Trends in Apolipoprotein B, Non-High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, and Hemoglobin A1C Among US Adults with Diagnosed Diabetes, 2005-2018

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Abstract

Background: The control of blood glucose and atherogenic cholesterol particle concentrations is fundamental for patients with diabetes. The objective of this study was to examine trends in levels of apolipoprotein B (apo B), non-high-density lipoprotein (non-HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and hemoglobin A1c (A1C) and changes in the proportion of patients who achieved their glycemic and lipid goals between 2005 and 2018.

Methods: We conducted a serial cross-sectional analysis of the US nationally representative data from the National Health and Nutrition Examination Surveys from 2005 through 2018.

Results: In total, 5536 adults aged 20 years or older with diabetes were included (weighted mean age, 60.2 years; female, 50.1%). Among all adults with diabetes, the age-adjusted mean apo B levels did not decrease significantly from 2005 to 2016 ($P=0.077$). The age-adjusted mean non-HDL cholesterol levels reduced significantly ($P=0.004$) from 2005 to 2018. In 2017-2018, 55.3% of patients achieved the A1C goal of $<7\%$ and 43.8% achieved the non-HDL cholesterol goal of <130 mg/dl. In 2015-2016, 47.3% achieved the apo B goal of <90 mg/dL, 57.2% achieved the LDL cholesterol goal of <100 mg/dl, while 30.6% achieved all four glycemic and lipid goals. The success rates for achieving the goals of apo B, non-HDL cholesterol, and LDL cholesterol were higher in older compared with younger subjects, while white patients exhibited better glycemic control than Mexican Americans and non-Hispanic black patients.

Conclusion: Among adults with diabetes, there was a significant reduction in non-HDL cholesterol level while there was no change in levels of apo B, LDL cholesterol or A1C over the past decade. Nevertheless, large percentages of adults with diabetes continue to have higher levels of apo B, non-HDL cholesterol, LDL cholesterol, and A1C.

Introduction

Diabetes is associated with an increased risk of cardiovascular disease, which remains the primary cause of morbidity and mortality among individuals with both type 1 and type 2 diabetes [1]. To prevent microvascular complications and macrovascular disease in individuals with diabetes, the control of blood glucose and atherogenic cholesterol particle concentrations is fundamental for patients with diabetes. In particular, early intensive management of dyslipidemia is warranted to decrease the significant risk of atherosclerotic cardiovascular disease in patients with diabetes.

There is emerging evidence of the importance of monitoring apolipoprotein levels for the management of dyslipidemia [2–6]. Apo B has repeatedly been shown to be superior to low-density lipoprotein (LDL) cholesterol in identifying the risk of cardiovascular disease events [7]. Particularly for individuals with hypertriglyceridemia, the measurement of apo B may be the most clinically useful since it is a direct measure of the total number of circulating atherogenic lipoprotein particles. By contrast, calculated LDL cholesterol values is systematically underestimated when triglyceride levels range from 1.5 to 4.5 mmol/L and cannot be assessed reliably at all when triglyceride levels are above 4.5 mmol/L. Alternatively, some studies have suggested the use of non-high-density lipoprotein (non-HDL) cholesterol rather than LDL

cholesterol to enhance risk prediction, particularly in patients with elevated triglyceride levels [8, 9]. The concentration of non-HDL cholesterol reflects the total cholesterol content of all atherogenic lipoproteins [10] and thus can provide another method for evaluating the risks of atherogenic lipoproteins.

The guidelines updated in 2017 provides recommendations for lowering cholesterol in patients with diabetes [11]. Patients with diabetes are recommended to achieve goals of apo B, non-HDL cholesterol, and LDL cholesterol levels, based on the risk stratification. Similar recommendations also have also been made by the American Association of Clinical Endocrinologists [12]. For individuals with diabetes with no other risk factors, the recommended goals are LDL cholesterol < 100 mg/dL, non-HDL cholesterol < 130 mg/dL, and apo B < 90 mg/dL [11, 12]. For individuals with diabetes at very high risk [i.e., patients with one or more risk factor(s)], the recommended goals are LDL cholesterol < 70 mg/dL, non-HDL cholesterol < 100 mg/dL, and apo B < 80 mg/dL.

However, most previous research has focused only on the achievement of LDL cholesterol goals in individuals with diabetes [13]. One study examined levels of apo B, but only in two survey circles from 2005 to 2008 [14], and another, by Carroll et al., focused only on the mean levels of apo B, non-HDL cholesterol, and LDL cholesterol from 2005 to 2014, and only among adults over the age of 60 [15]. However, diabetes is becoming increasingly common in young and middle-aged adults. Further, few data exist on whether individuals with diagnosed diabetes achieved apo B, non-HDL cholesterol, and LDL cholesterol goals per the updated guidelines.

