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Economic and clinical impact of alternative disease management strategies for secondary prevention in type 2 diabetes in the Swiss setting

Valerio Gozzoli[a], *A. J. Palmer*[b], *A. Brandt*[a], *Giatgen A. Spinas*[c]

[a] Institute for Medical Informatics and Biostatistics (IMIB), Riehen, Switzerland
[b] Centre for Outcome Research (CORE), Basel, Switzerland
[c] Department of Endocrinology and Diabetology, University Hospital Zürich, Switzerland

Summary

Principles: Different intervention strategies for the optimisation of disease management of diabetes exist and have been shown to increase the proportion of patients receiving screening and examinations and to improve risk factors such as Hb_{A1c}, lipids, and blood pressure. Thus, in the long-term, a decrease in diabetic complications and the associated costs could be expected. To address this question, the current analysis used a published diabetes simulation model to analyse the long-term clinical and economic implications of implementing various interventions in the Swiss setting.

Methods: Based on data from the literature, the short-term effects on clinical variables of multifactorial interventions, including screening for nephropathy and retinopathy, educational programmes and control of cardiovascular risk profile were assessed, and a cost-effectiveness analysis in comparison to standard care was performed. Life expectancy (LE) and total lifetime costs (TC) from the perspective of the health insurance payer were calculated using a long-term Markov simulation model.

Results: The multifactorial intervention led to an improvement in undiscounted LE of 0.56 years (LE = 10.73 and 11.29 years for standard care and multifactorial intervention respectively), and a reduction in 3%-discounted TC of CHF 7313 (10.7%) per patient compared to current standard practice. Extrapolation to the whole Swiss type 2 diabetes population (285 000) showed yearly cost savings of CHF 194 million from the multifactorial intervention.

Conclusions: The implementation of multifactorial interventions, including improved control of cardiovascular risk factors, combined with early diagnosis and treatment of diabetic complications, could be both cost- and life-saving in the Swiss setting.

Keywords: diabetes mellitus; cost-effectiveness; screening; secondary prevention

Introduction

Diabetes mellitus is the most common metabolic disease worldwide. In Switzerland some 285 000 patients are affected and the number of newly diagnosed cases is increasing [1]. Because of its chronic course and the appearance of severe, cost-intensive micro- and macrovascular complications such as diabetic retinopathy and nephropathy, coronary heart disease, stroke, and peripheral vascular disease possibly involving amputation, diabetes has a major clinical and economic impact. In the St. Vincent declaration of 1989, concrete endpoints for the improvement of disease management of diabetic patients were defined to which the Swiss government was also willing to adhere [2]. Some of the endpoints defined are reduction of the rate of amputations to half and reduction of blindness and endstage renal disease by a third. In addition, the incidence of diabetes-related myocardial infarction and stroke is to be reduced and the life expectancy of diabetic patients improved. New forms of disease management in diabetes suggest that better short- and long-term results could be obtained by optimisation of treatment conditions [3–7]. Such forms of disease management include treatment and educational programmes for patients and physicians, various forms of intensive insulin therapy, electronic patient recording with implementation of international treatment guidelines, and multidisciplinary team-based patient care. Optimisation of care by disease management,

in the sense of secondary prevention (and possibly primary prevention too), may lead to improved life expectancy and quality of life, and may presumably pay off by reducing treatment costs for diabetic complications. To address this question, the long-term clinical and economic implications of implementing various intervention strategies in patients with type 2 diabetes in the Swiss setting were analysed, using a published computer-based diabetes simulation model.

Methods

Model structure. For the cost-effectiveness analysis of alternative disease management strategies a published computer-based diabetes model was used [5]. The model simulates the clinical and economic implications of six diabetes-related short- and long-term complications (hypoglycaemia, nephropathy, retinopathy, acute myocardial infarction, stroke, amputation) under various treatment strategies. Life expectancy, incidence, prevalence, and cumulative event rate of complications, as well as the treatment costs for diabetes and its complications, are calculated for a patient cohort over lifetime. The precise structure of the model and its submodels is described elsewhere in detail [5].

