

# Stratified Patient-Centered Care in Type 2 Diabetes

A cluster-randomized, controlled clinical trial of effectiveness and cost-effectiveness

ANNABELLE S. SLINGERLAND, MD, DSC, MPH,  
MS<sub>CHSR</sub><sup>1,2</sup>  
WILLIAM H. HERMAN, MD, MPH<sup>3</sup>  
WILLIAM K. REDEKOP, PHD<sup>2</sup>

ROB F. DIJKSTRA, MD, PHD<sup>4</sup>  
J. WOUTER JUKEMA, MD, PHD<sup>1</sup>  
LOUIS W. NIESSEN, MD, PHD<sup>2,5</sup>

**OBJECTIVE**—Diabetes treatment should be effective and cost-effective. HbA<sub>1c</sub>-associated complications are costly. Would patient-centered care be more (cost-) effective if it was targeted to patients within specific HbA<sub>1c</sub> ranges?

**RESEARCH DESIGN AND METHODS**—This prospective, cluster-randomized, controlled trial involved 13 hospitals (clusters) in the Netherlands and 506 patients with type 2 diabetes randomized to patient-centered ( $n = 237$ ) or usual care (controls) ( $n = 269$ ). Primary outcomes were change in HbA<sub>1c</sub> and quality-adjusted life years (QALYs); costs and incremental costs (USD) after 1 year were secondary outcomes. We applied nonparametric bootstrapping and probabilistic modeling over a lifetime using a validated Dutch model. The baseline HbA<sub>1c</sub> strata were <7.0% (53 mmol/mol), 7.0–8.5%, and >8.5% (69 mmol/mol).

**RESULTS**—Patient-centered care was most effective and cost-effective in those with baseline HbA<sub>1c</sub> >8.5% (69 mmol/mol). After 1 year, the HbA<sub>1c</sub> reduction was 0.83% (95% CI 0.81–0.84%) (6.7 mmol/mol [6.5–6.8]), and the incremental cost-effectiveness ratio (ICER) was 261 USD (235–288) per QALY. Over a lifetime, 0.54 QALYs (0.30–0.78) were gained at a cost of 3,482 USD (2,706–4,258); ICER 6,443 USD/QALY (3,199–9,686). For baseline HbA<sub>1c</sub> 7.0–8.5% (53–69 mmol/mol), 0.24 QALY (0.07–0.41) was gained at a cost of 4,731 USD (4,259–5,205); ICER 20,086 USD (5,979–34,193). Care was not cost-effective for patients at a baseline HbA<sub>1c</sub> <7.0% (53 mmol/mol).

**CONCLUSIONS**—Patient-centered care is more valuable when targeted to patients with HbA<sub>1c</sub> >8.5% (69 mmol/mol), confirming clinical intuition. The findings support treatment in those with baseline HbA<sub>1c</sub> 7–8.5% (53–69 mmol/mol) and demonstrate little to no benefit among those with HbA<sub>1c</sub> <7% (53 mmol/mol). Further studies should assess different HbA<sub>1c</sub> strata and additional risk profiles to account for heterogeneity among patients.

Type 2 diabetes causes an enormous economic burden in almost every country. Diabetes treatment must be both effective and efficient (1–7). In 2011, diabetes affected at least 366 million people or 5% of the world's population (8% of adults) and was responsible for 4.6 million

deaths (8). The prevalence of diabetes is expected to increase to 552 million in 2030 (8). In 2011, diabetes care consumed at least 465 billion USD, accounting for 11% of healthcare expenditures in adults 20–79 years of age (8). The main cause of the high-cost burden of diabetes is its acute

and chronic complications, leading to a 3–13-fold increase in costs per patient (9–14). The occurrence of complications is related to nonmodifiable risk factors such as age, sex, and socioeconomic status. It is also related to modifiable risk factors, such as BMI and waist circumference, as well as risk factors not directly related to diabetes, such as comorbidities including depression. HbA<sub>1c</sub> is widely monitored as a measure of the risk of complications and as a target for intervention. HbA<sub>1c</sub> may also be important in defining a more comprehensive risk-based approach to diabetes management.

We have previously explored patient-centered care as a treatment strategy for type 2 diabetes (15–17). Earlier, we conducted a cluster-randomized, controlled clinical trial that compared patient-centered care versus professional-directed and usual care (control) in 13 hospitals (clusters). Patient-centered care had very acceptable incremental cost-effectiveness ratios (ICERs) as compared with professional-directed and usual care. These findings stimulated additional studies of self-management promotion, which is presently regarded as an essential and potentially very cost-effective approach to diabetes management (18–20).

