# **Goal Attainment in Patients with Type 2 Diabetes, Part 2**

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Are patients at a military treatment facility being screened often enough and being treated appropriately according to their disease progression?

The primary goals of diabetes mellitus management are to reduce mortality, ameliorate symptoms, reduce the risk of microvascular and macrovascular disease complications, and to improve quality of life. Of the many complications encountered in patients with diabetes, cardiovascular (CV) disease and end-stage renal disease (ESRD) are two of the most critical to prevent and treat. According to the American Diabetes Association (ADA), CV disease is the leading cause of death in patients with type 2 diabetes. And type 2 diabetes is statistically the largest contributor to the development of ESRD in the United States.2 Patients who develop ESRD require dialysis and, eventually, kidney transplantation.

In order to prevent CV disease, ESRD, and other diabetes complications, it is essential for patients to keep their blood glucose, blood pressure (BP), and cholesterol levels under control. For those patients who are unsuccessful at achieving

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their goal levels through diet and exercise alone, pharmacologic therapy is warranted. It has been shown that the reduction of CV disease risk factors through pharmacologic therapy can prevent or slow the progression of CV events significantly.

For example, a meta-analysis of six primary prevention studies by Vijan and Hayward demonstrated that lipid lowering medications resulted in a 3% absolute reduction in the risk of CV events over 4.3 years of treatment, with a number needed to treat of 35.3 The authors also conducted a meta-analysis of eight secondary prevention studies, which showed an absolute risk reduction of 7% over 4.9 years of treatment and a number needed treat of only 14.3

The ADA recommends that a number of routine screening assessments be completed for all patients with diabetes and that pharmacologic therapy be provided to assist patients in controlling their BP, cholesterol, and hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels.<sup>1</sup> National data, however, show that about 12% of diabetic patients do not have HbA<sub>1c</sub> testing, 17% do not have low-density lipoprotein cholesterol (LDL) screenings, and 20% do not have nephropathy assessments at least once a year. Furthermore, more than 90% of adult diabetic patients do not meet the recommended goals of therapy for HbA<sub>1c</sub>, BP, and cholesterol levels.4

In an effort to improve diabetes care, performance measures have

been developed by the ADA and by the National Committee for Quality Assurance to encourage health care organizations and providers to develop quality improvement interventions. These performance measures are tracked by several coalitions and programs, including the Diabetes Physician Recognition Program (DPRP) and the Healthcare Effectiveness Data and Information Set (HEDIS), which provide national benchmark information. The availability of these benchmarks allows smaller health care organizations to compare their own diabetes care performance to national data.

The purpose of the analysis reported here was to identify the adherence rates to the ADA 2006 diabetes treatment guidelines in patients receiving care for type 2 diabetes at a military treatment facility (MTF) and to compare these results to the national benchmarks. In the first part of this two-part series, which appeared in the August 2008 issue of Federal *Practitioner*, we focused on patients' HbA<sub>1c</sub>, LDL, and BP goal attainment rates. In this month's concluding article, we report patients' screening rates, medication treatment patterns, and CV disease and other diabetes complications. We start by reviewing the ADA's standards of care regarding screening for BP, lipids, HbA<sub>1c</sub>, and nephropathy complications; pharmacologic treatment for BP, lipids, HbA<sub>1c</sub>, nephropathy, and CV disease; and smoking cessation counseling.

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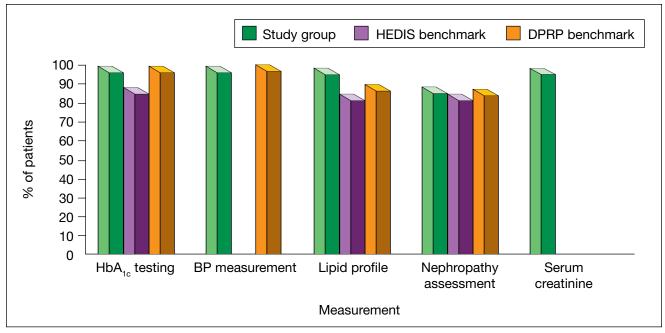