Table 1

General characteristics of the type 2 diabetes cohort analysed [8].

Variable	
Age	63 years
Sex	46.4% women
Duration of diabetes	13 years
Hb_{A1c}	7.4%**
Arterial hypertension	16.9%*
Total cholesterol	6.0 mmol/l**
HDL-cholesterol	1.01 mmol/l**
Triglycerides	2.46 mmol/l**
Smokers	15.4%
Retinopathy screening	75.2%
Nephropathy screening	15.5%
Proliferative retinopathy	14.4%
Microalbuminuria	17.2%**
Macroalbuminuria	10.2%**
Endstage renal disease	5.5%
History of acute myocardial infarction	9.8%
History of stroke	5.7%**
History of amputation	3.0%

* 90% with antihypertensive treatment
** Data from Germany [35]

Cohort and intervention strategies. The clinical and economic implications of the various intervention strategies were simulated for a cohort representing the Swiss type 2 diabetes population (table 1) [8]. The following interventions were combined in the model and compared with standard care: (1) Educational programme (2) Nephropathy screening with ensuing ACE-inhibitor therapy (3) Retinopathy screening with ensuing laser therapy (4) Multifactorial intervention. Standard care was defined as treatment with insulin (57%, in 45% combined with oral antidiabetic agents), oral antidiabetic agents (35%) and diet alone (8%), whereas 50% of patients on insulin, 10% on oral antidiabetic agents and 5% on diet performed regular blood and urine glucose self-measurement [8]. In some 50% of patients Hb_{A1c} was measured twice yearly. Screening for nephropathy and retinopathy was assumed in 15.5% and 75.2% respectively [8]. The educational programme, consisting of 5 lesson units of 90 to 120 minutes each, included learning of metabolic self-monitoring, dietary recommendations, influence of physical activity and illnesses on glucose metabolism, behaviour during hypoglycaemia, diabetic complications, foot care, and general health education [9]. For the simulation it was assumed that the educational programme was repeated every five years and that it reduced the Hb_{A1c}-level by 1.3% (absolute reduction) and the proportion of smokers by 25% (relative reduction) [10,11]. Nephropathy screening included a yearly test for microalbuminuria by test strip, followed by treatment with ACE inhibitors in the presence of microalbuminuria. Retinopathy screening consisted of annual 7-field fundus photography followed by laser photo-

Table 2

Overview of studies assessing the short-term effects of educational programmes and multifactorial interventions on clinical variables.

Author, year	study design	patient number	intervention	major finding
Schiel, 1997 [10]	observational, uncontrolled	59	educational programme	no effect on Hb_{A1c}, reduction of 25% in smokers
Schlottmann, 1996 [11]	observational, uncontrolled	243	educational programme	reduction of 1.5% in Hb_{A1c}
Hanefeld, 1991 [12]	randomised, controlled	382	multifactorial	reduction of 10 mm Hg in SBP, no effect on total cholesterol
Chicoye, 1998 [13]	observational, uncontrolled	5100	multifactorial	reduction of 24% in smokers
Ginsberg, 1998 [14]	observational, uncontrolled	507	multifactorial	reduction of 2% in Hb_{A1c}
Kelly, 1998 [15]	observational, uncontrolled	2163	multifactorial	reduction of 1.6% in Hb_{A1c}, reduction of 23% in smokers
Overland, 1999 [16]	observational, uncontrolled	86	multifactorial	reduction of 0.8% in Hb_{A1c}, reduction of 5 mm Hg in SBP, reduction of 1.2 mmol/l in total cholesterol
Rubin, 1998 [17]	observational, uncontrolled	18000	multifactorial	reduction of 25% in smokers
Smith, 1998 [18]	observational, uncontrolled	39	multifactorial	reduction of 0.5% in Hb_{A1c}, reduction of 3 mm Hg in SBP

