Has Control of Hypercholesterolemia and Hypertension in Type 1 Diabetes Improved Over Time?

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OBJECTIVE — To determine the extent to which patients' awareness, treatment, and control of hypertension and hypercholesterolemia have changed over time and to examine factors associated with awareness and treatment in a type 1 diabetes population.

RESEARCH DESIGN AND METHODS — Data from six examinations conducted over 10 years from the Pittsburgh Epidemiology of Diabetes Complications Study, a prospective study of subjects with childhood-onset (<17 years of age) type 1 diabetes diagnosed between 1950 and 1980 and followed since 1986, were analyzed. Hypertension and hypercholesterolemia were defined according to the concurrent Joint National Committee and National Cholesterol Education Program Adult Treatment Panel criteria, respectively.

RESULTS — Results demonstrated that awareness of both conditions has improved; however, control is not optimal (e.g., only 32.1 and 28% of those with hypertension in 1986–1988 and 1996–1998 were controlled, while for hypercholesterolemia, the rates were 0 and 5.5%, respectively). Stratified by age-group (18–29, 30–39, and >40 years), the youngest subjects with hypercholesterolemia were least likely to be treated and controlled to goal levels. Older age and physician contact were correlates of awareness and treatment of hypertension at baseline, while presence of renal or coronary complications was also associated with awareness and treatment of both hypertension and hypercholesterolemia at the 10-year follow-up.

CONCLUSIONS — There is a considerable treatment gap, particularly for hypercholesterolemia. Improved treatment of both hypertension and hypercholesterolemia are clearly needed, particularly hypercholesterolemia in younger age-groups who have not yet experienced long-term complications.

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Hypertension and hypercholesterolemia are important risk factors for the development of micro- and macrovascular complications in people with diabetes. Studies examining cardiovascular events among people with type 2 diabetes demonstrate that controlling these risk factors can directly impact the occurrence of both new (1) and repeat (2) events. Additionally, data suggest that people with type 1 diabetes and renal disease may experience remission or regression of their renal disease with aggressive antihypertensive treatment (3).

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Abbreviations: CAD, coronary artery disease; DSP, distal symmetric polyneuropathy; EDC, Pittsburgh Epidemiology of Diabetes Complications Study; LEAD, lower-extremity arterial disease; ON, overt nephropathy; PR, proliferative retinopathy.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

While primary and secondary prevention of complications should be paramount, reports of suboptimal levels of treatment and control of these risk factors are abundant in the literature. The proportion of hypertensive individuals treated and controlled in the general population range from 10 to 41% (4,5), while for people with diabetes, rates range from 11 to 23% (6–9). For hypercholesterolemia, reports indicate that 18–37% of those treated and at high risk for an event in the general population are controlled (10), while 16–35% of those with diabetes are controlled (8,9). Reasons for inadequate control are often centered on lack of access to health care, yet 90% of people with diabetes have access to a health care provider and have health insurance (8), demonstrating a "missed opportunity" for preventive care.

Over the past two decades, effective treatment options and more aggressive treatment guidelines have been introduced; however, little is known about the impact of these efforts on the level of treatment and control of hypertension and hypercholesterolemia, particularly in type 1 diabetes. It was our objective to determine the extent to which patients' awareness, treatment, and control of hypertension and hypercholesterolemia has changed over time and to examine factors associated with awareness and treatment in a type 1 diabetes population.

RESEARCH DESIGN AND METHODS

— The Pittsburgh Epidemiology of Diabetes Complications Study (EDC) is an observational prospective cohort study of type 1 diabetic subjects that has been previously described (11). Briefly, study participants were diagnosed between 1950 and 1980 and seen within 1 year of diagnosis at Children's Hospital of Pittsburgh. Although this population is clinic based, it has been shown to be epidemiologically representative of the type 1 diabetes population of Allegheny County, Pennsylvania (12). A total of 658 subjects participated in the baseline exam (1986–1988). While attendance at Chil-

Table 1—*Definitions for hypertension and hypercholesterolemia during the 10-year follow-up period in the EDC*

