

# Hypertension Prevalence, Awareness, Treatment, and Control in an Adult Type 1 Diabetes Population and a Comparable General Population

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**OBJECTIVE** — To compare the prevalence, awareness, treatment, and control of hypertension in a population-representative sample of adults with type 1 diabetes and comparable nondiabetic control subjects.

**RESEARCH DESIGN AND METHODS** — In 2000–2002, the Coronary Artery Calcification in Type 1 Diabetes Study enrolled 1,416 individuals aged 19–56 years with no known history of coronary artery disease: 652 type 1 diabetic patients (46% male, mean age 37 years) and 764 nondiabetic control subjects (50% male, mean age 39 years). Subjects were asked if they had been told by a physician that they had hypertension or were on a blood pressure medication. Blood pressure was measured using standardized Joint National Committee (JNC) protocol.

**RESULTS** — Type 1 diabetic subjects, compared with nondiabetic subjects, had higher rates of hypertension prevalence (43 vs. 15%,  $P < 0.001$ ), awareness (53 vs. 45%,  $P = 0.11$ ), treatment (87 vs. 47%,  $P < 0.001$ ), and control (55 vs. 32%,  $P < 0.001$ ) for the JNC 6 goal (130/85 mmHg). Only 42% of all type 1 diabetic hypertensive subjects met the new JNC 7 goal (130/80 mmHg). Type 1 diabetic subjects had better blood pressure control (72 vs. 32%,  $P < 0.0001$ ), using 140/90 mmHg as a common measure. The majority of treated subjects were on a single antihypertensive agent (75 vs. 64%).

**CONCLUSIONS** — Subjects with type 1 diabetes have higher rates of hypertension prevalence, treatment, and control than nondiabetic subjects. However, hypertension remains largely uncontrolled, even if treated in high-risk populations, such as type 1 diabetic subjects and undiagnosed individuals in the general population. Achieving more stringent blood pressure goals will require increased attention and may necessitate the use of multiple antihypertensive agents.

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**Abbreviations:** ADA, American Diabetes Association; CACTI, Coronary Artery Calcification in Type 1 Diabetes; JNC, Joint National Committee; NHANES, National Health and Nutrition Examination Survey.

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

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Numerous advances in care have led to improved health and longer survival in patients with type 1 diabetes. Hypertension has been estimated to affect ~30% of type 1 diabetic patients and usually reflects the development of diabetic nephropathy (1). Effective control of blood pressure is a well-established target to decrease morbidity and mortality in patients with type 1 diabetes and nondiabetic individuals as well (1,2).

In type 1 diabetes, hypertension is related to an increased risk of microvascular complications, such as retinopathy (3–5), and is a modifiable risk factor in the progression of nephropathy (6) as well as in the development of the macrovascular complications of cardiovascular disease (7,8). The risk of cardiovascular disease doubles with each increase of 20/10 mm/Hg beginning at 115/75 mm/Hg (2). It has been estimated that 35–75% of diabetes complications are due to hypertension (9). Recently revised guidelines have been published by both the American Diabetes Association (ADA) (1) and the Joint National Committee (JNC) 7 (2) regarding goals for blood pressure treatment.

Reports on prevalence, awareness, treatment, and control of hypertension exist for the general population (10,11) and the type 2 diabetic population (12–16), whereas data for patients with type 1 diabetes are limited, consisting of two EURODIAB reports (17,18) and one abstract from Pittsburgh (19). In the published reports on hypertension in type 1 diabetes, control groups are not included. Unique aspects of this report are the comparison between type 1 diabetic and nondiabetic subjects and a more detailed description of a U.S. population. The purpose of this study is to evaluate the prevalence, awareness, treatment, and control of hypertension in subjects with type 1 diabetes and nondiabetic control subjects from cross-sectional baseline data in the Coronary Artery Calcification in Type 1 Diabetes (CACTI) study.

