

Prevalence and clinical implications of American Diabetes Association-defined diabetes and other categories of glucose dysregulation in older adults: The Health, Aging and Body Composition Study

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Abstract

Using data on history of diabetes, fasting glucose (FG) and the oral glucose tolerance test (OGTT), the authors contrasted cardiovascular disease (CVD) risk factors (body mass index, blood pressure, lipids and glycated hemoglobin) in 3052 African-American and White adults aged 70–79 in mutually exclusive categories of diagnosed diabetes, undiagnosed diabetes defined by the American Diabetes Association (ADA), isolated post-challenge hyperglycemia (IPH; FG < 126 mg/dL and 2 h post-OGTT \geq 200 mg/dL), impaired fasting glucose (IFG; FG \geq 110 but < 126 mg/dL), and individuals who were non-diabetic by both ADA and World Health Organization (WHO) criteria (FG < 126 mg/dL and 2 h post-challenge glucose < 200 mg/dL). The prevalence of diagnosed diabetes, undiagnosed ADA diabetes and IPH were 15.2, 3.8 and 4.7%, respectively, with more diagnosed and undiagnosed ADA diabetes in African-Americans than Whites. Compared to mean glycated hemoglobin (HbA_{1c}) among ADA/WHO non-diabetic individuals (6.0%), HbA_{1c} was substantially higher in the diagnosed diabetes and undiagnosed ADA diabetes groups (8.0% and 7.7%), but not in the IPH group (6.3%). The diagnosed and undiagnosed ADA diabetic groups had worse CVD risk factor profiles than the ADA/WHO non-diabetic group. IPH subjects had elevated levels of some CVD risk factors, but differences were more modest than those for the diabetic groups. Among people with IPH, those who also had IFG had worse CVD profiles than those with IPH alone. Although the OGTT may identify additional adults with more CVD risk factors than normals, these differences appear to be clustered among those who also have IFG. © 2001 Elsevier Science Inc. All rights reserved.

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1. Introduction

Key to reducing the health and economic burden of diabetes in old age is determining what level of hyperglycemia is associated with increased risk to health, and what measures of hyperglycemia are most informative in providing this information. Based on the 1997 American Diabetes Association (ADA) criteria for diagnosis of diabetes [1], 37.7% U.S. adults aged \geq 60 years have diabetes mellitus [2]. Of these cases, 31.6% occur among older individuals who do not know that they have diabetes, highlighting the importance of screening for glucose abnormalities in old age.

Findings from a recent study [3] raised concerns that in older adults, the ADA criteria would underestimate the oc-

currence of glucose abnormalities relative to both the 1985 World Health Organization (WHO) criteria [4], and new criteria proposed by WHO in 1998 [5]. Differences in diabetes prevalence between the ADA and both sets of WHO criteria stem from the ADA's recommendation to use fasting glucose (FG) only (and not the oral glucose tolerance test [OGTT]) in identifying undiagnosed diabetes. Under ADA criteria, individuals with isolated post-challenge hyperglycemia (IPH; post-challenge glucose \geq 200 mg/dl and FG <126 mg/dl) would not be classified as diabetic, but this group is considered diabetic by WHO criteria.

Data from the Third National Health and Nutrition Examination Survey for adults aged 40–74 showed that with advancing age, the prevalence of IPH increased more rapidly than that of ADA diabetes, exceeding ADA diabetes by age 70 [6]. One study showed that IPH represented 72% of all newly diagnosed cases of diabetes in older adults [7], but

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another put this figure at 35% [8]. It is yet not clear which criteria are most sensitive and specific from the standpoint of identifying individuals at high risk of the most common late-life complications of diabetes, cardiovascular disease (CVD) and mortality. However, two prospective studies suggested that the ADA criteria may be less sensitive than WHO criteria for predicting CVD [7,9]. If findings from these studies were attributable to excess CVD mortality among individuals with IPH, IPH would constitute a clinically important subgroup of the population defined as non-diabetic by ADA criteria. Continued investigation of the prevalence and characteristics of individuals with ADA-defined diabetes and those with IPH will improve understanding of the impact of the ADA criteria on CVD health risk in old age.

This report has two objectives: (1) report by race and sex the prevalence of ADA-defined categories of glucose regulation in a large biracial cohort of adults aged 70–79; and (2) contrast CVD risk factor profiles of older individuals with diagnosed diabetes, undiagnosed ADA diabetes, IPH, and those who are non-diabetic by both ADA and WHO criteria (ADA/WHO non-diabetic). We hypothesized that older individuals with undiagnosed ADA diabetes would exhibit worse CVD risk factor profiles than those with IPH, and that individuals with IPH would have CVD risk factor profiles intermediate between those with undiagnosed ADA diabetes the ADA/WHO non-diabetic group. We further hypothesized that individuals with IPH would constitute a metabolically heterogeneous group, many of whom would also have impaired fasting glucose (IFG; $FG \geq 110$ but < 126 mg/dL). Last, we hypothesized that individuals with both IPH and IFG would have worse metabolic profiles than individuals with only one of these abnormalities.