Despite the controversies, hemoglobin A_{1c} (A1C) still serves as an indispensable index of long-term glycemic control and a reliable indicator of the development of long-term complications in diabetic patients [16, 17]. Achievement of the A1C target concentration of < 7% has been demonstrated to decrease the microvascular complications of type 1 and type 2 diabetes [18]. However, previous studies have found that many patients with diabetes are not achieving their recommended A1C goals [19], and poor glycemic control has been common among patients in general [20]. The significant changes in the treatments and interventions used for diabetes over the past decade, a fresh assessment of trends in the glucose and lipid control of individuals with diabetes is necessary by using the latest available representative data.

Therefore, the purpose of the present study was to analyze trends in the mean concentrations of serum apo B, non-HDL cholesterol, and LDL cholesterol, and A1C in US adults with diagnosed diabetes from 2005–2006 to 2017–2018. In addition, we evaluated changes in the proportion of individuals who achieved the LDL cholesterol, non-HDL cholesterol, and apo B goals, and assessed trends in the glycemic control achieved by US adults with diagnosed diabetes from 2005 to 2018.

Methods

This study was based on cross-sectional data from the National Health and Nutrition Examination Survey (NHANES), which has been a nationally representative surveys of the noninstitutionalized US population since 1999 [21]. Each of the NHANES survey uses a complex, multistage, and stratified sampling design. The study protocol of NHANES was approved by the research ethics review board of the National Center for

Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). Written informed consent was provided from all of the participants. The study design, data collection methods, and protocol for the survey have been previously reported [22].

Each NHANES survey included in-home interviews, mobile examinations, and laboratory measures. The in-home interviews gathered basic demographic and health information about the participants. They were then scheduled to participate in a mobile examination center for the physical examinations and laboratory tests.

Study Participants

The study population included adults aged 20 years or older who reported a diagnosis of diabetes. The diabetes section in the NHANES survey included personal interview data regarding diabetes, which were asked in the home by trained interviewers. The participants were asked whether they had ever been told by a health professional that they had diabetes or sugar diabetes. Those who answered “yes” were considered to have a diagnosis of diabetes. We excluded women who reported diagnosed diabetes during pregnancy. Based on the information that participants reported about race/ethnicity, participants were categorized by the NCHS (Mexican American, non-Hispanic white, non-Hispanic black, other Hispanic, or other). Other Hispanic and other were combined to create other racial/ethnic groups in the present study.

Survey Years

We accessed data from 2005–2006 through 2017–2018, thereby including all 7 continuous NHANES data cycles. We analyzed all of the available NHANES cycles for A1C (2005–2018), total cholesterol (2005–2018), HDL cholesterol (2005–2018), LDL cholesterol (2005–2016), and apo B (2005–2016). The data analysis was conducted in the United States from January to July 2020. In cases in which the relevant variables were missing, those individuals were excluded from particular analyses, and all available data were analyzed in this study.

Laboratory Methods

Serum specimens were collected, processed, and stored under appropriate frozen (–30 °C) conditions until they are shipped for testing. A1C was measured in a full sample with instruments certified by the National Glycohemoglobin Standardization Program and standardized according to the reference methods of the Diabetes Control and Complications Trial. Several changes were made to the methods for measuring serum lipids and the A1C over the 14-years of data collection from 2005 to 2018; the details are available from the NHANES laboratory data documentations [23]. Serum total cholesterol, HDL cholesterol, triglycerides, and apo B values were measured directly and standardized according to the CDC’s criteria of the lipid standardization program [24]. Non-HDL cholesterol levels were calculated as the difference between the levels of total cholesterol and HDL cholesterol. For serum samples with triglyceride levels of 400 mg/dL or

lower, the levels of LDL cholesterol were calculated for individuals who had fasted properly (≥ 8 to < 24 h) using the Friedewald equation [25]. Serum samples with triglyceride levels greater than 400 mg/dL were set as missing. For the patients with diagnosed diabetes, glycemic management was evaluated primarily based on the A1C measurement.

Outcome Assessment

The primary outcome measures were trends in mean concentrations of serum apo B, non-HDL cholesterol, and LDL cholesterol among US adults with diagnosed diabetes from 2005–2006 to 2017–2018. Additional outcome measures included changes in the percentages of patients who achieved an apo B goal of < 90 mg/dl, a non-HDL cholesterol goal of < 130 mg/dl, and an LDL cholesterol goal of < 100 mg/dl between 2005 and 2018. We also observed the percentages of patients who were achieving the more aggressive all-lipid goals (i.e., LDL-C targets of < 70 mg/dL, non-HDL-C targets of < 100 mg/dL, and apo B targets of < 80 mg/dL) at the end of the study period. Lastly, we evaluated changes in the levels of glycemic control achieved among U.S. adults with diagnosed diabetes between 2005 and 2018.