## RESEARCH DESIGN AND METHODS

The data presented in this report were collected as part of the baseline examination of 1,420 participants in the CACTI study. One hundred nine participants in this baseline cohort participated in the pilot study, which had slightly different inclusion criteria (20). A total of 4 of the 1,420 subjects were excluded from our analysis, including 1 subject who had a fasting blood glucose >140 mg/dl (173 mg/dl) and was subsequently diagnosed with type 2 diabetes, 2 pilot participants who were aged 58 (nondiabetic) and 59 (type 1 diabetic) years, and a 19 year old who was a sibling of a study participant but had only 4 years' duration of diabetes. Therefore, the 1,416 participants were 19–56 years of age and included 652 men and women with type 1 diabetes and 764 nondiabetic control subjects. All subjects were asymptomatic for coronary artery disease and had no history of coronary artery bypass graft, coronary angioplasty, or unstable angina. Patients with diabetes generally had been diagnosed at <30 years of age. Eighteen subjects aged >30 years were part of the pilot study, were antibody positive, and had a clinical course supporting type 1 diabetes, and all type 1 diabetic subjects had been treated with insulin within 1 year of diagnosis. The mean disease duration was  $23.2 \pm 8.9$  years on enrollment, with 12 subjects with type 1 diabetes duration of 4–9 years (most of whom originally enrolled in the pilot study and were kept in the larger cohort). Type 1 diabetic subjects were recruited from outpatient clinics at the Barbara Davis Center (52%), the Denver area Kaiser Permanente clinics (6%), endocrinology or subspecialty clinics (16%), or other sources (26%). All nondiabetic control subjects had never been diagnosed with diabetes, including gestational diabetes, and were generally spouses, friends, and neighbors of the case subjects. Demographic characteristics of the CACTI control group were similar to that of the general Colorado population based on the 2000 census data (U.S. Census Bureau): men accounted for 50% of both, and non-Hispanic whites for 84.0 vs. 84.8% of the study and the Colorado population aged 18 and over, respectively. All subjects provided informed consent, and the study was approved by the Colorado Combined Institutional Review Board.

## Examination and laboratory measurements

Participants completed the baseline examination between March 2000 and April 2002, and a more detailed description of this cohort has been published (21). Resting systolic blood pressure and fifth-phase diastolic blood pressure were measured three times while the subjects were seated, and the second and the third measurements were averaged. Fat measurements using computed tomography were determined as previously reported (21). Participants completed a standardized questionnaire including medical history and medication inventory as previously reported (21).

## Blood pressure medication

The CACTI database was queried to determine which subjects were on antihypertensive medications. Antihypertension medication use was determined by a medication inventory. (All subjects were asked to bring their medications to the study visit; or, if they failed to do this, the subjects then called from home with their medications.)

## Blood pressure definitions

Guidelines published by the ADA (22), JNC 6 (23), and JNC 7 (2) were used as definitions for hypertension. The diagnostic threshold for hypertension was  $\geq 140/90$  mmHg for both diabetic and nondiabetic patients, with <140/90 mmHg as the goal for nondiabetics. The JNC 6 goal for patients with diabetes is <130/85 mmHg, while the JNC 7 and ADA goal is <130/80 mmHg. Definitions used for prevalence, awareness, treatment, and control are as follows, and results are stratified by diabetes status.

**Prevalence.** Numerator: subjects with blood pressure above JNC or ADA guidelines ( $\geq 140/90$  mmHg) or subjects on antihypertension medication. Denominator: all study subjects. Those defined as hypertensive in the prevalence numerator become the denominator for awareness, treatment, and control.

**Awareness.** Numerator: subjects who answered yes to the question "Have you ever been told by an MD that you are hypertensive?" or subjects who reported that they were on medication for hypertension. Denominator: subjects with hypertension according to JNC or ADA guidelines plus those on antihypertensive

medication (numerator for the definition of prevalence).

**Treatment.** Numerator: subjects on antihypertensive medication. Denominator: subjects with hypertension according to JNC or ADA guidelines plus those on antihypertensive medication (numerator for the definition of prevalence).

**Control.** Numerator: subjects at goal blood pressure according to JNC or ADA guidelines (<130/85 mmHg according to JNC 6 and <130/80 mmHg for JNC 7 and the 2003 ADA Consensus Statement for type 1 diabetic subjects; <140/90 mmHg for nondiabetic subjects). Denominator: 1) subjects with hypertension according to JNC or ADA guidelines plus those on antihypertensive medication (numerator for the definition of prevalence) and 2) all subjects on treatment.

## Statistical analysis

Statistical analysis was performed using SAS version 8.2 software (SAS Institute, Cary, NC). Demographic data were analyzed using two-sided *t* tests for the means and  $\chi^2$  for differences in proportions. Differences between type 1 diabetic and nondiabetic groups in hypertension prevalence, awareness, treatment, and control were analyzed using  $\chi^2$  tests. A *P* value <0.05 was considered significant.

