

## Toward Tailored Disease Management for Type 2 Diabetes

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**R**ising costs, an aging population, and the recognition of severe deficiencies in traditional care have motivated the development of innovative models for chronic illness management. Examples include shared care, case management, and stepped care, but perhaps most well known internationally are disease management and the Chronic Care Model.<sup>1-3</sup> Differences aside, these concepts have in common their basic assumption that better treatment today will result in better health and less expensive care in the future. Specific quality improvement efforts tend to focus on (1) reducing fragmentation between providers and settings, (2) stimulating evidence-based practice, (3) promoting active and planned follow-up, and (4) supporting patients' self-management.<sup>4-7</sup>

Developed in the United States, disease management programs (DMPs) have quickly spread to other countries such as Canada, the United Kingdom, and Germany, which now has some of the largest DMPs in the world.<sup>8,9</sup> In the primary care-oriented Dutch health system, chronic disease management initiatives developed from the 1990s onward. Initially, uptake of these initiatives remained limited, mainly due to lack of a structured framework and fragmentary funding.<sup>10,11</sup> The 2006 health insurance reform granted health insurers extended power to negotiate with care providers and, in so doing, facilitated the development of a more integrated funding method, the so-called "bundled payment system."<sup>12-14</sup> Under this system, insurers pay care groups, which are provider networks based in primary care, a single fee for the full range of outpatient services for a specific chronic condition.<sup>15</sup> Bundled payments are seen as a way to stimulate primary care providers, predominantly general practitioners (GPs), to engage in multidisciplinary cooperation and deliver integrated, evidence-based disease management in an ambulatory setting, therefore limiting the need for specialist care.<sup>16,17</sup>

Although the evidence base for their impact on the quality and outcomes of care is limited, integrally financed DMPs for type 2 diabetes quickly achieved national coverage in The Netherlands. In March 2010, more than 100 groups representing approximately 80% of GPs

had a bundled payment contract for diabetes care.<sup>17,18</sup> In the same year, the payment system was expanded to cover the management of chronic obstructive pulmonary disease and vascular risks. Hence, the support for disease manage-

**Objectives:** To assess the differentiated effects of population-based disease management programs (DMPs) for type 2 diabetes on intermediary clinical outcomes in The Netherlands.

**Methods:** Data covering a period from 20 to 24 months between January 2008 and December 2010 were collected from 18 Dutch care groups (primary care provider networks that have bundled payment contracts for delivery of diabetes DMPs). Meta-analysis and meta-regression methods were used to conduct differentiated analyses of these programs' effects over time on 4 clinical indicators: glycated hemoglobin, low-density lipoprotein, systolic blood pressure, and body mass index. Heterogeneous average results were stratified according to various patient and process characteristics to investigate whether differences in these features could explain variation in outcomes.

**Results:** Between 56% and 71% of patients (N = 105,056) had valid first- and second-year measurements of the study outcomes. Although average changes in these measures over time were small, stratified analyses demonstrated that clinically relevant improvements were achieved in patients with poor first-year health values. Interactions with age, disease duration, comorbidity, and smoking status were not consistent across outcomes; nonetheless, heterogeneity in results decreased considerably when simultaneously correcting for known patient characteristics. Positive effects tended to diminish with longer length of follow-up, while greater measurement frequency was associated with improved results, especially in patients with poor health.

**Conclusions:** Our data suggest that tailored disease management, in which not only evidence-based guidelines but also patient characteristics directly determine care processes, including self-management support, has great potential to improve the cost-effectiveness of current chronic care delivery.

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### Take-Away Points

Correcting for heterogeneous care processes and patients resulted in differentiated insight into the effects of population-based disease management on intermediary outcomes of diabetes care.

- Patients with poorly controlled diabetes benefit more from standardized disease management than patients with better health, for whom self-management support might be equally effective.
- Positive effects of disease management diminish with longer length of follow-up; greater measurement frequency improves results, especially in patients with poor health.
- Tailored disease management, in which care content and dose are determined by patients' health, demographics, and social characteristics, has great potential for improving cost-effectiveness in chronic care.

ment in The Netherlands appears to be a matter more of faith than fact, as is the case in other countries as well. International studies and reviews of DMPs demonstrate highly heterogeneous results and so far have failed to answer the basic question of what works best for whom, not least because of variation in both methodology and nomenclature.<sup>3,19-22</sup> It is, however, especially the multicomponent and population-based nature of disease management that makes it difficult to draw unambiguous conclusions concerning effectiveness. Analyzing complex DMPs necessitates a clear framework that links expected outcomes to the characteristics of both the program and its target population, and measures effects over an adequate period of time.<sup>23</sup>

As part of the DISMEVAL (Developing and Validating Disease Management Evaluation Methods for European Healthcare Systems) project, this study's objective was to assess the effects of the Dutch diabetes DMPs on a range of intermediary clinical outcomes. To investigate heterogeneity in results across different care processes and patients, we designed the study as a population-based, multilevel meta-analysis and meta-regression. Given that experimental comparisons were not possible because of the nationwide rollout of the DMPs and the unsuitability of using historical controls,<sup>9</sup> these methods allow for the most in-depth assessment of effectiveness. Such differentiated insight, which goes beyond the "grand means" that currently inform many health system redesigns, can support professionals and policy makers in their efforts to better meet the complex care needs of the growing and inherently diverse population of chronically ill patients.

## METHODS

### Study Design and Participants

The bundled payment system for generic diabetes disease management in The Netherlands obliges care groups to provide insurers with a specific number of performance indicators for both processes and outcomes on an annual basis.<sup>24</sup> We retrospectively gathered individual patient data on these indi-

cators from a convenience sample of 18 groups, which were set up between 2006 and 2009 and represent nearly all regions of The Netherlands. Nine groups were part of an experimental pilot concerning bundled payments evaluated by the National Institute for Public Health and the Environment<sup>15</sup>; to include 9 other, nonexperimental groups, 14 care groups were approached (response rate 64.3%).

