Cost-Effectiveness of the Diabetes Care Protocol, a Multifaceted Computerized Decision Support Diabetes Management Intervention That Reduces Cardiovascular Risk

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OBJECTIVE — The Diabetes Care Protocol (DCP), a multifaceted computerized decision support diabetes management intervention, reduces cardiovascular risk of type 2 diabetic patients. We performed a cost-effectiveness analysis of DCP from a Dutch health care perspective.

RESEARCH DESIGN AND METHODS — A cluster randomized trial provided data of DCP versus usual care. The 1-year follow-up patient data were extrapolated using a modified Dutch microsimulation diabetes model, computing individual lifetime health-related costs, and health effects. Incremental costs and effectiveness (quality-adjusted life-years [QALYs]) were estimated using multivariate generalized estimating equations to correct for practice-level clustering and confounding. Incremental cost-effectiveness ratios (ICERs) were calculated and cost-effectiveness acceptability curves were created. Stroke costs were calculated separately. Subgroup analyses examined patients with and without cardiovascular disease (CVD+ or CVD− patients, respectively).

RESULTS — Excluding stroke, DCP patients lived longer (0.14 life-years, P = NS), experienced more QALYs (0.037, P = NS), and incurred higher total costs (€1,415, P = NS), resulting in an ICER of €38,243 per QALY gained. The likelihood of cost-effectiveness given a willingness-to-pay threshold of €20,000 per QALY gained is 30%. DCP had a more favorable effect on CVD+ patients (ICER = €14,814) than for CVD− patients (ICER = €121,285). Coronary heart disease costs were reduced (€−587, $P < 0.05$).

CONCLUSIONS — DCP reduces cardiovascular risk, resulting in only a slight improvement in QALYs, lower CVD costs, but higher total costs, with a high cost-effectiveness ratio. Cost-effective care can be achieved by focusing on cardiovascular risk factors in type 2 diabetic patients with a history of CVD.

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Every year a large percentage of the total health care budget is spent on diabetes-related care. In European countries percentages of 2.5–6.5% have been reported, and in the U.S. diabetes-related costs are even higher at 10% of the total health care budget (1,2). Long-term clinical follow-up studies (3–5) have shown that improvements in glycemic control, blood pressure, and cholesterol levels lead to fewer micro- and macrovascular complications and improve health outcomes. Intensive treatment, based on current guidelines, might lead to lower health care costs. However it seems difficult to follow guidelines, and many type 2 diabetic patients do not meet the strict targets for good glycemic and cardiovascular control.

New strategies like the Diabetes Care Protocol (DCP) have been developed to improve the quality and management of diabetes care (6). The DCP comprises several interventions, including a diabetes consultation hour run by a practice nurse, a computerized decision support system (CDSS), a recall system, and feedback on performance. A cluster randomized trial proved that the DCP reduces the cardiovascular risk of type 2 diabetic patients in primary care (6).

Although it is stated that information technology, like CDSS, in diabetes care may improve care processes, delay diabetes complications, and save health care costs (7), most studies in this field do not include a cost-effectiveness analysis (8). We therefore performed a cost-effectiveness analysis of the DCP versus usual care from a Dutch health care perspective.

RESEARCH DESIGN AND METHODS

Clinical trial

Between March 2005 and August 2007, we performed a cluster randomized trial in 55 primary care practices throughout the Netherlands. The practices were not involved in any other diabetes care improvement program and worked with an electronic medical record. Randomization was performed at practice level with stratification for the number of primary care physicians (PCPs) working in the practice and the presence of a practice nurse prior to the intervention. Twenty-six practices were randomized to the in-

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tervention group and 29 to the control group.

Patients in the intervention group were treated according to the DCP, which is described elsewhere (6). In brief, DCP consists of *1*) a diabetes consultation hour run by a practice nurse, *2*) a CDSS containing a diagnostic and treatment algorithm based on the Dutch primary care of type 2 diabetes guidelines (9) and providing patient-specific treatment advice, *3*) a recall system, and *4*) feedback at both practice and patient level every 3 months regarding the percentage of patients meeting the treatment targets (smoking cessation, A1C <7%, systolic blood pressure <140 mmHg, total cholesterol <4.5 mmol/l, LDL cholesterol <2.5 mmol/l, and BMI <27 kg/m^2) (9). The PCP remained responsible for new prescriptions and referrals. The control group continued receiving usual diabetes care, meaning that diabetes care was either provided by a PCP or by a practice nurse under PCP responsibility.