**RESULTS** — The baseline characteristics of subjects are shown in Table 1. Compared with the nondiabetic group, the type 1 diabetic subjects were slightly younger (37 vs. 39 years), were more likely non-Hispanic white (94 vs. 84%), had less visceral fat ( $3.1 \times 10^4$  vs.  $4.1 \times 10^4$  cm<sup>3</sup>), had higher systolic blood pressure (118 vs. 115 mmHg), had more hypertension (43 vs. 15%) and albuminuria (13.6 micro- and 8.1% macroalbuminuria vs. 2.2 and 0.4%), but had lower, though not clinically significant, diastolic blood pressure (78 vs. 79 mmHg).

Using JNC 6 criteria, hypertension prevalence, awareness, treatment, and control are reported in Table 2 stratified by diabetes status. Hypertension prevalence was 43% for type 1 diabetic subjects and 15% for nondiabetic subjects (*P* < 0.0001). Awareness of hypertension was 53% for type 1 diabetic subjects and 45% for nondiabetic subjects (*P* = 0.11). A total of 87% of type 1 diabetic subjects and 47% of nondiabetic subjects (*P* < 0.0001) were on hypertension treatment. Control of hypertension by JNC 6 guidelines, us-

Table 1—Baseline characteristics of the study group

	Type 1 diabetic patients	Nondiabetic patients	P value
n	652	764	—
Sex (% men)	46	50	0.11
Age (years)	37 ± 9	39 ± 9	<0.0001
BMI (kg/m <sup>2</sup> )	26.2 ± 4.4	26.1 ± 5.0	0.64
Ethnicity (% non-Hispanic white)	94	84	<0.0001
Duration of diabetes (years)	23.2 ± 8.9	NA	—
Years of education (622 type 1 diabetic and 735 nondiabetic subjects)	16.0 ± 10.2	16.8 ± 9.9	0.19
Systolic blood pressure (mmHg)	117 ± 14	114 ± 12	<0.0001
Diastolic blood pressure (mmHg)	78 ± 9	79 ± 8	0.003
Hypertension (%)	43	15	<0.0001
Current smoker (%)	10.3	7.9	0.11
Ever a smoker (%)	19.5	22.3	0.20
Albuminuria (micro/overt) (%)	13.6/8.2	2.2/0.4	<0.0001
HbA <sub>1c</sub> (%)	8.0 ± 1.3	5.5 ± 0.5	<0.0001
Fasting blood glucose (mg/dl) [median (interquartile range)]	180 (113–253)	89 (83–96)	—
Glycemic control (HbA <sub>1c</sub> <7.5%) (%)	36	NA	—
Continuous insulin infusion (pump use) (%)	37	NA	—
Insulin dose (units · kg <sup>-1</sup> · day <sup>-1</sup> )	0.61 ± 0.26	NA	—

Data are means ± SD unless otherwise indicated. Values were evaluated with Student's *t* test, and proportions were evaluated with  $\chi^2$ .

ing all subjects with hypertension as the denominator, was 55% for type 1 diabetic subjects and 32% for nondiabetic subjects ( $P < 0.0001$ ). Using only those treated as the denominator, control was 64% for type 1 diabetic subjects and 67% for nondiabetic subjects ( $P = 0.60$ ).

Evaluating these data obtained in 2000–2002 for type 1 diabetic subjects by the subsequent JNC 7/ADA 2003 Position Statement control goals (130/80 mmHg instead of the previous 130/85 mmHg) reduces the type 1 diabetic subjects in control from 55% (155 of 281) to

42% (117 of 281) among all type 1 diabetic hypertensive subjects. Among all type 1 diabetic subjects being treated for hypertension, control decreases from 64% (155 of 244) to 48% (117 of 244).

Next, we used a common standard (140/90 mmHg) to compare the level of blood pressure control between the type 1 diabetic and nondiabetic groups. More type 1 diabetic than nondiabetic subjects were in control when using 140/90 mmHg as the goal, among all subjects defined as hypertensive (72 vs. 32%,  $P < 0.0001$ , Fig. 1A) as well as among all sub-

jects treated (83 vs. 68%,  $P = 0.01$ , Fig. 1B).

The age-adjusted hypertension rates of 44.7% for type 1 diabetic and 14.5% for nondiabetic subjects reflect the slightly older age of nondiabetic subjects. The albuminuria-adjusted hypertension rate (dichotomizing albuminuria as yes/no) was 39.5% for type 1 diabetic and 16.6% for nondiabetic subjects. A total of 100 subjects did not have overnight urine specimens.