Statistical analysis

To obtain nationally representative estimates, the sample weights, clustering and stratification of the NHANES survey were incorporated into all of the analyses. The arithmetic means for non-HDL cholesterol and apo B and the percentage of participants who achieved the apo B, non-HDL cholesterol levels, and A1C goals are presented. Because of the skewed distribution of A1C, the geometric mean, calculated by back transforming the mean of the logarithm of the A1C concentration values, is presented. The means and percentages for adults with diabetes were age-adjusted, using the direct method to the projected 2000 U.S. Census population estimates [26].

For the primary analyses, the means and proportions were calculated by sex, age, and race/ethnicity strata, adjusting for age. We used multivariable linear regression, adjusting for age and race/ethnicity to examine trends by regarding the 2-year survey cycle as a continuous variable, and so regression coefficients (β) could be reported per one year. Trends in A1C concentrations were estimated using log-transformed values because of the skewed distribution for A1C. We used the survey procedures in SAS version 9.3 software (SAS Institute Inc) to account for the complex design. For all of the analyses, the statistical hypotheses were tested using an α level of 0.05 based on a 2-tailed test.

Results

Analytic Sample

A total of 5536 adults aged 20 years or older who reported a diagnosis of diabetes participated in an NHANES examination from 2005 to 2018 and were eligible for inclusion in the present study (weighted mean age, 60.2 years, standard error [SE] ± 0.27 ; female, 50.1%) (Table 1). Because the data relating to apo

B, non-HDL cholesterol level, LDL cholesterol, and/ or A1C were missing for some participants; therefore, the sample sizes vary slightly among these outcomes. LDL levels were calculated using the Friedewald formula. To calculate LDL cholesterol values by the formula, participants were excluded for whom total cholesterol or HDL cholesterol data were unavailable or whose triglyceride levels exceeded 400 mg/dL. More than half of the subjects had been told that they had diabetes for the first time when they were aged 40 to 59 years, while nearly one in five of the subjects was between aged 20 and 39 years.

Table 1

Sociodemographic characteristics of US adults with diabetes by NHANES survey cycle, 2005 to 2018

Characteristics	No. of Participants (Weighted %) *							
	2005– 2006	2007– 2008	2009– 2010	2011– 2012	2013– 2014	2015– 2016	2017– 2018	Overall
	(n = 513)	(n = 782)	(n = 775)	(n = 720)	(n = 764)	(n = 881)	(n = 921)	(n = 5356)
Age group, y †								
20–39	36 (10.2)	54 (9.3)	40 (7.1)	44 (6.5)	40 (6.5)	66 (9.3)	40 (7.1)	320 (7.9)
40–59	152 (39.7)	226 (39.4)	221 (36.6)	230 (38.8)	256 (39.1)	257 (33.4)	238 (33.6)	1580 (36.8)
≥ 60	313 (50.2)	483 (51.4)	497 (56.3)	441 (54.7)	451 (54.3)	545 (57.3)	626 (59.3)	3356 (55.3)
Sex								
Male	243 (43.9)	384 (47.7)	389 (50.4)	367 (49.1)	367 (48.4)	459 (53.2)	491 (53.4)	2700 (49.9)
Female	270 (56.1)	398 (52.3)	386 (49.6)	353 (50.9)	397 (51.6)	422 (46.8)	430 (46.6)	2656 (50.1)
Race/ethnicity								
Mexican American	113 (8.6)	133 (7.7)	164 (9.6)	76 (8.2)	131 (9.9)	201 (11.3)	142 (9.3)	960 (9.4)
Non-Hispanic white	193 (61.5)	309 (63.8)	284 (58.8)	224 (59.3)	277 (62.5)	232 (57.7)	307 (61.6)	1826 (60.7)
Non-Hispanic black	171 (18.4)	229 (18.1)	190 (17.2)	253 (16.9)	195 (14.7)	205 (14.3)	211 (11.3)	1454 (15.4)
Other‡	36 (11.5)	111 (10.4)	137 (14.4)	167 (15.6)	161 (12.8)	243 (16.8)	261 (17.8)	1116 (14.6)
Education level								
Less than high school	198 (27.1)	332 (30.4)	303 (29.4)	254 (25.5)	229 (20.9)	282 (20.6)	241 (15.8)	1839 (23.4)
High school	128 (27.3)	180 (25.9)	152 (20.1)	154 (26.3)	181 (24.2)	189 (21.1)	212 (29.4)	1196 (24.9)
More than high school	187 (45.6)	270 (43.7)	320 (50.5)	312 (48.2)	354 (54.9)	410 (58.3)	468 (54.8)	2321 (51.7)
Ratio of family income to poverty, %								