Figure 1. Monitoring rates for hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) testing, blood pressure (BP) and lipid measurement, nephropathy asssessment, and serum creatinine measurement in the study patients compared with patients treated in a commercial health care organization, according to the Healthcare Effectiveness Data and Information Set (HEDIS) 2007 national commercial benchmark<sup>4</sup> and patients treated by applicants to the Diabetes Provider Recognition Program (DPRP) from 1997 to 2003.<sup>8</sup>

# ADA STANDARDS OF CARE: SCREENING AND MEDICATION UTILIZATION

#### **BP**

The ADA recommends that a patient's BP be measured at every routine diabetes visit and that BP treatment target a systolic BP (SBP) of less than 130 mm Hg and diastolic BP (DBP) of less than 80 mm Hg.<sup>1</sup>

Initially, patients with elevated BP should be treated with a drug class that is demonstrated to reduce CV events in patients with diabetes—such as angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, diuretics, and calcium channel blockers.<sup>1</sup> All patients with diabetes who meet the criteria for hypertension should be treated with a regimen that includes either an ACE inhibitor or an ARB.<sup>1</sup>

#### Lipids

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, which plays a role in the higher rates of CV disease in this patient population. The ADA recommends testing for lipid disorders in adult patients at least annually and more often, if needed, to achieve LDL goals of less than 100 mg/dL in patients without CV disease and possibly less than 70 mg/dL in patients with CV disease.

Lipid management aimed at lowering LDL, raising high-density lipoprotein cholesterol (HDL), and lowering triglyceride levels has been shown to reduce macrovascular disease and mortality in patients with type 2 diabetes. In studies involving the use of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors (or statins), patients with diabetes achieved significant reductions in coronary and cerebrovascular events.<sup>1,5</sup> The ADA recommends statin therapy for all patients with CV disease and for those patients older than age 40 who don't have CV disease.<sup>1</sup> After LDL goals have been met, niacin or fibrate therapy may be needed to help patients reach target HDL and triglyceride levels.

#### HbA<sub>1c</sub>

Glycemic control is fundamental to diabetes management, and the goal of therapy is to achieve an HbA<sub>1c</sub> level as close to normal fasting and postprandial glucose concentrations as possible without developing hypoglycemia. The Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) have shown that improved glycemic control is associated with sustained, decreased rates of retinopathy, nephropathy, and neuropathy. The

HbA<sub>1c</sub> measurement provides a way to assess a patient's average glycemia over the preceding two to three months and evaluate treatment efficacy for glycemic control. The ADA recommends HbA<sub>1c</sub> testing be performed routinely in all patients with diabetes.<sup>1</sup>

#### Nephropathy

Diabetic nephropathy occurs in 20% to 40% of patients with diabetes and is the single leading cause of ESRD.1 Persistent microalbuminuria (defined as albuminuria in the range of 30 to 299 mg per 24 hours) has been shown to be the earliest stage of diabetic nephropathy in type 1 diabetes and a marker for the development of nephropathy in type 2 diabetes.<sup>1</sup> The ADA recommends annual testing for microalbuminuria in all patients with type 2 diabetes and in all patients with type 1 diabetes who have had the disease for at least five years. Serum creatinine also should be measured annually and used to estimate the glomerular filtration rate (GFR) in all adults with diabetes, regardless of their degree of urine albumin excretion.1

The UKPDS provided strong evidence that BP control can impede nephropathy development. Studies in patients with type 1 diabetes have demonstrated that achieving SBP levels of less than 140 mm Hg through the use of ACE inhibitors provides selective benefit over other antihypertensive drug classes in delaying the progression from microalbuminuria to macroalbuminuria and can slow the decline in GFR in patients with macroalbuminuria.1 ARBs also have been shown to reduce the rate of progression from microalbuminuria to macroalbuminuria, as well as ESRD in patients with type 2 diabetes. In the treatment of both microalbuminuria and macroalbuminuria, either ACE inhibitors or ARBs should be used. In diabetic patients with hypertension