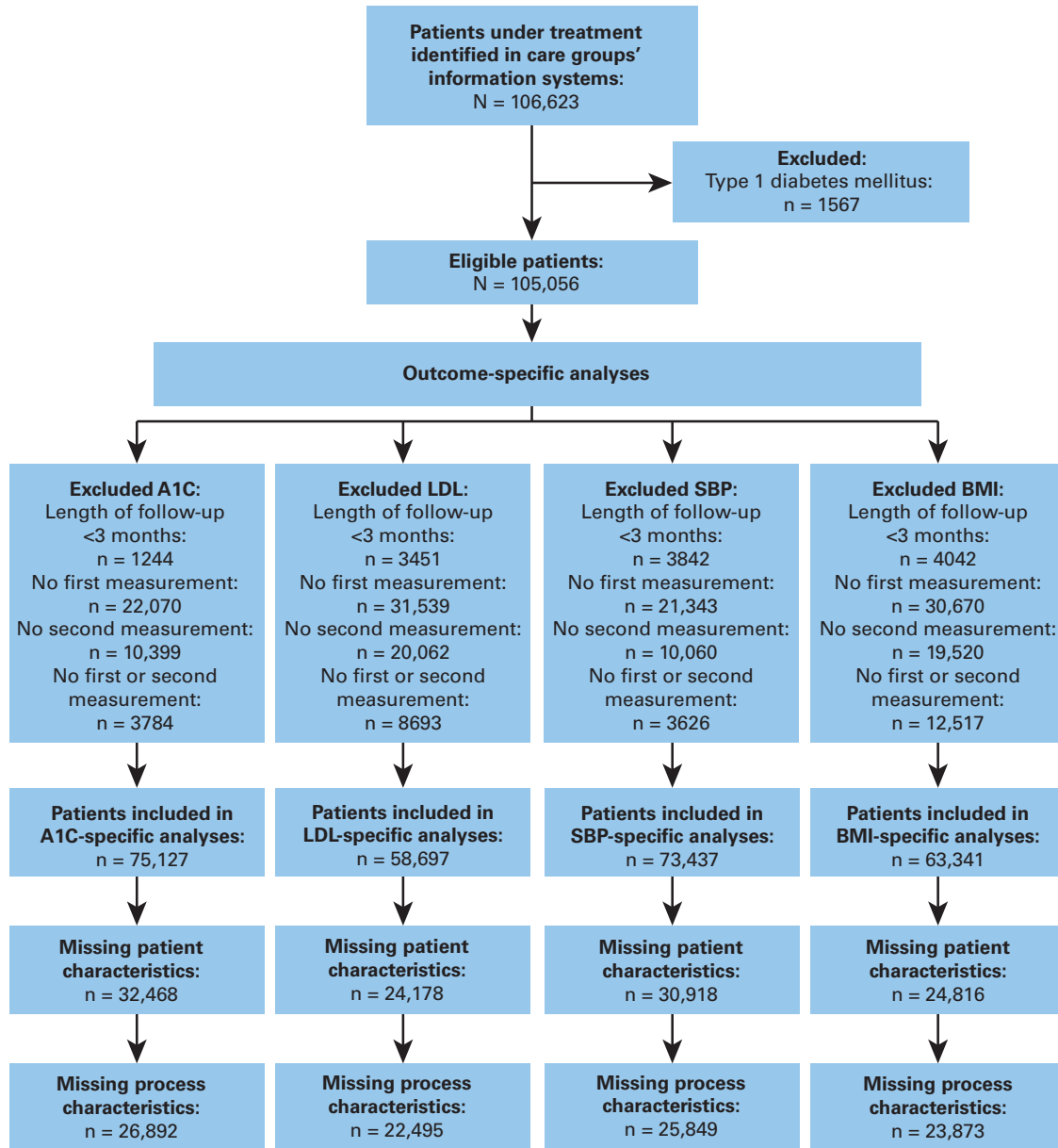
Across the included groups, 106,623 patients had at least 1 registered visit during the research period, which—depending on the availability of data—was either 20 or 24 months between January 2008 and December 2010. We excluded type 1 diabetes patients ( $n = 1567$ ) because they are treated primarily by specialists. Since patient data were drawn from groups' clinical information systems, plausibility was verified through range checks. Outliers were removed based on cutoff points determined by Dutch diabetes experts (see [eAppendix](#), available at [www.ajmc.com](http://www.ajmc.com)). Missing values were not imputed.

Because patient data were not available for the period before introduction of the bundled payment system, we assessed the effects of the diabetes DMPs by comparing the last measurement of each clinical outcome during the first year of the research period (or the first 8 months for the 2 groups with a 20-month research period) with the last measurement of that outcome in the second year. Per outcome-specific analysis, we excluded patients who (1) lacked registrations of the first- or second-year measurements, or both; (2) missed registrations of 1 or more of the patient and/or process characteristics used for stratification; and/or (3) had an observation period between first- and second-year outcome measurement of fewer than 3 months. The maximum length of follow-up per patient was 23 months. The study flow chart is shown in [Figure 1](#).