Unfortunately, most, if not all, studies focus on the average patient, whereas individual characteristics relate to the risk of developing complications (21–23), the effectiveness of treatment (23), and healthcare costs (24–26). More effective and efficient diabetes care might be achieved by focusing patient-centered strategies on patients with specific risk profiles. Such approaches have infrequently been described (27,28).

Therefore, we analyzed data from our trial using individual patient data to compare patient-centered with usual care. We stratified patients by baseline HbA<sub>1c</sub> and measured HbA<sub>1c</sub> and costs at 1 year, and quality-adjusted life years (QALYs) and healthcare costs over a lifetime. We tested the hypothesis that a policy of patient-centered care, provided to patients

From the <sup>1</sup>Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands; the <sup>2</sup>Institute of Health Policy and Management, Institute for Medical Technology Assessment, Erasmus MC, Erasmus University Rotterdam, Rotterdam, the Netherlands; the <sup>3</sup>University of Michigan Medical Center, Ann Arbor, Michigan; the <sup>4</sup>Dutch College of General Practitioners, Utrecht, the Netherlands; and the <sup>5</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland.

Corresponding author: Annabelle S. Slingerland, annabelle.s.slingerland@gmail.com.

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in higher baseline HbA<sub>1c</sub> strata, would result in significantly better outcomes and more efficient healthcare.

## **RESEARCH DESIGN AND METHODS**

### **Population and intervention (see CONSORT flow diagram online)**

We conducted a prospective cluster-randomized trial, aiming at 18 hospitals. Four did not participate and one dropped out for financial reasons. Eligible hospitals were situated across the Netherlands and met predefined eligibility criteria in terms of numbers of beds and diabetes specialist nurses. The 13 hospitals were representative of the 120 general hospitals in the Netherlands and delivered ambulatory secondary care. There was no systematic contamination due to geographical differences. The characteristics of the 13 hospitals that participated and the 5 that did not differ substantially. There was a small difference in mean HbA<sub>1c</sub> (SD) between participating and nonparticipating hospitals (7.8 [1.2] vs. 8.0 [1.4], respectively) (Table 1). In the 13 participating hospitals, internists recruited the first 150 patients with type 1 and type 2 diabetes who attended a diabetes clinic, excluding patients who were pregnant or had a poor life expectancy due to other diseases. Enrollment took place between November 1999 and March 2000. Exclusion criteria included participation in another study or being an academic hospital as we sought to study real-life day-to-day clinical care using a low-impact observational approach. After several pilot studies and preintervention baseline patient measurements, each hospital was randomized (without restrictions) to one of three intervention arms, allocating patients with type 2 diabetes into patient-centered, professional-directed, and usual care arms (see CONSORT flow diagram online). Allocation was performed by a noninvolved person, a so-called “third party,” outside the research group, and allocation results were concealed from the investigators until the start of the intervention. The allocation ratio was 4:4:5. Internists and patients allocated to the intervention group were aware of the allocated arm. The unit of randomization equaled the unit of analysis and was depicted as a continuous (the percentage of people benefiting) rather than as a dichotomous (success or failure) outcome. For practical reasons, and as the outcome was nonsubjective, the study was not blinded. The study design was clustered since the intervention strategy could

only be implemented by a provider team with a group of patients in a single hospital outpatient setting. Without clustering by hospital, patient, and provider level would have taken place. Ex ante, we made no modifications to the trial design or protocol in response to changing circumstances or allocation results.

The present paper compares two trial arms (see CONSORT flow diagram online) of randomly assigned clusters, the patient-centered arm with  $n = 240$  patients ( $n = 237$  with available HbA<sub>1c</sub> data at baseline) and the usual care arm with 276 patients ( $n = 269$  with available HbA<sub>1c</sub> data at baseline). Both subgroups are comparable with respect to baseline patient characteristics (Table 1). In the patient-centered care clusters, patients were not only seen by their internal medicine doctors and diabetes team as in usual care but additionally received detailed diabetes passports based on national guidelines that aim to educate and record results of medical examinations in order to promote shared disease management. Educational meetings for patients were organized in all of the hospitals where the diabetes passports were introduced. Physicians, diabetes specialist nurses, and dietitians attended these meetings with an opinion leader and received personal feedback with benchmarks on baseline data, adherence to key guidelines, and the use of the diabetes passports. Barriers and facilitators were discussed. Internists received personal feedback on clinical performance after 6 months as well as on the use of the diabetes passports. Leaflets and waiting room posters were also distributed. Usual care consisted of visits every 3 months to a specialized nurse and/or internist according to national evidence-based guidelines (CBO Banda Heereveen 1998, ISBN 90-6910-217-X). The standard protocol was rechecked, reexplained, re-emphasized, and followed-up in the hospitals involved.