Characteristics	No. of Participants (Weighted %) *							
< 1.3	160 (21.6)	247 (23.1)	247 (22.7)	279 (29.4)	274 (26.7)	305 (24.1)	228 (17.3)	1740 (23.4)
1.3–3.0	173 (34.2)	254 (32.4)	238 (31.2)	205 (31.9)	199 (25.7)	264 (28.8)	308 (31.5)	1641 (30.5)
> 3.0	144 (38.3)	190 (34.6)	210 (37.8)	155 (31.7)	237 (41.7)	215 (37.3)	267 (41.3)	2418 (37.8)
Missing	36 (5.8)	91 (10.0)	80 (8.3)	81 (7.0)	54 (5.9)	97 (9.7)	118 (9.9)	557 (8.2)
Take diabetic pills								
Yes	354 (69.0)	589 (72.2)	580 (73.6)	527 (73.5)	536 (70.1)	617 (72.6)	685 (72.0)	3888 (71.9)
No	156 (34.5)	187 (27.1)	191 (25.9)	192 (26.4)	226 (29.8)	259 (27.1)	236 (28.0)	1447 (27.8)
Age first told								
20–39	91 (24.2)	120 (21.6)	99 (16.5)	124 (18.3)	135 (19.7)	165 (19.7)	135 (17.6)	869 (19.4)
40–59	223 (48.0)	328 (49.9)	358 (52.8)	327 (55.3)	366 (55.8)	403 (54.9)	463 (56.2)	2468 (53.7)
≥ 60	144 (27.7)	232 (28.6)	225 (30.6)	188 (26.5)	182 (24.5)	201 (25.4)	212 (26.2)	1384 (26.8)
Abbreviations: NHANES, National Health and Nutrition Examination Survey.								
* Percentages were adjusted for NHANES survey weights.								
† Numbers may not sum to the total number of participants because of missing data.								
‡ “Other” includes race/ethnicity other than Mexican American, non-Hispanic white, and non-Hispanic black, including multiracial.								

Table 2

Age-adjusted percentage of achieving apo B < 90 mg/dL among U.S. adults with diabetes aged ≥ 20 years, 2005–2016

	2005– 2006	2007– 2008	2009– 2010	2011– 2012	2013– 2014	2015– 2016	<i>P</i> for linear trend
	apo B < 90 mg/dL	apo B < 90 mg/dL	apo B < 90 mg/dL	apo B < 90 mg/dL	apo B < 90 mg/dL	apo B < 90 mg/dL	
Total	28.8 (20.0 to 37.6)	51.0 (32.9 to 69.1)	53.7 (37.1 to 70.3)	42.4 (30.6 to 54.2)	50.1 (36.4 to 63.9)	47.3 (33.7 to 60.8)	0.184
Age group, y							
20–39	10.1 (-12.2 to 32.5)	44.9 (4.5 to 85.2)	55.5 (19.7 to 91.3)	38.3 (12.5 to 64.0)	48.5 (20.2 to 76.8)	43.5 (16.4 to 70.7)	0.044
40–59	40.3 (29.8 to 50.8)	46.5 (31.8 to 61.3)	47.4 (31.3 to 63.6)	33.2 (22.3 to 44.1)	47.9 (38.4 to 57.3)	44.8 (32.7 to 56.9)	0.490
≥ 60	42.8 (34.9 to 50.7)	68.9 (62.7 to 75.0)	60.7 (54.9 to 66.4)	64.3 (50.6 to 77.9)	56.5 (50.1 to 62.9)	57.6 (47.2 to 67.9)	0.559
Sex							
Male	39.5 (21.1 to 57.9)	65.3 (47.8 to 82.7)	61.2 (43.3 to 79.1)	57.0 (43.7 to 70.2)	75.5 (70.9 to 80.1)	51.1 (28.1 to 74.2)	0.995
Female	21.7 (14.8 to 28.6)	34.8 (25.9 to 43.7)	31.5 (22.4 to 40.5)	29.5 (18.3 to 40.7)	41.1 (23.6 to 58.6)	43.2 (29.3 to 57.2)	0.044
Race/ethnicity							
Mexican American	20.6 (8.8 to 32.3)	63.9 (58.2 to 69.7)	51.0 (36.1 to 65.9)	21.5 (11.5 to 31.6)	30.5 (18.2 to 42.8)	42.4 (24.8 to 60.0)	0.173
Non-Hispanic white	28.2 (18.3 to 38.0)	57.4 (32.0 to 82.8)	58.8 (37.3 to 80.2)	40.1 (20.2 to 60.1)	49.6 (30.9 to 68.3)	48.4 (20.4 to 76.5)	0.936
Non-Hispanic black	28.2 (20.9 to 35.5)	40.2 (21.1 to 59.3)	30.0 (22.2 to 37.9)	51.1 (29.6 to 72.6)	71.9 (62.1 to 81.7)	44.0 (27.0 to 60.9)	0.038
Other	39.2 (6.3 to 72.1)	58.2 (41.4 to 75.0)	46.9 (18.4 to 75.4)	44.8 (20.9 to 68.7)	72.5 (63.0 to 82.0)	70.8 (62.7 to 79.0)	0.217
apo B, apolipoprotein B.							