### Diabetes Disease Management Programs in The Netherlands

In 2007, 10 Dutch care groups started experimenting with a bundled payment system that allows the different components of care for generic type 2 diabetes to be purchased, delivered, and billed as a single product or service. Care groups are legal entities in primary care, which consist of multiple care providers, are most commonly owned by GPs, and form the principal contracting partners for health insurers involved in bundled payment contracts.<sup>17</sup> Groups either deliver the various components of a diabetes DMP themselves or subcontract other providers, including GPs, physical therapists, dieticians, laboratories, and/or specialists, to do so. The price of a specific

■ **Figure 1.** Study Flow Chart



A1C indicates glycated hemoglobin; BMI, body mass index; LDL, low-density lipoprotein; SBP, systolic blood pressure.

program (ie, care bundle) as well as the fees for individual subcontractors are freely negotiable between care groups on the one hand and health insurers or care professionals on the other. Patients are automatically enrolled by their GP.<sup>15,16</sup>

The services to be covered in the diabetes DMPs are codified by a national care standard for generic diabetes care.<sup>25</sup> This standard is based on existing evidence-based guidelines for GPs and includes general modules (eg, information, education and self-management support, smoking cessation, physical activity, nutrition and diet) as well as disease-specific

modules.<sup>24</sup> The latter comprise a defined frequency of GP visits, regular foot and eye examinations, and laboratory testing. To stimulate task redistribution from GPs to practice nurses, who traditionally play an important role in Dutch chronic care, the standard describes care in terms of functions rather than providers, defining what services must be delivered rather than by whom or where.<sup>16,25</sup> For more information on the contents of the Dutch diabetes DMPs, the diabetes care standard can be accessed online: <http://www.diabetesfederatie.nl/zorg/zorgstandaard.html>.

### Definition of Variables and Data Validation

We defined intermediary clinical outcomes as mean changes in glycated hemoglobin (A1C), low-density lipoprotein (LDL), systolic blood pressure (SBP), and body mass index (BMI) between the first- and second-year measurements. In addition, we assessed and compared the proportions of patients within 3 target range groups for glycemic control (A1C  $\leq 53$  mmol/mol; A1C = 54-74 mmol/mol; A1C  $\geq 75$  mmol/mol) at these 2 measurement points.<sup>25</sup>

Care processes were described in terms of measurement frequency and range, and duration of care. We codified measurement frequency as the number of registrations of each clinical outcome during follow-up; to describe measurement range, we assessed the number of different outcomes registered, which across care groups could be a maximum of 8 (ie, A1C, total cholesterol, LDL and high-density lipoprotein, SBP and diastolic blood pressure, BMI, and triglycerides). Duration of care was defined as the number of months between the first- and second-year measurements of each clinical outcome.

To describe patients, we used age in years, disease duration in years, health status, comorbidity, and smoking status. Health status was determined by the first-year values of each clinical outcome. Comorbidity was defined as the presence of 1 or more of the 4 most frequently registered co-occurring conditions across the included care groups (ie, angina pectoris, myocardial infarction, stroke, transient ischemic attack). We dichotomized smoking status as previous smoker or non-smoker versus current smoker.

### Data Analysis

We used a 2-step approach to population-based, multilevel meta-analysis, in which we clustered the individual patient data by care group.<sup>26,27</sup> During the first step, we conducted paired-sampled *t* tests (2 sided;  $\alpha = .05$ ) using SPSS version 18 (IBM Corporation, Armonk, New York) to calculate the group-specific mean differences in clinical values and associated standard deviations. In the second step, these were synthesized with Review Manager (RevMan version 5.1.1; The Cochrane Collaboration) into pooled mean differences and 95% confidence intervals, for which—owing to significant heterogeneity in results—we used the random-effects meta-analysis model of DerSimonian and Laird.<sup>28</sup> Using this model, we weighted the aggregate effects by the inverse of their variances while assuming random treatment effects across care groups.<sup>29</sup> To quantify heterogeneity, we calculated the  $I^2$  statistic—which can range from 0% to 100%—on the basis of the  $\chi^2$  test.<sup>30</sup> For outcomes showing moderate ( $I^2 > 50\%$ ) to high ( $I^2 > 75\%$ ) heterogeneity, subgroup analyses were conducted to examine the consistency of results across diabetes care processes and patients.<sup>26</sup> For this purpose, most continu-

ous variables were categorized into 2 or 3 groups on the basis of either scientific literature (age<sup>31,32</sup> and disease duration<sup>33</sup>) or median values (measurement frequency and length of follow-up). We dichotomized measurement range as 8 outcomes (the maximum number of clinical indicators that could be registered) versus fewer than 8 outcomes; first-year health status was categorized according to the target range values for clinical outcomes included in the diabetes care standard.<sup>25</sup>

We used multilevel meta-regression analysis of individual patient data, stratified by care group, to further assess the influence of potential effect modifiers as well as to investigate potential 3-way interactions between care processes, patient characteristics, and clinical outcomes.<sup>34,35</sup> To conduct the meta-regressions, we used the PROC MIXED command in the SAS 9.2 software (SAS Institute Inc, Cary, North Carolina), which uses a random-effects iterative method to provide a maximum likelihood estimate of the regression parameters. The meta-regression models were multivariable, though process and patient characteristics were included separately; continuous covariates were included as such. For each clinical outcome, we calculated the intraclass correlation coefficient to assess the percentage of total heterogeneity in effects occurring between care groups. The larger the intraclass correlation coefficient, the greater the proportion of variance that can be attributed to differences between rather than within groups.<sup>36</sup> We examined collinearity with the variance inflation factor: a variance inflation factor value of greater than 10 is generally taken as an indication of serious multi-collinearity.<sup>37</sup> Explained heterogeneity was expressed as the percent change in between-group variance ( $\tau^2$ ) and within-group variance ( $\sigma^2$ ).

## RESULTS

### Diabetes Care Processes and Patients

With regard to care processes, patients' SBP was assessed most frequently ( $n = 4$ ) during the period between the first- and second-year measurements, followed by BMI ( $n = 3$ ) and A1C ( $n = 2$ ). LDL was measured least often ( $n = 1$ ). Across care groups, the average share of patients with the maximum outcome measurement range varied from 44.4% to 86.7%, with a mean of 62.3%. Median length of follow-up varied from 10 to 12 months between groups.