2. Materials and methods

2.1. Sample selection

The Health, Aging and Body Composition Study (Health ABC) was established in 1996 to investigate in older, non-disabled adults, pathways by which multiple diseases, including diabetes and cardiovascular disease, affect morbidity, disability and risk of mortality. The cohort consists of 3075 men and women aged 70–79 recruited at two field centers, University of Pittsburgh and University of Tennessee, Memphis. One of the primary objectives of Health ABC is to understand predictors of early disability; therefore at baseline, all participants reported no difficulty walking one-quarter mile or walking up 10 steps without resting and also no difficulty with mobility-related Activities of Daily Living (ADL). Information on participant screening and recruitment is available [10].

2.2. Clinical measures and medication inventory

Height (mm) was measured twice by a Harpenden stadiometer (Holtain Ltd.) and weight was measured by a standard balance beam scale to the nearest 0.1 kg. Using the

mean of the two height measurements, body mass index (BMI; kg/m^2) was calculated as weight divided by the square of height. Sitting blood pressure was measured twice in immediate succession. Reported data are the means of these two measures. Participants were asked to bring both prescription and non-prescription medications used in the previous 2 weeks. In a medication inventory, examiners recorded the names and doses of these medications.

2.3. Definition of categories of glucose regulation

The WHO defines diabetes as $FG \geq 126$ mg/dl or 2 h post-OGTT of ≥ 200 mg/dl [5]. In contrast, the ADA defines diabetes by $FG \geq 126$ mg/dl, but does not recommend use of the OGTT. Health ABC interview and blood chemistry data were used to define mutually exclusive categories of glucose regulation. Participants completed an in-home interview during which they were asked “Has a doctor ever told you that you have diabetes or sugar diabetes?” Women were asked not to include diabetes that only occurred during pregnancy. Those who responded “yes” to this question, and those with medication inventory data showing use of hypoglycemic medications were categorized as “diagnosed diabetes.” Within several weeks of the interview, participants presented at the clinics in the morning and provided a blood sample following an overnight fast of at least 8 h. Except for those who were taking insulin or oral hypoglycemic medications, participants were administered a standard 2-h, 75-g OGTT.

Among subjects without diagnosed diabetes, “undiagnosed ADA diabetes” was present if the participant had $FG \geq 126$ mg/dL [1]. Among subjects without diagnosed or undiagnosed ADA diabetes, IFG was present if FG was between 110 and 125 mg/dL. “ADA non-diabetic” refers to subjects without diagnosed or undiagnosed ADA diabetes who had $FG < 110$ mg/dL. Among subjects without diagnosed or undiagnosed ADA diabetes, IPH was present if the subject had post-challenge glucose ≥ 200 mg/dL. Subjects without diagnosed or undiagnosed ADA diabetes or IPH who had $FG < 126$ mg/dL were described as “ADA/WHO non-diabetic.” Participants were further cross-categorized by IPH and IFG. In these analyses, the reference group consisted of individuals with $FG < 110$ mg/dl and post-challenge glucose < 200 mg/dL, who were described as having “no abnormality of fasting glucose.” With the exception of undiagnosed ADA diabetes and IFG, terms referring to various combinations of fasting and post-challenge glucose are solely descriptive, and are summarized in Appendix A.

2.4. Laboratory measurements

Fasting insulin (Abbot IMx) was measured on participants except those taking exogenous insulin. These values were log transformed because of their non-normal distribution. Data on fasting insulin and fasting and post-challenge glucose are not reported among participants with diagnosed diabetes since many of these individuals were taking hy-

poglycemic medications. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c) and triglycerides (TG) were measured, and low-density lipoprotein cholesterol (LDL-c) was calculated using the Friedewald equation [11]. Glucose and lipids were measured on a Johnson and Johnson Vitros 950 analyzer. Participants' glycated hemoglobin (HbA_{1c}) was also measured (Biorad). Biological specimens were processed according to standardized protocols by the Laboratory of Clinical Biochemistry at the University of Vermont [10]. HbA_{1c} reference values from this lab indicated that HbA_{1c} ≤ 6% is considered non-diabetic, a value consistent with standards reported in clinical practice guidelines published by the ADA [12].

