at midyear for the cohort of persons dying of ESRD in the year in question

g = rate of increase of labour productivity

H_{nsh} = annual mean imputed value of housekeeping services for all persons not in the workforce of a given sex in an age group where the midpoint age is n

H_{nsw} = annual mean imputed value of housekeeping services for all persons in the workforce of a given sex in an age group where the midpoint age is n

i = discount rate

s = sex

K_{ns} = average housekeeping participation rate of a given sex in the age group where the midpoint age is n

P^{n}_{as} = approximate probability that an individual of age a and sex s survives to age n

W_{ns} = average workforce participation rate of a given sex in the age group where the midpoint age is n

Y_{ns} = annual mean earnings for all persons of a given sex with earnings in an age group where the midpoint age is n

[56] For consistency, notation and methods match those used in a recent Health Canada study (2002).

Thus, mortality costs are calculated as the sum of lost production in the year of death and in subsequent years that an individual with ESRD would have been expected to live.[57] This method takes into account a cross sectional profile of age- and sex-specific earnings (adjusted for labour productivity growth), workforce participation, life expectancy, and unpaid work.[58] The latter is typically, although some would argue inappropriately, left out of macroeconomic metrics, such as the gross domestic product (Mankiw and Scarth, 1995; Colman, 1998). Nevertheless, the value of foregone home production (non-market activity) is included here because it is an important consequence of illness particularly for those in certain demographic groups and may require the purchase of market services to replace unpaid work (e.g. home support and maintenance services). While the contribution of this component to the overall economic burden of illness is relatively small, this approach is consistent with methods used in similar studies. A sensitivity analysis was conducted to evaluate the impact of this assumption (see Table 9).

All calculations discount the value of future production to reflect assumptions about time preference (Lazaro, 2002). Internationally, there has been considerable debate about the appropriate discount rate to use (Weinstein and Stason, 1977; Cairns, 1992; Parsonage and Neuburger, 1992; Drummond and Jefferson, 1996; Hutton, 2000). Baseline estimates in this study use a discount rate of 5%, as recommended by the Canadian Coordinating Office for Health Technology Assessment (1997). To test the sensitivity of results to this assumption, estimates with discount rates of 3% and 7% were also calculated.

---

[57] As underlying cause of death information from death certificates was not available, mortality estimates reflect all deaths for persons with ESRD in the relevant time period. This approach may somewhat overestimate mortality costs directly related to ESRD.

[58] While earnings are adjusted for labour productivity growth, current values for other variables such as age- and sex- specific survival and labour force participation are used. This essentially reflects the experience of a fixed cohort, projected forward to their estimated life expectancy. Note that given that most persons with ESRD tend to be older, the time horizons involved are relatively short. Changing this decision would therefore have relatively little impact on overall results.

To be consistent with the expected use of this analysis and with established practice in this field in Canada and internationally, these estimates do not take into account the potential lost consumption that would partially or completely offset lost productivity. At the extreme, a "net output" (subtracting consumption) rather than a "gross output" approach implies that the death of someone who consumes more than s/he produces confers a net benefit to society (Mishan, 1971). Since many persons with serious chronic illnesses fall in this category, subtracting consumption would imply that in order to optimize societal welfare, options that result in early death (with as few direct costs as possible) are preferred (Kuchler and Golan, 1999). This is inconsistent with the broader objective of this analysis, which is to reflect the burden of illness and how it might change over time under different assumptions. As Rice and colleagues state (1985), "individuals, not just the output they contribute in excess of consumption, are valued by society." In this respect, productivity losses can be interpreted as conservative estimates of societal welfare loss.

Additional key assumptions underlying the estimates of indirect costs due to premature mortality in this and subsequent chapters include:

- Average annual earnings of all earners in 1998 reflect future earnings, subject to adjustments for labour productivity growth. It is therefore assumed that Canadians' work and productivity patterns during their expected lifetime after 1998 would be consistent with current patterns by age group and sex.

- Lost production is measured by aggregating the expected gross income for individuals with ESRD who die, based on the argument that wage rates represent the value of marginal productivity (Brouwer, et al., 1997).[59] For this study, costs due to premature mortality in 2000 are derived using age/sex-specific profiles of total annual earnings for all years of expected life, based on earnings data reported by Statistics Canada's 1997 Survey of Consumer Finances. See section 5.2.2 for further information. Using the friction cost method (see previous chapter) would reduce these estimates since this approach assumes that workers who die (or are disabled) can be replaced by otherwise unemployed persons.

[59] This equivalence holds from a societal point of view under strict assumptions (Brouwer, et al., 1997).

- Had those with ESRD not had the disease, they would have produced the same potential average annual economic output and had the same labour force and housekeeping participation profiles as the population as a whole. As a result, cost estimates do not take into account the fact that persons with end-stage renal disease may have reduced productivity (e.g. because of reduced labour force participation) prior to their death compared to typical persons of their age and sex (Hirth, et al., 2003; Tawney, et al., 2003).

- Mortality is evenly distributed within a year. Accordingly, cost estimates for 2000 are calculated by dividing expected annual earnings for deceased individuals in 2000 in half (sometimes known as the 'half cycle' correction) (Briggs and Sculpher, 1998).

- Due to a lack of data, children age 0 to 14 are assumed to have no earnings and no value of household work is attributed to this age group. (As there were no deaths among ESRD patients aged 0 to 14 in 2000, this assumption applies only to projections in subsequent chapters).

- Average earnings, the value of unpaid work, and life expectancy were estimated by sex across 12 age groups (see Figure 9). Information on the number of ESRD deaths in 2000 was available by sex for 4 age groups (15-44, 45-64, 65-74, and 75+). For estimation purposes, the average age of ESRD patients in 2000 in each of the age groups was used to combine death and productivity information.

- Deaths among persons with ESRD are attributed entirely to ESRD, rather than to other conditions that may also affect their health.

Parameters for Productivity and Income Estimates

For comparability, productivity and income parameter estimates used for the latest national estimates of the overall economic burden of illness were used to calculate the economic burden of end-stage renal disease (Health Canada, 2002). Age- and sex-specific unpublished tabulations of the following parameters were obtained from Health Canada:

- Average annual adjusted non-investment income, taking into account earnings, income from the Canada/Quebec Pension Plans (including disability benefits), worker's compensation, unemployment insurance, and similar sources;[60]

- Average value of unpaid labour among the employed and unemployed, calculated using the replacement cost generalist method based on workforce participation and time-use data from Statistics Canada's *1998 General Social Survey* and an average wage rate from the 1996 Census projected to 1998 using Statistics Canada's index of labour costs;[61,62] and

- Workforce participation rates from the *1998 General Social Survey.*

Figure 9 illustrates the values of key parameters for men. Figure 10 shows the same parameters for women. Figure 11 presents the derived average annual productivity estimates for both sexes. These estimates are used to calculate indirect morbidity costs in a particular year, as well as to estimate the discounted present value of lost future production for deaths in that year (mortality costs).

Baseline estimates reflect an annual labour productivity growth rate of 1.1%, a value chosen by Health Canada to reflect Canadian historical rates over the preceding decade (Health Canada, 2002; Statistics Canada, 2004a).[63] Recent trends, however, demonstrate that labour productivity growth fluctuates over time (Crawford, 2002). Accordingly, a sensitivity analysis was conducted with growth rates of –0.3% and 2.8%, the minimum and maximum average annual labour

---

[60] Based on custom tabulations obtained by Health Canada from Statistics Canada's *1997 Survey of Consumer Finances* (Statistics Canada, 1999).

[61] Based on custom tabulations obtained by Health Canada from Statistics Canada's Income and Expenditure Accounts Division.

[62] Note that these data are not adjusted for cohort effects, such as the change in the shape of age/sex-specific earnings curves that has been observed in recent years.

[63] This approach assumes that growth in labour productivity would be reflected through earnings.

productivity growth rates for Canada between 1990 and 2000 (Organisation for Economic Cooperation and Development, 2004).

Figure 9: Average Annual Earnings/Unpaid Labour (Males)

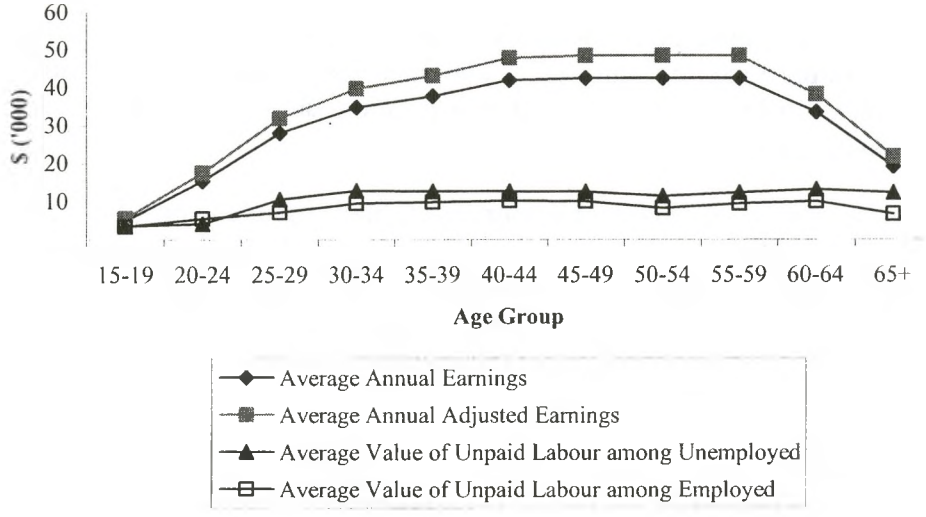


Figure 10: Average Annual Earnings/Unpaid Labour (Females)

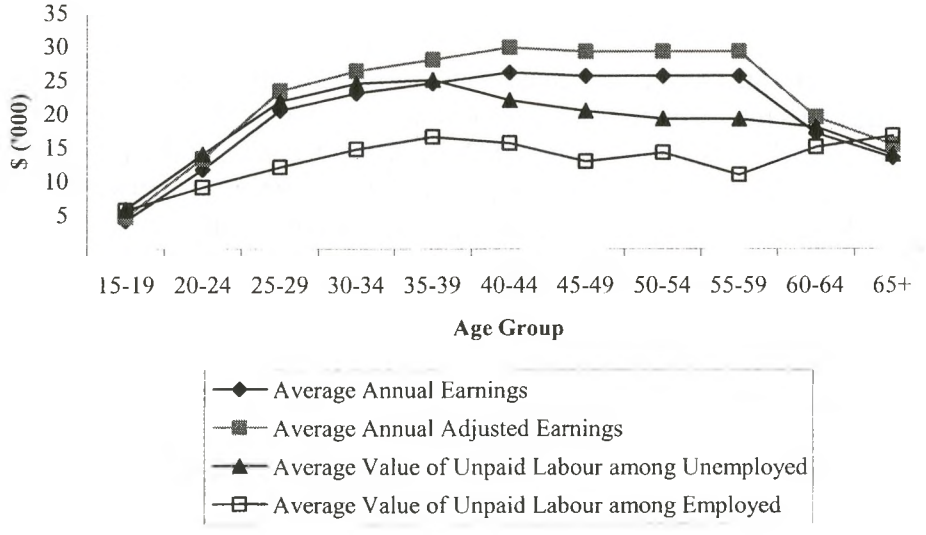
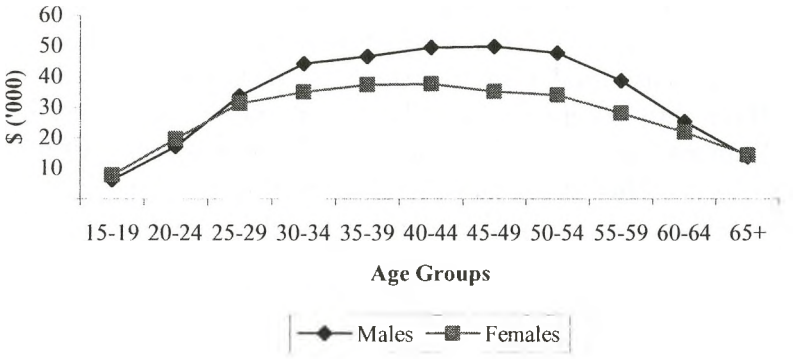


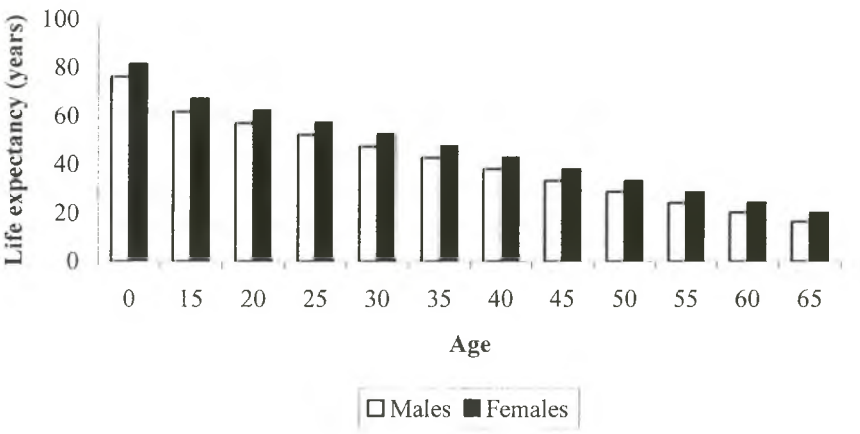
Figure 11: Average Annual Marginal "Productivity" from Paid and Unpaid Labour



Life Expectancy Estimates

Estimates of the economic burden due to mortality require not only estimates of the value of paid and unpaid work, but also estimates of life expectancy by age and sex. For the purposes of this analysis, age-specific life expectancy at birth and for the same age categories for which productivity data were available for 2001 were extracted from PMEDS-D (Version 2001 11.29). This software has been described in detail elsewhere (for instance, Denton, et al., 1989) and is used in other chapters of this thesis. The resulting life expectancy estimates are shown in Figure 12.

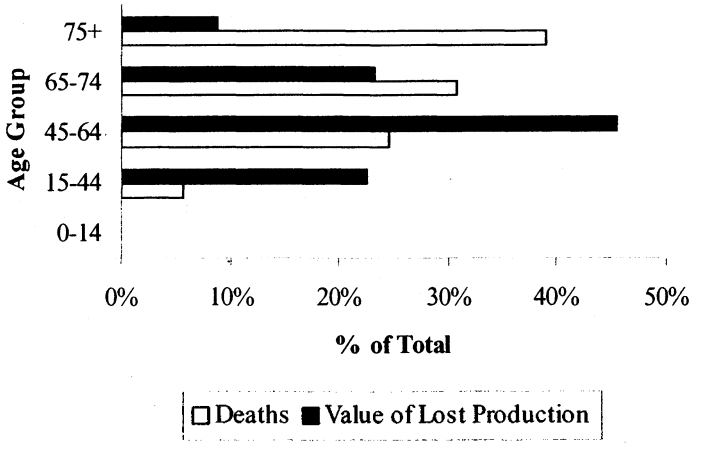
Figure 12: Life Expectancy at Birth and Each 15 Years to Age 65, 2001



Results ~ Economic Burden Related to Mortality

Just over 2,200 persons with end-stage renal disease died in 2000. The discounted present value of future production lost due to their premature deaths is estimated at more than $415 million.[64] This is higher than Health Canada estimates for conditions such as blood, musculoskeletal, and skin and related diseases ($19-126 million), but lower than those for major causes of death such as cancer at $10,622 million and cardiovascular disease at $8,250 million (Health Canada, 2002). As for many other diseases, while most deaths occur in older age groups, deaths among younger persons with ESRD contribute disproportionately to the total estimated value of lost production due to premature mortality (see Figure 13).

Figure 13: Distribution of Deaths and Value of Lost Production due to Premature Mortality for ESRD Patients in 2000 by Sex and Age Group



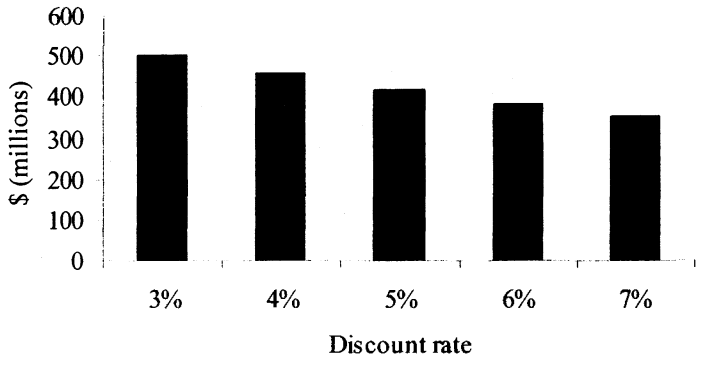
Additional analyses (see Table 8) show that overall ESRD estimates are more sensitive to changes in assumptions regarding discount rates than to variations in those related to labour productivity growth. For example, varying the assumed discount rate between three and seven percent leads to an almost $146 million difference in the estimated present value of lost production due to premature mortality.

[64] All currency values in this section are expressed in terms of 1998 Canadian dollars.

Table 8: Results of Sensitivity Analysis on Estimates of Premature Mortality Costs for ESRD Patients

Discount Rate	Labour Productivity Growth Rate	Estimate of Cost of Premature Mortality ($ millions)
Baseline Estimate		
5%	1.1%	$415
Sensitivity Analysis ~ Discount Rate		
3%	1.1%	$499
7%	1.1%	$353
Sensitivity Analysis ~ Labour Productivity Growth		
5%	-0.3%	$372
5%	2.8%	$480

Figure 14: Effect of Varying Discount Rates on Estimates of the Present Value of Lost Production Due to Premature Mortality among Persons with ESRD, 2000



The estimates of mortality costs related to ESRD described above include foregone earnings in the labour market, as well as other non-investment earnings and the value of unpaid labour. This approach, consistent with that used in Canadian studies of the total economic burden of illness, is designed to be inclusive of effects on those in the formal labour market and those who are not, responding to concerns that some experts have raised regarding equity issues arising from the potential to undervalue the impact of illness on segments of the population with lower or no labour market earnings (Koopmanschap, et al., 1995; Health Canada, 2002). In addition, when unpaid labour (e.g. housework) cannot be performed because of illness, paid services may be required to fill this gap. Either public programs or individual households may cover the cost of these services.

Analyses were conducted to test the sensitivity of the estimates of the economic burden of end stage renal disease to the inclusion of earnings from sources other than the labour market. Since sources of income such as the Canada/Quebec Pension Plans, worker's compensation, and unemployment insurance effectively represent transfers, some argue that they should not be included in estimates of the societal burden of illness since they shift resources between individuals but do not change society's overall resources (Brouwer, et al., 1997; Choi and Pak, 2002). Removing them caused estimates of mortality costs related to ESRD to fall only slightly. Simultaneously dropping the value of unpaid labour from the calculations had a more significant effect, particularly for women and older persons. The total mortality 'cost' based on paid labour market earnings only was $126 million, rather than $415 million.

5.3 Indirect Costs – Morbidity

Estimates of the economic burden of illness in the literature typically take into account lost productivity due to short-term and long-term disability/morbidity. In total, Health Canada (2002) estimated $9.8 billion in lost productivity due to short-term disability and $32.2 billion due to long-term disability in Canada in 1998.[65]

Like many other chronic health problems, end-stage renal disease significantly affects a person's quality of life and productivity. Some effects are related to the disease itself; others are attributable to the time-consuming and intrusive treatments that are required or patients' other health problems (Manns, et al., 2002).

Methodology

The morbidity measures of the economic burden of illness in this study attempt to capture productivity reductions for persons living with ESRD. Research suggests that quality of life varies by ESRD treatment type.

For many patients, transplantation is clearly preferable, reducing the risk of both mortality and morbidity (Evans, 1990; Simmons, et al., 1990; Rebello, et al., 1998; Gokal, et al., 1999). Several studies have found that the quality of life of those with functioning transplants is relatively comparable to the general population (Evans, et al., 1985; Bremer, et al., 1989; Baltzan, et al., 1997; Rebello, et al., 1998). Accordingly, only short-term productivity effects related to

[65] The national study defined morbidity costs as those "incurred when the illness or injury results in some form of disability and, as a result, time is lost from major activities like paid work and unpaid household work."

the transplantation procedure are estimated in this study (using an incidence-based approach).

The same is not true for patients on dialysis. Researchers have consistently found that these individuals experience a worse health-related quality of life; a few even elect to discontinue treatment (de Wit, et al., 1998; Rebello, et al., 1998; Gokal, et al., 1999). Given that quality of life effects of dialysis are on-going, the estimates in this chapter focus on its impact on long-term, not short-term, productivity.[66] The morbidity burden is calculated using a prevalence-based human capital approach.

As with national estimates of the overall economic burden of illness, weights for loss of production for different levels of disability were assigned to each person with ESRD. To estimate the annual value of lost production, disability weights for each of these individuals were multiplied by average values of paid and unpaid work by age group and sex, adjusted for labour force and housekeeping participation rates (see section 5.3.2 below).[67] The sum of these values represents the estimated effect of long-term ESRD morbidity on lost production. Key assumptions underlying these estimates include:

- Losses of production for persons with ESRD are attributed entirely to ESRD, rather than to other conditions (e.g. cardiovascular disease) that may also affect their health.

- Disability and lost production are correlated, but not perfectly.[68] The distribution of loss of autonomy from the Quebec Health and Social Survey and the resulting disability weights from Health Canada are assumed to be an appropriate representation for the ESRD population. This methodology is described in section 5.3.2. Note: Given that these weights are somewhat arbitrarily assigned, sensitivity analyses were conducted to determine the extent to which weights affect results.

- Quality of life variations between patients on different types of dialysis have been found, but they appear to attenuate after

[66] This is consistent with the approach used by Health Canada (2002). They defined long-term disability as "the presence of a restriction of activity that has lasted or is expected to last at least six months."

[67] This approach assumes that earnings and the value of unpaid work reflect marginal productivity and so can be used to estimate lost production.

[68] Following conventions in the literature, the estimates of the indirect economic burden of illness due to long-term disability in this chapter reflect estimated production losses only. As a result, they may not fully reflect some welfare-reducing effects of the disease, such as pain and psychological distress.

differences in patient demographics and rates of comorbidity are taken into account (Khan, 1998; Manns, et al., 2002). Accordingly, the same disability weights were used for all types of dialysis.

- Had those with ESRD not had the disease, they would have produced the same potential average annual economic output and had the same labour force and housekeeping participation patterns as the population as a whole.[69]

- Average annual earnings and wage supplements in 1998 provide a reasonable estimate of lost productivity.[70]

- Due to a lack of data, children age 0 to 14 are assumed to have no earnings and no value of household work is attributed to this age group. Neither loss of schooling time for this age group nor resultant effects on future earning opportunities are included in cost estimates. (As there were are few cases of ESRD among those aged 0 to 14 in 2000, this assumption has relatively little impact on final results).

- Average earnings, the value of unpaid work, and life expectancy were estimated by sex across 12 age groups. Information on the number of ESRD patients by treatment type in 2000 was available by sex for 5 age groups (0-14, 15-44, 45-64, 65-74, and 75+). For estimation purposes, productivity levels in the constituent detailed age groups were averaged to derive a productivity level for each of the 5 broader age groups. Since the age distribution of Canadian living organ donors was not available, the approximate age distribution of US living kidney donors in 2000 (from the United Network for Organ Sharing) was applied to Canadian totals.

- Patients' treatment status at the end of the year was used to calculate any lost productivity for the year as a whole. This somewhat underestimates lost productivity for those who die during the year

[69] Given that persons with ESRD tend to have multiple chronic conditions and that incidence rates are higher among lower socio-economic groups(Cass, et al., 2001; Cass, et al., 2002b; Krishnan, et al., 2002; Fored, et al., 2003; Cass, et al., 2004), this assumption may result in an overestimate of productivity losses.

[70] As for mortality estimates, all currency values in this section are in 1998 Canadian dollars to facilitate comparisons with other diseases from the latest overall national estimates of the economic burden of illness. In the summary in section 5.4, these figures are converted into 2000 Canadian dollars to facilitate integration with estimates of the direct costs of treatment and for consistency with the data year for the ESRD population used in the analysis.

and overestimates it for those who are diagnosed with ESRD during the year.

- Many patients with ESRD receive significant informal support from friends and family (Wicks, et al., 1997; Wicks, et al., 1998; Belasco and Sesso, 2002). In some cases, this may lead to lost production for these individuals, but these losses are not captured in this chapter.

Disability Weights

To facilitate comparability, disability weights were derived using a process similar to that employed by Health Canada in their latest overall economic burden of illness report (Health Canada, 2002). This approach assigns somewhat arbitrary weights based on losses in autonomy using information derived from the 1992-1993 Quebec Health and Social Survey. These weights may overestimate productivity losses for individuals who are able to adapt to their condition and underestimate them for those who experience more significant productivity effects (e.g. if the nature of their work is such that a schedule of centre-based dialysis treatments means that they cannot be employed in their previous profession) (Moore, et al., 1997a). In addition, they reflect discrete levels of disability and productivity loss, rather than what may be a non-linear relationship between disability and earnings loss.

Building on the approach used in the national economic burden of illness study (Health Canada, 2002), weights for persons in the community with long-term disability are as follows:

- 'Very severe' disability (defined by the Quebec survey as dependence for personal care): productivity weight of 0.2 out of 1.0 (full productivity),[71]
- 'Somewhat severe' (dependence for instrumental activities): weight of 0.5,
- 'Somewhat major' (disabled in performance of a main activity, such as working or keeping house): weight of 0.7, and
- 'Minor' (other activity limitations): weight of 1.0.

[71] The original research suggests a range for the production weight for this category of 0.0 to 0.2, but Health Canada's study uses the 0.2 weight in its baseline calculations. For the purposes of this study, a sensitivity analysis (described below) tests the effects of varying this assumption.

For transplantation, weights were assigned to reflect short-term losses of productivity that donors and recipients experience following the procedure. Since data on disability levels could not be disaggregated from national sources, this analysis relies on findings from research studies as a reasonable proxy for the experience of persons with ESRD across the country. Given that the resulting assumptions are somewhat arbitrary, sensitivity analyses were conducted.

Live donors were assumed to be in hospital and off work for the median periods (6 and 46 days respectively) measured in a 2000 Toronto-based study with 33 patients who had undergone an open nephrectomy (Pace, et al., 2003a; Pace, et al., 2003b).[72,73] A sensitivity analysis for the time off work evaluated the effects of varying this assumption to the minimum (14 days) and maximum (64 days) periods observed in the study.[74] Consistent with methods used in national studies of the economic burden of illness, days in hospital were weighted at a productivity of 0.2; other days off work were weighted at 0.5 (Health Canada, 2002).[75] That is, for the baseline estimates, a productivity loss of [0.2 (the productivity weight used for days in hospital) * 0.0164 (6 days in hospital/365 days per year) + 0.5 (the productivity weight used for other days off work) * 0.1096 (40 additional days off work/365 days per year)] times the relevant age/sex-specific annual dollar amount for each individual who was a live donor in a particular year was added to the indirect cost estimates.

Transplant recipients were assumed to be in hospital for 11 days, the mean length of stay measured by the Canadian Institute for Health Information in 2000/01 (special tabulation). As for kidney donors, this time was assigned a productivity weight of 0.2. Recent studies on the average time to return to normal activities for Canadian transplant recipients were not found in the literature. An estimate of 6 weeks post-surgery, or 31 days post-discharge, was derived from information for patients on the web sites of major international transplant

---

[72] These data are for patients who had their kidneys removed using an open surgical procedure. Patients receiving a newer laparoscopic procedure typically had less time off work (median of 18 days), but this procedure was not widely implemented in Canada in the period under consideration in this analysis.

[73] The study did not report results by age or sex of donor. Accordingly, the period of lost productivity is assumed to be the same for all live kidney donors.

[74] Published results from the study include only the minimum, median, and maximum periods of time off work for subjects. Information required to calculate the standard deviation of time off work was not available so this metric could not be used to inform the selection of parameters for the sensitivity analysis.

[75] Days in hospital were assumed to have been "spent in bed" (the national study's categorization for short-term disability among the household population, weighted at 0.2). On other days off work, the organ donor was assumed to have "cut down on things."

programs. The sensitivity analysis varied this assumption from 3 to 10 weeks. Productivity weights of 0.5 were applied to this time.

Patients on dialysis experience sustained, long-term effects on productivity. According to a 1999 study from Alberta, approximately 7% of hemodialysis patients and 5% of peritoneal dialysis patients require 24-hour/long-term care (Manns, et al., 2002). These patients were assumed to have a 'very severe' disability and assigned a productivity weight of 0.2. A further 31% and 35% respectively required part-time home care. These patients were assumed to have a 'somewhat severe' disability and assigned a productivity weight of 0.5. Remaining dialysis patients were assigned a weight of 0.7.[76]

Results ~ Economic Burden Related to Morbidity

Almost 25,000 Canadians had end-stage renal disease in 2000. For many, the disease had a significant impact, translating into almost $143 million in estimated productivity losses.[77] This total is about the same as Health Canada's (2002) estimates for other much more common conditions, such as hip problems ($174 million) and chronic obstructive pulmonary disease ($161 million),[78] reflecting the degree to which ESRD affects patients' lives.[79]

---

[76] This approach potentially overestimates productivity losses for patients on dialysis since some patients began dialysis part way through the year (and hence do not experience the full productivity loss). On the other hand, it potentially underestimates losses since some patients on dialysis will die during the year (and so are not reflected in the year-end census figures used for prevalence calculations) and some patients who have new functioning transplants at the end of the year will have spent part of the year on dialysis. In 2000, there were about 4,386 new ESRD patients; most started on dialysis although some had pre-emptive kidney transplants. In the same year, over 1,100 patients received new kidney transplants and almost 2,500 dialysis patients died.

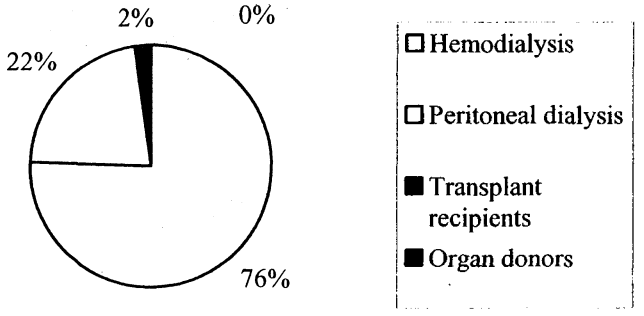
[77] All currency values in this section are expressed in terms of 1998 Canadian dollars.

[78] In 1998/99, for example, about 498,400 Canadians reported having been diagnosed by a physician with chronic bronchitis or emphysema, conditions seen as markers of chronic obstructive pulmonary disease, on the National Population Health Survey (CIHI, Canadian Lung Association, Health Canada, Statistics Canada, 2001).

[79] Estimates of the economic burden of end-stage renal disease could not be derived using the approach taken by the national study; a more specific study, such as this one, using different data sources was required. While attempts have been made to be as consistent as possible with the methodologies used in Health

The morbidity-related economic burden was much higher for dialysis patients than for those with transplants (see Figure 15), reflecting both the larger numbers of persons who receive dialysis and the fact that transplants typically offer a higher quality of life. In 2000, an estimated $107.9 million in productivity was lost due to morbidity experienced by patients on hemodialysis. A further $31.8 million was attributed to peritoneal dialysis patients. The difference between the two types of dialysis primarily reflects the number of patients receiving each therapy. In both cases, the estimates are highly sensitive to assumptions about productivity weights (see Table 9).[80]

Figure 15: Morbidity-Related Economic Burden of End-Stage Renal Disease in 2000 by Treatment Type



A further $3.2 million in short-term productivity losses were accrued by kidney transplant donors and recipients in 2000. The majority of these losses were attributed to transplant recipients, mostly because of their much larger numbers.[81] For the same reason, the sensitivity analyses that varied recovery time for transplant patients had more effect than those that varied the time that donors spent off work (see Table 9). In both cases, however, the changes had relatively little impact on the overall estimates of the economic burden of ESRD.

Canada's study (2002), the necessary variations in methods and data sources may affect the comparability of results.

[80] The overall national estimates of the economic burden of disease were equally sensitive to these types of assumptions.

[81] Most transplant recipients receive organs from cadaveric donors.

5.4 Summary of the Economic Burden of End-Stage Renal Disease

Traditionally, estimates of the economic burden of disease include direct health care costs and indirect costs related to both morbidity and mortality. In the case of end stage renal disease (ESRD), the total is significant: approximately $1.9 billion in 2000.[82,83] This is higher than for conditions such as skin and infectious diseases, about the same as genitourinary and endocrine disease, and lower than diseases such as cancer and stroke (Health Canada, 2002). This weight is, however, borne by a relatively small number of individuals. As a result, the economic burden of ESRD is higher per person affected than for most other diseases.

---

[82] Based on baseline estimates for each cost category.

[83] All direct cost estimates have been converted to 2000 Canadian dollars using CIHI's implicit price index (e.g. $0.963 in 1998 is equivalent to $1.00 in 2000). See section 5.1 for details. Other cost estimates (e.g. for the value of labour) have been converted to 2000 Canadian dollars using Statistics Canada's Consumer Price Index (Statistics Canada, 2004b). Based on this index, $0.957 in 1998 is equivalent to $1.00 in 2000.

Table 9: Results of Sensitivity Analysis on Estimates of Morbidity Costs for ESRD Patients (Millions of 1998 Dollars)

Assumptions	Hemo-dialysis	Peritoneal Dialysis	Trans-plant	Total
Baseline Estimate				
Baseline	$ 107.9	$31.8	$3.2	$ 142.9
Sensitivity Analysis ~ Disability Weights				
Much higher productivity loss weights[84]	$ 170.7	$50.7	$3.2	$ 224.6
Somewhat higher productivity loss weights[85]	$ 135.1	$39.8	$3.2	$ 179.2
Somewhat lower productivity loss weights[86]	$ 80.7	$23.7	$3.2	$ 107.6
Much lower productivity loss weights[87]	$ 40.5	$11.7	$3.2	$ 55.4
Sensitivity Analysis ~ Recovery Time				
Transplant donors are, on average, off work for less time (14 days)	$ 107.9	$31.8	$2.7	$ 142.4
Transplant donors are, on average, off work for more time (64 days)	$ 107.9	$31.8	$3.4	$ 143.1
Transplant patients more quickly resume regular activities (average of 3 weeks)	$ 107.9	$31.8	$2.1	$ 141.8
Transplant patients less quickly assume regular activities (average of 10 weeks)	$ 107.9	$31.8	$4.3	$ 144.0
Sensitivity Analysis ~ Non-Market Earnings				
Only includes paid labour market earnings (assumptions as in baseline)[88]	$75.8	$20.8	$1.9	$ 98.5

[84] For the 'much higher loss' case, days in hospital and days requiring 24-hour care/long-term care were assigned a productivity weight of 0 (instead of 0.2 as in the baseline analysis); dialysis patients requiring part-time home care were given a weight of 0.2 (not 0.5); others on dialysis were given a weight of 0.5 (not 0.7).

[85] For the 'somewhat higher loss' case, all baseline weights were decreased by 0.1. That is, days in hospital and days requiring 24-hour care/long-term care were assigned a productivity weight of 0.1 (not 0.2); dialysis patients requiring part-time home care were given a weight of 0.4 (not 0.5); others on dialysis were given a weight of 0.6 (not 0.7).

[86] For the 'somewhat lower loss' case, all baseline weights were increased by 0.1. Days in hospital and days requiring 24-hour care/long-term care were assigned a productivity weight of 0.3 (not 0.2); dialysis patients requiring part-time home care were given a weight of 0.6 (not 0.5); others on dialysis were given a weight of 0.8 (not 0.7).

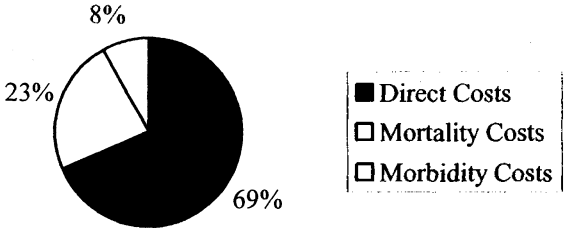
[87] For the 'much lower loss' case, dialysis patients requiring part-time home care were assigned a productivity weight of 0.7 (not 0.5); dialysis patients not requiring care were assigned a weight of 1.0 (not 0.7).

