End-stage renal disease in Canada: prevalence projections to 2005

Evidence

Études

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Abstract

Background: The incidence and prevalence of end-stage renal disease (ESRD) have increased greatly in Canada over the last 2 decades. Because of the high cost of therapy, predicting numbers of patients who will require dialysis and transplantation is necessary for nephrologists and health care planners.

Methods: The authors projected ESRD incidence rates and therapy-specific prevalence by province to the year 2005 using 1981–1996 data obtained from the Canadian Organ Replacement Register. The model incorporated Poisson regression to project incidence rates, and a Markov model for patient follow-up.

Results: Continued large increases in ESRD incidence and prevalence were projected, particularly among people with diabetes mellitus. As of Dec. 31, 1996, there were 17 807 patients receiving renal replacement therapy in Canada. This number was projected to climb to 32 952 by the end of 2005, for a relative increase of 85% and a mean annual increase of 5.8%. The increased prevalence was projected to be greatest for peritoneal dialysis (6.0% annually), followed by hemodialysis (5.9%) and functioning kidney transplant (5.7%). The projected annual increases in prevalence by province ranged from 4.4%, in Saskatchewan, to 7.5%, in Alberta.

Interpretation: The projected increases are plausible when one considers that the incidence of ESRD per million population in the United States and other countries far exceeds that in Canada. The authors predict a continued and increasing shortfall in resources to accommodate the expected increase in ESRD prevalence.

The incidence and prevalence of end-stage renal disease (ESRD) have increased greatly in Canada over the last 2 decades.[1] Although relatively rare, ESRD is an important health problem because of the high cost of renal replacement therapy,[2] the associated high mortality and the effect on patients' quality of life. Projecting future numbers of patients who will require dialysis and transplantation is of interest to health care planners in order to forecast equipment, facility and other resource requirements. Previously, we provided ESRD prevalence projections to the year 2000 at the national level.[3] However, because the funding of renal centres is a provincial responsibility, in this article we have projected ESRD incidence rates and therapy-specific year-end prevalence by province to the year 2005, using enhanced methods previously described.[4]

Methods

Data were obtained from the Canadian Organ Replacement Register, a population-based national organ failure registry of the Canadian Institute for Health Information.[1] Data on demographic characteristics (e.g., date of birth, sex, province of residence, ethnic background), comorbid conditions and underlying causes of renal failure (primary renal diagnosis) are collected by each of the 86 renal centres from all patients at the start of therapy. Clinical data (e.g., method of dialysis assigned and switches, transplantations and transplant failures) are submitted annually. Deaths are reported along with the other follow-up information.

Data were available for patients starting renal replacement therapy in Canada between Jan. 1, 1981, and Dec. 31, 1996. For our analysis, we classified patients by age (≤ 44 years,

45–64, ≥ 65) and primary renal diagnosis (diabetes mellitus status). Population data were obtained from Statistics Canada.

The projection model we used has 2 components: incidence and prevalence. Modelling was done separately for each province to allow for differences in the parameters of the incidence and prevalence components by province. Annual incidence rates were projected for the years 1997 to 2005 based on extrapolations from diabetes status-specific Poisson regression[5] models fitted to the 1981–1996 data. Under the Poisson model, the logarithm (base e) of the incidence rate is assumed to be a linear function of age and year within each province/diabetes cross-classification. Separate models for people with diabetes and those without diabetes were fitted to allow the time trend to differ by both age and diabetes status, while eliminating the potential need for third-order interaction terms. Interaction and polynomial terms were included when indicated. The relative goodness-of-fit of the models was compared using the deviance.[6] Variance estimates were appropriately adjusted when evidence of under- or overdispersion was observed (i.e., variability in the data was inconsistent with that of a Poisson distribution).[7] We computed 95% confidence intervals (CIs) for the incidence projections using the large-sample normal approximation.[6] As a supplementary analysis, prevalence projections to 2005 were produced, using the average annual incidence rate during 1994–1996 instead of the Poisson-based incidence projections. That is, the incidence rate was assumed to be constant between 1997 and 2005.

Follow-up was projected for 1997–2005 incident cases and "currently prevalent" patients (i.e., patients receiving therapy as of Dec. 31, 1996) using a Markov model.[8] The Markov model consists of a sequence of matrices, where each matrix contains interstate-transition probabilities pertaining to a specific follow-up interval. In this setting, the "states" included hemodialysis, peritoneal dialysis, functioning kidney transplant and death. The familiar survival model can be cast as a special case of the Markov model with only 2 states (survival and death), and such a model would have sufficed if our goal had been to project the total, as opposed to the therapy-specific, number of prevalent ESRD patients. The Markov model permitted us to estimate therapy-specific projections and thereby accommodated switches in therapeutic modality by patients.