2.5. Statistical methodology

The prevalence of categories of glucose regulation are presented both for the full analysis sample, and also by race and sex. The chi-square statistic was used to compare the distribution of these categories across race–sex strata. To examine evidence of hyperglycemia across these categories, mean levels of fasting and post-challenge glucose and of HbA_{1c} were examined with generalized linear models with ADA/WHO non-diabetic individuals as the reference group. Levels of CVD risk factors were compared across the groups. Using data from the medication inventory, blood pressure and lipids were examined with adjustment for use of anti-hypertensive medications and anti-lipemics, respectively. These analyses were subsequently conducted by race and sex to determine if cohort-level associations were consistent across the sub-groups. CVD risk factors were then examined among participants cross-categorized by IPH and IFG. In these analyses, the reference group consisted of individuals with FG < 110 mg/dL.

3. Results

Of the 3075 participants in Health ABC, 23 were missing both FG and the OGTT and were excluded, leaving an analysis sample of 3052 individuals (99.2% of the cohort) who could be categorized according to ADA criteria. The mean

age of these individuals was 73.6 years. Slightly over one-half of the participants were female (51.5%), and 41.6% of participants were African-American. The two clinical centers each examined approximately one-half of the participants.

3.1. Prevalence of ADA-defined categories of glucose regulation

Four hundred sixty-five participants (15.2%) had diagnosed diabetes at study entry (Table 1). As expected, the race-specific prevalence of diagnosed diabetes varied greatly. While 13.8% of White males had diagnosed diabetes, 21.8% of African-American males had diagnosed diabetes, a significant difference (relative prevalence for African-American males:White males = 1.58, $P < .001$). Similarly, 21.1% of African-American females had diagnosed diabetes, compared to 7.6% of White females, also a significant difference (relative prevalence for African-American females:White females = 2.79, $P < .001$).

A total of 117 participants (3.8%) had undiagnosed ADA diabetes. Individuals with diagnosed and undiagnosed ADA diabetes totaled 19.0% of the cohort. Undiagnosed ADA diabetes was more common among men than women, and somewhat higher in African-Americans compared to Whites. The relative prevalence of undiagnosed ADA diabetes among White men:White women was 3.35 ($P < .001$), and the corresponding statistic for African-Americans was 1.77 ($P < .05$). A total of 183 participants (6.0% of the sample) had IFG. IFG was more common than undiagnosed ADA diabetes in all race–sex groups, and was more common in men than women, but this difference was significant only among Whites (relative prevalence 1.76, $P < .01$).

3.2. Prevalence of isolated post-challenge hyperglycemia

Of participants without diagnosed or undiagnosed ADA diabetes, 91 did not have an OGTT, leaving 2379 participants whose IPH status could be determined. Of these, 143 had IPH, a group considered to have undiagnosed diabetes by WHO, but not ADA criteria. Fig. 1 shows the prevalence of undiagnosed ADA diabetes and IPH for the full sample

Table 1

Baseline prevalence of glucose abnormalities according to criteria proposed by the American Diabetes Association, by race and sex, Health ABC, 1997–1998 ($n = 3052$)^a

Categories of ADA diabetes ^b	White males		White females		African-American males		African-American females		Total	
	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>
Diagnosed diabetes	13.8	129	7.6	64	21.8	119	21.1	153	15.2	465
Undiagnosed ADA diabetes	5.1	48	1.5	13	5.9	32	3.3	24	3.8	117
Impaired fasting glucose	7.5	70	4.2	36	7.0	38	5.4	39	6.0	183
ADA non-diabetic	73.6	689	86.7	734	65.3	356	70.2	508	75.0	2,287
Total	100.0	936	100.0	847	100.0	545	100.0	724	100.0	3,052

^aSubjects have non-missing data for diagnosed diabetes and fasting glucose.

^bDiagnosed diabetes: subject reported being told by a physician that they have diabetes or have hypoglycemic medications on medication inventory; undiagnosed ADA diabetes: no diagnosed diabetes and fasting glucose ≥ 126 mg/dl; impaired fasting glucose: no diagnosed diabetes and fasting glucose between 110 and 125 mg/dl; ADA non-diabetic: no diagnosed diabetes and fasting glucose < 110 mg/dl.

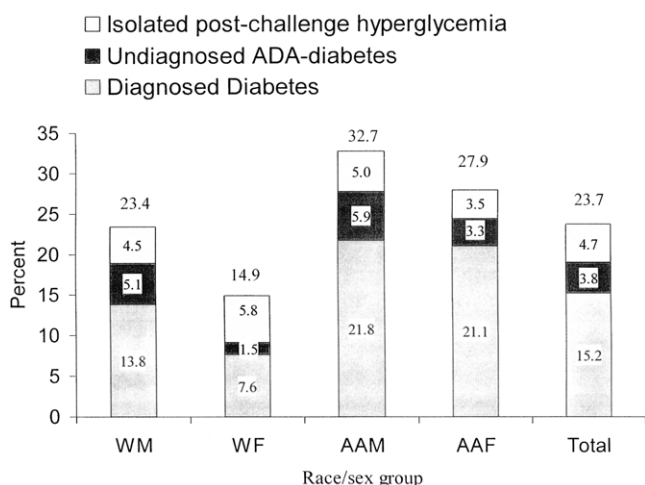


Fig. 1. Prevalence of undiagnosed ADA diabetes and isolated post-challenge hyperglycemia, by race and sex, Health ABC. WM = White men; WF = White females; AAM = African-American men; AAF = African-American females.