SBP = systolic blood pressure

coagulation if proliferative retinopathy was present. The multifactorial intervention included an educational programme, screening for nephro- and retinopathy, and control of cardiovascular risk factors, e.g. by electronic patient recording with implementation of evidence-based international treatment and control guidelines for optimisation of metabolic control, early diagnosis and treatment of complications, and health education. In the model the multifactorial intervention was simulated assuming two additional Hb_{A1c}-tests per year; one additional measurement of the lipid profile (cholesterol, HDL, triglycerides) per year; one annual screening for nephropathy and retinopathy in 100% of patients; an educational programme and control of blood pressure and smoking. From published sources it was estimated that the multifactorial intervention reduced Hb_{A1c} by 1.6% (absolute reduction), systolic blood pressure by 9 mm Hg, total cholesterol by 0.23 mmol/l (9 mg/dl) and the percentage of smokers by 25% (relative reduction) [12–18].

Clinical and economic data. The short-term effects of the interventions on clinical variables (Hb_{A1c}, lipids, blood pressure, nicotine abuse) were estimated by a literature search (MEDLINE), while the weighted averages were calculated and integrated in the diabetes model (table 2) [10–18]. General mortality was taken from Swiss mortality tables [19]. Due to lack of specific Swiss data, the event probabilities used in the model were mainly from other countries [3, 4, 20–22]. The costs of complications and interventions from the perspective of the health insurance payer were taken from published sources or were based on our own calculations (table 3).

Primary endpoints of the analysis were life expectancy, total direct lifetime costs, and cumulative event rates of diabetic complications. Indirect costs (loss of productivity) were not considered in the analysis. To take into account the time course of the accumulating costs, results were discounted at a real discount rate of 3%. Additionally, undiscounted costs and costs discounted at 5% were also calculated. Life expectancy was discounted at the same discount rates, but since discounting LE is more controverted, undiscounted results were discussed. Discounting takes into consideration the fact that the cost and utilities of an intervention incurred later in the course of a disease must be valued at a lower level than present cost and utilities. Consequently, in the cost-effectiveness analysis future values must be computed at a lower, "discounted" rate. To detect the variables with the highest influence on the final results an extensive sensitivity analysis was performed by varying all probabilities and cost elements in the model by ±10%. Break-even analysis was performed on annual costs of multifactorial intervention and the percentage of patients complying with the intervention. To compare the cost-effectiveness of an intervention with that of standard care, the incremental cost-effectiveness ratio (ICER) was calculated, which is defined as: $ICER = (C_i - C_o) / (E_i - E_o)$, where: C_o = total cost with standard care, C_i = total cost with an intervention, E_o = life expectancy with standard care, E_i = life expectancy with an intervention. If an intervention is less expensive and more effective than standard treatment, in terms of health economics the intervention is defined as "dominant" compared to the standard and calculation of the ICER is superfluous. In the opposite case (higher costs, lower effectiveness) the intervention is "dominated" by the standard.

Table 3

Cost data used in the model (CHF in 1996 values).

Cost element	event and first year	following years
Type 2 diabetes standard care [36–40]	1256	1256
Educational programme (every 5 years) [9, 38]	149*	–
Multifactorial intervention [9, 36, 38]	711*	114*
Nephropathy screening [38]	29	29
ACE-inhibitor therapy [36]	888	888
Retinopathy screening [38]	208	208
Photocoagulation [9]	743	–
Acute myocardial infarction [39–41]	23024	1700
Stroke [39–41]	33578	8687
Amputation [39–41]	35271	594
Haemodialysis [37]	63935	63935
Peritoneal dialysis [37]	48231	48231
Kidney transplantation [37]	209500	147500
Blindness (estimation)	1000	1000
Hypoglycaemia [39, 42]	620	–

* Costs additional to standard care

Results

Table 4 sums up the results of the mean life expectancy (LE) and the total lifetime costs (TC) with standard care and the interventions analysed. Table 5 shows the TC broken down by cost elements. As expected, the treatment costs for complications decrease with increasing prevention costs. Compared to standard care, all interventions with the exception of the educational programme resulted in lower TC with an improvement in LE, and thus in terms of health economics they are dominant compared to standard care. The greatest effect on LE was obtained by the multifactorial intervention, with an improvement in undiscounted LE of 0.56 years (standard care 10.73 years, multifactorial intervention 11.29 years). In table 6 cumulative event rates for the major dia-

betic complications are listed under standard care and multifactorial intervention. Implementation of the intervention resulted in a marked reduction in cost-intensive complications such as endstage renal disease, which was reduced by 53.01% with the multifactorial intervention. The reduction of acute myocardial infarction by 3.89% and stroke by 5.15% was less marked.

