Supplemental Material

Data S1.

Supplemental Methods

Methods used to determine piece-wise spline models to model nonlinear trends

We used the midpoint of each 2-year survey time as a continuous variable to test for linear trends using linear or logistic regression models. If the overall model fit improved after adding a quadratic term of survey time based on the likelihood ratio test, we then modeled the trends using spline models to facilitate the interpretations of a nonlinear relationship between time and outcome measures in a clinical context. The number of inflection points was determined based on the flexible and informed Bayesian regression analysis with multiple change points (the R package [mcp]). The test results favored use of one inflection point for trends analysis.

Multiple imputation

We first examined missing data patterns for our primary analysis. Among 50,928 study participants included, 3,141 (6.2%) participants had missing values for total cholesterol and 3,143 (6.2%) participants had missing HDL-C values. Among 24,651 participants who had fasting blood samples, 1,666 (6.8%) participants had missing values for both triglycerides and LDL-C. To account for data missingness and reduce bias derived from non-response, we conducted multiple imputation under the assumption that data were missing at random. The multiple imputation model included 8 variables, 4 of key outcomes (total cholesterol, triglycerides, LDL-C, and HDL-C) and 4 variables with no missing information as predictors of missing values (age, sex, survey weights, and a unique identifier combing both primary survey unit and stratum of NHANES).[36] Examination weights were used for total cholesterol and HDL-C and fasting weights were used for triglycerides and LDL-C. Multivariate normal distribution was used with five imputed datasets. Triglycerides were log-transformed before imputation and then transformed back before analysis. Stata, version 15.1 (StataCorp, College Station, TX) and code mi set, mi register, and mi impute were used to conduct multiple imputation.

Table S1. Age-Sex-Adjusted Point Estimates (95% Confidence Intervals) in Lipid Levels after Multiple Imputation

Mean Lipid Levels, mg/dL	NHANES 2017-2018	NHANES 2017-March 2020 Pre-Pandemic
Total cholesterol	188.6 (185.5-191.7)	186.5 (184.1-188.8)
Triglycerides	91.5 (88.4-94.6)	90.6 (87.9-93.4)
LDL-C	111.6 (108.9-114.4)	110.5 (108.1-112.9)
HDL-C	53.5 (52.6-54.3)	53.5 (52.8-54.2)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NHANES, National Health and Nutrition Examination Survey.

Table S2. Age-sex-adjusted proportions (95% confidence intervals) of cholesterol screening by race and ethnicity, NHANES 1999-2018

Cholesterol Screening	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	2015-2016	2017-2018	*P* for linear trend	*P* for non-linear trend
Ever Screened, %												
Non-Hispanic Asian	-	-	-	-	-	-	74.2 (70.1, 77.8)	78.5 (73.8, 82.5)	79.7 (74.8, 83.9)	80.5 (75.6, 84.6)	.056	
Hispanic	59.8 (54.8, 64.6)	57.4 (52.4, 62.3)	59.3 (53.8, 64.7)	57.3 (53.6, 60.9)	60.9 (58.5, 63.3)	59.9 (57.4, 62.3)	64.1 (60.9, 67.2)	70.0 (67.5, 72.4)	70.7 (67.2, 74.1)	72.6 (67.4, 77.3)		.003
Non-Hispanic Black	60.2 (56.2, 64.0)	64.8 (60.0, 69.3)	66.7 (64.8, 68.5)	69.6 (66.6, 72.4)	72.3 (69.9, 74.6)	68.9 (64.8, 72.7)	75.2 (70.1, 79.7)	75.3 (72.0, 78.4)	78.8 (75.9, 81.5)	76.8 (74.0, 79.4)	<.001	
Non-Hispanic White	74.9 (70.1, 79.1)	73.7 (71.7, 75.6)	74.7 (71.4, 77.7)	77.3 (75.1, 79.3)	75.8 (72.7, 78.6)	75.6 (73.6, 77.5)	76.9 (75.1, 78.7)	80.2 (78.3, 82.0)	83.4 (80.9, 85.6)	84.2 (81.0, 86.9)		.014
P for group difference	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001		<.001
Screened within 5 Years, %												
Non-Hispanic Asian	-	-	-	-	-	-	68.3 (65.0, 71.5)	73.1 (68.0, 77.6)	74.1 (68.0, 79.3)	75.0 (69.5, 79.8)	.052	
Hispanic	56.5 (51.3, 61.6)	51.1 (45.7, 56.4)	52.6 (47.1, 58.0)	52.0 (47.9, 56.0)	55.6 (52.8, 58.4)	54.8 (52.4, 57.2)	58.8 (55.4, 62.2)	62.7 (59.8, 65.4)	64.2 (60.2, 68.0)	65.8 (60.7, 70.5)	<.001	
Non-Hispanic Black	55.8 (51.5, 60.0)	57.7 (52.8, 62.4)	62.4 (59.0, 65.6)	62.3 (59.4, 65.1)	66.8 (63.9, 69.5)	64.9 (61.4, 68.3)	70.2 (64.9, 75.0)	71.5 (67.8, 74.8)	71.9 (68.9, 74.7)	70.7 (67.2, 73.9)	<.001	

