Published in final edited form as:

Ann Intern Med. 2017 June 20; 166(12): 876–882. doi:10.7326/M16-2052.

Prevalence of Elevated Cardiovascular Risks in Young Adults: A Cross-sectional Analysis of National Health and Nutrition Examination Surveys

Krishna K. Patel, MD¹, Glen B. Taksler, PhD², Bo Hu, PhD³, and Michael B. Rothberg, MD, MPH²

¹Department of Cardiology, University of Missouri-Kansas City, Kansas City, Missouri

²Center for Value-Based Care Research, Medicine Institute, Cleveland Clinic, Cleveland, Ohio

³Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio

Abstract

Background—The 2013 American College of Cardiology/American Heart Association (ACC/AHA) cholesterol management guidelines recommend screening lipids in all adults aged >20 years to identify individuals with elevated atherosclerotic cardiovascular disease (ASCVD) risk. Statins can be considered for elevated ten-year risk (> 5%) or LDL cholesterol ≥ 190 mg/dL.

Objective—To describe the prevalence of elevated ASCVD risk among non-diabetic adults aged <50 years.

Design—Cross-sectional

Settings—National Health and Nutrition Examination Survey (NHANES), 1999–2000 through 2011–2012.

Participants—Adults aged 30–49 years without known ASCVD or diabetes.

Corresponding Author: Dr. Krishna K. Patel, MD, Department of Cardiology, Mid America Heart Institute, Saint Luke's Hospital of Kansas City, University of Missouri-Kansas City, 4401 Wornall, 9th Floor/CV Research, Kansas City, Missouri 64111, patelkris@umkc.edu, Phone: 216-776-2196.

Current mailing addresses of the authors: Krishna K Patel: Department of Cardiology, Mid America Heart Institute, Saint Lukes Hospital of Kansas City, University of Missouri-Kansas City, 4401 Wornall, SLNI 5603, Kansas City, Missouri 64111, patelkris@umkc.edu Phone: 216-776-2196; Glenn B. Taksler, Bo Hu and Michael B. Rothberg: Center for Value-based Care Research, Medicine Institute, Cleveland Clinic, 9500 Euclid Avenue, Desk G-10, Cleveland, Ohio 44195

Reproducible Research Statement

Protocol: not available

Statistical Code: Available to interested readers working on related analyses by contacting Dr. Krishna Patel at patelkris@umkc.edu

Data: available for download at http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm

AUTHOR CONTRIBUTIONS

Krishna K Patel: study design, data acquisition, data analysis, data interpretation and drafting of manuscript.

Glen B Taksler: data analysis, data interpretation and revision for intellectual content.

Bo Hu: data analysis, data interpretation and revision for intellectual content.

Michael B Rothberg: study concept, design, supervision, data interpretation, drafting of manuscript and revision for intellectual content.

Authors Krishna K. Patel and Michael B. Rothberg had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Measurements—Ten-year ASCVD risk was estimated using the 2013 ACC/AHA ASCVD risk calculator. Participants were subdivided by age, gender and history of smoking and hypertension. The percentage of adults with 10-year ASCVD risk > 5% and adults with LDL 190mg/dL in each subgroup were estimated. Low prevalence subgroups were defined as those in which we could rule out a prevalence of elevated cardiovascular risk of more than 1% (upper 95% confidence bound for the prevalence was 1%).

Results—Overall, 9,608 NHANES participants representing 67.9 million adults were included, with approximately half (47.12%, representing 32 million adults) in low prevalence subgroups. In the absence of smoking or hypertension, 0.09% (95% CI: 0.02%, 0.35%) of adult men aged <40 years and 0.04% (95% CI: 0.0%, 0.26%) of women under 50 years had an elevated risk. Among other subgroups, 0% – 75.9% of participants had an elevated risk. Overall, 2.9% (95% CI: 2.3%, 3.5%) had LDL cholesterol 190 mg/dL.

Limitations—No information available regarding cardiovascular outcomes.

Conclusions—In the absence of risk factors, the prevalence of increased ASCVD risk is low among women below the age of 50 years and men below 40 years.