Using individual patient data, we stratified all patients into three groups according to baseline HbA<sub>1c</sub> (<7% [53 mmol/mol], 7–8.5%, >8.5% [69 mmol/mol]) (Table 1) and examined the effectiveness and cost-effectiveness of patient-centered care in each stratum. The analyses described in the present paper were not part of the original analyses of the cluster randomized control trial and were therefore performed as secondary analyses.

The institutional review board (Medical Ethics Committee of University Medical Center Nijmegen) and the Committee

for Scientific Research with Human Subjects (CWOM 9810–0208) approved of the study. All patients gave written informed consent. The trial has been assigned the ISRCTN number ISRCTN3581744 at the Commissie Mensgebonden Onderzoek (CMO), with the title The Diabetes Guidelines Implementation in Hospitals Study. The full protocol can be requested from the CMO and the authors; at the time, an online trial registry was not in place.

During and after the study, there were no departures from the initial study protocol. There were no changes to eligibility criteria, interventions, examinations, data collection, methods of analysis, and outcomes. The initial study had HbA<sub>1c</sub> as the primary outcome measure for the sample size calculations. A mean HbA<sub>1c</sub> of 7.9% (63 mmol/mol) was specified that could drop 0.5% (3.1 mmol/mol) after the intervention.  $\alpha$  was set at 0.05 and  $\beta$  at 0.20. Sample sizes for cluster-randomized trials were inflated to adjust for clustering. The intraclass correlation coefficient was set at  $\rho = 0.01$ . Given a potential of four hospitals per arm and a 70% response rate, the sample size needed was 150 patients (with a single medical record) per arm. The power is further indicated by the confidence interval. Potential inconsistencies in laboratory outcomes in pre- and post-measurements were checked by the Dutch Foundation for Quality Assessment in Clinical Laboratories, in which all hospitals participate. Calibration of HbA<sub>1c</sub> was performed according to the guidelines of the National Glycohemoglobin Standardization Program. No interim analyses were warranted or performed. Using the healthcare perspective, our analyses of trial effect and cost include health-related outcomes and healthcare costs related to the individual patients for the 1-year duration of the trial and during a simulated patient lifetime. Individual patient outcome and cost data from the trial follow-up were entered into an existing national diabetes model multiple times. This model has been used and described in previous studies, including one that estimated the long-term costs of diabetes and cardiovascular complications and hospitalizations (15).

### **Health effects (HbA<sub>1c</sub>), costs, and cost-effectiveness over 1 year**

The end points regarding the impact of stratification over 1 year were the effectiveness of HbA<sub>1c</sub> reduction, costs, and ICERs. The latter were obtained from nonparametric bootstrapping and estimated mean (95% CI). Each of these simulations used

