Abstracts

Scientific Poster Abstracts Selected for the National Lipid Association 2019 Scientific Sessions, May 16-19, 2019, Miami, FL

2019 Program Planners: Alan S. Brown, MD, FNLA; Anne C. Goldberg, MD, FNLA; Sergio Fazio, MD, PhD, FNLA; Edward Gill, MD, FNLA; Antonio M. Gotta, Jr., MD, DrPhil, FNLA; Elizabeth Jackson, MSN, ACNS-BC, CLS, FNLA; Peter H. Jones, MD, FNLA; Carol Kirkpatrick, PhD, RDN, MPH, CLS, FNLA; Pamela B. Morris, MD, FNLA; Carl E. Orringer, MD, FNLA; Joseph J. Saseen, PharmD, CLS, FNLA; Daneil E. Soffer, MD, FNLA

2019 Abstracts Committee: Pamela B. Morris, MD, FNLA (Chair); Dean A. Bramlet, MD, FNLA; Deborah S. Croy, DNP, CLS, FNLA; Dave L. Dixon, PharmD, CLS, FNLA; John Casey Elkins, DNP, MEd, CLS, FNLA; Peter H. Jones, MD, FNLA; and Thomas White, MD, FNLA; The National Lipid Association (NLA) is pleased to announce that 87 abstracts were accepted for presentation in the poster format for the NLA 2019 Scientific Sessions. Each abstract was reviewed by the NLA Scientific Sessions Abstracts Committee prior to acceptance.

Posters may be viewed from Thursday, May 16 at 6 p.m., through 2 p.m. on Saturday, May 18. The NLA Young Investigator Awards Ceremony will take place on Saturday, May 18 from 12:45-1:15 p.m. Posters were judged on quality of science, originality, interest to the field of lipidology, and overall impression with cash awards of $1,000 for first place, $750 to second place, and $500 to third place. The first place Young Investigator winner also was selected to give an oral presentation during the sessions.

Three additional abstracts are selected to give an oral presentation during the abstract session.

Note: Young Investigator abstract titles are marked with an asterisk. Encore abstracts are marked with a dagger symbol. The Foundation of the NLA Hunninghake FH Abstract award winner is marked with a caret.

Clinical Applications of Biomarkers, Lipoprotein Testing

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Establishing reference parameters for total and active PCSK9 levels: A pilot study

Diane Allen, PhD, Catherine Wooten, BS, Quantil Melendez, PhD, K. Kimbro, PhD, Undi Hoffler, PhD, Dayami Lopez, PhD, (Fort Bragg, NC)

Lead Author’s Financial Disclosures: None.

Study Funding: Support for work at Womack Army Medical Center (WAMC), Fort Bragg, NC was supported from an AMEDD Advanced Medical Technology Initiative (AAMTI) Rapid Innovation Award. Support for the work at NCCU: The work at NCCU was supported by funds from the State of North Carolina, the BRITE Institute, an AAMTI Rapid Innovation Award from WAMC (Fort Bragg, NC), a research contract from Quest Diagnostics (Secaucus, NJ), and a Technology Enhancement Grant from the North Carolina Biotechnology Center.

Background/Synopsis: Genetic testing for PCSK9 is complicated and expensive, but it is an excellent tool to predict resistance or sensitivity to statins and qualify patients for new drugs. Several assays that measure total PCSK9 levels in human serum are currently available, but they are unable to provide information on the functionality of PCSK9 (active PCSK9). A simple, inexpensive blood test that could identify patients with gain-of-function (GOF) or loss-of-function (LOF) PCSK9 mutations is needed.

Objective/Purpose: The objective of this study was to establish reference parameters for active PSCK9 levels in healthy individuals using a novel ELISA assay.

Methods: A cross-sectional study using a defined population at a single time point was done. Demographics such as age, ethnicity, and the use of medication, alcohol, and
Results: Forty participants (50% Caucasian Americans or CAs; 50% African Americans or AAs) who met the inclusion criteria were recruited. The median age of the population was 22.0 years, and the median BMI was 23.2 kg/m². Participants had healthy blood pressure and levels of total cholesterol, triglycerides, hemoglobin A1c, and glucose. Median values for LDL (99.5 mg/dL) and HDL (50 mg/dL) were just outside of normal ranges. CAs had significantly lower HDL than AAs (p = 0.0059), but significantly higher triglycerides (p = 0.0305). The population mean for total PCSK9 was 453 ng/mL whereas the mean for active PCSK9 was 160 ng/mL. The ratio of active to total PCSK9 was used to identify participants with GOF (ratio >0.7) and LOF (ratio <0.2) mutations. 50% of the participants had wild-type PCSK9. 43% had LOF mutations whereas 7% had GOF mutations. Glucose levels were significantly directly correlated with active PCSK9 (p = 0.042) and the ratio of active to total PCSK9 (p = 0.017).

Conclusions: Reference parameters for total and active PCSK9 levels in a healthy population were established. The assays proved to be useful in identifying participants with GOF and LOF PCSK9 mutations.

Table 1 Sample Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall N=40</th>
<th>Black n=20</th>
<th>White n=20</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.0 [21.0-23.0]</td>
<td>22.5 [21.0-23.0]</td>
<td>21.5 [20.0-23.0]</td>
<td>0.1241</td>
</tr>
<tr>
<td>Height (m)</td>
<td>70.0 [68.5-72.0]</td>
<td>69.0 [67.0-72.0]</td>
<td>70.0 [69.0-73.0]</td>
<td>0.0966</td>
</tr>
<tr>
<td>Weight (lb)</td>
<td>162.9 [151.7-173.6]</td>
<td>156.5 [144.4-171.4]</td>
<td>164.8 [156.6-178.9]</td>
<td>0.0819</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.2 [21.8-24.1]</td>
<td>23.2 [21.8-24.1]</td>
<td>23.2 [22.3-24.1]</td>
<td>0.8297</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td>0.3962</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>14 (35.0)</td>
<td>7 (35.0)</td>
<td>7 (35.0)</td>
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<tr>
<td>1-7 times/week</td>
<td>23 (57.5)</td>
<td>13 (65.0)</td>
<td>10 (50.0)</td>
<td></td>
</tr>
<tr>
<td>8-14 times/week</td>
<td>2 (5.0)</td>
<td>0 (0.0)</td>
<td>2 (10.0)</td>
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<tr>
<td>15+ times/week</td>
<td>1 (2.5)</td>
<td>0 (0.0)</td>
<td>1 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Tobacco Use</td>
<td></td>
<td></td>
<td></td>
<td>0.1274</td>
</tr>
<tr>
<td>None</td>
<td>31 (77.5)</td>
<td>18 (90.0)</td>
<td>13 (65.0)</td>
<td></td>
</tr>
<tr>
<td>&lt;1 Pack/day</td>
<td>9 (22.5)</td>
<td>2 (10.0)</td>
<td>7 (35.0)</td>
<td></td>
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<tr>
<td>1-2 Packs/day</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
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<td>3+ Packs/day</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
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<td>Systolic BP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td>0.6670</td>
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<tr>
<td>111.5 [107.5-120.0]</td>
<td>113.5 [107.5-121.0]</td>
<td>111.0 [107.0-119.5]</td>
<td></td>
<td></td>
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<tr>
<td>Diastolic BP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td>0.1658</td>
</tr>
<tr>
<td>63.0 [59.0-69.5]</td>
<td>64.0 [61.0-69.5]</td>
<td>62.0 [57.5-68.0]</td>
<td></td>
<td></td>
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<tr>
<td>Total Cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td>0.3165</td>
</tr>
<tr>
<td>161.5 [148.0-194.0]</td>
<td>164.0 [148.5-202.0]</td>
<td>160.0 [139.5-185.5]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Density Lipoprotein (mg/dL)</td>
<td>99.5 [82.0-121.5]</td>
<td>104 [79.0-127.0]</td>
<td>95.5 [86.5-115.5]</td>
<td>1.0000</td>
</tr>
<tr>
<td>High Density Lipoprotein (mg/dL)</td>
<td>55.0 [46.5-59.0]</td>
<td>57.0 [54.5-69.0]</td>
<td>48.5 [44.5-55.5]</td>
<td>0.0059</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
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<td></td>
<td></td>
<td>0.0305</td>
</tr>
<tr>
<td>64.0 [51.0-102.0]</td>
<td>56.0 [48.5-81.0]</td>
<td>80.9 [58.0-123.0]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.1974</td>
</tr>
<tr>
<td>5.2 [5.0-5.4]</td>
<td>5.2 [5.1-5.4]</td>
<td>5.1 [5.0-5.3]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td>0.1403</td>
</tr>
<tr>
<td>93.0 [87.5-96.5]</td>
<td>90.5 [85.0-96.5]</td>
<td>95.0 [90.5-97.0]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taking Medications</td>
<td></td>
<td></td>
<td></td>
<td>0.6050</td>
</tr>
<tr>
<td>36 (90.0)</td>
<td>19 (95.0)</td>
<td>17 (85.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data reported in N (%) or Median [Q1-Q3]
Results: Within the LDL-C sub-fraction a nuclear magnetic resonance (NMR) or ion mobility (IM) laboratory tests can assess the total LDL-C particle concentration and particle size (small, intermediate, or large). It is thought that smaller, dense LDL particles are more atherogenic than the larger, "buoyant" LDL particles because they can infiltrate a damaged endothelium with greater ease and contribute to plaque formation.

A systematic review of 24 studies demonstrated that high LDL particle number is indeed associated with increased CVD risk. This is relevant because within the physiology of insulin resistance there is a disconnect between LDL-C and LDL particle concentration; LDL-C levels do not change with more insulin resistance, however small LDL particle count increases with increasing severity of insulin resistance.

Many epidemiological studies use the ratio of TC or to HDL-C to stratify populations into higher and lower risk classes. There is consistent literature demonstrating that non-HDL-C (TC minus HDL-C) or TC to HDL-C ratio is a better CHD risk predictor than LDL-C on its own: to support this notion here we cite a prospective cohort study using the Framingham data (n=3322), a meta-analysis of 68 long-term prospective studies (n=302,430), and second meta-analysis of patients allocated to statin therapy from 8 trials (n=38,153).

Conclusions: In patients with metabolic syndrome risk factors we propose measuring LDL particle size to develop more nuanced CVD risk stratification and guide statin therapy. We also recommend the clinician’s judicious use of either TC:HDLC or non-HDL-C:LDL-C ratios over the current use of TC, HDL-C, or LDL-C.

Table 1 Lipoprotein(a) Levels measured in an outpatient Preventive Cardiology clinic on 121 patients presenting with family history of premature cardiovascular disease and no personal history of CVD.

<table>
<thead>
<tr>
<th>Lp(a) Level</th>
<th>Total Patients</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 mg/dL</td>
<td>72 (59.5%)</td>
<td>14</td>
<td>58</td>
</tr>
<tr>
<td>30-49 mg/dL</td>
<td>13 (10.7%)</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>50-99 mg/dL</td>
<td>23 (19.0%)</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>100-149 mg/dL</td>
<td>9 (7.4%)</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>&gt;150 mg/dL</td>
<td>4 (3.3%)</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

Clinical Applications of Biomarkers, Lipoprotein Testing
all children from ages 9 to 11 years. However, Wald et al., suggested screening of children from ages 1 to 9 years provided the most optimal balance of high detection and low false positive rates. These authors initiated a cholesterol screening program of children aged 1 to 2 years in the United Kingdom, screening over 13,000 participants to assess feasibility of screening at a younger age.

Based upon these findings, Cook Children’s Medical Center has initiated a program providing point-of-care cholesterol screening for 2-year-old children seen one of its 6 neighborhood general pediatric ambulatory clinics. Screening was incorporated into the 2-year health maintenance visit.

**Objective/Purpose:** The purpose of this study was to summarize the results of cholesterol testing and describe the challenges that were encountered.

**Methods:** At the time of a patient’s 2-year health maintenance visit, point-of-care cholesterol testing is conducted in each of the seven Cook Children’s sponsored ambulatory clinics that provide care for children in a 6 county area in Dallas Fort-Worth. Data is reported from 4/1/2017 to 2/1/2018.

**Results:** 4,954 children underwent a 2-year-old health maintenance visit from 4/1/2017 - 2/1/2018. Of the total population seen, 2,247 (45%) underwent cholesterol testing. Of the 2,247 screened, the median LDL-C level was 78 mg/dL. To assess criteria for referral to Cook Children’s Medical Center’s REACH clinic, multiple LDL-C value thresholds were assessed (Table 1).

**Conclusions:** Successful implementation of a cholesterol screening program at 2-years-of-age is not without challenges. In addition to initial and ongoing efforts to educate the medical and clinic support staff, logistics, cost and clinical workflow need to be very carefully considered when implementing additional testing in a busy ambulatory Pediatric Clinic. While guidelines for clinical management were helpful, PCP’s often did not follow through with the appropriate recommendation for dietary counseling or referral. Information obtained from this study will provide important information to facilitate process and quality improvement.

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**Table 1** Population percentages and estimated prevalence based on LDL-C value thresholds.

<table>
<thead>
<tr>
<th>LDL-C value (mg/dL)</th>
<th>Percent of population</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥119&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.8&lt;sup&gt;*&lt;/sup&gt;</td>
<td>1:17</td>
</tr>
<tr>
<td>≥122&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.2%</td>
<td>1:29</td>
</tr>
<tr>
<td>≥130&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.1%</td>
<td>1:32</td>
</tr>
<tr>
<td>≥139&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1%</td>
<td>1:83</td>
</tr>
<tr>
<td>≥160&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.5%</td>
<td>1:200</td>
</tr>
<tr>
<td>≥185&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.1%</td>
<td>1:1,000</td>
</tr>
<tr>
<td>≥190&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.1%</td>
<td>1:1,000</td>
</tr>
</tbody>
</table>

<sup>a</sup>1.53 Multiple of the Median (MoM).
<sup>b</sup>95% of population.
<sup>c</sup>estimated 95% of the general population < 20 years, 20 – 29 years, and 30+ years, respectively (JCL, 2011).
<sup>d</sup>99% of population.
<sup>e</sup>99.9% of population.
healthcare providers may help inform current educational needs and future recommendations for clinical practice guidelines.

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Marked reduction of Lipoprotein (a) with PCSK9 Inhibition in a statin intolerant patient: An Illustrative Case Report

Dean A. Bramlet, MD, FNLA, (St. Petersburg, FL)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Elevated levels of Lipoprotein(a) (Lp(a)) are not uncommon in patients with ASCVD and are not typically screened for with standard US lipid panels. Reports of 25-30% typical reductions in levels of Lp(a) are attributed to PCSK9 inhibitor therapy, and often are discordant with the 50-60% reduction seen in LDL-C with PCSK9i therapy. Potentially, elevated Lp(a) may be especially clinically important in cases when statin intolerance leads to inadequately controlled levels of LDL-C.

Objective/Purpose: This case report illustrates the insight gained from advanced cardiovascular diagnostic testing utilization in identifying a root cause predisposition to statin intolerance, and the important recognition of previously overlooked genetic elevation of Lp(a) for over 25 years post myocardial infarction treated elsewhere, including multiple subsequent stent deployments. It also demonstrates that in select individuals a much greater response in Lp(a) reduction can be seen with PCSK9i therapy, and that low dose pitavastatin can be tolerated in some individuals with even genetically predisposed statin intolerance.

Methods: An 81 year old white male with remote myocardial infarction and small abdominal aortic aneurysm, had 3 coronary stents deployed 2 years previously, with ongoing low dose aspirin and clopidogrel therapy. He also has chronic obstructive pulmonary disease, corrected hypothyroidism, hypertension controlled with lisinopril and amlopidine, and became intolerant or simvastatin, rosuvastatin, and atorvastatin due to myalgias. Despite identification of T/C genotype for SCLO1B1, he was able to tolerate pitavastatin 1 mg. three times a week. Advanced cardiovascular diagnostic testing was performed utilizing Boston Heart Diagnostics (TM) to assist in cardiac risk assessment and management.

Results: On pitavastatin his direct LDL-C was 114 mg/dl, Non-HDL-C 137 mg/dl, HDL-C 60 mg/dl. Elevated Lp(a) level of 85 mg/dl was identified along with LDL particle count of 1553 nmol/L and Apolipoprotein B of 109 mg/dl. After addition of evolocumab 140 mg. subcutaneous injections every 2 weeks, his values 14 weeks later were: direct LDL-C 61 mg/dl, Non-HDL-C 70 mg/dl, HDL-C 67 mg/dl, LDL particle count 843 nmol/L, and Apolipoprotein B 55 mg/dl. Lp(a) dropped to 40 mg/dl. This 53% reduction in Lp(a) exceeded the 46% reduction in LDL-C, the 45% reduction in LDL particle count and 50% reduction in Apolipoprotein B.

Conclusions:

1. Individual reductions in Lp(a) can exceed 50% in some individuals, making PCSK9i a more optimal second therapy to statin baseline, when reductions in Lp(a) are additionally desired by the patient/clinician collaboration
2. Pitavastatin in this case was tolerated in low doses even in the setting of unfavorable SCLO1B1 genetic polymorphism
3. Advanced cardiovascular diagnostics were useful in identifying root cause of predisposition to statin intolerance, in this case, and in identifying potentially useful targets of residual risk to consider for management alternatives.

Diabetes, Insulin Resistance and Dyslipidemia

A Randomized Study of Evolocumab in Patients With Type 2 Diabetes and Dyslipidemia on Background Statin: Primary Results of the BERSON Clinical Trial

Alberto J. Lorentzatti, MD, Freddy Eliaischewitz, MD, Yundai Chen, MD, Junming Lu, MD, Alexis Baass, MD, Maria Laura Monsalvo, MD, Nan Wang, PhD, Andrew Hamer, MD, Junbo Ge, MD, (Cordoba, Argentina)

Lead Author’s Financial Disclosures: Advisory board and steering committee member for and has received research grants and speaker fees from Amgen Inc.

Study Funding: This study was funded by Amgen Inc.

Background/Synopsis: BERSON was a phase 3, double-blind trial designed to evaluate the lipid-lowering efficacy and safety of the proprotein convertase subtilisin/kexin type 9 inhibitor evolocumab in patients with type 2 diabetes mellitus (T2DM) and hyperlipidemia or mixed dyslipidemia on background statin.

Objective/Purpose: We report the preliminary results of BERSON.

Methods: Patients ≥ 18 to ≤ 80 years with T2DM, on stable pharmacotherapy for diabetes for ≥ 6 months, and a screening low-density lipoprotein cholesterol (LDL-C) level of ≥ 100 mg/dL or ≥ 130 mg/dL, and with or without statin treatment at screening, respectively, were enrolled and started on atorvastatin 20 mg/day for at least 4 weeks. Patients were then randomized 2:2:1:1 to daily atorvastatin 20 mg plus either evolocumab 140 mg every 2 weeks (Q2W), evolocumab 420 mg every month (QM), placebo Q2W, or placebo QM. Co-primary outcome measures were percentage change from baseline in LDL-C at week 12 and percentage change from baseline in LDL-C at the mean of weeks 10 and 12. Additional measures
Table

<table>
<thead>
<tr>
<th></th>
<th>Evolocumab Q2W (N = 325)</th>
<th>Placebo Q2W (N = 164)</th>
<th>Evolocumab QM (N = 332)</th>
<th>Placebo QM (N = 160)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline LDL-C (mg/dL), mean (SD)</td>
<td>92.4 (38.8)</td>
<td>92.2 (32.0)</td>
<td>93.5 (33.6)</td>
<td>91.0 (30.7)</td>
</tr>
<tr>
<td>Baseline non-HDL-C (mg/dL), mean (SD)</td>
<td>121.3 (38.1)</td>
<td>119.2 (38.2)</td>
<td>121.2 (37.0)</td>
<td>119.4 (36.0)</td>
</tr>
</tbody>
</table>

### Safety

| Any adverse event (AE), n (%) | 137 (42.2) | 72 (43.9) | 151 (45.5) | 66 (41.3) |

### Mean of Weeks 10 and 12

#### Lipids

| Percent change from baseline in LDL-C, mean (SE) | -56.35 (3.1) | 4.94 (3.5) | -69.05 (3.0) | 0.99 (3.3) |
| Percent change from baseline in non-HDL-C, mean (SE) | -56.57 (2.7) | 4.33 (3.1) | -59.08 (2.6) | 0.33 (3.0) |
| Achievement of LDL-C < 70 mg/dL, n (%) | 281 (90.1) | 34 (21.7) | 292 (91.3) | 30 (19.4) |

#### Glycemic Control

| Change from baseline in FSG in mg/dL, mean (SE) | 1.8 (−12.6, 19.8) | 3.6 (−12.6, 16.2) | 2.7 (−12.6, 21.6) | 1.8 (−9.0, 16.2) |
| Change from baseline in HbA1c in percent, median (Q1, Q3) | 0.10 (−0.30, 0.60) | 0.10 (−0.10, 0.50) | 0.10 (−0.30, 0.50) | 0.10 (−0.30, 0.50) |

#### Notes

- *Serious AEs were reported in 4.9% of patients in the overall evolocumab group and 3.4% in the overall placebo group. No serious AEs were reported in ≥ 1% of patients in either the overall evolocumab or the overall placebo groups.
- **Values reflect LS means (SE) from a repeated-measures linear effect model.
- *P < 0.0001 for evolocumab versus placebo comparison.
- IP, investigational product; FSG, fasting serum glucose; HbA1c, glycated hemoglobin; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol; SE, standard error.

### Funding

Funding: Amgen Inc.

Maria Laura Monsalvo, MD, Nan Wang, MD, Andrew Hamer, MD, Junbo Ge, MD, (Beijing, China)

### Discussion

In patients with T2DM and hyperlipidemia, evolocumab significantly reduced LDL-C and non-HDL-C, was generally well tolerated, and had no notable impact on glucose or hemoglobin A1c levels.

### Conclusions

In patients with T2DM and hyperlipidemia or mixed dyslipidemia on statin therapy, evolocumab significantly reduced LDL-C and non-HDL-C, was generally well tolerated, and had no notable impact on glucose or hemoglobin A1c levels.