Table 1. Study patients' utilization patterns
of blood pressure medications (n = 299)

Blood pressure medication	Patients, no. (%) <sup>a</sup>
ACE <sup>b</sup> inhibitor	182 (60.9)
Thiazide diuretic	110 (36.8)
Beta-blocker	107 (35.8)
ARB°	91 (30.4)
Nondihydropyridine CCBd	31 (10.4)
Loop diuretic	30 (10.0)
Dihydropyridine CCB	17 (5.7)
Alpha-agonist	15 (5.0)
Direct vasodilator	12 (4.0)
Alpha-beta blocker	6 (2.0)
Alpha-blocker	5 (1.7)
Potassium sparing diuretic	4 (1.3)
Angiotensin II blocker	0 (0.0)

 $^{a}$ Twenty-nine patients (9.7%) were not taking any blood pressure medications.  $^{b}$ ACE = angiotensin converting enzyme.  $^{\circ}$ ARB = angiotensin receptor blocker.  $^{d}$ CCB = calcium channel blocker.

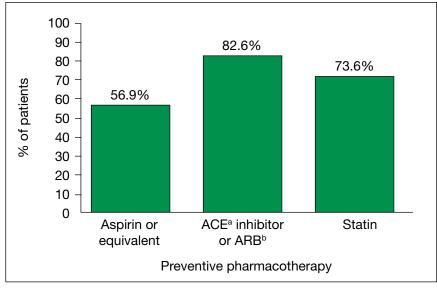


Figure 2. Utilization of preventive pharmacotherapy recommended by the American Diabetes Association among the study patients. <sup>a</sup>ACE = angiotensin converting enyzme. <sup>b</sup>ARB = angiotensin receptor blocker.

and any degree of albuminuria, ACE inhibitors or ARBs have been shown to delay the progression to macroal-buminuria and nephropathy.<sup>1</sup>

#### **Antiplatelet therapy**

Type 2 diabetes is a major risk factor for macrovascular disease and is now considered a CHD risk equiva-

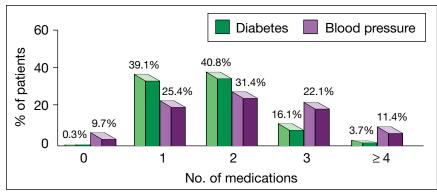


Figure 3. Number of diabetes and blood pressure medications used by the study patients (n = 299).

lent.6 Aspirin is recommended as primary and secondary therapy to prevent CV events in patients with diabetes.1 Many trials have shown a 30% decrease in myocardial infarction and a 20% decrease in stroke in a wide range of patients. The ADA recommends using aspirin therapy as a secondary prevention strategy in patients with diabetes and a history of CHD.1 In patients without CHD, the ADA recommends aspirin therapy in patients at increased risk for CV disease—those who are older than age 40 and have additional CV risk factors.1 Aspirin therapy also should be considered in younger patients (those between ages 30 and 40) who have other CV risk factors.1

#### **Smoking cessation counseling**

Studies of patients with diabetes consistently found an increased risk of morbidity and premature death associated with the development of macrovascular complications among smokers. Smoking is also related to premature development of microvascular diabetes complications. The ADA recommends that providers advise all patients not to smoke and include smoking cessation counseling as a routine component of diabetes care.<sup>1</sup>

#### **METHODS**

The study design, patient population, and data analysis for this investigational review board-approved retrospective, observational, cohort analysis of 299 patients were described in detail in part 1 of this series, as were the primary outcomes.<sup>7</sup> The secondary outcomes, which we describe herein, consisted of screening and prevention parameters. These included monitoring of BP, lipids, HbA<sub>1c</sub>, urine albumin, and serum creatinine levels; utilization patterns of BP, lipid lowering, and diabetes medications; use of aspirin therapy; use of tobacco cessation counseling for documented current smokers; and incidence of CV and other diabetes complications.