Table 1—Baseline characteristics

	Randomized hospitals				Excluded hospitals				Usual care				Patient-centered care				Total population				Population HbA <sub>1c</sub> at baseline		
	n	Mean (SD)	SD	%	n	Mean (SD)	SD	%	n	Mean (SD)	SD	%	n	Mean (SD)	SD	%	n	Mean (SD)	SD	%	<7	7–8.5	>8.5
Women (%)	13	14.65			5	4.50			276				240				506				99	244	163
Age ± SD, years	53	58 ± 16			54	59 ± 16			54.1	65.4 ± 10.4			54.1	64.0 ± 11.0			55	65 ± 11			45	59	55
Mean years since diagnosis ± SD	13.4 ± 10.2			12.5 ± 9.7		14.6 ± 10.3		12.6 ± 11.5					65 ± 11			65 ± 11				66 ± 11		64 ± 10	
Type 1 diabetes, %	31			27																			
Duration of diabetes, median (IQR), years																	11 (6–17)				7.5 (3–15)	11 (6–17)	12 (8–17)
Medication, n (%)																							
Tablets only																	52 (10)				17 (17)	22 (9)	12 (7)
Insulin only or in addition to tablets																	432 (84)				77 (78)	209 (86)	138 (85)
Tablets and insulin																	361 (70)				69 (70)	168 (69)	119 (73)
Mean HbA <sub>1c</sub> ± SD, %	7.8 ± 1.2			8.0 ± 1.4		7.9 ± 1.1		8.1 ± 1.2					8.1 ± 1.2				8.1 ± 1.3				6.5 ± 0.4	7.7 ± 0.4	9.5 ± 0.9
mmol/mol	62 (11)			64 (13)		63 (10)		65 (11)					65 (12)				65 (12)				48 (2)	61 (2)	80 (8)
Mean total cholesterol ± SD, mmol/L	5.3 ± 1.0			5.4 ± 1.1		5.5 ± 1.0		5.3 ± 1.0															
Mean weight ± SD, kg	84 ± 24			83 ± 16		30.0 ± 5.5		30.3 ± 5.0									30 ± 5				29 ± 5	30 ± 6	31 ± 5
Mean BMI ± SD, kg/m <sup>2</sup>																							
Mean systolic blood pressure ± SD, mmHg	145 ± 22			146 ± 23		150 ± 21		148 ± 23															
Mean diastolic blood pressure ± SD, mmHg	80 ± 11			80 ± 11		80 ± 11		81 ± 11															
Diabetes control 1 year trial data																							
Effectiveness																							
HbA <sub>1c</sub> , %						8.1 ± 1.3		7.8 ± 1.2															
HbA <sub>1c</sub> , mmol/mol						6.5 (12)		6.2 (11)															
Proportion of patients (%), HbA <sub>1c</sub> , % (mmol/mol)						16%/54%/30%		24%/56%/20%															
<7.0 (53), 7–8.5 (53–69), >8.5 (69)						0.161/0.540/0.299		0.242/0.560/0.198															
Costs																							
Percentage of patients taking insulin						71%		79%															
Mean costs of glucose control (USD)						1,880		2,627															

The first two columns (randomized and excluded hospitals) have been modified after Table 1 published in Dijkstra et al. Patients and nurses determine variation in adherence to guidelines at Dutch hospitals more than intensists or settings. Diabet Med 2004;21:586–591. The second two columns (usual and patient-centered care) have been modified after Table 1 published in Dijkstra et al. Patient-centered and professional-directed implementation strategies for diabetes guidelines: a cluster-randomized trial-based cost-effectiveness analysis. Diabet Med 2005;23:164–170.

1,000 bootstrap samples drawn from the original dataset containing the individual patient records. Direct costs per patient were estimated and standardized by multiplying each resource use component by the unit cost and summing the results at baseline and after 1 year for the main cost drivers: costs of medication (unit costs: insulin, -497 USD; tablets, -223 USD), costs of glucose monitoring (236 USD for glucose testing once every 6 weeks), and costs of implementation strategies (3.7 USD per patient) (29).

### Health gain, medical costs, and cost-effectiveness over a lifetime

The primary end points with respect to efficacy over a lifetime were effectiveness, QALYs (assessing the long-term complications and the excess cardiovascular morbidity and mortality associated with diabetes), as well as costs, based on the estimated events and prevalence of complications. These were estimated by extrapolating and bootstrapping individual patient data in a probabilistic cost-effectiveness analysis with 10,000 iterations using a per intervention arm validated probabilistic Markov diabetes model (10,30–33). Progression of diabetes complications was based on the

formula  $\beta^{(HbA_{1c}/10)}$  (10,31,34). We adjusted for the natural increase in HbA<sub>1c</sub> over time, ageing of patients, and the age-related increase in complication risk, accounting for uncertainties by including distributions in values of input variables, including HbA<sub>1c</sub> at the end of the trial and mortality risk (10,31). We only discounted costs (3%) and did not discount QALYs (32,33). Costs and health outcomes of the probabilistic analyses are presented as point estimates with 95% CIs.

### Statistical analysis

The primary and secondary outcomes by HbA<sub>1c</sub> strata were compared using ANOVA for continuous normally distributed variables (mean and SD, such as HbA<sub>1c</sub> and age), the Kruskal-Wallis test for continuous nonnormally distributed variables (median or interquartile range), like duration of diabetes, as well as the  $\chi^2$  test for categorical variables (numbers, sex, etc.). All tests were two tailed, and the limit of statistical significance was defined as  $P < 0.05$ . An intention-to-treat analysis was performed in this study. We used SPSS version 11.0 (SPSS Inc., Chicago, IL) and Excel version 9.0 (Microsoft, Seattle, WA).