### Methods

Patients ≥ 18 to ≤ 80 years with T2DM, on stable pharmacotherapy for diabetes for ≥ 6 months, and a screening low-density lipoprotein cholesterol (LDL-C) level of ≥ 100 mg/dL or ≥ 130 mg/dL, and with or without statin treatment at screening, respectively, were enrolled and started on atorvastatin 20 mg/day for at least 6 months, and then randomized 1:1 to add-on evolocumab or placebo Q2W or QM.
4 weeks. Patients were then randomly assigned 2:2:1:1 to daily atorvastatin 20 mg plus either evolocumab 140 mg every 2 weeks (Q2W), evolocumab 420 mg every month (QM), placebo Q2W, or placebo QM. Co-primary outcome measures were the % change from baseline in LDL-C at week 12 and the % change from baseline in LDL-C at the mean of weeks 10 and 12. Additional measures included change in non-high-density lipoprotein cholesterol (non-HDL-C), proportion achieving LDL-C ≤70 mg/dL, and measures of glycemic control. **Results:** In total, 451 (46%) of patients that were randomized and dosed were from China. The mean age (SD) of these patients was 60.0 (8.4) years and 51% were women. Table 1 reports baseline and end-of-study efficacy results and safety data. **Conclusions:** This study demonstrated that evolocumab administered every two or four weeks significantly reduced LDL-C and was well tolerated in Chinese patients with type 2 diabetes and dyslipidemia, with no notable impact on glycemic control.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Evolocumab Q2W (N = 150)</th>
<th>Placebo Q2W (N = 75)</th>
<th>Evolocumab QM (N = 152)</th>
<th>Placebo QM (N = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline LDL-C (mg/dL), mean (SD)</strong></td>
<td>86.9 (32.9)</td>
<td>88.9 (34.7)</td>
<td>90.3 (33.1)</td>
<td>82.7 (27.1)</td>
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<tr>
<td><strong>Baseline non-HDL-C (mg/dL), mean (SD)</strong></td>
<td>113.5 (36.5)</td>
<td>116.0 (41.7)</td>
<td>116.8 (34.1)</td>
<td>109.5 (30.2)</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td></td>
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<tr>
<td>Any adverse event (AE), n (%)</td>
<td>85 (56.7)</td>
<td>39 (52.0)</td>
<td>89 (58.6)</td>
<td>40 (54.1)</td>
</tr>
<tr>
<td>Serious AE, n (%)</td>
<td>8 (5.3)</td>
<td>2 (2.7)</td>
<td>16 (10.5)</td>
<td>4 (5.4)</td>
</tr>
<tr>
<td>Leading to discontinuation of IP</td>
<td>1 (0.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (1.4)</td>
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<tr>
<td><strong>Mean of Weeks 10 and 12</strong></td>
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<tr>
<td><strong>Lipids</strong></td>
<td></td>
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<tr>
<td>Percent change from baseline in LDL-C, mean (SE)</td>
<td>−72.0 (1.9)c</td>
<td>8.4 (2.7)</td>
<td>−73.2 (1.6)c</td>
<td>7.8 (2.3)</td>
</tr>
<tr>
<td>Percent change from baseline in non-HDL-C, mean (SE)</td>
<td>−61.0 (1.8)c</td>
<td>7.1 (2.5)</td>
<td>−63.1 (1.4)c</td>
<td>5.5 (2.0)</td>
</tr>
<tr>
<td>Achievement of LDL-C &lt; 70 mg/dL, n, %</td>
<td>139 (97.2)c</td>
<td>18 (24.3)</td>
<td>141 (95.3)c</td>
<td>17 (23.6)</td>
</tr>
<tr>
<td><strong>Week 12</strong></td>
<td></td>
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<tr>
<td><strong>Lipids</strong></td>
<td></td>
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<tr>
<td>Percent change from baseline in LDL-C, mean (SE)</td>
<td>−73.0 (0.3)c</td>
<td>12.0 (0.2)</td>
<td>−65.4 (4)c</td>
<td>9.5 (5.7)</td>
</tr>
<tr>
<td>Percent change from baseline in non-HDL-C, mean (SE)</td>
<td>−61.1 (1.1)c</td>
<td>9.2 (2.9)</td>
<td>−56.2 (2.6)c</td>
<td>6.7 (7.3)</td>
</tr>
<tr>
<td>Achievement of LDL-C &lt; 70 mg/dL, n, %</td>
<td>132 (96.4)c</td>
<td>17 (23.6)</td>
<td>137 (95.1)c</td>
<td>18 (25.0)</td>
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<tr>
<td><strong>Glycemic Control</strong></td>
<td></td>
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<tr>
<td>Change from baseline in FSG in mg/dL, median (Q1, Q3)</td>
<td>5.4 (−11.7, 22.5)</td>
<td>2.7 (−7.2, 16.2)</td>
<td>1.8 (−16.2, 17.1)</td>
<td>0 (−9.0, 10.8)</td>
</tr>
<tr>
<td>Change from baseline in HbA1c in percent, median (Q1, Q3)</td>
<td>0.30 (−0.20, 0.80)</td>
<td>0.20 (−0.10, 0.70)</td>
<td>0.10 (−0.40, 0.80)</td>
<td>0.10 (−0.30, 0.60)</td>
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</table>

*a* Serious AEs were reported in 7.9% of patients in the overall evolocumab group and 4.0% in the overall placebo group. No serious adverse events were reported in >1% of patients in either the overall evolocumab or the overall placebo groups.

*b* Values reflect LS means (SE) from a repeated-measures linear effect model.

*c* *P* < 0.0001 for evolocumab versus placebo comparison.

**Funding:** Amgen Inc.

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**Identifying patient perceptions and attitudes regarding statin-associated diabetes mellitus**

Cheryl A. Gibson, PhD, Rebecca Mount, MS, Jaehoon Lee, PhD, Jim Backes, PharmD, (Kansas City, KS)

**Lead Author's Financial Disclosures:** None.

**Study Funding:** Kowa Pharmaceuticals America, Inc.

**Background/Synopsis:** In 2012, the FDA published a communication on statin safety label changes in response to reports that statin use can result in increases in glucose levels. It is not known how the FDA communication influenced patients attitudes towards and perceptions of statin therapy. In our clinical setting, patients often express apprehension about statin therapy and the potential risk of diabetes mellitus (DM). Despite these concerns, formal data have not been captured to assess patient perceptions about statin-induced DM.

**Objective/Purpose:** To evaluate attitudes and perceptions of statin-associated DM among patients receiving a
stain or those who are candidates for statin therapy; and
to determine how these beliefs might influence
adherence.

**Methods:** A mixed methods design, using surveys and
semi-structured interviews among patients who were taking
a statin or potentially statin-eligible, was employed.
Patients completed an adapted Beliefs About Medicines
Questionnaire (aBMQ) to ascertain concerns about poten-
tial adverse effects of statins, the necessity of therapy, and
how these beliefs might influence adherence. Scores were
used to calculate a necessity-concerns differential about
patients beliefs about statin therapy. Interviews explored
factors influencing medication beliefs over the course of
treatment.

**Results:** Seventy-three (49 females; mean age 57 years)
individuals completed the aBMQ. Current statin users
had stronger beliefs about the necessity of statin therapy
(p<0.01), and indicated fewer concerns (p<0.01) and
less cost than benefit (p<0.001) compared to candidate
users. Participants with higher cholesterol levels had
weaker beliefs about the necessity of statin therapy
(p<0.001) and more concerns (p<0.01), and perceived
greater cost than benefit (p<0.001) compared to those
with lower cholesterol levels. Among the 73 participants,
14 completed interviews. Most interviewees had con-
cerns about statin side effects but indicated their pre-
scription did not share any information about potential
adverse effects of statins, including how statins might
affect glucose control. However, most interviewees
believed the benefits of statins outweigh the potential
risk of DM and this risk would not prevent them from
initiating or continuing statin therapy. Further, most
indicated they also would be willing to start or continue
their statin medication if the risk of raising their blood
glucose was less with a lower dose.

**Conclusions:** There are significant differences in the
perceived need and benefit of statin therapy in relation to
the potential risk of statin-associated DM. The need for
prescribers to address patients concerns and beliefs about
statin therapy is warranted.

**Enhancing Adherence, Compliance to Therapies**

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**Changing Between PCSK9 Inhibitor Medications**

*James Trippi, MD, FNLA,*

*Billie Jones, RN, (Indianapolis, IN)*

**Lead Author’s Financial Disclosures:** Speaker -
Sanofi, Amgen, Amarin, Pfizer.

**Study Funding:** None.

**Background/Synopsis:** PCSK9 inhibitors (alirocumab
and evolocumab) became commercially available in July
and August of 2015, respectively. They have been shown to
be effective in improving cardiovascular outcomes in
patients not adequately responding to statin and other
cholesterol lowering therapies. Over time some patients
change from one PCSK9 inhibitor to the other.

**Objective/Purpose:** We sought to determine the extent
of patients changing PCSK9 inhibitor medications and their
characteristics.

**Methods:** A retrospective review of electronic medical
records from our heart center showed PCSK9 inhibitors
were prescribed 371 times for 332 individual patients from
the time of commercial launch until November 2018.

**Results:** Most PCSK9 inhibitors prescriptions origi-
nated from the lipodologist on staff; recently other
cardiologists have begun prescribing as well. 39 patients
(11.7%) patients changed from one medication to the
other during this time. All patients switching medica-
tions had atherosclerotic heart disease and 4 patients had
definite familial hypercholesterolemia by Dutch Lipid
Clinics score or genetic testing. They were 12 females and
27 males, average age 63.5 years. 21 patients were not
on a statin, 8 were on high, 2 on intermediate and 8 on
low dose statin therapy. 15 patients were on ezetimibne
10 mg daily. None of the patients changing medications
were on advanced therapies such as lomitipide or
apheresis. 13 patients started on alirocumab 75 mg SQ
q 2 wks, 8 started on alirocumab 150 mg SQ q 2wks and
18 patients started on evolocumab 140 mg SQ q 2 wks.
The average duration on the first PCSK9 inhibitor was
6.3 months (range 17 to 1 months). Reasons for changing
between medications included insurance coverage (33),
cost (5) and side effects (1). No changes occurred
because of medication ineffectiveness. 30 of the 39
patients were noted to achieve LDL-C < 70 mg/dl
(average 60, range 171 to 5mg/dl) on the second
PCSK9 medication compared to pre-treatment LDL-C
(average 167, range 309 to 107mg/dl). Pre and post
LDL-C levels with alirocumab (152 to 62mg/dl, 59% 
reduction) and evolocumab (173 to 58 mg/dl, 70%
reduction) were noted. Because of numerous extraneous
variables, incomplete lab testing and the small numbers
of patients, the effectiveness of the respective medica-
tions should not be compared. The one patient having
PCSK9 inhibitor side effects later concluded that her
hair loss was not from evolocumab but from the
simultaneous steroid therapy administered for a pulmo-
nary disease exacerbation.

**Conclusions:** Changing between PCSK9 inhibitors oc-
curs frequently in clinical practice. Unfortunately, insur-
ance coverage and cost leading to switching medications,
decreases patient compliance to medical therapy, consistent
lipid reduction and convenience. Changing PCSK9 medi-
cations creates additional work and time burdens on
medical staff as well. As insurance coverage stabilizes
and familiarity with insurers preferred medication in-
creases, fewer changes between PCSK9 inhibitors will
improve patient care.
Perceived fatigue may be an overlooked barrier to successful therapeutic lifestyle change.

Todd Jarvis IV, OMS, Ben Bopp II, OMS, Tyler Hamby, PhD, Luke Hamilton, MS, Don Wilson, MD, (Fort Worth, TX)

Lead Author’s Financial Disclosures: None.
Study Funding: None.

Background/Synopsis: Children and adolescents at-risk of developing premature cardiovascular disease (CVD) due to genetic disorders and acquired conditions, such as obesity and insulin resistance, are often referred to a pediatric lipid clinic. While adoption of a lifelong, heart-hearty lifestyle is encouraged, those with genetic disorders may benefit from lipid-lowering medications. Recommendations for therapeutic lifestyle change in those who are obese, especially the need for less sedentary time and 30-60 min/d of moderate-to-vigorous physical activity, may be hindered by a perception of fatigue. An increased perception of fatigue in obese youth vs healthy controls has previously been reported in those referred to an obesity clinic.

Objective/Purpose: The purpose of this study was to examine perceived fatigue in a sample of obese youth (<18 yrs. of age; BMI 95th percentile) with acquired CVD risk factors, who were referred to a pediatric lipid clinic.

Methods: This study was a retrospective chart review of 237 youth referred to the Risk Evaluation to Achieve Cardiovascular Health (REACH) clinic at Cook Children’s Medical Center between January 1, 2014 and August 31, 2018. During the initial clinic visit, each subject and the child’s parent independently completed the PedsQL Multi-dimensional Fatigue Scale, a validated survey with 18 items divided into 3 subscales - General, Sleep/Rest, and Cognitive - each containing 6 questions. A total score was computed, the range of possible scores ranging from 0 to 100 for each subscale. Higher scores indicate less perception of fatigue. A t-test was used to compare study subjects to previously reported obese youth (N=43) referred to an obesity clinic and normal weight, healthy controls (N=157). A p-value < 0.05 was used to determine statistical significance.

Results: The study population consisted of 200 subjects, 50.5% of whom were morbidly obese (99th percentile). Study subjects had statistically significantly more perception of fatigue for each sub- and total scale for both self- and parent-reported scales (p < 0.001) compared to healthy controls. However, there were no statistically significant differences between our study subjects and the obese youth previously reported (Figure).

Conclusions: Obese youth with and without reported acquired CVD risk-factors experience greater perceived fatigue than healthy controls. It is important to consider barriers to implementation of lifestyle modification, such as perception of fatigue, when recommending less sedentary time and 30-60 min/d of moderate-to-vigorous physical activity to improve health.

Epidemiology of Cardiovascular Disease

Enhanced Prediction of the Population at Risk of Atherothrombotic Disease†

W. E. Feeeman Jr, MD, (Bowling Green, OH)

Lead Author’s Financial Disclosures: None.
Study Funding: None.

Background/Synopsis: The prediction of the population at risk of atherothrombotic disease (ATD) is essential to the prevention of clinical ATD. The chief ATD risk factors for ATD are cigarette smoking, dyslipidemia, and hypertension, with some contribution by the very high blood sugar levels of uncontrolled diabetes. These risk factors do not act in a vacuum, but rather are interdependent. Combining these three risk factors into a single predictive tool enhances the ability to predict the population at risk of ATD. Dyslipidemia is best interpreted as a ratio between LDL- and HDL-cholesterol, in the form of the Cholesterol Retention Fraction, or CRF. Hypertension’s contribution to ATD risk is best made by the systolic blood pressure (SBP).

Objective/Purpose: The purpose of this presentation is to present an updated version of the prediction of the population at risk of ATD, such that it is possible to stratify ATD risk in terms of higher ATD risk (patients aged 64 years or less at time of ATD onset), middle risk (patients aged 65-74 years at time of ATD onset), and lower risk
(patients aged 75 years of older at time of ATD presentation). A comparison with a similar graph using LDL-cholesterol instead of the CRF will be shown.

**Methods:** Chart review of the ATD database of the author’s medical practice.

**Results:** When the CRF is graphed against SBP (blood pressures at presentation levels, which include blood pressures which have been treated), one notes a layering effect with virtually all of the higher risk patients lying above the CRF of 0.70 or higher zone, most of the middle risk patients lying in the CRF of 0.60-0.69 zone, and those lower risk patients mostly lying in the CRF of 0.59 or lower zone. Some zonal overlap is present. This layering effect is eradicated by cigarette smoking, is more pronounced in ex-smokers, and marked in never smokers. This layering effect is not seen when LDL-cholesterol is used instead of the CRF.

**Conclusions:** It is possible to predict the population at risk of ATD with high accuracy using factors readily available to practicing physicians. This in turn affords the ability to prevent clinical ATD events.
Predicting Cardiovascular Disease in Familial Hypercholesterolemia: Risk Factors Counting

Alessa Baass, MD, Martine Paquette, MSc, Sophie Bernard, MD, PhD, (Montreal, QC)

Lead Author’s Financial Disclosures: A.B. received research grants from Merck Frosst, Amgen, Sanofi, Astra Zeneca and the Fondation Leducq. He has participated in clinical research protocols from Pfizer, Regeneron Pharmaceuticals Inc., The Medecines Company, Amgen, Acasti Pharma Inc., Novart.

Study Funding: None.

Background/Synopsis: Due to the important lifelong LDL cholesterol burden, patients with familial hypercholesterolemia (FH) have a high risk of cardiovascular disease (CVD). In recent years, many clinical and genetic factors have been shown to modulate the CVD risk in FH. It is thus essential to better stratify the CVD risk in this population.

Objective/Purpose: The objective of this study is to verify whether simple risk factor counting could efficiently stratify the risk of prevalent CVD in a large cohort of FH patients.

Methods: A total of 1412 adult patients diagnosed with FH from the FH Canada registry were included in the analysis. The risk factors used for the risk factor count (RFC) are the five variables of the Montreal-FH-SCORE (MFHS), namely age, HDL-C, sex, hypertension and smoking.

Results: Both the MFHS (AUC 0.805 [0.779-0.831]) and the RFC (AUC 0.797 [0.770-0.823]) were good predictors of prevalent CVD events and were not statistically different (P=0.20 for difference). Furthermore, we observed a significant difference in the prevalence of CVD events between the low risk group (0 to 2 risk factors) and the high risk group (3 to 6 risk factors) (% vs 37%, respectively, P<0.0001).

Conclusions: Even if the RFC represents a simplified method to assess the CVD risk in FH, it is a good predictor of prevalent CVD events. FH patients with multiple CVD risk factors would likely benefit from further risk factor reduction. Larger prospective studies are required to validate if RFC in FH is associated with better patient outcomes.

Hypertension and Tuberous Xanthomas predict Cardiovascular Disease in Familial Dysbetalipoproteinemia

Alessa Baass, MD, Martine Paquette, MSc, Sophie Bernard, MD, PhD, (Montreal, QC)

Lead Author’s Financial Disclosures: A.B. received research grants from Merck Frosst, Amgen, Sanofi, Astra Zeneca and the Fondation Leducq. He has participated in clinical research protocols from Pfizer, Regeneron Pharmaceuticals Inc., The Medecines Company, Amgen, Acasti Pharma Inc., Novart.

Study Funding: None.

Background/Synopsis: Familial dysbetalipoproteinemia (FDBL), also referred as Type III hyperlipoproteinemia, is an autosomal recessive disorder associated with a reduced clearance of remnant lipoproteins from the circulation. The resulting accumulation of cholesterol-enriched IDL and remnant chylomicrons particles is associated with a very high cardiovascular risk. The most frequent genetic predisposition of FDBL is apoE2 homozygosity. However, the penetrance of this genetic defect is low and secondary factors such as obesity, insulin resistance or alcohol consumption must be present to precipitate FDBL. Unfortunately, this disease is largely underdiagnosed and untreated. Furthermore, little is known about the cardiovascular risk factors in this population.

Objective/Purpose: The objective of this study is to describe the clinical characteristics of an FDBL cohort and to investigate what are the predictors of cardiovascular disease in this population.

Methods: Inclusion criteria were the following: age ≥ 18 years, apoE2/2 phenotype, triglycerides (TG) > 1.5 mmol/L (or 133 mg/dL) and VLDL-C/TG ratio > 0.69 (in mmol/L, or > 0.3 in mg/dL). Clinical data were collected retrospectively to the baseline visit at the lipid clinic.

Results: A total of 224 FDBL patients were included in the analysis. The cohort was comprised of 59% of men and the average age was 52 years. The vast majority (94%) had the presence of broad-beta band on electrophoresis. A total of 51 subjects (23%) had history of CVD. The univariate predictors of CVD were hypertension (β=0.323, P=0.00003), diabetes (β=0.191, P=0.01), tuberous xanthomas (β=0.250, P=0.004) and tuberoeruptive xanthoma (β=0.165, P=0.03), whereas only hypertension (β=0.299, P=0.0002) and tuberous xanthomas (β=0.217, P=0.02) remained significantly associated with CVD in multivariate analysis.

Conclusions: The presence of hypertension or tuberous xanthomas are independently associated with a significant increase of CVD risk in FDBL subjects. Due to the high prevalence of cardiovascular disease in FDBL, aggressive treatment should be initiated in these patients.

LDL-C Values and Lipid Lowering Therapy Utilization in a Medicare Fee For Service (FFS) Population

Nihar Desai, MD, MPH, Stefan DiMario, PharmD, Kiran Philip, MD, Alison Petrilla, PhD, Xian Shen, PhD, Kevin Dietz, BA, BS, (New Haven, CT)
Background/Synopsis: LDL-C is a causal risk factor for atherosclerotic cardiovascular disease (ASCVD). CVD is the leading cause for morbidity, mortality, and health care spending among Medicare beneficiaries. In patients with clinical ASCVD, the 2018 ACC/AHA Guidelines recommends decreasing LDL-C with high intensity or maximally tolerated statin therapy. Little is known about contemporary patterns of LDL-C values and lipid lowering therapy (LLT) utilization among Medicare FFS beneficiaries.

Objective/Purpose: To assess LDL-C values and LLT utilization in the overall Medicare FFS population, patients with ASCVD, and those with a recent acute myocardial infarction (AMI).

Methods: This retrospective cohort study used the 100% Medicare Parts A/B/D claims linked to the Prognoz LDL-C database. Patients were indexed on their latest LDL-C value in calendar year 2017 and were required to have one year of continuous enrollment pre-index. Use of LLT was assessed in the 30-day pre-index period. LLT included statin, ezetimibe, and/or PCSK9i. Three cohorts were defined; all Medicare FFS beneficiaries, those with clinical ASCVD as defined by the 2018 ACC/AHA guidelines, and those with an AMI hospitalization in the one year pre-index. LDL-C values and LLT utilization were assessed for each cohort.