and by race and sex. In Health ABC, the prevalence of IPH exceeded that of undiagnosed ADA diabetes (4.7% vs 3.8%). The prevalence of undiagnosed diabetes in Health ABC would therefore be 8.5% by WHO criteria, and 3.8% by ADA criteria, a > 50% underestimation of undiagnosed glucose disorders using ADA criteria. The prevalence of undiagnosed ADA diabetes exceeded that of IPH among men, but IPH was more common among women.

3.3. HbA_{1c} across categories of glucose regulation

Significant differences in HbA_{1c} were observed across the glucose categories, with all groups having statistically

significantly higher values than the ADA/WHO non-diabetic group (Table 2). Although statistically significant, the smallest difference in HbA_{1c} was observed between the IPH group and the ADA/WHO non-diabetic group (6.3% vs 6.0%).

Fig. 2 shows the 25th, 50th and 75th percentiles of HbA_{1c} by race and sex, and also for the full sample. Participants with diagnosed diabetes and undiagnosed ADA diabetes had less favorable distributions of HbA_{1c}, compared both to the IPH and ADA/WHO non-diabetic groups. HbA_{1c} among IPH participants was less favorable than that of ADA/WHO non-diabetic individuals, but this difference was slight. In the full sample, median HbA_{1c} was 7.4% among participants with undiagnosed ADA diabetes, 6.3% among participants with IPH, and 6.0% among ADA/WHO non-diabetic individuals.

3.4. CVD risk factors across categories of glucose regulation

Mean BMI was 29.3 and 29.4 kg/m² in the diagnosed and undiagnosed ADA diabetic groups respectively, significantly higher than the ADA/WHO non-diabetic group (26.9 kg/m²; Table 2). Participants with IPH had mean BMI intermediate between the diabetic and non-diabetic groups (27.8 kg/m²). Participants with diagnosed and undiagnosed ADA diabetes had significantly lower HDL-c than the ADA/WHO non-diabetic group, but HDL-c was similar in the IPH and ADA/WHO non-diabetic groups. Triglycerides were elevated in all groups compared to ADA/WHO non-diabetic. Both total cholesterol and LDL-c were lower in the diagnosed diabetic group compared to the ADA/WHO non-diabetic group. Systolic blood pressure was slightly higher and diastolic pressure slightly lower among subjects with

Table 2

Baseline measures of glucose regulation and cardiovascular disease risk factors, by category of glucose regulation, Health ABC, 1997–1998 (*n* = 2961)^a

Characteristic	Diagnosed diabetes ^b <i>n</i> = 465	Undiagnosed ADA diabetes ^b <i>n</i> = 117	Isolated post-challenge hyperglycemia ^b <i>n</i> = 143	ADA/WHO Non-diabetic ^b <i>n</i> = 2236
Age	73.6	73.8	73.8	73.6
Fasting glucose (mg/dl)	N/A	159 ^c	102 ^c	93
Post-challenge glucose (mg/dl)	N/A	278 ^c	232 ^c	120
Log fasting insulin (U/ml)	N/A	2.36 ^c	2.11 ^c	1.91
HbA _{1c} (%)	8.0 ^c	7.7 ^c	6.3 ^c	6.0
BMI (kg/m ²)	29.3 ^c	29.4 ^c	27.8 ^d	26.9
Systolic blood pressure (mm Hg)	137 ^d	137	140 ^e	135
Diastolic blood pressure (mm Hg)	70 ^e	72	72	72
Cholesterol (mg/dl)	197 ^e	207	205	203
HDL cholesterol (mg/dl)	50 ^e	48 ^c	55	55
LDL cholesterol (mg/dl)	117 ^e	124	118	122
Triglycerides (mg/dl)	153 ^c	186 ^c	161 ^c	132

^aSubjects have non-missing data for diagnosed diabetes, fasting glucose and post-challenge glucose.

^bDiagnosed diabetes: subject reported being told by a physician that they have diabetes, or have hypoglycemic medications on medication inventory; undiagnosed ADA diabetes: no diagnosed diabetes and fasting glucose \geq 126 mg/dl; isolated post challenge hyperglycemia: no diagnosed or undiagnosed ADA diabetes and post-challenge glucose \geq 200 mg/dl; ADA/WHO non-diabetic: no diagnosed or undiagnosed ADA diabetes or IPH, and fasting glucose < 126 mg/dl and 2-h glucose <200 mg/dl.