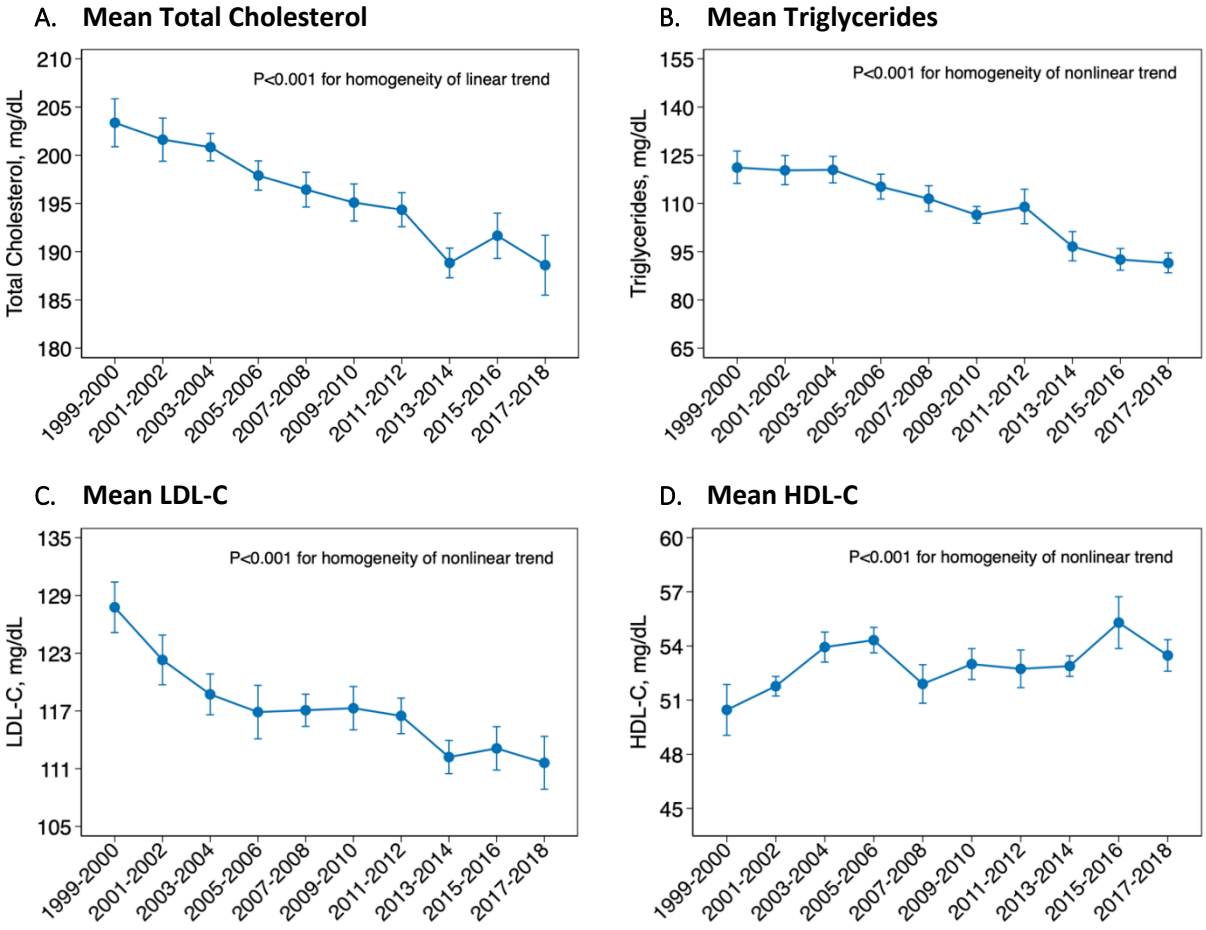
Non-Hispanic White	66.4 (61.9, 70.7)	64.5 (61.8, 67.1)	66.6 (62.7, 70.3)	68.2 (65.4, 71.0)	67.8 (64.7, 70.6)	68.7 (66.8, 70.6)	70.1 (67.5, 72.7)	73.5 (71.5, 75.4)	74.2 (71.1, 77.1)	74.1 (70.9, 77.2)	<.001	
P for group difference	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	
Non-linear trend was tested by adding a quadratic term of survey time into regression models. If not significant, linear trend was tested.												