Whereas the educational program alone led to additional costs (CHF 155 per patient and lifetime), the multifactorial intervention showed the highest savings (CHF 7313 per patient and lifetime), equivalent to a 10.7% reduction in TC (table 5). The savings were achieved after 3–4 years (figure 1). As a sign of early savings, the results were robust after discounting with 0% and 5%, with the exception of TC with an educational programme (table 4).

Extrapolation of the results to the Swiss setting was performed with a prevalence of type 2 diabetes of 3.5% (285 000 diabetic patients) [1]. Figure 1 shows the extrapolated cumulative costs of the interventions compared to standard care. Over lifetime the 3% discounted additional costs were CHF 44 million with the educational programme, and the savings with the other interventions were CHF 1.99-2.09 billion. After consideration of the increase in diabetes prevalence (P) due to the improved LE, according to the formula $P_{Intervention} = P_{Standard} \times LE_{Intervention} / LE_{Standard}$, extrapolation of the average 3% discounted annual costs per patient (= TC / LE) to the whole Swiss type 2 diabetes population resulted in annual additional costs of CHF 4.1 million with the educational programme and annual savings of CHF 185 million if combined with screening for nephro- and retinopathy, CHF 193 million if combined with nephropathy screening, and CHF 194 million with the multifactorial intervention.

In the sensitivity analysis the incidence of myocardial infarction and endstage renal disease had the most marked impact on LE. The cost elements with the strongest influence on TC were the annual costs for haemodialysis and treatment of diabetes (figure 2). In break-even analysis of the additional annual costs of the multifactorial intervention and the percentage of patients complying with the intervention, the break-even points were CHF 732 per patient and 46% for additional annual costs and compliance respectively (figure 3).

Table 4.

Discounted and undiscounted mean life expectancy (LE) (years) and total lifetime costs (TC) (CHF in 1996 values) per type 2 diabetes patient with and without interventions.

Intervention	annual discount rate					
	0%		3%		5%	
	LE	TC	LE	TC	LE	TC
Standard care	10.73	85 357	8.81	68 418	7.86	60 281
+ EP	10.83	85 292	8.87	68 573	7.91	60 523
+ EP + NS	11.09	75 417	9.04	61 156	8.04	54 315
+ EP + NS + RS	11.09	75 745	9.04	61 446	8.04	54 586
Multifactorial intervention	11.29	75 235	9.17	61 105	8.14	54 338

EP = educational programme, NS = nephropathy screening, RS = retinopathy screening

Table 5

3%-discounted mean total lifetime costs (TC) (CHF in 1996 values) per type 2 diabetes patient with and without interventions, broken down by cost element.

	standard care	EP	EP+NS	EP+NS+RS	multifactorial intervention
Diabetes management	11 066	11 146	11 351	11 351	11 519
Screening & prevention	1036	2403	2591	2944	3267
Myocardial infarction	5646	5592	5705	5705	5409
Stroke	11 050	10 974	11 327	11 327	10 635
Amputation	954	747	763	763	731
Nephropathy	37 594	36 723	28 254	28 254	28 430
Retinopathy	847	763	787	724	731
Major hypoglycaemia	225	225	378	378	382
Total	68 418	68 573	61 156	61 446	61 105

EP = educational programme, NS = nephropathy screening, RS = retinopathy screening

Table 6

Cumulative event rates (%) of diabetic complications per lifetime in type 2 diabetes patients with standard care and with multifactorial intervention.