Age-Adjusted Trends in Mean Levels of Apo B, Non-HDL cholesterol, and LDL Cholesterol

Supplementary Table 1 shows the age-adjusted mean levels of apo B and trend in mean levels of apo B. The age-adjusted mean levels of apo B for all adults with diabetes declined from 102 mg/dL (95% CI, 95 to 110 mg/dL) in 2005–2006 to 95 mg/dL (95% CI, 88 to 102 mg/dL) in 2015–2016 (β , -0.90 mg/dL [95% CI, -1.90 to 0.10 mg/dL] per year), but the linear trend did not reach statistical significance ($P = 0.077$ for linear trend) (**Supplementary Table 1 and Fig. 1**). From 2005 to 2018, a significant linear decreasing trend was observed in the age-adjusted mean non-HDL cholesterol level for all adults with diabetes (from 143 mg/dL (95% CI, 135 to 151) mg/dL in 2005–2006 to 136 mg/dL (95% CI, 127 to 144) mg/dL in 2017–2018) ($P = 0.004$) (**Supplementary Table 2 and Fig. 1**). The age-adjusted mean LDL cholesterol level for all adults with diabetes was not significantly improved from 107 mg/dL (95% CI, 96 to 117) mg/dL in 2005–2006 to 105 mg/dL (95% CI, 98 to 112) mg/dL in 2015–2016 ($P = 0.138$ for linear trend) (**Supplementary Table 4 and Fig. 1**).

In subgroup analyses by age, sex and race/ethnicity, significant declining trends in age-adjusted mean levels of apo B and non-HDL cholesterol were generally observed for patients aged 60 years or older, for Mexican Americans, and for non-Hispanic blacks. Also, a declining trend in mean non-HDL cholesterol level was observed for women ($P = .014$). No statistically significant declining trends in the age-adjusted mean LDL cholesterol levels were observed for both men and women, all race/ethnicity subgroups, and every age group except for patients aged 60 years or older.

Age-adjusted Trends In Geometric Mean Concentrations Of A1c

From 2005 to 2018, the age-adjusted geometric mean concentration of A1C was not significantly reduced for all adults with diabetes from 7.3% (95% CI, 6.9–7.7%) in 2005–2006 to 7.1% (95% CI, 6.7–7.5%) in 2017–2018, and the linear trend was not statistically significant ($P = 0.202$ for linear trend) (**Supplementary Table 6**). Also, there is no statistically significant change in the age-adjusted geometric mean concentrations of A1C for every age group, both men and women, and all race/ethnicity subgroups.

Age-Adjusted Trends in the Percentage of Participants Meeting Apo B, Non-HDL Cholesterol, and LDL Cholesterol Goals

The age-adjusted percentage of participants with diagnosed diabetes who had a level of apo B < 90 mg/dL increased from 28.8% (95% CI, 20.0–37.6%) in 2005–2006 to 47.3% (95% CI, 33.7–60.8%) in 2015–2016, but the linear trend was not statistically significant ($P = 0.184$) (**Table 2 and Supplementary Fig. 1**). From 2005 to 2018, there was an increasing linear trend in the age-adjusted percentage of patients who achieved the non-HDL cholesterol goal of levels < 130 mg/dL for all adults with diabetes, from 42.4% (95% CI, 31.2–53.7%) in 2005–2006 to 54.2% (95% CI, 45.7–62.7%) in 2017–2018, but the trend were also not significant ($P = 0.098$) (**Supplementary Table 3 and Supplementary Fig. 1**). From 2005 to 2016, the age-adjusted

proportion of patients who achieved the LDL cholesterol goal of levels < 100 mg/dL did not significantly increase in all adults with diabetes ($P = 0.379$) (**Supplementary Table 4 and Supplementary Fig. 1**).

In subgroup analyses by age, sex and race/ethnicity, a linear increase was observed in the age-adjusted proportion of all adults with diabetes who achieved the apo B goal of levels < 90 mg/dL or the non-HDL Cholesterol goal of levels < 130 mg/dL among women but not among men. The increase in the age-adjusted proportion of all adults with diabetes who had the apo B goal of levels < 90 mg/dL was observed for patients aged 20 to 39 years ($P = 0.044$) and for non-Hispanic blacks ($P = 0.038$). The age-adjusted proportion of patients meeting the non-HDL cholesterol goal of levels < 130 mg/dL increased significantly for those aged 60 years or older ($P = 0.031$), and for Mexican Americans ($P = 0.029$). The age-adjusted proportion of patients meeting the LDL cholesterol goal of levels < 100 mg/dL did not significantly increase for every age group, both sexes, and every racial/ethnic group.