**Table 1** shows the patients' main characteristics and first-year clinical values. Age ranged from 15 to 105 years with a mean of 65.7 ( $\pm 11.9$ ) years. Diabetes duration varied from 0 to 76 years with a mean of 4.8 ( $\pm 5.6$ ) years. Approximately 16% of patients had a known comorbidity; 18.4% were registered as current smokers. Depending on the clinical outcome of interest, roughly 56% to 71% of patients ( $n = 105,056$ )

had both a first- and second-year measurement. For most outcomes, the mean first-year values for patients were within normal range. Mean first-year BMI ( $29.7 \pm 5.2 \text{ kg/m}^2$ ), however, signified severe overweight to borderline obesity.

**Clinical Outcomes**

**Table 2** shows the overall results of the random-effects meta-analysis across 18 care groups, presented per clinical outcome. Mean A1C increased by 0.17 mmol/mol (95% confidence interval [CI]  $-0.60$  to  $0.93$ ) between the first- and second-year measurements. LDL was reduced significantly by a mean of  $0.09 \text{ mmol/L}$  (95% CI  $-0.13$  to  $-0.05$ ); SBP decreased significantly by an average of  $0.95 \text{ mm Hg}$  (95% CI  $-1.25$  to  $-0.64$ ). There was a small average decrease in BMI of  $0.04 \text{ kg/m}^2$  (95% CI  $-0.10$  to  $0.02$ ). Except for BMI, the effects of the diabetes DMPs on all intermediary outcomes were moderately to highly heterogeneous, with  $I^2$  values ranging from 57% for SBP to 98% for A1C.

**Figure 2** shows the proportions of patients within 3 target range groups for glycemic control at the first- and second-year measurements. Glycemic control improved in the vast majority of patients, especially in the group with highly uncontrolled diabetes ( $A1C \geq 75 \text{ mmol/mol}$ ). Diabetes was brought under control in roughly 68% of these patients; in 19%, the values improved to  $53 \text{ mmol/mol}$  or lower. Of the patients with first-year A1C concentrations between 53 and  $75 \text{ mmol/mol}$ , approximately 36% improved their glycemic control, 60% remained within the same range, and 4% deteriorated. Of those within target range at the first measurement ( $A1C \leq 53 \text{ mmol/mol}$ ), 83% maintained their A1C control, whereas A1C control deteriorated up to levels of  $<75 \text{ mmol/mol}$  in

**Table 1.** Characteristics of the Research Population

Characteristic	Patients for Whom Characteristic Was Known, % (n)	Estimate, Mean $\pm$ SD
<b>First-year age, y</b>	99.9 (105,013)	$65.7 \pm 11.9$
<b>First-year diabetes duration, y</b>	71.9 (75,498)	$4.8 \pm 5.6$
<b>First-year health status</b>		
A1C (mmol/mol; target $<53$ )	71.5 (75,127)	$50.2 \pm 9.8$
LDL cholesterol (mmol/L; target $<2.5$ )	55.9 (58,697)	$2.6 \pm 0.9$
SBP (mm Hg; target $<140$ )	69.9 (73,437)	$140.4 \pm 18.0$
BMI ( $\text{kg/m}^2$ ; target $<25$ )	60.3 (63,341)	$29.7 \pm 5.2$
<b>Comorbidity<sup>a</sup></b>		
None	84.2 (75,357)	
One or more	15.8 (14,165)	
<b>Smoking status</b>		
Nonsmoker or ex-smoker	81.6 (63,943)	
Current smoker	18.4 (14,441)	

A1C indicates glycated hemoglobin; BMI, body mass index; LDL, low-density lipoprotein; SBP, systolic blood pressure; SD, standard deviation.  
<sup>a</sup>Included were 4 major comorbidities associated with diabetes mellitus: angina pectoris, myocardial infarction, stroke, and transient ischemic attack.

16.5%. Roughly 0.5% saw their A1C increase to  $\geq 75 \text{ mmol/mol}$ . In terms of mean age and disease duration, the patients within target range at the first-year measurement were most comparable to the overall patient population. Those in the subgroups with initial A1C values above  $53 \text{ mmol/mol}$  and  $75 \text{ mmol/mol}$  were significantly younger but had a longer-than-average disease duration.

**Investigating Heterogeneity**

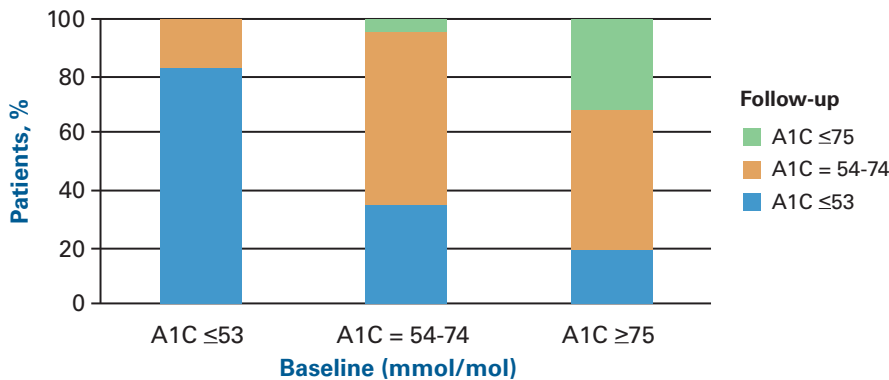
With regard to heterogeneity, the intraclass correlation coefficients identified in the meta-regression—ranging from 0.1% to 4.3% across outcomes—suggest that the vast majority of variance in effects on A1C, LDL, and SBP occurs within rather than between care groups. Subgroup meta-analysis and meta-regression were conducted to investigate