Table S3. Age-sex-adjusted mean (95% confidence intervals) lipid levels by race and ethnicity, NHANES 1999-2018

Cholesterol Screening	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	2015-2016	2017-March 2020	*P* for linear trend	*P* for non-linear trend
Total Cholesterol, mg/dL												
Non-Hispanic Asian	-	-	-	-	-	-	191.0 (187.6, 194.5)	190.4 (187.1, 193.7)	190.5 (186.4, 194.6)	191.7 (186.3, 197.1)	.92	
Hispanic	201.9 (198.2, 205.6)	201.9 (196.0, 207.8)	201.6 (198.6, 204.7)	202.2 (199.3, 205.2)	198.4 (196.1, 200.8)	196.8 (194.4, 199.2)	195.1 (192.4, 197.9)	192.6 (189.5, 195.7)	190.3 (187.9, 192.8)	188.6 (184.0, 193.1)	<.001	
Non-Hispanic Black	196.0 (193.6, 198.4)	198.8 (194.0, 203.6)	196.3 (193.3, 199.3)	189.8 (187.4, 192.1)	192.4 (189.4, 195.5)	190.0 (187.8, 192.2)	188.9 (186.7, 191.2)	182.6 (179.9, 185.3)	185.1 (181.4, 188.8)	185.3 (181.7, 189.0)	<.001	
Non-Hispanic White	204.7 (201.7, 207.7)	201.5 (199.0, 204.0)	201.8 (200.1, 203.5)	198.4 (196.7, 200.2)	196.8 (194.7, 198.8)	195.5 (193.1, 197.9)	195.2 (192.8, 197.7)	189.3 (187.4, 191.1)	192.7 (190.2, 195.1)	188.3 (184.3, 192.4)	<.001	
P for group difference	.18	.89	.92	.045	.17	.50	<.001	.003	.002	.003	<.001	
Triglycerides, mg/dL												
Non-Hispanic Asian	-	-	-	-	-	-	106.9 (101.1, 113.0)	96.2 (88.8, 104.1)	93.9 (87.5, 100.9)	97.6 (88.4, 107.9)	.084	
Hispanic	128.1 (120.8, 135.8)	130.7 (119.3, 143.3)	129.1 (121.9, 136.8)	127.2 (118.7, 136.2)	122.2 (117.3, 127.4)	122.5 (115.9, 129.6)	117.2 (111.9, 122.7)	108.7 (102.5, 115.4)	101.9 (98.1, 105.8)	103.2 (97.3, 109.6)		.004
Non-Hispanic Black	91.7 (88.7, 94.8)	94.4 (85.9, 103.7)	97.6 (92.4, 103.1)	94.7 (89.9, 99.6)	85.5 (77.7, 94.1)	89.6 (84.6, 95.0)	85.0 (80.1, 90.3)	75.6 (70.1, 81.5)	71.3 (66.5, 76.4)	70.9 (68.0, 73.9)		<.001
Non-Hispanic White	124.1 (118.1, 130.5)	122.6 (117.8, 127.7)	122.2 (116.6, 128.0)	117.2 (112.0, 122.5)	113.5 (108.7, 118.5)	106.3 (103.1, 109.5)	112.5 (106.9, 118.4)	98.1 (93.5, 102.9)	93.9 (90.0, 98.0)	91.0 (86.4, 95.9)		.006