Event	standard care	multifactorial intervention	% reduction
Acute myocardial infarction	24.05	23.12	–3.89
Amputation	3.00	2.26	-24.43
Stroke	21.45	20.35	–5.15
Blindness	10.40	7.62	–26.7
Endstage renal failure	8.56	4.02	–53.01

Figure 1

Cumulative discounted savings (discount rate 3%) of various intervention strategies compared to standard care, extrapolated to the Swiss type 2 diabetes population.
◆ = educational programme, ■ = educational programme with nephropathy screening, ▲ = educational programme with nephropathy and retinopathy screening, X = multifactorial intervention.

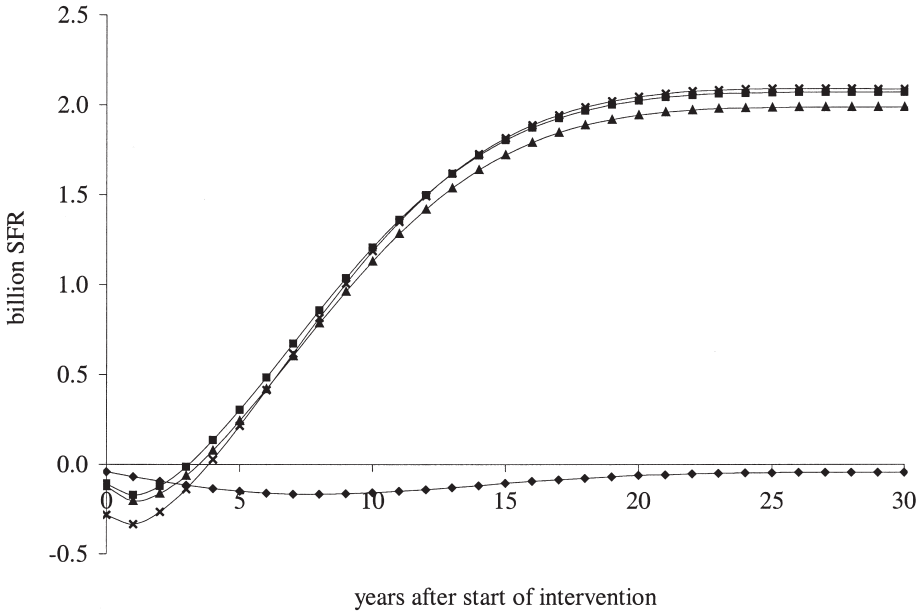
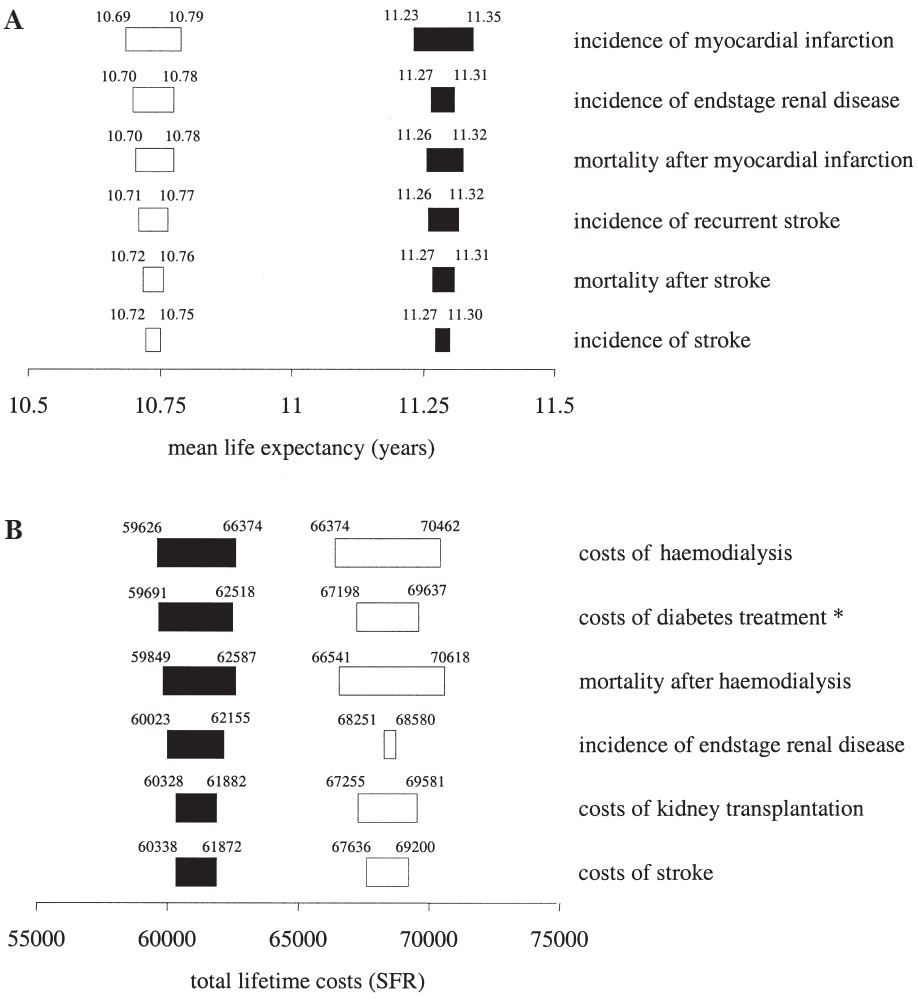