Primary funding source—None

Introduction

Elevated cholesterol levels have been long known to be a strong risk factor for cardiovascular disease, myocardial infarction and stroke.(1–3) Screening for dyslipidemia can identify asymptomatic individuals at risk of developing atherosclerotic cardiovascular disease (ASCVD), allowing them to pursue lifestyle interventions or medical therapy. The 2013 American College of Cardiology/American Heart Association (ACC/AHA) cholesterol management guidelines recommend checking a first lipid panel for all adults above 20 years of age and repeating it every 4–6 years to identify individuals at a high-risk for atherosclerotic cardiovascular disease.(4) For primary prevention, the high risk population has been defined as adults with a 10-year risk of ASCVD above 7.5% or a lifetime risk above 30%, as well as those with very high LDL cholesterol levels or primary genetic hyperlipidemias, for whom models may not accurately reflect risk.(5) In contrast, the US Preventive Services Task Force (USPSTF) 2008 guideline recommends starting screening at 35 years for men or 45 years for women unless they have one or more traditional risk factors for atherosclerosis.(6) One reason for this discrepancy is the lack of clinical trial evidence to support cholesterol screening for primary prevention in the young adult population.(7)

Because total and HDL cholesterol levels are required to calculate ASCVD risk, the decision to institute primary prevention requires a screening cholesterol level. However, based on the underlying distribution of cholesterol in the population, it may be possible to identify patients who, based on their lack of other risk factors, are very unlikely to have an ASCVD risk high enough to warrant treatment and therefore are unlikely to benefit from cholesterol screening. To help decide between the approach of the AHA/ACC and that of the USPSTF, we aimed to describe the prevalence of elevated ASCVD risk in young adults by extrapolating the Pooled Cohort risk prediction equation to a nationally representative sample of adults 30–49 years of age. We identify the prevalence of elevated 10-year ASCVD

risk in different subgroups based on age, sex, smoking and the presence of hypertension. We also describe the prevalence of very high LDL cholesterol levels identified by routine lipid screening in this population.

Methods

Study Design and Participants

This study involved a cross-sectional analysis of adults aged 30 to 49 years who participated in the examination component of the National Health and Nutrition Examination Survey (NHANES).⁽⁸⁾ NHANES is conducted by the Centers of Disease Control (CDC)/National Center for Health Statistics (NCHS) and utilizes a complex, multi-stage, clustered probability sampling method of non-institutionalized US civilians to provide nationally representative estimates. NHANES data from 1999–2000 through 2011–2012 were analyzed; 2013–2014 sample was excluded because prescription drug data are not yet available. Participants with missing data and those with self-reported stroke, coronary artery disease, other cardiovascular disease (congestive heart failure, myocardial infarction, or angina) and diabetes were excluded. In our primary analysis we also excluded participants who were already taking a statin or any other lipid-lowering drug at the time of the visit when lipid profiles were drawn, because their results would not represent their true lipid levels, but included them in a sensitivity analysis. All participants provided written informed consent. The study protocol was approved by NCHS Institutional Review Board.⁽⁸⁾

Covariates—We used the following self-reported information: age, gender, race, smoking status and treatment with anti-hypertensive medications. Systolic blood pressure (SBP), Total cholesterol (TC) and High Density Lipoprotein cholesterol (HDL-C) measurements were available and included for all examined participants, but only the morning session participants had fasting Low Density Lipoprotein cholesterol (LDL-C) and triglyceride (TG) measurements. Although standardized laboratory protocol was employed to perform all lipid analyses, there were some changes in the laboratories, methods and instruments used to make these measurements across the study period.⁽⁹⁾ The Friedewald equation was used to calculate LDL-C levels for participants with TG level ≥ 400 mg/dL. Hypertension was defined as blood pressure $\geq 140/90$ mmHg [average of ≥ 3 readings] as measured at the NHANES examination, self-report that a doctor/health professional diagnosed hypertension on at least 2 different occasions, and/or current receipt of an anti-hypertensive medication. Family history of premature ASCVD (a first degree relative with heart attack before age 50 years) was self-reported for participants in the NHANES surveys beginning in 2005–06.

Definition of Elevated Cardiovascular Risk and Low Prevalence Groups—The purpose of our study was to identify subgroups for which screening for cholesterol would not provide actionable information. Therefore, we defined elevated cardiovascular risk as a 10-year ASCVD risk of greater than 5%—the lowest ASCVD risk at which statin therapy might be considered according to the guideline—using the 2013 ACC/AHA ASCVD pooled cohort equation.⁽⁵⁾ Because the equation may overestimate risk in low-risk patients,^(10–12) our choice represents a conservative threshold which might be more sensitive in younger age groups.⁽¹³⁾ We then created subgroups of participants by age, gender and history of

smoking and hypertension, and calculated the prevalence of elevated cardiovascular risk within each subgroup. We found no studies to inform a threshold prevalence of risk that would justify screening. We defined low prevalence subgroups as those groups in which we could rule out a prevalence of elevated cardiovascular risk of more than 1% (i.e. upper bound of the 95% confidence limit was 1%). This seemed a reasonably conservative estimate, since the number-needed-to-treat with statins to prevent one fatal or non-fatal CHD event in primary prevention is approximately 56.(14) At a prevalence of <1%, the number-needed-to-screen to prevent one cardiovascular event would be at least 100 times as great (i.e. more than 5,600).

