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The cost-effectiveness of losartan in type 2 diabetics with nephropathy in Switzerland – an analysis of the RENAAL study

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Summary

Background: The prevalence and incidence of diabetic nephropathy with endstage renal disease (ESRD) have increased globally over recent decades. Diabetic nephropathy with ESRD for type 2 diabetes mellitus (DM) now has to be recognized as a growing public health problem. Several studies have found that angiotensin-II receptor antagonists have a renoprotective effect in type 2 diabetics with diabetic nephropathy, independently of their antihypertensive effects. These studies have shown a prevention of the progression of nephropathy to ESRD, or a slowing of that progression. The RENAAL study demonstrated the clinical benefits of losartan in patients with DM type 2 and advanced diabetic nephropathy.

Aim: The aim of this cost-effectiveness analysis of the RENAAL study was to evaluate the effect of losartan compared to a placebo from a Swiss third party payer perspective.

Methods: Using a decision analytic model, we evaluated the cost-effectiveness for losartan on the basis of the RENAAL study. A follow-up period of 3.5 years was used. Effectiveness was defined as the number of ESRD days saved. We valued haemodialysis, peritoneal dialysis and kidney transplantation. A weighted mean value was calculated for the daily costs of an ESRD (CHF 215.05). In the case of renal transplantation follow-on costs, resource utilization was determined through a telephone-based interview with 5 of the 6 Swiss transplantation centres. Expert consensus methodology was used to determine the proportion of health care resource utilization in type 2 diabetics. The percentage of patients receiving each of the 3 treatment alternatives was derived from a cross-sectional national study conceived for this purpose. The daily costs for haemodialysis and peritoneal dialysis were derived from figures provided by insurers. The costs of treatment with losartan were calculated on the basis of an average daily dose of losartan over a period of 3.5 years.

Results: Over a period of 3.5 years, losartan significantly reduced the number of ESRD days of type 2 diabetics with nephropathy by an average of 33.6 days (95% CI: 10.9, 56.3) compared to the placebo. This reduction in the number of ESRD days resulted in ESRD-associated cost savings of CHF 7,226 per patient over a period of 3.5 years (the ESRD-associated costs savings increased to CHF 10,086 per patient after 4 years). If the average costs per patient for treatment with losartan for the same period (CHF 3,142) are subtracted from the CHF 7,226 then the reduction in ESRD days yields net cost savings of CHF 4,084 per patient over 3.5 years. The univariate sensitivity analyses for the variables ESRD daily costs and percentage distribution of the 3 treatment modalities always yielded net cost savings.

Discussion: This evaluation revealed net cost savings of CHF 4,084 (€ 2,687) for patients with diabetic nephropathy and type 2 diabetes when given 50 to 100 mg losartan once daily over a period of 3.5 years compared to placebo. The net cost savings that administration of losartan yielded are of considerable importance given that the annual costs of diabetic nephropathy with ESRD in type 2 diabetics in Switzerland are approximately CHF 46 million. On the basis of the scientific evidence currently available, the use of losartan to prevent the advance of diabetic nephropathy is worthwhile from both a clinical and economic perspective.

Key words: losartan; cost-effectiveness analysis; diabetes; nephropathy; Switzerland

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Introduction

This analysis provides an evaluation of the incremental costs and effectiveness of losartan in patients with type 2 diabetes mellitus and nephropathy. We anticipate that the findings of this cost-effectiveness analysis will prompt a more efficient allocation of healthcare resources in Switzerland for patients with type 2 diabetes with hypertension and overt nephropathy.

Background

The prevalence and incidence of diabetic nephropathy with endstage renal disease (ESRD), in patients with diabetes mellitus type 2 (type 2 diabetes) has increased globally over recent decades. The increase was first seen in the USA and Japan, followed by all countries with a western lifestyle. This fact was viewed by Ritz et al. 1999 as a medical catastrophe with a global dimension [1, 2]. In most industrialized nations, diabetic nephropathy in patients with type 2 diabetes is now the most frequent cause of ESRD [3].