Results: A total of 3.8 million patients were included in the overall cohort, 1.4 million in the ASCVD cohort, and 23,064 in the AMI cohort. For the overall cohort, the mean age was 71 years, 43% were male, 40% had diabetes, and 78% and hypertension. Forty seven percent were not receiving LLT, 37% low- or moderate-intensity, and 12% high-intensity statin therapy. Mean (SD) LDL-C was 96 mg/dL (35), and 77% had an LDL-C ≥70 mg/dL. Among patients with ASCVD, 34% were not receiving LLT, 41% low- or moderate-intensity, and 20% high-intensity statin therapy. The mean LDL-C was 87 mg/dL (35), and 67% had an LDL-C ≥70 mg/dL. Among patients with an AMI, 19% were not receiving LLT, 29% low- or moderate-intensity, and 47% high-intensity statin therapy. The mean LDL-C was 77 (36), and 52% had an LDL-C ≥70 mg/dL.

Females and African Americans had higher levels of LDL-C across cohorts.

Conclusions: Among Medicare beneficiaries with ASCVD, one third are not treated with any LLT and nearly 7 out of 10 had an LDL-C value ≥70 mg/dL. Intensifying LLT among this group of patients remains a priority for performance improvement efforts, especially when considering over half of patients with an AMI had LDL-C ≥70 mg/dL.

LDL-C Distribution in Medicare FFS:

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Harvey Kaufman, MD, MBA, FCAP,
Kathryn Schurr, MS,
James Underberg, MD, (Needham, MA)

Lead Author’s Financial Disclosures: Employee of Quest Diagnostics.

Study Funding: None.

Background/Synopsis: In the US, cholesterol levels have declined for 50 years, until 2008, remaining flat from 2008-2011. From 2001-2008 low-density lipoprotein (LDL) cholesterol declined an average 2 mg/dL/year.

Objective/Purpose: We describe more recent LDL cholesterol trends, from 2010 to 2017.

Methods: LDL results from adults 20-99 years, tested at Quest Diagnostics, 2010-2017, were included, using the first result for each patient in each calendar year. Testing was performed on Olympus AU analyzers. LDL was calculated by Friedewald until 09/2017 and then by Martin-Hopkins. In addition, the population percent at varying levels of LDL was compared for each year, over time.

Results: 126,000,570 LDL results were obtained in 50,386,603 US adults (56% women, mean + SD age 52±17; 44% men, mean + SD age 52±16). Mean population LDL did not change meaningfully over the study period, for men (103-105 mg/dL) or women (107-109 mg/dL), across all age ranges (not shown). Similarly, there were no meaningful distribution changes across LDL ranges (Table).

Conclusions: In this study, mean LDL remained essentially constant from 2010-2017, for both men and women, across age ranges, with no meaningful distribution changes

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<td>Mean LDL Cholesterol (mg/dL)</td>
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<td>Overall</td>
<td>105.3</td>
<td>105.3</td>
<td>106.8</td>
<td>107</td>
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<td>106.7</td>
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<tr>
<td>Men</td>
<td>103.5</td>
<td>103.4</td>
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across LDL ranges. In light of clinical data suggesting lower LDL is associated with improved clinical outcomes, the lack of progress over the past decade suggests that efforts to lower LDL need to be re-examined. This has significant public health implications in the US.

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trends and goal achievement in LDL cholesterol according to cardiovascular risk in Chile: Overview from 2003 to 2016-2017

National Health Surveys

Guadalupe Echeverria, MSc, Paulina Mendoza, MD, Salinas Lorena, MD, Valentina Serrano, MD, MSc, Alvaro Passi, MSc, Alberto Maiz, MD, Attilio Rigotti, MD, PhD, Paula Margozzini, MD, MSc, (Santiago, Chile)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: High levels of LDL cholesterol (LDL-C) are an established risk predictor of cardiovascular disease (CVD) and the main target in dyslipidemia treatment for atherosclerosis management. Thus, trend assessments of LDL-C are needed to set and adjust lipid intervention priorities as well as to evaluate achievement of therapeutic lipid goals proposed by national clinical guidelines.

Objective/Purpose: To determine changes from 2003 to 2016-2017 in LDL-C levels, lipid lowering therapy use and LDL-C goal achievement according to CVD risk among Chilean adult population.

Methods: Chilean National Health Surveys (NHS) are cross-sectional household surveys performed by complex design random selection in non-institutionalized adults aged ≥18 years. In randomly selected subsamples, fasting total cholesterol, HDL cholesterol, and triglycerides were directly measured, whereas LDL and non-HDL cholesterol were calculated. Study analysis samples were as follows: 2003 (NHS2003) n=1,813; 2009-2010 (NHS2009-2010) n=2,581; and NHS 2016-2017 (NHS2016-17), n=3,382. Lipid lowering drug use was defined using ATC-WHO code C10 of nurse drug inventory. Local national guidelines were used for CVD risk stratification. Weighted 2003, 2009-2010 and 2016-2017 NHS LDL cholesterol means were compared using age-sex adjusted linear regression.

Results: From NHS2003 to NHS2009-10, LDL-C levels remained stable, but they decreased by 12 mg/dl in 2016-2017 (from 115 mg/dl in 2003 to 103 mg/dl in 2016-2017, p<0.001 adjusted by sex and age). This change in LDL-C levels was seen in all subgroups (sex, age, educational level, and urban/rural areas). Lipid lowering drug use increased from 1.9% in NHS2003 to 12.1% in NHS2016-17 in the total adult population as well as from 27.3% in NHS2009-2010 to 42.1% in NHS2016-2017 in subjects with previous CVD events. However, overall achievement of LDL-C goals in NHS2016-2017 based on national guidelines was only 56.9%. In this latter survey, attainment of LDL-C objectives was 83.1% in subjects at low CVD risk, 42.1% in moderate risk, and 19.6% at the high risk subgroup. Prevalence of LDL-C <70 mg/dl in individuals with known CVD was 8.5% in NHS2009-2010 versus 27.5% in NHS2016-2017.

Conclusions: Overall, these findings indicate a significant reduction in LDL-C levels in Chile over a 14-year period with better LDL-C goal achievement and higher lipid lowering drug use. Drug therapy in high CVD risk population and CVD survivors have also improved but still shows unacceptably low coverage. There is need for a more intensive approach in high risk groups in order to increase cost effectiveness of healthcare investment in CVD prevention in Chile.

Genetics, Gene Therapy and Atherosclerosis

263

Prevalence of Pathogenic Variants of Lipoprotein Metabolism Genes in a Single Lipidology Clinic*

Lane B. Benes, MD, Kent Brummel, MD, Michael Davidson, MD, (Chicago, IL)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Mendelian randomization and genome-wide association studies have identified genes causally related to and associated with dyslipidemia and coronary artery disease (CAD), however genetic testing is not routinely performed in the management of most lipid disorders.

Objective/Purpose: To determine the prevalence of pathogenic variants predisposing to dyslipidemia in a single lipidology clinic.

Methods: Patients in a single lipidology clinic were chosen by a lipidologist to undergo genetic testing based on the presence of at least one of the following: hypertriglyceridemia (defined as fasting serum triglycerides >150 mg/dL), elevated low-density lipoprotein-cholesterol (LDL-C) >190 mg/dL, low high-density lipoprotein-cholesterol (HDL-C) <40 mg/dL, elevated lipoprotein a (Lp(a)) >50 mg/dL or >100 nmol/L or history of premature CAD (defined as an acute coronary syndrome or revascularization before age 40 years in men and 50 years in women). Genetic testing was performed using GBinsight Comprehensive Dyslipidemia Panel that uses next-generation DNA sequencing (NGS) to analyze 127 genes known or suspected to be associated with dyslipidemia or CAD.

Results: Data for 84 patients are currently available, 82 (97.6%) of which were found to have at least one genetic variant predisposing to dyslipidemia or CAD. Known
Impact of Monogenic Familial Hypercholesterolemia and Polygenic Hypercholesterolemia Cardiovascular Disease Risk*

Liam R. Brunham, MD, PhD, Mark Trinder, MSc, Lubomira Cermakova, MSc, Gordon Francis, MD, G. B. Mancini, MD, (Vancouver, BC)

Lead Author’s Financial Disclosures: None.
Study Funding: Canadian Foundation for Innovation and Genome British Columbia.

Background/Synopsis: In 30–80% of patients with clinically-diagnosed Familial Hypercholesterolemia (FH), a pathogenic variant can be detected in the LDLR, APOB, or PCSK9 genes. Alternatively, ~20% of clinical FH is thought to be due to a polygenic cause. The cardiovascular disease (CVD) risk associated with polygenic versus monogenic FH has not been previously determined.

Objective/Purpose: We evaluated the impact of monogenic and polygenic causes of FH on CVD risk in a cohort of patients with clinically-diagnosed FH.

Methods: We prospectively recruited patients with ‘possible’, ‘probable’ or ‘definite’ FH, according to Dutch Lipid Clinic Network Criteria (n=555). We performed targeted sequencing of genes known to cause FH, and to detect common variants known to influence LDL levels to calculate polygenic risk scores. Cardiovascular events included premature unstable angina, myocardial infarction, cardiovascular revascularization, or stroke.

Results: We identified an FH-causing variant in 8.2% of possible, 25.6% of probable, and 51.0% of definite FH patients. A high polygenic risk score (>80th percentile) was identified in 33.5% of patients. Patients with an FH-causing variant had significantly higher levels of low-density lipoprotein cholesterol (LDL-C) than those without an FH-causing variant. A monogenic cause of FH was associated with significantly greater risk of CVD, whereas the risk of CVD in patients with polygenic FH was not significantly different than that of patients without an FH-causing variant. Interestingly, the presence of a high LDL-C polygenic risk score further increased risk among patients with monogenic FH.

Conclusions: Patients with monogenic FH are at increased risk of CVD compared to those with polygenic FH or those without an FH-causing variant. Genetic testing for FH can identify patients at greatest risk of CVD who may derive the most benefit from intensive lipid-lowering therapies.

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Incorporation of Genetic Testing for Familial Hypercholesterolemia Nearly Doubles Diagnosis Rate^

Emily Brown, MGC, Kathleen Byrne, CRNP, Dorothy Davis, RN, Rebecca McClellan, MGC, Thorsten Leucker, MD, Steven Jones, MD, Seth Martin, MD, (Baltimore, MD)

Lead Author’s Financial Disclosures: None.
Study Funding: None.

Background/Synopsis: Familial hypercholesterolemia (FH) is a hereditary condition characterized by elevated LDL-C from birth leading to premature coronary artery disease and physical sequelae of lipid deposition in tissues. Early diagnosis is critical since timely treatment can prevent atherosclerosis and coronary heart disease. Nevertheless, less than 10% of prevalent cases of FH in the United States have been diagnosed. Low rates of diagnosis may be attributable in part to affected patients not meeting the clinical diagnostic criteria of the Dutch Lipid Clinic Network (DLCN), Simon Broom diagnostic criteria, or MEDPED diagnostic criteria.

Objective/Purpose: To assess the utility of incorporating genetic testing into a patient’s evaluation for FH.

Methods: We retrospectively reviewed patients seen in the Advanced Lipids Disorders Clinic at Johns Hopkins Hospital between January 2015 and May 2018. Between June 2018 and December 2018, patients were consented to a prospective registry. DLCN, Simon Broom, and MEDPED criteria were applied to each patient, before and after genetic testing. Genetic testing included sequencing and deletion duplication analysis of four genes (LDLR, PCSK9, APOB, and LDLRAP1). Variants were classified according to the 2015 ACMG guidelines.

Results: The retrospective review and prospective study identified 135 adult, probands who were seen in our clinic for evaluation for heterozygous FH. Twenty-six individuals (19%) were determined to be heterozygous for a pathogenic or likely pathogenic variant. Using the DLCN criteria, 15 (57.7%) individuals met criteria for a definite diagnosis of FH prior to genetic testing. Thirteen patients (50%) met criteria using Simon Broom, and 16 (61.5%) patients met criteria using MEDPED prior to genetic analysis. None of the patients who did not meet DLCN or Simon Broom criteria had xanthomas or corneal arcus upon physical exam. Three patients who did not meet MEDPED criteria...
did have a history of xanthomas, and one patient also had corneal arcus prior to age 45 years. All of the patients not meeting criteria prior to genetic testing had a history of statin therapy.

Conclusions: Incorporating genetic testing nearly doubled the rate when of FH diagnosis compared to classification solely on clinical grounds. Affected individuals may not have originally met diagnostic criteria for a variety of reasons including having a mild phenotype or prior lipid lowering therapy modifying the clinical phenotype. Therefore, our data support genetic testing in evaluation for FH, as a definitive diagnosis has important implications for patients and their relatives.

### 324 Personalized Medicine for Dyslipemias by RNA Interference-Mediated Reductions in Apolipoprotein C3 or Angiopoietin-Like Protein 3

So C. Wong, PhD, Zhen Li, PhD, Bruce Given, MD, Mark Seefeld, PhD, Aaron Andersen, BS, Rui Zhu, PhD, Peter Havel, PhD, James Hamilton, MD, James Graham, PhD, Tao Pei, PhD, Julia Hegge, BS, Casi Schienebeck, BS, Gary Christensen, BS, Lucas Trilling, BS, Holly Hamilton, PhD, Qili Chu, PhD, Jeremy Briggs, BS, Meredith Hinkes, BS, Stephan Bertin, BS, (Madison, WI)

Lead Author’s Financial Disclosures: Employee of Arrowhead Pharmaceuticals.

Study Funding: None.

Background/Synopsis: Human genetic analysis has identified that individuals with loss-of-function mutations in either apolipoprotein-C3 (APOC3) or angiopoietin-like protein 3 (ANGPTL3) have very low plasma levels of triglycerides (TGs) and low-density lipoprotein (LDL-C), and a reduced risk of cardiovascular disease.

Objective/ Purpose: ANGPTL3 and APOC3 are primarily expressed in hepatocytes. An RNA interference (RNAi) based therapy using Arrowhead Pharmaceuticals’ TRiM platform to reduce APOC3 or ANGPTL3 production in the liver by gene silencing may be an effective approach to treat dyslipidemias and metabolic diseases (AHA 2018).

Methods: Highly potent and specific RNAi conjugates were identified targeting human and non-human primate (NHP) APOC3 transcripts (ARO-APOC3) or ANGPTL3 transcripts (ARO-ANG3). Rodent or NHP (high fructose diet-fed rhesus macaques) dyslipidemic animal models were used to study pharmacodynamic effects in target protein reduction and reductions in TGs and LDL-C.

Results: ARO-ANG3 was evaluated in LDL receptor knockout (LDLr KO) mice, diet-induced obese (DIO) mice, and leptin receptor defective mice, as well as a dyslipidemic NHP models. In all animal models, maximum serum reductions in ANGPTL3 of 96% were achieved and persisted for at least 8 weeks. Reductions in TGs and LDL-C were also observed. In DIO mice, improvements in glucose tolerance and reduction in hepatic steatosis were observed. Compared to LDLr KO mice treated with atorvastatin or ARO-ANG3 alone, reductions in TGs and LDL-C showed additive benefits when ARO-ANG3 and atorvastatin were administered in combination. ARO-APOC3 was evaluated in human APOC3 transgenic mice where dose-dependent reductions in serum human APOC3 protein (maximum 91%) and liver mRNA were observed along with reductions in TGs and LDL-C. In a dyslipidemic NHP model, reductions in serum APOC3 (up to 80%), TGs and LDL-C were observed, and the magnitudes of reductions correlated to the degree of dyslipidemia in the NHPs. Both ARO-ANG3 and ARO-APOC3 were well-tolerated in animal safety studies.

Conclusions: Our results support an RNAi therapeutic targeting APOC3 or ANGPTL3 as a treatment for dyslipidemia. ARO-ANG3 may also provide metabolic benefits in the liver and impact LDL in familial hypercholesterolemia. Both development candidates can be used to target specific patient populations depending on underlying genetic and metabolic profiles. ARO-APOC3 and ARO-ANG3 have recently entered human clinical trials.

### 325 Familial Hypercholesterolemia GENETic evaluation of Minority patients with an LDL-C >190mg/dL: FH GENE-Minority Study

Mary Katherine Cheeley, PharmD, CLS, FNLA, Allison Hester, PharmD, Adrian Brown, PharmD, Juliane Padgett, PharmD, Terry Jacobson, MD, FNLA, (Atlanta, GA)

Lead Author’s Financial Disclosures: Speakers bureau- Regeneron/Sanofi; Investigator Initiated Study Grant- Regeneron/Sanofi.

Study Funding: Funded by an investigator initiated study grant from Sanofi/Regeneron.

Background/Synopsis: Diagnosis of Familial Hypercholesterolemia (FH) can include use of multiple validated clinical tools that may rely on family history and/or genetic testing as well as other criteria. However, it was identified in an earlier study of patients at Grady Health System (GHS), an indigent health care system with a predominately minority population, that their family history is largely unknown; thus, making it difficult to accurately give a clinical diagnosis of FH. Genetic prevalence of FH, in a primary prevention population, has been shown to be about 2%; it has not been characterized in a predominately minority population.

Objective/Purpose: Data regarding FH in minority populations is lacking. This study reports the results of...
genetic testing and lp(a) levels for 100 patients at GHS with an LDL-C >190mg/dL.

**Methods:** All patients had a 7 gene genetic test (LDLR, PCSK-9 apoB, apoE, CETP, LDLRAP1, SREBF2) and Lp(a) measured in mg/dL. Patient were prospectively included from either the advanced lipid clinic or a system list of patients with an LDL-C >190 mg/dL. Patients were excluded if they had a secondary cause for elevated LDL-C, were pregnant, were incarcerated, or were age < 18 years old. Coronary Calcium Scoring was also conducted for primary prevention patient and is reported separately.

**Results:** One hundred patients were included in the study. Ninety-seven black, 2 hispanic, and 1 caucasian. Median baseline LDL-C 229 (IQR 214-250). Forty-three percent of patients have ASCVD. Baseline Dutch Lipid Score was 5 (IQR 3-5). Overall, 12 patients had a positive genetic test. Nine percent of patients had an LDL-C raising genetic defect. Eight patients had an LDLR mutation, 1 an apoB, and 3 patients had an apoE mutation. LDL-C in genetically positive patients was significantly higher than the negative group at 272 (238-289) vs 227 (211-245), median (IQR). Fifty patients had an Lp(a) above 50 mg/dL (median 52 [IQR 19.5-127.5]. Only 1 patient with a positive genetic test had a physical exam finding listed in the Dutch Lipid Criteria.

**Conclusions:** The incidence of genetically positive FH is similar in this minority population, compared to other studied groups. There was no difference in median Dutch Lipid Score, prior to genetic testing, between those who had a positive genetic test and those who were negative. There was no difference between the two groups with regards to median Lp(a). Existing population based clinical tools for a diagnosis of FH, such as the Dutch Lipid Criteria, failed to adequately identify genetically positive FH in this minority population.

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**Coronary Artery Calcium scores in asymptomatic minority subjects with phenotypic Familial Hypercholesterolemia**

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Adrian Brown, PharmD,
Terry Jacobson, MD, FNLA, (Atlanta, GA)

**Lead Author’s Financial Disclosures:** None.

**Study Funding:** Funded by an investigator initiated study grant from Sanofi/Regeneron.

**Background/Synopsis:** There is very little data about using coronary calcium (CAC) scores to further risk stratify those who present with the FH phenotype (LDL-C levels <190 mg/dL). Coronary artery calcium (CAC) scoring may be one method to identify those at higher CV risk who may require more aggressive treatment or an alternative way to identify those with the FH genotype.

**Objective/Purpose:** As part of the GENE-Minority study at Grady Health System (GHS) in Atlanta, Georgia, the probability of FH was determined. Within this indigent minority population, a large proportion of patients are unaware of their family history. Thus tools that rely heavily on patient-reported family history make the diagnosis of FH difficult without a genetic test. An alternative approach may be the use of CAC scores as an option to help risk stratify primary prevention patients. The aim of this study was to characterize the CAC scores of asymptomatic patients with baseline LDL-C <190 mg/dL, and to compare the CAC scores of patients with a positive versus negative genetic test.

**Methods:** Patients were included if they presented with an LDL-C <190 mg/dL and had no ASCVD. All patients had a genetic test and CAC scan. The genetic test evaluated 7 mutations associated with FH. CAC score and percentile, based on patient demographics, were compared across patients with positive versus negative genetic tests.

**Results:** Of a total of 54 patients, 98% of whom were African-American, 29 (53.7%) had a calcium score of 0. Of the 25 patients with a positive CAC score, the median adjusted population CAC percentile was 97% [IQR 78-99]. Those with a positive CAC score were generally older than the zero CAC group (mean age 57 vs 53 years). Of the 6 patients who had a FH genetic defect, only 2 had a positive CAC score (mean age 61 years) while 4 had a score of zero (mean age 34 years).

**Conclusions:** In this predominately African-American population, a clear association between elevated CAC scores and the FH phenotype was not demonstrated. Less than half of the cohort exhibited a positive CAC score and most of the genetically positive patients had a CAC score of zero. These data show that while CAC is a helpful tool at stratifying risk, it cannot replace genetic testing for patients with baseline LDL-C >190 mg/dL.

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**Increasing Diagnostic Yield for Inherited Lipidemias: Next-Generation Sequencing of An Expanded Panel**

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**Lead Author’s Financial Disclosures:** This author is a full-time employee of Phosphorus Diagnostics, the location where this research was performed.

**Study Funding:** None.
Background/Synopsis: The diagnosis of inherited lipid disorders is complicated by clinical overlap between syndromes, contributions of lifestyle and environment, and a spectrum of genetic risk, ranging from monogenic Mendelian disease to polygenic risk. Targeted genetic testing based only on clinical and biochemical phenotype can therefore be difficult due to these confounding variables. Multi-gene panel testing has been demonstrated to be an effective method of increasing diagnostic yield in inherited cancers and other clinical specialties, and could therefore be useful in inherited lipidaemia testing.

Objective/Purpose: We sought to determine the yield of testing of a multi-gene panel associated with a spectrum of inherited lipidaemias in a consecutive series of patients referred for clinical testing.

Methods: Next-generation-sequencing (NGS) analyzing a 21 gene panel was performed on 91 consecutive patients referred for inherited lipidaemia testing. Variants were classified in accordance with ACMG criteria.