	Exams 1–4 (1986–1993)	Exams 5 and 6 (1994–1998)
Hypertension		
Case definition	>140/90 mmHg or treatment with antihypertensive medication*	130/85 mmHg or treatment with antihypertensive medication*
Goal for treatment	<140/90 mmHg	<130/85 mmHg
Hypercholesterolemia		
Case definition	Above LDL cholesterol goal or treatment with anihyperlipidemic medication†	
Goal for treatment		
	• LDL cholesterol <160 mg/dl if less than two risk factors‡	• <160 mg/dl if less than two risk factors§
	• Initiate medication therapy if >190 mg/dl	• Initiate medication therapy if >190 mg/dl
	or	**or**
	• LDL cholesterol <130 mg/dl if CAD or two or more risk factors‡	• <130 mg if two or more risk factors
	• Initiate medication therapy if >160 mg/dl	• Initiate medication therapy if >160 mg/dl
		or
		• <100 mg /dl if CAD
		• Initiate medication therapy if >130 mg/dl

*Antihypertensive medications include ACE inhibitors, β-blockers, calcium channel blockers, diuretics, and other antihypertensives. Subjects also had to indicate that the reason for taking the medication was hypertension. If the reason was not hypertension, subjects were not considered to be taking an antihypertensive medication. If no reason was listed, the presumption was antihypertensive use. †Lipid-lowering medications include HMG-COA reductase inhibitors, fish oil (more than six capsules per day), bile acid resins, probucol, and niacin ≥750 mg/day. ‡Male sex, smoker, hypertension, family history of premature coronary heart disease, HDL cholesterol <35 mg/dl, diabetes, cerebrovascular or peripheral vascular disease, and BMI >45 kg/m^2. §Male age >45 years, female age >55 or postmenopausal without hormone replacement therapy, family history of premature coronary heart disease, smoker, hypertension, HDL cholesterol <35 mg/dl, and diabetes.

dren's Hospital was one of the eligibility criteria, the EDC participants subsequently received their diabetes care in the general community, with ~50% receiving care from diabetes specialists (13). The present cross-sectional analyses represent data available for adults (age >18 years) followed for the first 10 years (six examination periods) of the EDC.

Primary outcomes

Blood pressure was measured with a random zero sphygmomanometer, according to the Hypertension Detection and Follow-up Program protocol (14). Case definition of hypertension and level of control were defined for the time period studied according to the concurrent Joint National Committee (15,16) recommendations as outlined in Table 1.

HDL cholesterol was determined by a precipitation technique (heparin and manganese chloride) with a modification (17) of the Lipid Research Clinics method (18). Cholesterol and triglycerides were measured enzymatically (19,20). LDL cholesterol levels were calculated from measurements of the levels of total cholesterol, triglycerides, and HDL cholesterol using the Friedewald equation (21). Hypercholesterolemia and level of control were defined for the time period studied according to the concurrent National Cholesterol Education Program Adult Treatment Panel (22,23), as outlined in Table 1.

Patient awareness of hypertension was defined by a positive response to the question "has a physician ever told you that you had high blood pressure?" Patient awareness of hypercholesterolemia was defined by a positive response to the question "has a physician ever told you that you had high cholesterol/triglycerides?"

Data collection and variable definitions

Before their scheduled clinic visit, participants were sent questionnaires to document demographic, health care, self-care, lifestyle characteristics, and medical history information. Complication status was determined using a standardized protocol throughout the study period and defined as follows: Proliferative retinopathy (PR) was determined by stereo fundus photography (classified by the Arlie House System) (24) or a history of laser therapy for proliferative disease. Overt nephropathy (ON) was defined as an albumin excretion rate >200 μg/min on two of three timed urine samples or, in the absence of urine, serum creatinine >2 mg/dl, renal failure, or transplant. Distal symmetric polyneuropathy (DSP) was considered present if on examination, according to the Diabetes Control and Complications Trial protocol (25), the participant had at least two of the following: symptoms consistent with DSP, decreased or absent deep tendon reflexes, and signs of sensory loss. At the 4-year follow-up exam and thereafter (i.e., for 101 of 108 incident subjects), DSP was confirmed (CDSP) by the presence of a vibratory threshold above the age-specific normal range using the Vibratron II tester (Physitemp instruments, Clifton, NJ). Coronary artery disease (CAD) was determined by EDC physician-diagnosed angina or myocardial infarction, confirmed by Q waves on electrocardiogram or hospital records (Minnesota codes 1.1 or 1.2), or by angiographic stenosis >50%, coronary artery bypass surgery, angioplasty, or ischemic electrocardiogram (non–Q wave) (Minnesota codes 1.3, 4.1, 4.2, 5.1, 5.2, and 7.1). Lower-extremity arterial disease (LEAD) was determined