The reasons for the enormous increase in both the incidence and prevalence of ESRD in patients with type 2 diabetes include the increasing prevalence of such diabetes as a result of increased caloric food intake, a sedentary lifestyle, an aging population, the failure to prevent the disease, the ability to make a timely correct diagnosis and to implement a consistent treatment strategy. The observed secular trend of a higher life expectancy of type 2 diabetics is primarily attributable to the advances in the management of cardiovascular complications, coupled with the availability of improved antihypertensive compounds and the consistent and better treatment of coronary heart disease [4]. Many of the type 2 diabetics who are alive today would in the past have succumbed to cardiovascular death [5] before they could develop renal insufficiency. Diabetics now increasingly live long enough to develop renal insufficiency later on in life [6]. ESRD in patients with type 2 diabetes could therefore be viewed as a consequence of therapeutic advances in medicine [2, 7, 8]. Diabetic nephropathy with ESRD for type 2 diabetes now has to be recognized as a growing public health problem.

The increase in the prevalence and incidence of ESRD in type 2 diabetics means that the economic implications of this late complication – in principle avoidable – are becoming increasingly important [9]. Considerable economic importance has been attached to the complications of type 2 diabetes, including diabetic nephropathy [10, 11, 18, 38]. Caro et al. have estimated the average costs of complications in type 2 diabetics to be USD 47,240 per patient over a period of 30 years. The management of macrovascular complications alone accounts for 52% of these costs. The other costs are split between nephropathy (21%), neuropathy (17%) and retinopathy (10%) [11].

Details of the costs associated with diabetic nephropathy with ESRD for type 2 diabetics in other countries are not readily available and, given the differences in healthcare, cannot be extrapolated *a priori* and unconditionally to Switzerland [12, 13]. The costs of diabetic nephropathy with ESRD for type 2 diabetics are calculated for Switzerland for the first time in the main section of this study, enabling a cost-effectiveness analysis of the **R**eduction of **E**ndpoints in **N**IDDM with the **A**ngiotensin II **A**ntagonist **L**osartan, RENAAL study [14].

A number of new studies, some of them on a large scale, have found a clinical advantage of the administration of angiotensin-II receptor antagonists such as losartan (RENAAL study), irbesartan (**I**rbesartan Type II **D**iabetic **N**ephropathy **T**rial, IDNT [15] and **Ir**besartan in Patients with Type 2 Diabetes and **M**icro**A**lbuminuria Study Group, IRMA2 [16] studies) and valsartan (**M**icro**A**lbuminuria **R**eduction With **VAL**sartan, MARVAL [17] study). These studies have demonstrated a renoprotective effect in type 2 diabetics with diabetic nephropathy, independently of their antihypertensive effects [18]. These studies have shown a prevention of the progression of nephropathy to ESRD, or a slowing of that progression.

The RENAAL study, an international, multicentre, double-blind, randomized and placebo-controlled study in 1,513 patients evaluated, *inter alia*, the renoprotective effect of 50–100 mg losartan in type 2 diabetics with advanced diabetic nephropathy in 250 centres in 28 countries in Asia, Europe, Central America, South America, and North America. The inclusion criteria for RENAAL were an age in the range 31–70 years with a diagnosis of type 2 diabetes and nephropathy.

The patients were randomly assigned to losartan and placebo. Both losartan (50 or 100 mg once daily) and the placebo were given in addition to conventional antihypertensive treatment (calcium channel blockers, diuretics, alpha-blockers, beta-blockers and centrally acting drugs, but no ACE inhibitors or angiotensin-II receptor antagonists) to allow evaluation of the effects of losartan independently of the blood pressure lowering effect. The losartan group was comprised of 751 patients, 71% of whom were given 100 mg of losartan once daily. The other 29% received 50 mg losartan once daily. The placebo group was comprised of 762 patients. After an additional eight weeks antihypertensive agents of the types described above (but not ACE inhibitors or angiotensin I receptor antago-

nists) were added or their doses increased to achieve the target blood pressure. The patients were given 50 mg losartan or 50 mg placebo once daily during the first 4 weeks of the study, in addition to the above-mentioned conventional antihypertensive treatment. The dose of losartan or placebo was increased to 100 mg or the placebo equivalent once daily after 4 weeks if the blood pressure of the patient was above the systolic target level of less than 140 mm Hg systolic and 90 mm Hg diastolic pressure. The patients received standard treatment for diabetes over the entire period of the study, including measurement of glycosylated haemoglobin (HbA_{1c}) and fasting serum glucose concentrations. The drug treatment and follow-up for both the losartan and placebo patients in the RENAAL study was over an average period of 3.4 years. The primary endpoint was specified as a doubling of the baseline serum creatinine concentration, the onset of ESRD or death. The secondary endpoints were cardiovascular morbidity and mortality, proteinuria or a progression of renal disease.