Type 2 diabetic patients were selected from the electronic medical records. Patients under primary care treatment were eligible. We excluded patients if they were unable to visit the primary care practice, were under specialist treatment, or had a short life expectancy. The final, mainly Caucasian, study population consisted of 3,391 patients (1,699 intervention group, 1,692 control group). All patients were seen for their annual diabetes checkup at baseline and after 1 year follow-up (6).

Lifetime extrapolation of trial results to costs and effects

Lifetime costs and health effects were estimated using a modified probabilistic diabetes model for the Netherlands. This validated model has been used before and is described in more detail elsewhere (10–12). In brief, the model simulates the natural history of type 2 diabetes and calculates costs and quality-adjusted life-years (QALYs) for Dutch type 2 diabetic patients (12). It accounts for aging, temporal increases in A1C, and the age-related increase in complication risks.

The model includes a health state for cardiovascular disease (CVD) (angina pectoris and myocardial infarction), major type 2 diabetes–related complications (blindness, end-stage renal disease [ESRD], or lower-extremity amputation), minor type 2 diabetes complications (retinopathy or diabetic ulcers), uncomplicated type 2 diabetes, and death. The model computes the occurrence of the above-mentioned diabetes-related complications and the excess mortality due to diabetes. Based on the estimated events and prevalence of complications, it computes diabetes-related lifetime medical costs and QALYs. To calculate lifetime costs and outcomes, each health state is assigned a value in terms of medical costs and utility (health-related quality of life), and this value is multiplied by the prevalence of the health states over time.

Absolute Dutch excess mortality risk estimates for type 2 diabetes were calculated by multiplying sex and age-specific national mortality rates by the observed excess mortality hazard ratio for diabetic patients (10). The computed life-years were adjusted by quality-of-life results for major complications (blindness/poor vision, ESRD, or lower-extremity amputation), as observed in earlier Dutch studies, to derive the QALYs (10,12–14). The A1C levels for individual patients are used to adjust the baseline risks (transition probabilities) of blindness, renal failure, and lower-extremity amputation (10,15).

For this study, three adaptations were made to the original Dutch model. First, the distribution of the difference in 10-year UK Prospective Diabetes Study (UKPDS) coronary heart disease (CHD) risk estimate between intervention and control group was used to account for the difference in the probability of first events and death from CHD (16). Second, because patients with a history of CVD have an even higher increased risk of another cardiovascular event than diabetic patients without such a history, a separate extra risk for this subpopulation was added to the model. This correction was based on (W.K.R., L.W.N., unpublished data) subgroup analyses of the original in-file Dutch data from the EUROPA trial in secondary cardiovascular prevention. In that population, men with diabetes and a history of CVD showed a risk of a cardiovascular death that was 3.27 times that seen in the general population; in women, this relative risk was 4.63 (17). Finally, the costs of CHD complications were included in the model, based on resource use observed among Dutch diabetic patients with the mix of CHD complications observed in the EUROPA study (17).

In addition to the model input data described above, medication costs of glucose-lowering drugs (oral drugs and insulin), ACE inhibitors, angiotensin-renin blockers, and cholesterol-lowering drugs (ATC codes A10, C09, and C10) used during the 1-year follow-up period were included in the cost calculation. The mean 1-year follow-up medication costs were €326.30 in the DCP group and €325.10 in the control group. These costs were extrapolated to estimate lifetime medication costs, assuming the cost difference between DCP and usual care remained constant over time (Dutch Farmacotherapeutisch Kompas 2008). Because differences in use and costs of diuretics, β-blocking agents, and calcium channel blockers (ATC codes C03, C07, and C08) between both groups were negligible, they were left out of the medication cost calculations.