Table 2—*Characteristics of the study population (EDC) aged ≥18 years at baseline (1986–1988) and exam 6 (1996–1998)*

	Baseline	Exam 6
n	592	402
Age (years)	29.1 ± 6.8	37.4 ± 8.0
Duration (years)	20.4 ± 7.1	29.1 ± 7.6
Sex (% male)	49.2 (291)	50.6 (206)
Income (% >$20,000)	81.6 (386)	79.6 (300)
Education (% more than high school)	63.2 (354)	69.4 (121)
Saw physician in previous year (% yes)	82.1 (449)	91.6 (340)
Health insurance (% yes)	92.5 (371)	94.2 (376)
Hypertension (% positive)*	18.8 (106)	35.3 (140)
Age 18–29 years	10.3 (32)	13.4 (10)
Age 30–39 years	28.4 (59)	32.4 (57)
Age >40 years	34.1 (59)	49.3 (73)
Mean systolic blood pressure (mmHg)	114.9 ± 16.2	118.1 ± 18.2
Mean diastolic blood pressure (mmHg)	73.7 ± 11.0	70.7 ± 10.9
Hypercholesterolemia (% positive)*	26.3 (135)	39.8 (142)
Age 18–29 years	17.3 (51)	29.2 (19)
Age 30–39 years	37.1 (69)	32.7 (52)
Age >40 years	36.6 (15)	53.4 (71)
Mean LDL cholesterol (mg/dl)	118.3 ± 35.1	117.6 ± 32.2
Complications (% positive)		
CAD	8.3 (49)	22.1 (90)
LEAD	8.0 (47)	14.4 (57)
PR	34.8 (203)	51.0 (204)
ON	28.7 (170)	23.3 (95)
DSP	31.4 (185)	36.4 (146)

Data are percent (*n*) or means ± SD. *See Table 1 for definitions.

by history of amputation, or claudication, or ankle brachial index <0.9 at rest.

Statistical analyses

Prevalence, level of awareness, treatment, and control of hypertension and hypercholesterolemia were evaluated for each of the six examination periods, overall and by specific age strata (18–29, 30–39, and >40 years). All univariate comparisons were conducted using the Student's *t* test or χ^2 test for proportions.

RESULTS

Demographic data

Demographic and clinical characteristics of the population from the baseline and sixth exams are presented in Table 2. The mean age and diabetes duration at baseline were 29.1 and 20.4 years, respectively. The prevalence of both hypertension and hypercholesterolemia (defined by concurrent national criteria for the exam period) increased from exam 1 to exam 6, overall and within each age-group with the exception of hypercholesterolemia in the 30- to 39-year age-group. As noted in Table 2, mean diastolic blood pressure and LDL cholesterol were also lower at exam 6 than at baseline. Applying baseline criteria to exam 6, the prevalence of hypercholesterolemia remained unchanged; however, the prevalence of hypertension was lower (28.5%). Furthermore, because the prevalence of risk factors was determined at one time point, we examined the proportion of subjects with hypertension and hypercholesterolemia for two consecutive exams. When exams 1 and 2 were combined, 15.7% had hypertension and 22.5% had hypercholesterolemia. We also repeated the analyses for exams 5 and 6 combined and found 19.4% had hypertension and 22.2% had hypercholesterolemia.

Figure 1*A* and *B* describe the level of awareness, treatment, and control of hypertension and hypercholesterolemia in prevalent cases during exams 1–6 using concurrent definitions (Table 1). We do not present the proportion of patients by cut point or using mean values as these do not consider treatment.