^c*P* < .001 compared to ADA/WHO non-diabetic.

^d*P* < .05 compared to ADA/WHO non-diabetic.

^e*P* < .01 compared to ADA/WHO non-diabetic.

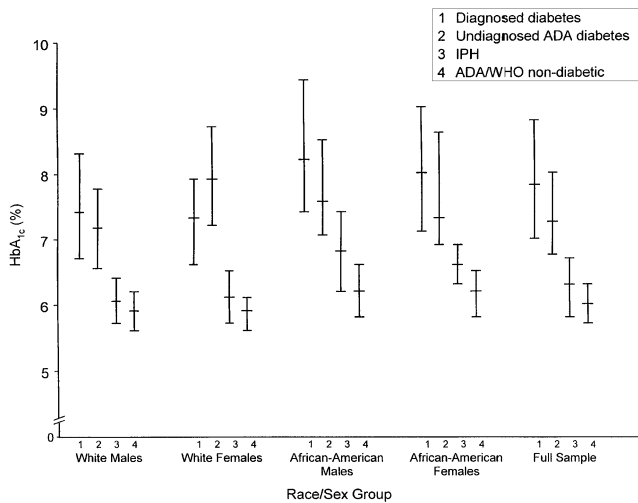


Fig. 2. Quartiles of HbA_{1c} according to glucose category, by race and sex, Health ABC.

diagnosed diabetes compared to those with no diagnostic abnormality.

3.5. Race, sex, and CVD risk factors by category of glucose regulation

Among White males, there was no difference in HbA_{1c} between the IPH and ADA/WHO non-diabetic groups (Table 3). Among White females, those with IPH had significantly higher BMI, TG and systolic blood pressure compared to the ADA/WHO non-diabetic group. Differences in HbA_{1c} between the two groups were statistically significant, but small (6.1% vs 5.9%). Among African-American males, HbA_{1c} and TG were higher in the IPH group compared to the ADA/WHO non-diabetic group, and in African-American females, HbA_{1c} was higher. Compared to ADA/WHO non-diabetics, the number and magnitude of elevated CVD risk factors was greater for diagnosed and undiagnosed ADA diabetes, and differences in HbA_{1c} were more pronounced. Importantly, African-Americans with diagnosed diabetes had markedly worse HbA_{1c}, BMI, HDL-c and TG compared to their White counterparts.

Analyses focusing on impaired fasting glucose revealed that 48 of the 143 participants with IPH also had IFG. Individuals with IFG+IPH had worse glucose and CVD risk factors levels than those with IPH alone (Table 4). CVD risk factors among participants with IPH alone did not differ markedly from those without an abnormality of fasting glucose.

Clinical cutpoints for HbA_{1c} and BMI proposed by the ADA [11] and the National Heart, Lung and Blood Institute [13] are shown by glycemic group in Table 5. One-third of participants with IFG alone had HbA_{1c} < 6%, but only 12.5% of those with IFG+IPH were below 6%. In contrast, 47% and 57% of IPH and those with no abnormality were below 6%. More than 30% of the IFG+IPH group had HbA_{1c} ≥ 7%, compared to 9.6% or less among the other groups. BMI followed a similar pattern: smaller proportions

of IFG and IFG+IPH subjects had BMI <25 kg/m² (18.9% and 20.8%) than the IPH alone and no abnormality groups (32.6% and 36.2%). Conversely, larger proportions of the IFG and IFG+IPH groups had BMI ≥30. The largest proportion of obese individuals was in the IFG+IPH group (39.6%).

4. Discussion

Type 2 diabetes mellitus is among the most common chronic diseases affecting older adults in the United States, with an estimated 3.2 million adults aged ≥65 having been diagnosed with this condition. The public health burden of diabetes in the elderly extends beyond direct medical expenditures for diabetes among adults aged ≥65, a cost estimated at more than \$27 billion in 1997. Forgone productivity and premature mortality contribute an additional \$4.8 billion to the attributable economic costs of diabetes in old age [14]. In Health ABC, the prevalence of diagnosed diabetes was 15.2% in adults aged 70–79, with African Americans having significantly more diabetes than their White counterparts. Our finding of substantial ethnic differences in diabetes are consistent with data from the National Health Interview Surveys, and indicate that the ethnic disparity in the impact of diabetes continues into old age [2,15]. However, the prevalence of diabetes was considerably lower in Health ABC compared to older adults in HANES III [2], possibly due to the selection of relatively healthy older adults in Health ABC.