Table 10: Economic Burden of End Stage Renal Disease in 2000 (Millions of dollars)

Category	Total
Direct Health Care Costs	$1,273
Morbidity Costs	$ 149
Mortality Costs	$ 434
Total Costs	$1,857

Direct costs account for the majority ($1.3 billion or 69%) of the total economic burden, reflecting the very high costs of caring for persons with ESRD and the fact that many of those affected are seniors and so past their peak earning years (see Figure 16). Indirect costs are also significant, however, both in terms of mortality ($434 million or 23%) and morbidity ($149 million or 8%), particularly for patients on dialysis. For example, direct costs for patients on hemodialysis are 5.9 times morbidity costs; for transplants, health care costs are more than 120 times the costs of short-term disability. These differences reflect the significant effects that being on dialysis has on people's productivity, as well as on their lives more generally.

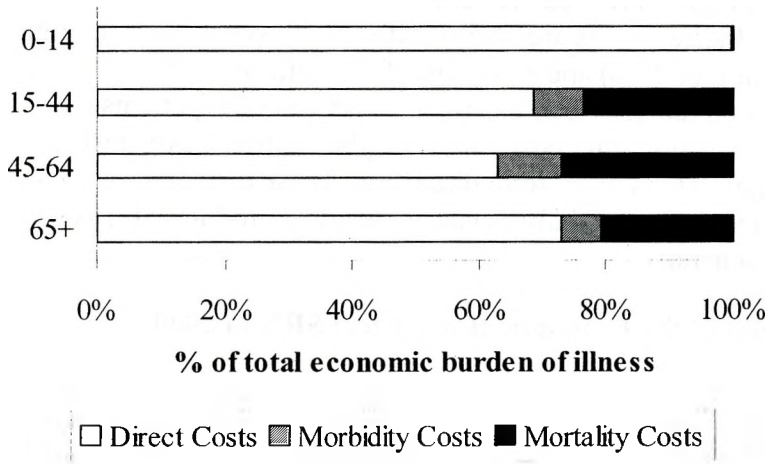
Figure 16: Distribution of the Economic Burden of ESRD in 2000



[88] This analysis drops income sources such as CPP/QPP, UI, and worker's compensation, as well as the value of foregone unpaid labour. These items were all excluded in the sensitivity analysis because they collectively reflect imputed value of time/home production in the economic burden calculations. This is an imperfect measure but is commonly used in research of this kind, partly because of the lack of well-validated alternatives.

Persons age 45 and over account for the vast majority of the economic burden of illness (77%), reflecting the large proportion of ESRD patients (74%) who are in this age bracket. The distribution of costs by type, however, varies over the life course. Direct costs account for more than half of the burden of illness in all age groups, but the proportion of indirect costs is highest for persons in middle adulthood (see Figure 17).[89] This reflects the fact that indirect costs are primarily based on earnings and the value of unpaid labour, which typically peak in a person's 40's and 50's.

Figure 17: Economic Burden of ESRD in 2000 by Age Group and Type of Cost



[89] Based on the methods used in this calculation, persons aged 0-14 contribute almost nothing to the total indirect costs of ESRD. This reflects the fact that no earnings are attributed to this group and hence no morbidity costs are assigned for these patients. (Indirect morbidity costs for living donors who donate kidneys for transplant to persons in this age group are included, but they are relatively modest.) There are also few deaths in this age group and, because of the 5% discount rate used in the baseline analysis, the value of future productivity losses related to mortality is very low or nil.

Chapter 6: A Systems Model of End-Stage Renal Disease and its Care

6.1 Introduction

The disease progression and treatment processes for end-stage renal disease (ESRD) are complex. This chapter provides both graphical and mathematical representations of this process. These models form the foundation of the incidence, prevalence, and economic burden of illness projections in subsequent chapters.

6.2 Graphical Representation of the Process

The figures in this section provide a high-level overview of the dynamics of the ESRD disease and treatment process. The starting point (at the top of Figure 18) is the total population at the beginning of a given time period, divided into those who do and do not have ESRD.

A small number of those with ESRD recover kidney function, but most do not. Their survival chances, quality of life, and the associated economic burden of their illness may depend on what type of treatment they receive. Accordingly, the next fork in the flowchart groups ESRD patients based on whether or not they have previously received a transplant that is still functioning. For those who have, a key determinant of their course of treatment and the on-going economic burden of their illness is whether or not their transplant (or "graft") fails. When graft failure occurs, patients typically return to dialysis. Depending on their circumstances, they may or may not then join the waiting list for a transplant.

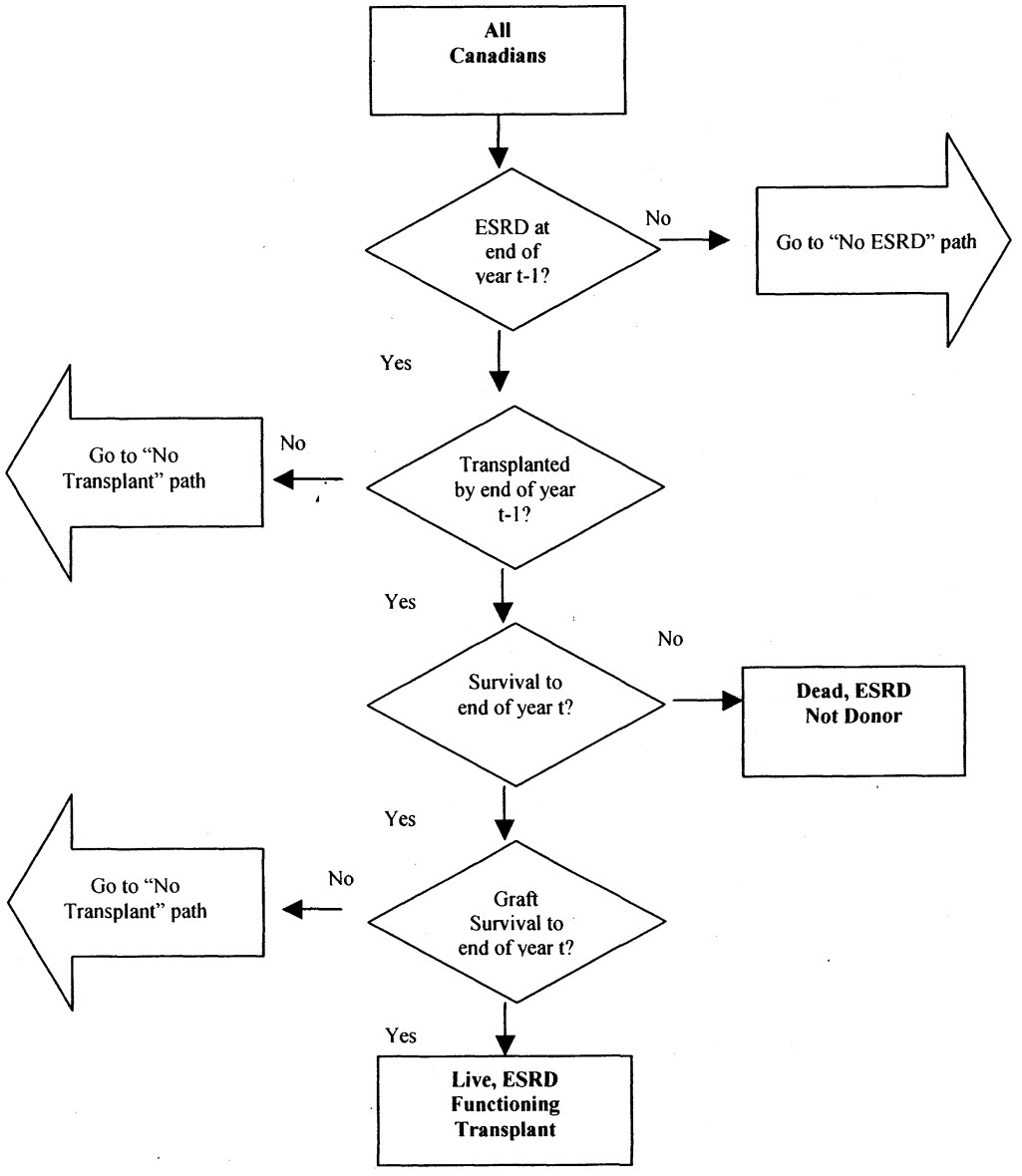
Most patients with ESRD who do not have a functioning transplant are assessed against the criteria to receive one (see Figure 19). Each year, some transplant candidates receive a new kidney, but many others are on the waiting list for surgery. They (as well as most of those who do not qualify for transplants) receive hemodialysis or peritoneal dialysis.

Nevertheless, over the course of a year, some of those with and without ESRD die. When deaths occur, they may or may not be in circumstances

conducive to organ donation (see Figure 20). For each potential donor where consent is obtained and organ retrieval is initiated, one or two kidneys may become available for transplantation. Live donors are the other source of kidneys for transplant.

Individuals without ESRD who survive may or may not develop the disease over a specified period of time (see Figure 21). Those who develop the disease typically begin hemodialysis or peritoneal dialysis.

Figure 18: ESRD and Treatment Dynamics - Entry Path[90]



[90] For simplicity, patients with ESRD are assumed not to be potential kidney organ donors.

Figure 19: ESRD and Treatment Dynamics - No Transplant Path

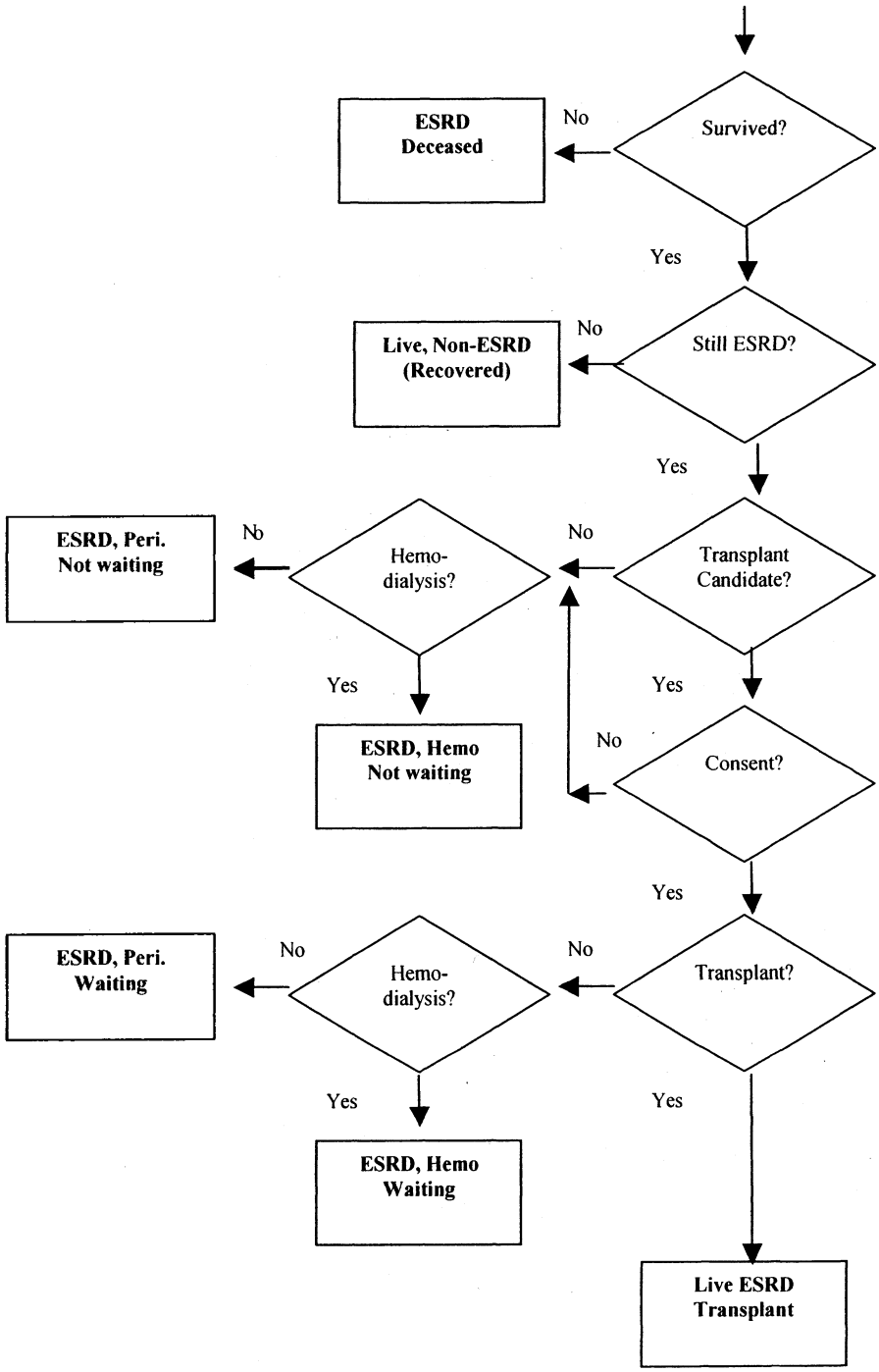


Figure 20: ESRD and Treatment Dynamics - No ESRD Path

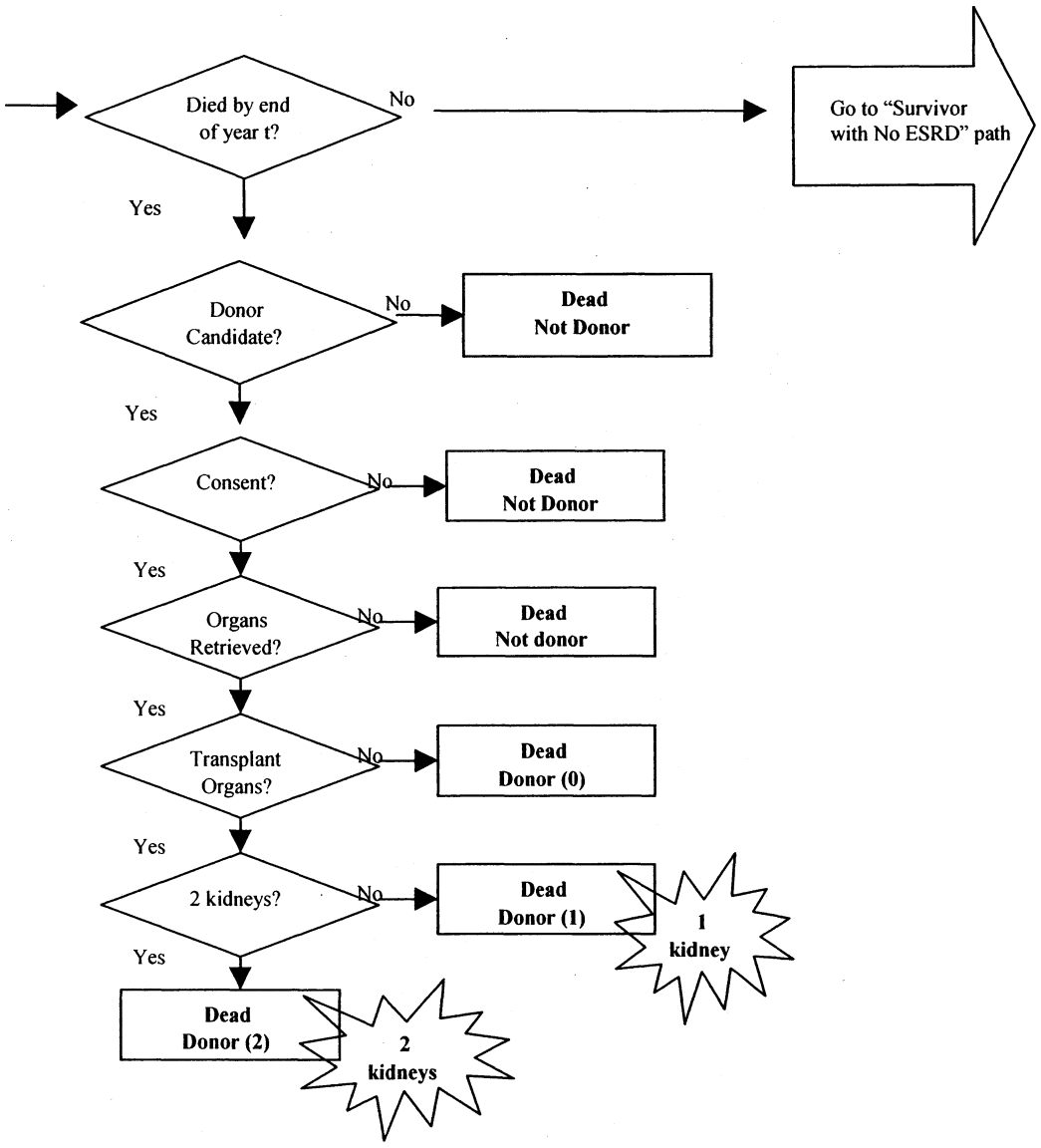
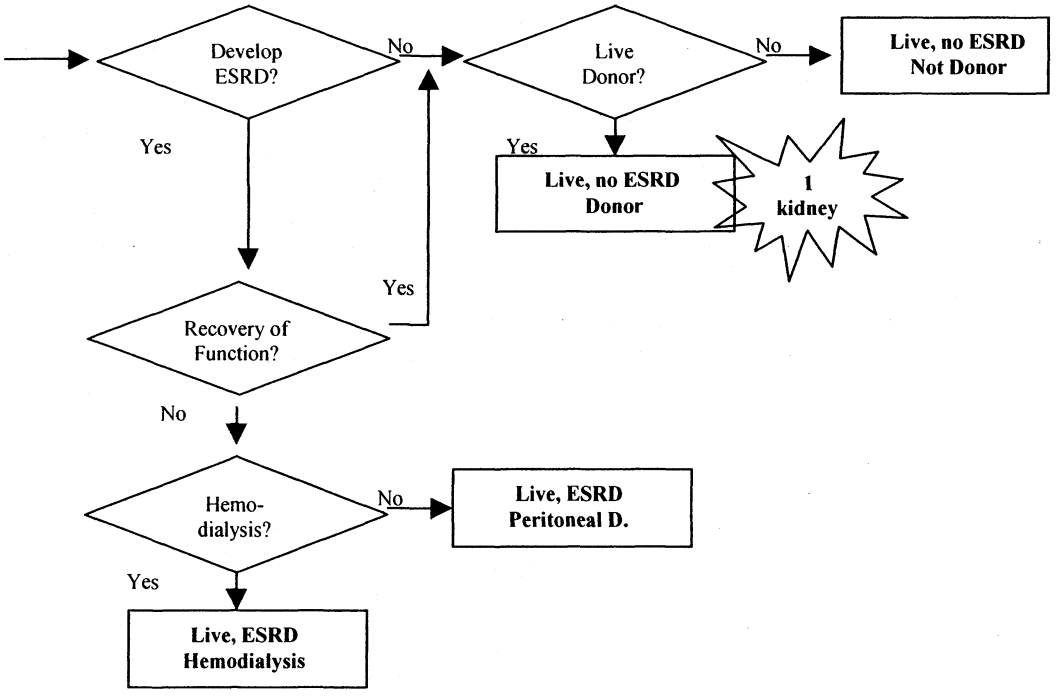


Figure 21: ESRD and Treatment Dynamics - Survivor with No ESRD Path



6.3 Mathematical Representation

Each of the population groups described above, as well as the transitions between different treatment and survival states, can be represented mathematically. A recursive, non-stochastic model of these processes is described below. A detailed description of each of the variables in the model is provided in Appendix C.

The Population and Disease Process

Canada is home to more than 30 million people. Of these, only a relatively small proportion develop ESRD each year. In the model, the expected number of people with ESRD at time t+1 equals the number of people with ESRD at time t plus the number of new ESRD cases between time t and t+1 (the incidence) minus the number of deaths and recoveries among people with ESRD.[91]

[91] In this case, as in many other areas, the operationalization of the model includes a vector by population characteristics. For example, the total ESRD population is

$$ES\_TOT_{t+1} = ES\_TOT_t + ES\_NEW_{t,t+1} - ES\_DEATHS_{t,t+1} - ES\_REC_{t,t+1} \quad \textbf{Eq. 4}$$

The expected number of incident cases of ESRD between time t and t+1 is calculated as the probability of developing the disease over this period times the total population at time t.[92,93,94]

$$ES\_NEW_{t,t+1} = PR\_ES\_NEW * POP\_TOT_t \quad \textbf{Eq. 5}$$

The expected number of deaths among people with ESRD between time t and time t+1 equals the probability of death among ESRD patients over this period multiplied by the number of people with ESRD at time t. These mortality rates vary by treatment modality (TTx), as well as other factors (DTx).

$$ES\_DEATHS_{t,t+1} = \sum_{DTx,TTx} PR\_ES\_DEATH_{DTx,TTx} * ES\_TOT_{t,DTx,TTx} \quad \textbf{Eq. 6}$$

---

the sum of the ESRD population in each age group. For ease of presentation, age and sex subscripts are not shown in this chapter.

[92] Technically, this should be calculated as the incidence in the total population excluding the population with ESRD. Nevertheless, in order to be consistent with the way that data available to populate the model are presented, the total population (including those with ESRD) is used. Given that the size of the ESRD population is small relative to that of the total population, the effect on projections is small.

[93] Changes in the distribution of incident cases, for example in terms of underlying risk factors, may cause second order effects. For instance, they might affect the probability of recovery. Nevertheless, since these effects are likely to be relatively minor and are difficult to track with available data, they are not included in the model at this time.

[94] Throughout the model, all transition probabilities are one-step probabilities (i.e. between time t and t+1). To simplify notation, the time subscripts (t,t+1) are not shown. In operationalizing the model in subsequent chapters, proportions estimated from actual data are used as the basis of probabilities that are applied at a patient level in the simulation model. These estimates therefore reflect actual patient experience, rather than the hypothetical trajectories developed by expert panels that are often employed in research of this kind because of a lack of longitudinal data or suitable analytical techniques.

The expected number of people with ESRD who recover kidney function between time t and time t+1 equals the probability of recovery among ESRD patients over this period times the number of people with ESRD at time t.

$$ES\_REC_{t,t+1} = PR\_ES\_REC * ES\_TOT_t \quad \textbf{Eq. 7}$$

In fact, equations five, six, and seven are examples of a generic equation in the model: the expected value in the next period equals the sum of the probabilities for individual sub-groups multiplied by the population size of those groups. To simplify notation, expected and actual variables are shown using the same symbol.

The probability of survival for ESRD patients between time t and time t+1 is the complement of the probability of death:

$$PR\_ES\_SURV = 1 - PR\_ES\_DEATH \quad \textbf{Eq. 8}$$

ESRD Treatment

Well over half of all patients with end-stage renal disease (78% in Canada at the end of 2000) are on dialysis (CORR/CIHI, 2002). Most of the remainder had a functioning kidney transplant. Many patients on dialysis have met clinical and other eligibility criteria and are on the waiting list for a transplant. At the end of 2000, 3,278 Canadians were waiting for kidney transplants.

In the model, the number of ESRD patients at time t equals the sum of the number receiving dialysis, plus the number with functioning transplants.[95] Dialysis patients can receive either haemodialysis or peritoneal dialysis.

$$ES\_TOT_t = ES\_DIAL_t + ES\_TRAN_t \quad \textbf{Eq. 9}$$

$$ES\_DIAL_t = ES\_HEMO_t + ES\_PERI_t \quad \textbf{Eq. 10}$$

[95] At any given time, a few patients will have been diagnosed with ESRD but not yet started therapy. Others have refused treatment. Since the numbers in both groups are small and the patients are expected to transition relatively rapidly to dialysis/transplant or death, these treatment states have not been included in the model.

The expected number of patients on a particular type of dialysis at time t+1 equals the number who were on that therapy at time t, adjusted for changes that occurred during the period. Those who switched from the other type of dialysis and patients who have newly developed ESRD or had a transplanted kidney fail and were placed on this therapy are added to the total. On the other hand, those on the dialysis therapy who recovered function, received a transplant, switched types of dialysis, or died are subtracted from the sum.

$$
\begin{aligned}
ES\_HEMO_{t+1} = \quad & ES\_HEMO_t \\
& + \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHG_{d2,d1} \end{pmatrix} \\
& + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d1}) \\
& + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d1} \end{pmatrix} \\
& - (ES\_HEMO_t * PR\_ES\_REC) \\
& - (ES\_HEMO_t * PR\_TRAN\_CHG_{r1,r2}) \\
& - \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHG_{d1,d2} \end{pmatrix} \\
& - (ES\_HEMO_t * PR\_ES\_DEATH_{d1})
\end{aligned}
\qquad \textbf{Eq. 11}^{96}
$$

[96] The following codes are used in equations in this chapter: d1=hemodialysis, d2=peritoneal dialysis, d3=no dialysis, r1=waiting for transplant, r2=functioning transplant, r3=other (e.g. not a candidate for transplant).

$$
\begin{aligned}
ES\_PERI_{t+1} = \quad & ES\_PERI_t \\
& + \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHNG_{d1,d2} \end{pmatrix} \\
& + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d2}) \\
& + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d2} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_REC) \\
& - (ES\_PERI_t * PR\_TRAN\_CHG_{r1,r2}) \\
& - \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHG_{d2,d1} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_DEATH_{d2})
\end{aligned}
\qquad \textbf{Eq. 12}
$$

The expected number of people with ESRD who have functioning transplants at time t+1 equals the number who had functioning transplants at time t, adjusted for changes that occur over the period. Patients from the waiting list at time t with newly-received functioning transplants by time t+1 are added to the totals. Those who die or suffer graft failure and return to dialysis (and in some cases are placed again on the transplant waiting list) are subtracted from the overall counts.[97]

$$
\begin{aligned}
ES\_TRAN_{t,t+1} = \quad & ES\_TRAN_t \\
& + (WAIT\_LIST_t) * PR\_TRAN\_CHG_{r1,r2} \\
& - ES\_TRAN_t * PR\_ES\_DEATH_{r2} \\
& - ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\
& - ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r1}
\end{aligned}
\qquad \textbf{Eq. 13}
$$

The probability that a person with ESRD who does not have a functioning transplant at time t will be placed on the waiting list is a non-linear function of the length of the waiting list, personal patient characteristics, clinical practices, and policies/legislation. For example, a survey of Canadian kidney transplant centres (Noorani and McGahan, 1999) explored factors considered in determining

[97] Canadian ESRD patients who receive transplants outside the country and then return to Canada would normally be reported as transplanted through the Canadian Organ Replacement Register (CORR) and hence included in these totals. Foreign ESRD patients (with or without a functioning transplant) migrating to Canada would typically be treated as "new" ESRD patients when registered with CORR.

eligibility to receive cadaveric kidney transplants. Many centres reported giving consideration to:

- *Employment and demographic factors*, such as age (in some cases patients aged 75 years or over were not eligible for transplants), insurance status (particularly post-surgery prescription drug coverage), and nationality (programs were often restricted to Canadian citizens or landed immigrants);

- *Comorbid conditions*, such as HIV infection, cardiovascular disease, malignancy, mental competence, pulmonary disease, liver disease, Hepatitis B, and other conditions; and

- *Health behaviours*, such as abstinence from alcohol and illicit drug substance abuse.

Some centres also reported giving consideration to other factors, such as whether or not the patient has appropriate social and community support systems. Additional factors may also be relevant but were not covered by the survey. Examples include blood type and other clinical match factors, organ size (e.g. child or adult), distance between donor centre and recipient centre, medical urgency, and the amount of time that potential recipients have been waiting.

Reflecting these and other research findings, a variety of possible influences on decisions regarding the distribution of organs for transplant are incorporated into the model. As with all transition probabilities in the model described in this chapter, those referred to below are conditional on an individual surviving to the next period.

$$PR\_TRAN\_CHG_{r1,r2} = f(WAIT\_LIST_t, PERS\_CHAR_t, CLINICAL\_P_t, POLICIES_t) \quad \textbf{Eq. 14}$$

The probability that a person with ESRD who does not have a functioning transplant at time t will receive one by time t+1 is a function of the probability that s/he will receive a transplant from either a living or a cadaveric donor.

$$PR\_TRAN\_CHG_{r1,r2} = f(PR\_NEW\_CAD, PR\_NEW\_LVG) \quad \textbf{Eq. 15}$$

Given that a patient receives a transplant, the probability that s/he receives a cadaveric transplant is the complement of the probability that s/he receives a transplant from a living donor.

$$PR\_CAD\_TRAN = 1 - PR\_LVG\_TRAN \qquad \textbf{Eq. 16}$$

The probability that patient *i* on the waiting list will receive a transplant from a cadaveric donor depends on the supply of cadaveric organs, patient characteristics, the length of the waiting list, clinical practices, and policies/legislation. These factors also affect the probability of receiving a transplant from a living donor. In this case, however, different weight may be placed on certain patient characteristics and other factors.

$$PR\_NEW\_CAD = f\begin{pmatrix} KDNY\_CAD_t, PERS\_CHAR_t, WAIT\_LIST_t, \\ CLINICAL\_P_t, POLICIES_t \end{pmatrix} \qquad \textbf{Eq. 17}$$

$$PR\_NEW\_LVG = f\begin{pmatrix} KDNY\_LVG_t, PERS\_CHAR_t, WAIT\_LIST_t, \\ CLINICAL\_P_t, POLICIES_t \end{pmatrix} \qquad \textbf{Eq. 18}$$

The expected number of people on the waiting list for a kidney transplant at time t+1 equals the number who were on the waiting list at time t, adjusted for changes that occurred over the period. Those who joined the waiting list between time t and time t+1 are added to the total, but those who received a transplant between time t and time t+1 are subtracted, as are those who died while waiting for a transplant. Individuals may also be taken off the waiting list for medical or other reasons (e.g. if they are alive but their condition has deteriorated in such that they are no longer a candidate for transplantation).

$$\begin{aligned} WAIT\_LIST_{t+1} = \quad & WAITLIST_t \\ & -WAIT\_LIST_t * PR\_TRAN\_CHG_{r1,r2} \\ & -WAIT\_LIST_t * PR\_ES\_DEATH_{r1} \\ & -WAITLIST_t * PR\_TRAN\_CHG_{r1,r3} \\ & +ES\_DIAL_t * PR\_DIAL\_CHG_{d3,r1} \end{aligned} \qquad \textbf{Eq. 19}$$

The Supply of Kidneys for Transplant

Over 1,000 kidney transplants are performed in Canada each year (CORR/CIHI, 2002). The organs come from both living and cadaveric (deceased) donors. As a result, the total expected number of kidneys successfully harvested for transplantation between time t and time t+1 equals the sum of the expected number successfully harvested from these two types of donors.[98]

$$KDNY\_TOT_{t,t+1} = KDNY\_LVG_{t,t+1} + KDNY\_CAD_{t,t+1} \qquad \textbf{Eq. 20}$$

The expected number of organs successfully harvested from cadaveric donors equals the number from donors where only a single organ was harvested plus two times the number from donors where both kidneys were harvested. The former is calculated as the number of candidate donors over the period multiplied by the probability that consent is received and the probability that only a single kidney is harvested. The latter is calculated in the same way, except that the probability that both kidneys are harvested is used.

$$\begin{aligned} KDNY\_CAD_{t,t+1} = \quad & \left(DONOR\_CAN_{t,t+1} * PR\_CONSENT \right. \\ & \left. * PR\_HARV\_1 \right) \\ & +2 * \left(DONOR\_CAN_{t,t+1} * PR\_CONSENT \right. \\ & \left. * PR\_HARV\_2 \right) \end{aligned} \qquad \textbf{Eq. 21}$$

[98] The model considers the supply of cadaveric and living organs separately (as in the equations that follow), since different factors may influence their supply. In the future, it is possible that xenotransplantations may occur. In this case, the number of such transplants would be added to the total in Equation 20.

Zero, one, or two kidneys can be successfully harvested for transplantation from a cadaveric donor. The probability that two will be harvested is the complement of the sum of the probabilities that zero or one will be retrieved.

$$PR\_HARV\_2 = 1 - (PR\_HARV\_1 + PR\_HARV\_0) \qquad \textbf{Eq. 22}$$

The expected number of candidates for cadaveric organ donation between time t and time t+1 equals the probability that a person alive at time t dies in circumstances that would make him/her a potential candidate for organ donation by time t+1, multiplied by the number of people alive at time t.

$$DONOR\_CAN_{t,t+1} = PR\_EL\_DEATH * POP\_TOT_t \qquad \textbf{Eq. 23}$$

The probability of an "eligible" death depends on many factors. For example, policies and legislation, such as seatbelt legislation, may have an impact on the number of deaths from head injuries. Personal behaviours, such as the propensity to drive after drinking alcohol, and clinical practices can also have an effect on the number of potential cadaveric organ donors.

$$PR\_EL\_DEATH = f\begin{pmatrix} POLICIES_t, CLINICAL\_P_t \\ PERS\_BHVR_t \end{pmatrix} \qquad \textbf{Eq. 24}$$

When someone dies in circumstances that might permit cadaveric organ donation, the probability that consent will be obtained to allow harvesting of organs depends on policies and legislation that are in place as well as public preferences regarding organ donation.

$$PRCONSENT = f(POLICIES_t, PERS\_PREF_t) \qquad \textbf{Eq. 25}$$

As for cadaveric donations, policies, legislation, and public preferences can have an impact on the expected number of living organ donations. The length of the transplant waiting list, clinical practices, and characteristics of persons with ESRD may also influence living donors' decisions. For example, data show that children with ESRD are more likely to be recipients of living donations than adults are (CORR/CIHI, 2002). Other factors may also be important. For instance, family size and other characteristics may matter since most living donors are related to transplant recipients. Nevertheless, this factor and others that are similarly not readily amenable to clinical or policy intervention have been omitted from the model for tractability.

$$KDNY\_LVG_{t,t+1} = f(POLICIES_t, PERS\_PREF_t, WAIT\_LIST_t, CLINICAL\_P_t, ES\_TOT_t, POP\_TOT_t) \quad \textbf{Eq. 26}$$

Chapter 7: End-Stage Renal Disease ~ Baseline Projections

7.1 Introduction

The direct and indirect economic burden of end-stage renal disease (ESRD) depends on the number of patients with ESRD, how many recover kidney function or die, and the types of treatment that they receive. Accordingly, projections of these parameters are required for any estimates of the future economic burden of the disease. The results themselves may also be of interest to managers and policy-makers who are projecting resource requirements for ESRD patients, planning purchases of major capital equipment, identifying future training requirements and programs, attempting to understand and mitigate potential public health implications, or exploring related issues.

This chapter highlights approaches and findings from previous projections, in addition to presenting new baseline projections for incidence, patient follow-up, and numbers of new transplants in Canada to 2015. The incidence of ESRD is projected using an autoregression model. Recovery, mortality, and treatment patterns for patients with the disease are estimated using a multi-state discrete time Markov model.

The resulting projections are then used to estimate the future economic burden of end stage renal disease. Chapter 8 extends the analysis by exploring the effects of alternate demographic and policy scenarios on the economic burden of ESRD. Chapter 9 investigates the gap between the demand for transplants and available living and cadaveric organ donations, as well as various policy alternatives to address this challenge.

7.2 Background ~ Projections of Chronic Disease Incidence and Prevalence and Health Care Utilization

Both the prevalence of chronic conditions and associated resource use fluctuate over time depending on trends in demographics, underlying risk factors, patient survival, treatment patterns, and other factors. The behavioural model of health services utilization offers one approach to understanding these

relationships that allows consideration of both individual-level and system-level factors. According to this model, usage depends on people's "predisposition to use services, factors which enable or impede use, and their need for care," in the context of the broader health care system and external environment (Andersen, 1995).

One such determinant is demographics. Certain groups of individuals, often defined by demographic characteristics, are more likely to have chronic conditions and thus to use more health services than the rest of the population. For example, on a per capita basis, the elderly consume substantially more health services than their younger counterparts. This trend holds for physician services (Barer, et al., 1989; Denton, et al., 2001; Denton, et al., 2002), nursing home care (Burner, et al., 1992), hospital services (McGrail, et al., 1998), and other health care services (Getzen, 1992). Seniors are also more likely to be diagnosed with ESRD and tend to receive different types of care for kidney failure (CORR/CIHI, 2002).