The RENAAL study demonstrated the clinical benefits of losartan in patients with diabetes mellitus type 2 and advanced diabetic nephropathy. Losartan was well tolerated and yielded a significant 25% reduction in the incidence of a doubling of the serum creatinine concentration ($p = 0.006$) and a significant 28% reduction in the incidence of ESRD ($p = 0.002$). It had no effect on the mortality rate. The renoprotective effect of angiotensin-II receptor antagonists has recently only been granted as a label for losartan in Switzerland.

Expanding health care costs and restricted health care budgets make it essential to conduct an economic evaluation on the recent evidence of the renoprotective effect of losartan. This is particularly necessary in view of the fact that spending on pharmaceuticals and healthcare as a whole in Switzerland and other European countries has grown more rapidly over the last 20 years than the gross national product [19]. It is therefore more necessary than ever to know whether the prescription of a medicine is cost-effective.

Aim

The aim of this cost-effectiveness analysis of the RENAAL study was to evaluate the effect of losartan compared to a standard treatment (placebo arm) in terms of the costs associated with ESRD from a Swiss third party payer perspective.

Methods

Using a decision analytic model, we evaluated the cost-effectiveness from the perspective of the Swiss healthcare payers (Krankenkassen) for losartan, compared with placebo on the clinical data of the multinational, double-blind, randomized and placebo-controlled RENAAL study [14].

The data relevant for this evaluation were taken from the RENAAL study or from the cost-effectiveness analysis of the RENAAL study for the USA [20, 31]. This included the definition of the patient population, the duration and dosage of treatment with losartan and the number of ESRD days for both groups of patients. A follow-up period of 3.5 years was defined for economic evaluation purposes since the number of ESRD days was available for this from the cost-effectiveness analysis of the RENAAL study for the USA. Effectiveness was defined as the number of ESRD days saved.

A separate investigation served as a database for the costs of ESRD and supplied the calculation of the daily costs of ESRD for Switzerland. The detailed calculation is given in that study [21]. A weighted mean value was calculated for the daily costs of a patient with ESRD (CHF 215.05). In the case of renal transplantation follow-on costs, resource utilization was determined through a telephone-based interview with 5 of the 6 Swiss transplantation centres. An additional expert consensus methodology was used to determine the proportion of health care resource utilization in type 2 diabetics. The percentage of patients receiving each of the 3 treatment alternatives was derived from a cross-sectional national study conceived for this purpose (haemodialysis: 85.36%, peritoneal dialysis: 10.46% and transplantation: 4.18%). The daily costs for haemodialysis and peritoneal dialysis were derived from figures provided by the Schweizerische Verband für Gemeinschaftsaufgaben der Krankenversicherer (SVK) [Swiss Association for Shared Responsibilities of Health Insurance Providers] (SVK) [22, 23]. The costs of transplantation were calculated on the basis of SVK lump sums and the response of experts to questions on the utilization of health resources for kidney transplantation [24–26]. The cross-sectional study and utilization of health resources are not described in greater detail here since they are discussed in detail by Sandoz et al. [21].

The costs of treatment with losartan were calculated on the basis of an average daily dose of losartan over a period of 3.5 years. The necessary number of packs is derived from this. Since type 2 diabetes is a chronic disease, the largest pack size was assumed and a pack that had been opened was regarded as such and not calculated as a full pack. The basis for the tariff was the healthcare payer-approved price to the public on the List of Specialties (Spezilitätenliste) for 2001, minus the cost stabilization rebate (3.2%) that pharmacies grant to the healthcare providers [27]. It was assumed that the drugs were dispensed through a usual pharmacy every 3 months and that the payment was based on the Leistungsorientierten Abgeltung für Apotheker (LOA) [Schedule of Service-related Payments to Pharmacists] which laid down government-fixed prices for pharmacists and patients for 2001 [28]. The mandatory 10% patient co-pay for the drug costs was subtracted. The statutory minimum annual insurance franchise of CHF 230 was not taken into consideration in the drug costs as it was assumed that this franchise would have been exhausted for those with a chronic illness in the course of routine consultations [29].

The ESRD-associated costs and cost savings were arrived at by multiplying the average number of days of ESRD for the 2 groups (losartan and placebo) by the daily costs of ESRD and then subtracting the costs of the losartan treatment to arrive at the net cost savings.