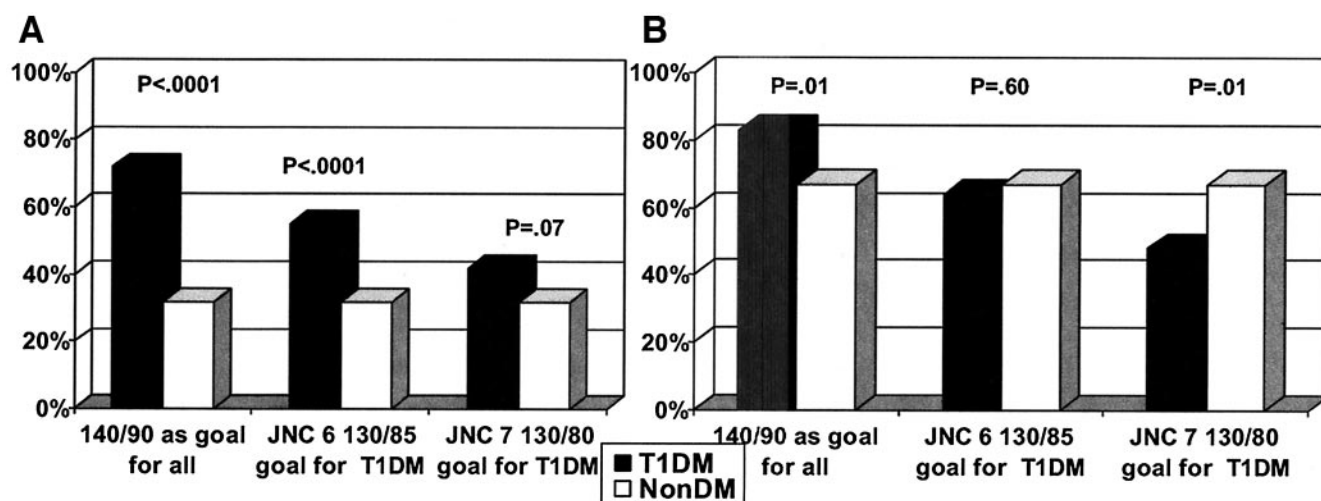
The majority of subjects being treated for hypertension were on a single drug. Of the 244 type 1 diabetic subjects on anti-hypertensive treatment, 182 (75%) were on a single drug, 40 (16%) were on two drugs, 17 (7%) were on three drugs, 4 (2%) were on four drugs, and 1 subject (0.4%) was on five drugs. Among the nondiabetic subjects ( $n = 55$ ), 35 (64%) were on single drug therapy, 15 (27%) were on two drugs, 4 (7%) were on three drugs, and 1 (2%) was on four drugs. Among the type 1 diabetic subjects, 210 (86%) were on ACE inhibitors and 34 (14%) were on angiotensin receptor blockers. Comparing rates of control by single versus multidrug therapy was not different for nondiabetic subjects (74 vs. 55%,  $P = 0.14$ ) or for type 1 diabetic subjects for JNC 7 control goals (130/80 mmHg) (48 vs. 47%,  $P = 0.83$ ) but was for type 1 diabetic subjects for JNC 6 control goals (130/85 mmHg) (68 vs. 50%,  $P = 0.01$ ).

In summary, as lower control goals for blood pressure are used for type 1 diabetic subjects, the proportion who are in control decreases, both among all hypertensive subjects (72, 55, and 42% for 140/90, 130/85 [JNC 6], and 130/80 mmHg

Table 2—Prevalence, awareness, treatment, and control of hypertension in adults with type 1 diabetes versus nondiabetic control subjects based on JNC 6 guidelines

Prevalence		Awareness		Treatment		Control	
Type 1 diabetic subjects	Non-diabetic subjects	Type 1 diabetic subjects	Non-diabetic subjects	Type 1 diabetic subjects	Non-diabetic subjects	Type 1 diabetic subjects	Non-diabetic subjects
n = 281	n = 116	n = 150	n = 52	n = 244	n = 55	n = 155	n = 37
43%*	15%	53%†	45%	87%*	47%	55%*	32%
						Control among treated	
						64%‡	67%
						155/244	37/55

\* $P < 0.0001$ , † $P = 0.11$ , ‡ $P = 0.60$ .