Demographic variables collected included age, gender, race, height, weight, tobacco use, and history of CV and diabetes complications. Laboratory and monitoring variables collected included HbA<sub>1c</sub>; SBP and DBP; lipid profiles, including LDL, HDL, triglycerides, and total cholesterol; urine albumin; and serum creatinine. Medication assessments included patients' use of aspirin, antiplatelet agents, warfarin, all BP medications, all lipid lowering medications, and all diabetes medications.

#### **RESULTS**

The mean age of the study group was 59.9 years (range, 18 to 85 years). More than half (56%) of the patients were male and the majority (60%) were white.

#### **BP**

Almost all (293, or 98%) of the 299 patients in the study group had a BP measurement completed in the past 12 months. This percentage is slightly lower than the average number of patients of DPRP applicants from 1997 to 2003 who had their BP measured in the previous year (Figure 1).8

Twenty-nine patients (9.7%) were not taking any BP medications. Although their mean BP was 125/73 mm Hg, 14 patients in this group (48.3%) had BP levels that were above the ADA-recommended value.

A total of 270 patients were taking at least one BP medication. The drug classes most often prescribed were ACE inhibitors (61%), thiazide diuretics (37%), beta-blockers (36%), ARBs (30%), and calcium channel blockers (16%) (Table 1). Many of the patients (82.6%) were taking either an ACE inhibitor or an ARB (Figure 2).

The mean number of BP medications prescribed for the entire study group was 2 (range, 0 to 6) (Figure 3). The mean number was slightly lower for patients who had reached their BP goal compared to those who hadn't (1.9 [range, 0 to 6] versus 2.2 [range, 0 to 6], respectively).

#### **Lipids**

Most (285, or 95.3%) of the 299 study patients had a lipid profile completed within the past 12 months. This rate is higher than the 2007 national HEDIS benchmarks<sup>4</sup> and higher than the average number of patients of DPRP applicants from 1997 to 2003 who had their lipid profile measured in the previous year.<sup>8</sup>

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#### DIABETES GOAL ATTAINMENT

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Lipid lowering therapy
None

in the study patients according to lipid lowering therapy							
ing	LDL level in mg/dL, mean (range) <sup>b</sup>	Patients with LDL level < 100 mg/dL, no. (%) <sup>c,d</sup>	Patients with triglyceride level < 150 mg/dL, no. (%)e	Patients with HDL <sup>f</sup> level > 40 mg/dL, no. (%) <sup>e</sup>	Patients with non-HDL level < 130 mg/dL, no. (%)e		
	97.9 (10–212)	31 (56.4)	29 (51.8)	34 (60.7)	28 (50.0)		

88.0 (28-189) 114 (72.2) 95 (59.7) Statin monotherapy 99 (62.3) 105 (66.0) Other LLAg 101.4 (39-157) 8 (47.1) 8 (47.1) 8 47.1) 9 (52.9) monotherapy Statin combination 81.9 (31–182) 43 (82.7) 34 (64.2) 24 (45.3) 35 (66.0) therapy with other LLA All patients 89.6 (10-212) 196 (69.5) 171 (60.0) 161 (56.5) 176 (61.8)

 $^a$ LDL = low-density lipoprotein cholesterol.  $^b$ One-way analysis of variance, P = .013.  $^o$ Chi square, P = .004.  $^d$ 282 patients had this lipid level recorded; n = 55 for no lipid lowering therapy, n = 158 for statin monotherapy, n = 17 for other LLA monotherapy, and n = 52 for statin combination therapy with other LLA.  $^o$ 285 patients had this lipid level recorded; n = 56 for no lipid lowering therapy, n = 159 for statin monotherapy, n = 17 for other LLA monotherapy, and n = 53 for statin combination therapy with other LLA.  $^o$ 1HDL = high-density lipoprotein cholesterol.  $^o$ 1LLA = lipid lowering agent.