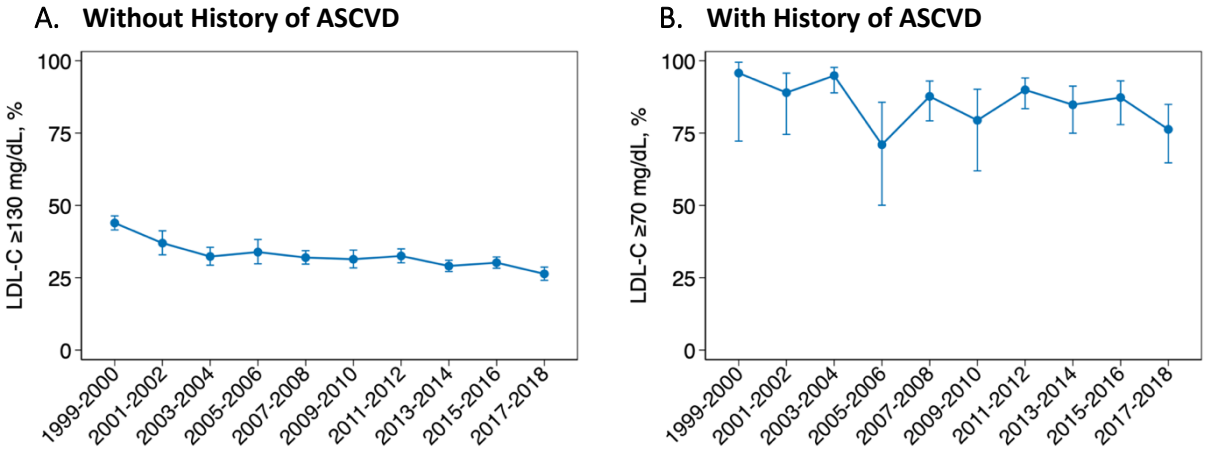
P for group difference	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001		<.001
LDL-C, mg/dL												
Non-Hispanic Asian	-	-	-	-	-	-	115.7 (110.0, 121.5)	109.6 (104.7, 114.6)	113.0 (107.7, 118.3)	114.6 (106.8, 122.5)	.98	
Hispanic	126.9 (124.2, 129.7)	118.3 (114.3, 122.2)	118.5 (114.5, 122.4)	122.5 (118.2, 126.8)	120.1 (117.4, 122.9)	119.3 (116.1, 122.4)	118.9 (116.2, 121.6)	115.4 (110.7, 120.2)	113.6 (111.7, 115.6)	113.4 (108.5, 118.3)	<.001	
Non-Hispanic Black	121.4 (117.3, 125.5)	121.2 (116.8, 125.6)	115.5 (112.2, 118.8)	112.1 (108.5, 115.8)	113.8 (109.6, 118.0)	116.2 (113.5, 118.9)	112.8 (109.6, 115.9)	109.2 (105.5, 112.8)	108.9 (103.4, 114.5)	110.8 (106.8, 114.8)	<.001	
Non-Hispanic White	128.6 (125.1, 132.1)	123.0 (120.0, 126.1)	119.9 (117.3, 122.6)	117.4 (114.1, 120.7)	117.2 (115.4, 119.0)	116.6 (113.3, 120.0)	116.4 (114.0, 118.8)	112.9 (110.8, 115.0)	113.3 (110.4, 116.2)	110.6 (107.0, 114.1)	<.001	
P for group difference	.041	.167	.091	.016	.036	.471	.098	.243	.512	.752		<.001
HDL-C, mg/dL												
Non-Hispanic Asian	-	-	-	-	-	-	53.5 (52.5, 54.6)	53.5 (52.2, 54.7)	54.7 (53.4, 56.1)	53.7 (52.4, 55.0)	.56	
Hispanic	47.5 (46.5, 48.5)	49.1 (48.3, 50.0)	51.1 (50.0, 52.3)	51.2 (49.8, 52.6)	49.1 (48.2, 50.0)	50.3 (48.8, 51.7)	49.6 (48.8, 50.5)	50.0 (49.1, 50.9)	50.1 (48.6, 51.6)	50.2 (49.4, 51.1)		.035
Non-Hispanic Black	53.4 (51.9, 54.9)	54.3 (53.0, 55.6)	56.4 (55.0, 57.9)	57.0 (56.2, 57.9)	56.5 (55.5, 57.5)	54.9 (53.5, 56.2)	54.5 (53.5, 55.4)	54.7 (53.6, 55.8)	58.0 (57.0, 59.1)	56.3 (55.4, 57.3)	.01	
Non-Hispanic White	50.5 (48.6, 52.4)	51.8 (51.0, 52.6)	54.1 (53.0, 55.1)	54.4 (53.6, 55.2)	51.8 (50.2, 53.3)	53.4 (52.2, 54.5)	53.0 (51.7, 54.3)	53.3 (52.6, 54.1)	56.4 (54.9, 57.9)	53.9 (52.7, 55.2)	<.001	
P for group difference	.016	.002	<.001	<.001	.010	.013	<.001	<.001	<.001	<.001		<.001
Non-linear trend was tested by adding a quadratic term of survey time into regression models. If not significant, linear trend was tested.												