Many researchers have attempted to quantify the effect of aging and other demographic shifts on future health and health care, primarily using an actuarial approach (Manton, et al., 1993; Evans, et al., 2001). This methodology answers the question, "what if a future population used health care at the same rate as today's population?" Researchers forecast future prevalence rates, utilization of health services, and costs based on current age-specific rates and population projections. For example, broad health services or acute care projections have been made for Germany (Leidl, 1992), Sweden (Gerdtham, 1993), the United States (Burner, et al., 1992; Warshawsky, 1994; Knickman and Snell, 2002), Canada (Denton and Spencer, 1975; Lefebvre, et al., 1979; Johansen, et al., 1996; Rosenberg, 2000), Ontario (Denton, et al., 1995), Manitoba (Stewart, et al., 2002), and other jurisdictions. Estimated changes in resource requirements given current practice patterns and utilization rates are often in the 0.5% - 2% per year range.

These studies typically explore the effects of demographic change holding all else (e.g. age/sex specific utilization patterns) equal, but recent experience suggests that, in practice, all else is *not* equal. Risk factors, disease rates, treatment options, practice patterns, and other factors change over time. At the aggregate level, researchers have found that differences in age-specific utilization rates can be at least as important as variations in population age distributions in explaining utilization trends. Evans and colleagues (1989) and Anderson and colleagues (1990), for instance, found that changes in age-specific relative rates of utilization have been at least as important as population aging in determining overall hospital usage in British Columbia. More recently, Denton, Gafni, and Spencer (1995); Evans and colleagues (Evans, et al., 2001); and Mennec and colleagues (Menec, et al., 2002) have come to similar conclusions based on evidence from across the country.

These overall patterns also apply to ESRD. There have been marked changes over time in age-specific incidence rates, particularly for the elderly, and in the distribution of patients among different types of treatments (CORR/CIHI, 2002). In fact, sixty years ago, there were no viable treatment options for people with ESRD. Today there are several, and patients' survival chances continue to improve.

Most published projections of ESRD incidence have endeavoured to take at least some demographic, risk factor, survival and/or treatment trends into account. In doing so, they have used many different methodological approaches (see Table 11). Some have simply extrapolated current trends in the number of new and/or prevalent cases of ESRD (e.g. Port, 1995). This approach is computationally simple, but resulting long-term projections do not take into account potential shifts in factors known to affect ESRD trends, such as demographics. Other researchers have made assumptions about incidence rates and applied these to projections of the population (e.g. Blanchard, et al., 1999). Still other studies have developed complex models based on probabilities of acquiring ESRD, of ESRD patient survival, and of transitioning between various ESRD treatments, often stratified by demographic and other characteristics (e.g. Schaubel, et al., 1998a; Schaubel, et al., 1999). This approach is computationally intense, but it allows for the development of rich projections, incorporating a variety of underlying trends.

Table 11: Selected Projections of ESRD Incidence and Prevalence

Population (Source)	Period	Methods
Ontario (Minister's Task Force on Kidney Donation, 1985)	To 2004	- Incidence projection method not described - Follow-up incorporates specific numerical assumptions regarding changes in mortality, transplant, and graft failure rates over time
Japan (Motohashi and Nishi, 1991)	To 2000	- System dynamics model - Assumes constant incidence rates of underlying diseases (e.g. diabetes) - Incorporates two different assumptions regarding changes in the number of transplants
United States (Krakauer, 1993)	To 1990	- Technology assessment in terms of effectiveness and cost - Actuarial and Kaplan-Meier survival analysis under various assumptions
Canada (Desmeules, et al., 1995)	To 2000	- Incidence: Poisson regression by age and diabetes status or maintenance of recent incidence rates - Markov model for patient follow-up

Population (Source)	Period	Methods
United States (Port, 1995)	To 2000	- Incidence: continuation of current exponential trend or maintenance of recent incidence rates - Prevalence not projected
Britain (Mallick, 1997)	To 2018	- Assumes quick progression to "target rate" for new patients - Survival analysis by risk group with sensitivity analysis - Constant "target rate" of transplants
Holland (de Wit, et al., 1998)	To 2000	- Extrapolation of number of new cases based on linear regression model - Markov model for patient follow-up
Canada (Schaubel, et al., 1998a)	To 2005	- Incidence: Poisson regression by age and diabetes status or maintenance of recent incidence rates - Markov model for patient follow-up
Manitoba, Canada (Blanchard, et al., 1999)	To 2025	- Projects diabetic population and then applies current ESRD incidence rates by age, gender, aboriginal status to projections - Moves population forward year by year
Canada by province (Schaubel, et al., 1999)	To 2005	- Incidence: Poisson regression by age and diabetes status or maintenance of recent incidence rates - Markov model for patient follow-up
United States (US Renal Data System, 2000)	To 2010	- Stepwise autoregression used to project new patient counts, patient numbers by treatment type, and Medicare payments - Point prevalence projection uses exponential smoothing
United States (Xue, et al., 2001)	To 2010	- Stepwise autoregression model or exponential smoothing for growth in patient numbers and point prevalence
World-wide (Lysaght, 2002)	To 2010	- Constant annual growth rate for dialysis population prevalence extrapolated based on recent trends
Northern Territory, Australia (You, et al., 2002)	To 2003	- Dialysis-specific univariate ARIMA model for the number of hemodialysis treatments

Regardless of the approach used, when the studies were conducted, or what population they covered, all consistently projected significant increases in the population with ESRD. As we plan for the future, more detailed models that project the size and nature of these types of chronic disease trends under various demographic assumptions and policy scenarios are being sought (Manton, et al., 1993; National Coordinating Committee for Organ and Tissue Donation Distribution and Transplantation, 1999; Alberta Advisory Committee on Organ and Tissue Donation and Transplantation, 2000). The analysis presented here and in subsequent chapters aims to help to fill this gap for ESRD in the Canadian context.

7.3 Methods ~ Projecting ESRD Patient Follow-up

This chapter describes baseline projections of survival, recovery, and treatment patterns for patients who had ESRD at the start of projection period, as well as those who would acquire the disease during that period. Recovery, mortality, and treatment patterns for patients with the disease are estimated using a multi-state discrete time Markov model, essentially a simplified version of the model described in Chapter 6. This type of model uses a transition matrix to characterize the natural progression of the disease and of the types of treatments used (Craig and Sendi, 2002). SAS analytical software was used for all analyses.

Data Sources

The patient follow-up projections use anonymized patient-level data from the Canadian Organ Replacement Register (CORR) for two cohorts of patients: those alive with ESRD in Canada in 1990 and those alive with ESRD in 1995. The data sets included basic contextual data (e.g. age at ESRD incidence, date of ESRD incidence, and primary renal disease), as well as information on death, recovery, and any switches in treatment status from incidence to December 31, 2000. Results are based on data included in the Register as of July 2002. For more information about CORR, see Appendix A.

In order to prepare the data for model estimation, several transformations were required. These included converting the file from one record per treatment status change at any time during the follow-up period (see top of Figure 22) to a series of observations on the treatment received as of a particular date in each year of the period (as in the table at the bottom of Figure 22). December 31st was chosen to coincide with available aggregate level data. For hemodialysis, peritoneal dialysis, and transplant treatment states, it was also possible to differentiate between patients in their first year (Y1) of a therapy and patients in the second or subsequent years (Y+) of that therapy.

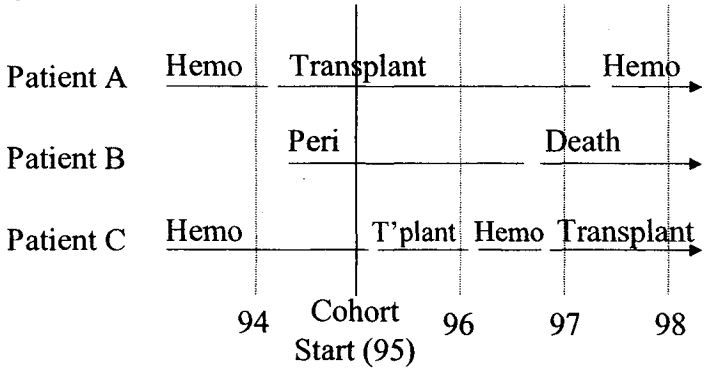
Other variables necessary for subsequent analysis were also derived. For example, the number of years that each patient had had ESRD at the start of the cohort ("ESRD duration") and the number of treatment switches each year were calculated.[99] In addition, extraneous observations for the purposes of the model

[99] Relatively few patients had more than one treatment switch within a year. Accordingly, the model only considers this factor in the case of transplants (having a transplant fail and receiving a new organ within a single year). Tracking transplants is important because of the relatively high costs associated with the surgery in the short-term and in order to estimate total organs used in a given year.

(e.g. those that related solely to a transfer between treatment centres, rather than a change in treatment itself) were dropped.

Figure 22: Sample ESRD Patient Status as in the Original Data Set and Derived Follow-up States[100]

Original Data Structure



Derived Follow-up Status

	1995	1996	1997	1998
A-	T'plant (Y1)	T'plant (Y+)	T'plant (Y+)	Hemo (Y1)
B-	Peri (Y1)	Peri (Y+)	Dead (n/a)	Dead (n/a)
C-	Hemo (Y+)	T'plant (Y1)	T'plant (Y1)	T'plant (Y+)

ESRD Study Populations

There were 9,626 ESRD patients in the 1990 cohort and 16,049 in the 1995 cohort (see Table 12).[101] Eight-eight (88) and 424 patients respectively were lost-

[100] Note: in the case of Patient C, the transition to hemodialysis would not be captured by the approach used since they transitioned to and from this treatment type within a single year.

[101] These numbers differ from those in Appendix B since the record-level data exclude patients who had recovered kidney function in previous years and are defined using a different cut-off date.

to-follow-up or deceased prior to the projection initiation time (December 31st of the reference year). They were excluded from further analysis.

Table 12: Characteristics of 1990 and 1995 ESRD Cohorts[102,103]

Cohort	1990	1995
Total number of patients	9,626	16,049
Average age	49	52
% age 65+	22.4%	28.6%
% diabetic	16.4%	19.1%

Over a given period of time, a patient with ESRD can receive one of several different types of ESRD therapy, can die, or (rarely) can recover kidney function. A Markov chain model can be used to estimate patients' transitions between these states over time (Gilks, et al., 1996; Gilks, 1998). Markov chain models have been used to study a wide range of research questions, including how individuals in similar situations progress through various disease states. In doing so, it offers an approach useful for economic analysis that can link clinical trajectories or disease progression with an understanding of the resources that are consumed by patients over time (Briggs and Sculpher, 1998; Bentkover, et al., 1999; Craig and Sendi, 2002).

In this class of models, the state that a patient will occupy in the next period depends on his/her previous state(s). Accordingly, how patients are distributed among states in the future depends on their current distribution among the states, the probability of moving from one state to another, and the inflow into the population over time (de Wit, et al., 1998).

Following Gilks (1998), suppose that a sequence of random variables $\{X_t, 0 \le t < \infty\}$ is a discrete time Markov chain. These variables take on one of a discrete set of possible states, $S = \{0,1,...,K\}$. The Markov property defines the dependency structure as follows:

$$\Pr(X_{t+1} = j \mid X_1 = i_1, X_2 = i_2, ..., X_{t-1} = i_{t-1}, X_t = i) = \Pr(X_{t+1} = j \mid X_t = i) \quad \textbf{Eq. 27}$$

[102] Patients lost-to-follow-up or deceased prior to projection initiation time were excluded from the calculation of descriptive characteristics.

[103] These are the characteristics of patients alive with ESRD at the given point in time. The profile of patients newly diagnosed with the condition is somewhat different. For example, the average age of new patients in 1995 was 59 years (CIHI/CORR, 2001).

The one-step transition probabilities are described in a square matrix P of dimension S where each element $p_{ij} = \Pr(X_1 = j \mid X_0 = i)$, $p_{ij} \geq 0$ and $\sum_{j \in S} p_{ij} = 1$.

Assuming that the transition probabilities are stable over time (i.e. P is time-stationary), by knowing the state space S, the transition matrix P, and the initial distribution over the states ($\Pr(X_0 = i)$, $i \in S$), it is possible to derive the evolution of the Markov chain at any discrete point in time. For example, it is possible to show that the n-step transition matrix, $P^{(n)}$, is the n^{th} power of the one-step transition matrix or P^n (see, for example, the proof in Gilks, 1998). This approach can be adapted when transition probabilities are not time-stationary (Chib and Greenberg, 1996; Gilks, et al., 1996).

One of the challenges in using a Markov chain model is appropriately defining the states to be included in the model. A balance must be struck between parsimony to maintain sufficient sample size for robust estimation and sufficient detail to ensure that important differences in transition probabilities are captured.

In the case of ESRD, a number of factors affected the choice of states to be included in the model. For example, the literature shows patient follow-up is a second-order process, at least for some groups of patients (Schaubel, et al., 1998a). That is, the patient's current and previous states must both be known to estimate accurately the probability that s/he will transition to a given state in the next period. In addition, the cost of treatment tends to be significantly different in the first year of a treatment compared to subsequent years (Prichard, 1997; de Wit, et al., 1998; Lysaght and O'Loughlin, 2000).[104] Finally, transition probabilities tend to differ in the first few years after ESRD diagnosis compared to later years, at least for some groups of patients. For example, few patients recover kidney function after their first year with ESRD.

[104] Consideration of this factor and its incorporation into the Markov chain model is important since the projections of incidence, prevalence, and the distribution among follow-up states are the foundation for the projections of the economic burden of ESRD in subsequent chapters.

Accordingly, the ESRD patient follow-up process was modeled as a modified second-order Markov process with the following states[105]:

- Death,
- First year of centre-based hemodialysis,
- Second or subsequent year of centre-based hemodialysis,
- First year of limited care or home hemodialysis (hereinafter referred to as "self-hemodialysis"),
- Second or subsequent year of self-hemodialysis,
- First year of peritoneal dialysis,
- Second or subsequent year of peritoneal dialysis,
- New transplant,[106]
- Second or subsequent year with same transplant, and
- Recovery of kidney function.

In the model, death is an "absorbing" state. Once patients reach this state, they stay in it for all remaining projection periods. Likewise, the small number of patients who recover kidney function rejoin the non-ESRD population group. They could re-enter the ESRD population through the ESRD incidence process, at which time they would be treated as if they were new patients.

Costs, survival chances, the use of different types of therapy, and other factors also vary by patient age and whether or not s/he has diabetes (CORR/CIHI, 2001; Powe, 2001; Yang, et al., 2001). Accordingly, state transition probabilities were estimated separately for diabetics and non-diabetics[107] in three age groups (0-44, 45-64, and 65+ years).[108,109] Since Schaubel and colleagues (1998a) have shown that transition probabilities stabilize five years after ESRD incidence, these probabilities were estimated separately for each diabetes/age

---

[105] A very small number of patients received more than one treatment simultaneously (e.g. hemodialysis and peritoneal dialysis). For the purposes of this analysis, these patients were deemed to be receiving the treatment with a higher associated direct and indirect economic burden of illness.

[106] This category includes both patients who receive a transplant for the first time and patients who receive a second or subsequent "new" transplant in the year in question.

[107] A patient was considered to be diabetic if CORR listed their "primary renal disease" as diabetes.

[108] To preserve the confidentiality of individual patients, information on the precise date of birth was not available from CORR. Age as of December 31st is imputed based on year of birth information provided by the Register.

[109] Due to relatively small numbers in some age/diabetes status categories, particularly for younger age groups, state transition probabilities were not estimated separately for males and females.

group combination for patients in their first, second, third, fourth, and fifth or subsequent years with ESRD.[110]

These transition probabilities were then applied to the starting populations and new incident cases to generate projections of their follow-up status. Monte Carlo techniques was used to produce 1,000 simulations of the paths that patients might follow. The baseline analysis described in this chapter assumes that transition probabilities remain constant over time. These projections answer the question "what if practice patterns and survival/recovery chances were to stay the same over time but the population grows and ages and recent trends in ESRD incidence continue?"

Estimating the One-Step Transition Matrices

The transition matrix (P) shows the probability of moving between treatment states from one period to the next. Values for some of the cells in the matrix are determined *a priori*. For example, those in the first year (Y1) of centre-based hemodialysis, self-hemodialysis, peritoneal dialysis, or transplant treatment may continue on that therapy or may switch to another one, recover, or die during the year. However, by definition they may not enter immediately into the second or subsequent year (Y+) of any other type of treatment for ESRD. Accordingly, these transitions are assigned a probability of zero. Likewise, death is an "absorbing" state so the probability that a dead patient transitions to the deceased state in the following period is 1. In contrast, the various treatments are "non-absorbing." For example, except for transplants, patients cannot remain in the initial year-state for the same therapy for more than one year.[111]

Table 13 shows the transition matrix *a priori*. A value of zero in a cell indicates that, by definition, the transition is ruled out. Conversely, a value of one indicates that only one transition is possible from the state in question. A question mark appears in cells that represent one of many possible transitions from the initial state. These probabilities were estimated empirically for each age group, diabetes, and ESRD duration category combination, generating a total of 30 separate transition matrices.[112]

---

[110] In deriving the transition matrices, each follow-up year for each invidual in a cohort was considered a separate observation. For example, patients in the 1995 cohort would generate 5 observations based on their follow-up experience (1995 to 1996, 1996 to 1997, 1997 to 1998, 1998 to 1999, and 1999 to 2000).

[111] Transplants are an exception because it is possible, although rare, for a patient to receive a new transplant within the same year as their previous graft failed.

[112] Three age groups, two diabetes states, and five duration categories were used.

Table 13: The *a priori* Transition Matrix

New State / Non-ESRD	Transplant		Centre Hemodialysis		Self-Hemodialysis		Peritoneal Dialysis		Death
Initial State	n/a	Y1	Y+	Y1	Y+	Y1	Y+	Y1	Y+	n/a
Non-ESRD	?	?	0	?	0	?	0	?	0	?
Transplant (Y1)	?	?	?	?	0	?	0	?	0	?
Transplant (Y+)	?	?	?	?	0	?	0	?	0	?
Centre Hemo. (Y1)	?	?	0	0	?	?	0	?	0	?
Centre Hemo. (Y+)	?	?	0	0	?	?	0	?	0	?
Self-Hemo. (Y1)	?	?	0	?	0	0	?	?	0	?
Self-Hemo. (Y+)	?	?	0	?	0	0	?	?	0	?
Peri. Dial. (Y1)	?	?	0	?	0	?	0	0	?	?
Peri. Dial. (Y+)	?	?	0	?	0	?	0	0	?	?
Death	0	0	0	0	0	0	0	0	0	1

Table 14 (1990 cohort) and Table 15 (1995 cohort) show estimated probabilities for these transitions based on annual state changes throughout a five-year follow-up period for ESRD patients alive in 1990 and 1995 respectively.[113] Patients who were lost to follow-up are not included in this analysis. This effectively assumes that these patients have the same distribution of state transitions as others do.

Differences between these two matrices are consistent with results from the literature that describe improved survival for ESRD patients and related trends over the past decade (CORR/CIHI, 2002; Schaubel, et al., 2002).

[113] For ease of presentation, results for diabetics and non-diabetics in all age groups have been combined. Results are also averaged over all patients, regardless of how long they have had ESRD.

Table 14: Estimated Annual (One-Step) Transition Probabilities based on Five-Year Follow-up ~ 1990 ESRD Cohort, Age/Diabetes/Duration Categories Combined[114]

	Non-ESRD	Transplant		Centre Hemodialysis		Self-Hemodialysis		Peritoneal Dialysis		Death
Initial State	n/a	Y1	Y+	Y1	Y+	Y1	Y+	Y1	Y+	n/a
Transplant (Y1)	0.00	0.00	0.94	0.02	-	0.01	-	0.01	-	0.02
Transplant (Y+)	0.00	0.00	0.94	0.02	-	0.00	-	0.01	-	0.03
Centre Hemo. (Y1)	0.01	0.1	-	-	0.59	0.06	-	0.05	-	0.19
Centre Hemo. (Y+)	0.00	0.06	-	-	0.72	0.02	-	0.01	-	0.19
Self-Hemo. (Y1)	0.00	0.15	-	0.09	-	-	0.69	0.01	-	0.07
Self-Hemo. (Y+)	0.00	0.11	-	0.08	-	-	0.73	0.01	-	0.08
Peri. Dial. (Y1)	0.01	0.1	-	0.09	-	0.01	-	-	0.64	0.15
Peri. Dial. (Y+)	0.00	0.08	-	0.08	-	0.01	-	-	0.62	0.22
Death	-	-	-	-	-	-	-	-	-	1.00

[114] Totals may not add to 1.00 due to rounding error. A dash indicates a transition that has been ruled out *a priori*.

Table 15: Estimated Annual (One-Step) Transition Probabilities based on Five-Year Follow-up ~ 1995 ESRD Cohort, All Age/Diabetes/Duration Categories Combined[114]

New State / Initial State	Non-ESRD	Transplant		Centre Hemodialysis		Self-Hemodialysis		Peritoneal Dialysis		Death
	n/a	Y1	Y+	Y1	Y+	Y1	Y+	Y1	Y+	n/a
Transplant (Y1)	0.00	0.00	0.95	0.02	-	0.01	-	0.00	-	0.02
Transplant (Y+)	0.00	0.00	0.95	0.02	-	0.00	-	0.01	-	0.02
Centre Hemo. (Y1)	0.00	0.07	-	-	0.66	0.07	-	0.03	-	0.16
Centre Hemo. (Y+)	0.00	0.05	-	-	0.74	0.02	-	0.01	-	0.19
Self-Hemo. (Y1)	0.00	0.09	-	0.09	-	-	0.75	0.01	-	0.06
Self-Hemo. (Y+)	0.00	0.11	-	0.06	-	-	0.73	0.01	-	0.09
Peri. Dial. (Y1)	0.00	0.09	-	0.1	-	0.02	-	-	0.65	0.14
Peri. Dial. (Y+)	0.00	0.07	-	0.1	-	0.01	-	-	0.62	0.2
Death	-	-	-	-	-	-	-	-	-	1.00

The Projection Process

The one-step transition matrices reflect the probability of transitioning from one state to another over the course of a year, based on patient characteristics. In order to project results several years into the future, many one-step matrices need to be applied in sequence. Two possible approaches were explored: patient-level simulation and Markov-chain based analysis. Results from both were qualitatively similar.

The patient-level simulation approach applies annual transition probabilities, year by year, to each individual patient in the starting and incident cohorts. That is, a follow-up state for each patient is selected based on the probability distribution associated with their underlying characteristics and initial treatment state, as well as a random number generated by SAS from the uniform distribution. This process is repeated for each year of the projection period to obtain a distribution of possible outcomes at the end of the projection period. Given the relatively large number of ESRD patients and follow-up states, as well

as the length of the projection period and the desire to test the implications of different policy options, however, this procedure was not used extensively. It was undertaken for the baseline case only (projecting 500 iterations of the 1995 cohort forward for five years based on the first five-year follow-up experience for the 1990 cohort).

Instead, the number of ESRD patients in each follow-up state at time y was projected as follows using the properties of Markov chains:

- Estimate one-step transition probability matrices by age group, diabetes status, and ESRD duration category.

- For each year of age,[115] diabetes status, and ESRD duration category combination, estimate $P^{(y)}$.[116] This requires multiplying the relevant one-step transition probability matrices for each year of the projection period to generate multi-step transition matrices. The end result is a set of 1090 matrices (109 age categories x 2 diabetes groups x 5 duration categories) that show the probability of a patient with particular characteristics moving from each possible initial state to each possible follow-up state at time y.[117] Table 16 and Table 17 show sample 15-step transition matrices based on the five-year follow-up experience of the 1990 and 1995 cohorts combined.

- For each patient in the starting cohort, apply the relevant y-step transition matrices to assign a follow-up state at the end of the projection period based on the position in the cumulative distribution function indicated by a random number generated using the SAS UNIFORM function.[118] Repeat this process 1,000 times and aggregate the results to estimate the expected number of patients in each follow-up state at time y.

---

[115] Estimation by year of age, not age group, is required since over a long projection period a significant number of patients move to a new age group. Note that constant probabilities are assumed within each age group.

[116] Consistent with other ESRD research and given the relatively small number of ESRD patients in many age/diabetes/duration categories, the patient groups were not further sub-divided by sex.

[117] 109 years of age were used to be consistent with the most recent life tables prepared by Statistics Canada (Duchesne, et al., 2002).

[118] This simulation approach was used since some age/diabetes/duration groups had very small numbers of patients.

- For each patient incident in each year of the projection period (generated from applying the incidence projection model), apply the relevant transition matrices to assign a follow-up state at the end of the projection period. As for the initial patients, repeat this simulation 1,000 times, aggregate the results, and combine them with those from the previous step.

Table 16: 15 Year Transition Probability Matrix for 45 Year-Old Non-Diabetics who have had ESRD for 5 or More Years[119]

New State / Non-ESRD	Transplant		Centre Hemodialysis		Self-Hemodialysis		Peritoneal Dialysis		Death
Initial State	n/a	Y1	Y+	Y1	Y+	Y1	Y+	Y1	Y+	n/a
Transplant (Y1)	0.00	0.01	0.50	0.01	0.04	0.00	0.01	0.00	0.01	0.41
Transplant (Y+)	0.00	0.01	0.50	0.01	0.04	0.00	0.01	0.00	0.01	0.41
Centre Hemo. (Y1)	0.00	0.01	0.18	0.01	0.05	0.00	0.01	0.00	0.01	0.74
Centre Hemo. (Y+)	0.00	0.01	0.16	0.00	0.05	0.00	0.01	0.00	0.00	0.75
Self-Hemo. (Y1)	0.00	0.01	0.27	0.01	0.05	0.00	0.03	0.00	0.01	0.62
Self-Hemo. (Y+)	0.00	0.01	0.26	0.01	0.05	0.00	0.03	0.00	0.01	0.64
Peri. Dial. (Y1)	0.00	0.00	0.18	0.01	0.04	0.00	0.01	0.00	0.01	0.74
Peri. Dial. (Y+)	0.00	0.00	0.18	0.01	0.04	0.00	0.01	0.00	0.01	0.75
Death	-	-	-	-	-	-	-	-	-	1.00

[119] Non-ESRD not listed as an initial state since this population has ESRD.

Table 17: 15 Year Transition Probability Matrix for 65-Year-Old Non-Diabetics who have had ESRD for 5 or More Years[119]

New State / Non-ESRD		Transplant		Centre Hemodialysis		Self-Hemodialysis		Peritoneal Dialysis		Death
Initial State	n/a	Y1	Y+	Y1	Y+	Y1	Y+	Y1	Y+	n/a
Transplant (Y1)	0.00	0.00	0.30	0.00	0.01	0.00	0.00	0.00	0.00	0.68
Transplant (Y+)	0.00	0.00	0.29	0.00	0.01	0.00	0.00	0.00	0.00	0.69
Centre Hemo. (Y1)	0.00	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.98
Centre Hemo. (Y+)	0.00	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.98
Self-Hemo. (Y1)	0.00	0.00	0.04	0.00	0.01	0.00	0.01	0.00	0.00	0.94
Self-Hemo. (Y+)	0.00	0.00	0.03	0.00	0.01	0.00	0.01	0.00	0.00	0.95
Peri. Dial. (Y1)	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.99
Peri. Dial. (Y+)	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.98
Death	-	-	-	-	-	-	-	-	-	1.00

Validation of Model

Data-splitting was used to assess the performance of the ESRD patient follow-up model empirically. Transition matrices estimated using data from the first five years of follow-up for the 1990 cohort were used to project the follow-up experience of the 1995 cohort in 2000.

Projection results were then compared to the actual distribution of the 1995 cohort among follow-up states in 2000 (see Table 18). The mean projected distribution of follow-up states was significantly different from the actual distribution in 2000 based on a χ^2 test at p=0.05 (Kanji, 1999). As expected, for example, the Markov chain model projected more deaths than actually occurred. This reflects improvements in survival and related trends seen in recent years. It suggests that the net effect of these changes was to reduce the 5-year crude

mortality rate for the 1995 cohort from an expected 43.5% to 37.7%, a non-trivial improvement in survival for persons with ESRD.[120]

Table 18: Projected Follow-up Status of 1995 Cohort Members in 2000 Based on Five-Year Follow-up Transition Probabilities of 1990 Cohort

	Actual[121]	Projected			
		Mean	Median	Range	Std Dev
Deceased	5839	6776	6776	6611-6923	50.3
Centre Hemodialysis	1955	1673	1673	1538-1819	38.0
Self-hemodialysis	587	568	568	495-650	22.1
Peritoneal Dialysis	450	577	577	509-643	22.9
Transplant	6633	5973	5974	5838-6123	45.5
Recovered	20	19	19	7-33	4.1

7.4 Methods ~ Projecting ESRD Incidence

In addition to projecting the follow-up status of patients who currently have ESRD, it is necessary to estimate the number and follow-up status of newly diagnosed patients.

Data Sources

The incidence projections use anonymized patient-level data from CORR for two cohorts of patients: those incident in 1990 and 1995. As above, results are based on data included in the Register as of July 2002. Additional aggregate data on ESRD incidence counts and rates by year and age group between 1981 and 2000 were obtained from CORR publications (CORR/CIHI, 2002). For more information about CORR, see Appendix A.

[120] This calculation excludes a small number of patients who were lost-to-follow-up over the five-year follow-up period.

[121] Excludes a small number of patients lost-to-follow-up since this category was not included in the projections.

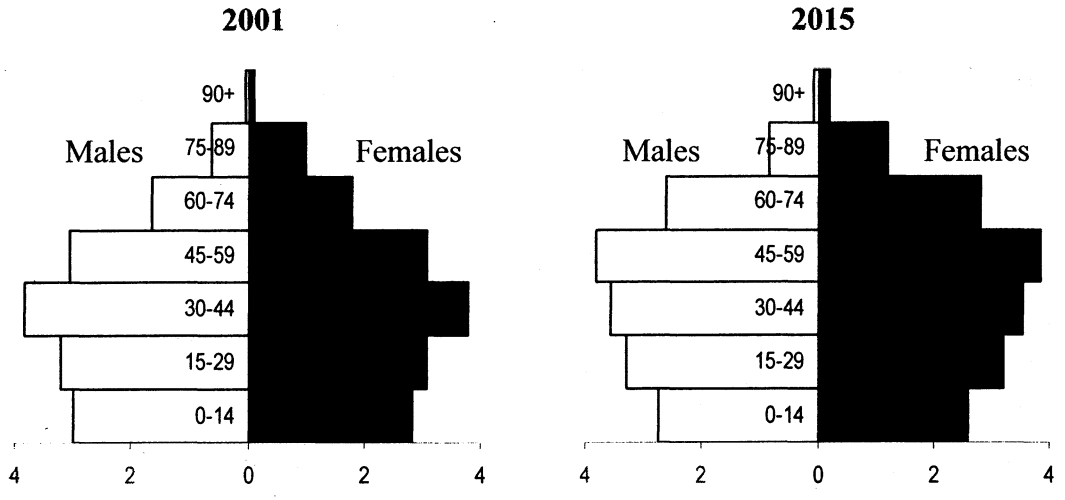
The incidence projections also required data on the size and age distribution of the total Canadian population. For model validation (which required population estimates from 1996 to 2000), population estimates were extracted from Statistics Canada's CANSIM system (Statistics Canada, 2002d).

Population Projections

PMEDS-D (Version 2001.11.29), customized software designed to project the future size and distribution of the Canadian population by age and sex, was used to generate the population projections used to estimate the annual number of new ESRD cases in the future. This software has been described elsewhere (for instance, Denton, et al., 1989).

In this chapter, a standard set of assumptions was used to project the population in five age groups (0-14, 15-44, 45-64, 65-74, and 75 and over) by year to 2015 (see Figure 23). Specifically, it was assumed that most parameters – including fertility rates, immigration and emigration levels, and their age/sex distribution – would remain relatively unchanged from recent values throughout the projection period. A continued decline in mortality rates was also incorporated. The associated assumptions would generate an increase in life expectancy at birth for men from 76.3 years in 2001 to 78.2 years in 2015. For females, life expectancy would rise from 81.7 years to 82.7 years over the same period.

Figure 23: Distribution of the Population by Age Group and Sex in 2001 and 2015



Projection Methods

Two different approaches to projecting ESRD incidence were explored. The first used only information on historical trends in the number of incident cases. Specifically, stepwise autoregression with a quadratic time trend model was used to project the annual number of new ESRD cases. This maximum likelihood approach uses the Yule-Walker method (SAS Institute, 1999; Brockwell and Davis, 2002). In doing so, it "combines a time-trend regression with an autoregressive model for departures from trend" (Duchesne, et al., 2002). Specifically, the procedure first fits a time trend. The residuals are modeled using many autoregressive lags, parameters that are then dropped in sequence until all those remaining are significant.[122] This method produces forecasts where more recent observations receive more weight than earlier ones.

[122] Note: this is a different procedure from stepwise regression, which uses a stepwise approach to the selection of independent variables.

Schaubel and colleagues (1998a) have shown that, at least over relatively short projection periods, estimates based solely on historical trends in the number of cases of ESRD can work well. To evaluate the particular model described here, incidence data from 1981 to 1995 were used to project the number of new cases from 1996 to 2000. For each year, the actual number of cases observed was within the projected 95% confidence interval (see Figure 24).[123]

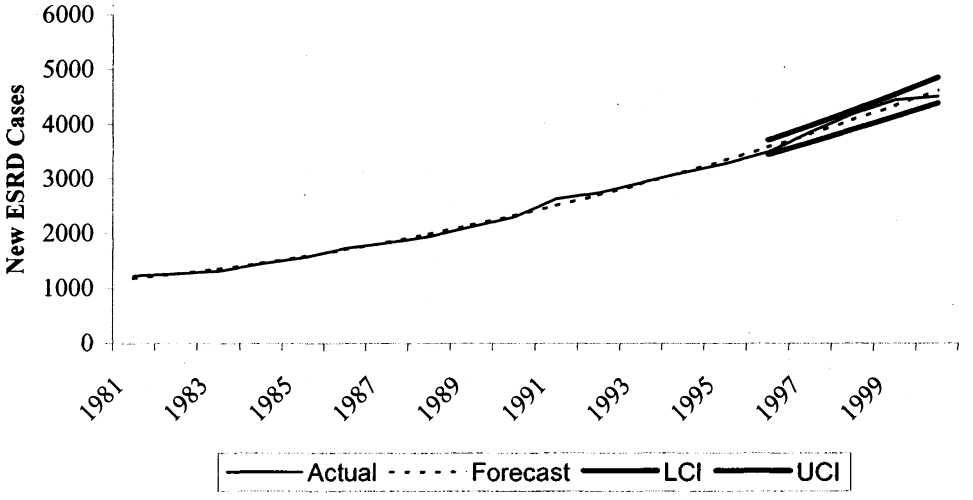
The second set of incidence projections used the same technique but modeled incidence rates per million population by age group (0-14, 15-44, 45-64, 65-75, and 75 and over), rather than the number of cases.[124] As before, stepwise autoregression with a quadratic time trend model was used. Estimated incidence rates were then applied to the standard population projections to generate an expected number of new ESRD cases by age group.

When data from 1981 to 1995 were used to project incidence between 1996 and 2000, there was a very high correlation between the actual and projected total number of incident cases (see Figure 25). As before, all actual values fell within the 95% confidence limits around the projected values.

[123] Projections for incidence in 2000 were compared to the number of observed cases reported in CORR's preliminary report (CORR/CIHI, 2002), plus the Register's estimate of the number of cases not yet reported at the time that these data were released.

[124] Ideally, diabetes and age-group specific incidence rates would have been calculated, but the lack of historical data on diabetes prevalence precluded this possibility.