Sixty-two (20.7%) of the 299 study patients were not prescribed any lipid lowering therapy, 166 (55.5%) were prescribed statin monotherapy, 17 (5.7%) were prescribed monotherapy with another lipid lowering agent, and 54 (18.1%) were prescribed a statin in combination with another agent. Of the 237 patients being treated with a lipid lowering agent, 73.6% were prescribed a statin, either alone or in combination with another lipid lowering agent.

Patients prescribed statins, either as monotherapy or in combination, were significantly more likely to achieve their LDL goals (P = .004) and had a significantly lower mean LDL level (P = .013) compared with patients taking other lipid lowering medications (Table 2). Patients prescribed statins were also more likely to achieve the triglyceride goal of less than 150 mg/dL and the non-HDL goal of less than 130 mg/dL, although this finding was not statistically significant.

For the 166 patients taking statins as monotherapy, 120 (72%) were tak-

ing simvastatin and 46 (28%) were taking a high potency agent (either atorvastatin or rosuvastatin) (Figure 4). In comparison, 54 patients (37%) prescribed a statin in combination therapy were taking the higher potency agents.

Almost all (99.5%) of the patients who were taking statins were taking them at doses providing greater than or equal to a 30% reduction in LDL. And 19% of those patients who were taking statins were taking them at doses providing greater than or equal to a 50% reduction in LDL. The mean doses for all of the statins increased slightly with combination therapy, with the exception of simvastatin (Figure 5). Fifty-five percent of atorvastatin and 92% of rosuvastatin usage was at the higher dosages (which provide the most aggressive LDL reductions of greater than or equal to 50%).

Among combination therapy patients, statins were most commonly used with fibrates (46.3%), ezetimibe (46.3%), and niacin (25.9%). The use of combination therapy was slightly higher in the patients treated by the

pharmacist-managed lipid clinic compared with patients treated by their primary care providers (21.1% versus 17.9%, respectively).

#### HbA<sub>1c</sub>

Almost all (296, or 99%) of the 299 study patients had at least one HbA<sub>1c</sub> measurement completed within the most recent 12-month period. This percentage was higher than the 2007 national HEDIS benchmarks.<sup>4</sup>

The mean number of diabetes medications used by the 299 patients overall was 1.8 (range, 0 to 4). The majority of patients were taking either one (39%) or two (41%) diabetes medications. Patients with HbA<sub>1c</sub> values below 7% were taking a mean of 1.7 diabetes medications (range, 0 to 4). Patients with an HbA<sub>1c</sub> value of 7% or greater were taking a mean of 2.2 diabetes medications (range, 1 to 4).

The most common medication regimens were metformin monotherapy (30%), metformin in combination with a sulfonylurea (14%), and metformin in combination with

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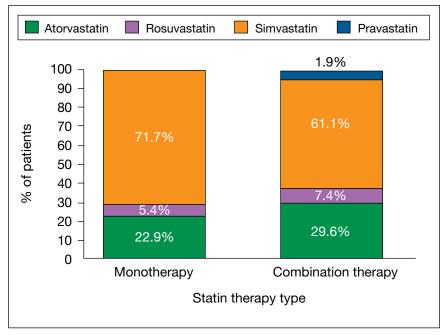


Figure 4. Distribution of statin medication types prescribed as monotherapy and in combination to the study patients.

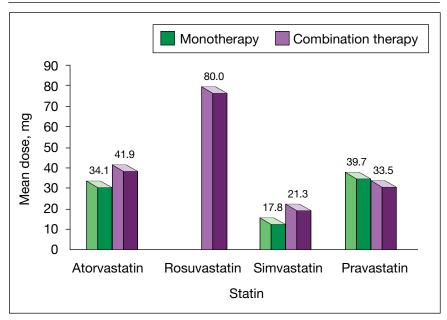


Figure 5. Distribution of statin medication mean doses (in mg) prescribed as monotherapy and in combination to the study patients.

a thiazolidinedione (13%) (Table 3). Twenty-five percent of patients were taking insulin, either as monotherapy or in combination with other agents.