Figure S1. Age-Sex-Adjusted Trends in Lipid Levels in US Adults after Multiple Imputation, NHANES 1999-2018



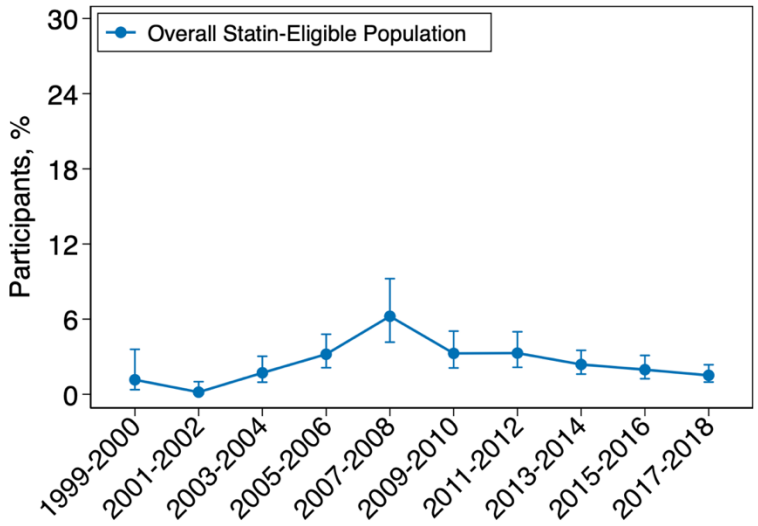
Error bars indicate 95% confidence intervals. Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NHANES, National Health and Nutrition Examination Survey.