Figure 24: Actual and Forecast ESRD Incidence to 2000 based on Stepwise Autoregression using Incidence Counts from 1981 to 1995

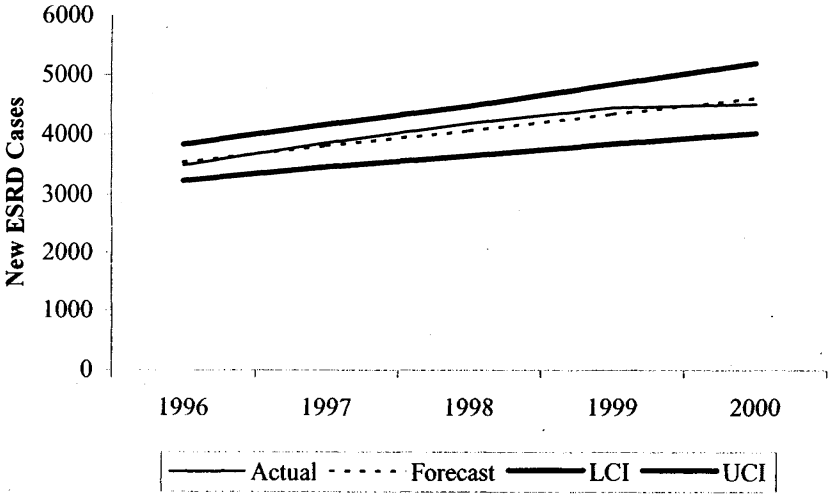


Given that over a longer time horizon, shifts in population demographics may result in significant effects on disease incidence (as was shown in Chapter 3), the second approach was used in all subsequent analyses. It also has the advantage of slightly lower root mean square error than the alternate approach, although the mean absolute percentage error is higher (see Table 19). As the implicit test tends to weight large forecast errors more heavily, it may be a more useful metric for the types of long range forecasts undertaken in this thesis (Kennedy, 1992).

Table 19: Comparison of Characteristics of Two Approaches to Forecasting ESRD Incidence Between 1996 and 2000

Criterion	Forecast based on actual number of cases in previous years	Forecast based on rates of new cases per million population
Actual values within 95% confidence intervals of forecasts	Yes	Yes
Correlation between actual and forecast values	0.970	0.974
Mean absolute percentage error (deviation between actual and forecast values)	-0.3% (range: -2.4% to +2.3%).	–0.6% (range: -3.0% to +2.2%)
Root mean square error	94.3	91.1

Figure 25: Actual and Forecast ESRD Incidence (Number of New ESRD Cases) to 2000 based on Stepwise Autoregression using Incidence Rates by Age Group from 1981 to 1995 and Actual Population Data for 1996 to 2000



Once the aggregate incident cohorts were established[125], the distribution of ESRD patients by specific year of age within each age group, by diabetes status, and by initial treatment was imputed based on the experience of the 1995 cohort. For each simulated incident patient, follow-up experience was then projected as described in section 5.3. This generates an expected number of new ESRD patients and their distribution across follow-up states at the end of the projection period based on 1,000 iterations of the simulation model.

7.5 Results

The number of patients with ESRD has risen rapidly for several decades. The baseline projections described in sections 7.3 and 7.4 suggest that this growth will continue, even accelerate, at least until 2015.[126]

By the end of this period, the projected number of patients newly diagnosed with ESRD is more than double levels in 2000 (see Table 20). Their diagnoses are projected to swell the total number of Canadians with ESRD to more than 102,700 in 2015.

Table 20: Patients with ESRD in 1985, 2000, and 2015 (Projected)

Year	# New Patients	# Patients Alive with ESRD
1985	1,563	7,749
2000	4,386	24,921
2015 (Baseline Projection)	11,157	102,735

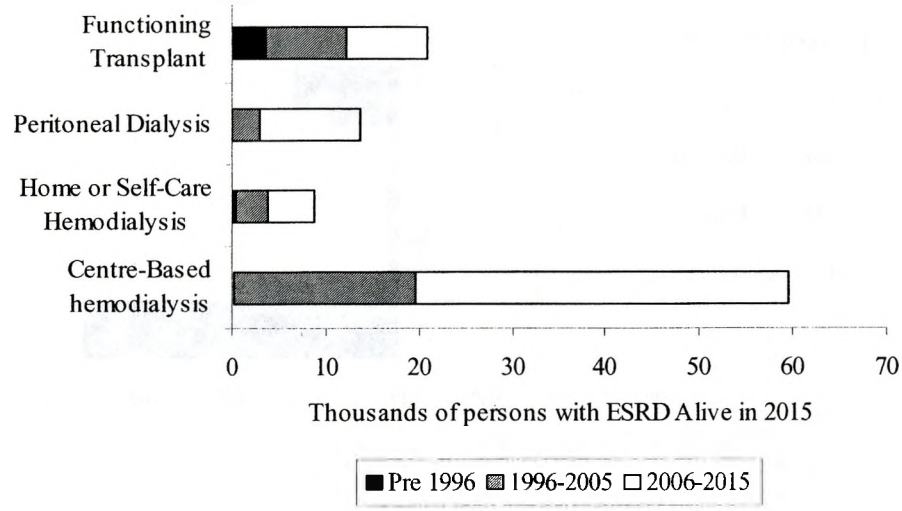
Time of Diagnosis

Under the baseline assumptions, more than a third of ESRD patients alive in 2015 (38%) would have developed the disease within the previous five years (see Figure 26). The proportion is higher for patients on dialysis but lower for those with transplants. This reflects the fact that patients with kidney failure who receive transplants tend to have high survival rates (Schaubel, et al., 1995).

[125] For incidence projections to 2015, all available data (1981-2000) were used in the model, not just those from 1981-1995.

[126] These projections are based on state transition matrices derived from the combined first five-year follow-up experience of the 1990 and 1995 ESRD cohorts.

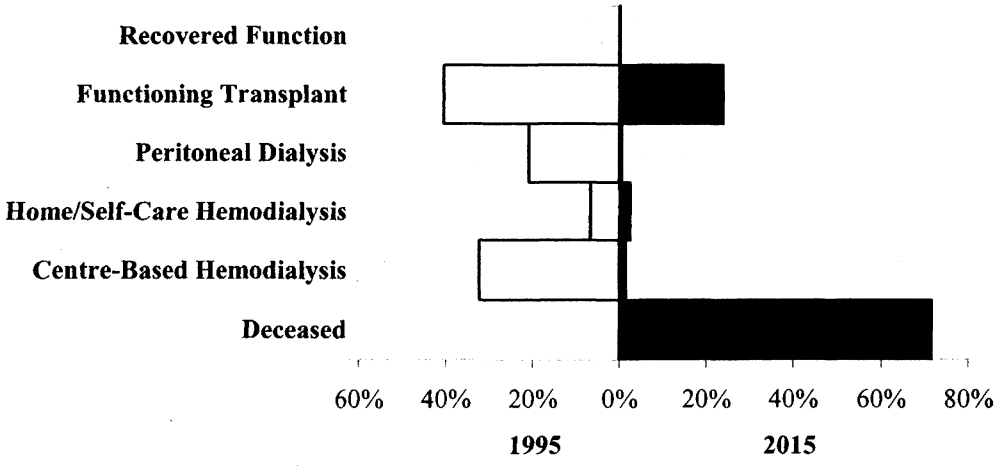
Figure 26: Projected Persons with ESRD in 2015 by Treatment Type and Cohort of Diagnosis



In contrast, 71% of those alive with ESRD in 1995 would have died by the end of the projection period. This reflects the relatively high average ages and mortality rates of ESRD patients. As Figure 27 shows, survival chances are much better for patients who have received transplants than for those on any type of dialysis.[127]

[127] This reflects research from around the world that has found better survival (as well as quality of life) for transplant patients, even after adjusting for differences in health status (Ojo, et al., 1994; Schaubel, et al., 1995, Laupacis, et al., 1996).

Figure 27: Treatment Status in 1995 and 2015 (Projected) for Patients with ESRD Before 1996



Types of Treatment

If current treatment patterns were to continue, dialysis would remain the predominant treatment for ESRD in 2015, with centre-based hemodialysis still the most frequently prescribed type of dialysis (see Table 21). Patients alive with functioning transplants would continue to account for a significant, but declining, share (20%) of the ESRD population. Even this level relies on more than doubling the current number of transplants performed (2,662 are projected for 2015 compared to the 1,105 reported in 2000).

This growth significantly exceeds current transplant levels and may not be realistic. An inability to achieve the projected level of surgery would imply more patients on dialysis in 2015, as well as a higher number of deaths over the projection period (given the lower survival rates for patients on dialysis).

Table 21: Projected Follow-Up Status in 2015 of Patients Alive with ESRD in 1995 and Cases Incident Between 1996 and 2015 (Based on 1,000 Iterations of the Projection Model)

	Total	1995 Cohort		Patients Incident 1996-2015	
		Mean	Std Dev	Mean	Std Dev
Deceased	46,576	11,035	42.8	35,541	124.6
Centre Hemodialysis	59,470	228	10.6	59,241	117.3
Home or Self-Care Hemodialysis	8,733	383	18.8	8,350	80.0
Peritoneal Dialysis	13,621	89	9.4	13,532	83.0
New Transplant	2,662	56	7.6	2,606	46.6
Functioning Transplant	18,249	3,625	43.4	14,624	94.7
Recovered	1,473	28	5.2	1,445	38.0

7.6 The Future Economic Burden of ESRD

As the number of new and continuing cases of ESRD grows, so too does the economic burden of the disease. Using the methods described in Chapter 5 and the baseline projections from this chapter, the total direct and indirect economic burden of ESRD in 2015 is estimated to be $7.9 billion, about four times more than the estimate for 2000.[128,129] This includes $5.8 billion in direct health care

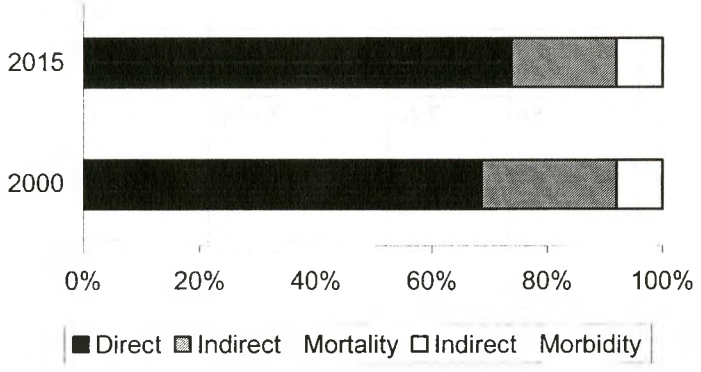
[128] All amounts are expressed in year 2000 Canadian dollars using the appropriate deflators for direct and indirect costs as described in Chapter 5. These calculations assume that the proportion of living and cadaveric organ donors for transplantation is the same as in 2000. Varying this assumption has relatively little impact on the overall economic burden of the disease.

[129] As described earlier in this chapter, Markov transition probabilities used for projections of future treatment status and survival were calculated separately for age/diabetes/duration of treatment groups. They were not further stratified by sex due to sample size considerations. Age and sex-specific profiles of earnings, unpaid work, labour force participation, and other factors were, however, used in the economic burden of illness calculations. For patients forecast to be diagnosed

costs, as well as $1.4 and $0.6 billion related to mortality and morbidity respectively [130]

The larger number of individuals with the disease, particularly the increased numbers on dialysis, explains most of this increase. The distribution among direct and indirect costs, however, is relatively consistent throughout the projection period (see Figure 28). Direct costs account for a somewhat larger percentage of the total in 2015 (74% compared to 69%), and mortality-related costs for a smaller share, reflecting the relatively large increase in new cases of the disease in later years of the projection period.

Figure 28: Components of the Economic Burden of ESRD in 2000 and 2015 (Baseline Projections)



7.7 Discussion ~ ESRD Projections

Since the mid-1980s, the findings of studies projecting future numbers of ESRD patients in Canada and around the world have been remarkably consistent. Under a range of assumptions and using a wide variety of methodologies, all have projected a significant increase in the prevalence of the disease over time.

Most of these studies based their models on data from the early to mid-1990s or before. The projections described in this chapter incorporate actual experience through 2000. Nevertheless, if recent trends continue, significant

---

with ESRD during the projection period, sex was randomly assigned based on the current proportion of males and females in the relevant population group (using a random draw from a uniform distribution).

[130] As in Chapter 5, mortality costs were also estimated using the value of paid labour only (removing transfer payments, such as pensions and employment insurance, and the value of unpaid labour). Under this scenario, the economic burden associated with ESRD mortality fell to $351 million.

increases in both the incidence and prevalence of ESRD through at least 2015 are expected. This represents a large and growing public health and economic burden. It also has important implications for health care managers, planners, and policy-makers, particularly given that ESRD-related direct health care costs are projected to be 4.6 times higher in 2015 than in 2000 under standard assumptions regarding population growth.

Unlike previous studies, this chapter compares projections of the volume of transplants (i.e. the number that is likely to occur if current organ donation patterns continue) to projections of the number of transplants required to maintain today's practice patterns (i.e. the likelihood that a patient on dialysis will receive a transplant). This analysis suggests that the problem is likely to worsen in the coming years as the gap grows between the projected number of available transplants and the projected number of patients who, given current practice patterns, would have received the surgery (see Chapter 9 for further discussion). As a result, waiting lists are likely to continue to rise unless there are significant changes to the underlying burden of ESRD, practice patterns, technology, and/or health policy.[131] Given that transplants offer, on average, lower long-term health care costs, improved quality of life, and better survival chances, the burden of kidney failure can be expected to grow in parallel with waiting lists.

[131] Significant changes in policies and other factors would be required to bring this about (see section 8.6).

Chapter 8: Sensitivity Analysis

8.1 Introduction

Projecting the future level or economic burden of a disease is complex because of the number of possible interrelated factors that may influence trends. A change in a single variable can have far-reaching effects over time. As a result, long-range projections rarely match exactly with what actually eventuates, often because the assumptions on which they are based shift over time. What is important, therefore, is to understand what types of factors may influence the many potential "futures" and the extent to which shifts in these underlying factors would affect projections. That is, how sensitive are the results obtained to different plausible assumptions or policy scenarios?

In the case of end-stage renal disease (ESRD), many factors may affect the future economic burden of the illness. Most projections in the literature incorporate limited or no sensitivity analysis (see Table 22). In contrast, projections presented here evaluate the impact of a broad range of changes in the model's assumptions on the number of patients alive with ESRD to 2015, their distribution across possible follow-up states, and the associated direct and indirect economic burden of illness.

Table 22: Types of Sensitivity Analysis Included in Studies Projecting ESRD Incidence and Prevalence Described in Table 11 and in This Thesis

Study	Trans-plant # or rates	Other practice patterns survival	Incidence # or rates	Other
(Minister's Task Force on Kidney Donation, 1985)	✓	×	×	×
(Motohashi and Nishi, 1991)	✓	×	×	×
(Desmeules, et al., 1995)	×	×	✓	×
(Port, 1995)	×	×	✓	×
(Mallick, 1997)	×	~[132]	×	×
(de Wit, et al., 1998)	✓	✓[133]	×	Various methods for valuation of quality of life
(Schaubel, et al., 1998a)	×	×	×	×
(Blanchard, et al., 1999)	×	×	✓	×
(Schaubel, et al., 1999)	×	×	×	×
(US Renal Data System, 2000)	×	×	×	×
(Xue, et al., 2001)	×	×	×	Linear versus quadratic forecast models
(Lysaght, 2002)	×	×	×	×
(You, et al., 2002)	×	×	×	×
This Thesis	✓	✓[134]	✓	**Various assumptions about:** **- Demographics (fertility, immigration, emigration, & mortality)** **- Disability weights** **- Recovery time for donors & recipients of transplants** **- Inclusion of non-market earnings** **- Discount rates** **- Labour productivity**

[132] This paper describes an analysis comparing steady state survival and an improvement in survival rates but results are not shown in the article.
[133] The analysis explored the effect of substitution among dialysis modalities.

Specifically, the sensitivity analysis described in this chapter concentrates on three factors that might influence the economic burden of ESRD: population demographics, the rate at which new cases of ESRD are diagnosed, and changes in treatment and survival patterns.[135] To better understand the potential impact of each factor, its effects are isolated in a separate scenario.

For each scenario[136], the mechanism by which a change in the given factor influences ESRD projections is described by outlining the first three stages of impact on the systems model of ESRD and its care presented in Chapter 6. Subsequently, these effects would continue to ripple through the entire structure of the model. The results of this process are highlighted by comparing projections based on altering the particular assumptions relevant to each scenario with the baseline projections of the number of patients with ESRD, their distribution across follow-up states, and the economic burden of the disease.

8.2 Scenario 1 ~ Effect of Demographic Shifts

Changes in the demographic structure of the population (or the overall size of the population) can have an effect on long-term projections of the future economic burden of ESRD. This can occur, for instance, through changes in fertility, mortality, or migration patterns since the probability of developing end stage renal disease increases with age. Other factors, including survival rates and the selection of dialysis modalities, are often also related to demographics.[137]

---

[134] The effect of changes in the probability of switching treatments (including to/from both dialysis and transplants), of recovery, and of dying were evaluated.

[135] The effect of changes in cost-related factors, such as the discount rate used and the inclusion/exclusion of non-wage earnings in lost productivity calculations, were explored in Chapter 5.

[136] The exception is the scenario on the effect of shifts in direct and indirect costs since this scenario relies on the base case projections of the future ESRD population and treatment patterns.

[137] The likelihood of becoming a cadaveric organ donor may also differ by age and sex. The nature of this relationship, however, continues to change. For example, the introduction of road safety measures, such as helmet and seatbelt legislation, has reduced the number of potential donors. On the other hand, expansions in criteria for organ donation (e.g. to accept older donors and non-heart-beating donors) have expanded or may expand the potential donor pool (Kievit, et al., 1997; Campbell and Sutherland, 1999; Whiting, et al., 2000). Likewise, there have been actual or potential changes in criteria and policies related to living organ donation (e.g. regarding the acceptability of organs from non-related, child, and older donors). As a result, the relationship between

The Baseline ESRD Projection described in Chapter 7 is based on an intermediate projection of population growth and change that assumes a continuation of recent trends. This section considers the effect of varying assumptions about fertility rates, mortality rates, and levels of immigration on the annual number of new cases of ESRD and resulting effects on patient numbers, follow-up status, and the economic burden of the disease.

Additional subtle effects from changes in the composition of the population may also occur. For example, changes in the age distribution of migrants, their numbers, or other patterns of migration may lead to shifts in patient and family preferences, personal behaviours, or similar factors that in turn affect the risk of developing ESRD, treatment and survival chances, and organ donation and transplant patterns. For a variety of reasons, including the limited data on possible effects and the likelihood that a one-time or short-term shock would have little long-term impact, these factors are not considered here.

Impact of Demographic Changes on Systems Model of ESRD

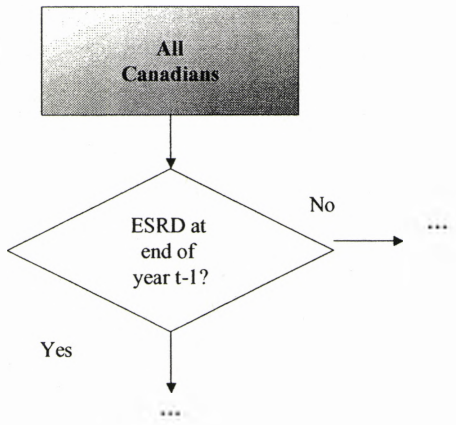
Stage 1

Changes in immigration patterns, mortality rates, or other demographic factors might systematically affect the current and future size and age/sex structure of the population. In the model, this is mathematically expressed through population (Pop) variable and graphically through changes to the "All Canadians" population at the top of the "Entry Path" (see Figure 29).

---

population demographics and organ donation has not been stable over time. Changes in organ supply are therefore considered in detail in Chapter 9 and the potential (relatively minor) effects of shifts in population demographics on organ supply over the next fifteen years are not considered in this scenario.

Figure 29: Initial Impact of Demographic Change (Where Shaded)



Stage 2

ESRD Incidence Impact: The number of new ESRD cases is a function of the population size/structure (from stage 1) and the probability of ESRD incidence. This is expressed through the equation below.

$$ES\_NEW_{t,t+1} = PR\_ES\_NEW * POP\_TOT_t$$

Eq. 28

Organ Donor Impact: All else being equal, changes in the size and composition of the general population also affect the potential pool of live and cadaveric organ donors, as the equations below show.

$$DONOR\_CAN_{t,t+1} = PR\_EL\_DEATH * POP\_TOT_t \qquad \textbf{Eq. 29}$$

$$KDNY\_LVG_{t,t+1} = f(POLICIES_t, PERS\_PREF_t, WAIT\_LIST_t, CLINICAL\_P_t, ES\_TOT_t, POP\_TOT_t) \qquad \textbf{Eq. 30}$$

Stage 3

Stage 2 effects then spread through the model in many ways, including affecting the distribution of ESRD patients by treatment status, as shown below.

Impact on On-Going Size of ESRD Population: The size of the ESRD population at time t+1 is a function of its size at time t, as well as the number of incident cases (from stage 2), deaths, and recoveries of function between time t and time t+1.

$$ES\_TOT_{t+1} = ES\_TOT_t + ES\_NEW_{t,t+1} - ES\_DEATHS_{t,t+1} - ES\_REC_{t,t+1} \quad \textbf{Eq. 31}$$

Impact on Hemodialysis Use: The number of patients on hemodialysis is a function, among other things, of the number of new ESRD cases (from stage 2) and the probability that a patient will be assigned to hemodialysis.

$$\begin{aligned} ES\_HEMO_{t+1} = \; & ES\_HEMO_t \\ & + \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHNG_{d2,d1} \end{pmatrix} \\ & + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d1}) \\ & + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d1} \end{pmatrix} \\ & - (ES\_HEMO_t * PR\_ES\_REC) \\ & - (ES\_HEMO_t * PR\_TRAN\_CHG_{r1,r2}) \\ & - \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHG_{d1,d2} \end{pmatrix} \\ & - (ES\_HEMO_t * PR\_ES\_DEATH_{d1}) \end{aligned} \quad \textbf{Eq. 32}^{138}$$

Impact on Peritoneal Dialysis: The number of patients on peritoneal dialysis is a function, among other things, of the number of new ESRD cases (from stage 2) and the probability that a patient will be assigned to peritoneal dialysis.

[138] Consistent with the notation in Chapter 4, the following codes are used in equations in this chapter: d1=hemodialysis, d2=peritoneal dialysis, d3=no dialysis, r1=waiting for transplant, r2=functioning transplant, r3=other (e.g. not a candidate for transplant).

$$
\begin{aligned}
ES\_PERI_{t+1} = \quad & ES\_PERI_t \\
& + \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHNG_{d1,d2} \end{pmatrix} \\
& + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d2}) \\
& + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d2} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_REC) \\
& - (ES\_PERI_t * PR\_TRAN\_CHG_{r1,r2}) \\
& - \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHG_{d2,d1} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_DEATH_{d2})
\end{aligned}
\qquad \textbf{Eq. 33}
$$

Methods

This chapter considers the effect of two sets of alternate demographic assumptions (see Table 23) on projections of ESRD and its economic burden. As before, population projections based on these assumptions were generated using PMEDS-D (Version 2001.11.29), customized software designed to project the future size and distribution of the Canadian population by age and sex. The resulting population projections were then applied in the same way and to the same estimated age-specific rates of diagnosis of new cases of ESRD as in Chapter 7.

Table 23: Assumptions Underlying Population Projections

Parameter	Low Growth	Baseline	High Growth
Fertility Rate	1999 – 1.52 2015 – 1.40	1999 – 1.52 2015 – 1.52	1999 – 1.52 2015 – 1.75
Immigration Levels	2001 – 252,000 2002 – 225,000 2006 – 175,000 2015 – 175,000	2001 – 252,000 2002 – 225,000 2015 – 225,000	2001 – 252,000 2002 – 225,000 2006 – 275,000 2015 – 275,000
Emigrants (% previous year population)	2002 – 0.2 2015 – 0.2	2002 – 0.2 2015 – 0.2	2002 – 0.2 2015 – 0.2
Male Mortality (ratio to change between 1971 and 1991)[139]	1996 – 0.85 2015 – 0.5	1996 – 0.85 2015 – 0.736	1996 – 0.85 2015 – 1.0
Female Mortality (ratio to change between 1971 and 1991)	1996 – 0.4 2015 – 0.2	1996 – 0.4 2015 – 0.4	1996 – 0.4 2015 – 0.6
Resulting Projected Life Expectancy in 2015	77.8 – male 82.4 – female	78.2 – male 82.7 – female	78.6 – male 83.1 – female

Results

While demographic factors can have profound effects over several decades, their effects over the relatively short projection period considered here (15 years) were modest. The projected size of the Canadian population in 2015 was 33.5, 34.4, and 35.4 million under the low growth, baseline, and high growth demographic assumptions respectively. This translated into 134,717-135,958 patients newly diagnosed with ESRD between 1996 and 2015.[140]

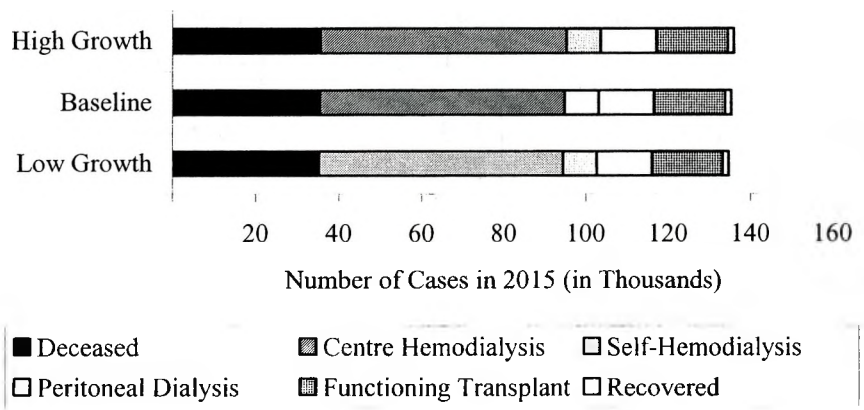
Gaps in numbers of deaths, recoveries, and in the distribution by treatment modality in 2015 were equally modest under the three sets of assumptions, as

[139] The improvement in mortality rates between 1971 and 1991 was converted to an annualized rate of change. A value of 1.0 implies that this rate of change continues to occur. A value of 0.5 assumes that mortality rates improve only half as quickly as in the 1970s and 1980s.

[140] This analysis evaluates the effects of changes in demographic assumptions on ESRD incidence only. Accordingly, patients diagnosed with ESRD before the projection period are not included in these figures as their follow-up results do not vary across the three sets of demographic assumptions.

shown in Figure 30.[141] In large part, this reflects the fact that kidney failure is typically progressive. ESRD is usually a disease of middle to late adulthood, although precursor conditions may begin at much younger ages. Accordingly, even significant changes in fertility rates, which would increase the number of children, would have little effect on the ESRD caseload by 2015. Similarly, changes in mortality rates and other assumptions have a relatively modest impact on the number of new ESRD cases over a 15-year time horizon.

Figure 30: Projected Follow-Up States in 2015 of ESRD Cases Incident After 1995 Under Three Population Projections[142]



Just as the demographic shifts have only modest effects on projections of the 2015 ESRD population and distribution by treatment pattern, they have relatively little impact on the projected future economic burden of the disease. Direct costs in 2015 for persons diagnosed with ESRD after 1995 ranged between $5.66 billion (low growth) and $5 71 million (high growth); indirect costs were $2.01-$2.02 billion.[143]

[141] For comparability, these estimates are based on the same assumptions, calculation methods, and parameters as were used for the base case calculation in Chapter 5 Unless otherwise specified, this is true for all economic burden of illness projections described in this chapter

[142] The "self-hemodialysis" category in this figure and in others in this chapter refers to home and self-care hemodialysis.

[143] Calculated using the base case assumptions. All figures are in year 2000 dollars.

8.3 Scenario 2 ~ Effect of Change in Incidence of Diagnosed ESRD

A number of factors influence the rate at which people are diagnosed with ESRD (the "incidence rate"). These include variations in underlying risk factors, such as the prevalence of diabetes, hypertension, or substance abuse; secondary prevention programs affecting whether or not a person with risk factors develops ESRD, such as those designed to prevent kidney disease as a complication of diabetes; and clinical diagnosis thresholds and practices. Changes in any of these factors can affect the future economic burden of illness related to ESRD.

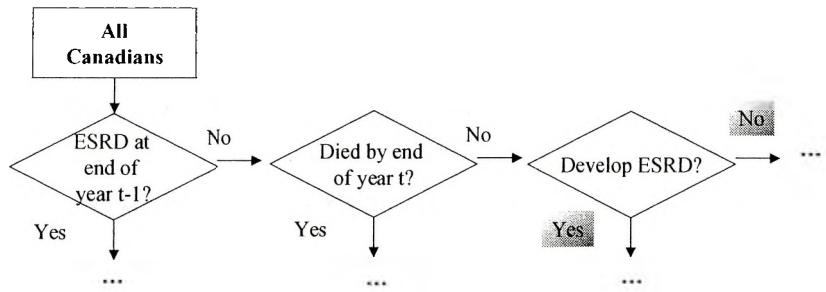
The Baseline Projection described in Chapter 7 is based on an intermediate projection of age-specific incidence rates that assumes a continuation of recent trends. Since age-specific incidence patterns have changed over time, it is appropriate to assess the sensitivity of the results to the assumptions that underlie this portion of the model.

Impact of Changes in the Incidence Rate on Systems Model of ESRD

Stage 1

Change in Incidence Rates: Changes in underlying risk factors, diagnostic thresholds and practice patterns, or other factors may alter age-specific incidence rates. In the systems model of ESRD and its care, this is expressed through the probability of ESRD incidence variable (PR_ES_NEW). Graphically, this is equivalent to a change in the proportion of people alive without ESRD at time t who follow the "yes" and "no" paths shaded in Figure 31

Figure 31: Initial Impact of Changes in the Incidence Rate



Stage 2

Change in Number of New Cases: The number of new ESRD cases is a function of the population size/structure and the age-specific probability of ESRD incidence (from stage 1). This is expressed through the equation below.

$$ES\_NEW_{t,t+1} = PR\_ES\_NEW * POP\_TOT_t \qquad \textbf{Eq. 34}$$

Stage 3

Change in the On-Going Size of ESRD Population: As in the previous scenario, the size of the ESRD population at time t+1 is a function of its size at time t, as well as the number of incident cases (from stage 2), deaths, and recoveries of function between time t and time t+1.

$$\begin{aligned} ES\_TOT_{t+1} = {} & ES\_TOT_t + ES\_NEW_{t,t+1} \\ & -ES\_DEATHS_{t,t+1} - ES\_REC_{t,t+1} \end{aligned} \qquad \textbf{Eq. 35}$$

Change in Hemodialysis Use: The number of patients on hemodialysis is a function, among other things, of the number of new ESRD cases (from stage 2) and the probability that a patient will be assigned to hemodialysis.

$$\begin{aligned} ES\_HEMO_{t+1} = {} & ES\_HEMO_t \\ & + \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHNG_{d2,d1} \end{pmatrix} \\ & + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d1}) \\ & + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d1} \end{pmatrix} \\ & - (ES\_HEMO_t * PR\_ES\_REC) \\ & - (ES\_HEMO_t * PR\_TRAN\_CHG_{r1,r2}) \\ & - \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHG_{d1,d2} \end{pmatrix} \\ & - (ES\_HEMO_t * PR\_ES\_DEATH_{d1}) \end{aligned} \qquad \textbf{Eq. 36}$$

Change in Peritoneal Dialysis Use: Likewise, the number of patients on peritoneal dialysis is a function, among other things, of the number of new ESRD cases (from stage 2) and the probability that a patient will be assigned to peritoneal dialysis.

$$
\begin{aligned}
ES\_PERI_{t+1} = \quad & ES\_PERI_t \\
& + \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHNG_{d1,d2} \end{pmatrix} \\
& + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d2}) \\
& + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d2} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_REC) \\
& - (ES\_PERI_t * PR\_TRAN\_CHG_{r1,r2}) \\
& - \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHG_{d2,d1} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_DEATH_{d2})
\end{aligned}
\qquad \textbf{Eq. 37}
$$

Methods

The baseline results in Chapter 7 used point estimates of age-specific incidence rates now and in the future to project future ESRD numbers, distribution across follow-up states, and economic burden of illness. This scenario considers the effect on ESRD and its economic burden of using the lower and upper 95% confidence intervals around the baseline age-specific rate projections.[144] As before, a quadratic time trend model was used to project incidence rates per million population by age group (0-14, 15-44, 45-64, 65-74, and 75 and over). The upper and lower confidence interval rates were then applied to the baseline population projections to generate an expected number of new ESRD cases by age group for each year between 1996 and 2015. The distribution of these cases across follow-up states in 2015 (recovery, death, centre hemodialysis, self-hemodialysis, peritoneal dialysis, or functioning transplant) was then projected as in Chapter 7.

In addition, a separate set of projections was conducted by applying age-specific incidence rates for the year 2000 to the baseline population projections. This approach addresses the question 'what if current rates of diagnosis of ESRD continue but the population grows and ages?'.

[144] For more information about the fit characteristics of these models, please see Chapter 7.

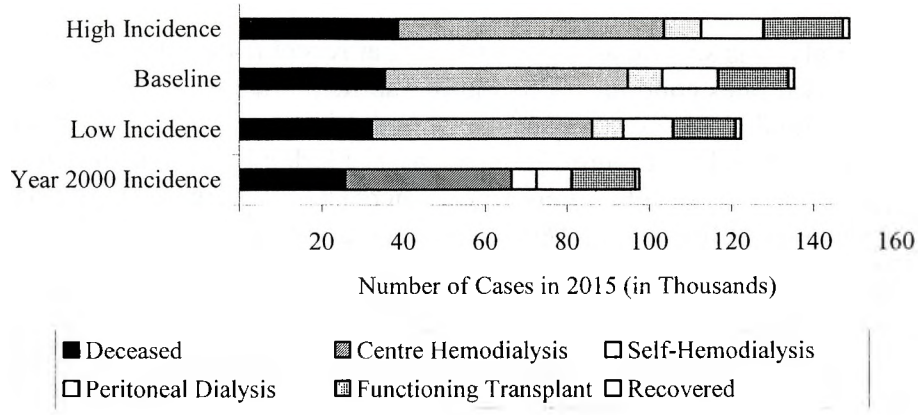
Results

Chapter 3 showed that the rise in diabetes and changes in age-specific incidence rates brought about by other causes explain a large proportion of the increase in the number of ESRD cases in recent years. Similarly, varying the assumptions regarding age-specific incidence rates has a substantial effect on the projected number of cases of ESRD and its economic burden in 2015.[145] For example, the model predicts that over 26,000 more patients would be diagnosed with ESRD by the end of the projection period when the upper bound forecast of incident rates is used instead of the lower bound forecast (see Figure 32). This translates into almost 4,000 "additional" patients with functioning transplants and more than 15,000 "extra" patients on dialysis in 2015. On the other hand, if current age-specific incidence rates were to continue (rather than recent *trends* in rates), there would be only a modest increase in the number of cases of ESRD compared to today (see Figure 32).

These findings also suggest that, given recent increases in the rate at which Canadians are being diagnosed with ESRD, the numbers of transplants in Canada in 2015 would need to be more than double today's level if current practice patterns are to continue, even under the low incidence rate projection. Given that current levels of transplantation are insufficient to meet demands, unless the supply of transplants or alternatives to transplantation improve dramatically, waiting lists for kidney transplants are likely to grow substantially in the coming years. Since patients with transplants have better survival chances and lower direct and indirect costs, shortages of organs for transplant can also be expected to affect mortality rates and the total economic burden of ESRD.

[145] While the impact is substantial, given that it is based on the lower and upper bounds of the 95% confidence interval around the projection resulting from a continuation of recent trends, the effects measured here can be considered to be based on strong, rather than conservative, assumptions regarding potential changes in incidence rates.