Costs regarding development and implementation of DCP were based on costs actually invoiced to Pfizer B.V.; maintenance costs of DCP were based on costs invoiced to PCPs. DCP costs were calculated per patient per year for a period of 10 years based on the CHOICE method (18). The total DCP costs included practice nurse instructions working with DCP, reorganizing primary care practice type 2 diabetes care, CDSS with recall system, and 3-monthly feedback. The costs of developing the DCP and a pilot study were divided by the total Dutch type 2 diabetic population, resulting in costs of €1 per patient. Implementation costs (first 3 years) and the yearly maintenance costs thereafter were divided by the number of patients in the participating type 2 diabetic population. Annual implementation costs were €90 per patient for the first 3 years and annual maintenance costs were €12 per patient for years 4–10. Because time spent on diabetes care was not registered adequately, we performed a survey among the participating practices to study if there were extra costs for personnel, education, and medical equipment (response rate: 50% intervention vs. 65% control). Since no differences were found, these costs were left out of the model.

Stroke was left out of the model calculations because there are no accurate Dutch data on survival rates of type 2 diabetic patients with stroke. In the online appendix (available at http://care.diabetesjournals.org/cgi/content/full/dc09-1232/DC1), the estimated stroke costs are calculated.

Analyses

The 1-year follow-up data from the trial were used, based on intention to treat with baseline values carried forward in

Table 1—*Baseline characteristics and clinical trial outcome* (n = *3,391*)

	Intervention group (n = 1,699)		Control group (n = 1,692)		Difference in change between groups*	95% CI difference between groups*
	Baseline	After 1 year	Baseline	After 1 year		
Age (years)	65.2 ± 11.3		65.0 ± 11.0			
Sex (% male)	48.2		49.8			
Caucasian (%)	97.7		97.6			
Duration of diabetes	5.8 ± 5.7		5.4 ± 5.8			
History of CVD (%)	47.1		63.3			
Current smoking (%)	22.6	20.7	16.6	15.5	1.1†	0.7–1.7
Clinical outcome						
A1C (%)	7.1 ± 1.3	6.9 ± 1.1	7.0 ± 1.1	6.9 ± 1.0	0.07	−0.02 to 0.16
Systolic blood pressure (mmHg)	149 ± 22	143 ± 20	149 ± 21	147 ± 20.8	3.3‡	0.5–6.0
Diastolic blood pressure (mmHg)	83 ± 11	80 ± 11	82 ± 11	82 ± 10.6	2.2‡	1.0–3.5
Total cholesterol (mmol/l)	5.0 ± 1.0	4.6 ± 0.9	4.9 ± 1.1	4.8 ± 1.1	0.2‡	0.1–0.3
HDL cholesterol (mmol/l)	1.36 ± 0.36	1.37 ± 0.37	1.32 ± 0.35	1.33 ± 0.36	−0.007	−0.038 to 0.023
LDL cholesterol (mmol/l)	2.8 ± 0.92	2.5 ± 0.88	2.8 ± 0.95	2.6 ± 0.97	0.15‡	0.07–0.23
10-year UKPDS CHD risk (%)	22.5 ± 16.5	20.6 ± 15.0	21.7 ± 15.8	21.6 ± 15.6	1.4‡	0.3–2.6

Data are means ± SD unless otherwise indicated. The 10-year UKPDS CHD risk (%) was calculated using date of onset of diabetes (age-duration of diabetes), sex, ethnicity, smoking, A1C, systolic blood pressure, total cholesterol, and HDL cholesterol. *GEEs to correct for clustering at practice level. †For percentages, the odds ratio is given. ‡Improvements of intervention group compared with control group significant ($P < 0.05$).

case of missing values. The model used the following parameters from the 1-year follow-up results to calculate lifetime disease outcomes: age, sex, duration of diabetes, A1C, systolic blood pressure, total cholesterol, HDL cholesterol, BMI, smoking, diabetes complications at 1-year follow-up (myocardial infarction, angina pectoris, stroke, lower-extremity amputation, retinopathy [no, background, or proliferate], neuropathy, and nephropathy [no, microalbuminuria, or macroalbuminuria]).