Figure S2. Trends in prevalence of high LDL-C in US adults, NHANES 1999-2018



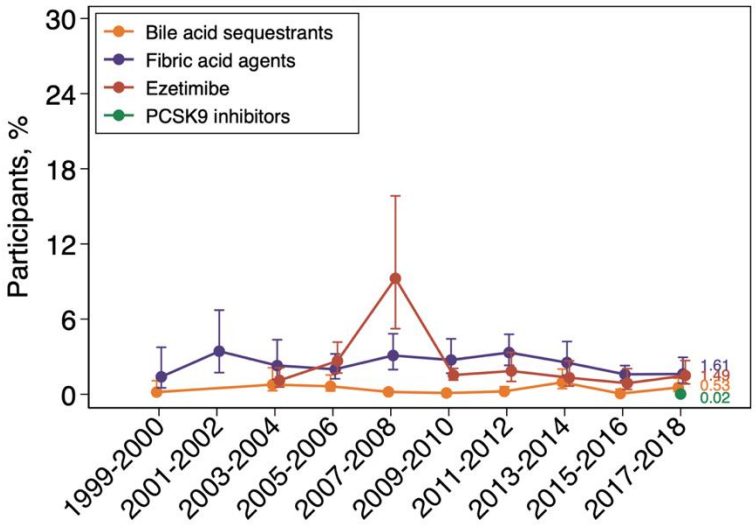
ASCVD was defined as a self-reported history of coronary heart disease, heart attack, stroke, or angina. Error bars indicate 95% confidence intervals. Abbreviations: ASCVD, atherosclerotic cardiovascular disease; NHANES, National Health and Nutrition Examination Survey.

Figure S3. Trends in use of statin and another lipid-lowering drug in statin-eligible US adults, NHANES 1999-2018



Error bars indicate 95% confidence intervals.

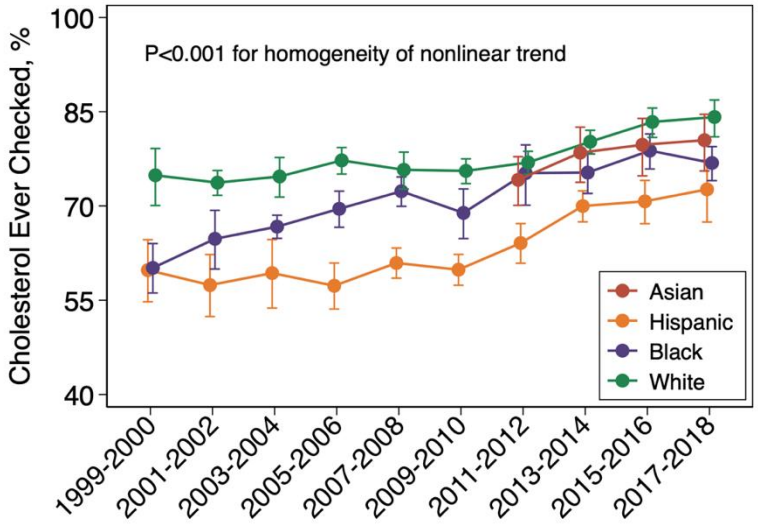
Figure S4. Trends in non-statin use in statin-eligible US adults by drug class, NHANES 1999-2018



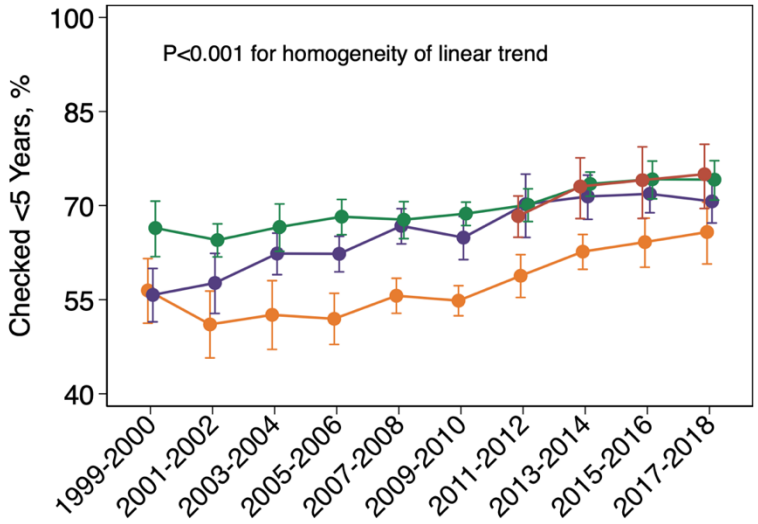
Error bars indicate 95% confidence intervals.