To establish robustness, the results were subjected to univariate sensitivity analyses with the 3 variables – a) daily costs of ESRD, b) the percentage distribution of the 3 modes of treatment (haemodialysis, peritoneal dialysis and transplantation) and c) the number of ESRD days saved. The daily costs of ESRD were varied upwards and downwards by 30%, a range our group has successfully used in other economic analyses in Switzerland. The transplantation percentage value (4.18%) was left unchanged in the sensitivity analysis of the percentage distribution. The remaining 95.82% was varied firstly a) for 60% haemodialysis (corresponding to 57.5% of 95.82%) and 40% peritoneal dialysis (corresponding to 38% of 96%) and secondly b) for 100% haemodialysis (corresponding to 95.82%) and 0% peritoneal dialysis. The transplantation percentage of 4.18% was not varied as there is no information on the variability of this percentage and it may reasonably be assumed that the value is relatively constant given the shortage of organs and the continued reticence of surgeons to carry out transplants for type 2 diabetics. The variation of the haemodialysis and peritoneal dialysis percentages is based on the results of the aforementioned cross-sectional study. So, for a) the percentages of the dialysis centre of the cross-sectional study with the lowest haemodialysis percentage (60% haemodialysis and 40% peritoneal dialysis) were used and for b) the percentages of the dialysis centre with the greatest haemodialysis percentage (100% haemodialysis) were used. This approach was adopted since the cross-sectional study delivered concrete figures for the relationship between haemodialysis and peritoneal dialysis, and haemodialysis had the highest daily costs of the 3 modes of treatment.

Results

Over a period of 3.5 years, losartan significantly reduced the number of ESRD days of type 2 diabetics with nephropathy by an average of 33.6 days (95% CI: 10.9, 56.3) compared to the placebo (table 1). This reduction in the number of ESRD days resulted in ESRD-associated cost savings of CHF 7,226 per patient over a period of 3.5 years (the ESRD-associated costs savings increased to CHF 10,086 per patient after 4 years) (table 2). If the average costs per patient for treatment with losartan for the same period (CHF 3,142) are subtracted from the CHF 7,226 then the reduction in ESRD days yields net cost savings of CHF 4,084 per patient over 3.5 years (table 3, figure 1)

Table 4 shows the results of univariate sensitivity analysis. The 2 univariate sensitivity analyses

Table 1

Average number of ESRD days and days of ESRD saved per patient.

Follow-up	Losartan (+CT*) (n = 751)	Placebo (+CT*) (n = 762)	ESRD days saved	95% CI
2 years	19.2	24.9	5.7	(–2.7, 14.1)
2.5 years	34.7	46.9	12.2	(–0.7, 25.1)
3 years	53.6	74.7	21.1	(3.5, 38.7)
3.5 years**	76.1	109.7	33.6	10.9, 56.3
4.years	102.0	148.9	46.9	(19.1, 74.7)

* CT = Conventional antihypertensive treatment
** Defined time frame for economic evaluation

Table 2

Average ESRD-associated costs and ESRD-associated cost savings per patient (CHF).

Follow-up	Losartan (+CT*) (n = 751)	Placebo (+CT*) (n = 762)	Average ESRD-associated cost savings
2 years	4,129	5,355	1,226
2.5 years	7,462	10,086	2,624
3 years	11,527	16,064	4,538
3.5 years**	16,365	23,591	7,226
4 years	21,935	32,021	10,086

* CT = Conventional antihypertensive treatment
** Defined time frame for economic evaluation

Table 3

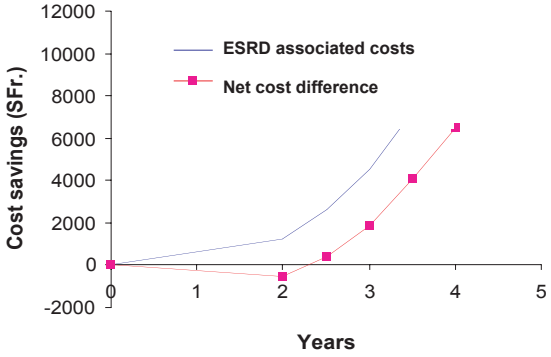
Net cost savings per patient (CHF).

Follow-up	Average ESRD-associated cost savings	Average treatment costs for losartan	Net cost savings
2 years	1,226	1,774	-548
2.5 years	2,624	2,224	400
3 years	4,538	2,674	1,864
3.5 years*	7,226	3,142	4,084
4 years	10,086	3,575	6,511

* Defined time frame for economic evaluation

Figure 1

Cost savings per patient (ESRD-related costs; Net cost difference).



for the variables ESRD daily costs and percentage distribution of the 3 treatment modalities always yielded net cost savings. By contrast, the sensitivity analysis in respect of the variable ESRD days saved showed substantial net cost savings only for the 56.3 days and additional costs of CHF 798 for the 10.9 days.