Hypertension

Over time, improvements in awareness and control were observed during exams 3 and 4, but control and awareness worsened during the 5th and 6th exam periods. Control was best at 48% in exam 3 but worsened to 28% at exam 6. As results may differ by age-group, results for exams 1 and 6 were repeated and stratified by age-groups (18–29, 30–39, and >40 years). The proportion of patients unaware of their hypertension increased between exams 1 and 6 in all age-groups and increased the most in the oldest age-group (6.7 to 21.5%, $P = 0.10$). The proportion untreated decreased in the 18–29 and 30–39 age-group but increased in those >40 years of age although not significantly. The proportion controlled was relatively stable in 18–29 year olds (15.6–20.0%, $P = 0.87$) and 30–39 year olds (37.3 to 35.1%, $P = 0.96$) but decreased in those >40 years of age (46.7 to 23.3%, $P = 0.13$).

Hypercholesterolemia

Figure 1*B* represents the level of awareness, treatment, and control of hypercholesterolemia. Patient awareness of hypercholesterolemia increased between exams 1 and 6 as did the proportion of patients untreated. No patients had their LDL cholesterol levels controlled to goal levels during the first two exam periods, and only 1–5.6% had achieved control during exams 3 and 6, respectively. When stratified by age, the proportion of subjects unaware of their hypercholesterolemia decreased in all age-groups from exam 1 to exam 6: 80.4 to 68.4%, $P = 0.45$ (18–29 years of age); 87.0 to 63.5%, $P = 0.005$ (30–39 years of age); and 93.3 to 57.7%, $P = 0.02$ (>40 years of age). However, the proportion untreated increased across all age-groups, although differences were not statistically significant. The proportion treated and controlled increased for the older two groups: 0–7.7% ($P = 0.03$) and 0–5.6% ($P = 0.79$) for ages 30–39 and >40 years, respectively, while no one in the youngest group was treated and controlled at either exam period.

Correlates of awareness and treatment

To determine the correlates of awareness and treatment of hypertension and hypercholesterolemia, analyses were performed for baseline and exam 6 data. At baseline,