#### **Nephropathy**

The majority (86.6%) of the patients had a microalbuminuria assessment and almost all (97.3%) had a serum

creatinine level documented in their medical record within the past 12 months. More people in the study group had a microalbuminuria assessment in the past year than patients enrolled in commercial health care organizations, according to the 2007 national HEDIS benchmarks.<sup>4</sup>

About 83% of the study patients were taking either an ACE inhibitor or an ARB. There were 52 patients who were not taking either medication. Of these, 32 (61.5%) had documented microalbuminuria, hypertension, or both.

#### **Antiplatelet therapy**

More than half (170, or 56.9%) of the study patients were taking either aspirin, another antiplatelet agent, warfarin, or a combination of the three agents. The majority within this group (133, or 78.2%) were taking aspirin only. Of the 61 patients with CHD in the study group, 42 (68.9%) were taking aspirin, another antiplatelet agent, or warfarin. Of the 238 patients without CHD, 55.3% of those over 40 years of age and 28.6% of those between the ages of 30 and 40 years were prescribed antiplatelet or anticoagulation therapy.

#### **Smoking cessation counseling**

Current smokers comprised 8.4% of the study group. Of these 25 patients, 11 (44%) had documentation of smoking cessation counseling. This rate is lower than the average 82% of patients of DPRP applicants from 1997 to 2003 who received smoking cessation counseling.<sup>8</sup>

## CV and other diabetes complications

Four percent of the study group already had a CV event in the past and 9% had a history of a CV event, heart disease, angina, or heart failure (Table 4). Overall, 20.4% of the study group

Table 3. Study patients' utilization patterns of diabetes medications (n=299)				
Agents used	Patients, no. (%) <sup>a</sup>			
Metformin	89 (29.8)			
Sulfonylurea + metformin	41 (13.7)			
TZDb + metformin	39 (13.0)			
Sulfonylurea + metformin + TZD	24 (8.0)			
Insulin + metformin	22 (7.4)			
Insulin + metformin + TZD	15 (5.0)			
TZD	14 (4.7)			
Insulin + TZD	13 (4.3)			
Insulin + sulfonylurea + metformin + TZD	10 (3.3)			
Sulfonylurea	9 (3.0)			
Insulin + sulfonylurea + metformin	6 (2.0)			
Insulin	5 (1.7)			
Sulfonylurea + TZD	4 (1.3)			
Insulin + sulfonylurea	2 (0.7)			
Insulin + sulfonylurea + TZD	2 (0.7)			
Sulfonylurea + AGI°	1 (0.3)			
Insulin + AGI + TZD	1 (0.3)			
Sulfonylurea + AGI + metformin + TZD	1 (0.3)			
AGI	0 (0)			
Meglitinide	0 (0)			
<sup>a</sup> One patient did not use any diabetes medications. <sup>b</sup> TZD = thiazolidinedione. <sup>c</sup> AGI = alpha-glucosidase inhibitor.				

already had some form of CV disease in their medical history.

The most common diabetes complication present in the study group was microalbuminuria, with 110 patients (37%) with documented microalbuminuria and one patient (0.3%) receiving dialysis. Overall, 11.4% of the study group already exhibited a severe diabetes complication, such as retinopathy, dialysis, amputation, peripheral neuropathy, or erectile dysfunction.

The mean number of CV and diabetes complications was 0.76 per patient (range, 0 to 5), with 46.2% of the study group having no complications present at the time of data col-

lection, 38.5% having one present, 10.7% having two present, 3% having three present, and 1.6% having four or more present.

#### **DISCUSSION**

Multiple drug therapy (two or more agents at proper doses) is generally required to achieve BP targets in patients with diabetes. This was the case with this study population, whose mean number of BP medications was two. The fact that the mean number of medications was slightly lower in patients who were at BP goal compared to those with elevated BP values could indicate that the latter patients either have more difficult to

control BP that requires additional add-on therapy or are not adherent to their current therapeutic regimen.