Furthermore, the age-adjusted percentage of participants with diagnosed diabetes who met the more aggressive apo B goal of levels < 80 mg/dL was 33.6% (95% CI, 18.7–48.5%) in 2015–2016. The age-adjusted percentage of patients who achieved the more aggressive LDL cholesterol goal of levels < 70 mg/dl was 10.9% (95% CI, 7.7–14.1%) in 2015–2016. The age-adjusted percentage of patients who achieved the more aggressive non-HDL cholesterol goal of levels < 100 mg/dl was 23.0% (95% CI, 14.7–31.4%) in 2017–2018.

Age-Adjusted Trends in the Percentage of Participants Achieving Glycemic Goals or Showing Poor Glycemic Control

From 2005 to 2018, the age-adjusted percentage of adults with diabetes who achieved the A1C target concentration of < 7% increase from 53.1% (95% CI, 44.7–61.5%) in 2005–2006 to 55.3% (95% CI, 41.8–68.8%) in 2017–2018, but the change was not statistically significant ($P = 0.275$) (**Table 3 and Supplementary Fig. 2**). Also, the age-adjusted percentage of participants showing poor glycemic control for adults with diabetes improved slightly from 23.2% (95% CI, 15.9–30.4%) in 2005–2006 to 16.1% (95% CI, 9.4–22.7%) in 2017–2018, but there were no statistically significance ($P = 0.996$) (**Supplementary Table 7 and Supplementary Fig. 2**).

Table 3

Age-adjusted percentage of achieving hemoglobin A1c concentration < 7% among U.S. adults with diabetes aged ≥ 20 years, 2005–2018

	2005– 2006	2007– 2008	2009– 2010	2011– 2012	2013– 2014	2015– 2016	2017– 2018	<i>P</i> for linear trend
	A1C < 7%	A1C < 7%	A1C < 7%	A1C < 7%	A1C < 7%	A1C < 7%	A1C < 7%	
Total	53.1 (44.7 to 61.5)	53.4 (42.5 to 64.3)	51.0 (39.0 to 63.0)	51.5 (41.4 to 61.7)	49.1 (40.9 to 57.4)	57.6 (51.7 to 63.4)	55.3 (41.8 to 68.8)	0.275
Age group, y								
20–39	46.7 (27.8 to 65.7)	52.6 (30.3 to 75.0)	48.5 (24.2 to 72.7)	48.2 (22.9 to 73.5)	50.1 (33.0 to 67.3)	70.3 (60.7 to 80.0)	62.6 (35.4 to 89.7)	0.136
40–59	52.4 (39.5 to 65.2)	53.8 (43.2 to 64.5)	49.9 (36.7 to 63.0)	50.8 (40.1 to 61.5)	43.3 (34.4 to 52.1)	44.4 (33.8 to 55.1)	46.4 (34.2 to 58.6)	0.113
≥ 60	65.2 (53.8 to 76.6)	54.1 (46.5 to 61.6)	57.2 (50.2 to 64.2)	58.4 (49.3 to 67.4)	56.8 (47.2 to 66.4)	56.8 (48.7 to 64.8)	56.9 (47.3 to 66.5)	0.423
Sex								
Male	47.8 (34.8 to 60.8)	49.4 (36.3 to 62.5)	45.4 (29.2 to 61.6)	49.4 (36.1 to 62.7)	50.4 (38.1 to 62.6)	48.6 (35.6 to 61.7)	54.6 (40.2 to 69.0)	0.124
Female	57.7 (47.1 to 68.2)	56.4 (44.4 to 68.4)	58.3 (42.8 to 73.7)	53.5 (37.3 to 69.8)	49.9 (37.0 to 62.7)	63.9 (58.7 to 69.1)	58.8 (42.3 to 75.3)	0.838
Race/ethnicity								
Mexican American	54.8 (35.1 to 74.5)	48.4 (32.9 to 63.8)	44.7 (23.8 to 65.5)	26.2 (16.1 to 36.2)	48.5 (30.2 to 66.8)	33.1 (19.1 to 47.1)	50.5 (32.8 to 68.2)	0.824
Non-Hispanic white	49.3 (36.0 to 62.7)	52.2 (37.5 to 67.0)	53.6 (37.7 to 69.5)	59.2 (42.5 to 75.8)	47.6 (36.9 to 58.3)	70.8 (61.9 to 79.6)	55.3 (31.3 to 79.4)	0.414
Non-Hispanic black	43.9 (32.5 to 55.2)	54.1 (36.5 to 71.8)	46.9 (26.2 to 67.7)	50.1 (31.8 to 68.4)	52.0 (39.5 to 64.5)	46.6 (39.4 to 53.8)	50.6 (35.4 to 65.7)	0.961
Other	64.6 (36.6 to 92.5)	76.0 (65.5 to 86.5)	46.8 (24.6 to 69.1)	46.5 (33.3 to 59.7)	51.8 (32.1 to 71.5)	65.7 (56.0 to 75.4)	70.4 (65.3 to 75.4)	0.351

In the subgroup analyses, the proportion of patients who achieved the A1C goals of < 7% was not statistically significant changes over the 14-year period for every age group, both men and women, and all

race/ethnicity subgroups. Similar trends over this 14-year period were observed in the proportion of those who achieved the A1C of > 9%.