Figure 32: Projected Follow-Up States in 2015 of ESRD Cases Incident After 1995 Under Four Assumptions Regarding Incidence Rates[146]



Different assumptions about ESRD incidence rates also result in significant variations in the projected future economic burden of ESRD. There is a $1 1 billion gap between direct cost projections in 2015 based on the low and high growth trends in incidence assumptions. The gap in indirect costs is smaller ($0.4 billion). Projections using year 2000 incidence rates lead to much smaller estimates of the total economic burden of ESRD· $5.5 billion compared with $6.9-$8.5 billion for the low and high growth trends in incidence projections, respectively

8.4 Scenario 3 ~Effect of Evolution of Treatment Patterns

The direct costs of care, quality of life, and survival rates for ESRD patients depend on the type of treatment that they receive, among other factors. As a result, patient preferences, patient characteristics, clinical practice patterns, the cost and availability of services, the supply of organs for transplantation, and other factors that may influence ESRD treatment modality selection also affect the economic burden of illness. Likewise, both direct and indirect costs depend on how long patients with ESRD survive and their state of health while they are alive. Survival and disability rates vary significantly depending on whether or not the patient has a functioning transplant and/or the type of dialysis s/he receives.

[146] The "high incidence" category refers to the projection based on the upper 95% confidence interval projection of trends in ESRD incidence. The "low incidence" category" is based on the lower 95% confidence interval. The "year 2000 incidence" category is based on the continuation of age-specific incidence rates from the year 2000 for the rest of the projection period.

The baseline ESRD Projection described in Chapter 7 assumes that current practice patterns and survival rates continue. Recent experience, however, suggests that this may be an unrealistic assumption (see Chapter 2).

Accordingly, this section assumes instead that recent *trends* in practice patterns and survival rates continue. This implies shifts in the proportion of the population receiving dialysis versus transplants, in the types of dialysis treatment provided (see recent trends in Figure 2), in recovery of kidney function, and in survival rates. These changes ultimately lead to increases or decreases in the size, treatment, and quality of life of the ESRD population and to the economic burden of illness.

Impact of Changes in Practice Patterns and Survival Rates on Systems Model of ESRD

Stage 1

Changes in practice patterns, such as in the propensity to choose a particular type of dialysis, and in survival rates translate into changes in transition probabilities. In the model, these probabilities are expressed mathematically through the PR_DIAL_CHG, PR_TRAN_CHG, PR_ES_DEATH, and PR_ES_REC variables. In the graphical representation of the model, this is equivalent to changes in the proportion of ESRD patients who travel down the branches of the path that separate those who receive peritoneal dialysis from those on hemodialysis; those who receive a transplant or who experience graft failure from those who do not; those who survive from those who die; and those who recover kidney function from those who do not.

Stage 2

Impact on Hemodialysis Use: The number of patients on hemodialysis is a function, among other things, of the probability that new and on-going patients receive hemodialysis.

$$
\begin{aligned}
ES\_HEMO_{t+1} = \quad & ES\_HEMO_t \\
& + \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHG_{d2,d1} \end{pmatrix} \\
& + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d1}) \\
& + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d1} \end{pmatrix} \\
& - (ES\_HEMO_t * PR\_ES\_REC) \\
& - (ES\_HEMO_t * PR\_TRAN\_CHG_{r1,r2}) \\
& - \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHG_{d1,d2} \end{pmatrix} \\
& - (ES\_HEMO_t * PR\_ES\_DEATH_{d1})
\end{aligned}
\qquad \textbf{Eq. 38}
$$

Impact on Peritoneal Dialysis Use: The same is true for the number of patients on peritoneal dialysis. This is expressed through the equation below.

$$
\begin{aligned}
ES\_PERI_{t+1} = \quad & ES\_PERI_t \\
& + \begin{pmatrix} ES\_HEMO_t * PR\_ES\_SURV_{d1} \\ * PR\_DIAL\_CHNG_{d1,d2} \end{pmatrix} \\
& + (ES\_NEW_{t,t+1} * PR\_NEW\_TX_{d2}) \\
& + \begin{pmatrix} ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ * PR\_DIAL\_CHG_{d3,d2} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_REC) \\
& - (ES\_PERI_t * PR\_TRAN\_CHG_{r1,r2}) \\
& - \begin{pmatrix} ES\_PERI_t * PR\_ES\_SURV_{d2} \\ * PR\_DIAL\_CHG_{d2,d1} \end{pmatrix} \\
& - (ES\_PERI_t * PR\_ES\_DEATH_{d2})
\end{aligned}
\qquad \textbf{Eq. 39}
$$

Impact on Transplant Population: Changes in practice patterns can also affect the probability of getting a transplant and, as a result, the size of the transplant population.

$$\begin{aligned} ES\_TRAN_{t,t+1} = \quad & ES\_TRAN_t \\ & +(WAIT\_LIST_t) * PR\_TRAN\_CHG_{r1,r2} \\ & -ES\_TRAN_t * PR\_ES\_DEATH_{r2} \\ & -ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ & -ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r1} \end{aligned} \qquad \textbf{Eq. 40}$$

Impact on the Total ESRD Population: As recovery and (more significantly) survival rates change, so does the size of the overall ESRD population. Recent improvements in long-term survival rates, for example, mean that more Canadians alive today are living with ESRD. These relationships are expressed through the equations below.

$$ES\_DEATHS_{t,t+1} = \sum_{DTx,TTx} PR\_ES\_DEATH_{DTx,TTx} * ES\_TOT_{t,DTx,TTx} \qquad \textbf{Eq. 41}$$

$$ES\_REC_{t,t+1} = PR\_ES\_REC * ES\_TOT \qquad \textbf{Eq. 42}$$

Stage 3

Changes in the number of people on hemodialysis, on peritoneal dialysis, and with transplants cause ripple effects throughout the model, too numerous to list here in detail. For example, the number of people alive with ESRD, the number of deaths from ESRD, and the size of the transplant waiting list are all affected. These effects carry through many years into the future.

Methods

In order to explore the potential effects of changing practice patterns and survival rates on projections of ESRD patients, their care, and the economic burden of illness, alternate assumptions regarding transition probabilities were used. That is, instead of assuming constant transition probabilities (as in the baseline projection), a constant *rate of change* in probabilities was assumed. This causes a change from the stationary transition matrix used in the baseline case in Chapter 7 to a non-stationary Markov model (also known as a time-dependent model). This approach continues to use information on the probability that an individual in a certain treatment state will stay in that state or move to another

within a given period of time to simulate the distribution of patients by treatment state at a future time, but it allows the one-step transition probabilities to evolve.

Specifically, the number of ESRD patients in each follow-up state in 2015 was projected as follows:

- Estimate one-step (year-to-year) transition probabilities by age group, diabetes status, and ESRD duration category for the 1990 and 1995 cohorts of ESRD patients based on their experiences over a five-year follow-up period.

- Instead of applying the 1995 cohort transition probabilities throughout the projection period (as in the baseline projection), calculate new transition probability matrices for the 2000, 2005, and 2010 cohorts. For example, the probability of changing from a given initial treatment state (e.g. peritoneal dialysis) to a specific new treatment state (e.g. death) for the 2000 cohort was assumed to equal the probability for the 1995 cohort for the same diabetes, age, and ESRD duration group, adjusted by the percentage change in probabilities for that group between the 1990 and 1995 cohorts. The 2005 and 2010 matrices were constructed in a parallel fashion.

- Where there were no individuals in a specific age group, diabetes, treatment, and ESRD duration category in either the 1990 or 1995 cohort, assume that the transition probabilities from the cohort for which data were available apply for both time periods and are constant throughout the projection period. This situation occurred most often for the youngest age group (ages 0-14) where ESRD is relatively rare. Given the small numbers of persons in this group, this assumption has a minor effect on final results. Likewise, where there were no individuals in an age group, diabetes, and ESRD duration category who had had a given treatment for more than one year (e.g. were in their second or subsequent year of peritoneal dialysis), first year transition probabilities were assumed to apply to future years on the same treatment.

- Adjust the sum of probabilities of transitioning to each new treatment state for a given diabetes, age, and ESRD duration group to 1.00 (since each patient must be in one and only one state at a given point of time) where the calculations above were affected by

rounding error (adjustments were conducted so that probabilities remained proportional to the original weights).[147]

- For each year of age, diabetes status, ESRD duration category, and year of diagnosis[148] combination, estimate the probability of transitioning from a given initial treatment state to each treatment state in 2015. This requires multiplying the relevant one-step transition probability matrices for each year of the projection period to generate multi-step transition matrices.[149]

- For each patient in the starting cohort, apply the relevant multi-step transition matrices to assign a follow-up state at the end of the projection period in 2015 based on the position in the cumulative distribution function indicated by a random number generated using the SAS UNIFORM function. Repeat this process 1,000 times and aggregate the results to estimate the expected number of patients in each follow-up state at time y.

- For each patient incident in each year of the projection period (generated from applying the incidence projection model described in Chapter 7),[150] apply the relevant transition matrices to assign a follow-up state at the end of the projection period in 2015. As for the initial patients, repeat this simulation 1,000 times, aggregate the results, and combine them with those from the previous step.

Results

Changes in practice patterns can have significant effects in both the short- and long-term. Given that the probability that a given patient will receive a transplant has been falling as waiting lists have lengthened, results of the

---

[147] This is to ensure that the one-step transition probability matrix P of dimension S complies with the requirement that each element $p_{ij} = \Pr(X_1 = j \mid X_0 = i)$, $p_{ij} \geq 0$ and $\sum_{j \in S} p_{ij} = 1$.

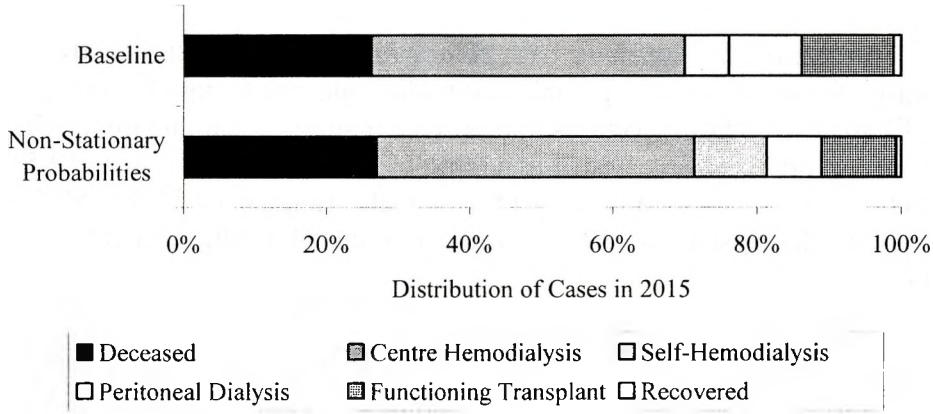
[148] Separate calculations were required for each year of incidence after 2000 since the new patients diagnosed in each year experience different transition probabilities to 2015 than those diagnosed in other years.

[149] In the stationary transition probabilities projections, the one-step transition probability matrices were the same for each year of the projection period. In these projections, different one-step matrices (for the 2000, 2005, or 2010 five-year follow-up periods) were used in the calculations.

[150] To isolate the effects of practice changes, no alterations were made to the baseline demographic and ESRD incidence projections.

sensitivity analysis project about 2,822 more patients receiving dialysis in 2015 than in the baseline case.[151] The distribution of patients by type of dialysis is also different, reflecting the growth in home and self-care hemodialysis and the reduced use of peritoneal dialysis observed between the early and late 1990s (see Figure 33).

Figure 33: Projected Follow-Up States in 2015 of ESRD Cases Incident After 1995 Under Stationary (Baseline) and Non-Stationary Transition Probabilities



Likewise, the number of *new* transplants performed under the non-stationary transition probabilities case in 2015 (1,397) was 54% of the amount projected for the baseline case. Even this level of surgery is higher than the 1,105 new kidney transplants reported in 2000. It is, however, relatively close to the 1,438 surgeries estimated based on projections of recent transplant growth (see Figure 37) and hence may be a more achievable level of surgery based on current organ donation trends.

All else being equal, patients on dialysis have reduced medium to long-term survival chances compared to their counterparts with transplants. Offsetting this effect are recent improvements in survival rates, reflected in a decreasing probability of death over time. The net result is a 3% increase in the number of deaths by 2015 among patients diagnosed with ESRD after 1995 relative to the baseline case. The distribution of these deaths differs, however, with a higher number of deaths occurring earlier in the projection period.

[151] The figures discussed in this section refer to outcomes projected for patients diagnosed with ESRD after 1995.

These trade-offs are also reflected in estimates of the economic burden of illness. While the distribution of persons with ESRD by treatment status differs substantially under the baseline and non-stationary transition probabilities scenarios, estimates of the total economic burden in 2015 are remarkably similar: $7.8 billion and $7.3 billion respectively. The lower amount in the latter case is due primarily to the smaller number of persons with ESRD alive in 2015 than in the baseline case. Other factors, such as the shift in the distribution of patients by type of dialysis, play a less significant role.

8.5 Discussion

The number of Canadians with kidney failure soared in the 1990s, partly because of changes in demographic and underlying risk factors for kidney disease (see Chapter 3). The projections in this chapter suggest that this trend will continue. Under a wide range of assumptions, the economic burden of ESRD is expected to rise dramatically by 2015. Estimates range from $6.9 to $8.5 billion for patients diagnosed after 1995, compared to the $1.9 billion calculated for 2000.

Driving this increase is the expected growth in the number of persons living with ESRD. Under all scenarios, about 100,000 or more Canadians would be living with the disease in 2015 (see Table 24). This number seems very large compared to the approximately 25,000 who had the disease at the end of 2000, but the growth rate is comparable to that experienced in recent years.

The baseline case presented in Chapter 7 used an intermediate projection of population growth and assumed that recent incidence trends, practice patterns, and survival rates would continue. Altering assumptions about population growth had relatively little impact on results in 2015, but changing the assumptions about the rate at which new patients would be diagnosed with ESRD (the incidence rate) led to a larger effect. In both cases, however, the distribution of patients by type of treatment was almost identical. There was slightly more variation in the projected number of new transplants in 2015 (between 2,274 and 2,989), but each of the scenarios forecast much larger numbers of transplants than are currently taking place. This suggests significant increases in waiting times for transplants if current practice patterns and policies continue.

Unlike these scenarios, relaxing the assumption that practice patterns would remain static had a significant effect on the projected number of transplants and the distribution of patients by treatment type in 2015. If recent *trends* in practice patterns and survival rates were to continue, transplantation rates would continue to fall. In 2000, about 4.4% of persons living with ESRD received a kidney

transplant. It would drop to about 1.4% in 2015 under scenario 3. All else being equal, the waiting list for transplants can be expected to increase accordingly.

Table 24: Results of Changing Projection Assumptions on Projected ESRD Numbers and Outcomes by 2015 for Patients Diagnosed after 1995[152]

Scenario	# patients diagnosed by 2015	# deceased by 2015	# new transplants in 2015	ESRD patients alive in 2015, % distribution by treatment status[153]		
				Hemo-dialysis	Peritoneal Dialysis	Functioning Transplant
Baseline	135,341	35,541	2,606	69%	14%	18%
Low Pop. Growth	134,717	35,341	2,584	69%	14%	17%
High Pop. Growth	135,958	35,704	2,625	69%	14%	17%
Lower 95% CI Incidence Rate Trend	122,349	32,327	2,274	69%	13%	17%
Higher 95% CI Incidence Rate Trend	148,632	38,710	2,989	68%	14%	18%
Continuation of Year 2000 Incidence Rates	97,642	25,778	2,276	66%	12%	22%
Changing Transition Probabilities	135,341	36,509	1,397	75%	10%	14%

The sensitivity analysis in this chapter also shows how the economic burden of illness varies under different assumptions (see Figure 34). Once again, altering the assumptions regarding population growth and aging has relatively little impact. The implications of differing incidence rates, however, are more significant. Depending on the assumptions used, the economic burden of illness ranges from $5.5 to $8.5 billion. Somewhat surprisingly, assuming that recent trends in practice patterns and survival rates continue (rather than holding these rates static) makes little difference to the estimated total economic burden of illness. Increases in costs in some areas are offset by decreases in others.

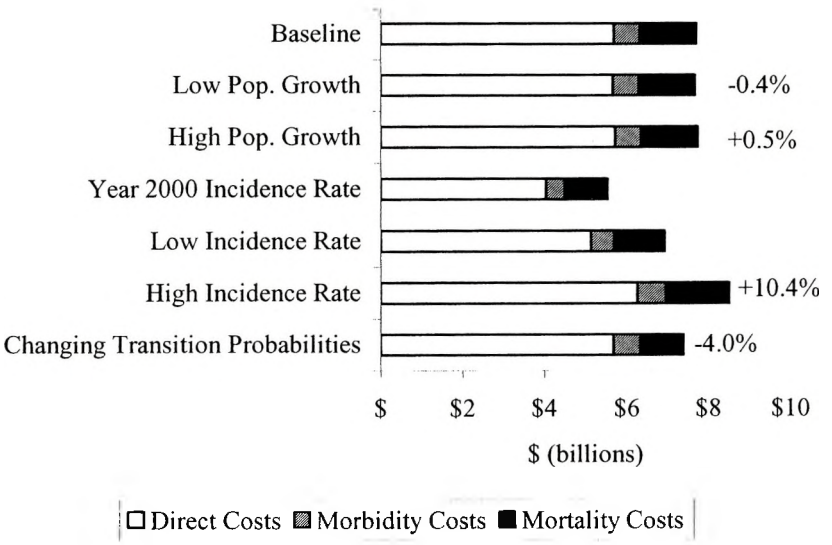
---

[152] This table includes patients diagnosed in 1996 and later to facilitate comparisons among the sets of assumptions. Patients diagnosed prior to this period represent approximately 3.0-4.5% of projected cases in 2015. Their outcomes in 2015 would vary by chance alone (i.e. as a result of a different random distribution of outcomes in the 1,000 iterations of the projection model) under the projections that vary population growth or incidence rates.

[153] This distribution does not include patients who recovered kidney function. Also, totals may not add to 100% due to rounding error.

The results of the sensitivity analysis in this chapter suggest that prevention strategies that affect risk factors for ESRD (e.g. by reducing diabetes rates) or that lessen/delay the onset of ESRD for those with risk factors could be effective in reducing the rate of growth of the numbers of people with disease and of its economic burden. They also highlight the challenge of the widening gap between the availability of organs and the demand for kidney transplants. Chapter 9 explores the impact of potential policy options on transplantation rates in more detail.

Figure 34: Projected Economic Burden of ESRD in 2015 for Patients Diagnosed After 1995 Under Different Assumptions and Percentage Difference from Baseline Projection



Chapter 9: Transplantation and the Future of ESRD

9.1 Introduction

Patients with end-stage renal disease who receive kidney transplants tend to survive longer and typically enjoy a better quality of life than their counterparts on dialysis. Unfortunately, waiting lists for transplant continue to grow. A record 2,760 Canadians were waiting for kidney transplants as of March 31, 2004; an additional 119 were waiting for combined kidney-pancreas transplants (CORR/CIHI, 2004b). At the current rate of transplantation, it would take more than 2.5 years (approximately 33 months) to clear this waiting list alone.

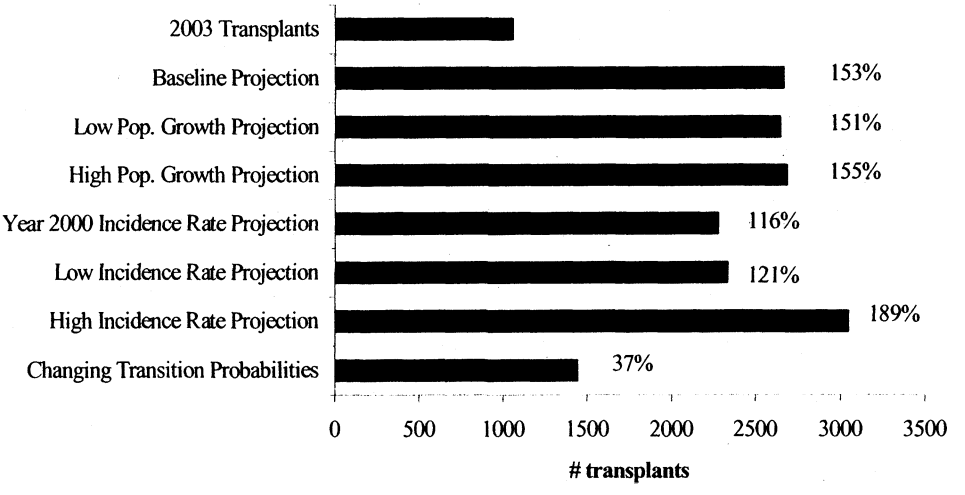
Lengthening waiting lists for transplants in Canada and elsewhere can, in part, be explained by long-standing shortages in the supply of organs available for transplant. Any number of changes in policy, clinical practice, public attitudes, or other factors could cause constraints on the supply of organs available for transplant to tighten or relax. This chapter explores the potential impact of several policy alternatives for increasing organ donations from both cadaveric and living donors.

9.2 The Widening Gap Between the Supply and Demand for Kidney Transplants

Already, there is a substantial gap between the supply of organs and the demand for kidney transplants, a gap that has widened considerably in recent years (CIHI, 2001). The projections in Chapters 7 and 8 suggest that, all else being equal, to maintain even the current probability that a person with ESRD will receive a transplant, the supply of organs will have to expand considerably (see Figure 35). The growth in the gap between the supply and demand for transplants would be somewhat more modest if it proves possible to hold the line on increases in the rate at which new cases of ESRD are diagnosed, but, even then, the projected number of transplants in 2015 still exceeds the volume of surgery undertaken today. In fact, unless the supply of organs for transplant grows, the

drop in the transplant rate[154] would be more rapid than has been seen in recent years. The Changing Transition Probabilities scenario shows that even if recent trends were to continue (including the steady decline in the transplant rate), the number of transplants in 2015 is projected to be 37% higher than the number of surgeries in 2003.

Figure 35: Actual Kidney Transplants in 2003 and Projections for 2015 – Absolute Number of Transplants and the Percentage Increase from 2003 Transplant Levels[155]



To evaluate to what extent this growth can be accommodated if recent transplant experience continues, independent projections of the number of transplants in the future were conducted. For consistency with earlier analyses in Chapter 7 and 8, these projections are based on aggregate data on the total number of transplants from live and cadaveric donors per year between 1981 and 2000, as reported by the Canadian Organ Replacement Register (CORR) (CORR/CIHI, 2002).

[154] Expressed in terms of transplants per person with ESRD.

[155] 2003 Figures are drawn from the cumulative E-Quarterly report for 2003 produced by the Canadian Organ Replacement Register (CORR/CIHI, 2004a). 2015 numbers include projection results for each scenario for patients diagnosed with ESRD after 1995, as well as those who acquired the disease before this date. For this reason, the numbers of transplants shown are close to, but do not match exactly, those reported in Chapter 8 (which included only new patients).

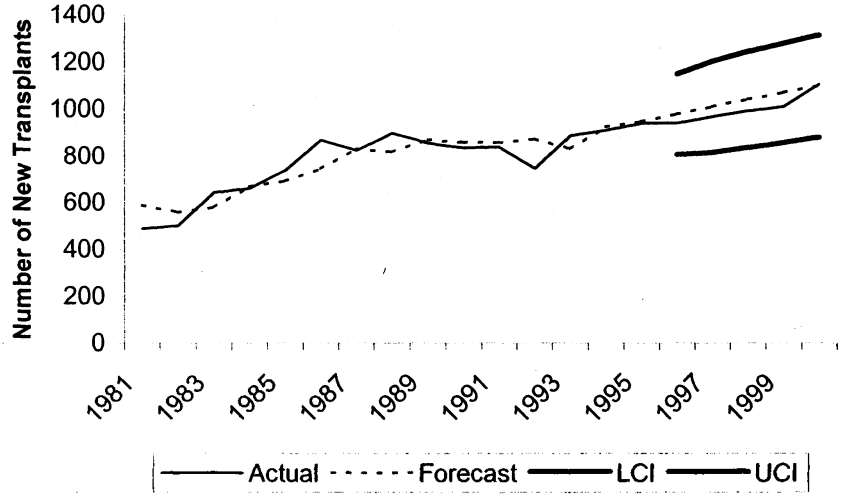
Projection Method

Stepwise autoregression with a linear time trend model was used to project the annual number of new transplants. Separate projections were also performed for organs from both cadaveric and live donors. This approach, rather than projecting rates per million population, was chosen because of the wide range of factors other than population age and size that may impact the number of transplants performed annually. In particular, there are significant constraints on (and potential facilitators of) the supply of organs for transplant that are related to policies, practice patterns, and similar factors.

Model Validation

When data from 1981 to 1995 were used to project transplants between 1996 and 2000, all actual values fell well within the 95% confidence limits around projected numbers (see Figure 36). The mean absolute percentage error of the forecasts compared to actual values between 1996 and 2000 was 3.7%. The root mean square error of the forecasts was 42.

Figure 36: Actual and Forecast Number of New Kidney Transplants to 2000 Using Data on the Number of Transplants Between 1981 and 1995



Results

Using the methods described above, projections of the number of transplants suggest that if recent trends continue, we can expect about 1438±208 transplants in 2015 (see Figure 37). While most transplants would continue to be from

cadaveric donors, the proportion from living donors would rise slightly, reflecting recent trends (see Figure 38).

Figure 37: Actual and Forecast Number of New Kidney Transplants to 2015 Based on Data from 1981 to 2000

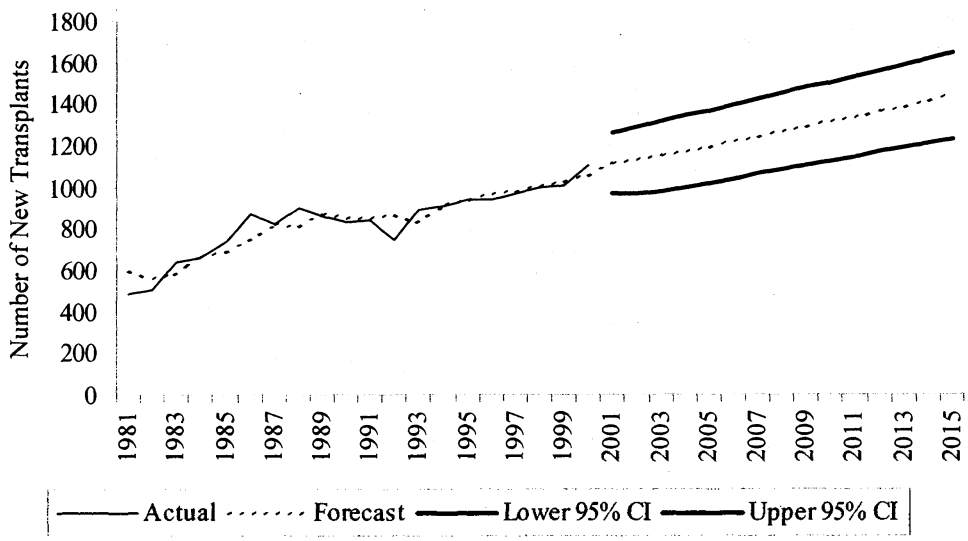
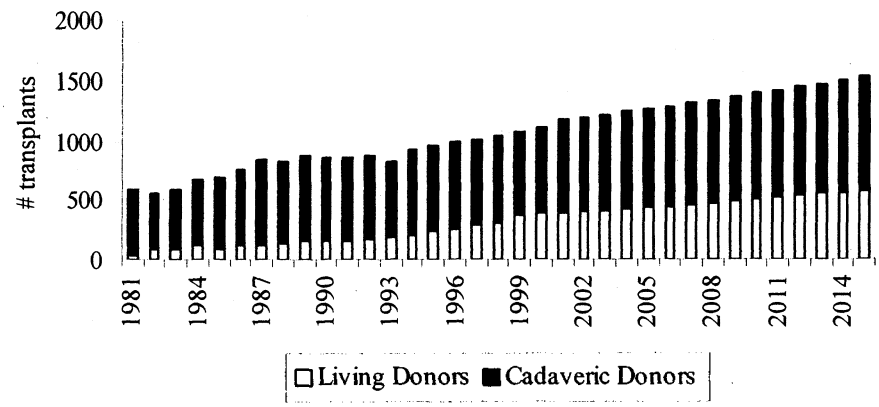


Figure 38: Actual and Forecast Number of Kidney Transplants by Type of Donor, 1981 to 2015



The total number of transplants projected for 2015 is significantly less than that required to accommodate the projected number of surgeries that would occur if current patterns of treatment for patients with ESRD were to continue (e.g. as per the baseline projection in Chapter 7). It is, however, about the same as

the number of transplants that projected under the Changing Transition Probabilities scenario in Chapter 8. Nevertheless, given that even this scenario starts from today's reality of rising waiting lists, the gap between the need for kidney transplants and their availability would widen in all cases. This suggests that waiting lists will continue to grow at least until 2015 unless there are significant changes in policies or practice.

There are three ways to address the large and growing mismatch between the demand and supply of kidneys for transplant: decrease the need for human organ transplants, increase the effective number[156] of cadaveric organs, or expand the effective number of organs from living donors. Each of these options is discussed in more detail below. Potential market-based strategies that cut across these options are discussed in section 9.6.

9.3 Policy Alternatives to Narrow the Gap ~ Decreasing Demand

Preventing kidney failure can reduce the need for transplants. This could occur, for example, because of reductions in risk factors for kidney disease (e.g. diabetes and hepatitis) or in the rate at which kidney disease progresses to ESRD.[157] The potential impact of such strategies was implicitly considered in the sensitivity analysis in Chapter 8 through the scenarios that explored different incidence rates and changing practice/survival patterns. These analyses suggest that changes in incidence rates could significantly affect the need for transplants in the future. Nevertheless, under a wide range of assumptions, this effect would be insufficient to reduce transplant waiting lists.

Improvements in dialysis – including better survival rates, quality of life for patients, and overall cost effectiveness relative to transplantation – would also potentially reduce the demand for transplants. Likewise, some commentators have suggested that xenotransplantation will reduce the need for human organ transplants in the long-term (Henderson, 2000). Xenotransplantation involves transplanting animal organs into human hosts. To date, there have been no kidney transplants of this type in Canada, even as part of research programs. It is a highly controversial practice with proponents pointing to xenotransplantation as a potential solution to the current organ shortage and opponents pointing to ethical, cost, and potential disease risks of the practice (National Forum on

---

[156] The "effective" supply refers to the number of organs from cadaveric donors that are actually transplanted. It recognizes that organs are not retrieved in all cases where consent is obtained and that not all retrieved organs are used.

[157] For instance, researchers suggest that improved pre-dialysis care may improve survival for patients on dialysis (Porter, 1998; Cass, et al., 2002a; Cass, et al., 2003).

Xenotransplantation, 1999; Magoha and Ngumi, 2001; Public Advisory Group on Xenotransplantation, 2001; Ivinson and Bach, 2002; Wright Jr., 2002). Given the scale of the issues involved, it is highly unlikely that xenotransplantation will have a significant impact on the shortage of organs in the near future (Henderson, 2000).

9.4 Strategies to Increase Cadaveric Donation

When transplants are required, most organs come from cadaveric donors. Many factors have an effect on the supply of these organs, including those that influence the frequency of death in circumstances that may make individuals potential candidates for organ donation, the probability that candidate donors (and/or their families) consent to organ donation, and the likelihood that organs are harvested once consent has been obtained (National Coordinating Committee for Organ and Tissue Donation Distribution and Transplantation, 1999; Alberta Advisory Committee on Organ and Tissue Donation and Transplantation, 2000). Personal preferences and attitudes affect a number of these factors – and therefore the supply of cadaveric organs (Bennett and Savani, 2004). A wide variety of policy decisions, including some outside the direct control of the health system, also have an impact. These range from road safety legislation (e.g. laws requiring motorcycle riders to wear helmets)[158] to the availability of beds in hospital intensive care units (Joint Commission on Accreditation of Healthcare Organizations, 2004).

Canada's cadaveric organ donation rate (13 per million population in 2002) falls in the middle of rates in developed countries (CORR/CIHI, Baxter, 2001; 2003).[159] A 2001 study estimated that organs for transplantation were obtained from only 15%, 9%, and 4.5% of those who died in hospital from head injuries, cerebrovascular accidents, and other causes potentially leading to organ donation respectively between 1992 and 1998 (Canadian Institute for Health Information and Clarica, 2001). While not all of these individuals could have successfully

---

[158] The reduction in the mortality rate from motor vehicle accidents has been identified as a factor affecting the current supply of cadaveric organs (Molzahn, et al., 2003). Statistics Canada data show that transport accidents caused 2,877 deaths in 2001, down from 5,690 in 1971 (Organization for Economic Cooperation and Development, 2003; Statistics Canada).

[159] Some have argued, however, that this method of calculating donation rates does not fully reflect the current situation because of differences in how the number of donors is counted and because Canada has lower rates of some types of death, such as motor vehicle accidents, than some countries with higher donation rates (Baxter, 2001).

become a donor, these statistics suggest that it may be possible to build on gains in cadaveric donation that have been made in recent years.

A number of strategies have been proposed to increase the supply of cadaveric organs, although there is little information about their relative effectiveness (and even less about cost-effectiveness). Some attempt to close the well-publicized gap between the number of actual and potential donors; others try to increase the pool of potential donors or to improve the use of available organs (Levine, 2000; McAlister, et al., 2003). Examples include:

- *Social marketing campaigns*: In a 2001 survey conducted for Health Canada, 93% of Canadian adults strongly or somewhat approved of organ and tissue donation, but only 40% said that they had signed an organ donor card or registered as an organ donor (Health Canada, 2003). Although some experts believe that more effective strategies to increase donation rates exist, governments and not-for-profit agencies have invested significant resources in social marketing campaigns to close this gap (Verble and Worth, 1996; Health Canada, 2003). They include messages encouraging donation, advice on how to register to be a donor, and requests to talk to your family about donation.[160] For example, the 2001 survey found that almost half of those surveyed remembered seeing an advertising campaign sponsored by Health Canada earlier that year. 45% of undecided donors said that seeing the advertising made them more likely to consider donation, but the proportion of decided/undecided donors was about the same as in a pre-campaign survey.

- *Training of clinical staff*: Clinicians have historically received little formal training about issues such as the organ donation/transplantation process and how best to request consent from families to harvest organs. Organ procurement organizations and other groups have developed training programs to address this gap. Research suggests that such interventions can be effective, albeit often only for a relatively short period of time (Riker and White, 1995; Morton, et al., 2000; Molzahn, et al., 2003).

- *Creation of organ procurement organizations*: Organ procurement organizations typically manage the organ donation process within a given geographic area. This may include sponsoring comprehensive

[160] Even when an individual has consented to organ donation, health professionals will typically seek consent from his/her family. Surveys and other research consistently find that families are less likely to consent if they are not aware of the potential donors' wishes (Rocheleau, 2001; West and Burr, 2002; Smith, et al., 2004).

strategies to improve how often families are asked to consent to organ donation, education for hospital staff, transplant coordination services, the development of consistent policies and practice guidelines, compensation to hospitals for the costs of organ procurement, and other programs. Experts suggest that integrated approaches can improve both organ donation rates and the effective utilization of donated organs (Beasley, et al., 1997; National Coordinating Committee for Organ and Tissue Donation Distribution and Transplantation, 1999). Many point to Spain as an example of the success of this type of approach (Martinez, et al., 2001; Matesanz, 2001; Matesanz, 2003).

- *Expansion in the types of donors from whom organs can be obtained*: For example, a study at the Foothills Hospital in Calgary, Alberta suggested that accepting organs from non-heart-beating donors might increase the supply of cadaveric kidneys for transplantation by 48% (Campbell and Sutherland, 1999). Others point out that there are many logistical and ethical challenges inherent in this approach (Canadian Critical Care Society, 2001).

- *Changes in legislation*: It has been suggested that changes in broad public policy, particularly legislation, could significantly increase organ donation rates. Although sometimes controversial, possible strategies include requiring that all adults register whether they do or do not wish to be organ donors ("mandated choice"), requiring that clinicians ask the families of all potential donors to consent to organ donation ("required request"), and assuming consent for donation unless an individual explicitly registers his/her refusal to consent ("presumed consent") (Sutherland, 1997; Chouhan and Draper, 2003; Oz, et al., 2003). Each of these strategies is in place in some parts of the world and there is some evidence that they can be effective. For example, Abadie (2004) found that western countries with presumed consent legislation have donation rates that are 25%-30% higher than countries that rely on an informed consent model.