**RESULTS**—Participant flow, for each arm and for each stratum is provided in the CONSORT 2010 flow diagram online. The trial was completed after 1 year of follow-up as planned. There was no reason to stop or end prematurely. Baseline characteristics of the participating and nonparticipating hospitals were similar (Table 1) as were the baseline characteristics of subjects in the two arms, patient-centered and usual care, apart from HbA<sub>1c</sub> (Table 1). Baseline characteristics of subjects in the three strata were also comparable, apart from longer duration of diabetes and more insulin use in the highest HbA<sub>1c</sub> stratum (Table 1).

A summary of the continuous outcomes in each trial arm according to stratum (HbA<sub>1c</sub> reduction, QALYs, and costs) as well as the effect size representing their contrast (differences between patient-centered and usual care and the ICERs) and their 95% CIs are presented in Table 2.

### Health effects (HbA<sub>1c</sub>), costs, and cost-effectiveness at 1 year

Change and distribution of HbA<sub>1c</sub> are depicted in Fig. 1. Over 1 year, the ICER for patient-centered care was highest in the highest HbA<sub>1c</sub> stratum (Table 2). In general,

**Table 2—HbA<sub>1c</sub> reduction and extra costs for patient-centered and usual care after the 1st year, and QALYs and extra costs over a lifetime**

	Stratified according to HbA <sub>1c</sub> at baseline		
	<7 (53 mmol/mol)	7–8.5 (53–69 mmol/mol)	>8.5 (69 mmol/mol)
Effect HbA <sub>1c</sub> reduction (mean [95% CI])			
Usual care (UC), %	-0.42 (0.43 to -0.42)	-0.31 (-0.31 to -0.30)	0.24 (0.23 to 0.25)
mmol/mol	-0.22 (0.23 to -0.22)	-1.0 (-1.0 to -9)	
Patient centered guideline-based care (PC), %	-0.34 (-0.35 to -0.34)	0.18 (0.17 to 0.18)	1.07 (1.06 to 1.08)
mmol/mol	-1.4 (1.5 to -1.4)	1.7 (1.6 to 1.7)	9.3 (9.2 to 9.5)
Difference between PC and UC, %	0.08 (0.07 to 0.09)	0.49 (0.48 to 0.49)	0.83 (0.81 to 0.84)
mmol/mol	0.64 (0.53 to 0.75)	3.0 (2.9 to 3.0)	6.7 (6.5 to 6.8)
Costs			
Usual care (UC)	115 (112 to 117)	-4 (-6 to -2)	-80 (-83 to -77)
Patient-centered care (PC)	14 (11 to 17)	4 (1 to 6)	119 (116 to 121)
Difference between PC and UC	-101 (-105 to -97)	9 (4 to 12)	199 (194 to 202)
ICER (USD/HbA <sub>1c</sub> %)			
Patient-centered care over usual care	-1.262 (-2.022 to 4.862)	18 (10 to 27)	261 (235 to 288)
Effect QALY not discounted (mean [95%])*			
Usual care (UC)	10.61 (8.90 to 12.32)	10.41 (9.33 to 11.48)	10.13 (8.71 to 11.55)
Patient-centered care (PC)	10.36 (8.34 to 12.38)	10.64 (9.39 to 11.89)	10.67 (9.30 to 12.04)
Difference between PC and UC	-0.24 (-0.66 to 0.18)	0.24 (0.07 to 0.41)	0.54 (0.30 to 0.78)
Costs discounted at 3% (USD)			
Usual secondary care (UC)	21,114 (17,183 to 25,044)	21,511 (18,900 to 24,122)	23,290 (19,013 to 27,567)
Patient-centered care (PC)	25,782 (19,345 to 32,219)	26,243 (22,236 to 30,250)	26,772 (22,209 to 31,334)
Difference between PC and UC	4,688 (3,504 to 5,832)	4,731 (4,259 to 5,205)	3,482 (2,706 to 4,258)
ICER (USD/QALY)			
Patient-centered care over usual care	Indecisive	20,086 (5,979 to 34,193)	6,443 (3,199 to 9,686)

\*A minus sign denotes an increase in HbA<sub>1c</sub> to allow a reduction being positive in the cost-effectiveness plane.