Projected incident cases and currently prevalent cases were multiplied by the appropriate sequence of transition matrices to project the distribution of patients as time progressed. Therapy-specific year-end prevalence by province was projected for 1997–2005 inclusive. A more detailed description and evaluation of the projection model was the subject of a previous report.[4]

For internal validation of the projection model empirically, we used 1981–1989 data to project year-end prevalence by province for the years 1990–1996 using the methods described above. The projected and observed prevalence on Dec. 31, 1996, were compared.

Results

The demographic and basic clinical characteristics of the 34 710 ESRD patients who initiated renal replacement therapy between Jan. 1, 1981, and Dec. 31, 1996, are presented in Table 1. Diabetes was the underlying cause of renal failure for 23.0% of the patients. The mean number of new patients per year rose from 1366 during 1981–1985, to 1990 during 1986–1990 and to 2988 during 1991–1996. At the end of 1996, 41.7% of the registered patients receiving therapy were receiving hemodialysis, 19.5% were receiving peritoneal dialysis, and 38.9% had a functioning kidney transplant. Most of the patients (39.5%) initiated therapy in Ontario.

The observed ESRD incidence rates per million population by diabetes status and province during 1981–1996 are listed in Table 2, along with the age-adjusted mean annual relative increase. In each province the observed increase in incidence was much more pronounced among people with than among those without diabetes. Nationally, the age-adjusted annual relative increase was estimated at 9.1% among patients with diabetes and 4.1% among those without diabetes. The relative increase was greatest in Manitoba and lowest in Ontario, irrespective of diabetes status.

The observed (1981 and 1996) and projected (2000 and 2005) incidence rates are listed by province in Table 3, along with the age-adjusted mean annual observed and projected increases. Manitoba had the highest observed incidence rate in 1996 (143.8 per million population) and the highest projected relative increase (8.9%). The 95% CIs were narrowest for Ontario and widest for Manitoba. Clearly, precision decreased as the year increased, as evidenced by the wider CIs for 2005 than for 2000. In general the ordering of provinces remained the same with respect to the observed and projected rates. Nationally, the projected mean annual

Table 1: Characteristics of Canadians with end-stage renal disease (ESRD) who initiated renal replacement therapy after Jan. 1, 1981

Characteristic	No. (and %) of patients *n = 34 710*
Age at start of therapy, yr	
≤ 44	9 557 (27.5)
45–64	12 666 (36.5)
≥ 65	12 487 (36.0)
Period therapy started	
1981–1985	6 831 (19.7)
1986–1990	9 951 (28.7)
1991–1996	17 928 (51.7)
Has diabetes mellitus	
No	26 718 (77.0)
Yes	7 992 (23.0)
Therapy status*	*n = 17 807*
Hemodialysis	7 415 (41.6)
Peritoneal dialysis	3 467 (19.5)
Functioning kidney transplant	6 925 (38.9)
Vital status*	
Alive	17 807 (51.3)
Dead	16 903 (48.7)
Province†	
Atlantic provinces	3 438 (9.9)
Quebec	7 698 (22.2)
Ontario	13 714 (39.5)
Manitoba	1 800 (5.2)
Saskatchewan	1 344 (3.9)
Alberta	2 931 (8.4)
British Columbia	3 785 (10.9)

*As of Dec. 31, 1996.
†Province in which therapy was started.

increase in incidence was 5.5% during 1997–2005, compared with 6.2% observed during 1981–1996.

The annual incidence rates for Canada by diabetes status are displayed in Fig. 1. The increase in projected rates was highest among patients 65 years of age and older, irrespective of diabetes status. Great increases were projected among patients 45–64 with diabetes. Patients aged 44 and less were projected to have stable incidence rates irrespective of diabetes status. In general the incidence trends projected for 1997–2005 were consistent with those observed between 1981 and 1996.