Forty-four percent of the patients who were not taking any lipid lowering therapy had LDL levels greater than 100 mg/dL and, therefore, required treatment that they were not receiving at the time of our analysis. In the 79 patients who were not treated with a statin, 74 (93.7%) would qualify for statin therapy based on the ADA recommendations, mainly due to age over 40 years (73.4%) and presence of overt CHD (17.7%). Most patients who were taking a statin were prescribed simvastatin-which is attributable to simvastatin's preferred status on the MTF's formulary. It appears that before going to maximal doses of any of the statins, the MTF providers were more likely to prescribe another agent as add-on therapy. Patients may have been switched to a higher potency statin in order to reach LDL targets.

The mean number of diabetes medications used by the study patients was 1.8. As the number of diabetes medications increased, the mean HbA<sub>1c</sub> level also increased slightly, thus indicating the possibility of more difficult to control diabetes or less adherence to the medicines.

Nearly 87% of the patients had a documented microalbuminuria assessment. Of those assessed, 37% had microalbuminuria, warranting aggressive monitoring and treatment. About 17% of the study patients were not taking either an ACE inhibitor or an ARB and 65% of them had either microalbuminuria or uncontrolled BP and would benefit from these agents.

A large proportion of the study patients were nonsmokers according to chart records of self-reported smoking history. Even so, our findings suggest the MTF needs to make improvements in smoking cessation

Table 4. Presence of CV <sup>a</sup> disease and other
diabetes complications in the study population

Complication	Patients, no. (%)			
CV disease				
CV event <sup>b</sup>	13 (4.3)			
Heart disease/angina	15 (5.0)			
Heart failure	8 (2.7)			
Other CV disease equivalent <sup>c</sup>	44 (14.7)			
Any CV complication	61 (20.4)			
Other diabetes complications				
Microalbuminuria	110 (36.8)			
Macroalbuminuria	0 (0.0)			
Dialysis	1 (0.3)			
Retinopathy	1 (0.3)			
Peripheral neuropathy	16 (5.4)			
Foot ulcer	2 (0.7)			
Amputation	1 (0.3)			
Erectile dysfunction	16 (5.4)			
Any severe diabetes complication	34 (11.4)			
<sup>a</sup> CV = cardiovascular <sup>b</sup> Acute myocardial infarction, acute coronary syndrome, coronary artery				

<sup>a</sup>CV = cardiovascular. <sup>b</sup>Acute myocardial infarction, acute coronary syndrome, coronary artery bypass graft, or percutaneous coronary intervention. <sup>c</sup>Peripheral arterial disease, cerebrovascular accident, coronary artery disease, or abdominal aortic aneurysm.

counseling for patients with diabetes who currently smoke and to increase the use of antiplatelet therapy and statins in high risk patients in order to further reduce CV risk.

### What do we take away from this?

The risk of CHD in patients with diabetes is fourfold that of patients without diabetes. CHD is the major source of mortality for patients with diabetes, and multiple risk factor interventions—treatment for hypertension and dyslipidemia, antiplatelet therapy, and smoking cessation—are indicated to reduce excess macrovascular events. Overall, we found that the patients managed by the MTF were receiving the appropriate risk factor interventions. Yet, diabetes complications still plagued this population,

with 20% of the patients having existing CV disease and 11% having other existing diabetes complications. The results of our study therefore show that many patients with diabetes treated in the outpatient setting have existing complications, and aggressive management is warranted to prevent further progression.

#### Author disclosures

Dr. ter Riet reports being an employee of Pfizer Inc. Dr. Emanuel, Dr. Jones, Ms. Andrews, Ms. Powell, and Ms. Williams report no actual or potential conflicts of interest with regard to this article.

#### Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of Federal Practitioner, Quadrant HealthCom Inc., the U.S.

government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.

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