The model calculated six lifetime health outcomes (life-years, QALYs) and costs for each patient (discounted and undiscounted). The averages of the six individual model outcomes were then analyzed using generalized estimating equations (GEEs) to correct for clustering at practice level. To correct for confounding and to improve model estimates of the difference in outcomes between DCP and control, the following baseline covariates were used: age, sex, duration of diabetes, history of CVD, smoking, A1C, systolic blood pressure, total cholesterol, and HDL cholesterol.

The primary outcome in our analysis was the cost-effectiveness of DCP versus current usual care, expressed as the incremental cost-effectiveness ratio (ICER), calculated by dividing the incremental costs by the incremental QALYs or incremental life-years. As recommended by the Dutch pharmacoeconomic guidelines, costs were discounted at 4%, QALYs at 1.5%, and life-years were undiscounted (19,20). We also examined differences in diabetes-related costs, cardiovascular event costs, and number of cardiovascular events.

Uncertainty surrounding the cost-effectiveness ratios as calculated from the model was expressed using a cost-effectiveness plane. A cost-effectiveness acceptability curve was created to determine whether implementation of DCP was cost-effective given different thresholds of willingness to pay for QALYs (e.g., a threshold of €20,000 per QALY).

After calculating the mean individual costs for each patient, we examined the cost-effectiveness of DCP for all patients in the study population, patients with a history of CVD (CVD+) and patients without a history of CVD (CVD−).

RESULTS

Trial

The mainly Caucasian study population had a mean age of 65 years and a mean diabetes duration of 5.5 years (Table 1). Baseline characteristics of the two groups were comparable, except for smoking status, history of CVD, and HDL cholesterol level. At 1-year follow-up, patients in the intervention group showed significantly greater reductions in blood pressure, total cholesterol, and 10-year UKPDS CHD risk than patients in the control group. No significant difference in A1C% was found (6).

Cost-effectiveness

Patients in the DCP group showed slightly more QALYs (0.037), slightly more life-years (0.14), and higher costs (€1,415) than patients in the control group (Table 2). However, none of these differences were statistically significant. In the total population, patients receiving DCP care had significantly fewer cardiovascular events than patients receiving usual care (i.e., 0.11 fewer events). This was also true for patients without a history of CVD (CVD−) (0.14 fewer events) (Table 2). The costs of CHD in the DCP group were significantly lower than those in the control group (total population €−517; CVD+ patients €−433; CVD− patients €−721). The ICER for the total population was €38,243 per QALY gained (i.e., €1,415/0.037), for the CVD+ patients €14,814 per QALY gained, and for CVD− patients €121,285 per QALY gained.

Figure 1 shows the degree of uncertainty around the differences in costs and QALYs between the DCP and control groups for the total population. The percentage of dots in the southeast quadrant (meaning lower costs and improved health) for these patients is 3%. Conversely, the percentage of dots in the northwest quadrant (where DCP increases costs and reduces health) is 26%. The cost-effectiveness acceptability curves (Fig. 2) show that the DCP for CVD+ patients is more likely to be cost-effective at any willingness-to-pay threshold than DCP for all patients or DCP for

Table 2—*Costs and effects of DCP compared with usual care*

	Total population (n = 3,391)		Patients with history of CVD (n = 1,743)		Patients without history of CVD (n = 1,648)	
	Mean difference*	95% CI	Mean difference*	95% CI	Mean difference*	95% CI
Differences in health, model calculations						
Healthy years (QALYs, discounted)	0.037	−0.066 to 0.14	0.07	−0.051 to 0.19	0.014	−0.141 to 0.169
Life-years	0.14	−0.12 to 0.40	0.19	−0.07 to 0.45	0.10	−0.26 to 0.46
Number of cardiovascular events	−0.11	−0.18 to −0.04	−0.08	−0.17 to 0.007	−0.14	−0.25 to −0.036
Differences in costs, model calculations						
Diabetes-related (excluding CHD) (€, discounted)	1,698	187–3,209	1,167	−620 to 2,954	2,146	−189 to 4,482
CHD (€, discounted)	−587	−880 to −294	−433	−847 to −18	−721	−1,177 to −265
DCP (€, discounted)	316	315–318	314	3,112–316	319	318–320
Total costs (€, discounted)	1,415	−130 to 2,961	1,037	−891 to 2,967	1,698	−692 to 4,089
Cost-effectiveness, model calculations						
Total costs per QALY gained	38,243		14,814		121,285	
Total costs per life-year gained	10,107		5,457		16,980	