Definition of elevated LDL-cholesterol level—To identify participants with LDL cholesterol high enough to directly qualify for statin treatment, we estimated the proportion of adults with LDL cholesterol levels of at least 190 mg/dL, which is the recommended screening threshold for identifying patients with familial hyperlipidemia.(15) To evaluate the utility of targeted screening of young adults for familial hyperlipidemia in patients with self-reported family history of premature ASCVD, we assessed whether the proportion of participants with LDL cholesterol levels of at least 190 mg/dL differ by presence of a positive family history of premature ASCVD. (15)

Statistical analysis—We generated nationally representative prevalence estimates after incorporating appropriate 2-year or 4-year sample weights (for the main analysis) or morning fasting subsample weights (for the LDL analyses), which accounted for the complex multistage probability sampling design of the NHANES survey. (16) We used appropriate morning fasting subsample weights for the subgroup of participants with data available on both LDL-cholesterol and family history (2005–06 to 2011–12), according to NCHS instructions.(16) Standard errors were obtained using first-order Taylor series linearization.(17) Confidence intervals were constructed using logit transformation for subgroups with positive numbers of individuals at elevated risk, or an exact binomial method for subgroups with 0 individuals at elevated risk.(9, 18) These prevalence estimates were intended to represent the civilian, non-institutionalized US population aged ≥20 years. We compared differences in the proportion of participants with elevated LDL-cholesterol levels between those with vs. without family history of premature ASCVD, using Pearson’s chi-square test and appropriate sample weights to account for the survey design. In sensitivity analyses, we included participants who were taking lipid-lowering drugs and estimated their lipid profiles (and corresponding 10-year ASCVD risk) in absence of these medications. Specifically, based on prior studies, we assumed that lipid-lowering drugs lowered TC by 21.18% and raised HDL-C by 3.57%.(19) All analyses accounted for complex survey design and appropriate subgroup weighting. NHANES analyses were performed using the “svy” prefix to the “prop” command (with the “subpop” option for subpopulations, such as individuals with LDL ≥190 mg/dL) and the “over” option for between-group comparisons, (such as males vs. females) in STATA/MP 13.1 (College Station, TX).

Primary funding source—None.

Results

Out of 10,862 NHANES participants between the ages of 30 and 49 years, 1,003 were excluded for having diabetes (n=735) or ASCVD or its equivalents (stroke n=116, coronary artery disease n=72, other cardiovascular disease n=223) or missing data (n=197) and 251 were excluded because they were already on statin therapy at the time of their visit. Our final population consisted of 9,608 adults representing 67.9 million US adults. The characteristics of the population are described in Table 1.

Overall, 9.1% (95% CI: 8.3%, 9.9%) of adults had a 10-year estimated ASCVD risk greater than 5% (i.e. elevated risk). Table 2 shows the percentage of patients with elevated cardiovascular risk in subgroups of young adults divided by age, gender and risk factors of smoking and hypertension. The percentage of elevated-risk adults varied substantially (from 0% to 75.9%) by age, gender, smoking and hypertension status. In the absence of smoking or hypertension, adult men under the age of 40 and adult women under 50 years constituted the low prevalence subgroups (represented by shaded cells).

Of non-smoking, non-hypertensive women under the age of 50 years, 0.04% (95% CI: 0.0%, 0.26%) had an elevated cardiovascular risk. Of non-smoking, non-hypertensive men under the age of 40 years, 0.09% (95% CI: 0.02%, 0.35%) had an elevated cardiovascular risk. About half of the young adult population aged 30 – 49 years (47.12%) was in the low prevalence subgroups. Of the few adults who had elevated risk in these low prevalence groups, all had a risk between 5.0% and 7.4% (Table 3). Non-smoking adults with hypertension had an intermediate prevalence of elevated risk (ranging from 0 – 29.3% depending on age and sex). At every age, smokers had the highest prevalence of elevated cardiovascular risk. Sensitivity analyses including patients who were taking lipid-lowering drugs demonstrated similar results and identified the same low prevalence subgroups, except that the 95% confidence interval for women without risk factors aged 45–49 crossed 1% (Appendix Table 1).