The therapy-specific ESRD prevalence (number of patients at year end) by province during 1981–2005 is displayed in Fig. 2, with summary data listed in Table 4. In general the

Table 2: Incidence rates (per million population) of ESRD in Canada during 1981–1996, by province and diabetes status

	No diabetes			Diabetes		
Province	Rate in 1981	Rate in 1996	Mean annual increase,* %	Rate in 1981	Rate in 1996	Mean annual increase,* %
Atlantic provinces	45.0	107.7	4.1	7.1	33.6	10.8
Quebec	37.2	77.6	4.7	5.8	23.6	9.6
Ontario	45.7	76.3	3.3	9.8	36.2	8.3
Manitoba	56.8	92.9	5.8	10.6	50.9	11.0
Saskatchewan	42.9	68.7	3.8	13.3	44.1	9.1
Alberta	33.9	83.1	4.9	9.1	31.5	9.3
British Columbia	38.1	73.4	4.1	1.8	21.8	8.9
Canada	41.7	79.8	4.1	7.7	31.4	9.1

*Estimated using Poisson regression, adjusted for age (age and province, for Canada).

Table 3: Incidence rates (per million population) of ESRD in 1981 and 1996 (observed) and in 2000 and 2005 (projected), by province

	Observed			Projected		
Province	Rate in 1981	Rate in 1996	Mean annual increase,* %	Rate in 2000 (and 95% CI)	Rate in 2005 (and 95% CI)	Mean annual increase,*† %
Atlantic provinces	52.1	141.3	5.4	207.6 (175.7–245.3)	341.7 (273.7–426.6)	8.1
Quebec	42.9	101.1	5.7	145.7 (130.9–162.3)	208.6 (181.5–239.8)	5.8
Ontario	55.6	112.5	4.4	147.4 (136.9–158.7)	187.6 (170.3–206.6)	4.0
Manitoba	67.4	143.8	7.3	252.5 (199.7–319.4)	417.3 (305.5–569.9)	8.9
Saskatchewan	56.2	112.8	5.4	160.6 (123.8–208.2)	219.4 (156.1–308.3)	5.5
Alberta	43.0	114.6	5.9	160.9 (136.3–189.9)	249.6 (200.6–310.6)	7.4
British Columbia	39.8	95.1	5.0	124.1 (110.6–139.2)	153.1 (131.6–178.1)	3.5
Canada	49.5	111.2	6.2	154.2 (147.0–161.7)	214.5 (201.5–228.2)	5.5

Note: CI = confidence interval.
*Estimated using Poisson regression, adjusted for age (age and province, for Canada).
†For period 1997–2005.

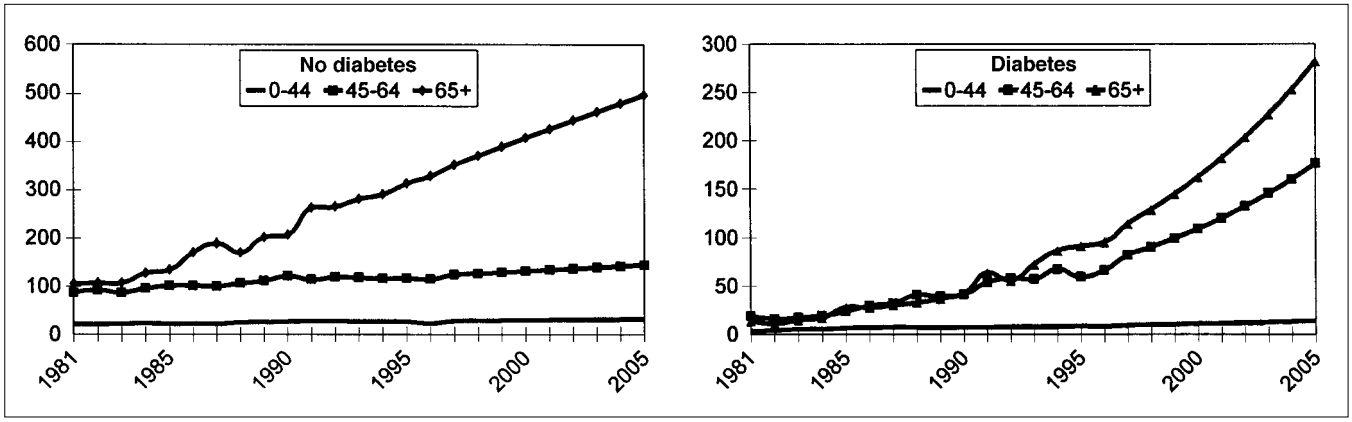

Fig. 1: Incidence rates (per million population) of end-stage renal disease (ESRD) in Canada during 1981–1996 (observed) and 1997–2005 (projected) among people without diabetes mellitus (left) and those with diabetes (right). Projected rates were extrapolated from Poisson regression models fitted to 1981–1996 data.