The aging of the so-called “baby boom” generation, longer life expectancy [16], increasing prevalence of obesity [17,18], and increasing representation of ethnic minorities at high risk of diabetes [16] may cause both the prevalence and absolute number of older adults with glucose abnormalities to increase in coming decades. Identifying age-appropriate tools for identification of older, high-risk individuals in the clinical setting is therefore a critical aspect of diabetes screening. Our results demonstrate that the ADA criteria, which emphasize use of fasting glucose, underestimate the prevalence of glucose abnormalities by more than 50% in older adults, when compared to WHO criteria, which also call for use of the OGTT. The >50% underestimation of diabetes cases is consistent with several previous epidemiologic studies of older adults [3,6,7], and stems from the large number of older individuals with isolated post-challenge hyperglycemia identified from the OGTT.

Despite the high prevalence of IPH in this and other cohorts of older adults, our findings indicated that mean HbA_{1c}, an indicator of long-term exposure to hyperglycemia, was considerably lower in IPH participants than in those with undiagnosed ADA diabetes: median HbA_{1c} was 7.4% in those with undiagnosed ADA diabetes, and 6.3% in people with IPH. While the distribution of HbA_{1c} was higher in these groups compared to the ADA/WHO non-diabetic group, HbA_{1c} was much higher in undiagnosed ADA

Table 3

Baseline measures of glucose regulation and cardiovascular disease risk factors, by sex, race and category of glucose regulation, Health ABC 1997–1998 ($n = 2961$)^a

Characteristic	Diagnosed diabetes ^b $n = 465$	Undiagnosed ADA diabetes ^b $n = 117$	Isolated post-challenge hyperglycemia ^b $n = 143$	ADA/WHO Non-diabetic ^b $n = 2236$
White males $n = 916$	$n = 129$	$n = 48$	$n = 42$	$n = 697$
Age	73.9	74.4	73.8	73.9
Fasting glucose (mg/dl)	N/A	159 ^c	104 ^d	94
2-h glucose (mg/dl)	N/A	277 ^c	225 ^c	116
Log fasting insulin (U/ml)	N/A	2.46 ^c	1.93	1.91
HbA _{1c} (%)	7.5 ^c	7.3 ^c	6.1	5.9
BMI (kg/m ²)	27.8 ^e	29.3 ^c	26.6	26.7
Systolic blood pressure (mm Hg)	136	137	139 ^d	132
Diastolic blood pressure (mm Hg)	69 ^d	72	73	71
Cholesterol (mg/dl)	184 ^d	198	199	192
HDL cholesterol (mg/dl)	41 ^c	40 ^e	48	46
LDL cholesterol (mg/dl)	107 ^c	116	122	119
Triglycerides (mg/dl)	182 ^c	229 ^c	151	137
White females $n = 819$	$n = 64$	$n = 13$	$n = 49$	$n = 693$
Age	73.3	73.8	73.8	73.6
Fasting glucose (mg/dl)	N/A	151 ^c	98 ^c	90
2-h glucose (mg/dl)	N/A	318 ^c	233 ^c	122
Log fasting insulin (U/ml)	N/A	2.55 ^c	2.11 ^c	1.82
HbA _{1c} (%)	7.3 ^c	7.9 ^c	6.1 ^c	5.9
BMI (kg/m ²)	28.6 ^c	29.4 ^e	27.5 ^c	25.7
Systolic blood pressure (mm Hg)	134	143 ^d	141 ^d	133
Diastolic blood pressure (mm Hg)	67	70	70	69
Cholesterol (mg/dl)	200	215	216	212
HDL cholesterol (mg/dl)	50 ^c	46 ^e	58	60
LDL cholesterol (mg/dl)	119	132	118	122
Triglycerides (mg/dl)	206 ^c	218 ^e	190 ^c	149
African-American males $n = 530$	$n = 119$	$n = 32$	$n = 27$	$n = 352$
Age	73.7	73.5	73.9	73.4
Fasting glucose (mg/dl)	N/A	160 ^c	104	94
2-h glucose (mg/dl)	N/A	261 ^c	236 ^c	118
Log fasting insulin (U/ml)	N/A	2.11	2.11	1.87
HbA _{1c} (%)	8.4 ^c	8.2 ^c	6.7 ^c	6.2
BMI (kg/m ²)	28.6 ^c	28.1	27.8	26.7
Systolic blood pressure (mm Hg)	140	137	143	138
Diastolic blood pressure (mm Hg)	73 ^d	73	75	76
Cholesterol (mg/dl)	186 ^d	202	196	194
HDL cholesterol (mg/dl)	48 ^e	51	56	53
LDL cholesterol (mg/dl)	113	125	112	120
Triglycerides (mg/dl)	122 ^d	132 ^d	142 ^c	109
African-American females $n = 696$	$n = 153$	$n = 24$	$n = 25$	$n = 494$
Age	73.4	73.0	73.8	73.4
Fasting glucose (mg/dl)	N/A	161 ^c	106 ^d	93
2-h glucose (mg/dl)	N/A	280 ^c	238 ^c	124
Log fasting insulin (U/ml)	N/A	2.38 ^d	2.42 ^e	2.08
HbA _{1c} (%)	8.3 ^c	7.6 ^c	6.6 ^d	6.1
BMI (kg/m ²)	31.4 ^c	31.2	30.3	29.3
Systolic blood pressure (mm Hg)	139	134	139	139
Diastolic blood pressure (mm Hg)	68 ^c	70	71	74
Cholesterol (mg/dl)	211	229	203	215
HDL cholesterol (mg/dl)	58 ^c	62	58	62
LDL cholesterol (mg/dl)	127	136	117	129
Triglycerides (mg/dl)	132 ^d	153 ^d	143	117