LDL cholesterol levels of at least 190 mg/dL were present in 2.9% (95% CI: 2.3%, 3.5%) of young adults in NHANES. Of these, 1.7% (95% CI: 1.1%, 2.4%) of adults in the low prevalence groups had an LDL level of at least 190 mg/dL. Based on our sample of 2562 young adults aged 30–49 years who had both an LDL level and family history available, 11.4% (95% CI: 9.9%, 12.9%) had a family history of premature ASCVD. The proportion of adults with LDL cholesterol levels ≥ 190 mg/dL in both men and women did not differ by family history (Table 4).

Discussion

In this cross-sectional analysis of a nationally representative population, we found that the prevalence of elevated cardiovascular risk was low in normotensive, non-smoking females younger than 50 years (~22.2 million women) and males younger than 40 years (~9.8 million men). This group constituted one-half of the population aged 30–49 years, representing 32 million people. Only 1.7% (95% CI: 1.1%, 2.4%) of these low risk adults had an LDL level of at least 190 mg/dL, and they were no more likely to report a family

history of premature heart attack than those with lower LDL levels. Given the low prevalence of patients at elevated cardiovascular risk, our findings would support the targeted approach of the USPSTF over the more general screening of the AHA/ACC. However, given the observed risk distribution, screening for adults without risk factors could begin at age 40 for men and 50 for women.

The primary purpose of checking serum cholesterol in healthy patients is to identify those who would benefit from lipid-lowering therapy. This includes patients with an elevated risk of developing cardiac events based on the Pooled Cohort equation, as well as patients whose cholesterol levels are extremely high, indicating probable familial hypercholesterolemia. It is thought that the latter group has an accelerated risk of developing ASCVD,(20) and initiation of statin treatment helps reduce their risk early in the course of treatment.(21, 22) The 2013 AHA/ACC guidelines recommend treatment with a statin for patients with a 10-year risk of 7.5%, although statin treatment can be considered even at a risk of 5%.(5) In contrast, the USPSTF recommends treating only those patients with a 10-year risk of 10% and at least one cardiac risk factor.(23) We examined the probability of patients having a risk >5% to decide a priori whether testing made sense. As the data are sparse regarding risk prediction for the young adult population,(4, 7) we extrapolated the Pooled Cohort equations to this subgroup. For young patients without risk factors, we found that very few (<0.5%) had a calculated risk >5%. Moreover, this threshold may be overly aggressive, as several studies have found that the Pooled Cohort equation overestimates risk in low risk patients (11, 12) especially women.(10) Using a higher threshold (e.g. 7.5%) would make screening these groups even less efficient, as there were not patients in these subgroups with a risk >7.5%. Some might argue that patients with risk levels in the 1–4% range should be made aware of their risk so that they can undertake therapeutic lifestyle changes. However, there is no evidence that showing patients they are at low risk will prompt positive behavior changes and could even have the opposite effect. If the patients chose not to make lifestyle changes, it would be unfortunate, since a healthy lifestyle, including proper diet and exercise, is beneficial for preventing both cardiovascular and non-cardiovascular diseases, and can be recommended for all, regardless of cholesterol level.(24)

Another argument for testing and potentially treating younger patients has to do with lifetime cardiac risk.(5) Although ten-year risks may be low, preventing atherosclerosis could prevent disease 20, 30 or even 40 years in the future. However, there are no trials to inform such a strategy, and treatment at later years is so effective (25) that it is unclear how much additional benefit would result from initiating treatment early.(7) Moreover, treatment with statins may increase risk for diabetes,(26) which could outweigh cardiovascular benefits in younger patients. More research is needed before statins can be recommended based on lifetime risk alone.

Lastly, universal screening could be used to identify people with familial hyperlipidemia, who experience early disease (20) and might benefit from early treatment with statins. A recent NHANES analysis estimated the prevalence of familial hypercholesterolemia as 1 in 250 using clinical criteria, with prevalence rising with increasing age and obesity.(27) However, only a very small fraction of patients with LDL cholesterol 190 mg/dL have a mutation for familial hyperlipidemia.(28) Identifying a broader population as potentially

having familial hyperlipidemia could lead to more testing or potentially to overtreatment. In the present study, 2.9% of the population had LDL cholesterol values of at least 190 mg/dL, 90% of whom presumably do not have familial hypercholesterolemia. Moreover, such patients were not more likely to have a family history of premature ASCVD.