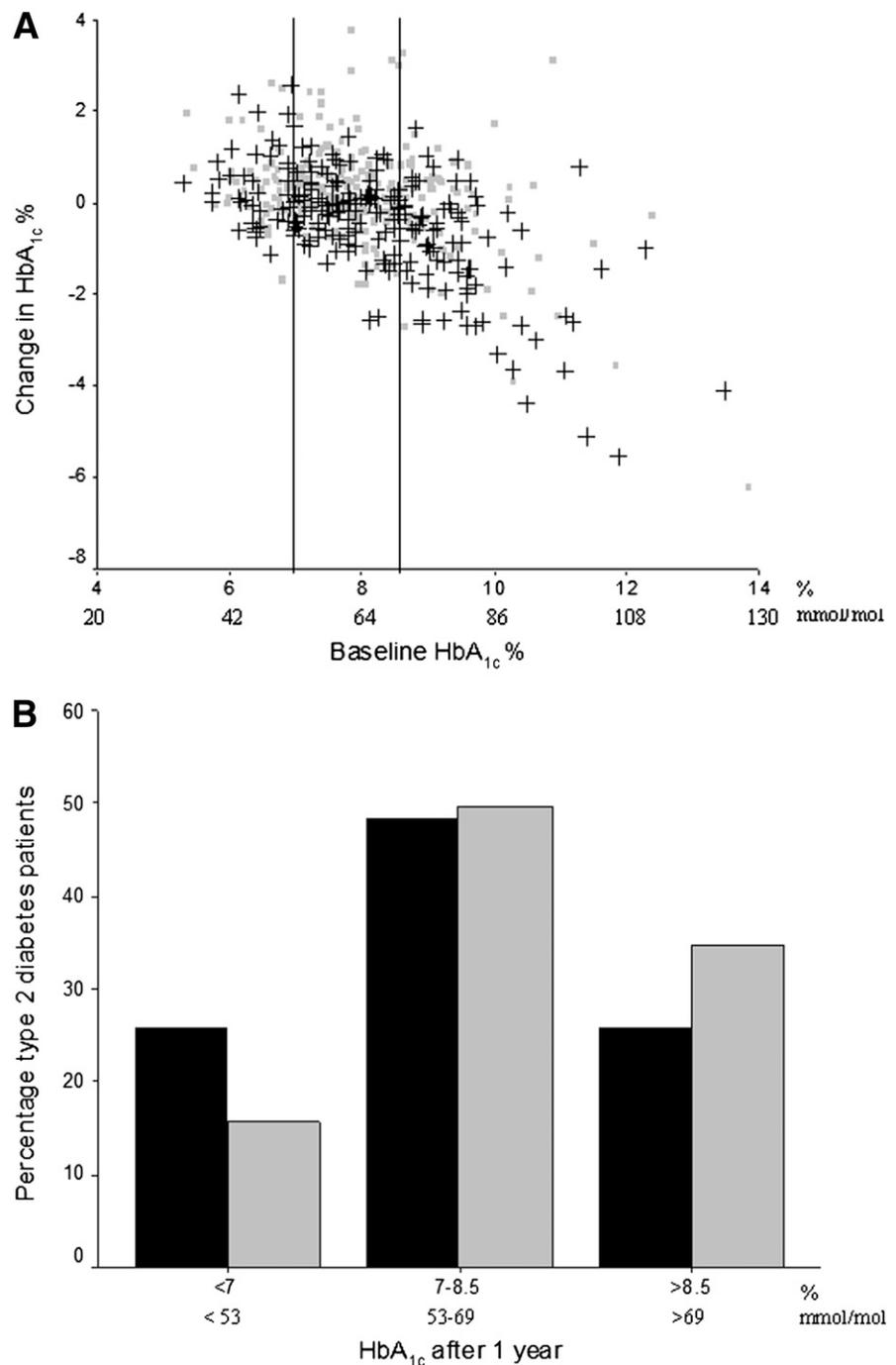
the ICERs were quite low. Bootstrapping the results of the individual patients and plotting the gain in a cost-effectiveness plane confirmed this (Fig. 2). The scatter plots at lower baseline HbA<sub>1c</sub> were in the two lower quadrants and with higher HbA<sub>1c</sub> at baseline in the upper right quadrant. Hence, for the highest stratum (baseline HbA<sub>1c</sub> >8.5 [69 mmol/mol]), patient-centered care showed a reduction in HbA<sub>1c</sub> at higher costs (dots above the x-axis). For patients with baseline HbA<sub>1c</sub> = 7–8.5% (53–69 mmol/mol), patient-centered care showed an HbA<sub>1c</sub> reduction and was cost saving in 45% of cases. For patients with a baseline HbA<sub>1c</sub> <7% (53 mmol/mol), the health effects were uncertain as points were divided over the left and right sides of the y-axis. With 64% of the points falling below the x-axis, there is a reasonable chance that patient-centered care would be dominant or cheaper than usual care.