Figure 2

Sensitivity analysis of mean life expectancy and total lifetime costs.
Variables und cost elements with the strongest impact on mean life expectancy (A) and total lifetime costs (B) with standard care (❒) and multifactorial intervention (■). For the sensitivity analysis all variables/cost elements were varied by ± 10%. The sensitivity analysis is performed on values discounted at a discount rate of 3%. * Costs of diabetes treatment include physician's consultations, laboratory analysis, insulin, oral antidiabetic agents, and blood glucose self-measurements.



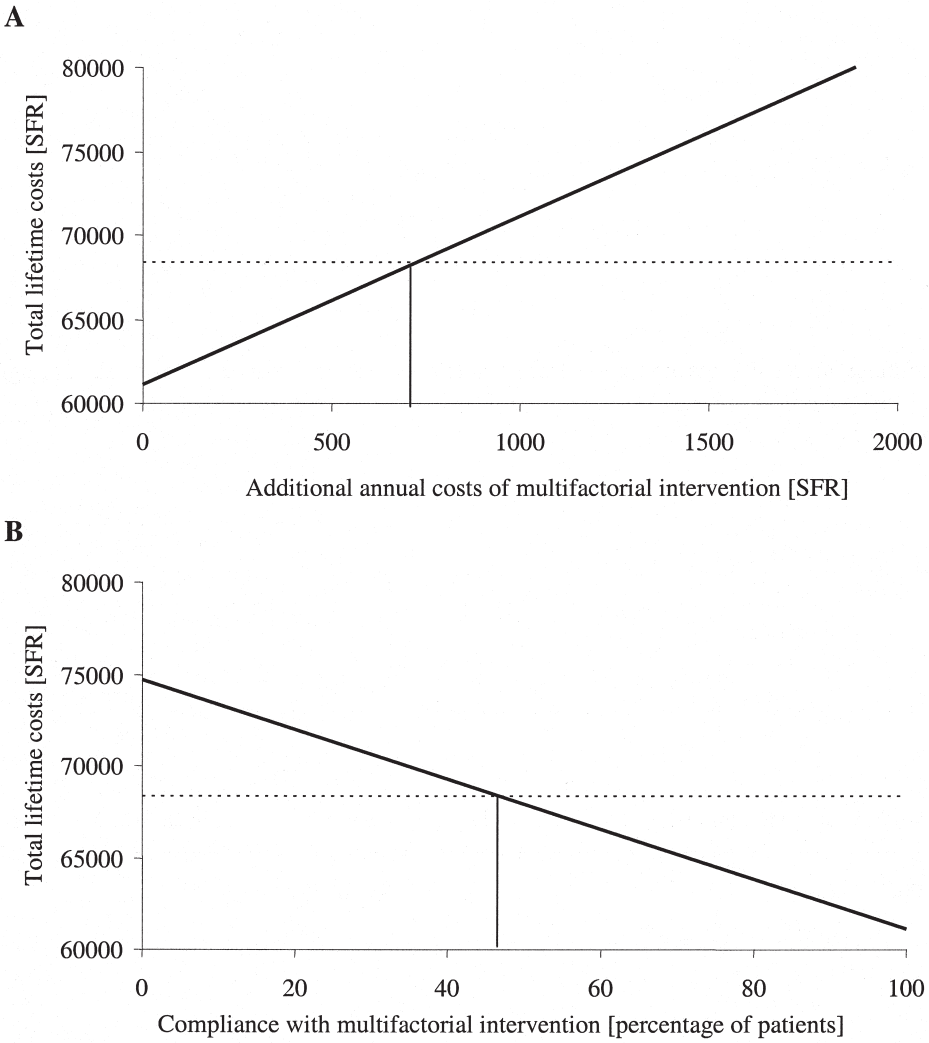


Figure 3

Break-even analysis of additional annual costs and compliance of multifactorial intervention. Horizontal dashed line = total lifetime costs per patient with standard care. Diagonal line = total lifetime costs per patient with multifactorial intervention as the additional annual cost (A) and the compliance (B) of the intervention are varied from CHF 0–2000, and from 0–100% respectively. Vertical line = break-even values: If the additional annual costs of the intervention are less than CHF 732 per patient, the total lifetime costs of the intervention will be lower than with standard care. If compliance with the intervention is greater than 46%, the total lifetime costs of the intervention will be lower than those of standard care. Break-even analysis is performed on values discounted at a discount rate of 3%.

Discussion

The cost-effectiveness analysis of different disease management strategies in patients with type 2 diabetes suggests that their implementation may lead to an improvement in life expectancy and a reduction in total lifetime costs compared to standard care. In the analysis, the multifactorial intervention was the most cost-effective disease management strategy. In the model simulation the improved control of cardiovascular risk factors such as blood glucose, lipids, blood pressure and smoking status, combined with early diagnosis and treatment of diabetic complications such as nephropathy and retinopathy, led to improvement of undiscounted life expectancy of 0.56 years with a reduction of 3%-discounted total lifetime costs of CHF 7313 (10.7%) per patient.