Results: Pathogenic/Likely Pathogenic variants were identified in 18 patients. LDLR variants associated with familial hypercholesterolemia (FH) were identified in 12/91 (13.2%) patients. Heterozygous ABCG5 variants (c.1336C>T; p.Arg446Ter and c.1166G>A; p.Arg389His) associated with sitosterolemia were identified in 2 patients, and one patient was compound heterozygous for an APOB variant (exon 19-20 deletion) associated with hypobetalipoproteinemia and an ABCG8 variant (c.547delC; p.Gln183fs) associated with sitosterolemia. Two patients carried the same LPL variant (c.953A>G; p.Asn318Ser) associated with risk for hypertriglyceridemia and lipoprotein lipase deficiency, and one patient carried the c.1214C>T (p.Thr405Met) LIPC variant associated with hepatic lipase deficiency. In 5/6 patients with non-LDLR variants, the indication for testing was a diagnosis of familial hypercholesterolemia (ICD10: E78.01).

Conclusions: The inheritance pattern of familial lipidaemia is a spectrum, ranging from monogenic disease to polygenic risk. Three patients were heterozygous carriers for autosomal recessive disease and a fourth was compound heterozygous for variants associated with two different recessive diseases, indicating that carrier status may contribute to the phenotype in these patients. In two others, a variant in a gene not related to the primary indication for testing was identified, further indicating that variants in other genes may contribute to the phenotype of patients clinically diagnosed with FH. In summary, NGS for an expanded panel of lipid disorders can identify variants that contribute to patient phenotype and is a cost-effective method of increasing diagnostic yield.

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Genetic Testing for Hypertriglyceridemia - Pilot Data from a Single Center Lipid Clinic

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Lead Author's Financial Disclosures: None.

Study Funding: None. Genetic testing from this pilot study was provided without charge by GBinsight.

Background/Synopsis: Severe elevations of triglycerides can cause pancreatitis and triglyceride (TG) rich lipoproteins are likely causal risk factors for atherosclerotic cardiovascular disease (ASCVD) based on epidemiologic and Mendelian randomization studies. Moreover, genetic linkage studies have provided novel targets for therapy against hypertriglyceridemia. While hypertriglyceridemia is often a polygenic disease, genetic testing has potential to affect clinical decision making.

Objective/Purpose: The aim of this pilot study is to evaluate the clinical utility of genetic testing in a lipid clinic for patients with hypertriglyceridemia.

Methods: In collaboration with GBinsight, we conducted a pilot study of 40 patients who had genetic testing. Patients presented to lipid clinic from January 2018 to December 2018 and provided informed consent and saliva samples. Monogenic variants were reported as pathogenic/likely pathogenic, variants of unknown significance projected as likely high-risk. The prevalence of diabetes was 25%. The mean (standard deviation) for relevant clinical data were: highest documented TG 1906 (192), high-density lipoprotein (HDL) cholesterol 31 (16), non-HDL cholesterol 204 (112), fasting glucose 117 (61), and BMI 27.0 (4.5). Genotypic data per individual are presented in Table 1.

Conclusions: Genetic testing in patients with hypertriglyceridemia has a high yield for pathogenic variants and variants of unknown significance projected as likely high risk. Larger studies are needed which include various ethnic groups, especially South Asians, as previous recommendations may have underestimated the benefit of routine genetic testing in this population.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Race</th>
<th>Variant</th>
<th>Zygosity</th>
<th>Polygenic Risk Score</th>
<th>Highest recorded TG level (mg/dL)</th>
<th><strong>Presenting lipid values (mg/dL)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hispanic</td>
<td>LPL(c.953A&gt;G(p.Asn318Ser)) ◊ APOA5(c.56C&gt;G(p.Ser19Trp)) APOE(E4(p.Cys130Arg)) APOE(E2(p.Arg176Cys)) ZPR1(c.*724C&gt;G)</td>
<td>Heterozygous</td>
<td>98</td>
<td>1493</td>
<td>TG 1493 HDL-C 28 Non-HDL-C 354</td>
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<tr>
<td>2</td>
<td>South Asian</td>
<td>ABCA1(c.1913G&gt;A(p.Arg638Gln))</td>
<td>Heterozygous</td>
<td>98</td>
<td>1518</td>
<td>TG 1371 HDL-C 11</td>
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<tr>
<td>3</td>
<td>Caucasian</td>
<td>LPL(c.929G&gt;A(p.Cys310Tyr)) CREB3L3(c.731_732insG(p.Lys244Glufs)) LMF1(c.1052G&gt;A (p.Arg351Gln)) SVEP1(c.8105A&gt;G (p.Asp2702Gly)) ZPR1(c.*724C&gt;G)</td>
<td>Homozygous</td>
<td>90</td>
<td>2353</td>
<td>Non-HDL-C 98 HDL-C 148</td>
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<tr>
<td>4</td>
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<td>417</td>
<td>TG 356 HDL-C 55 Non-HDL-C 208</td>
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<tr>
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<td>1119</td>
<td>HDL-C 24 Non-HDL-C 269</td>
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<td>ABCA7(c.274G&gt;T(p.Gly92Trp)) APOE(E4(p.Cys130Arg)) POMC(c.706C&gt;G(p.Arg236Gly)) PPARC(c.625G&gt;T(p.Ala237Ser))</td>
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<td>84</td>
<td>1000</td>
<td>TG 160 HDL-C 50 Non-HDL-C 143</td>
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<tr>
<td>7</td>
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<td>Homozygous</td>
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<td>1100</td>
<td>TG 531 HDL-C 15 Non-HDL-C 119</td>
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<tr>
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<td>4500</td>
<td>HDL-C 26 Non-HDL-C 444</td>
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<tr>
<td>9</td>
<td>Caucasian</td>
<td>ABCG8(c.55G&gt;C (p.Asp19His)) APOA5(c.553G&gt;T(p.Gly185Cys)) CD300LG(c.244C&gt;T(p.Arg82Cys))</td>
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<td>520</td>
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<tr>
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<td>7145</td>
<td>TG 1567 HDL-C 24 Non-HDL-C 276</td>
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<td>1359</td>
<td>TG 1109 HDL-C 13 Non-HDL-C 198</td>
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<td>12</td>
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<td>APOE(E2(p.Arg176Cys)) LPA(c.4262G&gt;A(p.Arg1421Gln)) ZPR1(c.*724C&gt;G)</td>
<td>Heterozygous</td>
<td>26</td>
<td>353</td>
<td>TG 160 HDL-C 35 Non-HDL-C 99</td>
</tr>
</tbody>
</table>

TG = triglyceride, HDL-C = high density lipoprotein cholesterol
◊ Indicates variant classified as pathogenic. All other variants are classified as variants of undetermined significance projected as likely high risk.
* Indicates a translation termination (stop) codon
**Lipid results are preclinic laboratory values from the visit that genetic testing sample was collected
Familial hypercholesterolemia (FH) is a common genetic disorder cause of premature atherosclerosis due to chronically elevated low-density lipoprotein cholesterol (LDL-C) levels from birth. Individuals with FH experience an increased risk of premature cardiovascular disease (CVD), and lack of early identification and treatment increases the risk of CVD-related coronary events later in life.

**Objective/Purpose:** We report two siblings with FH caused by a novel mutation in APOB.

**Methods:** Electronic medical records were reviewed for two patients with FH.

**Results:** Two biologically related siblings (male age 9, female age 11) were found to have LDL-C levels >95th centile for respective age and gender. Neither sibling had preexisting medical conditions nor a history of chronic medications. Both siblings were found to have the same missense variant in the APOB gene, a novel mutation causing hypercholesterolemia. Because of parental concerns regarding usage of statins, both were treated with a cholesterol absorption inhibitor.

**Conclusions:** Despite the benefits of early identification of those at moderate-to-severe risk, several knowledge gaps impede successful cholesterol screening of children: misunderstanding goals of screening, the best screening method, and ideal age for screening and for intervention. Current guidelines recommend universal cholesterol screening and selective screening starting at 10 and 2 years of age, respectively. Although not routinely preformed, identification of a genetic mutation helps to 1) confirm the diagnosis of FH; and 2) serve as an additional risk factor for CVD, aids risk stratification and clinical-decision making, and helps determine the timing and intensity of treatment that would provide the best long-term health benefits. In addition to lipid-lowering medications, treatment should include global reduction of all CVD risk factors through health education, and adoption of life-long, heart-healthy living with a goal to reduce LDL-C levels to <100mg/dL or at least 50% or more.

**Exome Secondary Findings identifies an incidental FH prevalence rate of 1 in 500**

Andrew Castro, MS, CGC, Kirsten Blanco, BS, Tami Johnston, MS, CGC, Benjamin Feldmann, MS, CGC, Jill Dolinsky, RN, MS, CGC, Zoe Powis, MS, CGC, (Aliso Viejo, CA)

**Lead Author’s Financial Disclosures:** Andrew Castro is an employee of Ambry Genetics.

**Study Funding:** None.

**Background/Synopsis:** The American College of Medical Genetics and Genomics (ACMG) recommends clinical genetic testing laboratories return secondary findings (SF) with diagnostic exome sequencing in 59 genes associated with medically actionable conditions. Among these genes are APOB and LDLR, genes associated with familial hypercholesterolemia (FH). Through clinical diagnostic exome sequencing, individuals and family members with disease-causing alterations in FH genes can be identified. These individuals may or may not have prior known symptoms of FH; however, a causative pathogenic alteration in the LDLR or APOB gene is sufficient for a definite diagnosis of FH, per Dutch Lipid Clinic Network criteria.

**Objective/Purpose:** We aim to assess the rate of pathogenic alterations in APOB or LDLR in individuals and their family members undergoing diagnostic exome sequencing.

**Methods:** We retrospectively analyzed SF results of APOB and LDLR and provided clinical information from 15,832 individuals from 7,990 families.

**Results:** In total, 13 individuals (0.08% of individuals) from 10 families (0.13%) were positive for a pathogenic alteration in APOB and 31 individuals (0.20% of individuals) from 24 families (0.30%) were positive for a pathogenic alteration in LDLR. Overall, 44 individuals (0.28%) from 34 families were positive for an FH pathogenic alteration. The average age of testing was 26.2 years (range <1 to 67), with 16 individuals <18 years old (36.4% of positive individuals). 10 (22.7%) positive individuals were under 9 years old. Among patients tested between ages 9-18 (n=2,349), 0.3% had a pathogenic FH alteration.

One family had a reported family history of hypercholesterolemia (paternal grandmother of proband), but the alteration present in this family was not paternally inherited. No individuals had a reported personal history of hypercholesterolemia. All individuals were heterozygous for reported pathogenic alterations.

**Conclusions:** The prevalence of FH-positive individuals within our cohort (1/500) is lower than some previously reported estimates of 1/200-1/250, but higher than that reported in a 1000 Genomes assessment (1/1000) even without the addition of the genes PCSK9 and LDLRAP1. It is uncertain if the scarcity of clinical history of hypercholesterolemia indicates a lack of blood cholesterol testing, under-reporting by patients, and/or lack of FH-related discussion between provider and patient. Regardless, no individuals with a pathogenic alteration had a reported personal or family history of FH.

**Lead Author’s Financial Disclosures:** Andrew Castro is an employee of Ambry Genetics.

**Study Funding:** None.

**Background/Synopsis:** Familial hypercholesterolemia (FH) is a common genetic disorder cause of premature atherosclerosis due to chronically elevated low-density lipoprotein cholesterol (LDL-C) levels from birth. Individuals with FH experience an increased risk of premature cardiovascular disease (CVD), and lack of early identification and treatment increases the risk of CVD-related coronary events later in life.

**Objective/Purpose:** We report two siblings with FH caused by a novel mutation in APOB.

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**Conclusions:** Despite the benefits of early identification of those at moderate-to-severe risk, several knowledge gaps impede successful cholesterol screening of children: misunderstanding goals of screening, the best screening method, and ideal age for screening and for intervention. Current guidelines recommend universal cholesterol screening and selective screening starting at 10 and 2 years of age, respectively. Although not routinely preformed, identification of a genetic mutation helps to 1) confirm the diagnosis of FH; and 2) serves as an additional risk factor for CVD, aids risk stratification and clinical-decision making, and helps determine the timing and intensity of treatment that would provide the best long-term health benefits. In addition to lipid-lowering medications, treatment should include global reduction of all CVD risk factors through health education, and adoption of life-long, heart-healthy living with a goal to reduce LDL-C levels to <100mg/dL or at least 50% or more.

**Exome Secondary Findings identifies an incidental FH prevalence rate of 1 in 500**

Andrew Castro, MS, CGC, Kirsten Blanco, BS, Tami Johnston, MS, CGC, Benjamin Feldmann, MS, CGC, Jill Dolinsky, RN, MS, CGC, Zoe Powis, MS, CGC, (Aliso Viejo, CA)
hypercholesterolemia, indicating the increased need for screening and genetic testing for FH. Given that FH mutation carriers have a higher risk of coronary artery disease at all LDL levels, patients with FH mutations identified through diagnostic exome sequencing warrant follow up by a cardiologist or lipid specialist, including a number of minor children, age.

Hypertriglyceridemia

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The Economic Burden of Hypertriglyceridemia Among US Adults With Diabetes or Atherosclerotic Cardiovascular Disease on Statin Therapy*

Brian C. Case, MD, Adam Bress, PharmD, MS, Paul Kolm, PhD, Sephy Philip, PharmD, Jennifer Herrick, Craig Granowitz, MD, PhD, Peter Toth, MD, PhD, Wenjun Fan, MD, MS, Nathan Wong, PhD, MPH, Michael Hull, MS, William Weintraub, MD, (Washington, DC)

Table 1 Generalized Linear Models with Bootstrapping for Total Health Care Costs (PPPM) in the Follow-up Period for Various Population Subsets

<table>
<thead>
<tr>
<th>Population Subset</th>
<th>Study Group: Triglycerides ≥ 150 mg/dL vs. Comparison: Triglycerides &lt; 150 mg/dL and HDL-C &gt; 40 mg/dL</th>
<th>Estimated Mean Difference</th>
<th>LCL (95%)</th>
<th>UCL (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td>194.79</td>
<td>147.57</td>
<td>241.43</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-64</td>
<td></td>
<td>232.63</td>
<td>148.85</td>
<td>331.60</td>
</tr>
<tr>
<td>55-64</td>
<td></td>
<td>174.30</td>
<td>99.89</td>
<td>253.19</td>
</tr>
<tr>
<td>65+</td>
<td></td>
<td>176.75</td>
<td>100.97</td>
<td>247.69</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>209.54</td>
<td>138.72</td>
<td>286.89</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>181.76</td>
<td>114.57</td>
<td>237.55</td>
</tr>
<tr>
<td>Coverage Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td></td>
<td>211.40</td>
<td>148.53</td>
<td>272.56</td>
</tr>
<tr>
<td>Medicare</td>
<td></td>
<td>136.28</td>
<td>69.56</td>
<td>208.02</td>
</tr>
<tr>
<td>Geographic Region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td></td>
<td>177.39</td>
<td>26.36</td>
<td>327.83</td>
</tr>
<tr>
<td>Midwest</td>
<td></td>
<td>209.11</td>
<td>76.05</td>
<td>357.89</td>
</tr>
<tr>
<td>West</td>
<td></td>
<td>178.72</td>
<td>15.36</td>
<td>343.56</td>
</tr>
<tr>
<td>South</td>
<td></td>
<td>194.48</td>
<td>137.36</td>
<td>246.60</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td>202.64</td>
<td>154.09</td>
<td>257.09</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>166.88</td>
<td>54.20</td>
<td>281.00</td>
</tr>
<tr>
<td>ASCVD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td>230.42</td>
<td>129.46</td>
<td>325.30</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>179.06</td>
<td>131.21</td>
<td>235.99</td>
</tr>
</tbody>
</table>

*Estimated mean differences were calculated using adjusted GLM models with gamma distribution and log link on the model outcome, total costs in the follow-up period as per patient per month (PPPM). A total of 1,000 bootstrap iterations were conducted for each analysis to produce bias-corrected upper and lower 95% confidence intervals (Cameron, A.C., Trivedi, P.K. Microeconomics Using Stata, Stata Press: College Station, 2009). Outcomes were adjusted for age, gender, insurance coverage, geographic region, diabetes in baseline, and ASCVD in baseline.

Figure 1 Inclusion and Exclusion Criteria of Participants

Lead Author’s Financial Disclosures: None.

Study Funding: Supported by a research grant from Amarin Pharma, Inc.
Methods: We estimated population sizes and annual healthcare costs associated with triglycerides $\geq 150$ mg/dL compared to $< 150$ mg/dL + HDL-C $> 40$ mg/dL overall and in subgroups.

Table 2  Projected number of US adults $\geq 45$ years taking a statin and with ASCVD or diabetes, adjusted incremental total healthcare costs, and total annual costs associated with triglycerides $\geq 150$ mg/dL compared to $< 150$ mg/dL + HDL-C $> 40$ mg/dL overall and in subgroups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Population Sizes (95% CI), in Millions from NHANES</th>
<th>Adjusted Incremental Total Healthcare Costs from OPTUM Research Database, USD</th>
<th>Projected annual cost burden due to triglycerides $\geq 150$ mg/dL vs $&lt; 150$ mg/dL + HDL-C $&gt; 40$ mg/dL, Billions of USD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>8.3 (7.1-22.3)</td>
<td>$2,340 ($1,770-$2,900)</td>
<td>$11.9 ($8.5-$15.3)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45 to &lt;55</td>
<td>1.0 (0.6-1.3)</td>
<td>$2,790 ($1,790-$3,980)</td>
<td>$2.2 ($1.1-$3.4)</td>
</tr>
<tr>
<td>55 to &lt;65</td>
<td>1.6 (1.2-2.2)</td>
<td>$2,090 ($1,200-$3,040)</td>
<td>$3.1 ($1.3-$4.9)</td>
</tr>
<tr>
<td>65+</td>
<td>5.7 (4.9-6.5)</td>
<td>$2,120 ($1,210-$2,970)</td>
<td>$5.9 ($3.3-$8.6)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4.4 (3.8-5.0)</td>
<td>$2,510 ($1,660-$3,440)</td>
<td>$6.5 ($3.8-$9.3)</td>
</tr>
<tr>
<td>Female</td>
<td>3.9 (3.1-4.7)</td>
<td>$2,180 ($1,370-$2,850)</td>
<td>$5.5 ($3.3-$7.7)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4.6 (4.0-5.2)</td>
<td>$2,430 ($1,850-$3,090)</td>
<td>$9.5 ($6.6-$12.4)</td>
</tr>
<tr>
<td>No</td>
<td>3.7 (2.9-4.5)</td>
<td>$2,000 ($650-$3,370)</td>
<td>$2.4 ($0.6-$4.2)</td>
</tr>
<tr>
<td>ASCVD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5.2 (4.2-6.2)</td>
<td>$2,770 ($1,550-$3,900)</td>
<td>$6.9 ($3.7-$10.2)</td>
</tr>
<tr>
<td>No</td>
<td>3.1 (2.7-3.5)</td>
<td>$2,150 ($1,570-$2,830)</td>
<td>$5.6 ($3.7-$7.5)</td>
</tr>
</tbody>
</table>

Background/Synopsis: Hypertriglyceridemia (HTG) is associated with increased cardiovascular disease (CVD) risk. However, the cost burden of HTG-related CVD in high-risk US adults is not well characterized.

Objective/Purpose: We estimated the HTG-related healthcare cost burden among US adults with CVD or diabetes taking statin therapy.

Methods: We estimated population sizes and annual healthcare costs among US adults age $\geq 45$ years with diabetes or CVD taking statin therapy with 'normal' triglycerides (TG) as defined as TG $< 150$ mg/dL and high-density lipoprotein cholesterol (HDL-C) $> 40$ mg/dL compared to those with HTG as defined as $\geq 150$ mg/dL regardless of HDL-C. Population sizes were estimated from the 2011-2014 National Health and Nutrition Examination Surveys. Adjusted total annual healthcare costs in 2015 US dollars were estimated using the Optum Research Database. The annual total healthcare cost burden was estimated by multiplying the population size by the mean annual total incremental healthcare costs overall and within subgroups.

Results: There were 5.1 (95% CI, 4.3-5.9) million and 8.3 (95% CI, 7.1-22.3) million US adults age $\geq 45$ years with diabetes and or CVD with TG $\geq 150$ mg/dL (HTG) and TG $< 150$ mg/dL + HDL-C $> 40$mg/dl ('normal'), respectively. The mean adjusted incremental total one-year healthcare costs in adults with TG $\geq 150$ mg/dL compared to those with TG $< 150$ md/dl + HDL-C $> 40$mg/dl was $2,340 (95% CI, $1,770-$2,900). This leads to a projected annual cost burden associated HTG in patients with diabetes or CVD of $11.9 billion (95% CI, $8.5B-$15.3B). The annual cost burden is higher for adults over the age of 65 years old, with 2.8 million (95% CI, 2.3M-3.3M) US adults with HTG, leading to a projected annual cost burden associated with HTG of $5.9 billion (95% CI, $3.3B-$8.6B). The mean adjusted incremental total one-year healthcare cost in adults with HTG and diabetes is $2,430 (95% CI, $1,850-$3,090), which leads to a total projected annual cost burden $9.5 billion. The
Hypertriglyceridemia is associated with increased atherosclerotic cardiovascular disease (ASCVD) risk and remains prevalent in US adults due to the increasing prevalence of obesity, insulin resistance, and other risk factors. Moderately elevated triglycerides (TG) are also associated with increased ASCVD risk, even in statin-treated patients with well-managed low-density lipoprotein cholesterol. The recently completed REDUCE-IT cardiovascular outcomes trial included statin-treated patients with high ASCVD risk and baseline TG 135 to 499 mg/dL.

**Objective/Purpose:** To examine the prevalence of TG $\geq 135$ mg/dL in the overall US adult population, in those who are statin-treated, and according to presence of ASCVD and/or diabetes.

**Methods:** We studied 9593 US adults aged 20 years and older (projected to 219.9 million) in the US National Health and Nutrition Examination Survey (NHANES; 2007-2014) who had available morning fasting TG. We determined the proportions of individuals with TG $\geq 135$ mg/dL according to statin use, LDL-C levels, diabetes, ASCVD, and/or age.