#### Lifetime extrapolation of costs and effects

The difference in total lifetime QALYs between patient-centered care and usual care varied according to the baseline HbA<sub>1c</sub> stratum (Table 2), and the difference was positively associated with HbA<sub>1c</sub>. The gain achievable from patient-centered care was greatest in patients with an HbA<sub>1c</sub> >8.5% (0.54) (69 mmol/mol) (0.36) and lowest in patients with an HbA<sub>1c</sub> <7% (53 mmol/mol). In both arms, costs were higher, the higher the baseline HbA<sub>1c</sub>, and the difference was lowest in the highest stratum. Hence, the ICER of patient-centered over usual care was most favorable in patients with HbA<sub>1c</sub> >8.5% (69 mmol/mol) (6,443 USD/QALY). The higher cost-effectiveness ratio of 20,086 USD/QALY measured in the second stratum (7 < HbA<sub>1c</sub> < 8.5 [53–69 mmol/mol]) was below prevailing thresholds used to decide whether or not an intervention is cost-effective (e.g., 50,000 USD for the U.S.) (35). The lowest stratum (HbA<sub>1c</sub> <7 [53 mmol/mol]) showed uncertain health gains and an unfavorable ICER.

The cluster design did not change the outcomes of the analyses. The intracluster-correlation for reduction in HbA<sub>1c</sub> and other long-term parameters was low and varied, except for HbA<sub>1c</sub> <7% (53 mmol/mol) for life years and QALYs. The latter was 0.06.

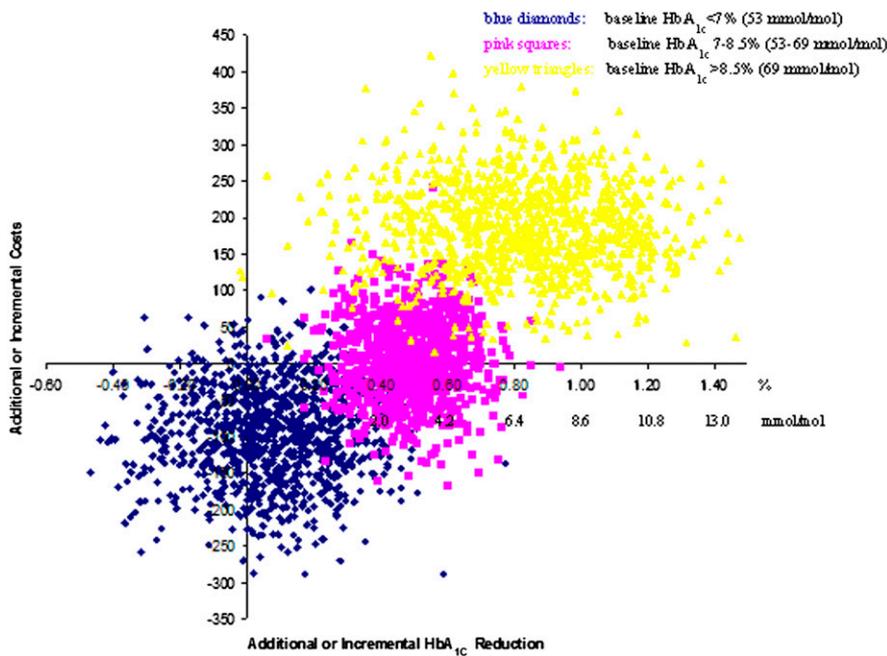
Analyses were only performed according to predefined protocol. No adverse events, harms, or unintended events were reported.



**Figure 1**—A: Change in HbA<sub>1c</sub> at 1 year, according to HbA<sub>1c</sub> at baseline. Change in HbA<sub>1c</sub> % in the 506 patients with type 2 diabetes after 1 year of patient-centered (black crosses, n = 237) or usual care (rectangles, n = 269) according to baseline HbA<sub>1c</sub> %. Vertical black lines represent the different strata: HbA<sub>1c</sub> <7 (53 mmol/mol), 7–8.5, or >8.5% (69 mmol/mol). B: HbA<sub>1c</sub> distribution of 506 type 2 diabetes patients at 1 year follow-up. HbA<sub>1c</sub> distribution of the 506 patients with type 2 diabetes according to HbA<sub>1c</sub> strata after having received patient-centered (black bars, n = 237) or usual care (white bars, n = 269) for 1 year.