Extrapolated to Switzerland (assuming a type 2 diabetes prevalence of 3.5% [1]) the average annual costs for the Swiss type 2 diabetes population are CHF 1.82 billion with standard care and CHF 1.62 billion with the multifactorial intervention. Through the avoidance of cost-intensive diabetes-related complications, the initial costs turn into savings after as little as 3–4 years, which on average would amount to CHF 194 million per year. Nevertheless, an intervention which pays off only in the later course of a disease often meets with resistance, because health policies tend more to consider present public health expenditures than long-term investments. In health economics this time preference for money and utilities is taken into account by discounting the results in the sphere of health economics [23]. Since there is controversy on which discount rate to apply, the analysis was performed with various discount rates. Even after discounting costs by 5% the annual savings would still be large at CHF 158 million, reflecting the early pay-off with the intervention.

The advantages in health economics of optimising disease management have been demonstrated previously for various interventions. Palmer et al. analysed the cost-effectiveness of different management strategies for type 1 diabetes in Switzerland and found savings of some CHF 42000 (13%) per patient and lifetime by adding screening for nephropathy and retinopathy to

conventional insulin therapy [5]. In the USA Rubin et al. estimated savings through the implementation of a multidisciplinary diabetes management programme in a mixed diabetes population of 12% after one year and 30% after 5 years [17]. According to Ginsberg et al. the lifetime costs could be reduced by US$ 27000 per type 1 diabetes patient by the use of a computerised disease management programme, the intervention paying off after 6–7 years compared to standard care [14]. While these results only count for specific intervention variants, there is a growing impression that optimised diabetes care may be financed by the complication costs avoided.