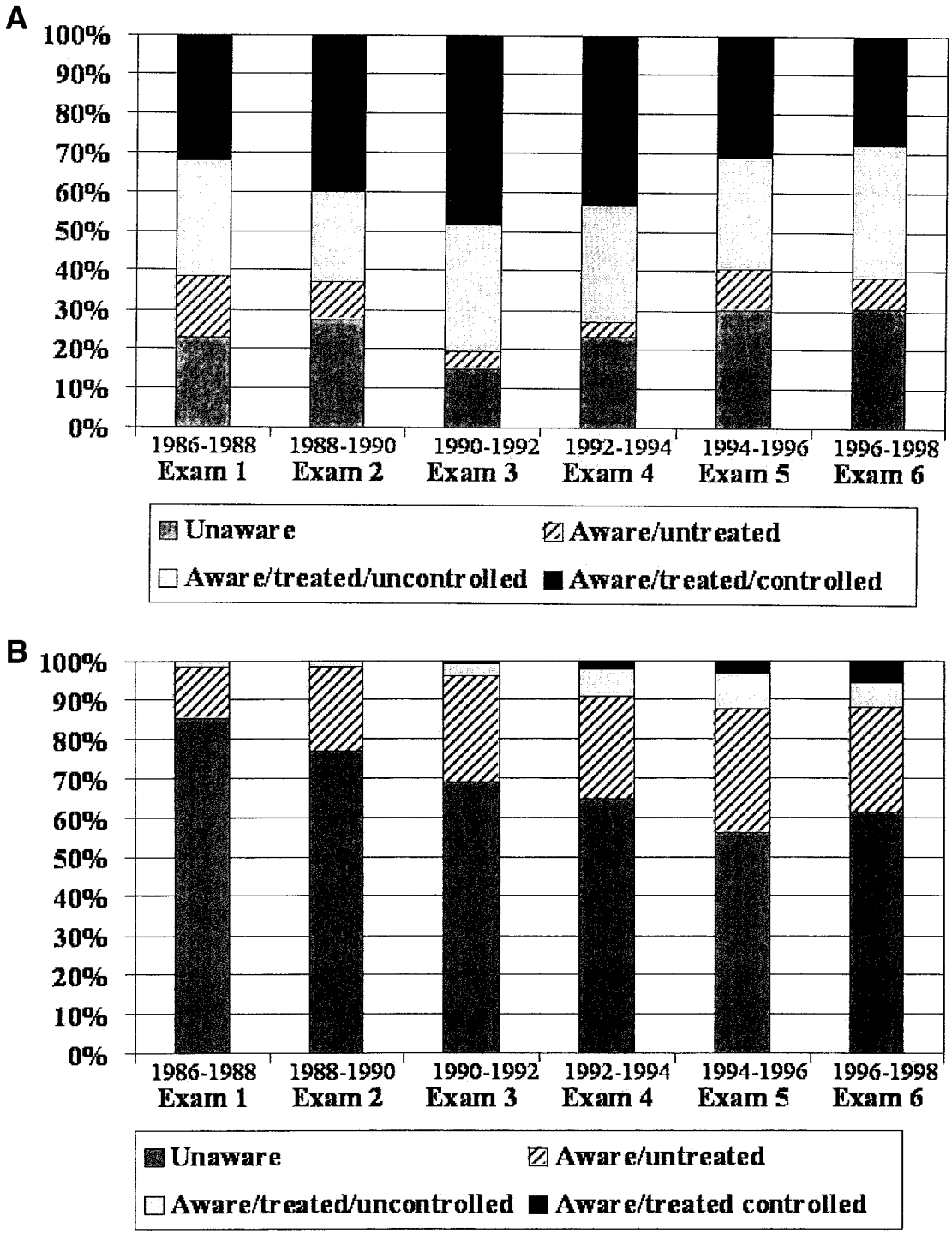

Figure 1—A: *Level of awareness, treatment, and control of hypertension: EDC 10-year follow-up.* B: *Level of awareness, treatment, and control of hypercholesterolemia; EDC 10-year follow-up.*

older age (33.9 vs. 30.4 years, $P < 0.01$) and seeing a physician in the previous year (96.3 vs. 68.2%, $P < 0.001$) were significantly associated with both awareness and treatment of hypertension (age 34.2 vs. 31.5 years, $P < 0.05$; physician contact 96.9 vs. 79.0%, $P < 0.01$). At exam 6, only the presence of ON or CAD was significantly associated with awareness (66.0 vs. 44.2%, $P < 0.05$).

For hypercholesterolemia, there were no significant associations with awareness at the baseline exam. Only two subjects were treated at baseline; thus, analyses were not conducted. At exam 6, the presence of ON or CAD were associated with awareness (72.7 vs. 49.4%, $P < 0.01$) and treatment (82.4 vs. 55.2%, $P < 0.05$), as were other complications (PR, CDSP, and LEAD) (88.9 vs. 73.8%, $P < 0.05$; 100.0 vs. 76.9%, $P < 0.05$, respectively).

CONCLUSIONS — In a representative cohort of people with type 1 diabetes receiving diabetes care in the general community of health care providers, we found an extremely low level of control of two major complication risk factors, with little improvement observed over a 10-year follow-up period. Only 27.8% of hypertensive individuals and 5.6% of those with hypercholesterolemia reached goal levels at the last exam period (1996–1998), demonstrating a considerable deficiency in complication risk factor management.

Results indicated that awareness, treatment, and control of hypertension were best at exam 3 and worsened progressively thereafter, perhaps due to the stricter treatment goals introduced in the fifth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (16), for exams 5 and 6. When we stratified our results according to age-group, the youngest group (18–29 years) had the poorest treatment and control rates at both exams 1 and 6. The prevalence of hypercholesterolemia increased over time as expected and could not be explained by the more conservative definition of hypercholesterolemia used in exams 5 and 6, as results did not change when the less aggressive criteria were applied (22). Awareness improved during the follow-up period between exams 1 and 6 in all age-groups; however, the proportion aware but untreated increased across all categories. Disturbingly, no one in the youngest groups was treated and controlled during either exam period. While awareness of these risk factors is increasing, there has been little improvement in treatment or control, particularly in younger age-groups. These results likely reflect the lack of clear guidelines for the treatment of dyslipidemia in young adults with type 1 diabetes, as the National Cholesterol Education Program and American Diabetes Association guidelines are primarily for type 2 diabetes. Because of this, we have previously advocated vigorous intervention for hypertension and hyperlipidemia for type 1 diabetes based on our epidemiological risk observations (26).