^aSubjects have non-missing data for diagnosed diabetes, fasting glucose and post-challenge glucose.

^bDiagnosed diabetes: subject reported being told by a physician that they have diabetes, or have hypoglycemic medications on medication inventory; undiagnosed ADA diabetes: no diagnosed diabetes and fasting glucose ≥ 126 mg/dl; isolated post challenge hyperglycemia: no diagnosed or undiagnosed ADA diabetes and post-challenge glucose ≥ 200 mg/dl; ADA/WHO non-diabetic: no diagnosed or undiagnosed ADA diabetes or IPH, and fasting glucose < 126 mg/dl and 2-hr glucose < 200 mg/dl.

^cP $< .001$ compared to ADA/WHO non-diabetic.

^dP $< .05$ compared to ADA/WHO non-diabetic.

^eP $< .01$ compared to ADA/WHO non-diabetic.

Table 4

Diabetes and cardiovascular risk factors, by glycemic group among subjects without diagnosed or undiagnosed ADA diabetes at baseline, Health ABC 1997–1998 ($n = 2379$)^a

Characteristic	IFG alone ^b $n = 127$	IFG + IPH ^b $n = 48$	IPH alone ^b $n = 95$	Normal fasting glucose ^b $n = 2109$
Age	73.6	73.7	73.9	73.6
Fasting glucose (mg/dl)	115 ^c	116 ^c	95	91
2-h (mg/dl)	145 ^c	240 ^c	228 ^c	119
Log fasting insulin (U/ml)	2.27 ^c	2.35 ^c	1.99	1.89
HbA _{1c} (%)	6.3 ^c	6.6 ^c	6.2 ^d	6.0
BMI (kg/m ²)	29.0 ^e	29.1 ^e	27.1	26.8
Systolic blood pressure (mm Hg)	138	140	140 ^d	135
Diastolic blood pressure (mm Hg)	73	74	71	72
Cholesterol (mg/dl)	204	198	209	203
HDL (mg/dl)	51 ^e	50 ^d	57	55
LDL (mg/dl)	126	113	121	122
Triglycerides (mg/dl)	145	170 ^e	157 ^e	131

^aData are presented for subjects without diagnosed or undiagnosed ADA diabetes who have both fasting and post-challenge glucose.

^bIFG alone: $110 \leq \text{FG} < 126$ mg/dl and post-challenge glucose < 200 mg/dl; IFG+IPH: $110 \leq \text{FG} < 126$ mg/dl and post-challenge glucose ≥ 200 mg/dl; IPH alone: $\text{FG} < 110$ mg/dl and post-challenge glucose ≥ 200 mg/dl.

^c $P < .001$ compared to no abnormality of fasting glucose.

^d $P < .05$ compared to no abnormality of fasting glucose.

^e $P < .01$ compared to no abnormality of fasting glucose.

diabetes, indicating that the ADA criteria are effective at identifying a group of older individuals with evidence of long-term exposure to hyperglycemia.

We also examined CVD risk factors, including BMI, blood pressure and lipids. Our data showed that BMI was highest in the diagnosed and undiagnosed ADA diabetic groups, intermediate in the IPH group, and lowest in ADA/WHO non-diabetic group. Although there was no difference in HDL-c between the IPH group and the ADA/WHO non-diabetic group, HDL-c was significantly lower in the diagnosed and undiagnosed ADA diabetic groups. For a number of CVD risk factors, the IPH group did not differ from the ADA/WHO non-diabetic group, or had risk factor levels intermediate between the diabetic and ADA/WHO non-diabetic groups.