Age-Adjusted Trends in the Percentage of Participants Achieving All Three Lipids Goals and the Glycemic Goal

Among all adults with diagnosed diabetes, the percentages of patients who achieved the apo B goal of < 90 mg/dL, the non-HDL cholesterol goal of < 130 mg/dl, the LDL cholesterol goal of < 100 mg/dl, and the A1C target of < 7% increased from 15.2% (95% CI, 7.4–23.0%) in 2005–2006 to 30.6% (95% CI, 18.1–43.1%) in 2015–2016, but the trend was not reach statistically significant ($P < 0.396$) (**Supplementary Table 8 and Supplementary Fig. 2**).

In the subgroup analyses, Mexican Americans and non-Hispanic blacks were less likely to meet all four goals than non-Hispanic whites, and men were less likely to achieve all four goals than women.

The proportion of all diabetic adults with at least one optimal level—either for apo B, non-HDL cholesterol, LDL cholesterol, or A1C—increased from 66.9% (95% CI, 55.4–78.5%) in 2005–2006 to 73.3% (95% CI, 65.4–81.1%) in 2015–2016, but the trend was also not statistically significant ($P < 0.996$).

We also found that the percentages of patients who were achieving all of the more aggressive goals (i.e., apo B < 80 mg/dL, non-HDL cholesterol < 100 mg/dl, LDL cholesterol < 70 mg/dl, and A1C < 7%) was 3.9% (95% CI, 1.8–5.9%) in 2015–2016.

Discussion

Among all adults with diabetes, significant declining trend in age-adjusted mean level of non-HDL cholesterol was observed from 2005 to 2018. No statistically significant decline in age-adjusted mean level of apo B was found from 2005 to 2016. Furthermore, the age-adjusted mean LDL cholesterol level and geometric mean A1C concentrations did not improve significantly. Significant declining trends in age-adjusted mean levels of apo B, non-HDL cholesterol, and LDL cholesterol were overall observed for patients aged 60 years or older. The increases observed in the percentages of patients who achieved the apo B goal of level < 90 mg/dL, the non-HDL cholesterol goal of level < 130 mg/dL, or the LDL cholesterol goal of level < 100 mg/dL but were not statistically significant. In addition, the age-adjusted percentage of those achieving the A1C target concentration of < 7% did not increase significantly from 2005 to 2018, and the age-adjusted percentage of adults with diabetes showing poor glycemic control (A1c > 9%) remained high (16.1%) in 2017–2018. The percentages of patients achieving all four goals was 30.6% (95% CI, 18.1–43.1%) in 2015–2016, and, compared with non-Hispanic whites, Mexican Americans and non-Hispanic blacks were less likely to achieve all four goals.

Some studies have indicated that individuals with diagnosed diabetes may alter their lifestyles to improve their glycemic control and lipid profiles through such steps as healthy eating, smoking cessation, weight management, and/or physical activity. In a previous study using a national sample of subjects with diabetes, most participants tried increase their physical activity, lose weight, and change their diet [27].

There is evidence that diet for reducing cholesterol concentration achieved a greater reduction in serum cholesterol concentration [28]. We found that the observed declines in the mean apo B levels were of relatively smaller magnitude and the mean non-HDL cholesterol levels declined significantly. The percentages of patients achieving the apo B goal of levels < 90 mg/dL, the non-HDL cholesterol goal of levels < 130 mg/dl, the LDL cholesterol goal of levels < 100 mg/dl, and the A1C target of concentrations < 7% increased from 15.2% in 2005–2006 to 30.6% in 2015–2016, although the results were not statistically significant. Several studies have shown that increased physical activity can prevent or delay the development of type 2 diabetes [29] and improve cardiovascular risk factors in persons with type 2 diabetes [30].

The increasing use of lipid-lowering medications may also have contributed to the observed improvements in patients' lipid profiles. A cohort study found that statin use has increased substantially among US adults in recent years, from 17.9% in 2002–2003 to 27.8% in 2012–2013 [31].