**Figure 1**—Control of Hypertension. A: Among subjects meeting the diagnosis of hypertension. B: Among subjects on treatment.

[JNC 7], respectively) and among those on antihypertensive treatment (83, 64, and 48% for the same classifications as above).

**CONCLUSIONS**— This is the first study to compare rates of hypertension prevalence, awareness, treatment, and control between type 1 diabetic subjects and nondiabetic control subjects and, other than one abstract (19), the first report on this subject in a U.S. type 1 diabetic population. As such, it raises several issues for improving clinical care. Hypertension is underdiagnosed in both the type 1 diabetic and nondiabetic populations, although type 1 diabetic subjects fared better in both treatment and control. Importantly, the new JNC 7 (2) and ADA (22) hypertension guidelines that lower the diastolic blood pressure target to 80 mmHg will require additional effort to achieve this goal and thereby optimize the health of type 1 diabetic subjects. CACTI was undertaken to identify targets for primary prevention of coronary artery disease in type 1 diabetic subjects compared with nondiabetic control subjects.

Our main finding in this study is that subjects with type 1 diabetes have increased prevalence of hypertension but also higher rates of treatment and control compared with nondiabetic subjects despite more stringent blood pressure treatment goals. However, only 55% of patients with type 1 diabetes met JNC 6 blood pressure goals. Applying the new JNC 7 guidelines that were issued in 2003 after the subjects' data were collected (the diastolic blood pressure goal in diabetes

was lowered from 85 to 80 mmHg), the proportion of type 1 diabetic subjects diagnosed with hypertension who were in control decreased from 55 to 42% and decreased from 64 to 48% among those subjects who were treated. Figure 1 provides a comparison at different levels of control as well as a historical overview of the progressive decreases in blood pressure goals for patients with type 1 diabetes, which have steadily decreased in the past decades (140/90 to 130/85 to the current 130/80 mmHg).

The majority of subjects in our study are seen at referral centers for type 1 diabetes, and we speculate that rates of control may be less in the general type 1 diabetic population as well as in those not volunteering for a research study. This also emphasizes the challenge presented by the more rigorous blood pressure goals for subjects with diabetes. However, when applying a common goal of 140/90 mmHg to compare type 1 diabetic and nondiabetic subjects, the type 1 diabetic subjects in this study had much better blood pressure control. Although subjects with type 1 diabetes have higher rates of hypertension, they have greater levels of control despite a lower blood pressure goal.

Our data are comparable to that from Pittsburgh, the only other available data on hypertension in type 1 diabetic subjects in the U.S., in which the prevalence of hypertension in adults ( $n = 386$ ) with type 1 diabetes in 1996–1998 was 29% (CACTI 43%), with 81.7% aware of hypertension (CACTI 53%), 74.7% on medication (CACTI 87%), and 49.5% on

medication and controlled (CACTI 64%) (19). Two European-wide studies of hypertension in type 1 diabetic subjects have been published by the EURODIAB group. In 3,250 type 1 diabetic subjects seen in 1989–1990 with a mean age of 32.7 years and duration of diabetes of 14.7 years, 24% had hypertension, of whom 48.5% were aware of the diagnosis and 42.2% were on treatment with only 11.3% controlled. Additionally, 81% of those on treatment were on only one antihypertensive medication (17). In the EURODIAB 7-year follow-up data, hypertension prevalence had increased from 412 to 631 subjects out of 1,866 subjects. They also reported an increase in hypertensive subjects who were treated (from 40 to 69%) as well as those in control (from 32 to 41%). Furthermore, the use of more than one antihypertensive medication increased from 19 to 33% (18). Multiple possible explanations exist for our higher hypertension prevalence in type 1 diabetic subjects (43%) compared with previous studies. These include age and duration of diabetes (the Pittsburgh cohort had a mean age of 28 years with 20 years of duration, whereas the EURODIAB cohort had a mean age of 33 years with mean duration of 15 years at baseline compared with our mean of 37 years of age and 23 years of duration) and renal protection treatment (in our cohort, 86% of type 1 diabetic subjects were on ACE inhibitors and 14% were on angiotensin receptor blockers; this is not reported in the Pittsburgh cohort, and in the EURODIAB reports, the use of ACE inhibitors increased from 57 to 82%). Finally, dif-



ferences of representative subjects and physicians' practice could contribute to differences, especially in the EURODIAB group, which included subjects from multiple European centers.