Table 4

Univariate sensitivity analyses.

	ESRD-associated cost savings (CHF)	Net cost savings per patient (CHF)
Daily costs of ESRD		
+30%	9,394	6,252
–30%	5,058	1,916
Percentage distribution across the 3 treatment modalities		
HD* 95.82%, PD# 0%, T§ 4.18%	7,463	4,321
HD* 57.49%, PD# 38.33%, T§ 4.18%	6,594	3,452
No. of ESRD days saved		
56.3	12,107	8,965
10.9	2,344	–798

* HD = Haemodialysis
# PD = Peritoneal dialysis
§ T = Transplantation

Discussion

The results of this economic evaluation revealed net cost savings of CHF 4,084 (€ 2,687) for patients with diabetic nephropathy and type 2 diabetes when given 50 to 100 mg losartan once daily over a period of 3.5 years compared to placebo. In addition to its clinical benefit (a significant 28% reduction in the incidence of ESRD [p = 0.002]) and therefore a reduction in the number of ESRD days, it also has economic benefits. Moreover, these appear to increase with a lengthening of the treatment period [14].

Cost-effectiveness analyses for the RENAAL study were also carried out for the USA, the European Union and Germany with similar results [30, 31, 33–35]. These analyses yielded net cost savings for the EU of € 3,718 per patient over a period of 3.5 years (rising to € 5,189 after 4 years). The savings for the USA were € 3,592 (€ 5,702 after 4 years) and for Germany € 1,911 (€ 3,212 after 4 years), assuming a then exchange rate of 1 € = CHF 1.5197, 1 dollar = CHF 1.7910. At current exchange rates the savings in the USA (in Euros) would be quite a lot higher. The calculated net cost savings for Switzerland of CHF 4,084, equivalent to € 2,687, are thus greater than those for Germany and below those for the European Union and the USA. The daily costs of ESRD adopted for this study are € 141.51 (CHF 215.05) for Switzerland, € 111 for the study for the EU and Germany € 180.31 (US$ 153) for the USA. The daily costs for ESRD adopted in the analyses are the latest available and the only ones available in the literature. The calculated net cost savings of the different values for the different countries reflect the variation in the daily ESRD costs between those countries.

A comparison of the different daily costs for ESRD, reflected in the different net cost savings, is only possible to a limited degree for several reasons. The ESRD costs embrace a different range of services depending on the country in question. The ESRD costs for Switzerland can therefore only be compared to those for Germany within certain limits, since the ESRD costs for Germany only take the dialysis costs into consideration and neglect the costs of transplantation. The German costs moreover include costs for erythropoetin, complications and transport. The dialysis costs for Switzerland only include erythropoetin and not the costs of complications or transport [32]. Possible reasons for the 20% lower daily costs in Germany compared to Switzerland, despite the more comprehensive scope of services, include the generally lower price level in Germany and the difference in the percentage distribution of the 3 treatment modalities. Haemodialysis is the commonest form of treatment in both countries. Switzerland,

however, has a higher percentage of patients on haemodialysis than Germany – 85.4% compared to 70%. The dialysis in centres is in both countries the most expensive form of dialysis, but it is still less costly in Germany than in Switzerland.

The results of our study are also in accordance with other model-based *cost-effectiveness* studies. Palmer et al. [1, 32] performed a cost-effectiveness study of the IDNT study [15]. They developed a Markov model which simulated the progression from nephropathy to ESRD and death in patients with hypertension, type 2 diabetes and overt nephropathy. They determined that the onset of ESRD was delayed with irbesartan by 1.41 and 1.35 years versus amlodipine and control, respectively. When a 10-year time horizon was considered, delay in ESRD onset led to anticipated improvements in life expectancy of 0.13 years versus amlodipine and 0.26 years versus control. Irbesartan was associated with cost savings of € 14,949 and € 9205/patient in Belgium, and € 20,128 and € 13,337 in France, versus amlodipine and control, respectively. Similar results for the IDNT study were obtained by Rodby et al. for the United States [34]. At three, resp. ten years, the model yielded net savings of US$ 2,778 resp. US$ 15,607 per patient treated with irbesartan. The cost-effectiveness of Losartan in the RENAAL was valued by Souchet at al. for the French health care system [35]. The mean cumulative cost of losartan over 4 years was € 1,603 per patient. The reduction in the number of ESRD days over 4 years in patients treated with losartan significantly decreased costs associated with ESRD by € 7,438 per patient. Compared to the placebo group, the average cost per patient over 4 years in the losartan group was lower by € 5,834.