**Results:** Overall, the proportion of adults with TG $\geq 135$ mg/dL was 32% (71M individuals; Table). Among statin-treated adults, the proportion with TG $\geq 135$ mg/dL was 39% (15M) and ranged from 35% to 48% for those who also had LDL-C controlled to <100 mg/dL, diabetes, and/or ASCVD (Table).

**Conclusions:** Based on our analysis, more than 30% (71M) of all US adults have TG $\geq 135$ mg/dL, including 39% (15M) of those being treated with statins. Better efforts are needed to identify and address 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.

---

**Prevalence of US Adults With Triglycerides $\geq 135$ mg/dL: NHANES 2007-2014**

<table>
<thead>
<tr>
<th>Prevalence, %</th>
<th>Patients With TG $\geq 135$ mg/dL, millions*</th>
<th>Total Number of Patients, millions*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>32.1</td>
<td>70.5</td>
</tr>
<tr>
<td>Statin treated</td>
<td>39.0</td>
<td>15.2</td>
</tr>
<tr>
<td>Statin treated and LDL-C $&lt;100$ mg/dL</td>
<td>35.0</td>
<td>7.6</td>
</tr>
<tr>
<td>Statin treated and diabetes</td>
<td>47.6</td>
<td>5.9</td>
</tr>
<tr>
<td>Statin treated and ASCVD</td>
<td>38.7</td>
<td>4.1</td>
</tr>
<tr>
<td>Statin treated and diabetes or ASCVD</td>
<td>43.0</td>
<td>8.1</td>
</tr>
<tr>
<td>Statin treated and diabetes or ASCVD and $\geq 45$ yrs</td>
<td>39.3</td>
<td>7.6</td>
</tr>
<tr>
<td>Statin treated and diabetes or ASCVD and $\geq 45$ yrs and LDL-C $&lt;100$ mg/dL</td>
<td>39.3</td>
<td>4.9</td>
</tr>
</tbody>
</table>

*Projected number of US adults.

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**Comparison of Atherosclerotic Plaque Characteristics among Normal and High Triglycerides (TG) Patients**

Lavanya Cherukuri, MD, Chandana Shekar, MD, April Kininger, MD, Divya Birudaraju, MD, Sajad Hamal, MD, Ferdinand Flores, MD, John Tayek, MD, Sion Roy, MD, Matthew Budoff, MD, John Nelson, MD, Amit Johanis, (Torrance, CA)
Table 1  Baseline characteristics among patients

<table>
<thead>
<tr>
<th>Baseline Demographics</th>
<th>High TGs group (n=48)</th>
<th>Normal TGs group (n=48)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>57.2 ± 8.8</td>
<td>57.46 ± 9.25</td>
<td>0.902</td>
</tr>
<tr>
<td>Male Gender (%)</td>
<td>31</td>
<td>31</td>
<td>1.00</td>
</tr>
<tr>
<td>BMI (kg/m²)*</td>
<td>32.7 ± 6.0</td>
<td>32.69 ± 7.52</td>
<td>0.986</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>32</td>
<td>32</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>36</td>
<td>34</td>
<td>0.646</td>
</tr>
<tr>
<td>Current Smoker (%)</td>
<td>1</td>
<td>6</td>
<td>0.0497</td>
</tr>
<tr>
<td>Family History of CAD (%)</td>
<td>15</td>
<td>22</td>
<td>0.1421</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>37.9 ± 9.1</td>
<td>49.3 ± 17.6</td>
<td>0.00</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>95.4 ± 42.2</td>
<td>71.4 ± 28.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>270.6 ± 82.9</td>
<td>106.1 ± 36.8</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Table 2  Quantitative plaque scores (median ± SD)

<table>
<thead>
<tr>
<th>Normalized Quantitative Plaque Scores</th>
<th>High TGs group (n=48)</th>
<th>Normal TGs group (n=48)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized Total Dense Calificated Volume</td>
<td>46.2 ± 145.4</td>
<td>23.5 ± 327.6</td>
<td>0.44</td>
</tr>
<tr>
<td>Normalized Total Fibrous Fatty Volume</td>
<td>25.2 ± 56.5</td>
<td>18.3 ± 78.8</td>
<td>0.32</td>
</tr>
<tr>
<td>Normalized Total Fibrous Volume</td>
<td>93.9 ± 175.5</td>
<td>132.3 ± 290.4</td>
<td>0.79</td>
</tr>
<tr>
<td>Normalized Total Low Attenuation Volume</td>
<td>13.8 ± 57.1</td>
<td>1.9 ± 45.4</td>
<td>0.02</td>
</tr>
<tr>
<td>TNCP Volume</td>
<td>132.2 ± 267.4</td>
<td>175.9 ± 384.6</td>
<td>0.94</td>
</tr>
<tr>
<td>Total Plaque Volume</td>
<td>195 ± 373.1</td>
<td>250.9 ± 639.5</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Hypertriglyceridemia is a major risk factor for cardiovascular disease (CVD). We compared patients with high triglycerides (TGs) enrolled in a double-blind, randomized trial EVAPORATE (Effect of Vascepa on Improving Coronary Atherosclerosis in people with High Triglycerides Taking Statin Therapy), with those with normal TGs.

Objective/Purpose: We intended to assess the differences in atherosclerotic plaque burden and characteristics between these two groups.

Methods: We identified 48 patients with TGs >200mg/dl undergoing Coronary Computed Tomography Angiography (CCTA) (31 male) enrolled in the EVAPORATE trial. We matched this cohort 1:1 by age, gender, body mass index and diabetes with individuals averaging TGs <150 mg/dl, (31 male) (Table 1). Using semi-automated plaque analysis software, we quantified coronary plaque (total, calcified, non-calcified including fibrous, fibrous-fatty and low attenuation plaque) volume on their CCTAs. Median levels between the cohorts normalized coronary plaque and lipids (HDL and TGs) were tested via the Wilcoxon Rank Sum test, whereas mean LDL, age and BMI were analyzed by independent t tests. Risk factor differences (DM, HTN, smoking, family history of CAD) between the cohorts were assessed with Chi-square.

Results: Patients with high TGs had more low attenuation plaque (LAP) volume when compared to the patients with normal TGs [13.8 +/- 57.1 mm³ v/s 1.9 +/- 45.4 mm³ (p value 0.02)]. (Table 2).

Conclusions: Individuals enrolled in the EVAPORATE trial, with higher TGs had more low attenuation plaque when compared to the individuals with normal TGs. As low attenuation plaque is more vulnerable to plaque rupture, prompt treatment to lower triglycerides are of vital importance.

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Meta-analysis of Effects of Triglyceride Modifiers on Cardiovascular Outcomes*

Hammod Rahman, MD, Safi Khan, MD, Swapna Talluri, MD, Muhammad Asif, MD, Tehseen Hammad, MBBS, Edo Kaluski, MD, FACC, (Sayre, PA)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: The impact of triglyceride (TG) lowering therapy on cardiovascular (CV) outcomes remains unclear.

Objective/Purpose: To investigate the effects of TG modifiers on CV disease.

Methods: 30 randomized trials having ≥200 patients with ≥6-month follow-up period were selected using PubMed/Medline, EMBASE and the CENTRAL (Inception- 30 May 2018) comparing TG modifiers (fibrates, niacin or omega-3 fatty acids (U-3)) with the control group. Outcomes were major adverse cardiovascular events (MACE) [composite of myocardial infarction (MI), stroke, CV mortality and coronary revascularization (CR)], its
components and all-cause mortality. These were reported as relative risk (RR) with 95% confidence interval (CI) using random effects model.

**Results:** In analysis of 140,529 patients with mean follow-up of 46 ± 19.8 months, TG-modifiers significantly reduced MACE (RR: 0.92; 95% CI, 0.89-0.96; P<0.001), CV mortality (RR: 0.94; 95% CI, 0.89-0.98; P=0.008), MI (RR: 0.86; 95% CI, 0.80-0.92; P<0.001) and CR (RR: 0.94; 95% CI, 0.91-0.98; P=0.005) but had neutral effect on stroke (RR: 1.02; 95% CI, 0.93-1.12; P=0.64) and all-cause mortality (RR: 0.99; 95% CI, 0.95-1.04; P=0.78).

Subgroup analysis revealed significantly lower MACE, CV mortality and MI rates limited to studies without background statin therapy. Significant reduction of MACE and MI was derived mostly from fibrates while CV mortality was limited to U-3 use. Moment of meta regression analyses demonstrated significantly decreased MI and CR associated with absolute reduction (mmol/L) of LDL-C; however no beneficial effect was noted by absolute reduction of triglycerides or absolute increase of HDL-C.

**Conclusions:** TG modifiers significantly reduced MACE, CV mortality and MI in the absence of concurrent statin therapy.

**Figure 1** Forest plot comparing Triglyceride (TG) modifiers for major adverse cardiovascular outcomes (MACE).

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**Severe Combined Hyperlipidemia, Heterozygous APOE p.V254E, Pancreatitis, Diabetes Mellitus, and Plantar Xanthomas***

Brian Cheung, MD, Barry Tedder, MD, FACC, Ernst Schaefer, MD, FNLA, Robert Hegele, MD, (Jonesboro, AR)

**Lead Author’s Financial Disclosures:** None.

**Study Funding:** Dyslipidemia Foundation.

**Background/Synopsis:** Severe combined hyperlipidemia is a condition caused by the APOE E2/2 genotype or other rare APOE mutations usually associated with other conditions, including diabetes mellitus and/or familial combined hyperlipidemia. The disease may be associated with premature cardiovascular disease, as well as tuberoeruptive and palmar xanthomas.

**Objective/Purpose:** Our goal was to fully evaluate a patient presenting with severe hypertriglyceridemia, pancreatitis, diabetes, and plantar xanthomas.

**Methods:** A careful history, physical examination, lipid and lipoprotein testing, standard clinical chemistry, and lipase and amylase measurements were performed. Computed tomography scans of the abdomen and pelvis were used to confirm the diagnosis of pancreatitis. APOE genotyping was carried out at Boston Heart Diagnostics in Framingham, MA, and next generation DNA sequencing was performed at the LPL, APOC2, APOA5, LF1, GPIHB1, GCKR, CREB3L3, GPD1, APOE, and APOC3 gene loci as well as other genes associated with lipid disorders, including LDLR, APOB, and PCSK9, on the Illumina MiSeq platform at the Roberts Research Institute at the University of Western Ontario, Canada.

**Results:** A 56-year-old obese Caucasian woman presented with pancreatitis, marked hypertriglyceridemia, and uncontrolled diabetes mellitus. She has a history of mild carotid disease, abdominal aorta non-obstructive atherosclerotic disease, and subclavian and coronary artery calcifications. She was noted to have right Achilles tendon xanthomas and multiple large chronic non-tender non-pruritic bilateral plantar xanthomas on the soles of her feet with no palmar or tuberoeruptive xanthomas. Her non-fasting lipids in mg/dL were: triglycerides (TG) >1575 and total cholesterol (TC) >650. Fasting lipid and apolipoprotein (apo) levels in mg/dL were: TG 1273, TC 493, direct low-density lipoprotein cholesterol (LDL-C) 210, high-density lipoprotein cholesterol (HDL-C) 36, apoB 224, and lipoprotein (a) 8. She was managed with intravenous fluids and insulin, and was subsequently placed on fish oil, fenofibrate, atorvastatin, ezetimibe, and pioglitazone, along with a low-fat, low-sugar diet. Her follow-up fasting lipid values in mg/dL were: TG 509, TC 216, direct LDL-C 66, HDL-C 48, and apoB 134. She had the APOE E3/3 genotype, and was heterozygous for the APOE missense

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**Plantar Xanthomas on Left Foot:**
lipolysis, leading to severe hypertriglyceridemia and high-risk of pancreatitis. Data on postprandial dietary fatty acid (FA) metabolism are however limited in this population.

**Objective/Purpose:** To compare postprandial metabolism among FCS patients, healthy controls and subjects with multifactorial chylomicronemia (MCM).

**Methods:** Twenty-one patients with FCS (11 women/10 men) aged 55 [43-60] (median [IQR]) with a body mass index (BMI) of 23.4 [21.6-25.5] kg/m2 underwent a low-fat (13g) liquid meal test labeled with 3H-palmitate and were compared to 32 healthy controls (18 women/14 men) aged 47 [33-55] with a BMI of 25.9 [24.9-27.6] kg/m2 and to 12 MCM subjects (4 women/8 men) aged 58 [50-62] with a BMI of 32.5 [29.2-34.2] who underwent a high-fat (100g) liquid meal test with either 3H- or 13C-palmitate labeling. A subset of participants simultaneously underwent intravenous infusion of d5-glycerol (9 FCS, 21 controls, 11 MCM) or d2-palmitate (7 FCS, 19 controls, 10 MCM) to measure plasma glycerol and nonesterified FA appearance rates and dietary FA spillover.

**Results:** Fasting plasma glucose levels and postprandial glucose area under the curve (AUC) were higher in FCS than in controls (P<0.05), but similar to MCM whereas plasma fasting insulin levels and postprandial insulin AUC in FCS were similar to levels in controls, but lower than in MCM (P<0.05). Fasting plasma TG levels were higher in FCS (23.50 [12.71-29.95]) than in controls (0.67 [0.50-1.11]) and MCM (2.42 [1.69-4.62]) (P<0.05). Plasma TG AUC was 22 and 7-fold higher in FCS than in controls and MCM, respectively (P<0.05). Chylomicron tracer activity AUC was also much higher in FCS (% ingested dose = 62 [40-115]) than in controls (17 [11-32], P<0.05) and MCM (22 [5-76], P = NS). Plasma glycerol appearance rate AUC, a marker of total TG lipolysis, was almost 3 and 4-fold lower in FCS than in controls and MCM, respectively (P<0.05) while plasma palmitate appearance rate was similar in all groups. Dietary FA spillover rate was almost 4-fold higher in FCS than in controls (4.3 [1.5-7.5] % vs. 1.0 [0.8-1.3] % ingested dose 360min) (P<0.05) but similar to MCM (5.0 [1.5-7.4]).

**Conclusions:** FCS is characterized by increased dietary FA spillover despite profound impairment in LPL-mediated chylomicron lipolysis, suggestive of impaired adipose tissue dietary FA storage. More studies are needed to determine the mechanisms of this pathophysiological feature of FCS.

**Correlation between chylomicronemia diagnosis scores and post-heparin lipoprotein lipase activity**

**Familial Chylomicronemia Syndrome is associated with increased dietary fatty acid spillover in the circulation despite lower total postprandial triglycerides**

André C. Carpentier, MD, Frederique Frisch, MSc, Diane Brisson, PhD, Daniel Gaudet, MD, PhD, (Sherbrooke, QC)

**Lead Author’s Financial Disclosures:** None.

**Study Funding:** IRSC grant (AC MOP 341582).

**Background/Synopsis:** Familial Chylomicronemia Syndrome (FCS) is a rare monogenic autosomal recessive disorder characterized by severe reduction of lipoprotein lipase (LPL)-mediated triglyceride (TG)-rich lipoprotein lipolysis, leading to severe hypertriglyceridemia and high-risk of pancreatitis. Data on postprandial dietary fatty acid (FA) metabolism are however limited in this population.

**Objective/Purpose:** To compare postprandial metabolism among FCS patients, healthy controls and subjects with multifactorial chylomicronemia (MCM).

**Methods:** Twenty-one patients with FCS (11 women/10 men) aged 55 [43-60] (median [IQR]) with a body mass index (BMI) of 23.4 [21.6-25.5] kg/m2 underwent a low-fat (13g) liquid meal test labeled with 3H-palmitate and were compared to 32 healthy controls (18 women/14 men) aged 47 [33-55] with a BMI of 25.9 [24.9-27.6] kg/m2 and to 12 MCM subjects (4 women/8 men) aged 58 [50-62] with a BMI of 32.5 [29.2-34.2] who underwent a high-fat (100g) liquid meal test with either 3H- or 13C-palmitate labeling. A subset of participants simultaneously underwent intravenous infusion of d5-glycerol (9 FCS, 21 controls, 11 MCM) or d2-palmitate (7 FCS, 19 controls, 10 MCM) to measure plasma glycerol and nonesterified FA appearance rates and dietary FA spillover.

**Results:** Fasting plasma glucose levels and postprandial glucose area under the curve (AUC) were higher in FCS than in controls (P<0.05), but similar to MCM whereas plasma fasting insulin levels and postprandial insulin AUC in FCS were similar to levels in controls, but lower than in MCM (P<0.05). Fasting plasma TG levels were higher in FCS (23.50 [12.71-29.95]) than in controls (0.67 [0.50-1.11]) and MCM (2.42 [1.69-4.62]) (P<0.05). Plasma TG AUC was 22 and 7-fold higher in FCS than in controls and MCM, respectively (P<0.05). Chylomicron tracer activity AUC was also much higher in FCS (% ingested dose = 62 [40-115]) than in controls (17 [11-32], P<0.05) and MCM (22 [5-76], P = NS). Plasma glycerol appearance rate AUC, a marker of total TG lipolysis, was almost 3 and 4-fold lower in FCS than in controls and MCM, respectively (P<0.05) while plasma palmitate appearance rate was similar in all groups. Dietary FA spillover rate was almost 4-fold higher in FCS than in controls (4.3 [1.5-7.5] % vs. 1.0 [0.8-1.3] % ingested dose 360min) (P<0.05) but similar to MCM (5.0 [1.5-7.4]).

**Conclusions:** FCS is characterized by increased dietary FA spillover despite profound impairment in LPL-mediated chylomicron lipolysis, suggestive of impaired adipose tissue dietary FA storage. More studies are needed to determine the mechanisms of this pathophysiological feature of FCS.

**Correlation between chylomicronemia diagnosis scores and post-heparin lipoprotein lipase activity**

Étienne Khoury, PhD, Daniel Gaudet, MD, PhD, Diane Brisson, PhD, (Sherbrooke, QC)

**Lead Author’s Financial Disclosures:** None.
**Study Funding:** None.

**Background/Synopsis:** Chylomicronemia (CM) is associated with plasma accumulation of chylomicrons and is characterized by severe hypertriacylglycerolaemia (triglyceride (TG) > 1000 mg/dl). CM phenotype is due to functional or genetic defects in lipoprotein lipase (LPL) mediated TG-rich lipoproteins lipolysis. Familial chylomicronemia syndrome (FCS) is a rare autosomal recessive form of CM caused by null loss-of-function variants in LPL or LPL-related genes. Post-heparin LPL activity is importantly reduced in FCS (<20% of normal). Most individuals with CM are not affected by FCS however and present multifactorial CM (MCM), in which plasma LPL activity levels are higher and more variable than in FCS. FCS and MCM importantly differ in term of risk, comorbidities and clinical management. Different scoring systems were proposed to help clinicians to accurately distinguish FCS and MCM.

**Objective/Purpose:** The aim of this study was to assess the relation between plasma post-heparin LPL activity and two CM diagnosis scoring systems: an European score and a Canadian score which includes surrogate markers of TG hydrolysis.

**Methods:** Post-heparin plasma LPL activity was measured using colorimetric assay among a sample of 29 subjects with chylomicronemia (21 FCS and 8 MCM). Spearman’s rank correlation and Mann-Whitney U test were used.

**Results:** There was an significant (p<0.001) difference in post-heparin LPL activity (median and interquartile range) between FCS (0% [0-6.6]) and MCM (83.2% [69.1-92.3]). Both the European (rs=-0.55, p=0.002) and the Canadian (rs=-0.64, p<0.001) scoring systems showed good correlations with post-heparin LPL activity.

**Conclusions:** Although these results were obtained among a small sample, they suggest that both the European and the Canadian diagnosis scoring systems fairly correlate with post-heparin plasma LPL activity and may contribute to adequately distinguish between FCS and MCM.

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Free glycerol correlate with post-heparin lipoprotein lipase activity and contribute to differentiate familial vs. multifactorial chylomicronemia

Diane Brisson, PhD,
Etienne Khoury, PhD,
Daniel Gaudet, MD, PhD, (Saguenay, Quebec)

**Lead Author’s Financial Disclosures:** None.

**Study Funding:** None.

**Background/Synopsis:** Lipoprotein lipase (LPL) is a key enzyme of triglyceride (TG) hydrolysis in TG-rich lipoproteins, namely chylomicrons and VLDLs. Patients with LPL deficiency (LPLD, omim: 238600) or familial chylomicronemia syndrome (FCS), a rare autosomal recessive disease, sustainably present TG levels above 1,000 mg/dl (chylomicronemia) due to genetically acquired very low LPL activity. Most patients with chylomicronemia do not have FCS however and present secondary or multifactorial chylomicronemia (MCM). Although FCS and MCM are both characterized by chylomicronemia, they importantly differ in term of risk, comorbidities and disease management. Compared to FCS, patients with MCM have higher and highly fluctuating LPL activity. Measuring LPL activity is not clinically simple since it is based on complex, expensive and time-consuming post-heparin methods. Plasma glycerol appearance rate (as assessed by using d5-glycerol labeled tracer) and free glycerol plasma concentrations are markers of TG hydrolysis and are both significantly lower in FCS than in MCM.

**Objective/Purpose:** This study aimed to estimate the relation between post-heparin plasma LPL activity and plasma free glycerol levels in subjects with chylomicronemia.

**Methods:** This study was performed in a sample of 25 subjects with chylomicronemia. Post-heparin plasma LPL activity was measured using 2 different colorimetric assays and glycerol with an enzymatic method. Analyses were performed by using Spearman’s rank correlation tests.

**Results:** Post-heparin LPL activity (median and interquartile range) was significantly lower in FCS (0% [0-6.6]) than in MCM (89.4% [80.6-103.4]) (p<0.001). There was a significant correlation between post-heparin LPL activity and free glycerol levels, whatever the method used (rs=0.67, p=0.03; rs=0.41 p=0.05). Adding plasma apolipoprotein (apo) B levels, anthropometrics and other covariates to the model further increase the relation, as suggested by the correlation observed between LPL activity and apoB (rs=0.56, p=0.01) or the body mass index (rs=0.47, p=0.03).