The distribution of ASCVD risk in adults below the age of 50 years has been studied by others. In a study using earlier data from NHANES, 95.7% of adults aged 30–39 years and 89.7% of adults aged 40–49 years had a 10-year risk <10% based on Framingham risk equation in the absence of ASCVD or risk equivalents.(29) Because this study preceded the 2013 guidelines, they did not address the 5% threshold. In a more recent analysis of risk distribution using the Pooled Cohort equations in NHANES, 86.6% of adults (78.1% of men and 95.2% of women) aged 40–50 years had a risk of <5%. This analysis considered all adults, including those with ASCVD, diabetes and other risk equivalents.(4) More importantly, these studies did not examine the risk distribution of different subgroups based on individual risk factors like smoking and hypertension. This is important because one could argue that if 4% of the population between 30 and 39 years of age has a risk of >10%, repeated screening of this age group is reasonable. Our study reveals that the overwhelming majority of those at high risk are smokers and, to a lesser degree, non-smokers with hypertension.

Our study has a number of strengths. We examined the prevalence of increased cardiovascular risk in a nationally representative sample of healthy young adults. By choosing risk factors that are readily available (age, sex, smoking status and hypertension) we could easily identify groups of patients for screening. In our sample, approximately one-third of tests among men and two-thirds among women under age 50 years could be avoided with minimal effect. At the same time, our study emphasizes the importance of smoking as a risk factor in younger patients. Almost all smokers had at least a 5.5% chance of having elevated risk, regardless of age or sex. This mirrors a recent finding that for patients under 50, smoking was associated with 8 times the risk of myocardial infarction faced by non-smokers.(30)

Our study also has several limitations intrinsic to the NHANES study design. Risk factors and family history were self-reported by participants. LDL cholesterol values were present only in the morning examination subsample. We also excluded patients who were taking a statin or other lipid-lowering drug at their initial visit. Sensitivity analyses including those participants produced similar results. We measured predicted risk, not actual cardiovascular outcomes. However, because treatment under the ACC/AHA guidelines as well as the USPSTF guidelines are based on predicted risk, our analysis reveals the likelihood that screened patients would be eligible for treatment, which is strongly associated with reduced events.(31) Finally, we used a conservative risk cut-off of 5% to identify a population which might benefit from therapy directed towards lowering cholesterol levels. Some have argued that the ASCVD overestimates risk.(10, 11) Using a different calculator or a higher cutoff would make screening the low-prevalence population even less attractive.

Conclusion

In a nationally representative adult population, the prevalence of elevated cardiovascular risk in absence of smoking or hypertension in men under the age of 40 years and women under the age of 50 years is low. There might be utility in one time screening of the entire population to identify patients with very high LDL cholesterol levels suggesting possible genetic hyperlipidemias. Targeted screening of young adults with a family history of premature heart disease is not more likely to identify patients with very high LDL cholesterol levels.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Disclosures:

Dr. Patel is supported by the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number T32HL110837. Dr. Taksler is supported by the National Center for Advancing Translational Sciences (NIH) under Award Number KL2TR000440. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Appendix

Appendix Table 1

Prevalence of elevated ASCVD risk in US Adults, aged 30–49 by risk factors; including participants on lipid-lowering medications: NHANES 1999 – 2012 (n=9,859)

Age group (years)	Male			Female		
	Smokers	Non-smokers, Hypertension	Non-smokers, No Hypertension	Smokers	Non-smokers, Hypertension	Non-smokers, No Hypertension
30–34	9.3% (6.3%–13.5%)	2.8% (0.6%–11.7%)	0.0% (0.0%–0.5% [*])	19.5% (14.0%–26.5%)	0.0% (0.0%–0.4% [*])	0.0% (0.0%–0.4% [*])
35–39	26.4% (21.9%–31.4%)	2.4% (1.3%–4.5%)	0.2% (0.1%–0.7%)	14.8% (11.0%–19.6%)	0.7% (0.2%–2.7%)	0.1% (0.0%–1.0%)
40–44	54.5% (48.1%–59.8%)	8.9% (5.7%–13.5%)	1.2% (0.4%–3.1%)	14.1% (9.8%–19.8%)	1.8% (0.8%–3.8%)	0.0% (0.0%–0.5% [*])
45–49	76.9% (70.2%–82.4%)	30.3% (24.0%–37.5%)	6.0% (3.9%–9.2%)	19.3% (14.5%–25.3%)	4.9% (2.4%–9.6%)	0.3% (0.0%–1.8%)

[#] Using 2013 ACC/AHA Pooled Cohort Equations ASCVD risk calculator.

^{*} Confidence intervals estimated using exact binomial methods.

Brackets show 95% confidence intervals for that subgroup.

Shaded cells represent low prevalence subgroups.