Some studies have found significant improvements in measures of 10-year coronary heart disease risk among adults with diabetes over the past decade [32] and reduced morbidity and mortality associated with atherosclerotic cardiovascular disease [33]. Because hypertriglyceridemia is commonly seen in individuals with diabetes, the measurement and monitoring of apolipoprotein levels have been recommended as a guide for lipid-lowering therapies [34, 35]. There is substantial evidence that, compared with LDL cholesterol, apo B is a superior marker of vascular disease, and non-HDL cholesterol is a better predictor of risk for cardiovascular disease. In the present study, we also estimated the percentages of patients who were achieving the more aggressive all lipid goals and found that few achieved the more aggressive target of lipid control. At the end of the study period, 33.6% had achieved the more aggressive apo B goal of levels < 80 mg/dL, 23.0% had achieved the more aggressive non-HDL cholesterol goal of levels < 100 mg/dl, and only 10.9% had achieved the more aggressive LDL cholesterol goal of levels < 70 mg/dl. Among patients who achieved the A1C target of concentration < 7%, only 3.9% achieved the more aggressive all three lipid goals just listed. Nonpharmacological correlates of serum lipid levels and use of medications may jointly influence the observed patterns.

For adults with diabetes, adherence to self-care recommendations naturally promotes overall diabetes control. A cross-sectional study of 476 type 2 diabetic patients found that good adherence to an appropriate diet was associated with a favorable serum lipid profile and that a relatively low BMI was associated with physical activity [36]. The present study showed that, compared with those of patients aged 60 years or older, the mean apo B, non-HDL cholesterol, and LDL cholesterol levels of young and middle-aged adults was higher and the proportion of patients who achieved the goals for apo B, non-HDL cholesterol, or LDL cholesterol was smaller. This result may indicate that older adults with diabetes tend to adhere better to lifestyle and/or medication therapy than younger adults. Also, it could be that older adults have been exposed more to the healthcare system than younger patients, and thus the cumulative effect of health interventions in older versus younger patients led to this particular result.

Moreover, the target for most adults with diabetes is an A1C concentration of less than 7%. Our findings indicated that Mexican Americans and non-Hispanic blacks tended to have higher A1C concentrations and

poorer glycemic control than non-Hispanic whites and were less likely to meet all four goals. The racial disparities in glycemic control are consistent with previous findings [19, 37]. Future research should explore factors that contributed to reducing the ethnic disparities and focus on interventions to eliminate disparities.

In the present study, poor glycemic control was more common in younger than older subjects and in men than in women. Previous studies also found that younger individuals were less likely to achieve their A1C goals [13]. Diabetes medication adherence has been associated with reduced A1C concentrations in the middle-aged to elderly type 2 diabetes patients [36]. Women may tend to demonstrate better adherence than men; a cross-sectional study of 6729 subjects found that the proportion of male diabetes patients adhering to regular treatment was low [38].

Strengths And Limitations

The strengths of this study include the use of a nationally representative sample, which makes it possible to draw generalizations about the U.S. adult population. The measurement of levels of apolipoprotein B, total cholesterol, HDL cholesterol, triglyceride and A1C were based on the criteria of the CDC's standardization program. This study also had some limitations. To begin with, individuals with diagnosed diabetes in the sample were the small number. Owing to limitations in power, subgroup analyses must be interpreted with caution. Participants in the fasting sample was limited, which lead to LDL estimates unreliable. Further, our analysis of trends in lipids levels and A1C concentration among adults was based on 6 or 7 NHANES survey periods, so data from future surveys are needed to further confirm our results.

Conclusions

This study found a significant declining trend in mean non-HDL cholesterol level for all adults with diabetes from 2005 to 2018 and no statistically significant decline in level of apo B from 2005 to 2016. The observed increases in the proportion of the diabetes patients who were achieving the apo B, non-HDL cholesterol, LDL cholesterol, or A1C goals were also not statistically significant. The proportion of poor glycemic control for adults with diagnosed diabetes remained high in 2017–2018. A significant opportunity exists to improve glycemic and lipid profiles further and, thus, to decrease diabetes-related complications.

Abbreviations

A1C: hemoglobin A1c; apo B: apolipoprotein B; CDC: Centers for Disease Control and Prevention; CI: confidence interval; HR: hazards ratio; LDL: low-density lipoprotein; NCHS: National Center for Health Statistics; NHANES: National Health and Nutrition Examination Survey; non-HDL: non-high-density lipoprotein; OR: odds ratio.

Declarations

Ethics approval and consent to participate

The study protocol of NHANES was approved by the research ethics review board of the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). Written informed consent was provided from all of the participants in the NHANES.

Consent for publication

Not applicable.

Availability of data and materials

Use of a Public Data.

Competing interests

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this study.

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Authors' contributions

XW and DZ contributed to the study concept and design, collected and analyzed data, contributed to discussion, and wrote, reviewed, and edited the manuscript. YD and YBS designed the study, collected and analyzed data, and contributed to discussion. LGS contributed to discussion and reviewed and edited the manuscript. All authors approved of the final version.

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Figures

Figure 1

Age-adjusted in mean levels of apo B, non-HDL cholesterol, and LDL cholesterol among U.S. adults with diabetes aged ≥ 20 years by NHANES survey cycle from 2005-2006 to 2017-2018. NHANES indicates National Health and Nutrition Examination Survey. Data were adjusted for NHANES survey weights to be nationally representative.

Figure 1

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