**CONCLUSIONS**—Stratification is an important tool to optimize effectiveness and efficiency. Patient-centered care is more effective when targeted at a subgroup defined by higher baseline HbA<sub>1c</sub>. Over a lifetime, patient-centered care is

particularly effective and a “better buy” for patients with baseline HbA<sub>1c</sub> >8.5% (69 mmol/mol) and does not provide value for patients with baseline HbA<sub>1c</sub> <7% (53 mmol/mol). This suggests that patient-centered care should focus on



patients with a baseline  $HbA_{1c} > 8.5\%$  (69 mmol/mol), be considered for those with  $HbA_{1c} = 7.0\text{--}8.5\%$  (53–69 mmol/mol), and not be implemented in those with baseline  $HbA_{1c} < 7\%$  (53 mmol/mol).

This paper transforms intuition into evidence and quantifies the benefits of targeting the patient-centered care intervention by baseline  $HbA_{1c}$ . Exploring additional criteria for stratification, as well as additional interventions aimed at the high-risk patient groups, seems warranted.

Our study is among the first to stratify patients with type 2 diabetes according to baseline risk in order to optimize lifetime benefits and lower costs. Our results are consistent with the recent literature on cost-effectiveness of interventions in people at high risk for diabetes and stratified analyses in other diseases (18,34,36–40). A recent Cochrane review suggests a benefit of individual education on glycemic control when compared with usual care in a subgroup of those with a baseline  $HbA_{1c} > 8\%$  (64 mmol/mol) in an at least 6-month follow-up (41). We extend these findings over a lifetime and show that such benefits persist.

Several limitations should be acknowledged. Further studies should replicate and refine these analyses and

include other risk profiles to account for heterogeneity among patients. This would also provide a more comprehensive picture of the additional key risk factors impacting the development of complications. Also, further studies should include primary care settings since treatment of chronic diseases like type 2 diabetes tends to occur in primary care settings. In addition, longer follow-up will be needed. We assumed that the level of improvement seen after 1 year would be maintained over a lifetime (as shown in the UK Prospective Diabetes Study [UKPDS]). This is especially relevant for the stratum with  $HbA_{1c} > 8.5\%$  (69 mmol/mol). Another potential limitation could relate to the generalizability of our findings. Although it is likely that our findings apply to other European and North American hospital settings, since the prevalence, characteristics, treatment strategies, and costs of type 2 diabetes are similar (37), the intensity of care might vary. Finally, more complex models might be needed that include side effects and disutilities related to insulin and oral medication use and other healthcare costs (related to patient admissions, primary care, or specialist visits).

Further insight can be achieved by replication of the present approach in

larger completed studies hypothesizing gradients or threshold levels below which patient-centered care is not cost-effective and above which it is cost saving. Moreover, a study using a priori stratification would provide valuable confirmatory evidence for the findings of our exploratory study. Conceptually, the terminology and emphasis of patient-centered care has evolved over the years. At the time of our study, it referred to care in which the patient through the use of self-monitoring was more involved in decision making than those enrolled in usual care. The current concept of patient-centered care is one where the patient plays a much more active role.

For now, our results have several implications. When faced with the question of whether intervention A is effective and cost-effective relative to intervention B, the answer may be “it depends” instead of an unequivocal “yes” or “no,” when referring to the average patient. Targeting treatments at specific risk groups may result in better outcomes and better use of resources. Targeting those with  $HbA_{1c} > 8.5\%$  (69 mmol/mol), those who are most in need, is preferable to targeting those who have little to gain. Especially in low- and middle-income countries, targeted implementation might reduce healthcare expenditures (3).

Future research should confirm our findings in primary care and investigate risk profiles other than  $HbA_{1c}$ . These might include BMI or waist circumference or cardiovascular risk factors that predict cardiovascular events.

Targeting interventions to the highest risk population may allow resources to be better used, costs to be reduced, and negative side effects to be reduced by avoiding unnecessary use of medications. Focusing on  $HbA_{1c}$  and examining a variety of  $HbA_{1c}$  reduction strategies is valuable for patients, healthcare organizations, and the economy.

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