In a US (non-modeling) study Herman and colleagues also determined net cost savings for losartan in the RENAAL study [36]. The results showed that losartan compared with placebo reduced the number of days with ESRD by 33.6 per patient over 3.5 years. This reduction in ESRD days resulted in a decrease in cost associated with ESRD of US$ 5144 per patient (p = 0.003, 95% CI US$ 1,701 to 8,587). After accounting for the cost of losartan, the reduction in ESRD days resulted in a net savings of US$ 3,522 US dollars per patient over 3.5 years (p = 0.041, US$ 143 to 6,900).

Several limitations are noteworthy. Multivariate sensitivity analyses would have been more informative, but were omitted in order to make interpretation of the results easier. The fact that no discounting was used for future costs and cost savings in this economic evaluation is justifiable given the relative short time frame of 3.5 years. Another limitation of this cost-effectiveness analysis is certainly the fact that the range of services taken into consideration in the resources consumed by a patient with ESRD is approximated to in reality, but not fully covered. In addition, the limitations of the RENAAL study – adopted as a clinical database for the economic evaluation – are a limitation for the cost-effectiveness analysis. The patients in the RENAAL study are thus selected ones and are not necessarily representative of patients in everyday practice. For instance, the compliance of patients in the clinical study is likely to be better than in everyday clinical practice. A further possible criticism is whether a placebo is really an adequate treatment comparator for losartan, or whether an ACE inhibitor should have been used. In a recently-published study it was found that angiotensin-II receptor antagonists and ACE inhibitors are first-line drugs for secondary prevention in type 2 diabetics beginning nephropathy. Angiotensin-II receptor antagonists alone are first-line drugs for tertiary prevention (overt nephropathy) [37]. Although the renoprotective effect is an evident one for ACE inhibitors, it is not yet approved as an indication in Switzerland so that a placebo is probably acceptable as a treatment comparator. Additionally, patients in the placebo group required more antihypertensive medication. These costs would obviously augment the cost-effectiveness ratio. However, we were not able to quantify this effect due to the inability to have access to the raw study data. Another issue which we could not address is the extent of savings beyond what has been demonstrated in the RENAAL study. Even though expected savings might increase in theory, empirical analysis might require extensive modeling, requiring data which is not readily available.

Conclusions

The net cost savings that administration of losartan brings that have been shown in this economic evaluation are of considerable importance given that the annual costs of diabetic nephropathy with ESRD in type 2 diabetics in Switzerland are approximately CHF 46 million [21]. On the basis of the scientific evidence currently available, the use of the angiotensin-II receptor antagonist losartan to prevent the advance of diabetic nephropathy is to be welcomed from both a clinical and economic perspective.

One of the aims of the St. Vincent Declaration of the WHO in 1989 was to reduce the incidence of chronic renal failure as a result of diabetes by more than one third [37]. Treatment of type 2 diabetics with nephropathy with losartan would help to attain this aim and at the same time save costs.

The findings of this study are very important from a public health perspective. The prevalence of diabetic nephropathy with ESRD in Switzerland for type 2 diabetes mellitus is 73 cases per million residents and the total direct medical costs of

this complication are CHF 46,065,788 per annum (0.11% of total health expenditure). This corresponds to CHF 215.05 per patient per day and CHF 1,569.87 per 100,000 residents per day. Of these costs, 82% relate to haemodialysis, 7% to peritoneal dialysis and 11% to kidney transplantation. Prevention of this complication is of extreme importance and would make a substantial contribution to the judicious allocation of resources within the healthcare system.