Appendix Table 2

Proportion of NHANES adults with LDL cholesterol ≥ 190 mg/dL, by risk factor (aged 30–49 years).*

Male, %			Female, %		
Smokers	Non-smokers, Hypertension	Non-smokers, No hypertension	Smokers	Non-smokers, Hypertension	Non-smokers, No hypertension
5.3% (3.2%–7.3%)	3.4% (1.1%–5.6%)	2.7% (1.4%–4.1%)	4.0% (1.9%–6.2%)	3.5% (0.9%–6.1%)	1.3% (0.7%–2.0%)

* Among 4,275 eligible NHANES participants in the morning examination subsample.

References

1. Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events: final report of the pooling project. The pooling project research group. *J Chronic Dis.* 1978 Apr; 31(4):201–306. [PubMed: 681498]
2. Kannel WB, Dawber TR, Friedman GD, Glennon WE, McNamara PM. Risk Factors in Coronary Heart Disease. An Evaluation of Several Serum Lipids as Predictors of Coronary Heart Disease; the Framingham Study. *Ann Intern Med.* 1964 Nov;61:888–99. [PubMed: 14233810]
3. Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. *BMJ.* 2000 Oct 21; 321(7267):983–6. [PubMed: 11039962]
4. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB Sr, Gibbons R, Greenland P, Lackland DT, Levy D, O'Donnell CJ, Robinson JG, Schwartz JS, Shero ST, Smith SC Jr, Sorlie P, Stone NJ, Wilson PW. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014 Jul 1; 63(25 Pt B):2935–59. [PubMed: 24239921]
5. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PW. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014 Jul 1; 63(25 Pt B):2889–934. [PubMed: 24239923]
6. United States Preventive Services Task Force. Lipid disorders in adults (cholesterol, dyslipidemia): screening. Jun. 2008 Available from: <http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lipid-disorders-in-adults-cholesterol-dyslipidemia-screening>. Last accessed February 20, 2017
7. Chou R, Dana T, Blazina I, Daeges M, Bougatsos C, Jeanne TL. Screening for Dyslipidemia in Younger Adults: A Systematic Review for the U.S. Preventive Services Task Force Screening for Dyslipidemia in Younger Adults. *Annals of Internal Medicine.* 2016; N/A(N/A):N/A–N/A.
8. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. Available from: <http://www.cdc.gov/nchs/nhanes/index.htm>. Last accessed February 20, 2017
9. Carroll MD, Kit BK, Lacher DA, Shero ST, Mussolino ME. Trends in lipids and lipoproteins in US adults, 1988–2010. *JAMA.* 2012 Oct 17; 308(15):1545–54. [PubMed: 23073951]
10. Cook NR, Ridker PM. Further insight into the cardiovascular risk calculator: the roles of statins, revascularizations, and underascertainment in the Women's Health Study. *JAMA Intern Med.* 2014 Dec; 174(12):1964–71. [PubMed: 25285455]
11. Ridker PM, Cook NR. Statins: new American guidelines for prevention of cardiovascular disease. *Lancet.* 2013 Nov 30; 382(9907):1762–5. [PubMed: 24268611]
12. DeFilippis AP, Young R, McEvoy JW, Michos ED, Sandfort V, Kronmal RA, McClelland RL, Blaha MJ. Risk score overestimation: the impact of individual cardiovascular risk factors and preventive therapies on the performance of the American Heart Association-American College of

Cardiology-Atherosclerotic Cardiovascular Disease risk score in a modern multi-ethnic cohort. *Eur Heart J*. 2016 Jul 19.