Our analysis emphasises that besides the economic advantage, the implementation of a multifactorial diabetes management programme also results in clinical benefits and is thus, in terms of health economics, to be considered "dominant" compared to standard care. The multifactorial intervention allows better control of cardiovascular risk factors by the implementation of treatment and control guidelines, e.g. using electronic patient recording with a reminder system, and screening of more patients for complications [12–18]. The integration of these data into our simulation model led to a major reduction in cost-intensive diabetic complications (table 6). The ultimate aims of the St. Vincent declaration, i.e. reduction of amputations by 50% and blindness by 30%, could nearly be achieved by a diabetes management programme of this kind, and even exceeded in the case of endstage renal disease. These results are underlined by several clinical studies, in particular by the DCCT and UKPDS, which outline the benefit of optimising metabolic control [3, 6, 24]. In addition, several randomised trials have shown that early treatment with ACE inhibitors delays [25–28] or even prevents [29–33] the progression of diabetic nephropathy to endstage renal disease. Since there are only a few long-term studies in type 2 diabetes which support stabilisation or improvement of nephropathy by ACE inhibitors, we performed the analysis conservatively, assuming a 50% reduction in the progression of microalbuminuria to more advanced stages of diabetic nephropathy [34].

Our cost-effectiveness analysis is limited by the following aspects: (1) diabetic neuropathy, diabetic foot syndrome, and diabetes-related infections are not considered in the model; (2) the short-term effects of an intervention on clinical variables must be considered estimates, since they were mainly derived from uncontrolled observational studies by calculation of weighted averages and not by meta-analysis; (3) the probable reduction in indirect costs (loss of productivity) and improvement of life quality by the decrease in morbidity and mortality have not been analysed. However, it is implicit that an intervention resulting in a reduction of complications with high morbidity, such as endstage renal failure, will also lead to a reduction in indirect costs and thus improve quality of life. Finally, a maximum intervention was simulated assuming that every patient is screened for complications. In real life, screening of 100% of patients is unlikely. However, the break-even analysis showed that if compliance with the intervention was greater than 46% the total lifetime costs of the intervention would still be lower than with standard care (figure 3).

Assessment of the economic and clinical impact of alternative disease management strategies in type 2 diabetes by the present cost-effectiveness analysis suggests – subject to the limitations of the model simulation – that implementation of a multifactorial diabetes management programme may result in lower costs and higher clinical effectiveness compared to standard care and the other interventions analysed. Thus, the multifactorial intervention is dominant compared to standard care and may pay off, after initial expenditure, by averting diabetic complications and their associated costs.

Correspondence
Dr. med. Valerio Gozzoli
Florastrasse 35
CH-4057 Basel
E-mail: gozzoli@econophone.ch

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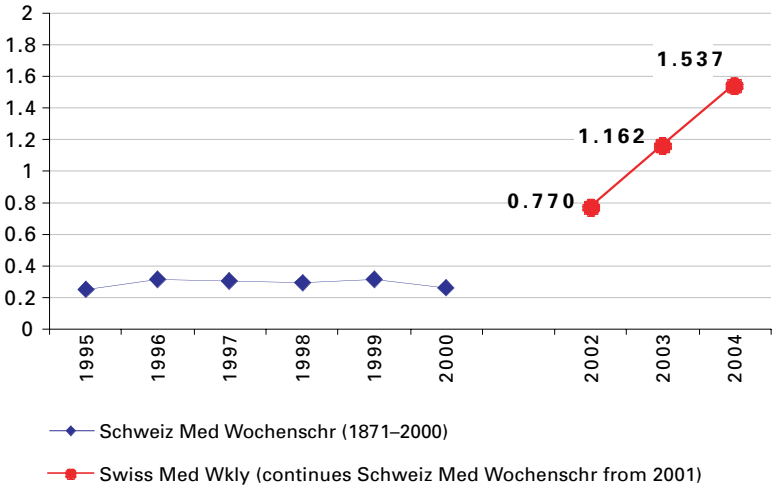

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