**Table 2.** Results of the Overall Random-Effects Meta-Analysis per Clinical Outcome

Intermediary Outcome	Care Groups, n	Patients, n	Mean Difference (95% CI)	Heterogeneity, $I^2$
A1C (mmol/mol)	18	75,127	$0.17 (-0.60 \text{ to } 0.93)$	98% <sup>a</sup>
LDL (mmol/L)	18	58,697	$-0.09 (-0.13 \text{ to } -0.05)$ <sup>a</sup>	93% <sup>a</sup>
SBP (mm Hg)	18	73,437	$-0.95 (-1.25 \text{ to } -0.64)$ <sup>a</sup>	57% <sup>a</sup>
BMI ( $\text{kg/m}^2$ )	18	63,341	$-0.04 (-0.10 \text{ to } 0.02)$	0%

A1C indicates glycated hemoglobin; BMI, body mass index; CI, confidence interval; LDL, low-density lipoprotein; SBP, systolic blood pressure.  
<sup>a</sup>Statistically significant ( $P < .05$ ).  
 $I^2$  quantifies the total level of heterogeneity in effects.

**Figure 2.** Glycemic Control From First- to Second-Year Measurements According to Target Values



A1C indicates glycated hemoglobin.

to what extent this heterogeneity can be explained by variation in care processes and patient characteristics. Evidence for multicollinearity (variance inflation factor >10) among the different covariates on these levels was not identified (see **Tables 3-6**).

**Variation in Care Processes**

Table 3 shows that subgroup meta-analyses identified 1 significant difference in effects based on a process characteristic: patients with a length of follow-up of 1 year or less achieved greater reductions in SBP than patients followed for more than 1 year. The meta-regressions demonstrated linear relationships between length of follow-up and all clinical outcomes, indicating that as the duration of care increases, the positive effects of the DMPs are difficult to maintain. A greater measurement frequency was also associated with progressively greater reductions in all included outcomes, although statistical significance was not achieved for A1C. The results for measurement range (<8 outcomes vs 8 outcomes) were inconsistent. Despite the identified interactions, simultaneously correcting for the 3 known process features resulted in no more than minor changes in the existing heterogeneity in effects within groups.

**Variation in Patient Characteristics**

The findings from the analyses stratified by patient characteristics are displayed in **Tables 4 to 6**. Both the subgroup meta-analyses and the meta-regressions demonstrated an association between progressively greater health improvements and initially poorer clinical values. Across the 18 care groups, patients with a first-year A1C of ≥75 mmol/mol achieved a mean reduction in this clinical measure of 16.8 mmol/mol, whereas those starting within the target range (≤53 mmol/mol) experienced a slight

deterioration (1.79 mmol/mol). For SBP and LDL, similar interactions were found. The results of the remaining analyses (ie, for age, disease duration, comorbidity, and smoking status) were less conclusive and inconsistent across clinical outcomes. Nevertheless, simultaneously including all patient characteristics into a meta-regression model allowed for substantial reductions in within-group variance in results.

**Combining Variation in Processes and Patients**

Meta-regression identified a significant 3-way interaction—between care processes, patients, and treatment effects—that was consistent across all included outcomes (**Table 7**). This interaction indicates that the poorer a patient’s initial values were, the more beneficial frequent measurement of that particular clinical outcome was in terms of achieving improvements.

DISCUSSION

As far as we are aware, this study is one of the largest to date (N = 105,056) that analyzed the effects of population-based disease management on the intermediary outcomes of diabetes care. In terms of the Chronic Care Model,<sup>14</sup> the DMPs for diabetes in The Netherlands can be considered a “light” form of practice redesign, focusing primarily on improvements in 2 areas: decision support and the delivery system design. During the 12-month evaluation of the bundled payment system, Dutch providers indeed reported improved evidence-based practice and coordination of care based on the guiding principles of the diabetes care standard.<sup>15-17</sup> Thus far, self-management support is not part of most contracts and, as such, is less of a target point for improvement efforts. While contracts do include record-keeping obligations and the diabetes care standard emphasizes the importance of adequate data exchange, clinical information systems also remain underdeveloped.<sup>15</sup>

Based solely on the undifferentiated mean changes in clinical values shown by our meta-analysis—which differ from a simple paired *t* test to the extent that they are pooled and weighted per care group—one would conclude that the Dutch DMPs have little impact on the health of patients suffering from type 2 diabetes. However, one of the strengths of multilevel meta-analysis and meta-regression of individual pa-

## Toward Tailored Disease Management

**Table 3.** Effect of Process Characteristics on Changes in Glycated Hemoglobin, Low-Density Lipoprotein, and Systolic Blood Pressure Levels Between First- and Second-Year Measurements