The potential impact of each of these strategies can be followed through the ESRD model outlined in Chapter 6. For simplicity, one was selected to illustrate the effects of a relaxation or tightening in the constraint on the supply of organs for transplantation. Specifically, the first three stages resulting from changes in the probability that persons alive at time t die in circumstances that would make them a potential candidate for organ donation (e.g. because of improvements in

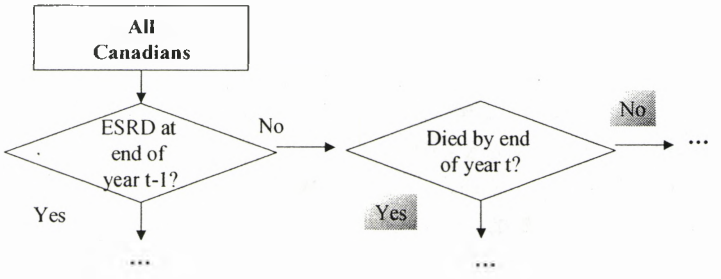
road safety or beginning to accept organs from non-heart-beating donors for transplantation) are shown below.[161]

Stage 1

Impact on Probability of "Eligible" Death: Changes in road safety policy and legislation can affect the probability that people alive at time t die in circumstances that would make them potential candidates for organ donation by time t+1 as Equation 43 shows. Graphically, this is the equivalent in a change in the proportion of people without ESRD at time t who follow the "yes" and "no" paths shaded in Figure 39.

$$PR\_EL\_DEATH_{t,t+1} = f(POLICIES_t, CLINICAL\_P_t, PERS\_BHVR_t) \quad \textbf{Eq. 43}$$

Figure 39: Initial Impact of Changes in the Probability of Death



Stage 2

Impact on Number of Eligible Deaths: The total number of candidates for cadaveric organ donation depends on the probability of "eligible" death (stage 1), as well as the size and structure of the general population.

$$DONOR\_CAN_{t,t+1} = PR\_EL\_DEATH_{t,t+1} * POP\_TOT_t \quad \textbf{Eq. 44}$$

Stage 3

Impact on Cadaveric Organ Supply: The number of candidate donors (stage 2), as well as the probabilities that consent is received and that kidneys are harvested, affect the total supply of cadaveric organs.

[161] Technically, these changes would also influence the probability of death among patients with ESRD. The impact on the size and age/sex structure of the ESRD population, however, is likely to be relatively minor and is not explicitly considered.

$$KDNY\_CAD_{t,t+1} = \begin{pmatrix} DONOR\_CAN_{t,t+1} * PR\_CONSENT_{t,t+1} \\ * PR\_HARV\_1_{t,t+1} \end{pmatrix} + 2 * \begin{pmatrix} DONOR\_CAN_{t,t+1} * PR\_CONSENT_{t,t+1} \\ * PR\_HARV\_2_{t,t+1} \end{pmatrix} \quad \textbf{Eq. 45}$$

9.5 Policy Alternatives to Increase Kidney Transplantation from Living Donors

Rates of transplantation from living donors have risen in recent years, prompting some experts to suggest increases in living donation as a potential solution to address the shortage of organs for transplant (Baran, 2004; Joint Commission on Accreditation of Healthcare Organizations, 2004). This enthusiasm is, however, tempered by the challenges involved, such as the ethical dilemmas associated with expanding the pool of living donors, the challenge in ensuring an equitable distribution of organs, and the potential risk to donors (Steiner and Gert, 2000; Rowinski and Walaszewski, 2002; Kayler, et al., 2003).

As for cadaveric organs, a number of factors affect the supply of organs from living human donors. Examples include:

- *Clinical and legal practices/policies:* Clinical and legal practices and policies govern the organ donation and transplantation process. For example, laws in most Western countries, including Canada, prohibit the sale of organs. Likewise, the World Medical Association has issued a statement about the principles that should govern organ donation which includes a discussion of acceptable and unacceptable practices (Zabinski, et al., 2001).

- *The scope of the donor pool:* Most of Canada's living donors (75% in 2000) are related to those who receive the organ transplant (CORR/CIHI, 2002). There is considerable interest, however, in opportunities to expand donations from groups such as spouses and emotionally committed friends (Gjertson and Cecka, 2000). In addition, there has been much discussion about organ exchange programs whereby a person who wants to donate an organ to a family member but cannot because of biological incompatibility donates his/her kidney to someone else on the understanding that his/her family member also receives a transplant (Matas and Schnitzler, 2004). There has also been limited transplantation from altruistically- or financially-motivated donors with no direct connection to a person with ESRD, but these practices remain highly controversial (Landolt, et al., 2001; Adams, et al., 2002; Friedlaender, 2002; Henderson, et al., 2003).

- *The length of the cadaveric waiting list*: Countries with longer waiting times for cadaveric organ transplants (or that restrict such practices) tend to have higher levels of living donation (Baxter, 2001).

- *The characteristics of patients on the waiting list*: Children and men are more likely to receive living donations than are others. For example 60% of kidney transplants received by children in 2000 were from living donors, compared to 25% overall (CORR/CIHI, 2002).

- *The costs experienced by organ donors*: Several authors have suggested that living donors should be recompensed for the out-of-pocket costs associated with their donation (Joint Commission on Accreditation of Healthcare Organizations, 2004). This may include health care costs, time off work, higher future insurance premiums, and other costs. Financial incentives, particularly if designed to go beyond a strict reimbursement of out-of-pocket costs, are highly controversial. Options that have emerged are discussed in further detail in section 9.6.

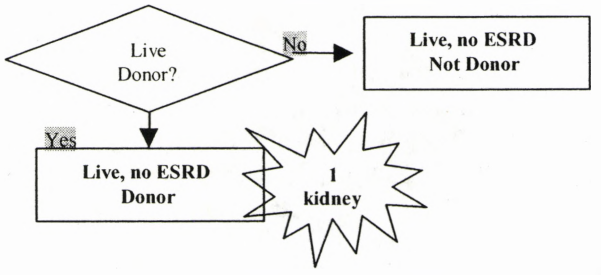
As with cadaveric transplants, changes in any of the above factors would have ripple effects through the model of ESRD and its care presented in Chapter 6. Consider, for example, a policy change that expanded the pool of potential living donors. The first three stages of impact resulting from such a shift (e.g. because of greater acceptance of spousal donors or a decision to permit altruistic anonymous donation) are illustrated below.

Stage 1

Impact on Supply of Living Kidney Donors: Changes in policies regarding eligibility for donation would potentially affect the number of individuals at time t who choose to donate a kidney to a person with ESRD for transplant by time t+1 as Equation 46 shows. Graphically, this is the equivalent in a change in the proportion of people without ESRD at time t who follow the "yes" and "no" paths shaded in Figure 40.

$$KDNY\_LVG_{t,t+1} = f(POLICIES_t, PERS\_PREF_t, WAIT\_LIST_t, CLINICALP_t, ES\_TOT_t, POP\_TOT_t) \quad \textbf{Eq. 46}$$

Figure 40: Initial Impact of Changes in Eligibility Criteria for Living Donors



Stage 2

Impact on Total Supply of Kidneys for Transplant: The total number of organs for transplant depends on the number of kidneys from living donors (stage 1). As a result, the total expected number of kidneys successfully harvested for transplantation between time t and time t+1 equals the sum of the expected number successfully harvested from these donors and from cadaveric donors.[162]

$$KDNY\_TOT_{t,t+1} = KDNY\_LVG_{t,t+1} + KDNY\_CAD_{t,t+1} \qquad \textbf{Eq. 47}$$

Impact on Probability of Obtaining a Transplant from a Living Donor: The probability that patient *i* on the waiting list will receive a transplant from a living donor depends on individuals' willingness to serve as living donors (and therefore the supply of organs), patient characteristics, the length of the waiting list, clinical practices, and policies/legislation.

$$PR\_NEW\_LVG = f\begin{pmatrix} KDNY\_LVG_t, PERS\_CHAR_t, WAIT\_LIST_t, \\ CLINICAL\_P_t, POLICIES_t \end{pmatrix} \qquad \textbf{Eq. 48}$$

Stage 3

Impact on Probability of Transplantation: The probability that a person with ESRD who does not have a functioning transplant at time t will receive one by

[162] The model considers the supply of cadaveric and living organs separately since different factors may influence their supply. In the future, it is possible that xenotransplantations may occur. In this case, the number of such transplants would be added to the total in Equation 20.

time t+1 is a function of the probability that s/he will receive a transplant from either a living or a cadaveric donor.

$$PR\_TRAN\_CHG_{r1,r2} = f(PR\_NEW\_CAD, PR\_NEW\_LVG) \quad \textbf{Eq. 49}$$

Impact on Number of Individuals with Transplants: Likewise, the expected number of people with ESRD who have functioning transplants at time t+1 equals the number who had functioning transplants at time t, adjusted for changes that occur over the period, including patients on the waiting list at time t who receive transplants from living donors by time t+1.

$$\begin{aligned} ES\_TRAN_{t,t+1} = \; & ES\_TRAN_t \\ & +(WAIT\_LIST_t) * PR\_TRAN\_CHG_{r1,r2} \\ & -ES\_TRAN_t * PR\_ES\_DEATH_{r2} \\ & -ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r3} \\ & -ES\_TRAN_t * PR\_TRAN\_CHG_{r2,r1} \end{aligned} \quad \textbf{Eq. 50}$$

Impact on the Waiting List for Transplants: Recipients of transplants from living donors between time t and time t+1 are removed from the waiting list, as measured at time t+1.

$$\begin{aligned} WAIT\_LIST_{t+1} = \; & WAITLIST_t \\ & -WAIT\_LIST_t * PR\_TRAN\_CHG_{r1,r2} \\ & -WAIT\_LIST_t * PR\_ES\_DEATH_{r1} \\ & -WAITLIST_t * PR\_TRAN\_CHG_{r1,r3} \\ & +ES\_DIAL_t * PR\_DIAL\_CHG_{d3,r1} \end{aligned} \quad \textbf{Eq. 51}$$

9.6 Market-Based Strategies to Increase Transplantation

Many of the strategies described above, and others, have been used in various parts of Canada and in other countries in recent years. Some gains have been made, but the demand for transplants has continued to outstrip the availability of cadaveric organs. For example, the analysis described earlier in this chapter shows that if recent trends continue, about 944±230 cadaveric

transplants are projected for 2015. Even the upper bound of this estimate falls well below the projected future need.

This gap has led some commentators to call for new, market-based strategies to increase donation. A number of potential strategies have been proposed, ranging from recompensing families for the funeral or other expenses for a donor to developing a futures market for organs, creating mutual insurance plans for organs, and paying living kidney donors (Levine, 2000). These proposals have many differences (e.g. how property rights would be assigned, whether price levels would be fixed by a public entity or not, and whether benefits would be available before or after transplantation), but all involve some type of financial incentive to encourage donation (Adams III, et al., 1999).[163]

Such proposals are highly controversial. Proponents argue that, given the persistent shortage of organs from other sources, market-based strategies could be an effective way to increase the supply of organs for transplant (Adams III, et al., 1999; Barnett II, et al., 2001; Friedlaender, 2002). Opponents often cite ethical, logistical, public policy, and other barriers to the implementation of a market for organs (Levine, 2000; Brooks, 2003). In addition, they argue that financial incentives might decrease altruistic donations (Sells, 1994). Some also point to mixed clinical outcomes for patients and donors (Sever, et al., 2001) and unfair practices (e.g. nonpayment of donors) in areas where limited commercial markets for organs do exist (e.g. India, Iraq, and Iran) (Zargooshi, 2001).

Public policy is clearly against market-based strategies,[164] but public and professional attitudes appear to vary. In 1993, for example, researchers reported that 40-49% of those surveyed would have allowed the purchase of kidneys based on two case scenarios (Guttmann and Guttmann, 1993). More recently, survey respondents reported that their decision to donate was more likely to be influenced by incentives such as upfront cash payments and priority on waiting lists than by more altruistic alternatives (Bennett and Savani, 2004). Likewise, recent polls of transplant professionals have found that at least half are in favour of indirect forms of compensation, such as providing some amount of money towards donors' funeral expenses (Oz, et al., 2003; Jasper, et al., 2004).

Although there are few examples of the use of financial incentives for donation in developed countries, a number of economists have explored the characteristics of the current mechanisms by which organs are distributed, as well

[163] Nelson and colleagues (1993) define financial incentives as "any material gain or valuable consideration obtained by those directly consenting to the process of organ procurement, whether it be the organ donor himself (in advance of his demise), the donor's estate, or the donor's family."

[164] The buying and selling of organs is illegal in most developed countries.

as potential alternatives. For example, Barney and Reynolds (1989; 1991) and Kaserman and Barnett (1991) have presented an economic analysis of the current situation.

While there are reports of willingness to pay very large amounts of money for a transplant,[165] Adams, Barnett, and Kaserman (1999) use survey data to argue that the equilibrium market-clearing price would be very low, far less than the $90,000 that Matas and Schnitzler (2004) estimate as the societal break-even point. Likewise, Barnett, Saliba, and Walker (2001) argue that a free market in kidneys could be efficient and equitable. This view, however, is vigorously disputed (Levine, 2000; Benatar, 2004).

Another option that has been proposed to encourage organ donation without using monetary incentives or a presumed consent legislative regime is a mutual insurance pool (Schwindt and Vining, 1998). Under this approach, individuals who elected to participate in the pool would agree to donate their organs should they die in circumstances that would make them potential organ donors. In return, they (and/or their immediate families) would receive priority access to organs from members of the pool, or potentially from any source.[166] This process can either be characterized as an insurance scheme or as a lottery where individuals pay a premium (i.e. the information and enrollment costs, as well as the delivery of organs contingent on dying in such a way that they are a candidate for donation) in exchange for the relatively low probability of a large gain (i.e. that they will receive a kidney transplant, or at least improve their odds of doing so, should they require one in the future). To address adverse selection problems, a number of potential solutions have been proposed, including allowing parents to enroll their children only shortly after conception or stratifying the pool by risk group (e.g. on the basis of a medical exam) (Schwindt and Vining, 1998).

A simple model of this process can illustrate some of the trade-offs involved for individuals facing a registration decision. Let u_D and u_N be the present value of expected utility realized with and without donation, respectively.[167] The utility gain derived from donation is $u_D - u_N = v$. Although all individuals will eventually die, not all will do so under circumstances that make them candidates

[165] For example, by the time e-Bay halted an on-line auction for a kidney (likely a false offer), bidding had reached almost $6 million US (BBC News, 1999).
[166] Schwindt and Vining suggest that this might be appropriate since to the extent that the pool increases the supply of organs in the face of an overall shortage, there are positive externalities for non-participants.
[167] For simplicity, this model assumes that everyone must make a decision to register or not.

to be organ donors. They do so with a probability of $p_{CAN} = E(candidate\_for\_donation\_at\_death) + \varepsilon_1$, where ε_1 is independent.

Likewise, let u_1 and u_2 be the utility levels that individuals in the pool and out of the pool respectively would realize should they acquire ESRD. This eventuality occurs with a probability of $p_{ESRD} = E(lifetime\_probability\_of\_ESRD) + \varepsilon_2$, where ε_2 is independent. Thus, $w = u_1 - u_2$ is the utility gain from quicker transplantation should ESRD develop. Finally, individuals who choose to register face registration costs (including contemplation costs) of c.[168]

Utility levels vary across individuals. An individual observes his/her own utility levels, as well as the distribution for society as a whole. For simplicity, c is assumed to be fixed and known to everyone. The lifetime probability of developing ESRD might vary between groups in society, but the distribution would be generally known, as is that of ε_1 and ε_2.[169]

This simple model of a mutual insurance organ pool can be represented as an extensive form game with incomplete information. First, individuals decide whether or not to register for the insurance pool after observing the registration costs (c), their utility gain from donation (v), their utility gain from quicker transplantation should ESRD develop (w), the likelihood that they will develop ESRD at some point in their life, and the probability that they will die in circumstances that would make them candidates for organ donation. With a probability of p_{ESRD}, individuals will develop ESRD during their lifetime. If they have registered for the organ pool, they can expect to receive a quicker transplant than if they had not registered which affects the utility they would realize. With a probability of p_{CAN}, the individual will be a candidate organ donor at the time of death, which would also affect their realized utility.

In this scenario, individuals will choose to donate if the expected utility that they would realize from so doing exceeds the expected utility associated with not registering. Thus, they would register if $E[(prob_{ESRD} \times w) + (prob_{CAN} \times v)] > E[c + (prob_{CAN} \times v)]$ or $E(prob_{ESRD} \times w) > c$. These trade-offs would vary, perhaps significantly among individuals.

---

[168] If the government or other groups chose to actively encourage participation in the insurance pool (e.g. because of the positive externalities to non-pool members), c might be negative. The existence of such potential positive externalities is, however, not considered in this simple model of the insurance pool.

[169] $E(\varepsilon_1) = E(\varepsilon_2) = 0$

Many factors, such as the rate of time preference, risk aversion, and the probable size of the mutual insurance pool would need to be considered in a more detailed analysis, but a simple calculation suggests that many individuals would participate in the insurance pool even with a non-trivial *c*. For example, the lifetime cumulative risk of developing ESRD in the United States has been estimated at 1.8% for 20 year-old white women, 2.5% for white men, 7.3% for black men, and 7.8% for black women (Kiberd and Clase, 2002). Once a patient has ESRD, quality of life tends to be much higher with a transplant than on dialysis. A recent study also estimated that utility gains decline significantly with longer waiting times (Jassal, et al., 2003).

9.7 Discussion

The gap between the number of people who need transplants and the supply of organs is large and growing. The analysis in this chapter demonstrates that large leaps, not incremental change, will be required simply to maintain current rates of transplantation in the future. While some promising strategies to increase donation rates have been tried – and still more proposed – this gap has persisted for many years. In addition, recent research suggests that the group who might benefit from transplants may be larger (e.g. including more elderly patients) than those who traditionally have been identified as candidates for surgery (Stack and Messana, 2000; Rao, 2002). If transplants were to become more available, these individuals might be added to the waiting list for surgery.

As a result, some commentators are calling for the use of controversial market-based strategies to increase donation rates. These might include direct or indirect payments to the families of cadaveric organ donors, financial and non-financial incentives for individuals who indicate that they are willing to donate their organs on their death, and payments to living organ donors. Although there is some evidence that such strategies may generate more organs for transplant, there are serious ethical, legal, and practical barriers to their use. As a result, it is unlikely that they will be implemented in the near future.

Chapter 10: Conclusion

> *For individuals and families, health brings the capacity for personal development and economic security in the future. Health is the basis for job productivity, the capacity to learn in school, and the capability to grow intellectually, physically, and emotionally. In economic terms, health and education are the two cornerstones of human capital.* (World Health Organization Commission on Macroeconomics and Health, 2001)

About ten percent of Canada's Gross Domestic Product is currently spent on health care (CIHI, 2003b), but the costs of illness are much higher when the economic burden of associated morbidity and early mortality are taken into account. This is particularly true for chronic diseases where individuals live with the consequences of their disease for years or even decades.

End-stage renal disease (ESRD), also known as kidney failure, is one such condition. Although less than 0.1% of Canadians have ESRD, the disease led to direct health care expenditures of about $1.27 billion in 2000, or about 1.3% of total spending. Added to this were an estimated $434 million in losses related to early deaths among persons with ESRD and about $149 million in disease-related lost productivity.

Since the early 1980s, the number of Canadians living with ESRD has more than quadrupled. Rising ESRD numbers have led to questions about the current and future impact of the disease on public health, quality of life, health spending, and overall economic burden.

In order to project future trends, it is helpful to understand key drivers of past experience. Chapter 3 shows that more than half of the growth in ESRD between 1994 and 2000 can be explained by three factors: population growth, changes in the population's age structure, and increases in the prevalence of diabetes. Chapter 7 takes these types of factors into account in developing projections of ESRD numbers and economic burden to 2015. These projections are based on a multi-state discrete time Markov model. They show that, if recent trends continue, ESRD numbers would rise considerably over the next fifteen years, and the total economic burden of the disease would grow to $7.9 billion.

Chapter 8 extends the literature by considering a variety of sensitivity analyses. It shows that the projections are much more sensitive to assumptions about incidence rates than to those about population growth and change. Assuming that treatment patterns would continue to evolve in line with recent trends (rather than being the same as those experienced in the late 1990s) also had an impact on the mortality rate and treatment patterns for persons with ESRD, but the economic burden of illness in 2015 was estimated to be relatively similar to the baseline case.

Nevertheless, under almost all assumptions, there was significant projected growth in the number of persons with ESRD through at least 2015. This represents a significant and increasing public health and economic burden. It also has important implications for health care managers, planners, and policy-makers, particularly given that direct health care costs form a relatively large component of the total economic burden of illness.

The projected widening gap between the need for transplants and the supply of organs is also a challenging public policy issue. Waiting lists are likely to continue to rise unless there are significant changes to the underlying burden of ESRD, practice patterns, technology, and/or health policy. Chapter 9 explores the potential magnitude of this mismatch and a number of options for addressing it. Some have already been implemented in parts of Canada or elsewhere. Others, such as mutual insurance pools for organs or xenotransplantation, would require fundamental policy change and/or scientific advances. Given the extensive transformations that they would require, it is not realistic to assume that it would happen any earlier than 2010 and, in fact, even 2010 is likely optimistic.

Extensions to the work presented in this thesis could proceed in a number of directions. For example, microsimulation approaches could be used to model the long-term effects of specific changes in upstream factors that affect the risk of developing ESRD. Combined with projections of the economic burden of illness, this approach could assist policy-makers in making difficult trade-offs between investing in the prevention of future illness or in care for individuals who could benefit from further care today. Similar approaches could be used to model other policy trade-offs (e.g. the impact of alternatives for encouraging transplantation). To do so, further primary research would also be required as there is little population-based research on the cost-effectiveness and long-term effects of various policy options. For example, experimental economics techniques could be used to explore the potential impact of different monetary and non-monetary incentives.

Bibliography

Abadie, A and S Gay. (2004). The Impact of Presumed Consent Legislation on Cadaveric Organ Donation: A Cross-Country Study. Boston: John F. Kennedy School of Government, Harvard University.

Adams III, AF, AH Barnett, and DL Kaserman. (1999). "Markets for Organs: The Question of Supply." Contemporary Economic Policy **17**(2): 147-55.

Adams, PL, DJ Cohen, GM Danovitch, RM Edington, RS Gaston, CL Jacobs, RS Luskin, RA Metzger, TG Peters, LA Siminoff, RM Veatch, L Rothberg-Wegman, ST Bartlett, L Brigham, J Burdick, S Gunderson, W Harmon, AJ Matas, JR Thistlethwaite, and FL Delmonico. (2002). "The Nondirected Live-Kidney Donor: Ethical Considerations and Practice Guidelines: A National Conference Report." Transplantation **74**(4): 582-9.

Alberta Advisory Committee on Organ and Tissue Donation and Transplantation. (2000). A Framework for Action: A Coordinated and Integrated Organ and Tissue Donation and Transplant System for Alberta, Alberta Health. http://www.health.gov.ab.ca/public/document/organs/Organ.PDF. Accessed in 2002.

Andersen, RM. (1995). "Revisiting the Behavioral Model and Access to Medical Care: Does It Matter?" Journal of Health and Social Behavior **36**(1): 1-10.

Anderson, GM, IR Pulcins, ML Barer, RG Evans, and C Hertzman. (1990). "Acute Care Hospitalization under Canadian National Health Insurance: The British Columbia Experience from 1969 to 1988." Inquiry **27**(4): 352-58.

Andersson, A, LA Levin, and BG Emtinger. (2002). "The Economic Burden of Informal Care." International Journal of Technology Assessment in Health Care **18**(1): 46-54.

Asche, CV, E Ho, B Chan, and PC Coyte. (1997). "Economic Consequences of Multiple Sclerosis for Canadians." Acta Neurologica Scandinavica **95**(5): 268-74.

Baltzan, MA, S Ahmed, RB Baltzan, RP Marshall, EL Thoma, and MF Nicol. (1997). "Variations in Living Donor Graft Rates by Dialysis Clinic: Effect on Outcome and Cost of Chronic Renal Failure Therapy." Clinical Nephrology **47**(6): 351-5.

Baran, D. (2004). "How to Improve Organ Donation Rates." Canadian Medical Association Journal **170**(3): 318-9; author reply 319.

Barer, ML, IR Pulcins, RG Evans, C Hertzman, J Lomas, and GM Anderson. (1989). "Trends in the Use of Medical Services by the Elderly in British Columbia." Canadian Medical Association Journal **141**(1): 39-45.

Barnett II, W, M Saliba, and D Walker. (2001). "A Free Market in Kidneys: Efficient and Equitable." The Independent Review **5**(3): 373-385.

Barney Jr., LD and RL Reynolds. (1989). "An Economic Analysis of Transplant Organs." Atlantic Economic Journal **17**(3): 12-20.

Barney Jr., LD and RL Reynolds. (1991). "An Economic Analysis of Transplant Organs: Reply." Atlantic Economic Journal **14**(2): 64-65.

Barrett, BJ, PS Parfrey, J Morgan, P Barre, A Fine, MB Goldstein, SP Handa, KK Jindal, CM Kjellstrand, A Levin, H Mandin, N Muirhead, and RM Richardson. (1997). "Prediction of Early Death in End-Stage Renal Disease Patients Starting Dialysis." American Journal of Kidney Disease **29**(2): 214-22.

Baxter, D. (2001). Beyond Comparison: Canada's Organ Donation Rates in an International Context. Vancouver: Urban Futures Institute.

BBC News. (1999). Kidney Sale on Web Halted, BBC Online Network. Accessed in 2004.

BC Renal Council. (1994). Resource Utilisation in Chronic Dialysis Patients. Victoria: Ministry of Health.

Beasley, CL, CL Capossela, LE Brigham, S Gunderson, P Weber, and SL Gortmaker. (1997). "The Impact of a Comprehensive, Hospital-Focused Intervention to Increase Organ Donation." Journal of Transplant Coordination **7**(1): 6-13.

Becker, BN and WJ Stone. (1997). "Options for Renal Replacement Therapy: Special Considerations." Seminars in Nephrology **17**(3): 176-87.

Belasco, AG and R Sesso. (2002). "Burden and Quality of Life of Caregivers for Hemodialysis Patients." American Journal of Kidney Disease **39**(4): 805-12.

Benatar, SR. (2004). "Blinkered Bioethics." Journal of Medical Ethics **30**(3): 291-2.

Bennett, R and S Savani. (2004). "Factors Influencing the Willingness to Donate Body Parts for Transplantation." Journal of Health and Social Policy **18**(3): 61-85.

Bentkover, JD, C Field, EM Greene, V Plourde, and JP Casciano. (1999). "The Economic Burden of Irritable Bowel Syndrome in Canada." Canadian Journal of Gastroenterology **13 Suppl A**: 89A-96A.

Bigam, D, R Zhong, G Levy, and D Grant. (1999). "Xenotransplantation." Canadian Journal of Surgery **42**(1): 12-16.

Birmingham, CL, JL Muller, A Palepu, JJ Spinelli, and AH Anis. (1999). "The Cost of Obesity in Canada." Canadian Medical Association Journal **160**(4): 483-8.

Blake, PG, J Floyd, E Spanner, and K Peters. (1996). "How Much Extra Does "Adequate" Peritoneal Dialysis Cost?" Peritoneal Dialysis International **16**(1): S171-5.

Blanchard, JF, A Wajda, and C Green. (1999). Epidemiologic Projections of Diabetes and Its Complications: Forecasting the Coming Storm, Manitoba Health. http://www.gov.mb.ca/health/publichealth/epiunit/docs/storm.pdf. Accessed in 2002.

Borghouts, JA, BW Koes, H Vondeling, and LM Bouter. (1999). "Cost-of-Illness of Neck Pain in the Netherlands in 1996." Pain **80**(3): 629-36.

Bremer, B, C McCauley, R Wrona, and J Johnson. (1989). "Quality of Life in End-Stage Renal Disease: A Reexamination." American Journal of Kidney Disease **7**: 751-62.

Briggs, A and M Sculpher. (1998). "An Introduction to Markov Modelling for Economic Evaluation." Pharmacoeconomics **13**(4): 397-409.

Brockwell, PJ and RA Davis. (2002). Introduction to Time Series and Forecasting. New York: Springer.

Brooks, M. (2003). "A Free Market in Kidneys Would Be Efficient and Equitable: A Case of Too Much Romance." The Independent Review **7**(4): 587-594.

Brouwer, WB, MA Koopmanschap, and FF Rutten. (1997). "Productivity Costs Measurement through Quality of Life? A Response to the Recommendation of the Washington Panel." Health Economics **6**(3): 253-9.

Burner, ST, DR Waldo, and DR McKusick. (1992). "National Health Expenditures through 2030." Health Care Financing Review **14**(1): 174-192.

Cairns, J. (1992). "Discounting and Health Benefits: Another Perspective." Journal of Health Economics **1**(1): 76-79.

Campbell, GMD and FR Sutherland. (1999). "Non-Heart-Beating Organ Donors as a Source of Kidneys for Transplantation: A Chart Review." Canadian Medical Association Journal **160**(11): 1573-76.

Canadian Burden of Illness Study Group. (1998a). "Burden of Illness of Multiple Sclerosis: Part I: Cost of Illness." Canadian Journal of Neurological Science **25**(1): 23-30.

Canadian Burden of Illness Study Group. (1998b). "Burden of Illness of Multiple Sclerosis: Part II: Quality of Life." Canadian Journal of Neurological Science **25**(1): 31-8.

Canadian Coordinating Office for Health Technology Assessment. (1997). Guidelines for Economic Evaluation of Pharmaceuticals. Ottawa: CCOHTA.

Canadian Critical Care Society. (2001). CCCS Position Paper on Organ and Tissue Donation. Toronto: Canadian Critical Care Society.

Canadian Institute for Health Information. (2001). 2001 Report: Dialysis and Renal Transplantation, Canadian Organ Replacement Register. Ottawa: Canadian Institute for Health Information.

Canadian Institute for Health Information. (2002a). 2002 DAD Resource Intensity Weights and Expected Length of Stay - Electronic Appendices. Ottawa: Canadian Institute for Health Information.

Canadian Institute for Health Information. (2002b). National Health Expenditure Trends 1975-2002. Ottawa: CIHI.

Canadian Institute for Health Information. (2003a). Canadian MIS Database: Moving toward the Reporting of Hospital Financial Performance Indicators, 1999-2000 and 2000-2001. Ottawa: CIHI.

Canadian Institute for Health Information. (2003b). National Health Expenditure Trends 1975-2003. Ottawa: CIHI.

Canadian Institute for Health Information and Clarica. (2001). Estimating Potential Cadaveric Organ Donors for Canada and Its Provinces, 1992 to 1998: A Discussion Paper. Ottawa: Canadian Institute for Health Information.

Canadian Organ Replacement Register/Canadian Institute for Health Information. (1997). Data Definitions and User Manual: Initial Registration and Follow-up for Renal Failure Patients. Ottawa: Canadian Institute for Health Information.

Canadian Organ Replacement Register/Canadian Institute for Health Information. (2002). Preliminary Report for Dialysis and Transplantation: Preliminary Statistics on Renal Failure and Solid Organ Transplantation in Canada 2002 (Includes Data 1981-2000). Ottawa: Canadian Institute for Health Information.

Canadian Organ Replacement Register/Canadian Institute for Health Information. (2003). Corr Insites - a Decade of Organ Donation in Canada: 1993 to 2002, CIHI. http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=statistics_results_topic_transplants_e&cw_topic=Health%20Conditions&cw_subtopic=Organ%20Donation%20and%20Transplantation. Accessed in 2004.

Canadian Organ Replacement Register/Canadian Institute for Health Information (CIHI). (2004a). E-Quarterly Report on Transplant, Waiting List and Donor Statistics: 2003 Summary Statistics, January 1 to December 31, 2003, Canadian Institute for Health Information. http://secure.cihi.ca/cihiweb/en/downloads/reports_corrstats2003c_t1a_e.pdf. Accessed in 2004.

Canadian Organ Replacement Register/Canadian Institute for Health Information (CIHI). (2004b). E-Quarterly Report on Transplant, Waiting List and Donor Statistics: 2004 First Quarter, January 1 to March 31, 2004, Canadian Institute for Health Information. http://secure.cihi.ca/cihiweb/en/downloads/Corrq1_2004_Table2A_e.pdf. Accessed in 2004.

Carabin, H, TW Gyorkos, JC Soto, J Penrod, L Joseph, and JP Collet. (1999). "Estimation of Direct and Indirect Costs Because of Common Infections in Toddlers Attending Day Care Centers." Pediatrics **103**(3): 556-64.

Cass, A, J Cunningham, PC Arnold, P Snelling, Z Wang, and W Hoy. (2002a). "Delayed Referral to a Nephrologist: Outcomes among Patients Who Survive at Least One Year on Dialysis." Medical Journal of Australia **177**(3): 135-8.

Cass, A, J Cunningham, P Snelling, and JZ Ayanian. (2003). "Late Referral to a Nephrologist Reduces Access to Renal Transplantation." American Journal of Kidney Disease **42**(5): 1043-9.

Cass, A, J Cunningham, P Snelling, Z Wang, and W Hoy. (2002b). "End-Stage Renal Disease in Indigenous Australians: A Disease of Disadvantage." Ethnicity and Disease **12**(3): 373-8.

Cass, A, J Cunningham, P Snelling, Z Wang, and W Hoy. (2004). "Exploring the Pathways Leading from Disadvantage to End-Stage Renal Disease for Indigenous Australians." Social Science and Medicine **58**(4): 767-85.

Cass, A, J Cunningham, Z Wang, and W Hoy. (2001). "Social Disadvantage and Variation in the Incidence of End-Stage Renal Disease in Australian Capital Cities." Australian and New Zealand Journal of Public Health **25**(4): 322-6.

Centre for Infectious Disease Prevention and Control. (2001). HIV/AIDS Epi Update, Bureau of HIV/AIDS, STD, and TB Update Series, Centre for Infectious Disease Prevention and Control, Health Canada. www.hc-sc.gc.ca/hpb/lcdc/bah/epi/estima_e.html. Accessed in 2002.

Chan, B, P Coyte, and C Heick. (1996). "Economic Impact of Cardiovascular Disease in Canada." Canadian Journal of Cardiology **12**(10): 1000-6.

Chapman, K, J Bourbeau, and L Rance. (2003). "The Burden of COPD in Canada: Results from the Confronting COPD Survey." Respiratory Medicine **97**(Suppl C): S23-31.

Chen, J and WJ Millar. (2000). "Are Recent Cohorts Healthier Than Their Predecessors?" Health Reports **11**(4): 9-23.

Chib, S and E Greenberg. (1996). "Markov Chain Monte Carlo Simulation Methods in Econometrics." Econometric Theory **12**(3): 409-31.

Choi, BC and AW Pak. (1996). "Health and Social Costs of Tobacco Use in Ontario, Canada, 1979 and 1988." Journal of Epidemiology and Community Health **50**(1): 81-5.

Choi, BK and AW Pak. (2002). "A Method for Comparing and Combining Cost-of-Illness Studies: An Example from Cardiovascular Disease." Chronic Diseases in Canada **23**(2): 47-57.

Choudhry, NK and CD Naylor. (1995). "Reflections on Supply-Demand Mismatch in Dialysis Services in Ontario." Canadian Medical Association Journal **153**(5): 575-81.

Chouhan, P and H Draper. (2003). "Modified Mandated Choice for Organ Procurement." Journal of Medical Ethics **29**(3): 157-62.

Clarke, AE, H Zowall, C Levinton, H Assimakopoulos, JT Sibley, M Haga, J Shiroky, C Neville, DP Lubeck, SA Grover, and JM Esdaile. (1997). "Direct and Indirect Medical Costs Incurred by Canadian Patients with Rheumatoid Arthritis: A 12 Year Study." Journal of Rheumatology **24**(6): 1051-60.

Clayton, D and A Barcel. (1999). "The Cost of Suicide Mortality in New Brunswick, 1996." Chronic Diseases in Canada **20**(2): 89-95.

Colman, R. (1998). Measuring Sustainable Development: Application of the Genuine Progress Index to Nova Scotia; Module 2: The Economic Value of Unpaid Housework and Child-Care in Nova Scotia. Halifax: GPI Atlantic.