In our study, rates of treatment and control of hypertension were somewhat higher compared with those reported in the literature (6). In the EuroDiab study (a prospective cohort study of people with type 1 diabetes from 16 countries in Europe), rates of treatment and control were 42.2 and 11.3%, respectively. Our treatment and control rates for the same time period were 63 and 40%, respectively. Several factors may account for these differences. The EuroDiab study used a different definition for the concurrent time period for control of hypertension of 130/85 mmHg, which is more conservative, thus resulting in lower rates of control. Additionally, the EDC population had a longer duration of diabetes and, thus, may have experienced more complications, which could lead to higher treatment rates as both patients and health care providers were more aware of their health status. Additionally, subjects in the EDC and EuroDiab studies are treated under different health systems, which could influence results. Other studies of hypertension control also report lower rates; however, these studies were conducted on subjects with type 2 diabetes, or the type of diabetes was not specified, making comparisons difficult (8,9).

For hypercholesterolemia, there appears to be little data available on treatment and control in type 1 diabetes. Again, available studies do not specify type of diabetes or that the study population is exclusively type 2 diabetes (8). Our data suggest that the abysmal rates of control are likely due to the younger age of this population, despite their longer duration of diabetes, compared with those with type 2 diabetes. The impression by health care providers and patients alike may be that because of their younger age, they may not be a high-risk group for the development complications, particularly cardiovascular disease.

Our data demonstrate that older age and the presence of any complications are correlates of awareness of hypercholesterolemia and that the presence of ON or CAD was associated with awareness of hypertension at exam 6. For hypercholesterolemia treatment, older age and complications are correlates of treatment. This may demonstrate a health system focus on secondary rather than primary prevention of diabetes complications. In the present analyses, those with complications were more likely to be aware of their risk factors, which supports the findings of Stafford et al. (27), who showed that comorbid conditions were associated with higher screening rates for hypercholesterolemia. Health insurance is often considered the gateway to adequate health care; however, we found no association between having health insurance and hypertension control, similar to the findings of Hyman et al. (5). These data demonstrate that both system and patient factors need appropriate attention in order to improve awareness, treatment, and control of hypertension and hypercholesterolemia (27). Our results also showed that having a physician visit in the previous year was a significant correlate of hypertension awareness and treatment at the baseline exam. Despite a large proportion of subjects having regular health care (at least one visit per year), control remained suboptimal throughout (5), which may represent a breakdown in communication between provider and patient. Previous studies assessing type of health care provider accessed by EDC participants indicated that at exam 6, ~50% of the cohort reported receiving care from a diabetes specialist (13,28); thus, it is unlikely that type of provider played a significant role in the results.

Limitations

We defined both hypertension and hypercholesterolemia according to the guidelines applicable at each exam period, which became more conservative over the study period. As this could significantly bias our results, these changes were taken into account for both case definition and level of control. To examine the effect of this change in criteria, data were analyzed further, applying the definition used for exam 1 to the data from exam 6, and we found no difference in the prevalence of awareness, treatment, and control of hypercholesterolemia. However, we did find a lower prevalence of hypertension, which was accompanied by higher levels of awareness, treatment, and control. Another limitation was that both blood pressure and lipids were measured at a single point in time for each exam and cannot be considered diagnostic; thus, subjects may have been misclassified. We investigated this potential bias and found that the prevalence of hypertension and hyercholesterolemia at two consecutive time points was indeed lower. However, exam periods were 2 years apart, and it is possible that those who did not have the risk factor at one exam may have developed it at the subsequent exam. Blood pressures were measured using a random zero sphygmomanometer, which may underrecord blood pressure, particularly systolic. There-

fore, the prevalence of hypertension may be underestimated while proportion controlled may be overestimated.

In conclusion, increased efforts for intensifying treatment of hypertension and hypercholesterolemia need to be implemented. More emphasis should be placed on coordinating care for people with diabetes, as multiple providers are likely involved in their care, and risk factors beyond glycemic control may be neglected. As treatment goals for blood pressure of 130/80 mmHg (29) and for LDL cholesterol of 100 mg/dl continue to get more conservative (29,30), intensive efforts aimed an increasing both patient and provider awareness of these goals need to be put into practice to have the greatest impact on prevention of diabetes complications.

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