Process Characteristic	Groups, n	Patients, n	Mean Difference (95% CI; I <sup>2</sup> )	RC <sup>a</sup>	Change in τ <sup>2</sup> , %	Change in σ <sup>2</sup> , %	VIF
<b>A1C, mmol/mol</b>	<b>18</b>	<b>75,127</b>	<b>0.17 (−0.60 to 0.93; 98)</b>		<b>26</b>	<b>−0.1</b>	
<b>Measurement frequency</b>	14			−			1.04
≤Median		27,322	0.09 (−0.85 to 1.03)				
>Median		20,913	−0.06 (−1.47 to 1.36)				
<b>Measurement range</b>	18			− <sup>b</sup>			1.05
<8 outcomes		15,641	0.13 (−1.08 to 1.34)				
8 outcomes		51,820	0.05 (−0.66 to 0.75)				
<b>Length of follow-up, y</b>	18			+ <sup>b</sup>			1.05
≤1		57,069	0.02 (−0.77 to 0.81)				
>1		18,058	0.53 (−0.22 to 1.27)				
<b>LDL, mmol/L</b>	<b>18</b>	<b>58,697</b>	<b>−0.09<sup>a</sup> (−0.13 to −0.05; 93<sup>a</sup>)</b>		<b>−36.9</b>	<b>0.7</b>	
<b>Measurement frequency</b>	14			− <sup>b</sup>			1.02
≤Median		25,420	−0.08 <sup>b</sup> (−0.12 to −0.05)				
>Median		10,782	−0.20 <sup>b</sup> (−0.26 to −0.15)				
<b>Measurement range</b>	18			−			1.00
<8 outcomes		6500	−0.10 <sup>b</sup> (−0.15 to −0.05)				
8 outcomes		45,301	−0.10 <sup>b</sup> (−0.14 to −0.06)				
<b>Length of follow-up, y</b>	18			+ <sup>b</sup>			1.02
≤1		43,901	−0.09 <sup>b</sup> (−0.13 to −0.05)				
>1		14,796	−0.11 <sup>b</sup> (−0.15 to −0.06)				
<b>SBP, mm Hg</b>	<b>18</b>	<b>73,437</b>	<b>−0.95<sup>a</sup> (−1.25 to −0.64; 57<sup>a</sup>)</b>		<b>15.6</b>	<b>5.2</b>	
<b>Measurement frequency</b>	14			− <sup>b</sup>			1.08
≤Median		21,764	−0.99 <sup>b</sup> (−1.57 to −0.41)				
>Median		25,824	−1.01 <sup>b</sup> (−1.38 to −0.64)				
<b>Measurement range</b>	18			+ <sup>b</sup>			1.06
<8 outcomes		14,397	−1.60 <sup>b</sup> (−2.02 to −1.17)				
8 outcomes		50,392	−0.79 <sup>b</sup> (−1.15 to −0.43)				
<b>Length of follow-up, y</b>	18			+ <sup>b</sup>			1.07
≤1		55,686	−1.27 <sup>b</sup> (−1.60 to −0.95)				
>1		17,751	−0.04 (−0.52 to 0.44)				

A1C indicates glycated hemoglobin; CI, confidence interval; LDL, low-density lipoprotein; RC, regression coefficient; SBP, systolic blood pressure; VIF, variance inflation factor.  
<sup>a</sup>Plus (+) = positive; minus (−) = negative.  
<sup>b</sup>Statistically significant (*P* < .05).

tient data is that these methods allow for the investigation of subgroups of patients for whom certain care processes might be more or less effective. Most notably, the stratified results suggest that the DMPs are considerably more beneficial for patients with poorly controlled diabetes than for those within the target range of important clinical indicators. A recent meta-analysis of the international literature conducted by Pimouguet et al<sup>21</sup> supports this finding, which—given that the

vast majority of patients included in our research had good first-year values for A1C, LDL, and SBP—provides a plausible explanation for the small average effects of the diabetes DMPs. Contrary to what is often assumed, the patients benefiting most from disease management in our study were not those recently diagnosed with diabetes, but rather patients with a longer-than-average disease duration. Stratified analysis for A1C showed that in patients with controlled diabetes

■ **Table 4.** Effect of Patient Characteristics on Changes in Glycated Hemoglobin Levels Between First- and Second-Year Measurements

Patient Characteristic	Groups, n	Patients, n	Mean Difference (95% CI; I <sup>2</sup> )	RC <sup>a</sup>	Change in τ <sup>2</sup> , %	Change in σ <sup>2</sup> , %	VIF
<b>A1C, mmol/mol</b>	<b>18</b>	<b>75,127</b>	<b>0.17 (−0.60 to 0.93; 98)</b>		<b>−12.5</b>	<b>−23.5</b>	
<b>Age, y</b>	18			− <sup>b</sup>			1.12
≤59		20,538	0.21 (−0.56 to 0.98)				
60-69		24,204	0.23 (−0.55 to 1.02)				
≥70		30,382	0.03 (−0.78 to 0.83)				
<b>Disease duration, y</b>	14			+ <sup>b</sup>			1.09
≤2		21,261	−0.12 (−1.12 to 0.88)				
3-5		13,342	0.11 (−0.76 to 0.98)				
≥5		20,474	−0.07 (−1.08 to 0.95)				
<b>First-year A1C, mmol/mol</b>	18			− <sup>b</sup>			1.05
≤53		51,545	1.79 <sup>b</sup> (1.17, 2.41)				
54-74		21,637	−2.62 <sup>b</sup> (−3.46 to −1.78)				
≥75		1945	−16.82 <sup>b</sup> (−18.67 to −14.96)				
<b>Comorbidity</b>	16			+ <sup>b</sup>			1.03
No		53,065	0.04 (−0.63 to 0.71)				
Yes		10,183	−0.06 (−0.76 to 0.65)				
<b>Smoking</b>	17			+ <sup>b</sup>			1.04
No/previously		46,277	0.23 (−0.28 to 0.73)				
Yes		10,375	0.20 (−0.85 to 1.25)				

A1C indicates glycated hemoglobin; CI, confidence interval; RC, regression coefficient; VIF, variance inflation factor.

<sup>a</sup>Plus (+) = positive; minus (−) = negative.

<sup>b</sup>Statistically significant (*P* < .05).