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References

1 Ritz E, Stefansky A. Diabetic nephropathy in type II diabetes. Am J Kidney Dis 1996;27:167–94.
2 Ritz E, Rychlík I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes: a medical catastrophe of worldwide dimensions. Am J Kidney Dis 1999;34:795–808.
3 Ismail N, Becker B, Strzelczyk P, Ritz E. Renal disease and hypertension in non-insulin-dependent diabetes mellitus. Kidney Int 1999;55:1–28.
4 Ritz E, Rychlik I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes: a medical catastrophe of worldwide dimensions. Am J Kidney Dis 1999;34:795–808.
5 Mackenbach JP, Kunst AE, Lautenbach H, Oei YB, Bijlsma F. Competing causes of death: a death certificate study. J Clin Epidemiol 1997;50:1069–77.
6 Thomas RJ, Palumbo PJ, Melton LJ 3rd, Roger VL, Ransom J, O'Brien PC, et al. Trends in the mortality burden associated with diabetes mellitus: a population-based study in Rochester, Minn, 1970–1994. Arch Intern Med 2003;163:445–51.
7 Ritz E. Nephropathy in type 2 diabetes. J Intern Med 1999;245: 111–26.
8 Fliser D, Haller H. nephropathy bei Diabetes mellitus type 2. Der Internist 2000;41:1363–73.
9 Bruno G, Biggeri A, Merletti F, Bargero G, Ferrero S, Pagano G, et al. Low incidence of end-stage renal disease and chronic renal failure in type 2 diabetes: a 10-year prospective study. Diabetes Care 2003;26:2353–8.
10 O'Brien JA, Shomphe LA, Kavanagh PL, Raggio G, Caro JJ. Direct medical costs of complications resulting from type 2 diabetes in the U.S. Diabetes Care 1998;21:1122–8.
11 Caro JJ, Ward AJ, O'Brien JA. Lifetime costs of complications resulting from type 2 diabetes in the U.S. Diabetes Care 2002; 25:476–81.
12 Liebl A, Carides GW, Gerth WC, Krobot KJ. losartan reduces the medical burden and costs associated with ESRD. Implications from the RENAAL Study for Germany. Poster des Kongresses der European Association for the Study of Diabetes, 38. Jahrestreffen, 1.–5. September 2002, Budapest, Ungarn.
13 USRDS Annual Report 2000. www.usrds.org. Zugegriffen am 27. November 2002.
14 Brenner BM, Cooper ME, De Zeeuw D, Keane WF, Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001;345:861–8.
15 Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al.; Collaborative Study Group. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345: 851–60.
16 Parving HH, Lehnert H, Brochner-Mortensen J, Gomis R, Andersen S, Arner P. Irbesartan in Patients with Type 2 Diabetes and microalbuminuria Study Group. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med 2001;345:870–8.
17 Viberti G, Wheeldon NM, for the MicroAlbuminuria Reduction With VALsartan (MARVAL) Study Investigators. Microalbuminuria reduction with valsartan in patients with type 2 diabetes mellitus: a blood pressure-independent effect. Circulation 2002;106:672–8.
18 Sica DA, Bakris GL. Type 2 diabetes: RENAAL and IDNT – the emergence of new treatment options. J Clin Hypertens 2002;4:52–7.
19 Ess SM, Schneeweiss S, Szucs TD. European healthcare policies for controlling drug expenditure. Pharmacoeconomics 2003;21:1–15.
20 Herman WH, Shahinfar S, Carides GW, Dasbach EJ, Brenner BM for the RENAAL Investigators. losartan reduces the costs associated with ESRD: economic evaluation. Poster ASN/ISN Weltkongresses der Nephrologie, 13.–17. Oktober 2001, San Francisco, USA.
21 Sandoz MS, Ess SM, Keusch GW, Schwenkglenks M, Szucs TD. Prevalence and direct medical costs of end-stage renal disease in patients with type 2 diabetes mellitus in Switzerland for 2001. Swiss Med Wkly 2004;134:448–58.
22 Schweizerischer Dialysevertrag zwischen H+ Die Spitäler der Schweiz, Aarau und dem SVK Schweizerischer Verband für Gemeinschaftsaufgaben der Krankenversicherer, Solothurn. Anhang: Tarif, Position 11*, per 1. Juli 1998.
23 Schweizerischer Dialysevertrag zwischen H+ Die Spitäler der Schweiz, Aarau und dem SVK Schweizerischer Verband für Gemeinschaftsaufgaben der Krankenversicherer, Solothurn. Anhang: Tarif, Position 22*, per 1. Juli 1998.
24 Schweizerischer Verband für Gemeinschaftsaufgaben der Krankenversicherer SVK. Vertrag über Transplantation solider Organe. Anhang 2 Abschnitt 1, per 1. November 2001.
25 Schweizerischer Verband für Gemeinschaftsaufgaben der Krankenversicherer SVK. Vertrag über HLA-Typisierung bei Nierentransplantationen bzw. Nieren-Pankreastransplantationen (bzw. Nieren und Langerhans'sche Inseln), per 1. November 1999.
26 Schweizerischer Verband für Gemeinschaftsaufgaben der Krankenversicherer SVK. Vertrag über Angabenbestimmung bezüglich Immunologie bei Nierentransplantationen bzw. Nieren-Pankreastransplantationen (bzw. Nieren und Langerhans'sche Inseln), per 1. Juli 1999.
27 Spezialitätenliste (Stand 1.07.2001). www.bsv.admin.ch/sl/liste/d/index.htm. Zugegriffen im Juli 2002.
28 Leistungsorientierte Abgeltung (LOA) für Apothekerinnen und Apotheker (mit Einführung ab 1. Juli 2001).
29 Krankenversicherungsgesetz KVG: Artikel 64, Absatz 2 und Verordnung über die Krankenversicherung (KVV) vom 27. Juni 1995: Artikel 103, Absatz 1 und 2.
30 Gerth WC, Viberti GC, Remuzzi G, Hannedouche T, Martinez-Castelao A, Shahinfar S, et al. losartan reduces the burden and cost of ESRD: Public health implications from the RENAAL study for the European Union. Poster des Kongresses der European Association for the Study of Diabetes, 38. Jahrestreffen, 1.–5. September 2002, Budapest, Ungarn.
31 Herman WH, Shahinfar S, Carides GW, Dasbach EJ, Gerth WC, Alexander CM, et al. losartan Reduces the Costs Associated With Diabetic End-Stage Renal Disease: The RENAAL study economic evaluation. Diabetes Care 2003;26:683–7.
32 Nebel M. Behandlungskosten der Nierenersatztherapie in Deutschland 1999. Nieren- und Hochdruckkrankheiten 2002; 31:85–92.
33 Palmer AJ, Annemans L, Roze S, Lamotte M, Rodby RA, Cordonnier DJ. An economic evaluation of irbesartan in the treatment of patients with type 2 diabetes, hypertension and nephropathy: cost-effectiveness of Irbesartan in Diabetic Nephropathy Trial (IDNT) in the Belgian and French settings. Nephrol Dial Transplant 2003;18:2059–66.