Figure S5. Trends in cholesterol screening in US adults by race and ethnicity, NHANES 1999-2018

A. **Cholesterol Ever Screened**

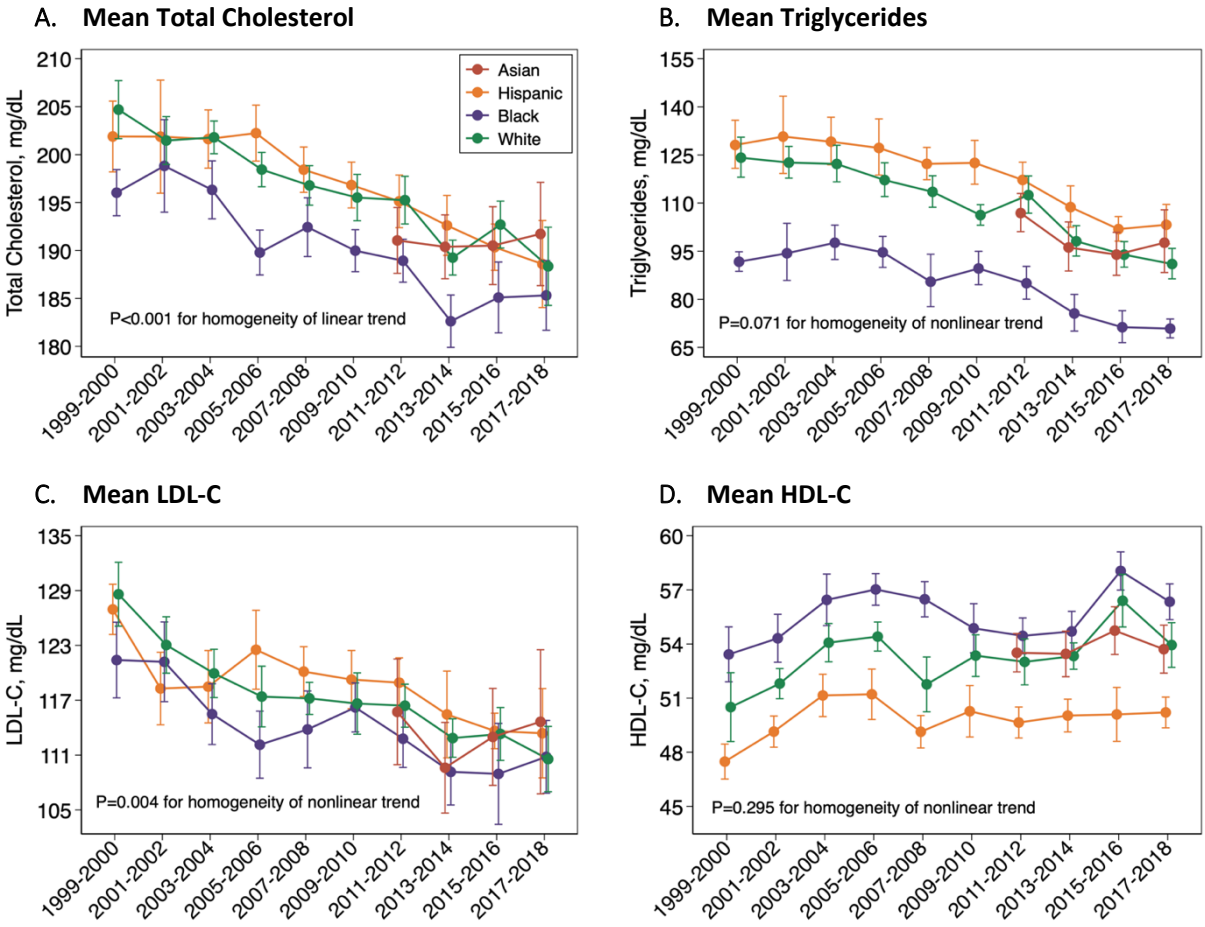


B. **Cholesterol Screened within 5 Years**



Error bars indicate 95% confidence intervals. Abbreviations: NHANES, National Health and Nutrition Examination Survey.

Figure S6. Trends in lipid levels in US adults by race and ethnicity, NHANES 1999-2018



Error bars indicate 95% confidence intervals. Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. Abbreviations: NHANES, National Health and Nutrition Examination Survey.