■ **Table 5.** Effect of Patient Characteristics on Changes in Low-Density Lipoprotein Levels Between First- and Second-Year Measurements

Patient Characteristic	Groups, n	Patients, n	Mean Difference (95% CI; I <sup>2</sup> )	RC <sup>a</sup>	Change in τ <sup>2</sup> , %	Change in σ <sup>2</sup> , %	VIF
<b>LDL, mmol/L</b>	<b>18</b>	<b>58,697</b>	<b>−0.09<sup>b</sup> (−0.13 to −0.05; 93<sup>b</sup>)</b>		<b>−33.9</b>	<b>−21.7</b>	
<b>Age, y</b>	18			+ <sup>b</sup>			1.11
≤59		15,857	−0.12 <sup>b</sup> (−0.16 to −0.07)				
60-69		19,364	−0.09 <sup>b</sup> (−0.13 to −0.05)				
≥70		23,474	−0.08 <sup>b</sup> (−0.12 to −0.03)				
<b>Disease duration, y</b>	14			−			1.05
≤2		16,756	−0.14 <sup>b</sup> (−0.19 to −0.08)				
3-5		10,607	−0.08 <sup>b</sup> (−0.12 to −0.03)				
≥5		15,857	−0.06 <sup>b</sup> (−0.10 to −0.01)				
<b>First-year LDL, mmol/L</b>	18			− <sup>b</sup>			1.02
<2.5		29,311	0.15 <sup>b</sup> (0.12, 0.18)				
2.5-3.5		19,984	−0.17 <sup>b</sup> (−0.20 to −0.14)				
>3.5		9402	−0.72 <sup>b</sup> (−0.77 to −0.67)				
<b>Comorbidity</b>	16			− <sup>b</sup>			1.04
No		39,721	−0.10 <sup>b</sup> (−0.14 to −0.06)				
Yes		7994	−0.08 <sup>b</sup> (−0.15 to −0.01)				
<b>Smoking</b>	17			−			1.03
No/previously		38,294	−0.09 <sup>b</sup> (−0.13 to −0.04)				
Yes		7762	−0.11 <sup>b</sup> (−0.15 to −0.06)				

CI indicates confidence interval; LDL, low-density lipoprotein; RC, regression coefficient; VIF, variance inflation factor.

<sup>a</sup>Plus (+) = positive; minus (−) = negative.

<sup>b</sup>Statistically significant (*P* < .05).



**Table 6.** Effect of Patient Characteristics on Changes in Systolic Blood Pressure Between First- and Second-Year Measurements

Patient Characteristic	Groups, n	Patients, n	Mean Difference (95% CI; I <sup>2</sup> )	RC <sup>a</sup>	Change in τ <sup>2</sup> , %	Change in σ <sup>2</sup> , %	VIF
<b>SBP, mm Hg</b>	<b>18</b>	<b>73,437</b>	<b>-0.95<sup>a</sup> (-1.25 to -0.64; 57<sup>a</sup>)</b>		<b>74.8</b>	<b>-29.9</b>	
<b>Age, y</b>	18			+ <sup>b</sup>			1.15
≤59		20,139	-0.57 <sup>b</sup> (-0.92 to -0.23)				
60-69		23,689	-1.00 <sup>b</sup> (-1.38 to -0.62)				
≥70		29,605	-1.34 <sup>b</sup> (-1.72 to -0.96)				
<b>Disease duration, y</b>	14			+			1.04
≤2		21,673	-1.04 <sup>b</sup> (-1.47 to -0.62)				
3-5		13,117	-0.55 <sup>b</sup> (-0.97 to -0.13)				
≥5		19,645	-1.22 <sup>b</sup> (-1.61 to -0.84)				
<b>First-year SBP, mm Hg</b>	18			- <sup>b</sup>			1.04
≤140		42,784	4.59 (4.21 to 4.97)				
>140		30,653	-8.91 (-9.67 to -8.16)				
<b>Comorbidity</b>	16			- <sup>b</sup>			1.04
No		50,780	-0.93 <sup>b</sup> (-1.29 to -0.58)				
Yes		9788	-1.25 <sup>b</sup> (-1.75 to -0.75)				
<b>Smoking</b>	17			-			1.04
No/previously		46,908	-0.90 <sup>b</sup> (-1.24 to -0.56)				
Yes		10,504	-1.07 <sup>b</sup> (-1.54 to -0.59)				

CI indicates confidence interval; RC, regression coefficient; SBP, systolic blood pressure; VIF, variance inflation factor.  
<sup>a</sup>Plus (+) = positive; minus (-) = negative.  
<sup>b</sup>Statistically significant (*P* < .05).

(A1C ≤53 mmol/mol), whose clinical values leave limited room for further improvement, the DMPs implemented in The Netherlands successfully maintained A1C levels within target range, thereby preventing the severe complications associated with deteriorating glycemic control.<sup>32,38</sup> Although the interactions between the effects of the DMPs and patient characteristics other than first-year health status were far less conclusive, the existing heterogeneity in results was reduced considerably after simultaneously correcting for patient features. Characteristics not included in our study (eg, level of education, socioeconomic status) may be equally important and informative, given their influence on people’s healthcare behaviors.<sup>39</sup>

The rising prevalence of long-term conditions strains the human and financial capital of current healthcare systems in many countries and urges cost-effective solutions.<sup>40,41</sup> Our study was based on the assumption that evaluations of DMPs should take into account the heterogeneous nature of care processes and patients (something that randomized controlled trials have thus far failed to do<sup>9,19,21</sup>) because this information can help healthcare professionals and policy makers to achieve such solutions. In its current form, the Dutch bundled payment system appears to motivate care providers to deliver highly standardized diabetes care based on performance indicators monitored by health insurers.<sup>15</sup> Among other things,

these indicators prescribe a defined intensity of service delivery and target values for clinical measures. Our findings support a move toward a more tailored approach to disease management, in which the characteristics of patients directly determine care processes. Frequent monitoring was shown to be especially useful for improving clinical values in patients with poorly controlled diabetes. For those in relatively good health, perhaps as a result of having previously been monitored intensively, a less physician-guided form of care that emphasizes self-management might be equally effective—and probably less costly—for maintaining glycemic control. Multiple studies have shown that self-management support programs can improve patients’ health behaviors and clinical and social outcomes, and reduce medical costs.<sup>42,43</sup> Further research is necessary to assess whether intensive, physician-guided disease management might indeed be redundant for relatively healthy subgroups of diabetes patients and could be replaced by adequate self-management support.