Commision d'étude sur les services de santé et les services sociaux. (2000). Emerging Solutions: Report and Recommendations, Government of Quebec. www.cessss.gouv.qc.ca. Accessed in 2002.

Commission on the Future of Health Care in Canada. (2002). Shape the Future of Health Care: Interim Report, Commission on the Future of Health Care in Canada. www.healthcarecommission.ca. Accessed in 2003.

Committee on Summary Measures of Population Health of the Institute of Medicine. (1998). Summarizing Population Health: Directions for the

Development and Application of Population Metrics. Washington: National Academy Press.

Cooper, BS and DP Rice. (1976). "The Economic Cost of Illness Revisited." Social Security Bulletin **39**(2): 21-36.

Coyte, PC, CV Asche, R Croxford, and B Chan. (1998). "The Economic Cost of Musculoskeletal Disorders in Canada." Arthritis Care Research **11**(5): 315-25.

Coyte, PC, CV Asche, and LM Elden. (1999). "The Economic Cost of Otitis Media in Canada." International Journal of Pediatric Otorhinolaryngology **49**(1): 27-36.

Coyte, PC, LG Young, BL Tipper, VM Mitchell, PR Stoffman, J Willumsen, and DF Geary. (1996). "An Economic Evaluation of Hospital-Based Hemodialysis and Home-Based Peritoneal Dialysis for Pediatric Patients." American Journal of Kidney Disease **27**(4): 557-65.

Craig, BA and PP Sendi. (2002). "Estimation of the Transition Matrix of a Discrete-Time Markov Chain." Health Economics **11**(1): 33-42.

Crawford, A. (2002). "Trends in Productivity Growth in Canada." Bank of Canada Review **Spring 2002**: 19-32.

Cuff, GB. (2001). It's Time to Act: A Report on the Health and Social Services System of the Northwest Territories, Government of the Northwest Territories. www.hlthss.gov.nt.ca. Accessed in 2002.

Dault, M, J Lomas, and M Barer. (2004). Listening for Direction II: National Consultation on Health Services and Policy Issues for 2004-2007, Advisory Committee on Governance and Accountability of the F/P/T Conference of Deputy Ministers of Health, Canadian Health Services Research Foundation, Canadian Institute for Health Information, Canadian Coordinating Office for Health Technology Assessment, Institute of Health Services and Policy Research of the Canadian Institutes of Health Research, and Statistics Canada. secure.cihi.ca/cihiweb/products/Listening_e.pdf. Accessed in 2004.

Dawson, KG, D Gomes, H Gerstein, JF Blanchard, and KH Kahler. (2002). "The Economic Cost of Diabetes in Canada, 1998." Diabetes Care **25**(8): 1303-7.

de Vecchi, AF, M Dratwa, and ME Wiedemann. (1999). "Healthcare Systems and End-Stage Renal Disease (ESRD) Therapies--an International Review: Costs and Reimbursement/Funding of ESRD Therapies." Nephrology, Dialysis, Transplantation **6**: 31-41.

de Wit, GA, PG Ramsteijn, and FT de Charro. (1998). "Economic Evaluation of End Stage Renal Disease Treatment." Health Policy **44**(3): 215-32.

Denton, FT, CH Feaver, and BG Spencer. (1989). MEDS -- Models of the Economic-Demographic System: A Report on the Project and Some Preliminary Analysis. Hamilton: Program for Quantitative Studies in Economics and Population, Faculty of Social Sciences, McMaster University.

Denton, FT, A Gafni, and BG Spencer. (1995). "The SHARP Way to Plan Health Care Services: A Description of the System and Some Illustrative Applications in Nursing Human Resource Planning." Socio-Economic Planning Sciences **29**: 125-137.

Denton, FT, A Gafni, and BG Spencer. (2001). "Population Change and the Requirements for Physicians: The Case of Ontario." Canadian Public Policy **27**(4): 469-85.

Denton, FT, A Gafni, and BG Spencer. (2002). "Exploring the Effects of Population Change on the Costs of Physician Services." Journal of Health Economics **21**(5): 781-803.

Denton, FT and BG Spencer. (1975). "Health-Care Costs When the Population Changes." Canadian Journal of Economics **8**: 34-48.

Department of Clinical Epidemiology and Biostatistics at the McMaster University Health Sciences Centre. (1998). "How to Read Clinical Journals: VII To Understand an Economic Evaluation (Part B)." Canadian Medical Association Journal **130**(12): 1542-1549.

Desmeules, M, D Schaubel, SS Fenton, and Y Mao. (1995). "New and Prevalent Patients with End-Stage Renal Disease in Canada. A Portrait of the Year 2000." American Society for Artificial Internal Organs Journal **41**(2): 230-3.

Dever, GEA. (1984). Epidemiology in Health Services Management. Rockville, Maryland: Aspen Publishers.

Donaldson, C and KM Narayan. (1998). "The Cost of Diabetes. A Useful Statistic?" Diabetes Care **21**(8): 1370-1.

Drummond, M, B O'Brien, G Stoddart, and G Torrance. (1997). Methods for Economic Evaluation of Health Care Programs. Oxford: Oxford University Press.

Drummond, MF and TO Jefferson. (1996). "Guidelines for Authors and Peer Reviewers of Economic Submissions to the British Medical Journal." British Medical Journal **313**(7052): 275-283.

Duchesne, D, P Tully, B Thomas, and R Bourbeau. (2002). Life Tables - Canada, Provinces and Territories 1995-1997. Ottawa: Statistics Canada.

Evans, RG, ML Barer, C Hertzman, GM Anderson, IR Pulcins, and J Lomas. (1989). "The Long Good-Bye: The Great Transformation of the British Columbia Hospital System." Health Services Research **24**(4): 435-59.

Evans, RG, KM McGrail, SG Morgan, ML Barer, and C Hertzman. (2001). "Apocalypse No: Population Aging and the Future of Health Care Systems." Canadian Journal of Aging **20**(suppl 1): 160-191.

Evans, RW. (1990). "Quality of Life Assessment and the Treatment of End Stage Renal Disease." Transplantion Reviews **4**: 28-51.

Evans, RW, D Manninen, L Garrison, G Hart, C Blagg, R Gutman, A Hull, and E Lowrie. (1985). "The Quality of Life of Patients with End-Stage Renal Disease." New England Journal of Medicine **13**: 200-9.

Fenton, SS, M Desmeules, JR Jeffery, and JL Corman. (1993). "Dialysis Therapy among Elderly Patients; Data from the Canadian Organ Replacement Register, 1981-1991." Advances in Peritoneal Dialysis **9**: 124-9.

Fored, CM, E Ejerblad, JP Fryzek, M Lambe, P Lindblad, O Nyren, and CG Elinder. (2003). "Socio-Economic Status and Chronic Renal Failure: A Population-Based Case-Control Study in Sweden." Nephrology Dialysis Transplantation **18**(1): 82-8.

Friedlaender, M. (2002). "The Right to Sell or Buy a Kidney: Are We Failing Our Patients?" Lancet **359**(9310): 971-3.

Fyke, KJ. (2001). Caring for Medicare: Sustaining a Quality System. Regina: Commission on Medicare.

Gafni, A and S Birch. (1997). "QALYs and HYEs: Spotting the Differences." Journal of Health Economics **16**(5): 601-8.

Gerdtham, U-G. (1993). "The Impact of Aging on Health Care Expenditure in Sweden." Health Policy **24**(1): 1-8.

Getzen, TG. (1992). "Population Aging and the Growth of Health Expenditures." Journal of Gerontology **47**(3): S98-S104.

Gilks, W. (1998). Markov Chain Monte Carlo. Encyclopedia of Biostatistics. P Armitage and T Colton. New York, John Wiley and Sons: 2415-2423.

Gilks, W, S Richardson, and D Spiegelhalter. (1996). Introducing Markov Chain Monte Carlo. Markov Chain Monte Carlo in Practice. W Gilks, S Richardson and D Spiegelhalter. London, Chapman & Hall: 1-16.

Gjertson, DW and JM Cecka. (2000). "Living Unrelated Donor Kidney Transplantation." Kidney International **58**(2): 491-9.

Goeree, R, J Manalich, P Grootendorst, ML Beecroft, and DN Churchill. (1995). "Cost Analysis of Dialysis Treatments for End-Stage Renal Disease (ESRD)." Clinical and Investigative Medicine **18**(6): 455-64.

Goeree, R, BJ O'Brien, G Blackhouse, K Agro, and P Goering. (1999a). "The Valuation of Productivity Costs Due to Premature Mortality: A Comparison of the Human-Capital and Friction-Cost Methods for Schizophrenia." Canadian Journal of Psychiatry **44**(5): 455-63.

Goeree, R, BJ O'Brien, P Goering, G Blackhouse, K Agro, A Rhodes, and J Watson. (1999b). "The Economic Burden of Schizophrenia in Canada." Canadian Journal of Psychiatry **44**(5): 464-72.

Gokal, R, M Figueras, A Ollé, J Rovira, and X Badia. (1999). "Outcomes in Peritoneal Dialysis and Haemodialysis - a Comparative Assessment of Survival and Quality of Life." Nephrology, Dialysis, Transplantation **14**(Suppl. 6): 24-30.

Government of British Columbia. (2001). Patients First: Renewal and Reform of British Columbia's Health Care System, Government of British Columbia. www.legis.gov.bc.ca/CMT. Accessed in 2002.

Government of New Brunswick. (2002). Health Renewal - a Discussion Paper, Government of New Brunswick. www.gnb.ca/op_cpm. Accessed in 2002.

Grover, SA, L Coupal, H Zowall, R Rajan, J Trachtenberg, M Elhilali, M Chetner, and L Goldenberg. (2000). "The Economic Burden of Prostate Cancer in Canada: Forecasts from the Montreal Prostate Cancer Model." Canadian Medical Association Journal **162**(7): 987-92.

Gutch, CF, MH Stoner, and AL Corea. (1999). Review of Hemodialysis for Nurses and Dialysis Personnel. St. Louis: Harcourt.

Guttman, M, P Slaughter, M Theriault, D DeBoer, and C Naylor. (2003). "Burden of Parkinsonism: A Population-Based Study." Movement Disorders **18**(3): 313-9.

Guttmann, A and RD Guttmann. (1993). "Attitudes of Healthcare Professionals and the Public Towards the Sale of Kidneys for Transplantation." Journal of Medical Ethics **19**(3): 148-53.

Hanvelt, RA, NS Ruedy, RS Hogg, S Strathdee, JS Montaner, MV O'Shaughnessy, and MT Schechter. (1994). "Indirect Costs of HIV/AIDS Mortality in Canada." AIDS **8**(10): F7-11.

Harris, TT, CM Thomas, MN Wicks, MS Faulkner, and DK Hathaway. (2000). "Subjective Burden in Young and Older African-American Caregivers of Patients with End Stage Renal Disease Awaiting Transplant." Nephrology Nursing Journal **27**(4): 383-91.

Health Canada. (1999a). Diabetes in Canada: National Statistics and Opportunities for Improved Surveillance, Prevention, and Control. Ottawa: Minister of Public Works and Government Services.

Health Canada. (1999b). National Diabetes Surveillance System, Health Canada. http://www.hc-sc.gc.ca/english/media/releases/1999/99135ebk1.htm. Accessed in 2002.

Health Canada. (2002a). Healthy Canadians: A Federal Report on Comparable Health Indicators 2002. Ottawa: Health Canada.

Health Canada. (2002b). Science Advisory Board Executive Summary for SAB Meeting on February 19-20, 2002 on the Canadian Council for Donation and Transplantation (CCDT) and Health Canada's Organ and Tissue Donation Public Awareness Strategy, Health Canada. http://www.hc-sc.gc.ca/sab-ccs/feb2002_exec_sum_otd_e.html. Accessed in 2004.

Health Canada. (2003). Reports: Organ and Tissue Donations: Canadian Public Awareness, Knowledge and Attitudes, Environics Research for Health Canada. http://www.hc-sc.gc.ca/english/socialmarketing/marketing_research/organ.html#2. Accessed in 2004.

Health Canada. (n.d.). FAQs About Organ and Tissue Donation, Health Canada. www.hc-sc.gc.ca/english/organandtissue/facts_faqs/index_faq.html. Accessed in 2002.

Health Canada Medical Services Branch. (1997). Diabetes among First Nations People: Information from the 1991 Aboriginal Peoples Survey Carried out by Statistics Canada. Ottawa: Government of Canada.

Henderson, AJ, MA Landolt, MF McDonald, WM Barrable, JG Soos, W Gourlay, CJ Allison, and DN Landsberg. (2003). "The Living Anonymous Kidney Donor: Lunatic or Saint?" American Journal of Transplantation **3**(2): 203-13.

Henderson, LW. (2000). "Future Developments in the Treatment of End-Stage Renal Disease: A North American Perspective." American Journal of Kidney Disease **35**(4 Suppl 1): S106-16.

Hicks, V, G Fortin, and G Ballinger. (2001). Price Indexes Used in National Health Expenditures. Ottawa: CIHI.

Hirth, RA, ME Chernew, MN Turenne, MV Pauly, SM Orzol, and PJ Held. (2003). "Chronic Illness, Treatment Choice and Workforce Participation." International Journal of Health Care Finance and Economics **3**(3): 167-81.

Holt, AW, GK Hodgeman, AE Vedig, and PE Heard. (1999). "Organ Donor Index: A Benchmark for Comparing Hospital Organ Donor Rates." Medical Journal of Australia **170**(10): 479-81.

Hörl, WH, F de Alvaro, and PF Williams. (1999). "Healthcare Systems and End-Stage Renal Disease (ESRD) Therapies--an International Review: Access to ESRD Treatments." Nephrology, Dialysis, Transplantation **6**: 10-5.

Hornberger, JC, AM Garber, and JR Jeffery. (1997). "Mortality, Hospital Admissions, and Medical Costs of End-Stage Renal Disease in the United States and Manitoba, Canada." Medical Care **35**(7): 686-700.

Hutton, G. (2000). Considerations in Evaluating the Cost Effectiveness of Environmental Health Interventions. Geneva: World Health Organization.

Hutubessy, RC, MW van Tulder, H Vondeling, and LM Bouter. (1999). "Indirect Costs of Back Pain in the Netherlands: A Comparison of the Human Capital Method with the Friction Cost Method." Pain **80**(1-2): 201-7.

Inskip, H, V Beral, and P Fraser. (1983). "Methods for Age-Adjustment of Rates." Statistics in Medicine **2**(4): 455-466.

Institute of Health Economics. (2000). A National List of Provincial Costs for Health Care: Canada 1997/98. Edmonton: Institute of Health Economics.

Ivinson, AJ and FH Bach. (2002). "The Xenotransplantation Question: Public Consultation Is an Important Part of the Answer." Canadian Medical Association Journal **167**(1): 42.

Jasper, JD, CA Nickerson, PA Ubel, and DA Asch. (2004). "Altruism, Incentives, and Organ Donation: Attitudes of the Transplant Community." Medical Care **42**(4): 378-86.

Jassal, S, M Krahn, G Naglie, J Zaltzman, J Roscoe, E Cole, and D Redelmeier. (2003). "Kidney Transplantation in the Elderly: A Decision Analysis." Journal of the American Society of Nephrology **14**(1): 187-96.

Jassal, SV, JE Brissenden, A Raisbeck, and JM Roscoe. (1998). "Comparative Cost-Analysis of Two Different Chronic Care Facilities for End-Stage Renal Disease Patients." Geriatric Nephrology and Urology **8**(2): 69-76.

Johannesson, M and G Karlsson. (1997). "The Friction Cost Method: A Comment." Journal of Health Economics **16**(2): 249-55; discussion 257-9.

Johansen, H, K Chagani, S Lessard, and C Nair. (1996). "Person-Based Information from Canadian Hospital Discharge Data." Leadership in Health Services **5**(5): 27-32.

Joint Commission on Accreditation of Healthcare Organizations. (2004). Health Care at the Crossroads: Strategies for Narrowing the Organ Donation Gap and Protecting Patients. Oakbrook Terrace, IL: JCAHO.

Kaiserman, MJ. (1997). "The Cost of Smoking in Canada, 1991." Chronic Diseases in Canada **18**(1): 13-9.

Kaminota, M. (2001). "Cost-Effectiveness Analysis of Dialysis and Kidney Transplants in Japan." Keio Journal of Medicine **50**(2): 100-8.

Kanji, GK. (1999). 100 Statistical Tests. London: SAGE Publications.

Kaserman, DL and AH Barnett. (1991). "An Economic Analysis of Transplant Organs: A Comment and Extension." Atlantic Economic Journal **19**(2): 57-63.

Katzmarzyk, PT, N Gledhill, and RJ Shephard. (2000). "The Economic Burden of Physical Inactivity in Canada." Canadian Medical Association Journal **163**(11): 1435-40.

Katzmarzyk, PT and I Janssen. (2004). "The Economic Costs Associated with Physical Inactivity and Obesity in Canada: An Update." Canadian Journal of Applied Physiology **29**(1): 90-115.

Kayler, LK, CS Rasmussen, DM Dykstra, AO Ojo, FK Port, RA Wolfe, and RM Merion. (2003). "Gender Imbalance and Outcomes in Living Donor Renal Transplantation in the United States." American Journal of Transplantation **3**(4): 452-8.

Kennedy, P. (1992). A Guide to Econometrics. Cambridge, Massachusetts: MIT Press.

Keshaviah, P, AJ Collins, JZ Ma, DN Churchill, and KE Thorpe. (2002). "Survival Comparison between Hemodialysis and Peritoneal Dialysis Based on Matched Doses of Delivered Therapy." Journal of the American Society of Nephrology **13**(Suppl. 1): 48-52.

Khan, IH. (1998). "Comorbidity: The Major Challenge for Survival and Quality of Life in End-Stage Renal Disease." Nephrology, Dialysis, Transplantation **1**: 76-9.

Kiberd, BA and CM Clase. (2002). "Cumulative Risk for Developing End-Stage Renal Disease in the US Population." Journal of the American Society of Nephrology **13**(6): 1635-44.

Kievit, J, A Oomen, E Heineman, and G Kootstra. (1997). "The Importance of Non-Heart-Beating Donor Kidneys in Reducing the Organ Shortage." EDTNA/ERCA Journal **23**(2): 11-3.

Klefter, R and B Nielsen. (2002). "Savings in Dialysis Treatment?" Artificial Organs **26**(1): 49-54.

Knickman, J and E Snell. (2002). "The 2030 Problem: Caring for Aging Baby Boomers." Health Services Research **37**(4): 849-84.

Koopmanschap, MA, FF Rutten, BM van Ineveld, and L van Roijen. (1995). "The Friction Cost Method for Measuring Indirect Costs of Disease." Journal of Health Economics **14**(2): 171-89.

Korn, EL and BI Graubard. (1999). Analysis of Health Surveys. New York: John Wiley & Sons, Inc.

Krahn, MD, C Berka, P Langlois, and AS Detsky. (1996). "Direct and Indirect Costs of Asthma in Canada, 1990." Canadian Medical Association Journal **154**(6): 821-31.

Krakauer, H. (1993). A Forecasting Model for the Assessment of Medical Technologies: End-Stage Renal Disease. Forecasting the Health of Elderly Populations. KG Manton, BH Singer and RM Suzman. New York, Springer-Verlag.

Krishnan, M, CE Lok, and SV Jassal. (2002). "Epidemiology and Demographic Aspects of Treated End-Stage Renal Disease in the Elderly." Seminars in Dialysis **15**(2): 79-83.

Kuchler, F and E Golan. (1999). Assigning Values to Life: Comparing Methods for Valuing Health Risks; Agricultural Economics Report No. 784. Washington: US Department of Agriculture.

Lameire, N and W Van Biesen. (1999). "The Pattern of Referral of Patients with End-Stage Renal Disease to the Nephrologist--a European Survey." Nephrology, Dialysis, Transplantation **6**: 16-23.

Landolt, MA, AJ Henderson, WM Barrable, SD Greenwood, MF McDonald, JG Soos, and DN Landsberg. (2001). "Living Anonymous Kidney Donation: What Does the Public Think?" Transplantation **71**(11): 1690-6.

Lang, TA and M Secic. (1997). How to Report Statistics in Medicine: Annotated Guidelines for Authors, Editors, and Reviewers. Philadelphia: American College of Physicians.

Laupacis, A, P Keown, N Pus, H Krueger, B Ferguson, C Wong, and N Muirhead. (1996). "A Study of the Quality of Life and Cost-Utility of Renal Transplantation." Kidney International **50**(1): 235-42.

Law, B, C Fitzsimon, L Ford-Jones, N MacDonald, P Dery, W Vaudry, E Mills, S Halperin, A Michaliszyn, and M Riviere. (1999a). "Cost of Chickenpox in Canada: Part I. Cost of Uncomplicated Cases." Pediatrics **104**(1 Pt 1): 1-6.

Law, B, C Fitzsimon, L Ford-Jones, J McCormick, and M Riviere. (1999b). "Cost of Chickenpox in Canada: Part II. Cost of Complicated Cases and Total Economic Impact. The Immunization Monitoring Program-Active (Impact)." Pediatrics **104**(1 Pt 1): 7-14.

Lazaro, A. (2002). "Theoretical Arguments for the Discounting of Health Consequences: Where Do We Go from Here?" Pharmacoeconomics **20**(14): 943-961.

Lefebvre, LA, Z Zsigmond, and MS Decereaux. (1979). A Prognosis for Hospitals: The Effects of Population Change on the Need for Hospital Space, 1967-2031. Ottawa: Statistics Canada.

Leidl, R. (1992). "Health Economic Issues Relevant to Countries with Aging Populations." World Health Statistics Quarterly **45**(1): 95-108.

Levine, DZ. (2000). "Nephrology Ethics Forum: Kidney Vending: "Yes!" or "No!"" American Journal of Kidney Disease **35**(5).

Locker, AR, JL Dorland, L Hartling, and W Pickett. (2003). "Economic Burden of Agricultural Machinery Injuries in Ontario, 1985 to 1996." Journal of Rural Health **19**(3): 285-91.

Longobardi, T, P Jacobs, L Wu, and C Bernstein. (2003). "Work Losses Related to Inflammatory Bowel Disease in Canada: Results from a National Population Health Survey." American Journal of Gastroenterology **98**(4): 844-9.

Lowance, DC. (2002). "Withholding and Withdrawal of Dialysis in the Elderly." Seminars in Dialysis **15**(2): 88-90.

Lysaght, MJ. (2002). "Maintenance Dialysis Population Dynamics: Current Trends and Long-Term Implications." Journal of the American Society of Nephrology **13**(1): S37-40.

Lysaght, MJ and JA O'Loughlin. (2000). "Demographic Scope and Economic Magnitude of Contemporary Organ Replacement Therapies." American Society for Artificial Internal Organs Journal **46**(5): 515-21.

Maetzel, A, LC Li, J Pencharz, G Tomlinson, and C Bombardier. (2004). "The Economic Burden Associated with Osteoarthritis, Rheumatoid Arthritis, and Hypertension: A Comparative Study." Annals of Rheumatic Diseases **63**(4): 395-401.

Magoha, GA and ZW Ngumi. (2001). "Renal Transplantation During the Twentieth Century: A Review." East African Medical Journal **78**(6): 317-21.

Mallick, NP. (1997). "The Costs of Renal Services in Britain." Nephrology, Dialysis, Transplantation **12**(Suppl. 1): 25-28.

Manitoba Health. (1998). Diabetes: A Manitoba Strategy, Manitoba Health. http://www.gov.mb.ca/health/publichealth/diabetes/strategy.html. Accessed in 2002.

Mankiw, GN and W Scarth. (1995). Macroeconomics. New York: Worth Publishers.

Manns, B, JA Johnson, K Taub, G Mortis, WA Ghali, and C Donaldson. (2002). Quality of Life in Patients with End-Stage Renal Disease over Time: The Impact of Dialysis Modality and Other Important Determinants. Edmonton: Institute of Health Economics.

Manns, B, D Meltzer, K Taub, and C Donaldson. (2003). "Illustrating the Impact of Including Future Costs in Economic Evaluations: An Application to End-Stage Renal Disease Care." Health Economics **12**(11): 949-58.

Manns, BJ, KJ Taub, and C Donaldson. (2000). "Economic Evaluation and End-Stage Renal Disease: From Basics to Bedside." American Journal of Kidney Disease **36**(1): 12-28.

Manton, KG, BH Singer, and RM Suzman. (1993). The Scientific and Policy Needs for Improved Health Forecasting Models for Elderly Populations. Forecasting the Health of Elderly Populations. KG Manton, BH Singer and RM Suzman. New York, Springer-Verlag.

Martin, M. (1996). "As Number of Patients Grows, So Do Critical Problems Facing MDs Who Provide Dialysis." Canadian Medical Association Journal **154**(6): 931-3.

Martinez, JM, JS Lopez, A Martin, MJ Martin, B Scandroglio, and JM Martin. (2001). "Organ Donation and Family Decision-Making within the Spanish Donation System." Social Science and Medicine **53**(4): 405-21.

Matas, AJ, ST Bartlett, AB Leichtman, and FL Delmonico. (2003). "Morbidity and Mortality after Living Kidney Donation, 1999-2001: Survey of United States Transplant Centers." American Journal of Transplantation **3**(7): 830-4.

Matas, AJ and M Schnitzler. (2004). "Payment for Living Donor (Vendor) Kidneys: A Cost-Effectiveness Analysis." American Journal of Transplantation **4**(2): 216-21.

Matesanz, R. (2001). "A Decade of Continuous Improvement in Cadaveric Organ Donation: The Spanish Model." Nefrologia **21 Suppl 5**: 59-67.

Matesanz, R. (2003). "Factors Influencing the Adaptation of the Spanish Model of Organ Donation." Transplant International **16**(10): 736-41.

McAlister, VC, K Badovinac, SS Fenton, and PD Greig. (2003). "Transplantation in Canada: Review of the Last Decade from the Canadian Organ Replacement Register." Clinical Transplation: 101-8.

McFarlane, PA, A Pierratos, and DA Redelmeier. (2002). "Cost Savings of Home Nocturnal Versus Conventional in-Center Hemodialysis." Kidney International **62**(6): 2216-22.

McGill University Health Centre. (1998). 100 True Life Stories of Courage from Québec to Inspire the Rest of Canada. www.muhc.mcgill.ca/Releases/p090698.html. Accessed in 2002.

McGrail, KM, RG Evans, ML Barer, SB Sheps, C Hertzman, and A Kazanjian. (1998). The Quick and the Dead: The Utilization of Hospital Services in British Columbia: 1969 to 1995/96. Vancouver: Centre for Health Services and Policy Research, University of British Columbia.

McKenzie, JK, AH Moss, TG Feest, CB Stocking, and M Siegler. (1998). "Dialysis Decision Making in Canada, the United Kingdom, and the United States." American Journal of Kidney Disease **31**(1): 12-8.

Mehrotra, R and KD Nolph. (2001). "Peritoneal Dialysis Should Be the First Choice of Initial Renal Replacement Therapy for More Patients with End-

Stage Renal Disease." American Society for Artificial Internal Organs Journal **47**(4): 309-11.

Mendelssohn, D and for the Professional and Public Policy Committee of the Canadian Society of Nephrology. (1997). "Policy Statement: Principles of End Stage Renal Disease Care." Annals of the Royal Society of Physicians and Surgeons of Canada **30**: 271-273.

Menec, VH, L MacWilliam, R-A Soodeen, and L Mitchell. (2002). The Health and Health Care Use of Manitoba's Seniors: Have They Changed over Time? Winnipeg: Manitoba Centre for Health Policy.

Miller, TR. (1995). "Costs Associated with Gunshot Wounds in Canada in 1991." Canadian Medical Association Journal **153**(9): 1261-8.

Minister's Task Force on Kidney Donation. (1985). Organ Donation in the Eighties: The Minister's Task Force on Kidney Donation. Toronto: Ontario Ministry of Health.

Mishan, EJ. (1971). "Evaluation of Life and Limb: A Theoretical Approach." Journal of Political Economy **79**(4): 687-705.

Molzahn, AE and JF Kikuchi. (1998). "Children and Adolescents of Parents Undergoing Dialysis Therapy: Their Reported Quality of Life." American Nephrology Nurses' Association Journal **25**(4): 411-7.

Molzahn, AE, R Starzomski, and J McCormick. (2003). "The Supply of Organs for Transplantation: Issues and Challenges." Nephrology Nursing Journal **30**(1): 17-26; quiz 27-8.

Mooney, G and S Jan. (1997). "Vertical Equity: Weighting Outcomes? Or Establishing Procedures?" Health Policy **39**(1): 79-87.

Moore, R, Y Mao, J Zhang, and K Clarke. (1997a). Economic Burden of Illness in Canada, 1993. Ottawa: Health Canada.

Moore, R, Y Mao, J Zhang, and K Clarke. (1997b). "Economic Burden of Illness in Canada, 1993. Executive Summary and Recommendations." Chronic Diseases in Canada **18**(2): 95-6.

Morton, J, GA Blok, C Reid, J van Dalen, and M Morley. (2000). "The European Donor Hospital Education Programme (EDHEP): Enhancing

Communication Skills with Bereaved Relatives." Anaesthesia and Intensive Care **28**(2): 184-90.

Motohashi, Y and S Nishi. (1991). "Prediction of End-Stage Renal Disease Patient Population in Japan by System Dynamics Model." International Journal of Epidemiology **20**(4): 1032-6.

Muir, T and M Zegarac. (2001). "Societal Costs of Exposure to Toxic Substances: Economic and Health Costs of Four Case Studies That Are Candidates for Environmental Causation." Environmental Health Perspectives **109 Suppl 6**: 885-903.

Murphy, SW, RN Foley, BJ Barrett, GM Kent, J Morgan, P Barre, P Campbell, A Fine, MB Goldstein, SP Handa, KK Jindal, A Levin, H Mandin, N Muirhead, RM Richardson, and PS Parfrey. (2000). "Comparative Mortality of Hemodialysis and Peritoneal Dialysis in Canada." Kidney International **57**(4): 1720-6.

Murray, CJL, JA Salomon, and C Mathers. (n.d.). A Critical Examination of Summary Measures of Population Health, World Health Organization. http://www3.who.int/whosis/discussion_papers/discussion_papers.cfm? Accessed in 2003.

National Cancer Institute of Canada. (2001). Canadian Cancer Statistics 2001, National Cancer Institute of Canada. http://66.59.133.166/stats/tables/table.htm. Accessed in 2002.

National Coordinating Committee for Organ and Tissue Donation Distribution and Transplantation. (1999). A Coordinated and Comprehensive Donation and Transplantation Strategy for Canada: A Report from the National Coordinating Committee for Organ and Tissue Donation, Distribution, and Transplantation, National Coordinating Committee for Organ and Tissue Donation, Distribution, and Transplantation. http://www.hc-sc.gc.ca/english/protection/biologics_genetics/organ_strategy/pdf/strategy.pdf. Accessed in 2002.

National Forum on Xenotransplantation. (1999). Viewpoint: A Summary of Recommendations from the National Forum on Xenotransplantation, Therapeutic Products Programme, Health Canada. www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/bgtd/forumsummary_e.html. Accessed in 2002.

National Health Strategy of the Department for Health Housing and Community Services (1993). Cost of Illness Studies: Their Strenths and

Limitations. Pathways to Better Health. D Nutbeam. Canberra, Commonwealth of Australia.

Nelson, EW, JE Childress, J Perryman, V Robards, A Rowan, MS Seely, S Sterioff, and M Rovelli Swanson. (1993). Financial Incentives for Organ Donation. A Report of the Payment Subcommittee, United Network for Organ Sharing Ethics Committee. Richmond, Virginia: United Network for Organ Sharing.

Nissenson, AR and RA Rettig. (1999). "Medicare's End-Stage Renal Disease Program. Current Status and Future Prospects." Health Affairs **18**(1): 161-79

Noorani, HZ and L McGahan. (1999). Criteria for Selection of Adult Recipients for Heart, Cadaveric Kidney, and Liver Transplantation. Ottawa. Canadian Coordinating Office for Health Technology Assessment.

O'Brien, JA, I Caro, D Getsios, and JJ Caro. (2001). "Diabetes in Canada. Direct Medical Costs of Major Macrovascular Complications." Value Health **4**(3): 258-65

Ojo, AO, FK Port, RA Wolfe, EA Mauger, L Williams, and DP Berling. (1994). "Comparative Mortality Risks of Chronic Dialysis and Cadaveric Transplantation in Black End-Stage Renal Disease Patients." American Journal of Kidney Disease **24**(1): 59-64.

Ontario Ministry of Health and Long-Term Care. (2003). Schedule of Benefits for Physician Services under the Health Insurance Act: Amended September 1, 2003, Ontario Ministry of Health and Long-Term Care. http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/J diagt h.pdf. Accessed in 2004.

Organisation for Economic Cooperation and Development. (2004). OECD Productivity Database, OECD. http://www.oecd.org/dataoecd/30/14/29861140.xls. Accessed in 2004.

Organization for Economic Cooperation and Development. (2003). OECD Health Data 2003, OECD.Accessed in 2004.

Ostbye, T and E Crosse. (1994). "Net Economic Costs of Dementia in Canada." Canadian Medical Association Journal **151**(10): 1457-64.

Oz, MC, AR Kherani, A Rowe, L Roels, C Crandall, L Tomatis, and JB Young. (2003). "How to Improve Organ Donation. Results of the ISHLT/FACT Poll." Journal of Heart and Lung Transplantation **22**(4): 389-410.

Pace, KT, SJ Dyer, V Phan, RJ Stewart, RJ Honey, EC Poulin, CM Schlachta, and J Mamazza. (2003a). "Laparoscopic Versus Open Donor Nephrectomy " Surgical Endoscopy **17**(1): 134-42.

Pace, KT, SJ Dyer, RJ Stewart, RJ Honey, EC Poulin, CM Schlachta, and J Mamazza. (2003b). "Health-Related Quality of Life after Laparoscopic and Open Nephrectomy " Surgical Endoscopy **17**(1): 143-52.

Parsonage, M and H Neuburger (1992). "Discounting and Health Benefits." Journal of Health Economics **1**(1): 71-76.

Pascual, M, T Theruvath, T Kawai, N Tolkoff-Rubin, and AB Cosimi. (2002). "Strategies to Improve Long-Term Outcomes after Renal Transplantation." New England Journal of Medicine **346**(8): 580-90.

Peeters, P, D Rublee, PM Just, and A Joseph. (2000). "Analysis and Interpretation of Cost Data in Dialysis: Review of the Western European Literature." Health Policy **54**. 209-27

Pindyck, RS and DL Rubinfeld. (1992). Microeconomics. New York: Macmillan Publishing Company

Policy Research Division of the Strategic Policy Directorate in the Population and Public Health Branch of Health Canada. (2002). Economic Burden of Illness in Canada, 1998. Ottawa. Health Canada.

Population Division of the Department of Economic and Social Affairs at the United Nations Secretariat. (1999). The World at Six Billion, United Nations Secretariat.
http://www.un.org/esa/population/publications/sixbillion/sixbillion.htm. Accessed in 2004.

Port, FK. (1993). "Worldwide Demographics and Future Trends in End-Stage Renal Disease." Kidney International Supplement **41**(7): S4-7

Port, FK. (1995). "End-Stage Renal Disease: Magnitude of the Problem, Prognosis of Future Trends and Possible Solutions." Kidney International Supplement **50**(6): S3-6.

Porter, E. (1998). "Pre-Dialysis: Initiatives in Canada." Nephrology News and Issues **12**(11): 15-6.

Powe, NR. (2001). "Patients, Populations and Policy· Patient Outcomes in Chronic Kidney Disease." Transactions of the American Clinical and Climatological Association. **112** 224-32.

Premier's Advisory Council on Health. (2001). A Framework for Reform, Premier's Advisory Council on Health. www.premiersadvisory.com. Accessed in 2002.

Prichard, S. (1996). "Socioeconomic and Health-Care Policies and Peritoneal Dialysis." Peritoneal Dialysis International **16**(1): S378-80.

Prichard, SS. (1997). "The Costs of Dialysis in Canada." Nephrology, Dialysis, Transplantation **1** 22-4.