13. Navar-Boggan AM, Peterson ED, D'Agostino RB Sr, Pencina MJ, Sniderman AD. Using age- and sex-specific risk thresholds to guide statin therapy: one size may not fit all. *J Am Coll Cardiol*. 2015 Apr 28; 65(16):1633–9. [PubMed: 25743624]
14. Taylor F, Huffman MD, Macedo AF, Moore TH, Burke M, Davey Smith G, Ward K, Ebrahim S. Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2013; (1):CD004816. [PubMed: 23440795]
15. Gidding SS, Champagne MA, de Ferranti SD, Defesche J, Ito MK, Knowles JW, McCrindle B, Raal F, Rader D, Santos RD, Lopes-Virella M, Watts GF, Wierzbicki AS. The Agenda for Familial Hypercholesterolemia: A Scientific Statement From the American Heart Association. *Circulation*. 2015 Dec 1; 132(22):2167–92. [PubMed: 26510694]
16. Centers for Disease Control and Prevention. Continuous NHANES Web tutorials. Specifying weighting parameters. Available from: <https://www.cdc.gov/nchs/tutorials/nhanes/SurveyDesign/Weighting/intro.htm>. Last accessed February 20, 2017
17. STATA Survey Data Reference Manual, Release 13. Available from: <http://www.stata.com/manuals13/svy.pdf>. Last accessed February 20, 2017
18. Wolter, K. Introduction to Variance Estimation [Electronic]. Springer-Verlag; New York: 2007.
19. Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhalra N, Peto R, Barnes EH, Keech A, Simes J, Collins R. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010 Nov 13; 376(9753):1670–81. [PubMed: 21067804]
20. Perak AM, Ning H, de Ferranti SD, Gooding HC, Wilkins JT, Lloyd-Jones DM. Long-Term Risk of Atherosclerotic Cardiovascular Disease in US Adults With the Familial Hypercholesterolemia Phenotype. *Circulation*. 2016 Jul 5; 134(1):9–19. [PubMed: 27358432]
21. Versmissen J, Oosterveer DM, Yazdanpanah M, Defesche JC, Basart DC, Liem AH, Heeringa J, Witteman JC, Lansberg PJ, Kastelein JJ, Sijbrands EJ. Efficacy of statins in familial hypercholesterolaemia: a long term cohort study. *BMJ*. 2008; 337:a2423. [PubMed: 19001495]
22. Besseling J, Hovingh GK, Huijgen R, Kastelein JJ, Hutten BA. Statins in Familial Hypercholesterolemia: Consequences for Coronary Artery Disease and All-Cause Mortality. *J Am Coll Cardiol*. 2016 Jul 19; 68(3):252–60. [PubMed: 27417002]
23. United States Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: Us preventive services task force recommendation statement. *JAMA*. 2016; 316(19):1997–2007. [PubMed: 27838723]
24. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, Lee IM, Lichtenstein AH, Loria CM, Millen BE, Nonas CA, Sacks FM, Smith JSC, Svetkey LP, Wadden TA, Yanovski SZ. 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2014; 63(25_PA)
25. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet*. 2005 Oct 8; 366(9493):1267–78. [PubMed: 16214597]
26. Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, Seshasai SR, McMurray JJ, Freeman DJ, Jukema JW, Macfarlane PW, Packard CJ, Stott DJ, Westendorp RG, Shepherd J, Davis BR, Pressel SL, Marchioli R, Marfisi RM, Maggioni AP, Tavazzi L, Tognoni G, Kjekshus J, Pedersen TR, Cook TJ, Gotto AM, Clearfield MB, Downs JR, Nakamura H, Ohashi Y, Mizuno K, Ray KK, Ford I. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet*. 2010 Feb 27; 375(9716):735–42. [PubMed: 20167359]
27. de Ferranti SD, Rodday AM, Mendelson MM, Wong JB, Leslie LK, Sheldrick RC. Prevalence of Familial Hypercholesterolemia in the 1999 to 2012 United States National Health and Nutrition Examination Surveys (NHANES). *Circulation*. 2016 Mar 15; 133(11):1067–72. [PubMed: 26976914]

28. Khera AV, Won HH, Peloso GM, Lawson KS, Bartz TM, Deng X, van Leeuwen EM, Natarajan P, Emdin CA, Bick AG, Morrison AC, Brody JA, Gupta N, Nomura A, Kessler T, Duga S, Bis JC, van Duijn CM, Cupples LA, Psaty B, Rader DJ, Danesh J, Schunkert H, McPherson R, Farrall M, Watkins H, Lander E, Wilson JG, Correa A, Boerwinkle E, Merlini PA, Ardisino D, Saleheen D, Gabriel S, Kathiresan S. Diagnostic Yield and Clinical Utility of Sequencing Familial Hypercholesterolemia Genes in Patients With Severe Hypercholesterolemia. *J Am Coll Cardiol*. 2016 Jun 7; 67(22):2578–89. [PubMed: 27050191]
29. Ford ES, Giles WH, Mokdad AH. The distribution of 10-Year risk for coronary heart disease among US adults: findings from the National Health and Nutrition Examination Survey III. *J Am Coll Cardiol*. 2004 May 19; 43(10):1791–6. [PubMed: 15145101]
30. Lloyd A, Steele L, Fotheringham J, Iqbal J, Sultan A, Teare MD, Grech ED. Pronounced increase in risk of acute ST-segment elevation myocardial infarction in younger smokers. *Heart*. 2016 Nov 29.2016
31. Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, Voysey M, Gray A, Collins R, Baigent C. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet*. 2012 Aug 11; 380(9841):581–90. [PubMed: 22607822]

