
Wenjun Fan¹, Sephy Philip², Peter P. Toth³, Craig Granowitz², Nathan D. Wong¹

¹Heart Disease Prevention Program, Division of Cardiology, University of California, Irvine, CA, USA
²Amarin Pharma Inc., Bedminster, NJ, USA
³Ciccarone Center for the Prevention of Cardiovascular Disease, Johns Hopkins University School of Medicine, Baltimore, MD and CGH Medical Center, Sterling, IL, USA

Hypertriglyceridemia is associated with increases in atherosclerotic cardiovascular disease (ASCVD) risk and remains prevalent among adults in the United States (US) due to an increasing prevalence of obesity, insulin resistance, diabetes mellitus, and other risk factors. Guidelines suggest target triglycerides (TG) should be < 150 mg/dL [1]. However, a number of studies have suggested that reduced cardiovascular risk is associated with lower TG [2–4]. Indeed, ASCVD risk remains even in patients with moderately elevated TG despite the control of low-density lipoprotein cholesterol (LDL-C) with statin therapy [2, 4–6]. The recently completed REDUCE-IT trial investigated the effects of icosapent ethyl 4 g/day in statin-treated patients with established cardiovascular disease, diabetes and other risk factors and TG 135–499 mg/dL. REDUCE-IT found a significant reduction in major adverse cardiovascular events when compared with a placebo (hazard ratio [HR] 0.75; 95% confidence interval [CI] 0.68–0.83; p < 0.001) over a median follow-up time of 4.9 years [4]. Subgroup analyses showed similar risk reduction both in persons with or without baseline TG ≥ 150 mg/dL [4]. Based on the findings of REDUCE-IT, the American Diabetes Association Standards of Care now includes a Level A recommendation that icosapent ethyl be considered for reducing cardiovascular risk in statin-treated patients with controlled LDL-C, elevated TG (135–499 mg/dL), diabetes, ASCVD or other cardiac risk factors [7].

The objective of this analysis was to examine the prevalence of TG ≥ 135 mg/dL in the overall US adult population and in those treated with statins, in accordance with the presence of ASCVD and/or diabetes.

This analysis included laboratory data, medical history, and prescription data from subjects aged 20 years and older who participated in the US National Health and Nutrition Examination Survey (NHANES; 2007–2014) and had morning fasting TG available. For the current report, the proportion and number (weighted in millions to the US population) of individuals with TG ≥ 135 mg/dL was estimated according to the following factors: statin use, LDL-C < 100 mg/dL, diabetes, ASCVD, and/or age ≥ 45 years, as well as the proportion and number of individuals with multiple risk factors. All analyses used the NHANES 8-year sample weighting to project the US population in millions. The general methodology of NHANES data collection was published previously [8].

Diabetes was defined as fasting glucose ≥ 126 mg/dL, non-fasting glucose ≥ 200 mg/dL, taking insulin or other medications to lower blood sugar, or diagnosed by a healthcare provider. LDL-C was calculated by the Friedewald equation.

The study sample included 40,617 individuals in the NHANES 2007–2014 survey. A total of 9593 subjects, projected to represent 219.9 million US adults, met the entry criteria and were included in the analysis. As shown in Table 1, the overall proportion of US adults with TG ≥ 135 mg/dL was 32.1% (representing 70.5 million individuals). Among statin-treated adults, the proportion with TG ≥ 135 mg/dL was 39.0% (15.2 million) and
ranged from 35.0% to 47.6% for those who also had LDL-C controlled to < 100 mg/dL, diabetes, and/or ASCVD (Table 1).

Based on the present analysis, more than 30% of all adults in the US (70.5 million) have TG \( \geq 135 \) mg/dL, including 39.0% (15.2 million) of those being treated with statins. In a recent study of this population, 56.9 million US adults were estimated to have TG \( \geq 150 \) mg/dL [9], resulting in 13.6 million having TG \( \geq 135 \) mg/dL and < 150 mg/dL based on that study and the present analysis.

Schwartz et al. [2] demonstrated a significant trend toward increased risk of both short- and long-term ASCVD following acute coronary syndrome, according to progressively higher tertiles or quintiles of TG concentrations (p = 0.03 and p < 0.001, respectively) [2]. They further reported that the adjusted risk of ASCVD increased by 1.8% for every 10 mg/dL increase in TG above 80 mg/dL. Another study reported a significantly elevated risk of myocardial infarction in patients with TG from 89 to 176 mg/dL, compared to those with TG < 89 mg/dL (HR 1.6; 95% CI 1.4–1.9), indicating substantially increased risk at higher TG levels [3]. In the placebo arm of REDUCE-IT, a primary composite endpoint event occurred in 22% of patients overall, and in 21% of the subset of patients with TG < 150 mg/dL, indicating substantial risk in such patients.

The current report estimates that 4.8 million US adults on statin therapy with either ASCVD or diabetes have TG \( \geq 135 \) mg/dL but LDL-C < 100 mg/dL and may be possible candidates for icosapent ethyl therapy for the reduction of ASCVD risk based on results from REDUCE-IT. Better efforts are needed to identify and address remaining residual ASCVD risk in statin-treated individuals with TG \( \geq 135 \) mg/dL, including lifestyle modification adherence measures and the use of evidence-based pharmacologic therapies shown to reduce ASCVD risk.

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### Conflict of interest

Dr. Nathan D. Wong receives research support from Amarin Pharma Inc. and Amgen through his institution and has participated on advisory boards or speaker bureaus for Amarin Pharma Inc., Sanofi, and Novartis. Dr. Sephy Philip and Dr. Craig Granowitz are employees and stock shareholders of Amarin Pharma Inc. Dr. Peter P. Toth is a consultant and speaker for Amarin Pharma Inc., Amgen, Kowa, Novo Nordisk, Regeneron, and Sanofi. Dr. Wenjun Fan has no conflicts to report.

### References