34 Rodby RA, Chiou CF, Borenstein J, Smitten A, Sengupta N, Palmer AJ, et al. Collaborative Study Group. The cost-effectiveness of irbesartan in the treatment of hypertensive patients with type 2 diabetic nephropathy. Clin Ther 2003;25:2102–19.
35 Souchet T, Durand Zaleski I, Hannedouche T, Rodier M, Gaugris S, Passa P. An economic evaluation of Losartan therapy in type 2 diabetic patients with nephropathy: an analysis of the RENAAL study adapted to France. Diabetes Metab 2003;29: 29–35.
36 Herman WH, Shahinfar S, Carides GW, Dasbach EJ, Gerth WC, Alexander CM, et al. Losartan reduces the costs associated with diabetic end-stage renal disease: the RENAAL study economic evaluation. Diabetes Care 2003;26:683–7.
37 Deferrari G, Ravera M, Deferrari L, Vettoretti S, Ratto E, Parodi D. Renal und cardiovascular protection in type 2 diabetes mellitus: Angiotensin II receptor blockers. J Am Soc Nephrol 2002;13(Suppl 3):224–9.
38 Gozzoli V, Palmer AJ, Brandt A, Spinas GA. Economic and clinical impact of alternative disease management strategies for secondary prevention in type 2 diabetes in the Swiss setting. Swiss Med Wkly 2001;131:303–10.

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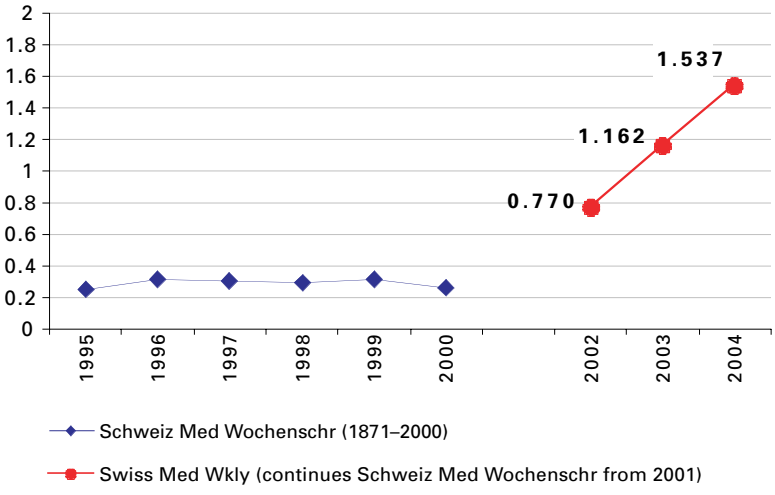

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