**Conclusions:** These results suggest that free glycerol, the end-product of TG hydrolysis, used alone or in association with other covariates, could represent a useful, low cost and easily available surrogate of post-heparin LPL activity measurement and may clinically contribute to differentiate FCS from MCM.

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Lipase Maturation Factor 1 Contributes to ER Redox Homeostasis†

Saskia Neher, PhD, (Chapel Hill, NC)

**Lead Author’s Financial Disclosures:** None.

**Study Funding:** American Heart Association and National Lipid Association.

**Background/Synopsis:** Lipoprotein lipase (LPL) is a secreted lipase that clears triglycerides from circulating...
Imaging in Atherosclerosis

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Relationship between Lipid Levels and Coronary Atherosclerotic Plaque Scores by Coronary Computed Tomography Angiography (CTA) in Subjects with Elevated Triglycerides

Alice Lee, April Kinninger, MPH, Eranthi Jayawardena, BS, Chandana Shekar, MD, Lavanya Cherukuri, MD, Christopher Dailing, BS, Sajad Hamal, MS, Ferdinand Flores, BS, Matthew Budoff, MD, John Nelson, MD, (Torrance, CA)

Lead Author's Financial Disclosures: None.

Study Funding: Amarin Pharma, Inc.

Background/Synopsis: We studied a population of patients undergoing coronary CT angiography for assessment of plaque progression in a double blind randomized trial – EVAPORATE. We evaluated factors that were associated with increased plaque burden in patients with elevated triglycerides at baseline. We did find an association between low HDL cholesterol levels and increased atherosclerosis. Therefore, HDL cholesterol levels should be considered when assessing coronary artery disease risk in persons with elevated triglycerides.

Objective/Purpose: To investigate the association between low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides and coronary plaque prevalence.

Methods: 72 subjects of the prospective, double-blind randomized multicenter EVAPORATE (Effect of Vascepa on Improving Coronary Atherosclerosis in people with High Triglycerides Taking Statin Therapy) trial underwent baseline Coronary Computed Tomography Angiography (CCTA). CCTA was evaluated using a modified 17-segment American Heart Association coronary tree model. Coronary Artery Calcium (CAC) Score, Total Plaque Severity (TPS: total amount of plaque in segment), Total Non-Calcified Plaque Score (TNPS) and Segment Involvement Score (SIS: total number of segments with plaque) were interpreted by expert readers. Triglycerides, LDL-C and HDL-C were analyzed for association with semi-quantitative plaque scores using multivariable regression analysis, after adjusting for confounding variables.

Results: The average age and body mass index were 56.3 + 8.6 years and 33.4 + 6.8 kg/m2, respectively. 41 (56.9%) of the participants were male. In a population of patients with elevated triglycerides, low HDL-C was independently associated with increased CAC (p = 0.024), and trends for both low HDL-C and non-calcified plaque (p = 0.06) as well as higher triglycerides and non-calcified plaque (p = 0.072) were noted.

Conclusions: Patients with low HDL-C levels had higher CAC scores after adjustment for age, gender, BMI, diabetes, hypertension, current smoking and family history of CAD. As higher CAC scores are associated with greater risk of coronary events, these findings show that low HDL-C is an independent risk factor for coronary artery disease in persons with high triglycerides.
For Whom The Lobe Folded.....When?

Robert Charles Lichtenberg, MD, Jyothsna Bandaru, MD, (Berwyn, IL)

Lead Author’s Financial Disclosures: None.
Study Funding: None.

Background/Synopsis: The diagonal ear lobe crease (ELC), first describe by Frank in 1973 (1) has been suggested to be an easily detectable sign of atherosclerosis by several studies (2-5). As recent as 2015 the diagonal bilateral ELC was independently associated with cardiovascular events comprising not only coronary but also cerebrovascular and vascular disease. Others have said it is simply a sign of aging (6). A post-mortem analysis of 376 patients with an average age of 70 years demonstrated a strong association with coronary atherosclerosis(7). What is not known is for those whom the lobe folded......when?

Objective/Purpose: This study investigated the onset of the ELC in patients being followed in a community based Cardiology clinic who have at least one ELC.

Methods: Patients seen in a single cardiologist office with Coronary Artery Disease who had single or bilateral ELC were asked to provide photographs going back to at least age 10 years, with one photo/ decade that showed their ears well enough to determine the presence of a diagonal ELC. Between 2004 and 2017, 205 submitted at least one photograph but only 68 patients submitted adequate photographs to be able to detect the ELC and its decade of onset. These 68 patients form the basis of this report.

Results: The 68 patients included 58 male (85%) with an age range of 37-74. The table below reports the number per decade at which time at least one ELC was detected.

<table>
<thead>
<tr>
<th>Decade</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
<th>6th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number with first ELC</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>46</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Percent of Total</td>
<td>6%</td>
<td>68%</td>
<td>20%</td>
<td>6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The photo depicts a typical diagonal ELC and gives an example of submitted photographs.

Top: Serial photos per decade from single patient Bottom: Example of Ear lob crease

Conclusions: The ELC is acquired and appears most commonly in the 4th decade. Once present, the crease remains and becomes more prominent with time. This study does not attempt to assess the association with coronary atherosclerosis or the cause but rather answers the clinical question: For Whom The Lobe Folded....When?

Association between Lipids and Coronary Atherosclerotic Plaque Characteristics

Lavanya Cherukuri, MD, Chandana Shekar, MD, April Kinninger, MPH, Divya Biradaraju, MD, Eranthi Jayawardena, Sajad Hamal, MS, Ferdinand Flores, BSN, John Tayek, MD, Sion Roy, MD, Matthew Budoff, MD, John Nelson, MD, (Torrance, CA)

Lead Author’s Financial Disclosures: None.
Study Funding: None.

Background/Synopsis: High Triglycerides (TGs) and low High-Density Lipoprotein Cholesterol (HDL-C) are associated with increased insulin resistance, hypertension, and obesity. HDL-C, in turn, has a cardioprotective effect because of its role in reverse cholesterol transport, endothelial cell function, and its antioxidant activity. Therefore, patients with low HDL-C and high TGs are at higher risk for coronary artery disease (CAD) and adverse cardiac events.

Objective/Purpose: We investigated the relationship between atherosclerotic plaque burden and lipids levels in patients with hypertriglyceridemia and low HDL-C.

Methods: 70 individuals (37 men) with hypertriglyceridemia (TGs >200mg/dl), enrolled in the EVAPORATE (Effect of Vascepa on Improving Coronary Atherosclerosis in people with High Triglycerides Taking Statin Therapy) trial and undergoing Cardiac Computed Tomography Angiography (CCTA) at our center were identified (Table 1). Using semi-automated plaque analysis software, we measured coronary plaque (total, calcified, non-calcified including fibrous, fibrous-fatty and low attenuation plaque) volume on the CCTA. Univariate regression analysis was used to measure the linear relationship between log-transformed normalized plaque type and burden and lipid metrics.

Results: Increasing HDL levels were linearly associated with decreasing normalized fibrous, total non-calcified, and total plaque volumes. A 1mg/dl increase in HDL resulted in a 4% decrease in normalized fibrous plaque and a 3% decrease in total non-calcified, and total plaque volumes. Increasing Non-HDL levels were also linearly associated with decreasing normalized fibrous plaque volumes. A 1mg/dl increase in non-HDL resulted in a 1% decrease in normalized fibrous plaque volume. No significant association was found between triglycerides and coronary plaque. (Tables 2 and 3).
Conclusions: As low HDL-C and high non-HDL are associated with non-calcified plaque, screening and optimal medical therapy targeted towards these lipids are important in preventing coronary artery disease. Further studies to investigate the association of these lipids and lipid lowering therapies on coronary plaque progression are also warranted.

Lipid Management Best Practices

The Role of Niacin in the Management of Dyslipidemia†

Joseph M. Keenan, MD, (Jordan, MN)

Lead Author’s Financial Disclosures: None.

Study Funding: Innovite Corporation, Lonza Corporation, Upsher-Smith corporation, NIH (NHLBI), Quaker Oats Corporation.

Background/Synopsis: This presentation will briefly review Niacin (NA) research literature and specifically review 4 RCTs (JMK is PI) using wax-matrix extended-release NA(WMER) to underscore the importance of the NA as both a primary agent and “add on” agent in the global management of CVD.

Objective/Purpose: The latest “Cholesterol Management Guidelines” endorsed by 12 national organizations literally “dumped” NA as a lipid agent, stating it has only a limited role in hypertriglyceridemia. This appears

Table 1 Demographics of the individuals enrolled

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Mean ± SD (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>56.31 ± 8.3</td>
</tr>
<tr>
<td>Male Gender (%)</td>
<td>37.00</td>
</tr>
<tr>
<td>BMI (kg/m²)*</td>
<td>33.7 ± 6.6</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>49.00</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>52.00</td>
</tr>
<tr>
<td>Current Smoker (%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Family History of CAD (%)</td>
<td>19.00</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>38.5 ± 9.4</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>95.6 ± 43.8</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>262.4 ± 74.2</td>
</tr>
<tr>
<td>Non-HDL Cholesterol (mg/dL)</td>
<td>142.4± 43.6</td>
</tr>
</tbody>
</table>

Table 2 Normalized Quantitative Plaque Volume

<table>
<thead>
<tr>
<th>Type of Plaque</th>
<th>Mean ± SD (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized Total Dense Calcified Plaque</td>
<td>106.1 ± 135.0</td>
</tr>
<tr>
<td>Normalized Total Fibrous Fatty Plaque</td>
<td>36.8 ± 52.1</td>
</tr>
<tr>
<td>Normalized Total Fibrous Plaque</td>
<td>154.1 ± 195.5</td>
</tr>
<tr>
<td>Normalized Total Low Attenuation Plaque</td>
<td>23.0 ± 48.3</td>
</tr>
<tr>
<td>Normalized Total Non Calcified Plaque</td>
<td>213.9 ± 271.8</td>
</tr>
<tr>
<td>Normalized Total Plaque</td>
<td>320 ± 369.6</td>
</tr>
</tbody>
</table>

Table 3 Univariate regression analysis

<table>
<thead>
<tr>
<th>Plaque Type *Log Adjusted</th>
<th>Lipid</th>
<th>β</th>
<th>sd</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized Total Dense Calcified Volume</td>
<td>HDL Cholesterol (0.035)</td>
<td>0.02</td>
<td>0.159</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDL Cholesterol (0.001)</td>
<td>0.01</td>
<td>0.823</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triglycerides (0.002)</td>
<td>0.00</td>
<td>0.570</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-HDL Cholesterol (0.003)</td>
<td>0.01</td>
<td>0.537</td>
<td></td>
</tr>
<tr>
<td>Normalized Total Fibrous Fatty Volume</td>
<td>HDL Cholesterol (0.031)</td>
<td>0.02</td>
<td>0.107</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDL Cholesterol (0.002)</td>
<td>0.00</td>
<td>0.712</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triglycerides (0.001)</td>
<td>0.00</td>
<td>0.595</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-HDL Cholesterol (0.002)</td>
<td>0.00</td>
<td>0.570</td>
<td></td>
</tr>
<tr>
<td>Normalized Total Fibrous Volume</td>
<td>HDL Cholesterol (0.036)</td>
<td>0.02</td>
<td>0.023</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDL Cholesterol (0.006)</td>
<td>0.00</td>
<td>0.096</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triglycerides (0.002)</td>
<td>0.00</td>
<td>0.384</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-HDL Cholesterol (0.007)</td>
<td>0.00</td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>Normalized Total Low Attenuation Volume</td>
<td>HDL Cholesterol (0.022)</td>
<td>0.02</td>
<td>0.348</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDL Cholesterol (0.003)</td>
<td>0.00</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triglycerides (0.001)</td>
<td>0.00</td>
<td>0.705</td>
<td></td>
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<tr>
<td></td>
<td>Non-HDL Cholesterol (0.002)</td>
<td>0.01</td>
<td>0.649</td>
<td></td>
</tr>
<tr>
<td>Normalized TNCP Volume</td>
<td>HDL Cholesterol (0.032)</td>
<td>0.02</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDL Cholesterol (0.004)</td>
<td>0.00</td>
<td>0.229</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triglycerides (0.002)</td>
<td>0.00</td>
<td>0.418</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-HDL Cholesterol (0.005)</td>
<td>0.00</td>
<td>0.133</td>
<td></td>
</tr>
<tr>
<td>Normalized Total Plaque Volume</td>
<td>HDL Cholesterol (0.036)</td>
<td>0.02</td>
<td>0.025</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDL Cholesterol (0.004)</td>
<td>0.00</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triglycerides (0.002)</td>
<td>0.00</td>
<td>0.457</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-HDL Cholesterol (0.006)</td>
<td>0.00</td>
<td>0.106</td>
<td></td>
</tr>
</tbody>
</table>
to be a significant oversight in the “Guideline’s” recommendations of best practices”.

Methods: NA was the first single agent to demonstrate significant reduction in CVD events and mortality. It has been shown in multiple studies, both alone and in combination (including statins) to be effective in reducing CVD events and mortality. NA has the broadest range of lipid/CVD benefits of any agent available.

Results: It lowers LDL-C (specifically small, dense LDL-c) up to 26%, raises HDL-C (specifically Apo-A1) up to 22%, reduces TG up to 15%, and is the only agent that reduces Lp(a) up to 22%. In addition, NA has non-lipid benefits that have been shown to reduce reactive oxygen species that are associated with the oxidation of LDL-C, and reduces vascular chemo-attractant particles and Monocyte adhesion protein associated with early atherosclerosis. The early knock on NA therapy was high rate of intolerance (flushing) which has been largely eliminated by WMER (WMER RCTs average 3-4% drop out). More recently, 2 large clinical trials (AIM-HIGH, HPS-2THRIVE) reported disappointing results using polygel NA in combination with a statin and they reported a negative conclusion on the NA/statin combination. Review of these studies revealed significant design flaws, and cast serious doubt on many of their conclusions. Another large combination NA/statin RCT done since these flawed studies yielded largely positive results. In addition to the broad lipid and non-lipid benefits NA is the least expensive lipid lowering agent available (about $10/month for WMER, $60/month generic ezetimibe).

Conclusions: The guidelines focus on LDL-C goals clearly makes statins the first choice for most dyslipidemias. However, with 18% of persons “statin intolerant” and an additional percentage of persons having significant residual CVD risk despite statin therapy, NA remains an appropriate and cost effective “add on” agent. Furthermore, for the “Guidelines” to be relevant and useful to the global epidemic of CVD they should offer alternative recommendations/options for nations or individuals that can’t afford $37,000 QALY (statins) or $330,000 QALY (PCSK9-1). NA is a logical first choice for Metabolic Syndrome and other mixed dyslipidemias with mild LDL-C elevation.

Study Funding: Research reported in this publication was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Number K12HL137942.

Background/Synopsis: Individuals with familial hypercholesterolemia (FH) are often undiagnosed and undertreated. Cholesterol guidelines recommended aggressive treatment, but often this is not implemented in practice. Although some strategies to promote the uptake of guideline-recommended care for non-familial hypercholesterolemia exist, these strategies for FH are lacking.

Objective/Purpose: The purpose of this study is to uncover barriers and facilitators to care that individuals with FH experience and organizational stakeholders face when treating individuals with FH.

Methods: Semi-structured interviews were conducted with individuals with FH, defined as having a problem list diagnosis (ICD 10: E78.01) or a pathogenic or likely pathogenic FH variant, and organizational stakeholders involved in the care of individuals with FH. Questions were tailored to each stakeholder group interviewed regarding barriers and facilitators to caring for FH. Audio recordings of the interviews were transcribed verbatim, assessed for accuracy, and independently coded by two reviewers.

Results: A total of 25 individuals with FH were interviewed. Two-thirds were female (18/25) and all were white. A majority were > or = 55 years of age (15/25) and about half (11/25) had a college degree or higher education. Many described only recently learning that their high cholesterol was a specific condition called FH. Most individuals described barriers related to medications, health insurance, or the healthcare system; however, a few reported no barriers to caring for their FH. Other barriers experienced by some were related to various personal demands, including medical or financial and caring for family members. Individuals mentioned that care teams and access to resources were important in facilitating their care.

Conclusions: Uncovering barriers and facilitators to caring for familial hypercholesterolemia*

Lead Author’s Financial Disclosures: None.
Lipid Management Best Practices

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An updated cost-effectiveness analysis of evolocumab therapy for reducing cardiovascular events in very high-risk patients with atherosclerotic cardiovascular disease according to the 2018 ACC/AHA guideline

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Lead Author’s Financial Disclosures: Reports consulting for Abbott, Amgen, Bayer, Janssen and Novartis.

Study Funding: Amgen.

Background/Synopsis: Based on FOURIER results, Fonarow et al. (2017) evaluated the cost-effectiveness of evolocumab when added to standard background therapy (maximally tolerated statin with/without ezetimibe) in patients with atherosclerotic cardiovascular disease (ASCVD). In October 2018, a 60% list price reduction for evolocumab was announced, aimed at improving value and lowering patient copays. Shortly thereafter, the 2018 American College of Cardiology/American Heart Association Multisociety Guideline on the Management of Blood Cholesterol (2018 ACC/AHA guideline) recommended proprotein convertase subtilisin-kexin type (PCSK9) inhibitors in very high-risk (VHR) patients with ASCVD whose low-density lipoprotein cholesterol levels remain ≥70 mg/dL despite standard background therapy, among other patient populations.

Objective/Purpose: To present an updated cost-effectiveness analysis of evolocumab added to standard background therapy in VHR patients with ASCVD defined according to the 2018 ACC/AHA guideline, using the new evolocumab list price.

Methods: This updated analysis, based on the original model by Fonarow et al. (2017), incorporates new data for 2 key parameters: (1) an evolocumab annual list price of $5,850 and (2) a baseline cardiovascular (CV) event rate (myocardial infarction, ischemic stroke, and CV death) reflecting the 2018 ACC/AHA guideline definition of VHR. The updated baseline rate was modeled by adjusting the real-world baseline rate from the original analysis, which modeled a mixture of VHR and non-VHR patients with ASCVD, by the rate ratio of VHR to non-VHR patients observed in FOURIER. Model outcomes included CV events, costs, quality-adjusted life-years (QALY), and incremental cost-effectiveness ratios (ICER).

Results: In FOURIER, VHR patients had approximately two-fold the baseline rate of non-VHR patients, yielding plausible baseline rates ranging from 6.4 to 12.3 per 100 patient-years for VHR patients with ASCVD in the real world. Evolocumab was associated with both increased costs and QALY when added to standard background therapy (maximally tolerated statin with/without ezetimibe). Incremental costs ranged from $22,228 to $3,411, depending on the baseline rate, and QALY gained ranged from 0.39 to 0.44. ICER ranged from $56,655 to $7,667 per QALY gained; therefore, for any baseline rate in VHR patients with ASCVD, ICER were below generally accepted willingness-to-pay thresholds. Moreover, ICER were below $50,000 per QALY gained for any baseline rate ≥6.9 per 100 patient-years. If background therapy included maximally tolerated statin with ezetimibe, ICER would range from $59,331 to $10,584.

Conclusions: At its current list price, the addition of evolocumab to standard background therapy demonstrates high value across a range of CV event rates in VHR patients with ASCVD.

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Evaluating a population health approach to statin use: pharmacist driven interventions in patients with type 2 diabetes mellitus*

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: In the context of value-based healthcare, a common population health initiative is initiation of statin therapy in patients with type 2 diabetes mellitus (T2DM). Many studies have shown that pharmacist managed services increase statin initiation rates; however, limited data have compared the effectiveness of different population health approaches targeting initiation of statin therapy.

Objective/Purpose: The purpose of this analysis is to compare statin initiation rates with a population health initiative among 4 University of Colorado primary care clinics with embedded clinical pharmacists to 5 clinics with non-embedded clinical pharmacists. Primary outcome is the rate of prescribing a statin among patients with T2DM who are not on statin therapy after statin therapy was recommended by the clinical pharmacist.

Methods: This retrospective cohort analysis evaluated a population health program that identified primary prevention patients with T2DM, age 40-75 years, with LDL-C of 70-189 mg/dL with no active statin prescription through electronic health record (EHR) registries. One cohort had embedded clinical pharmacists (interprofessional model within the primary care clinic) while the other had centrally-located clinical pharmacists. Each evaluated patients to determine if statin therapy was indicated. When indicated, statin therapy was recommended to providers using two approaches: (A) written EHR recommendation within 7 days prior to an upcoming office visit or (B)
provision of a list of pre-reviewed patients for whom the clinical pharmacist recommended statins. Providers could indicate approval and the pharmacist then performed telephone outreach to initiate therapy. Pharmacists recommended statin therapy in 870 patients between March 1, 2018 and November 10, 2018. Based on the a priori sample size calculation, 136 patients were randomly selected from each cohort. Data were analyzed using a Chi-square test, with p-values <0.05 identified as statistically significant.

Results: Statin initiation was 41.9% and 36.8% in the embedded and non-embedded cohorts, respectively (p=0.38). In the embedded cohort, all recommendations were made using approach A (EHR note prior to office visit); whereas, in the non-embedded cohort, 77 recommendations were made with approach A and 59 were made with approach B (prospective patient panel), with resultant statin initiation rates of 41.6% and 30.5% respectively (p=0.19).

Conclusions: This clinical pharmacist population health initiative increased the rate of statin prescribing in eligible patients with T2DM. Both embedded and non-embedded clinical pharmacists models were successful. Population health approaches that target eligible patients for statin therapy prior to their next office visit may be more effective than prospectively evaluating an entire patient panel.

327 Geographic Variation In LDL-C Levels And Lipid Lowering Therapy Use In Patients With Atherosclerotic Cardiovascular Disease

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Lead Author’s Financial Disclosures: S.J. Baum serves as President of the American Society of Preventive Cardiology, President of Northridge Heart Associates, President and CMO of Excel Medical Clinical Trials, and is a Clinical Affiliate Professor in the Department of Integrated Medical Sciences at the of Florida Atlantic University; serves on scientific advisory boards for Akcea Therapeutics, Amgen Inc., Regeneron, and Sanofi; is a consultant for Akcea Therapeutics, Amgen Inc., Cleveland HeartLab, Inc., Gerson Lehrman Group, Inc., Guidepoint Global, LLC, Novo Nordisk A/S, Regeneron, and Sanofi; and is a speaker for Akcea Therapeutics, Amgen Inc., Aralez Pharmaceuticals Inc., Boehringer Ingelheim, and Novo Nordisk A/S.