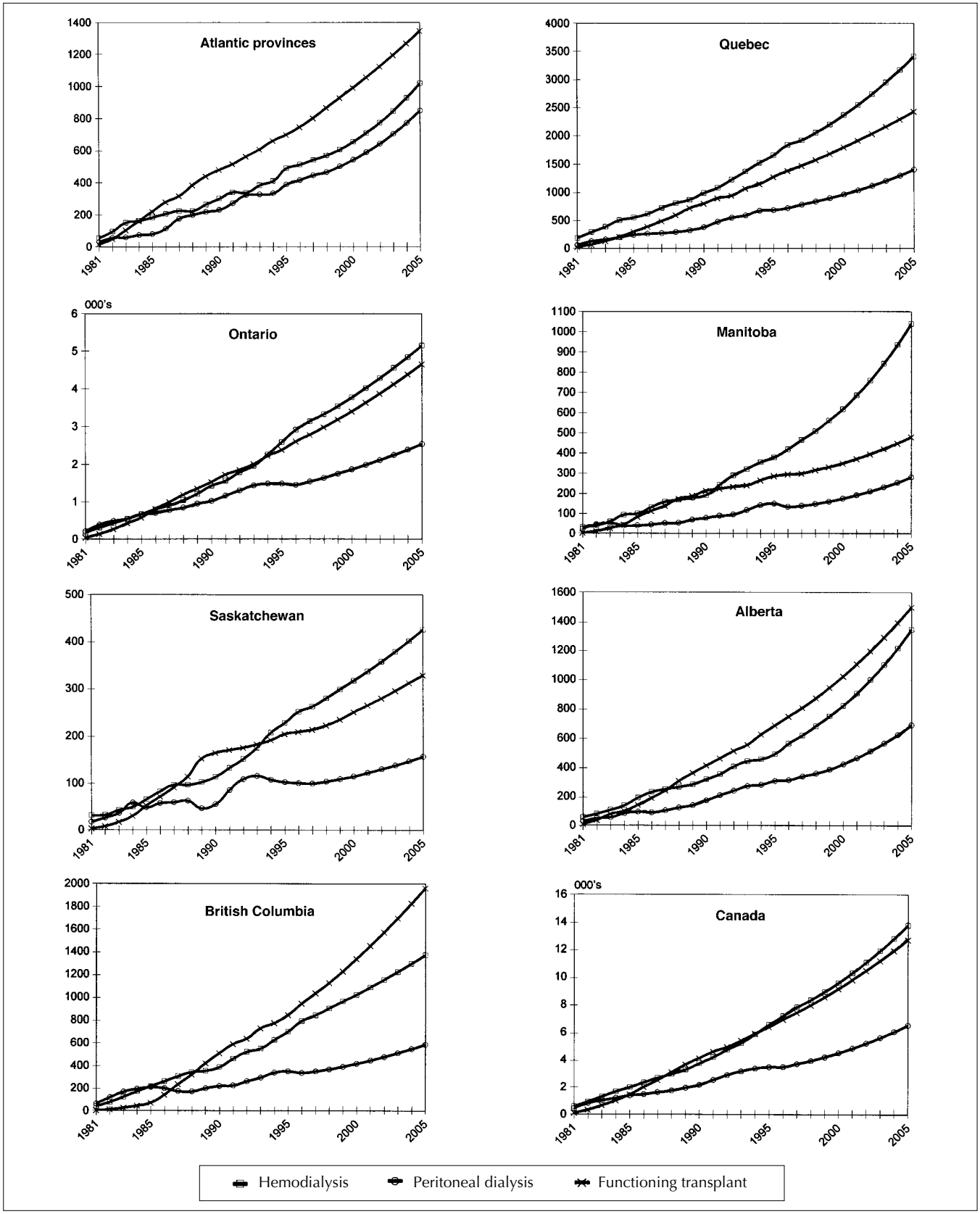

Fig. 2: Therapy-specific prevalence of ESRD (year-end number of registered patients [initiated therapy after Jan. 1, 1981]) by province during 1981–1996 (observed) and 1997–2005 (projected). Projections are based on a model that combined Poisson regression for incidence rates and a Markov model for patient follow-up.

prevalence trends projected were consistent with the observed prevalence. We projected that 32 952 patients will be receiving renal replacement therapy by the end of 2005; of these, 13 754 (41.7%) will be receiving hemodialysis, 6501 (19.7%) will be receiving peritoneal dialysis and 12 697 (38.5%) will have a functioning kidney transplant. The projected distribution by therapy for 2005 was virtually identical to that observed in 1996 (41.6%, 19.5% and 38.9% respectively). The mean annual increase in prevalence during 1997–2005 was projected to be highest in Manitoba (7.3%), lowest in Saskatchewan (4.4%) and 5.8% nationally.