Pritchard, C and M Schulper (2002). Productivity Costs: Principles and Practice in Economic Evaluation, Office of Health Economics. http://www.ohe.org/productivity_costs.htm. Accessed in 2003

Provincial Health Council. (2000). Core Clinical Services Identified by Nova Scotians: A Preliminary Report on Essential Health Services, Provincial Health Council. http://www.healthcouncil.ns.ca/report.pdf. Accessed in 2002.

Public Advisory Group on Xenotransplantation. (2001). Animal-to-Human Transplantation. Should Canada Proceed? Ottawa. Canadian Public Health Association.

Rabbat, CG, KE Thorpe, JD Russell, and DN Churchill. (2000). "Comparison of Mortality Risk for Dialysis Patients and Cadaveric First Renal Transplant Recipients in Ontario, Canada." Journal of the American Society of Nephrology **11**(5): 917-22.

Rae, A, P Craig, and G Miles. (1972). "Home Dialysis: Its Costs and Problems." Canadian Medical Association Journal **106**(12): 1305 passim.

Rao, VK. (2002). "Kidney Transplantation in Older Patients: Benefits and Risks." Drugs and Aging **19**(2): 79-84.

Rebello, P, F Ortega, JM Baltar, C Díaz-Corte, RA Navascués, M Naves, A Ureña, X Badía, F Alvarez-Ude, and J Alvarez-Grande. (1998). "Health-

Related Quality of Life (HRQOL) in End Stage Renal Disease (ESRD) Patients over 65 Years." Geriatric Nephrology and Urology **8**: 85-94.

Reikes, ST (2000). "Trends in End-Stage Renal Disease: Epidemiology, Morbidity, and Mortality " Postgraduate Medicine **108**(1): 124-6.

Rice, DP (1966). Estimating the Cost-of-Illness. Rockville, MD: US Department of Health, Education, and Welfare.

Rice, DP (1994). "Cost-of-Illness Studies: Fact or Fiction?" Lancet **344**(8936): 1519-20.

Rice, DP (2000). "Cost of Illness Studies. What Is Good About Them?" Inj Prev **6**(3): 177-9

Rice, DP, TA Hodgson, and AN Kopstein. (1985). "The Economic Costs of Illness: A Replication and Update." Health Care Financing Review **7**(1): 61-80.

Riegelman, RK. (2000). Studying a Study and Testing a Test: How to Read the Medical Evidence. Philadelphia: Lippincott Williams & Wilkins.

Riker, RR and BW White. (1995). "The Effect of Physician Education on the Rates of Donation Request and Tissue Donation." Transplantation **59**(6): 880-4.

Rocheleau, CA. (2001). "Increasing Family Consent for Organ Donation. Findings and Challenges." Progress in Transplantation **11**(3): 194-200.

Rockwood, K, M Brown, H Merry, I Sketris, and J Fisk. (2002). "Societal Costs of Vascular Cognitive Impairment in Older Adults." Stroke **33**(6): 1605-9

Rosenberg, M. (2000). The Effects of Population Aging on the Canadian Health Care System, SEDAP Research Paper No. 14, SEDAP, McMaster University http://socserv2.mcmaster.ca/sedap/ Accessed in 2002.

Rowinski, W and J Walaszewski. (2002). "Ethical and Societal Problems in Organ Transplantation." Annals of Transplantation **7**(4): 7-9

SAS Institute. (1999). Introduction to Forecasting Methods in SAS/ETS User's Guide, SAS Insitute. http://www.uwm.edu/IMT/Computing/sasdoc8/sashtml/ets/chap12/sect3.htm. Accessed in 2002.

Schaubel, D, M Desmeules, Y Mao, J Jeffery, and S Fenton. (1995). "Survival Experience among Elderly End-Stage Renal Disease Patients. A Controlled Comparison of Transplantation and Dialysis." Transplantation **60**(12): 1389-94.

Schaubel, DE, JR Jeffery, Y Mao, R Semenciw, K Yeates, and SS Fenton. (2002). "Trends in Mortality and Graft Failure for Renal Transplant Patients." Canadian Medical Association Journal **167**(2): 137-142.

Schaubel, DE, HI Morrison, M Desmeules, D Parsons, and SS Fenton. (1998a). "End-Stage Renal Disease Projections for Canada to 2005 Using Poisson and Markov Models." International Journal of Epidemiology **27**(2): 274-81.

Schaubel, DE, HI Morrison, M Desmeules, DA Parsons, and SS Fenton. (1999). "End-Stage Renal Disease in Canada: Prevalence Projections to 2005." Canadian Medical Association Journal **160**(11): 1557-63.

Schaubel, DE, HI Morrison, and SS Fenton. (1998b). "Comparing Mortality Rates on CAPD/CCPD and Hemodialysis. The Canadian Experience: Fact or Fiction?" Peritoneal Dialysis International **18**(5): 478-84.

Schwindt, R and A Vining. (1998). "Proposal for a Mutual Insurance Pool for Transplant Organs." Journal of Health Politics, Policy, and Law **23**(5).

Sekkarie, M, M Cosma, and D Mendelssohn. (2001). "Nonreferral and Nonacceptance to Dialysis by Primary Care Physicians and Nephrologists in Canada and the United States." American Journal of Kidney Disease **38**(1): 36-41.

Sells, R. (1994). Transplants. Principles of Health Care Ethics. R Gillon. London, John Wiley & Sons: 1004-1025.

Sever, MS, R Kazancioglu, A Yildiz, A Turkmen, T Ecder, SM Kayacan, V Celik, S Sahin, AE Aydin, U Eldegez, and E Ark. (2001). "Outcome of Living Unrelated (Commercial) Renal Transplantation." Kidney International **60**(4): 1477-83.

Simmons, RG, CR Anderson, and LK Abress. (1990). "Quality of Life and Rehabilitation Differences among Four ESRD Therapy Groups." Scandinavian Journal of Urology and Nephrology **Suppl 131**: 7-22.

Single, E, L Robson, X Xie, and J Rehm. (1998). "The Economic Costs of Alcohol, Tobacco and Illicit Drugs in Canada, 1992." Addiction **93**(7): 991-1006.

SmartRisk. (2001). Economic Burden of Unintentional Injury in British Columbia, BC Injury Research and Prevention Unit. http://www.injuryresearch.bc.ca/Publications/Reports/Economic%20Burden%20Report.pdf. Accessed in 2004.

SmartRisk. (2003). The Economic Burden of Unintentional Injury in Atlantic Canada, Atlantic Network for Injury Prevention. http://www.anip.ca/COI/ATL_COI-rev.pdf. Accessed in 2004.

Smith, EKM. (1987). Renal Disease: A Conceptual Approach. New York: Churchill Livingstone.

Smith, SW, JE Kopfman, LL Lindsey, J Yoo, and K Morrison. (2004). "Encouraging Family Discussion on the Decision to Donate Organs: The Role of the Willingness to Communicate Scale." Health Communication **16**(3): 333-46.

Stack, AG and JM Messana. (2000). "Renal Replacement Therapy in the Elderly: Medical, Ethical, and Psychosocial Considerations." Advances in Renal Replacement Therapy **7**(1): 52-62.

Standing Senate Committee on Social Affairs, Science, and Technology. (2002). The Health of Canadians: The Federal Role, Senate of Canada. www.parl.gc.ca. Accessed in 2002.

Starzomski, R and A Hilton. (2000). "Patient and Family Adjustment to Kidney Transplantation with and without an Interim Period of Dialysis." Nephrology Nursing Journal **27**(1): 17-8.

Statistics Canada. (1999). Estimates of Labour Income, Monthy Estimates, Supplementary Income Rate. Ottawa: Statistics Canada.

Statistics Canada. (2002a). Canadian Community Health Survey: A First Look. www.statcan.ca/Daily/English/020508/d020508a.htm. Accessed in 2002.

Statistics Canada. (2002b). Diabetes by Age Group and Sex, Household Population Aged 12 and Older, Canada Excluding Territories, 1994/95-1998/99, Statistics Canada. www.statcan.ca/english/freepub/82-221-XIE/00502/tables/html/1241.htm. Accessed in 2002.

Statistics Canada. (2002c). Diabetes by Age Group and Sex, Household Population Aged 12 and over, Canada, 2000/01, Statistics Canada. www.statcan.ca/english/freepub/82-221-XIE/00502/tables/html/1245.htm. Accessed in 2002.

Statistics Canada. (2002d). Table 051-0001: Estimates of Population, by Age Group and Sex, Canada, Provinces and Territories, Statistics Canada. http://cansim2.statcan.ca/cgi-win/cnsmcgi.exe?Lang=E&RootDir=CII/&ResultTemplate=CII/CII___&Array_Pick=1&ArrayId=0510001. Accessed in 2002.

Statistics Canada. (2003). Table 102-0540 - Deaths, by Cause - Chapter XX: External Causes of Morbidity and Mortality (V01-Y98), Age Group and Sex, Canada, Annual (Number), Statistics Canada. http://www.statcan.ca/english/freepub/84-208-XIE/2001/tables.htm. Accessed in 2004.

Statistics Canada. (2004a). The Canadian Productivity Accounts - Data (Catalogue # 15-003-XIE). Ottawa: Statistics Canada.

Statistics Canada. (2004b). Consumer Price Index, Historical Summary (Catalogue # 62-001-XPB), Statistics Canada. http://www.statcan.ca/english/Pgdb/econ46.htm. Accessed in 2004.

Steiner, RW and B Gert. (2000). "Ethical Selection of Living Kidney Donors." American Journal of Kidney Disease **36**(4): 677-86.

Stephens, T and N Joubert. (2001). "The Economic Burden of Mental Health Problems in Canada." Chronic Diseases in Canada **22**(1): 18-23.

Stewart, DK, R Tate, G Finlayson, L MacWilliam, and NP Roos. (2002). Projecting Hospital Bed Needs for 2020. Winnipeg: Manitoba Centre for Health Policy.

Sutherland, FR. (1997). "Legislating Organ Donation: Problems with This Approach." Annals (Royal College of Physicians and Surgeons of Canada) **30**(1): 33-4.

Szava-Kovats, G and JA Johnson. (1997). A Review of Diabetes Cost of Illness Studies. Edmonton: Institute of Pharmaco-Economics.

Tawney, KW, PJ Tawney, and J Kovach. (2003). "Disablement and Rehabilitation in End-Stage Renal Disease." Seminars in Dialysis **16**(6): 447-52.

Taylor, M, P Greig, A Detsky, R McLeod, A Abdoh, and M Krahn. (2002). "Factors Associated with the High Cost of Liver Transplantation in Adults." Canadian Journal of Surgery **45**(6): 425-34.

To, T and K Wu. (1995). "Health Care Utilization and Disability of Migraine: The Ontario Health Survey." Canadian Journal of Public Health **86**(3): 195-9.

Torrance, GW. (1986). "Measurement of Health State Utilities for Economic Appraisal: A Review." Journal of Health Economics **5**(1): 1-30.

Trillium Gift of Life Network. (2003). Trillium Gift of Life Network Annual Report 2002-2003, Trillium Gift of Life Network. http://www.giftoflife.on.ca/tgln/101019%20Trillium%20AR%20Eng.pdf. Accessed in 2004.

US Renal Data System. (2000). USRDS 2000 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases.

Van Manen, JG, JC Korevaar, FW Dekker, EW Boeschoten, PM Bossuyt, and RT Krediet. (2002). "How to Adjust for Comorbidity in Survival Studies in ESRD Patients: A Comparison of Different Indices." American Journal of Kidney Disease **40**(1): 82-9.

Verble, M and J Worth. (1996). "The Case against More Public Education to Promote Organ Donation." Journal of Transplant Coordination **6**(4): 200-3.

Wall, R, J Rehm, B Fischer, B Brands, L Gliksman, J Stewart, W Medved, and J Blake. (2000). "Social Costs of Untreated Opioid Dependence." Journal of Urban Health **77**(4): 688-722.

Warshawsky, MJ. (1994). "Projections of Heath Care Expenditures as a Share of the GDP: Actuarial and Macroeconomic Approaches." Health Services Research **29**(3): 293-313.

Weinstein, M and W Stason. (1977). "Foundations of Cost-Effectiveness Analysis for Health and Medical Practices." New England Journal of Medicine **296**(13): 716-21.

West, R and G Burr. (2002). "Why Families Deny Consent to Organ Donation." Australian Critical Care **15**(1): 27-32.

Whiting, JF, RS Woodward, EY Zavala, DS Cohen, JE Martin, GG Singer, JA Lowell, MR First, DC Brennan, and MA Schnitzler. (2000).

"Economic Cost of Expanded Criteria Donors in Cadaveric Renal Transplantation: Analysis of Medicare Payments." Transplantation **70**(5): 755-60.

Wicks, M, E Milstead, D Hathaway, and C M. (1997). "Subjective Burden and Quality of Life in Family Caregivers of Patients with End Stage Renal Disease." American Nephrology Nurses' Association Journal **24**(5): 527-8, 531-8; discussion 539-40.

Wicks, MN, EJ Milstead, DK Hathaway, and M Cetingok. (1998). "Family Caregivers' Burden, Quality of Life, and Health Following Patients' Renal Transplantation." Journal of Transplant Coordination **8**(3): 170-6.

Wiebe, S, DR Bellhouse, C Fallahay, and M Eliasziw. (1999). "Burden of Epilepsy: The Ontario Health Survey." Canadian Journal of Neurological Science **26**(4): 263-70.

Wight, JP, L Edwards, J Brazier, S Walters, JN Payne, and CB Brown. (1998). "The SF36 as an Outcome Measure of Services for End Stage Renal Failure." Quality in Health Care **7**(4): 209-21.

Wigle, D, Y Mao, T Wong, and R Lane. (1991). "Economic Burden of Illness in Canada, 1986." Chronic Diseases in Canada **12**(Suppl 3).

Williams, A. (1999). "Calculating the Global Burden of Disease: Time for a Strategic Reappraisal?" Health Econ **8**(1): 1-8.

Wilson, R, M Godwin, R Seguin, P Burrows, P Caulfield, E Toffelmire, R Morton, P White, M Rogerson, G Eisele, and G Bont. (2001). "End-Stage Renal Disease: Factors Affecting Referral Decisions by Family Physicians in Canada, the United States, and Britain." American Journal of Kidney Disease **38**(1): 42-8.

Winkelmayer, WC, MC Weinstein, MA Mittleman, RJ Glynn, and JS Pliskin. (2002). "Health Economic Evaluations: The Special Case of End-Stage Renal Disease Treatment." Medical Decision Making **22**(5): 417-30.

World Health Organization Commission on Macroeconomics and Health. (2001). Investing in Health for Economic Development: Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization.

Wright Jr., J. (2002). "Alternative Interpretations of the Same Data: Flaws in the Process of Consulting the Canadian Public About Xenotransplantation Issues." Canadian Medical Association Journal **167**(1): 40-2.

Xie, X, J Rehm, E Single, L Robson, and J Paul. (1998a). "The Economic Costs of Alcohol Abuse in Ontario." Pharmacology Research **37**(3): 241-9.

Xie, X, J Rehm, E Single, L Robson, and J Paul. (1998b). "The Economic Costs of Illicit Drug Use in Ontario, 1992." Health Economics **7**(1): 81-5.

Xie, X, L Robson, E Single, J Rehm, and J Paul. (1999). "The Economic Consequences of Smoking in Ontario." Pharmacology Research **39**(3): 185-91.

Xue, JL, JZ Ma, TA Louis, and AJ Collins. (2001). "Forecast of the Number of Patients with End-Stage Renal Disease in the United States to the Year 2010." Journal of the American Society of Nephrology **12**(12): 2753-8.

Yang, WC, SJ Hwang, SS Chiang, HF Chen, and ST Tsai. (2001). "The Impact of Diabetes on Economic Costs in Dialysis Patients: Experiences in Taiwan." Diabetes Research and Clinical Practice **54**(1): S47-54.

You, J, W Hoy, Y Zhao, C Beaver, and K Eagar. (2002). "End-Stage Renal Disease in the Northern Territory: Current and Future Treatment Costs." Medical Journal of Australia **176**(10): 461-5.

Young, EW. (1997). "An Improved Understanding of the Causes of End-Stage Renal Disease." Seminars in Nephrology **17**(3): 170-5.

Zabinski, RA, TA Burke, J Johnson, F Lavoie, C Fitzsimon, R Tretiak, and JV Chancellor. (2001). "An Economic Model for Determining the Costs and Consequences of Using Various Treatment Alternatives for the Management of Arthritis in Canada." Pharmacoeconomics **19 Suppl 1**: 49-58.

Zargooshi, J. (2001). "Iranian Kidney Donors: Motivations and Relations with Recipients." Journal of Urology **165**(2): 386-92.

Appendix A: Data Sources

A.1 Canadian Community Health Survey

The Canadian Community Health Survey (CCHS) is conducted by Statistics Canada. Its primary objective is "to provide timely cross-sectional estimates of health determinants, health status, and health system utilization at a sub-provincial level (health region or combination of health regions)" (Statistics Canada, 2002a). The first cycle of the CCHS collected information from over 130,000 household residents aged 12 and older in all Canadian provinces and territories between September 2000 and November 2001. Indian Reserves, Canadian Forces Bases, and some remote areas were excluded. The survey included questions on demographics, health risk factors and behaviours, health status and chronic conditions, use of health services, and other related information.

A.2 Canadian Organ Replacement Register

The Canadian Organ Replacement Register (CORR) includes demographic, treatment, risk factor, outcome, and other data on all dialysis patients who began treatment for end-stage renal failure in Canada since 1981 and on organ donation/transplant patients (heart, lung, liver, kidney, and pancreas) since 1990. Organ transplant waiting list data are available from 1991, and information on organ donors is available from 1992. Data are currently voluntarily submitted to CORR by 23 hospitals performing renal transplants, 85 dialysis centres, and the country's organ procurement organizations (CORR/CIHI, 2002).

Incorporated in 1990, the Canadian Institute for Health Information has managed CORR since 1995. The CORR Board of Directors is responsible for registry policies; an advisory committee provides advice on data collection, analysis, and ad hoc requests. The mandate of the registry is to "record, analyze, and report the level of activity and outcome of vital organ transplantation as well as renal dialysis activities" (CORR/CIHI, 2002).

Each year, participating dialysis centres and hospitals performing renal transplants submit summary facility-level information about the number of patients on various treatments as well as the activity and practices of each unit (CORR/CIHI, 1997). In addition, patient-specific questionnaires are completed

for all patients with end-stage renal disease who started treatment since January 1, 1981 ("registered patients").[170] Data on patients who received treatment prior to this date are gradually being added but are not comprehensively available at present. As a result, patients registered as of the 1999 data year accounted for approximately 97% of dialysis patients and 86% of patients with a functioning kidney transplant in Canada (CIHI, 2001).[171]

Questionnaires are completed at initial registration for any patients beginning long-term treatment for renal failure for the first time, as well as at annual follow-up intervals. Centres have the option of submitting follow-up data for patients who have died or transferred to another treatment centre prior to the end of the annual reporting cycle.[172]

Preliminary data for the 2000 calendar year were released in 2002. (CORR/CIHI, 2002) CORR estimates that approximately 129 new ESRD patients had not been registered at the time of cut-off for this preliminary reporting on December 13, 2001. In addition, follow-up data were missing for 247 patients from Quebec and Ontario. Final data for earlier years tends to be more complete than preliminary data for the latest year. Nevertheless, a small percentage of patients, primarily those with functioning transplants, are lost to follow-up. For the 1999 data year, 1.6% of registered patients fell into this category (CIHI, 2001).

---

[170] Every year, a number of patients may also receive dialysis treatment for short periods for treatment of acute renal failure. According to Registry protocols, they should not be included in the CORR patient registration process (CORR/CIHI, 1997).

[171] Transplant undercoverage primarily relates to the 1981 to 1990 period when CORR focused on information on patients receiving dialysis. Transplant data for these years were collected retrospectively for this period. Estimates of the degree of undercoverage are derived by comparing the number of registered patients captured through CORR to aggregate data supplied by provincial Ministries of Health. Dialysis undercoverage reflects the difference between the number of patients registered through CORR and aggregate point prevalence estimates provided by dialysis facilities. It primarily reflects patients who started dialysis prior to January 1, 1981. As a result, the degree of undercoverage is gradually decreasing over time.

[172] Note: CORR has instituted various procedures to avoid double-counting of patients who transfer between treatment centres.

A.3 National Population Health Survey

Statistics Canada's National Population Health Survey (NPHS) began in 1994/95 (Chen and Millar, 2000). It collects information about respondents' demographics, health risk factors and behaviours, health status and chronic conditions, use of health services, and related characteristics every two years. The main component of the survey covers household residents aged 12 and older in all provinces, except those living on Indian Reserves, Canadian Forces Bases, and in some remote areas. From 1994/95-1998/99, the NPHS had both cross-sectional and longitudinal components. Cross-sectional responses from the health file were used to derive diabetes prevalence estimates for 1994/95. It should be noted that since the survey only includes household residents (i.e. not those living in institutions), it likely underestimates the true prevalence of chronic conditions, such as diabetes (Chen and Millar, 2000).

Appendix B: Summary of Key End-Stage Renal Disease Parameters

The Canadian Organ Replacement Register (CORR) has been tracking key statistics on patients with end-stage renal disease (ESRD) since 1981. The table below provides a high-level summary of trends in key descriptors of ESRD incidence, prevalence, and treatment drawn from the Register's latest report. (CORR/Canadian Institute for Health Information, 2002) Data for 2000 are preliminary. The second column in the table identifies reporting units (either a count of cases or a rate per million population). The third column shows the period for the data – a "Y" indicates that the data represent annual totals; a "P" indicates that the data represent a point prevalence estimate for status on December 31st of the given year.

Table 25: Trends in Key ESRD Parameters, Canada, 1985-2000[173]

Variable	Units	Prd	1985	1990	1995	1999	2000(p)
Incidence: New ESRD Patients	# RPMP	Y Y	1563 60.3	2293 82.5	3274 110.6	4451 146.0	4386 142.6
Prevalence: Total ESRD Patients	#	P	7749	11987	17749	23820	24921
Cadaveric Organs	#	Y	635	719	739	689	769
Living Donors	#	Y	103	118	225	380	389
Kidney Transplants[174]	# RPMP	Y Y	738 28.4	837 30.1	942 31.8	1011 33.2	1105 35.9
Transplant Waitlist	#	P	n/a	n/a	2126	2808	3027
Functioning Transplant Patients	#	P	3446	5914	7943	9852	10354
Hemodialysis Patients	#	P	2766	3885	6409	10615	11320
Peritoneal Dialysis Patients	#	P	1537	2188	3397	3353	3247
% ESRD patients on dialysis	%	P	55.5	50.7	55.2	58.6	58.5
Deaths among ESRD patients	#	Y	775	1226	2029	2666	2675

[173] Data for 2000 are preliminary. CORR estimates that an additional 129 patients had not yet been registered at the cut-off time for preliminary reporting (December 13, 2001). In a limited number of cases, it was possible to subsequently obtain more recent data from CORR. This information was incorporated into the analysis in this thesis, as described in the text.

[174] Does not include kidneys transplanted in combination with other organs.

Appendix C: Model Variables

The mathematical model describing the dynamic nature of the economic burden of end-stage renal disease includes a range of stock variables, flow variables, and probabilities. Both exogenous variables (inputs to the model) and endogenous variables (those where values for future periods are determined through the projection model) are described below. Where subscripts used in the model are not self-explanatory (e.g. t as a subscript for a point in time), they are also described.

Age			*Label:* A
Description: A vector of population age.			
Values:	10 year age categories.		
Type:	☐ Stock ☒ Subscript	☐ Flow	☐ Probability
Endogeneity:	☐ Yes	☐ No	☒ Not applicable
Cadaveric Harvest			*Label:* $KDNY\_CAD_{t,t+1}$
Description: The total number of kidneys successfully harvested from cadaveric donors for transplantation between time t and t+1.			
Values:	Positive integer.		
Type:	☐ Stock ☐ Subscript	☒ Flow	☐ Probability
Endogeneity:	☒ Yes	☐ No	☐ Not applicable
Candidate Cadaveric Donors			*Label:* $DONOR\_CAN_{t,t+1}$
Description: The number of potential ("candidate") cadaveric donors between time t and time t+1.			
Values:	Positive integer.		
Type:	☐ Stock ☐ Subscript	☒ Flow	☐ Probability
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Clinical Practices			*Label:* CLINICAL_P_t
Description: Represents a range of clinical practices that may affect organ donation and transplantation.			
Values:	n/a		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Cost of ESRD			*Label:* $COST\_TOT_{t,t+1}$
Description: The total cost per person with ESRD, in constant $, of ESRD treatment between time t and time t+1.			
Values:	Positive value in constant Canadian dollars.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Direct Cost of ESRD			*Label:* $COST\_DIR_{t,t+1}$
Description: The total direct cost per person with ESRD, in constant $, of ESRD treatment between time t and time t+1.			
Values:	Positive value in constant Canadian dollars.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

ESRD Deaths			*Label:* $ES\_DEATHS_{t,t+1}$
Description: The number of people with end-stage renal disease at time t who have died by time t+1.			
Values:	Positive integer.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

ESRD Patients on Hemodialysis			*Label:* ES_HEMO_t
Description: The number of ESRD patients receiving hemodialysis at time t.			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

ESRD Patients on Peritoneal Dialysis			*Label:* ES_PERI_t
Description: The number of ESRD patients receiving peritoneal dialysis at time t.			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

ESRD Patients with Functioning Transplant			*Label:* ES_TRAN_t
Description: The number of ESRD patients with a functioning transplant at time t.			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

ESRD Population			*Label:* ES_TOT_t
Description: The number of people alive at time t who have been diagnosed with end-stage renal disease (ESRD).			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

ESRD Recoveries			*Label:* $ES\_REC_{t,t+1}$
Description: The number of people with end-stage renal disease at time t who have recovered kidney function by time t+1.			
Values:	Positive integer.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Incident Cases			*Label:* $ES\_NEW_{t,t+1}$
Description: The number of people developing end-stage renal disease between time t and time t+1.			
Values:	Positive integer.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Indirect Cost of Treatment			*Label:* $COST\_IND_{t,t+1}$
Description: The total indirect cost per person with ESRD, in constant $, of ESRD treatment between time t and time t+1.			
Values:	Positive value in constant Canadian dollars.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Living Harvest			*Label:* $KDNY\_LVG_{t,t+1}$
Description: The total number of kidneys harvested for transplantation from living donors between time t and t+1.			
Values:	Positive integer.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Number of ESRD Patients on Dialysis			*Label:* ES_DIAL_t
Description: The number of people with end-stage renal disease receiving any type of dialysis at time t.			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Number of Kidney Transplants			*Label:* $ES\_TRAN\_NEW_{t,t+1}$
Description: The number of new kidney transplants using organs from living human, cadaveric, and non-human sources between time t and time t+1			
Values:	Positive integer		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Number of Xenotransplants			*Label:* $KDNY\_XENO_{t,t+1}$
Description: The total number of kidneys harvested from non-human sources for transplantation between time t and t+1.			
Values:	Positive integer (currently zero)		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Patient Characteristics			*Label:* x
Description: Represents a range of clinical, demographic, and other patient characteristics that may influence ESRD care.			
Values:	n/a		
Type:	☐ Stock	☐ Flow	☐ Probability
	☒ Subscript		
Endogeneity:	☐ Yes	☐ No	☒ Not applicable

Personal Behaviours			*Label:* PERS_BHVR$_{t,char}$	
Description: Represents a range of personal behaviours (e.g. drinking and driving or wearing seatbelts) that may affect the probability that a member of the general population dies and is considered a potential cadaveric organ donor.				
Values:	n/a			
Type:	☒ Stock	☐ Flow	☐ Probability	☐ Subscript
Endogeneity:	☐ Yes	☒ No	☐ Not applicable	
Personal Characteristics			*Label:* PERS_CHAR$_i$	
Description: The personal characteristics (e.g. comorbid health conditions, socio-economic characteristics, race) other than age and sex that are associated with end-stage renal disease development, progression, treament, or cost.				
Values:	n/a			
Type:	☒ Stock	☐ Flow	☐ Probability	☐ Subscript
Endogeneity:	☐ Yes	☐ No	☒ Not applicable	
Personal Preferences			*Label:* PERS_PREF$_t$	
Description: Represents a range of personal preferences that may affect organ donation.				
Values:	n/a			
Type:	☒ Stock	☐ Flow	☐ Probability	☐ Subscript
Endogeneity:	☐ Yes	☒ No	☐ Not applicable	
Policies and Legislation			*Label:* POLICIES$_t$	
Description: Represents a range of possible clinical, legal, and other policies and legislation that may affect organ donation.				
Values:	n/a			
Type:	☒ Stock	☐ Flow	☐ Probability	☐ Subscript
Endogeneity:	☐ Yes	☒ No	☐ Not applicable	

Population			*Label:* POP_TOT_t
Description: Total population at time t.			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable
Probability Donor Candidate			*Label:* PR_CAND
Description: The probability that a person who dies between time t and t+1 is a candidate kidney donor.			
Values:	Ratio between 0 (certain non-candidate) and 1 (certain candidate).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable
Probability of Cadaveric Consent			*Label:* PR_CONSENT
Description: The probability that consent is received for harvesting kidneys from a candidate cadaveric donor for transplantation between time t and t+1. Note: this includes necessary consents from both the potential donor and his/her family, if required.			
Values:	Ratio between 0 (no consent with certainty) and 1 (guaranteed consent).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Cadaveric Transplant			*Label:* PR_CAD_TRAN
Description: The probability that a person receiving a transplant between time t and time t+1 will receive an organ from a cadaveric donor. It is the complement of the probability of receiving an organ from a living donor.			
Values:	Ratio between 0 (definitely from living donor) and 1 (definitely from cadaveric donor).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Death			*Label:* PR_DEATH
Description: The probability that a person who is alive at time t dies by time t+1.			
Values:	Ratio between 0 (guaranteed survival) and 1 (certain death).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Dialysis Change			*Label:* $PR\_DIAL\_CHNG_{d1,d2}$
Description: The probability that a person with a given dialysis treatment state (in this case d1 or hemodialysis) at time t is in a particular dialysis treatment state (in this case d2 or peritoneal dialysis) at time t+1. See "Type of Dialysis Treatment" for codes.			
Values:	Ratio between 0 (certain that will remain at same state) and 1 (certain that will change to new state).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Double Harvest			*Label:* PR_HARV_2
Description: The probability that two kidneys are successfully harvested for transplantation from a candidate cadaveric donor (given that consent has been received) between time t and t+1.			
Values:	Ratio between 0 (no double organ harvest with certainty) and 1 (guaranteed single organ harvest).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Eligible Death			*Label:* PR_EL_DEATH
Description: The probability that a person who is alive at time t dies by time t+1 in circumstances where they might be considered a candidate for organ donation, following criteria in Noorani and McGahan, 1999.			
Values:	Ratio between 0 (definitely not a candidate) and 1 (definitely a candidate).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of ESRD Incidence			*Label:* PR_ES_NEW
Description: The probability that a person who had not been diagnosed with ESRD at time t is diagnosed with the condition by time t+1.			
Values:	Ratio between 0 (no chance of diagnosis) and 1 (certain diagnosis).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of ESRD Mortality			*Label:* PR_ES_DEATH$_{d\ or\ r}$
Description: The probability that a person who has been diagnosed with ESRD and is alive at time t is dead by time t+1. The probability is specified for each dialysis and transplant treatment state. It is the complement of PR_ES_SURV.			
Values:	Ratio between 0 (certain survival) and 1 (certain death).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of ESRD Recovery			*Label:* PR_ES_REC
Description: The probability that a person who diagnosed with ESRD at time t recovered kidney function by time t+1.			
Values:	Ratio between 0 (no chance of recovery) and 1 (certain recovery).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of ESRD Survival			*Label:* PR_ES_SURV$_{d\ or\ r}$
Description: The probability that a person who has been diagnosed with ESRD and is alive at time t survives to time t+1; the probability is specified for each dialysis and transplant treatment state.			
Values:	Ratio between 0 (certain death) and 1 (certain survival).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Initial Treatment Type Assignment			*Label:* PR_NEW_TX$_d$
Description: The probability that a person newly diagnosed with ESRD between time t and time t+1 will be assigned to the dialysis treatment modality specified.			
Values: Ratio between 0 (certain non-assignment) and 1 (definite assignment to the treatment modality).			
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Living Donor			*Label:* PR_LVG_DONOR
Description: The probability that a person who is alive at time t becomes a living kidney donor by time t+1.			
Values: Ratio between 0 (certain non-donation) and 1 (certain donation).			
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Living Donor Transplant			*Label:* PR_LVG_TRAN
Description: The probability that a person receiving a transplant between time t and time t+1 receives a living transplant.			
Values: Ratio between 0 (definitely from a cadaveric donor) to 1 (definitely from a living donor)			
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Probability of No Harvest			*Label:* PR_HARV_0
Description: The probability that no kidneys are successfully harvested for transplantation from a candidate cadaveric donor (given that consent has been received) between time t and t+1.			
Values: Ratio between 0 (no organ harvest with certainty) and 1 (guaranteed harvest of at least one organ).			
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Receiving a Cadaveric Transplant *Label:* PR_NEW_CAD			
Description: The probability that a person on the waiting list for a transplant at time t receives a cadaveric transplant by time t+1.			
Values:	Ratio between 0 (certain non-receipt) and 1 (certain receipt)		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Probability of Receiving a Living Transplant *Label:* PR_NEW_LVG			
Description: The probability that a person on the waiting list for a transplant at time t recieves a transplant from a living donor by t+1.			
Values:	Ratio between 0 (certain non-receipt) and 1 (certain receipt)		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable

Probability of Single Harvest *Label:* PR_HARV_1			
Description: The probability that one and only one kidney is successfully harvested for transplantation from a candidate cadaveric donor (given that consent has been received) between time t and t+1.			
Values:	Ratio between 0 (no single organ harvest with certainty) and 1 (guaranteed single organ harvest).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Probability of Transplant Change *Label:* PR_TRAN_CHG$_{r1,r2}$			
Description: The probability that a person with a given transplant treatment state at time t (in this case r1 or on the waiting list) is in a particular transplant treatment state at time t+1 (in this case r2 or functioning transplant). See "Transplant Treatment State" for codes.			
Values:	Ratio between 0 (certain that will remain at same state) and 1 (certain that will change to new state).		
Type:	☐ Stock	☐ Flow	☒ Probability
	☐ Subscript		
Endogeneity:	☐ Yes	☒ No	☐ Not applicable

Sex			*Label:* s
Description: A vector representing the population sex distribution.			
Values:	Male, female		
Type:	☐ Stock	☐ Flow	☐ Probability
	☒ Subscript		
Endogeneity:	☐ Yes	☐ No	☒ Not applicable
Supply of Organs			*Label:* $KDNY\_TOT_{t,t+1}$
Description: The number of kidneys successfully harvested from cadaveric and living donors between time t and time t+1.			
Values:	Positive integer.		
Type:	☐ Stock	☒ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable
Time			*Label:* t
Description: A vector representing time.			
Values:	Positive integer		
Type:	☐ Stock	☐ Flow	☐ Probability
	☒ Subscript		
Endogeneity:	☐ Yes	☐ No	☒ Not applicable
Transplant Treatment State			*Label:* r
Description: The transplant treatment state of an ESRD patient			
Values:	Waiting for transplant (r1), functioning transplant (r2), other (r3)		
Type:	☐ Stock	☐ Flow	☐ Probability
	☒ Subscript		
Endogeneity:	☐ Yes	☐ No	☒ Not applicable
Type of Dialysis Treatment			*Label:* d
Description: The dialysis treatment state of an ESRD patient			
Values:	Hemodialysis (d1), peritoneal dialysis (d2), none (d3)		
Type:	☐ Stock	☐ Flow	☐ Probability
	☒ Subscript		
Endogeneity:	☐ Yes	☐ No	☒ Not applicable

Waiting List			*Label:* $WAIT\_LIST_t$
Description: The number of Canadians waiting for a kidney transplant on a given date. Those on the waiting list must meet certain clinical and other eligibility criteria and have consented to the procedure should an appropriate donor be found.			
Values:	Positive integer.		
Type:	☒ Stock	☐ Flow	☐ Probability
	☐ Subscript		
Endogeneity:	☒ Yes	☐ No	☐ Not applicable