Tailoring care provision for diabetes requires improvements in the clinical information systems used to register data in the daily practice of healthcare, as valid and reliable information concerning the patient under treatment must guide decisions on care content and dose. Despite record-keeping obligations, missing values were ubiquitous in the data sets gathered from our care groups. Tailored disease manage-

**■ Table 7.** Three-Way Interactions Between Measurement Frequency, First-Year Clinical Values, and Effects of the Diabetes Disease Management Programs on Glycated Hemoglobin, Low-Density Lipoprotein, and Systolic Blood Pressure

Clinical Value	Groups, n	Patients, n	Coefficient	Change in $\tau^2$ , %	Change in $\sigma^2$ , %
<b>A1C, mmol/mol</b>	<b>14</b>	<b>48,235</b>		<b>-11.2</b>	<b>-19.2</b>
Intercept			13.2497 <sup>a</sup>		
Measurement frequency			1.5295 <sup>a</sup>		
First-year A1C			-0.2743 <sup>a</sup>		
Measurement frequency × first-year A1C (interaction)			-0.02614 <sup>a</sup>		
<b>LDL, mmol/L</b>	<b>14</b>	<b>36,202</b>		<b>-62.2</b>	<b>-21.2</b>
Intercept			0.6997 <sup>a</sup>		
Measurement frequency			0.1095 <sup>a</sup>		
First-year LDL			-0.3024 <sup>a</sup>		
Measurement frequency × first-year LDL (interaction)			-0.05091 <sup>a</sup>		
<b>SBP, mm Hg</b>	<b>14</b>	<b>47,588</b>		<b>69.8</b>	<b>-23.0</b>
Intercept			63.5490 <sup>a</sup>		
Measurement frequency			1.8236 <sup>a</sup>		
First-year SBP			-0.4683 <sup>a</sup>		
Measurement frequency × first-year SBP (interaction)			-0.01115 <sup>a</sup>		

A1C indicates glycated hemoglobin; LDL, low-density lipoprotein; SBP, systolic blood pressure.

<sup>a</sup>Statistically significant ( $P < .05$ ).

ment further necessitates broad implementation of effective strategies for self-management support (which should reach beyond the boundaries of the healthcare system) to provide patients with the knowledge, skills, resources, and confidence to care for their illness(es).<sup>1,44,45</sup> Most importantly, however, the financial incentives embedded in funding systems should motivate providers to deliver high-quality care rather than to achieve overly standardized levels of service delivery, as appears to be the case with the Dutch bundled payment system. Healthcare professionals cannot be expected to work in a patient-centered—or for that matter, efficient—manner if they are reimbursed on the basis of performance indicators stipulating, for instance, that patients should be seen at least 4 times per year, regardless of their care needs or self-management skills.

Future evaluations of disease management should utilize longitudinal data in order to improve insights into the long-term impact on patients' health. In line with previous research,<sup>21,46</sup> our findings suggest that studies conducted over shorter periods of time might overestimate effects, as length of follow-up is negatively related to health outcomes. Coming to strong conclusions regarding how we can best treat patients who have 1 or more chronic diseases requires more population-based research. Randomized controlled trials, generally perceived as the gold standard for evaluating healthcare interventions, not only are difficult to apply to analyses of complex DMPs but also produce

results that are difficult to generalize to the larger and inherently more heterogeneous populations of chronically ill patients.<sup>47</sup> Future studies should take into account the variation in both patients and interventions, and focus on gaining differentiated insights into the modes of care provision that are most effective for treating specific subgroups of chronically ill patients such as those suffering from severe multimorbidity.

Most of the limitations of this study relate to the choice to collect data in a retrospective fashion. Of the 18 included care groups, no more than 2 were able to provide data on all of the requested process and patient characteristics, and intermediary outcomes. As a result, few analyses of the interactions between these variables could be conducted on the basis of data from all groups. Within care groups, we had to exclude considerable numbers of patients lacking valid registrations of included characteristics or outcomes. Nonetheless, our population did not differ from other diabetes populations studied in The Netherlands in terms of average age or disease duration, or from the overall Dutch population with respect to percentage of smokers.<sup>15,48,49</sup> The prevalence of co-occurring conditions was considerably lower in our research group than in the total cohort of Dutch diabetes patients,<sup>50</sup> which likely signifies registration problems. Gathering data retrospectively also limited our choice of effect measures to the included set of intermediary clinical outcomes; more patient-centered indicators (eg, health-related quality of life, self-efficacy, patient satisfaction) were not available. Fur-

thermore, we were not able to stratify patients based on information about their GP (practice) or their use of services offered by other professionals, even though variation on the provider level likely causes heterogeneity in effects. Finally, the recent implementation of the diabetes DMPs in The Netherlands did not allow for analyses of time series, nor were we able to assess changes in the processes of diabetes care as a consequence of the implementation of these programs.

Strengths of our study include the large sample size, the setting in daily healthcare practice, an adequate length of follow-up, and the analytic methods used for evaluation, which allowed us to determine the differential effects of disease management for diabetes across different care processes and patients.

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■ **eAppendix.** Cutoff Points for Data Cleaning

<b>Indicator</b>	<b>Lower</b>	<b>Upper</b>	<b>No. (%) Excluded</b>
Glycated hemoglobin, mmol/mol	18	108	913 (0.5)
Low-density lipoprotein, mmol/L	1	7.3	2110 (1.3)
Systolic blood pressure, mm Hg	70	250	25 (0.01)
Body mass index, kg/m <sup>2</sup>	16	70	123 (0.08)