Study Funding: This study was funded by Amgen Inc.

Background/Synopsis: Hyperlipidemia is a highly prevalent condition in the US, with research showing that only 1 out of every 3 adults with elevated LDL-C has their condition under control.

Objective/Purpose: To describe US geographic variations in utilization of lipid lowering therapy (LLT), LDL-C levels, and the proportion of patients with persistent LDL-C elevations among LLT-treated patients with atherosclerotic cardiovascular disease (ASCVD).

Methods: This retrospective cohort study used a nationally representative health claims database linked to data from a large national lab-data aggregator to characterize LDL-C levels and LLT use among approximately 23 million patients. Patients were indexed to their most recent LDL-C test date during the index-period (01/01/2016 to 06/30/2018). The LDL-C levels and current LLT use among ASCVD patients were assessed at the state level. Direct standardized rates for patients with elevated LDL-C (≥70mg/dL) despite treatment with LLT (prescription claim within 90 days pre-index) were reported adjusting for age and gender estimates from the latest census data available (2017 Current Population Survey).

Results: There were 4,259,270 ASCVD patients (mean age=69 years, males=52.2%, mean LDL-C=93.2 mg/dL) in our study population, with 46.7% patients having at least one claim of LLT (90 days pre-index). At the national level and after standardizing, overall 70.9% patients were found to have an elevated LDL-C at ≥70mg/dL, and 33.9% at ≥100mg/dL respectively; despite receiving LLT. At the national level, variations in standardized rates of patients with elevated LDL-C specific to age and gender were also observed (Table 2). Substantial geographic variation was observed - both in terms of receipt of current LLT and the proportion of patients with elevated LDL-C (≥70mg/dL) while under treatment. The proportion of ASCVD patients receiving any LLT (90 days pre-index) ranged from 55.9% in Massachusetts to 67.9% in Vermont. The overall standardized rate of patients with elevated LDL-C (≥70mg/dL) despite LLT treatment ranged from 58.0% in Colorado to 75.8% in Maine.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-44</td>
<td>71.2%</td>
<td>74.2%</td>
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<tr>
<td>45-64</td>
<td>68.1%</td>
<td>77.1%</td>
</tr>
<tr>
<td>65+</td>
<td>57.3%</td>
<td>69.3%</td>
</tr>
</tbody>
</table>

Table 2 Standardized rates of patients with LDL-C ≥70mg/dL despite current LLT
Conclusions: The current study highlights the persistent high burden of elevated LDL-C, pervasive underuse of LLT in patients with ASCVD and substantial geographic variations in the US. The study also highlights the need of better lipid management in such patients to reduce their cardiovascular risk.

Technological advancements in CME increase knowledge gains and the translation of education to practice within cardiovascular care.

Matthew Frese, MBA, Brooke Hefele, Lauren Welch, MA, Christina Gallo, Andrew Gryzbowski, (New York, NY)

Lead Author’s Financial Disclosures: None.
Study Funding: This activity was supported by an educational grant from Sanofi and Regeneron.

Background/Synopsis: Over the past three years, Med Learning Group (MLG) has incorporated virtual reality and augmented reality (VR and AR) tools into its educational platform to further engage learners, enhance comprehension, improve recall, and support practice change. These tools are also downloadable and re-scripted to help engage patients. This innovation makes the information ‘sticky’ by providing clear clinical insights in a concise manner while also giving participants clinical practice tools to improve the care of their patients.

In 2018, MLG conducted a variety of educational opportunities inclusive of VR and AR animations on the pathophysiology of hypercholesterolemia and the mechanism of action of the latest recommended therapies to ultimately reduce the risk of CVD. Outcomes from these programs demonstrate how this advanced continuing medical education (CME) results in greater knowledge gains, practice improvements, and patient engagement.

Objective/Purpose: Innovative VR and AR, when appropriately incorporated into CME, can improve cardiologists’ understanding of pathophysiology as well as current and emerging therapies in hypercholesterolemia care in order to reduce the risk of CVD.

Methods: MLG incorporated VR into 2018 CVD educational experiences, and offered participants VR and AR tools to view from their smart device for continuous learning and to share with their patients to enhance patient engagement. Pre/posttests, electronic surveys, and phone interviews were conducted to assess the value of these technologies in not only enhancing HCP knowledge but also supporting practice change and improving the patient experience.

Results: Over 2,300 participants have viewed MLG’s activities. Interspersing VR animations into education helped HCPs visualize how therapies work in a unique manner that improved recall and comprehension. From pretest to posttest, learners improved knowledge and competence on average 20% and 26% respectively (N=1794). Follow-up surveys indicate that the downloadable animations, posters, and AR tool have aided physician-patient communication. These tools have easily translated into practice with 80% of responding physicians indicating the VR/AR improved recall and 83% reporting change to their practice based on the innovate education (N=204), leading to a potential benefit for 7,841 CVD patients. This is a 22% gain in reported practice change compared to similar programs MLG conducted without VR/AR the year prior.

Conclusions: The inclusion of innovative technological tools has provided valued education and resources for HCPs and patients alike. This innovation positively affects the management of patients with hypercholesterolemia.

Lipid Management in Special Populations

Severe hypercholesterolemia secondary to drug-induced cholestatic liver injury

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Lead Author’s Financial Disclosures: None.
Study Funding: None.

Background/Synopsis: Hypercholesterolemia may manifest in cases of cholestatic liver disease or injury. Cholestasis may arise from various underlying causes and may be marked by severely elevated serum LDL-C on standard laboratory measures. In cholestasis, apparent LDL-C elevation may be due to production of Lipoprotein-X (Lp-X) rather than true excess of LDL or other atherogenic lipoproteins. Lp-X has similar density to LDL, resulting in its false identification as LDL on most assays. However, Lp-X does not contain apolipoprotein B (apoB) and is not considered atherogenic.

Objective/Purpose: This case report reviews the presentation and management of a patient with severe hypercholesterolemia secondary to drug-induced cholestatic liver injury and evaluation of suspected Lp-X elevation.

Methods: A retrospective review was performed of the patient’s pertinent history and objective testing preceding acute hepatic injury and course of care thereafter. A 61 year-old woman with asthma and hypertension was newly diagnosed with pulmonary asplereiosis. Treatment was initiated with a 4-month course of itraconazole, sulfamethoxazole/trimethoprim, and prednisone. After 3 months of therapy, she presented with marked elevations in hepatic function tests and was admitted for drug induced liver injury (DILI) in a cholestatic pattern, likely secondary to itraconazole and sulfamethoxazole/trimethoprim; both medications were held. She was re-admitted 2 months later
for evaluation of hyponatremia to 113-119 mg/dl, found to be pseudohyponatremia secondary to severe hypercholesterolemia with total cholesterol >2100 mg/dL, LDL cholesterol >1200 mg/dL (above upper limits of assay). For DILI, ursodiol was initiated and prednisone was continued. Atorvastatin 40 mg and ezetimibe 10 mg daily were initiated for hypercholesterolemia.

Results: This patient was followed in hepatology and lipid clinics for management of hepatic injury and hypercholesterolemia. Serum cholesterol improved with progressive resolution of DILI. Patient’s baseline ASCVD 10-year risk was 4%, on-treatment LDL was 54 mg/dL, apoB 95 mg/dL, and she had no other ASCVD risk factors or evident subclinical atherosclerotic disease on available imaging. Thus, ezetimibe was discontinued and coronary artery calcium scoring was recommended to guide the decision whether to discontinue atorvastatin, per the patient’s preference.

Conclusions: This patient’s lipid panel trend follows the course and resolution of hepatic injury. Initial severe cholesterol elevation was inconsistent with historic baseline and incongruent with measured apoB level. The authors propose that the apparent LDL-C elevation on assay was secondary to Lp-X elevation that resolved in parallel to resolution of hepatic injury.

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Abstract Title: Perceived Barriers to Lipid Management for Suspected Familial Hypercholesterolemia Franco-American Founder Populations

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Familial hypercholesterolemia (FH) is a common genetic disorder characterized by elevated cholesterol levels and is associated with an increased risk for developing premature coronary heart disease (CHD). Though FH affects all racial and ethnic groups, the condition is more prevalent among certain subpopulations, including French-Canadians and Franco-Americans. Less than 10% of the estimated 1.3 million individuals living with FH in the United States have been diagnosed. These trends not only support the need to evaluate barriers to effective lipid management, but also to better understand health-related behaviors for at-risk individuals.

Objective/Purpose: Our study applied components of the Health Belief Model to the Franco-American FH founder population in central Maine. This widely utilized theoretical framework was originally designed to predict health-related behaviors and examine disease perceptions. Survey responses were analyzed to determine common barriers to lipid management.

Methods: A multi-section questionnaire was disseminated to individuals living in central Maine. Targeted distribution efforts at local cultural and educational centers, healthcare organizations, and media outlets were implemented to maximize the representation of Franco-Americans. Univariate frequencies and bivariate correlations were conducted to assess model components and determine relationships between clinical indicators, health beliefs, and barriers to care.

Results: Approximately 83% (n = 170) of survey respondents were Franco-American or French-Canadian. In the total respondent cohort, 70% were female, and 51% were 65 years of age or older. Approximately 43% of individuals reported having high cholesterol, while nearly 70% indicated a family history of cardiovascular disease. Less than 9% of respondents expressed a personal FH diagnosis, and 10% reported experiencing a heart attack or stroke. We observed that affective barriers to lipid management, (e.g. knowing when to seek help (28%), trust in medicine (25%), worry about diagnosis (20%), and fear of judgment (13%)) were more frequently reported than instrumental barriers (e.g. health care costs (18%), time conflicts (15%), and lack of health insurance (12%). Moreover, we found the combined additive scales of each barrier category to be significantly correlated with an external health locus of control (p < 0.05).

Conclusions: Our findings affirm the importance for clinicians to consider common barriers to lipid management perceived by their patients, including their ability to proactively seek care, concern over potential diagnoses, and fear of resulting judgement. Sustained efforts to increase awareness of FH and its treatment strategies, particularly in founder populations, can help mitigate the consequences of these barriers and empower patients to engage in early health-promoting behaviors.

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Familial Chylomicronemia Syndrome: Distinguishing the Rare Among the Common in Adults for Appropriate Management†

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Hypertriglyceridemia (HTG) is common, but familial chylomicronemia syndrome (FCS)
is a very rare cause of severe HTG, associated with pancreatitis, which can be fatal. It is due to impaired lipoprotein lipase (LPL) function, commonly caused by bi-allelic LPL loss-of-function mutations. Mutations in the genes encoding apolipoprotein C-II, apolipoprotein A-V, lipase maturation factor 1, and glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein are also causes of FCS.

Although FCS generally presents in childhood with acute pancreatitis and HTG, it should also be considered as a diagnosis in adults with severe HTG. Unlike polygenic HTG, dietary fat-restriction is the mainstay of treatment in FCS which is critical in preventing pancreatitis since traditional medications are ineffective.

Objective/Purpose: We present three siblings, including fraternal twins, whose definitive diagnosis of FCS in their 50's prompted changes in dietary recommendations that stabilized their clinical picture. We also report a favorable finding from a clinical trial with a novel biologic in which the female twin partook.

Methods: The siblings participated in an institutionally approved study, investigating the genetic etiology of dyslipidemia at the University of Pennsylvania, and they consented to research genetic testing and allowed us to obtain their medical information.

Results: FCS diagnosis in the siblings was confirmed by finding of a homozygous LPL variant, c.617T>C, p.V206A, corroborated by reduced LPL activities, and altered molecular dynamics that indicated dysfunctional LPL.

The three siblings had suffered from multiple pancreatitis episodes, and the twins required multiple hospitalizations prior to their visit to our clinic. Their dietary history revealed the use of a low-carbohydrate diet, which was inappropriate for FCS, worsened their TG control. A very low-fat diet was promptly prescribed and their TG levels stabilized with a reduction in pancreatitis episodes.

The female twin qualified to enroll in a clinical study for the treatment of HTG, receiving multiple doses of an experimental APOC3 antisense oligonucleotide (ASO), volanesorsen, which lowered her TG from 3,447 to 201 mg/dL (~94% reduction) within 90 days which persisted for several months. The result seemed to indicate that inhibiting the production of APOC3 by ASO could effectively enhance the residual LPL lipolytic activity and lower TG.

Conclusions: Our case demonstrates the importance of identifying FCS even in adults with HTG for prescribing the most appropriate therapy. In particular, the favorable result of the clinical trial was promising that novel biologics may become an optional therapy in certain patients with FCS beyond dietary management in the future.

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Case Presentation: A family history of early myocardial infarction in a family with elevated lipoprotein(a)

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Daniel Soffer, MD,
Douglas Jacoby, MD, (Philadelphia, PA)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Patient XY is 52 year-old woman with dyslipidemia and a family history of fatal myocardial infarction in her father at 45 years of age. Her four daughters, ranging from 21 to 25 years-old, underwent cardiovascular risk assessment at our lipid clinic. The daughters have relatively benign traditional lipid profiles, with low-density lipoprotein cholesterol (LDL-C) levels ranging from 85 to 112 mg/dL (calculated by Friedewald formula). Their advanced lipid testing, however, reveals significant lipoprotein-(a) (Lp(a)) elevations, ranging from 70 to 236 mg/dL (30 mg/dL = upper limit of normal [ULN]; 90th to 99.8th percentile). Their carotid intimal media thickness (IMT) ranged from 0.49 mm to 0.57 mm, values in the highest two quartiles. In each daughter, the degree of Lp(a) elevation roughly corresponded to the extent of carotid intimal medial thickness.

Carotid IMT is an established surrogate marker for atherosclerosis and a strong independent predictor of cardiovascular events. Lipoprotein(a) is a cholesterol-rich lipid particle derived from LDL with apolipoprotein(a) crosslinked to apolipoprotein B (apoB). Clinical epidemiologic and genome wide association studies confirm that Lp(a) is a heritable marker of atherogenicity and arterial thrombosis. Despite multiple proposed pathogenic mechanisms linking Lp(a) to atherosclerosis and arterial thrombosis, it is unknown whether directly targeting (a) attenuates risk. Statins, traditionally the foundation of pharmacotherapy for atherosclerosis cardiovascular disease reduction, do not reduce Lp(a) levels in prospective trial, and can even cause Lp(a) elevations. Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) and niacin reduce Lp(a) levels by modest amounts, though the
mechanisms are still unknown. A phase III trial is underway with the antisense drug, AKCEA-APO(a)-Lrx, that specifically targets Lp(a) levels.

Objective/Purpose: Not applicable.

Methods: Not applicable.

Results: See attached table.

Conclusions: Multiple organizations have called for universal and directed screening of Lp(a) levels. The 2018 Cholesterol Guidelines recommend acknowledging high Lp(a) levels as a risk-enhancing feature for stratification in moderate ASCVD risk patients in whom the indication for use of statins may be uncertain. The European Atherosclerosis Society (EAS) issued a consensus statement calling for screening moderate-high ASCVD risk patients. Identification of family members of patients with premature ASCVD and high Lp(a) may help identify an important risk factor and ultimately, target of therapy early in life. The family described above represents the complexity of early identification of ASCVD risk without a clear recommendation for treatment. We believe that additional study is needed to clarify the role of primary prevention in patients with high Lp(a) and a family history of premature ASCVD, but low calculated ASCVD risk.

Table of Results: Advanced Lipid Testing and Subclinical Atherosclerosis Testing Results

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<th></th>
<th>LDL-C (mg/dL)</th>
<th>HDL (mg/dL)</th>
<th>LDL-P (mmol/L)</th>
<th>Apo-B (mmol/L)</th>
<th>Lp(a) mg/dL</th>
<th>Carotid IMT (mm)</th>
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<td>120 79 69</td>
<td>1533</td>
<td>149</td>
<td>0.71 (&gt;75th percentile) without plaques</td>
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<tr>
<td>Mother in 2018</td>
<td>112 79 69</td>
<td>70</td>
<td></td>
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<tr>
<td>Daughter A</td>
<td>120 79 69</td>
<td>71</td>
<td>96</td>
<td>0.49 (&gt;50th percentile) without plaques</td>
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<tr>
<td>Daughter B</td>
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<td>0.47 (&gt;50th percentile) without plaques</td>
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<td>70</td>
<td></td>
<td>0.45 (&gt;50th percentile) without plaques</td>
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Intensity and Timing of Statin Initiation in Patients with Initial LDL Greater Than 190 mg/dL in an Urban Medical Center: A Retrospective Observational Single Center University Experience*

Sanket R. Gokhale, MD, Noreen Nazir, MD, (Chicago, IL)

Lead Author’s Financial Disclosures: None.

Background/Synopsis: Severely elevated serum LDL level (>190mg/dL) is an independent risk factor in the development of premature complications of atherosclerotic cardiovascular disease (ASCVD) and current guidelines recommend immediate initiation of high intensity statin therapy. Unfortunately, limitations in care continue to exist, especially amongst patients from disadvantaged socioeconomic backgrounds. Thus, our study evaluated the demographics of an urban population with respect to the timeliness and appropriateness of initiating statin therapy in patients with initial LDL greater than 190mg/dL.

Methods: We performed a single center, retrospective observational study in a predominantly urban population. Patients with initial LDL levels greater than 190mg/dL presenting at The University of Illinois-Chicago Hospital and Clinics between Jan 1, 2013 and Dec 31, 2014 were included. These patients were then evaluated for intensity and timing of statin therapy after initial lipid profile and stratified according to race and gender. Data was recorded for 12 months after the initial lipid profile.

Results: 499 patients were included in the study. Mean age was 50.3 years, 61.9% identified as female, and 59.7% were black. 61.7% of patients had a diagnosis of hypertension, 32.2% with diabetes, and 30.8% had significant smoking histories. Mean initial LDL level was 231mg/dL. With regards to intensity of statin started, 38.2% of patients were not started on any statin therapy while 16.2% of patients were started on a high intensity statin started.

In terms of time to statin start, 38.2% were not started on any statin while 29.8% were immediately started on statin therapy (p=0.039). Again, no significant difference was seen between either race or gender with regards to intensity of statin started.

Conclusions: Although a significant difference between race or gender with regards to the intensity or timeliness of statin initiation was not observed, the undertreatment of severely elevated LDL across all study participants is significant. Given the high prevalence of other comorbid conditions amongst this vulnerable patient population, it is crucial that primary care physicians are educated on the importance of primary prevention of premature ASCVD complications and the aggressive treatment of severely elevated serum LDL levels.
Clinical Management of Elevated Lipoprotein(a) in a Large Cohort of Familial Hypercholesterolemia Patients

Daniel Rader, MD,
Douglas Jacoby, MD,
Daniel Soffer, MD, (Philadelphia, PA)

Lead Author's Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Familial hypercholesterolemia (FH) patients may exhibit both elevated low-density lipoprotein (LDL-c) and elevated lipoprotein(a) [Lp(a)] through genetic inheritance. Several studies suggest elevated Lp(a) as a clinical risk factor significantly and independently associated with cardiovascular disease risk in patients with FH. However, targeted modification of Lp(a) in FH patients in real-world settings remains poorly described.

Objective/ Purpose: To determine the cardiovascular disease burden and treatment patterns respective of Lp(a) in a large FH cohort at a tertiary academic center.

Methods: A retrospective query was conducted in The University of Pennsylvania Health System (UPHS) using the FH ICD-10 code, E78.01. Plasma Lp(a) concentrations were evaluated in these patients with results in the electronic health record. Elevated Lp(a) was defined as concentrations ≥50 mg/dL.

Results: The query returned 1417 FH patients [703 seen in the Penn Lipid Clinic, 714 seen elsewhere in UPHS] of whom 27% (389 of 1417) had an Lp(a) result. Of these patients, 87% of patients (338 of 389) had seen a provider in the Penn Lipid Clinic, and 50% of patients (194 of 389) had elevated Lp(a) with a median of 139 mg/dL (interquartile range, 84-225 mg/dL). Factors associated with elevated Lp(a) included the non-white race (odds ratio 1.37, confidence interval 0.82 to 2.30), the male gender (1.16, 0.77 to 1.75), prescription of niacin (1.91, 1.20 to 3.06), prescription of a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor (20.9, 1.40 to 3.13), and prevalent cardiovascular disease (1.42, 0.95 to 2.13). Among patients with a Lp(a) result, median age at initiation of lipid-lowering therapy was 50 years old and median age at FH diagnosis was 55 old years; among patients without a Lp(a) result, median age at initiation of lipid-lowering therapy was 50 years old and median age at FH diagnosis was 55 old.

Conclusions: In a large cohort of FH patients, particularly those not seen in a lipid clinic, a large majority have not been evaluated for Lp(a). Among those patients with at least one Lp(a) result, half demonstrate elevated Lp(a) which associates with a higher cardiovascular disease burden. The 2018 Cholesterol Guidelines suggest that high Lp(a) levels are a risk-enhancing feature that may support the need for intensification of cholesterol-lowering pharmacotherapy.
Results: Nine patients who received evolocumab underwent neuropsychological assessment with RBANS prior to initiation of therapy and follow-up testing after initiation of therapy. The mean age of the cohort was 58 (+/-9) and 44% were male. Average education was 15 years. Seven patients had known coronary artery disease. The mean change from baseline (standard deviation, p-value) over an average of 452 days (+/-157) in the raw score for the immediate memory, visuospatial/constructional, language, attention, delayed memory and total scale were -1.78 (13.26, p = 0.7), 6.56 (13.79, p = 0.19), -4.11 (12.58, p = 0.36), -1.67 (7.37, p = 0.51), 2.67 (8.31, p = 0.36), and 0.44 (6.11, p = 0.83) respectively.

Conclusions: There was no significant change in cognitive function in multiple domains observed in patients receiving evolocumab over an average of 15 months.