Table 1

Characteristics of the study population

Characteristic	Mean (SD) or % (95% confidence intervals) (N=9,608)
Age, years	39.4 (4.7)
Male gender, %	48.9% (47.8% – 50.1%)
Race, Caucasian, %	68.3% (65.9% – 70.8%)
African American, %	10.7% (9.5% – 12.0%)
Hispanic, %	15.1% (13.6% – 16.7%)
Other, %	5.8% (4.6% – 7.1%)
Hypertension, %	18.6% (17.4% – 19.8%)
Systolic Blood Pressure, mmHg	117.00 (11.3)
Diastolic Blood Pressure, mmHg	73.11 (8.7)
Current smokers, %	26.6% (25.3% – 28.0%)
Total Cholesterol, mg/dL	201.0(32.4)
High Density Lipoprotein Cholesterol, mg/dL	52.5 (13.2)
Low Density Lipoprotein Cholesterol, mg/dL	120.4 (27.4) [†]
10 year ASCVD risk [#] , %	1.9 (2.2)
Low Density Lipoprotein Cholesterol 160–189 mg/dL, %	69.5% (8.4% – 10.6%) [†]
Low Density Lipoprotein Cholesterol ≥ 190 mg/dL, %	2.9% (2.3% – 3.5%) [†]

[†] Among 4,275 eligible NHANES participants in the morning examination subsample.

[#] Risk calculated using 2013 ACC/AHA sex and race specific Pooled Cohort equations

Table 2

Prevalence of elevated ASCVD risk in US Adults, aged 30–49 by risk factors: NHANES 1999–00 to 2011–12 (n=9,608)

Age Group (years)	Male		Female	
	Smokers	Non-smokers, Hypertension	Smokers	Non-smokers, Hypertension
30–34	8.4% (5.5%–12.5%)	2.0% (0.3%–13.2%)	19.5% (14.0%–26.5%)	0.0% (0.0%–4.0% [*])
35–39	25.6% (21.1%–30.7%)	2.5% (1.4%–4.7%)	13.9% (10.4%–18.5%)	0.1% (0.0%–1.0%)
40–44	53.1% (47.2%–58.9%)	6.9% (4.4%–10.6%)	13.3% (8.9%–19.4%)	0.0% (0.0%–0.5% [*])
45–49	75.9% (69.1%–81.6%)	29.3% (22.6%–37.1%)	18.5% (13.5%–25.0%)	0.0% (0.0%–0.6% [*])

#Risk calculated using 2013 ACC/AHA Sex and Race specific Pooled Cohort Equations.

* Confidence Intervals estimated using exact binomial methods.

Brackets show 95% confidence intervals for that subgroup.

Shaded cells represent low prevalence subgroups.

Table 3

Distribution of 10-year ASCVD risk in the low-prevalence subgroups

10-year ASCVD Risk*	Men < 40 years (non-smokers, non-hypertensive) N=1,365	Women <50 years (non-smokers, non-hypertensive) N=3,281
<0.1%	2.2% (1.5%–3.4%)	7.7% (6.8%–8.8%)
0.1% – 0.49%	44.9% (41.9%–48.0%)	58.7% (56.3%–61.1%)
0.5% – 0.99%	27.3% (24.8%–29.9%)	23.3% (21.3%–25.4%)
1.0% – 2.4%	23.3% (20.6%–25.9%)	10.0% (8.6%–11.6%)
2.5% – 4.9%	2.2% (1.6%–3.2%)	0.2% (0.1%–0.5%)
5.0% – 7.4%	0.09% (0.02%–0.4%)	0.04% (0.0%–0.3%)

Brackets show 95% confidence intervals for that subgroup.

* Risk calculated using 2013 ACC/AHA Sex and Race specific Pooled Cohort Equations. Low-prevalence subgroups defined as those subgroups in which we could rule out a prevalence of elevated cardiovascular risk (10-year ASCVD risk >5%) of more than 1%; and included non-smoking, non-hypertensive men under age of 40 years and non-smoking, non-hypertensive women under age of 50 years.

Table 4

Proportion of US adults, aged 30–49 years, with LDL-cholesterol level 190 mg/dL; by family history of premature heart disease: NHANES 2005–06 to 2011–12 (n=2562)

Male, %		Female, %	
Family History	No Family History	Family History	No Family History
3.4% (0.0%–7.5%)	3.3% (1.9%–4.6%)	2.0% (0.0%–4.8%)	2.1% (1.1%–3.1%)
p-value#		p-value#	
0.83		0.89	

LDL cholesterol: Low Density Lipoprotein cholesterol

* Evaluated by self-report of a close relative (mother, father, sisters, brothers) having a heart attack before age of 50 years (NHANES cohorts 2005–06 through 2011–12).

using Pearson's chi-square test, accounting for complex survey design.