Literature also exists for type 2 diabetes, though given the differences in pathophysiology and treatment, direct comparisons cannot be made. An Australian study (15) reported that 69% of 2,331 patients with type 2 diabetes were hypertensive, with 59% under treatment, and only 31% of those treated were controlled. In a study of 800 male veterans with hypertension (16), the 274 subjects with diabetes were more likely to have a blood pressure  $\geq 140/90$  mmHg (73 vs. 66%) and to receive less intensive antihypertensive treatment. Using the National Health and Nutrition Examination Survey (NHANES) III database from the 1988 to 1994 period, Geiss et al. (12) reported that 71% of all U.S. adults with diabetes (no distinction was made between type 1 and type 2 diabetes) were hypertensive, with 71% aware, 57% treated, but only 12% meeting the JNC 6 goal of 130/85 mmHg, and 45% had blood pressure  $< 140/90$  mmHg.

In the general population, the most recent NHANES data reported that 28.7% of the participants had hypertension, an increase of 3.7% from 1988 to 1991. Overall, 68.9% were aware of their hypertension, 58.4% were treated, and 31% were controlled (10). This compares to 15% prevalence, 45% awareness, 48% treatment, and 32% control in our nondiabetic cohort. As our nondiabetic cohort was relatively young, this explains the decreased prevalence of hypertension compared with NHANES data, while the frequencies of treatment and control were relatively similar. Additionally, the use of spouses, friends, and neighbors as control subjects might introduce bias, as this group may be more health conscious than the general population. Prevalence of hypertension has been reported to be lower in the U.S. (28%) and Canada (27%) than in Europe (38–55%). Similarly, treatment was higher in the U.S. and Canada (53 and 36%, respectively) than in Europe (25–32%). However, control of blood pressure was low in the U.S. (29%), Canada (17%), and Europe ( $\leq 10\%$ ) (11).

Recent reports (24,25) have emphasized that traditional risk factors for cardiovascular disease account for the majority of cardiovascular disease events.

Similarly, reports such as ALLHAT (Anti-hypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) (26) and practice recommendations such as those from JNC 7 (2) and the ADA (1) emphasize increased attention to blood pressure control and the health benefit of lower blood pressure goals.

Limitations of this study include the possibility that subjects who volunteer for a research study may be more health conscious and therefore have higher rates of awareness, treatment, and control. Additionally, as the majority of type 1 diabetic patients were seen at referral centers, these subjects may be better educated, have increased access to medical care, and be more concerned about their health than the general type 1 diabetic population. If so, then the magnitude of effort required to obtain hypertension control in the general public (both with and without type 1 diabetes) would be even greater. On the other hand, our type 1 diabetic subjects may be more sick, as they are seen at tertiary care centers. No national cohort like NHANES exists for type 1 diabetes, but the ongoing SEARCH for Diabetes in Youth study is, in part, addressing this issue. The CACTI cohort is likely representative of the type 1 diabetic population seen at tertiary care centers. As these data are cross-sectional, longitudinal results from the CACTI study will provide more detailed data on the progression of hypertension in subjects with type 1 diabetes. Another possible limitation (similar to that reported by Collado-Mesa et al. [17]) is in our definition of treatment, which may include subjects (especially those with type 1 diabetes) who were on antihypertension medication for renal protective reasons. Finally, as a majority of patients with type 1 diabetes are non-Hispanic white, further analysis of our data by ethnicity, which is an important factor in hypertension, lacks adequate sample size.

Recent JNC 7 recommendations for diagnosis and treatment goals include the category of prehypertension and the statement that individuals who are normotensive at age 55 years have a 90% lifetime risk for developing hypertension (2). Our findings in this epidemiological study of 1,416 relatively healthy young adults asymptomatic for coronary artery disease demonstrate a need for improvement in diagnosis of hypertension and in blood pressure therapy to reach treatment

goals. Despite a higher prevalence of hypertension, the type 1 diabetic patients in this study, who were reasonably well controlled from a glycemic standpoint (mean  $HbA_{1c} = 8.0\%$ ), had better treatment and control of hypertension. In addition to providing baseline data on hypertension in a large cohort of type 1 diabetic and nondiabetic subjects, this report highlights the need for increased attention to diagnosing hypertension and meeting treatment goals for blood pressure in both the type 1 diabetic and nondiabetic populations to maximize cardiovascular health in all patients and diabetes care in patients with type 1 diabetes.

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