Results are corrected for clustering and baseline differences in age, duration of diabetes, sex, smoking, A1C, systolic blood pressure, total cholesterol, HDL cholesterol, and history of CVD (only total population). *Mean difference between intervention and control group.

CVD− patients. If a threshold of €20,000 is applied (21), there is a probability of cost-effectiveness of 59% for CVD+ patients versus 30% for all patients and 24% for CVD− patients (Fig. 2).

CONCLUSIONS — After 1 year, DCP results in reduced blood pressure, total cholesterol, and estimated 10-year UKPDS CHD risk in comparison with usual care. This resulted in a cost-effectiveness ratio of €38,243, which is higher than the often mentioned willingness-to-pay threshold of €20,000/QALY (21). In the long run, DCP is more costly and leads to only slightly more health than current care, although it does result in significantly lower CHD costs. The cost-effectiveness ratio for CVD+ patients is €14,814 and for CVD− patients €121,285. DCP for CVD+ patients has the highest probability of cost-effectiveness (59% at a willingness-to-pay threshold of €20,000/QALY) (21).

When considering the 1-year follow-up 10-year UKPDS CHD risk, 20.6% in the DCP group versus 21.6% in the control group, we see a significant though small relative risk reduction of 5%. Since DCP was compared with good usual care, this may explain why the size of improvements in QALYs (0.037) and life-years (0.14 years) was small. The costs per life-year gained were much smaller than the costs per QALY gained (total population €10,107; CVD+ €5,457; CVD− €16,980). Although there were no significant differences in A1C between the intervention and control group after 1-year follow-up, the increase in diabetes costs was mainly caused by an age-related cumulative increase in renal failure and amputation.

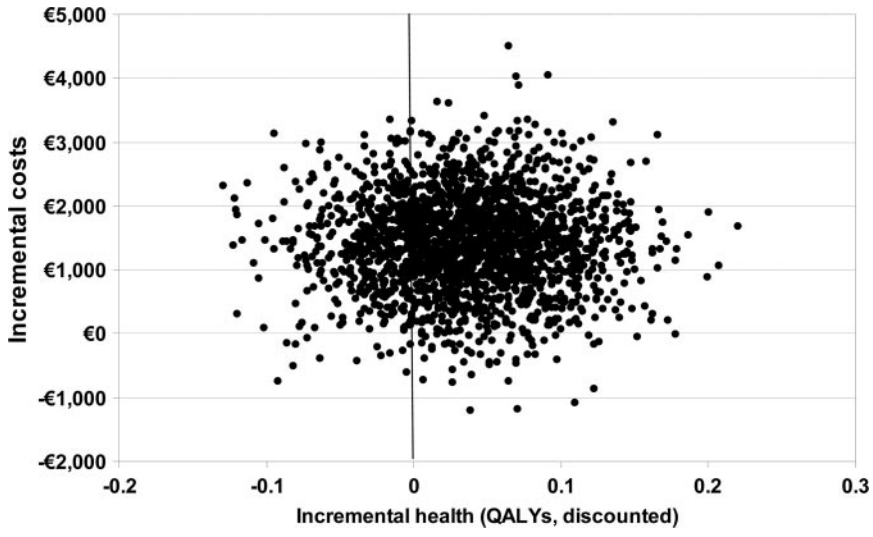

Figure 1—*Scatter-plot showing incremental costs and health (QALYs discounted). The dots represent different patient populations and are the result of a second-order uncertainty analysis.*

Strengths and limitations

The existing type 2 diabetic model used in this study was improved by including medication and CHD costs. The increase in diabetes medication costs after 1 year was, however, assumed to be constant over the lifetime. This might however be a conservative assumption, because it is likely that diabetes-related costs and medication costs will also increase in the control group when more type 2 diabetic patients are treated according to current guidelines and treatment targets, independent of the intervention used.