In the model in which the incidence rates of ESRD were assumed to remain constant during 1997–2005, we projected that 25 065 patients in Canada will be receiving therapy in 2005 (Table 5), an increase of 40.8% over the 1996 national prevalence.

To validate the accuracy of the projection model, we used 1981–1989 data to project ESRD prevalence by province to Dec. 31, 1996 (Table 6). The projected prevalence for 1996 differed from the observed prevalence by 1.3%. The relative error ranged from –2.3%, for Ontario, to 10.4%, for British Columbia. Projected therapy-specific counts closely approximated those observed in each province (data not shown).

Interpretation

Our projected mean annual increase in ESRD prevalence of 5.8% during 1997–2005 would result in 32 952 Canadians requiring renal replacement therapy by the end of 2005. This figure represents a relative increase of 85% over the prevalence in 1996. The increase is cause for concern because rationing of dialysis reportedly already occurs in Canada, with several renal centres currently working beyond their actual capacity.[9–11]

The validity of our projection model is supported from a methodological perspective. With respect to incidence, Poisson regression is frequently used for rate modelling,[6] and the Poisson model has a long history of being used in the modelling of rare events such as ESRD incidence.[6,8] Regarding patient follow-up, the Markov model has been successfully used previously in the context of ESRD planning[12–14] and is naturally suited to this setting.

In general our projected incidence and prevalence trends were consistent with the observed trends. That the rates of therapy initiation could further increase beyond current levels is supported by the fact that, despite the large increases already experienced in Canada, incidence rates are much higher in the United States and other developed countries such as Germany and Japan.[15–17] A potential liability is the assumption of exponential increase in incidence over time. The observed trends were indeed exponential, consistent with trends in other countries.[18,19] Although exponential trends may not persist for extended periods, the practical value of the Poisson model for incidence projections has been previously demonstrated.[20]

Table 4: Observed and projected prevalence of ESRD, by province and type of renal replacement therapy

Province	Therapy; prevalence, no. of patients at year end (and mean annual increase, %)			
	Hemodialysis	Peritoneal dialysis	Functioning kidney transplant	Total
			Observed (1996)	
Atlantic provinces	542	416	747	1 705
Quebec	1 832	717	1 382	3 931
Ontario	2 988	1 454	2 603	7 045
Manitoba	427	132	293	852
Saskatchewan	251	100	209	560
Alberta	582	312	746	1 640
British Columbia	793	336	945	2 074
Canada	7 415	3 467	6 925	17 807
			Projected (2005)*	
Atlantic provinces	1 020 (6.0)	849 (6.9)	1 347 (5.6)	3 216 (6.0)
Quebec	3 405 (5.9)	1 402 (6.5)	2 427 (5.3)	7 235 (5.8)
Ontario	5 149 (5.0)	2 538 (5.2)	4 655 (5.5)	12 342 (5.2)
Manitoba	1 039 (8.9)	280 (7.3)	478 (4.4)	1 796 (7.3)
Saskatchewan	426 (4.9)	157 (4.0)	329 (4.0)	911 (4.4)
Alberta	1 344 (8.3)	689 (7.8)	1 498 (6.7)	3 532 (7.5)
British Columbia	1 372 (5.1)	586 (5.2)	1 963 (7.1)	3 921 (6.1)
Canada	13 754 (5.9)	6 501 (6.0)	12 697 (5.7)	32 952 (5.8)

*Projections are based on a model that combined the Poisson model for incidence and a Markov model of patient follow-up. The sum of the numbers may not equal row and column totals because of rounding.

In terms of reconciling the increase in ESRD incidence, the issue of competing mortality has been raised[21] and applies to Canada and other developed areas of the world. That is, patients with coronary artery disease, which has risk factors common to ESRD (e.g., hypertension), are surviving longer because of vast improvements in treatment, and therefore they are at higher risk for ESRD. Increased diabetes prevalence is a hypothesized explanation for the rise in ESRD incidence in Canada and other countries.[22–24] Our findings indicated that the increase in ESRD incidence was more pronounced among patients with than among those without diabetes. Because reliable estimates of diabetes incidence or prevalence are unavailable, we cannot tell whether the prevalence of diabetes is increasing, or whether ESRD incidence is increasing in a perhaps constant population of people with diabetes. It is also possible that the proportion of diabetic patients with ESRD who are referred for therapy has increased.