What then has accounted for differences in incidence of CVD and of excess mortality in recent studies of IPH? The

answer may lie in the heterogeneity of older adults with IPH. In Health ABC, HbA_{1c} was higher among participants with IFG+IPH compared to those with IPH alone, indicating greater exposure to hyperglycemia. Several CVD risk factors were also worse in the IFG+IPH group compared to those with IPH alone. Thirty-three percent of the IFG+IPH group had HbA_{1c} $\geq 7\%$, and the IFG+IPH group had the highest proportion of obese individuals. Ascertainment of IFG, requiring only a fasting glucose measurement, combined with measurement of HbA_{1c}, may allow for identification of the subset of IPH individuals with long-term exposure to hyperglycemia, and increased risk of CVD. This group may have contributed to the excess morbidity and mortality observed in previous studies of IPH. Alternatively, it may even be possible to screen for undiagnosed type 2 diabetes using HbA_{1c} alone. A recent study reported that HbA_{1c} 2 standard deviations above the normal mean was 63% sensitive and 97% specific for identification of undiagnosed ADA diabetes [19]. The authors suggested that this measure might be an even easier tool than FG for identifying undiagnosed diabetic individuals at risk of complications. It should be emphasized, however, that HbA_{1c} values increase with age, and that large vessel complications are considerably more common than small vessel complications in older adults.

Retinopathy has been used as an example of vascular complications secondary to hyperglycemia [1], but this complication is relatively rare in old age, despite its strong association with vision loss. It is not yet clear whether hyperglycemia per se, or diabetes-associated abnormalities such as dyslipidemia or hypertension are responsible for the excess macrovascular disease and mortality observed in diabetes in old age. However, the question of greatest clinical importance is how well different definitions of diabetes predict the occurrence of adverse health events. This basic question is still under investigation.

Table 5

Baseline distribution of clinical cut points for glycated hemoglobin and body mass index, by glycemic group among subjects without diagnosed or undiagnosed ADA diabetes, Health ABC ($n = 2379$)^a

Variable/ cutpoints	IFG alone ^b $n = 127$	IFG+IPH ^b $n = 48$	IPH alone ^b $n = 95$	Normal fasting glucose ^b $n = 2109$
HbA _{1c} (%)				
<6	33.1	12.5	47.5	57.6
≥ 7	9.6	32.9	8.5	1.9
BMI (kg/m ²)				
≤ 25	18.9	20.8	32.6	36.2
25 to <30	45.7	39.6	44.2	42.6
≥ 30	35.4	39.6	23.2	21.2

^aData are presented for subjects without diagnosed or undiagnosed ADA diabetes who have both fasting and post-challenge glucose.

^bIFG alone: $110 \leq \text{FG} < 126$ mg/dl and post-challenge glucose < 200 mg/dl; IFG+IPH: $110 \leq \text{FG} < 126$ mg/dl and post-challenge glucose ≥ 200 mg/dl; IPH alone: $\text{FG} < 110$ mg/dl and post-challenge glucose ≥ 200 mg/dl.

Three important limitations of the study should be noted. First, Health ABC includes only non-disabled older adults, so our results may not be generalizable to the general population of adults aged 70–79. Second, clinical practice guidelines of the American Diabetes Association call for confirmation of elevated blood glucose measures on more than one occasion [20]. Participants in Health ABC and most other epidemiological studies are therefore not classified according to these guidelines since a single measure of fasting and post-challenge glucose was collected. Third, recent changes in the FG-based diagnostic guidelines from the WHO-based 140 mg/dL to the ADA-based 126 mg/dL means that the group called “diagnosed diabetes” in this study was identified under a higher level of FG than the group called “undiagnosed ADA diabetes.” Thus, if the new ADA fasting criteria (126 mg/dL) had been in place earlier, it is likely that a larger number of individuals in Health ABC would have been defined as diagnosed diabetes. These methodological limitations are common in large epidemiologic studies of diabetes mellitus and do not substantially detract from our findings that the ADA criteria are effective at identifying older adults with evidence of hyperglycemia who may also be at high risk of CVD, the major complication of diabetes in old age. Prospective analysis of Health ABC participants with IPH and IFG will determine if a lower fasting glucose cutpoint is useful in identifying the subset of IPH individuals at increased risk of CVD and mortality.

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Appendix A.

Category name	Diagnosed diabetes	Fasting glucose	OGTT	Reported in:
Diagnosed diabetes	yes	N/A	N/A	Tables 1,2,3; Fig.2
Undiagnosed ADA diabetes	no	≥126 mg/dl	N/A	Tables 1,2,3; Fig. 1,2
Impaired fasting glucose	no	110–125 mg/dl	N/A	Tables 1,4,5
ADA non-diabetic	no	<110 mg/dl	N/A	Table 1
Isolated post-challenge hyperglycemia	no	<126 mg/dl	≥200 mg/dl	Tables 2,3,4,5; Fig. 1,2
ADA/WHO non-diabetic	no	<126 mg/dl	<200 mg/dl	Tables 2,3; Fig.1
Normal fasting glucose	no	<110 mg/dl	<200 mg/dl	Tables 4,5