Although we included a large unselected primary care type 2 diabetic population, it is difficult to generalize the results to other countries and settings. If DCP were to be applied in populations with higher mean A1C levels, larger A1C reductions would probably be obtained and more costly A1C-related complications would be prevented; this would improve the cost-effectiveness of DCP. However, in countries where the diabetic

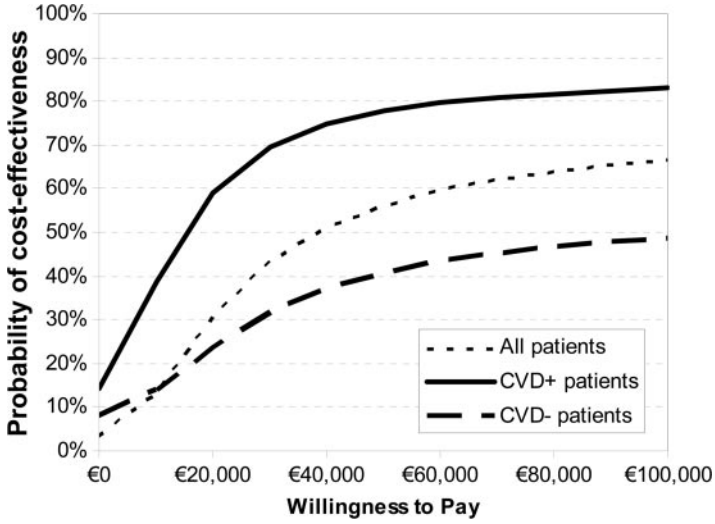

Figure 2—*Cost-effectiveness acceptability curve for patients with and without a history of CVD (CVD+ patients, CVD− patients).*

population is fairly adequately treated, the small improvement in QALYs will make cost-effectiveness less likely, even with less costly interventions. The results are limited by uncertainties in disease outcome. Although we calculated the average of six model outcomes per patient, this will probably not have led to a better cost-effectiveness estimation. Further, it is unlikely that the absence of many baseline values regarding history of CVD had any substantial effect on the results, since relatively few patients developed CVD in 1 year. Although stroke costs were not included in the model, the estimation of stroke costs did not have a significant effect on the study outcomes (online appendix).

Comparison with other studies

We observed that the DCP is more cost-effective for use among patients with a history of CVD. These patients can be considered as high-risk patients, just like type 2 diabetic patients with microalbuminuria or high CVD risk estimates, because they have an increased risk for a cardiovascular event. In fact, this was also shown by the intensive multifactorial intervention in the young high-risk type 2 diabetic population in the Steno-2 Study. They found a 53% reduction in cardiovascular events, which proved to be cost-effective (22).

The baseline values in our trial are in accordance with a world wide positive trend in the general therapeutic approach of type 2 diabetes with increasing percentages of patients achieving their targets for A1C, blood pressure, and lipids (23). Under these conditions, a potential cost-effective outcome will be more difficult to achieve. Unlike blood glucose level, there is strong evidence that controlling high blood pressure and high cholesterol levels significantly reduces both macro- and microvascular complications in type 2 diabetic patients. Recent trials suggest that early strict glycemic control is likely to be beneficial for many patients (24), but setting a glycemic target is definitely more difficult in people with existing diabetes-related complications (25). This implies that PCPs will have to provide a more personalized kind of diabetes care for different kinds of patients (i.e., those with a short duration of diabetes and those at high risk). Based on the results of our study, we think that DCP or comparable interventions are only useful instruments if they can identify these different categories of patients to facilitate structured personalized patient review.

In this study we showed that DCP, consisting of CDSS, a recall system, feedback, and case management, improves clinical outcome in an unselected primary care type 2 diabetic population and results in lower CVD-related costs but much higher diabetes-related costs and a high cost-effectiveness ratio. In the effort to improve health in a cost-effective manner, PCPs should not simply focus on A1C percentage but rather on personalized need-differentiated type 2 diabetes care.

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