The projection model's internal validity was demonstrated by the fact that the model using 1981–1989 data projected the prevalence during 1990–1996 adequately. Naturally, such "data–splitting" procedures understate the accuracy of the full-data model. That is, in the validation model, data for only 9 years were used, with the projected time span equal to 78% (7/9) of the time span of the data. In the main model, data for 16 years were available, with a projected time span equal to 56% (9/16) of the data's time span. Furthermore, for diseases such as ESRD, which have a high death rate, prevalence projections are very sensitive to the specified incidence model. This sensitivity increases greatly, as does the instability of the incidence model, as the number of available data points decreases.

The projected therapy-specific prevalence of ESRD was considerably lower when we assumed that the incidence would remain constant over time. The purpose of this model was to assess the impact of a plateau at current incidence rates. If the observed increase in therapy were due to increased acceptance of therapy, and all ESRD patients were indeed referred for treatment, then we would expect incidence to level off at current rates. There was evidence of plateauing in the age group most likely to be referred to a nephrologist (those 44 years of age and younger). However, we found no evidence of plateauing in the 2 groups currently generating the greatest number of new cases: patients aged 65 and older, and diabetic patients aged 45–64. In the United States the number of patients receiving renal replacement therapy per million population (949 in 1994[15]) greatly exceeds that in Canada, even after adjustment for race. There is no evidence yet of a plateau, even though predictions from the 1970s were that a plateau would occur in the 1980s.[18] Even if incidence rates were to remain constant, the projected increase of 40.8% in prevalence for 2005 is still sizeable, particularly for an already overburdened health care system. As well, the annual number of new cases per year would still increase, despite constant incidence rates, because continued population increases are projected, particularly of elderly people.

Our study has some limitations. Because we lacked data on the true underlying incidence and prevalence of ESRD, we could not estimate the proportion of patients

Table 6: Evaluation of model's accuracy in projecting ESRD prevalence

Region	Prevalence in 1996, no. of patients at year end			Relative error, %‡
	Observed	Projected*	Error†	
Atlantic provinces	1 705	1 835	+130	+7.6
Quebec	3 931	3 711	–220	–5.6
Ontario	7 045	6 886	–159	–2.3
Manitoba	852	807	–45	–5.3
Saskatchewan	560	536	–24	–4.3
Alberta	1 640	1 507	–133	–8.1
British Columbia	2 074	2 290	+216	+10.4
Canada	17 807	17 572	–235	–1.3

*Calculated using 1981–1989 data. Projections are based on a model that combined Poisson regression for incidence and a Markov model of patient follow-up.
†Difference between projected and observed numbers.
‡(projected – observed)/observed × 100%.

Table 5: Projected therapy-specific prevalence of ESRD in 2005, assuming constant incidence rate*

Province	Therapy; projected no. of patients†			
	Hemodialysis	Peritoneal dialysis	Functioning kidney transplant	Total
Atlantic provinces	579	461	1 202	2 242
Quebec	2 307	897	2 191	5 395
Ontario	3 960	1 820	4 275	10 055
Manitoba	540	145	387	1 071
Saskatchewan	297	97	299	693
Alberta	787	378	1 250	2 415
British Columbia	1 022	394	1 778	3 194
Canada	9 492	4 192	11 381	25 065

*The incidence rate of ESRD observed between 1994–1996 was assumed to remain constant between 1997 and 2005.
†The sum of the numbers may not equal row and column totals because of rounding.

receiving renal replacement therapy among those requiring treatment. As well, data were only available for registered patients (i.e., those who initiated therapy after Jan. 1, 1981). This would result in the ESRD prevalence in 2005 being underestimated to the degree that nonregistered patients survive and would primarily affect the number of patients undergoing transplantation. Our projections are limited by the contingency of their validity on the persistence of observed trends, a limitation inherent in forecasting.

The large projected increase in the number of ESRD cases has serious implications for Canada's health care system. The predicted rise in prevalence indicates that there will be a substantial burden on health care resources and on patients' health. We therefore urge social and health care planners to consider projections of ESRD rates in their planning of future services.

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