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Homozygous Familial Hypercholesterolemia in the United States: Data from the CASCADE-FH Registry

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Lead Author’s Financial Disclosures: Research Grant; Significant; RegenxBio, Regeneron, Akcea, NIH.

Study Funding: Amgen.

Background/Synopsis: Homozygous Familial hypercholesterolemia (HoFH) is a rare genetic condition (prevalence 1 in 250,000) characterized by extremely elevated LDL-C levels from birth, CVD that may manifest clinically in childhood, and often aortic stenosis. Treatment response is generally inadequate and multiple lipid lowering treatments are necessary. The CVD burden and treatment intensity among patients with HoFH in the US is poorly characterized.

Objective/ Purpose: To describe patients diagnosed with HoFH participating in the FH Foundation’s CASCADE FH (Cascade Screeening for Awareness and DEtection of Familial Hypercholesterolemia) patient registry.

Methods: We conducted an observational analysis of the baseline data from 40 HoFH patients enrolled in the CASCADE FH Registry through 17 US lipid clinics between April 2014 and January 2018.

Results: Out of 4549 FH patients present in the CASCADE FH Registry, 40 patients (18 males and 22 females) were identified as having HoFH on the basis of genetic diagnosis (n=29, 72.5%) or LDL-C levels above
500 mg/dl and positive family history. Median (Q1, Q3) age at diagnosis was 4 years (2, 12) and at time of enrolment in the registry was 24 (10, 42). LDL-C levels prior to the initiation of lipid lowering treatment were 694+/−167 mg/dl. At time of enrolment in the registry, 62.5% of HoFH had prior documentation of CAD, 40% had prior PCI or CABG, 12.5% prior valve replacement and 10% had received liver transplant. Thirty-four (85%) patients were receiving lipid lowering therapy: 80% statins (60% high intensity), 60% ezetimibe, 17.5% lomitapide, 7.5% each niacin, resins and PCSK9 inhibitors. Seventeen subjects (42.5%) received LDL apheresis. 45% of the patients were treated with two different therapies, 25% with three and 5% with four. Mean LDL-C levels during treatment remained elevated at 310+/−224 mg/dl (range 37 to 769).

Conclusions: Diagnosis of HoFH was made relatively early in this cohort of patients followed at US centers. However, CVD (both atherosclerotic and valvular) in these patients was highly prevalent, treatment was sub-optimal and LDL-C levels remained elevated, underscoring the difficult of treating this condition and the need for nationwide recognition for the optimization of the therapeutic approach.

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Characterization of Familial Hypercholesterolemia Management at an Academic Medical Center*

Danielle Hess, BS, Stephanie Seto, BS, Pramit Nadpara, PhD, Evan Sisson, PharmD, MSHA, Dave Dixon, PharmD, (Richmond, VA)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Familial hypercholesterolemia (FH) is an underrecognized inherited disorder and major cause of premature atherosclerotic cardiovascular disease (ASCVD). While several studies have evaluated patients meeting the FH phenotype, low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL, few have characterized the management of patients with higher LDL-C levels (≥250 mg/dL) who are more likely to have FH.

Objective/Purpose: To characterize the management of FH at an academic medical center as part of a quality improvement initiative.

Methods: Electronic health records were utilized to identify outpatients with earliest (baseline) documented LDL-C of ≥ 250 mg/dL between 2006 and 2016. We excluded patients < 21 years old, documented secondary cause(s) of dyslipidemia, or insufficient data due to an absence of clinical notes. Baseline characteristics included age, race/ethnicity, sex, ASCVD history, family history of ASCVD or elevated LDL-C, comorbidities, and use of lipid-lowering therapies. Follow-up lipid profiles were extracted for patients with a repeat lipid profile performed closest to 12 months from baseline along with documented use of lipid-lowering therapies. The Dutch Lipid Clinic Network Criteria was used to determine the probability of FH. The Wilcoxon Signed-Ranked Test was used to compare the change in median LDL-C from baseline to 12 months.

Results: A total of 278 individual patients with baseline LDL-C ≥250 mg/dL were identified and 159 met entry criteria. The majority (59%) were classified as having probable/definite FH. The mean age was 52 years, 53% were black, and 66% female. The median baseline LDL-C was 270 mg/dL (IQR 257-292). Established ASCVD was present in 35.8% of patients and 25% had premature ASCVD. Common comorbidities included hypertension (62.9%), obesity (42.7%), and diabetes (32.7%). Nearly three-fourths (74.2%) were not on statin therapy at baseline and non-statin use was rare. In a subgroup of 96 patients with a follow-up lipid panel, the LDL-C decreased by a mean of 37% to 170 mg/dL (p<0.001); however, 76% still had LDL-C levels ≥130 mg/dL. Statin use at follow-up was 77% with 38.5% receiving a high-intensity statin and 36.4% receiving a moderate-intensity statin. Non-statin use was infrequent (15.6%).

Conclusions: The management of FH at an academic medical center was poor among those with an initial LDL-C ≥250 mg/dL. A significant number of patients were eligible for therapy intensification. Next steps will include provider education and implementation of clinical decision support tools.

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How Can We Reduce Cardiovascular Disease Risks in Black Women?

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Synopsis: According to AHA data from 2015, 47.7% of Black females have
cardiovascular disease (CVD) compared to 35.1% of White, 33.0% of Hispanic, and 27.0% of Asian females. It is crucial to identify CVD risk factors in Black females early and implement targeted education and preventive care. As part of the Emory Women’s Heart Center 10,000 Women Hypertension Screening Project, we screened Black females for CVD risk factors.

**Objective/Purpose:** To assess CVD risk factors in Black Women and identify trends with increasing age to determine which age groups to target for education for risk reduction.

**Methods:** 789 Black women were screened for blood pressure and CVD risk factors from 2015-2018 as part of community based health screening. Personal medical information was collected along with blood pressure, body mass index (BMI) and point of care cholesterol levels were measured using Alere Cholestech LDX analyzer. Descriptive statistics, T-tests, and chi square analysis were performed.

**Results:** Mean age was 50.38 +/-13.82. For the group overall, the BMI was 31.61 +/-7.20, systolic blood pressure (SBP) 122.83 +/- 19.21, diastolic blood pressure (DBP) 81.21 +/-11.61 mmHg, total cholesterol (TC) 175.05 +/-32.85 mg/dL, triglycerides (TG) 122.42 +/-62.85 mg/dL, low-density lipoprotein cholesterol (LDL-C) 92.6 +/- 11.61 mg/dL, and high density lipoprotein cholesterol (HDL-C) 58.09 +/- 16.39 mg/dL.

**Conclusions:** CVD education programs need to be tailored toward Black women at different age ranges. 1-Hypertension education should started before age 20 and continue throughout the lifespan. 2-Education geared toward young Black women on diet, fats, exercise, healthy lifestyles and sodium restriction may diminish the rise in lipids and SBP seen between ages 20 to 40 and 40 to 60. 3-Targeting young Black females to maintain a healthy BMI prior to childbearing years is reinforced as Black women are entering their 20’s with a BMI >30 and this continues across the lifespan. The ongoing rise in SBP throughout the ages with the rise in TC, LDL-C and TG in women over 40 undoubtedly adds to the numbers of Black women being diagnosed with hypertension, metabolic syndrome and diabetes, and leads to a higher burden of CVD in Black women.

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**Evaluation of the Safety Profile of Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors in Patients with Chronic Kidney Disease**

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**Lead Author’s Financial Disclosures:** None.

**Study Funding:** None.

**Background/Synopsis:** Evidence has shown that patients with chronic kidney disease (CKD) have difficulty in obtaining optimal lipid levels with statin therapy, thereby increasing the risk for cardiovascular disease. This patient population often presents with increases in the total cholesterol (TC), low density lipoproteins (LDL), non-high-density lipoproteins (non-HDL), triglycerides (TG) and decreases in high density lipoproteins (HDL). There is currently limited data on PCSK9 inhibitor use in CKD patients because of exclusion criteria and limited patient populations from previous trials. PCSK9 inhibitors used as monotherapy or in combination with statin therapy have demonstrated significant LDL-C lowering. The results of this study will add to the limited literature to date regarding the safety profile of PCSK9 inhibitors in the CKD population.

**Objective/Purpose:** The objective of this study is to evaluate the safety of PCSK9 inhibitors in patients with chronic kidney disease (CKD).

**Methods:** This is a retrospective chart review of patients at NYU Langone Health (NYULH), a 1,069-bed tertiary hospital in New York City. All patients within NYULH with chronic kidney disease (CKD) receiving a PCSK9 inhibitor from January 2016 to June 2018 were reviewed. Patients’
demographics, comorbidities, laboratory data and details of lipid lowering therapy (medications, doses, frequencies, and duration) were collected based on the retrospective review of electronic health records (EHR). Patients were included in this study if they were greater than 18 years of age with a diagnosis of CKD stages III-V. Patients were excluded if they had an intolerance to PCSK9 inhibitors prior to the 180-day follow-up period. The primary outcome of this study is the change in kidney function as measured through blood urea nitrogen (BUN), serum creatinine (SCr), and estimated glomerular filtration rate (eGFR) over a follow-up of 6 months post-PCSK9 inhibitor initiation. Secondary measures of assessment will include changes in lipid values from obtained lipid panels, creatinine kinase (CK) levels, and any documented adverse drug events.

**Results:** Over 180 patients were identified to have reported CKD and a history of PCSK9 inhibitor use. However, only 18 patients met the inclusion criteria. At baseline, 15 patients had CKD stage 3, one patient had CKD Stage 4 and two patients had borderline CKD stage 2-3. Approximately, 50% of the patients had an increase in SCr (8/18), an increase in BUN (10/18) and a decrease in GFR (9/18) at the 6-month follow-up. A rise or decline in SCr (8/18), an increase in BUN (10/18) and a decrease in GFR (9/18) at the 6-month follow-up. The primary outcome of this study is the change in kidney function as measured through blood urea nitrogen (BUN), serum creatinine (SCr), and estimated glomerular filtration rate (eGFR) over a follow-up of 6 months post-PCSK9 inhibitor initiation. Secondary measures of assessment will include changes in lipid values from obtained lipid panels, creatinine kinase (CK) levels, and any documented adverse drug events.

**Conclusions:** Based on the limited evidence, the use of PCSK9 inhibitors after 6 months of treatment, appears to be safe in the CKD population, however monitoring of renal function is still warranted in these patients. Larger studies with longer follow-up periods are required to determine if use of non-statin therapies, specifically ezetimibe and alirocumab. At the time of their most recent clinic visits, all patients were tolerating their lipid lowering regimen and four of the patients had reached guideline specified LDL targets, with the fifth patient deferring further statin titration until resolution of a dermatomyositis flare (current LDL reduction 33%).

**Management of Dyslipidemia in Patients with Dermatomyositis: A Case Series**

**Lead Author’s Financial Disclosures:** None.

**Study Funding:** None.

**Background/Synopsis:** Statins remain the preferred initial therapy for most patients with hyperlipidemia and elevated cardiovascular risk. However, they may also cause statin associated muscle symptoms (SAMS) that can limit their use in many patients. Patients with dermatomyositis often have skeletal muscle weakness, making the use of statins challenging. The management of patients with this diagnosis has not been clearly defined. This case series describes five patients with dermatomyositis, seen at The Ohio State University Wexner Medical Center Cardiovascular Risk Reduction and Lipid Clinic between 2014 and 2018, their treatment, and subsequent relevant outcomes.

**Objective/ Purpose:** To review the management of dyslipidemias in patients with baseline musculoskeletal dysfunction secondary to dermatomyositis.

**Methods:** We performed a retrospective chart review of patients at an academic medical center lipid clinic with a diagnosis of dermatomyositis and indication for statin therapy. Patients were required to be seen for at least one follow up visit to verify tolerance.

**Results:** Five adult patients were included in our analysis, all with biopsy confirmed (intermediate or definite) dermatomyositis prior to establishing with the lipid clinic. Indications for statin therapy included coronary artery bypass grafting, recurrent myocardial infarction, non-obstructive coronary artery disease on left heart catheterization, possible familial hypercholesterolemia, and an elevated 10 year risk >20%; all also carried additional risk factors. At the initial visit, only one patient was on statin therapy, which was stopped shortly after at the request of her neuromuscular physician, and three of the remaining patients had failed statin therapy in the past due to SAMS. Therapies were chosen in conjunction with the patient’s dermatomyositis physician (rheumatology, neuromuscular) and based on patient tolerance and response. Three patients were approved for trial of statin therapy while managing physicians preferred avoidance of statins in the remaining two patients. Four patients were approved for use of non-statin therapies, specifically ezetimibe and alirocumab. At the time of their most recent clinic visits, all patients were tolerating their lipid lowering regimen and four of the patients had reached guideline specified LDL targets, with the fifth patient deferring further statin titration until resolution of a dermatomyositis flare (current LDL reduction 33%).

**Conclusions:** Though dermatomyositis patients have baseline myopathy, they often warrant lipid lowering therapy. Experience with our center’s small cohort demonstrates that tolerable and effective regimens, including statins, can be found for this patient population.
Background/Synopsis: The introduction of PCSK9 inhibitors in 2015 added a potent therapeutic option for lipid lowering therapy. Both FDA approved agents, alirocumab and evolocumab, have well documented LDL-C lowering effects as well cardiovascular event reduction data.

Objective/Purpose: Previous studies have demonstrated a trend for a more robust LDL-C reduction in men versus women with both alirocumab and evolocumab therapy. Anecdotal reports also suggest that women have a higher rate of significant hypo-responsiveness to PCSK9 inhibitor therapy than men. This study (1) examines the gender specific effects of alirocumab and evolocumab on LDL-C lowering and (2) examines the gender specific effects on the variability of response to PCSK9 inhibitor therapy.

Methods: A retrospective chart review was conducted at the Florida Lipid Institute in Orlando. Pre- and post- PCSK9 inhibitor therapy LDL-C levels were collected in patients started on the initial dose of alirocumab (75 mg sq every two weeks) and evolocumab (140 mg sq every two weeks).

Results: Data was collected from 160 patients on PCSK9 inhibitor therapy - 67 on alirocumab and 83 on evolocumab. There were no gender differences in the alirocumab group for LDL-C lowering: 51% +/- 16% for men and 54% +/-16% for women (p=0.48). In the alirocumab group the LDL-C lowering response ranged from 5% to 90% but there were no gender differences in the variability of response (p=0.94). In the evolocumab group men had a statistically significant better LDL-C lowering response (68% +/- 14%) compared to women (61% +/-12%) (p=0.01). In the evolocumab group the LDL-C lowering response ranged from 33% to 92% but there were no gender differences in the variability of response (p=0.99).

Conclusions: Alirocumab had no gender differences in LDL-C lowering response or the variability of LDL-C lowering effects as well cardiovascular event reduction effects. Among 211 OHT patients, average time to follow-up was 5.8 years (0.5-26). There were 19 deaths (9%) and 101 (48%) developed CAV. Statin intensity data was available in 195 patients- 40% (77) were on high-intensity, 42% (81) on moderate-intensity, 12% (22) on low-intensity statin respectively and 6% (11) were not on a statin. Compared to the non-CAV group, CAV patients had higher systolic BP and HbA1C (p<0.05) but no difference in lipid values or statin intensity. No difference in statin intensity or lipid values were also noted among patients who died. In a Cox Proportional Hazards model to predict time to occurrence of CAV, statin intensity (1.4; CI-1.05-1.8), history of kidney transplant (0.4; 0.78-0.97) and CMV viremia (1.72; CI-1.02-2.9) were significant predictors in a model that also included lipid values, BP, HbA1C and h/o diabetes.

Conclusions: The majority of OHT patients are on statin therapy including moderate to high-intensity statin. The intensity of statin therapy is associated with time to occurrence of CAV. Since we collected data on statin intensity at the time of diagnosis of CAV, this may be reflective of changes made after diagnosis of CAV. Lipid values are not related to intensity of CAV and therefore should not be used to assess need for escalation of therapy.
and 7.4% of adolescents age 12-19 years have elevated Low-density Lipoprotein cholesterol (>130 mg/dL).

Racial/Ethnic differences have been noted in prevalence of dyslipidemia in adults.

**Objective/Purpose:** The goal of our study was to describe the racial/ethnic differences in hyperlipidemia among youth referred to a tertiary care facility.

**Methods:** We queried the Electronic medical record at our institution for all patients seen in pediatric cardiology clinic between 2011 and 2018 and obtained their race/ethnicity, age, gender, height, weight, BMI, and lipid profile. SPSS was used to do statistical analysis. Chi-Square test was used to test differences between the groups.

**Results:** Lipid profiles for 12610 unique subjects were obtained between 2011 and 2018. The mean age of subjects was 10.4 years (range 3 months-21 years). 54% of subjects were male. The race/ethnic profile is shown in table 1 (see attachment).

**Conclusions:** Racial/ethnic differences exist in cholesterol profile in youth. Consideration of race/ethnic differences may benefit development of optimal screening strategies and treatment of youth with dyslipidemia. Further research is needed to determine how racial/ethnic differences in dyslipidemia in youth may affect the development of cardiovascular disease rates in future.

**Nutrition, Nutrigenomics, Nutraceuticals and Exercise Therapies**

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**Importance of Nutritional Intervention for Infants with Abetalipoproteinemia**

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Michelle Maeda, MS, RD, Adam McIntyre, MSc, Robert Hegele, MD,
Mary Malloy, MD, Daniel Rader, MD, (Philadelphia, PA)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

**Background/Synopsis:** Having low levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) are considered desirable due to evidence linking high levels to increased risk for cardiovascular disease. However, marked reductions may indicate the presence of devastating heritable disorders, such as abetalipoproteinemia, hypobetalipoproteinemia, and chylomicron retention disease due to bi-allelic mutations in MTP, APOB, and SAR1B, respectively. These disorders are associated with extremely low TC, LDL-C, and undetectable apolipoprotein B due to defective assembly and secretion of chylomicrons from the intestine and very low-density lipoproteins from the liver. Fat malabsorption, often beginning in infancy, is common in abetalipoproteinemia and can lead to failure to thrive with steatorrhea due to fat-intolerance to breast milk or formula. Abnormal lipoprotein levels, acanthocytosis and hepatic steatosis are other notable features. Devastating manifestations include retinal disease, bone and neurological abnormalities, and coagulopathy due to deficiencies of vitamins A, D, E, and K, respectively, that require lipoproteins for transport. There is no treatment for abetalipoproteinemia aside from large doses of fat-soluble vitamins. Thus, early diagnosis and dietary management can dramatically improve the patient’s overall condition.

**Objective/Purpose:** We present a young patient with abetalipoproteinemia whose growth and development have been positively impacted by appropriate nutritional intervention beginning in infancy.

**Methods:** The patient and her family participated in an institutionally approved study, investigating the genetic etiology of dyslipidemia at the University of Pennsylvania. Growth history was obtained from her parent, nutritionist, and medical records.

**Results:** The patient was clinically diagnosed with abetalipoproteinemia at 5 months. This diagnosis was confirmed by the presence of maternally inherited (Int 13+5 G>A -E13 skip), and paternally inherited (insA, p.N140K-141X (p.N140Kfs*1) MTP mutations. She was seen by a metabolic nutritionist at 7 months because of severe milk-intolerance and poor growth. Commercially available infant formulas were not tolerated, requiring the

**Table 1 Race/Ethnic differences in dyslipidemia in youth**

<table>
<thead>
<tr>
<th></th>
<th>Caucasian</th>
<th>Black</th>
<th>Asian</th>
<th>Hispanic</th>
<th>Other/Unknown</th>
<th>X²</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High TC</td>
<td>13.6%</td>
<td>21.1%</td>
<td>18.1%</td>
<td>24.1%</td>
<td>13.9%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low HDL C</td>
<td>32.6%</td>
<td>21.4%</td>
<td>24.1%</td>
<td>44.1%</td>
<td>30.4%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High LDL C</td>
<td>10.8%</td>
<td>10%</td>
<td>18.4%</td>
<td>6.5%</td>
<td>13.9%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High TG</td>
<td>32.6%</td>
<td>12.5%</td>
<td>35.3%</td>
<td>29.8%</td>
<td>27.5%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

High TC: Total Cholesterol ≥ 200, Low HDL C: High-density Lipoprotein Cholesterol ≤ 40, High LDL C: Low-density Lipoprotein Cholesterol ≥ 130, High TG: Triglycerides ≥ 130
preparation of a special modular formula containing ProVi- Min, Polycose, corn oil, and flaxseed to provide essential fatty acids that were critical for infant growth and development along with vitamin supplementation. The patient had remarkable catch-up growth on the new formula, and both her weight and height increased from <10th tile to 50th tile within a month. Although she has been diagnosed with hepatic steatosis and mild sensory abnormalities, her general health has been good and her development has been age-appropriate. She has been playing basketball without difficulties.

Conclusions: The case clearly shows the importance of appropriate nutritional intervention in infancy to minimize the devastating manifestations of abetalipoproteinemia.

Table Infant Formula Comparison: based on current data 100 g powder

<table>
<thead>
<tr>
<th></th>
<th>Special Formula</th>
<th>Monogen*</th>
<th>Tolerex</th>
<th>Alimentum*</th>
<th>Neocate Infant*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td></td>
<td>444</td>
<td>375</td>
<td>525</td>
<td>483</td>
</tr>
<tr>
<td>Protein %</td>
<td>12</td>
<td>11.6</td>
<td>8</td>
<td>11</td>
<td>11</td>
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<tr>
<td>Carbohydrate %</td>
<td>75</td>
<td>62.2</td>
<td>91</td>
<td>39</td>
<td>43</td>
</tr>
<tr>
<td>Fat %</td>
<td>11</td>
<td>26.1</td>
<td>2</td>
<td>50</td>
<td>46</td>
</tr>
<tr>
<td>LCT g/percent</td>
<td>5.5 g</td>
<td>2.1 g/16%</td>
<td>1 g/18%</td>
<td>19.2 g/67%</td>
<td>16.5 g/67%</td>
</tr>
<tr>
<td>MCT g/percent</td>
<td>0</td>
<td>10.8 g/84%</td>
<td>0%</td>
<td>9.6 g/33%</td>
<td>8 g/33%</td>
</tr>
<tr>
<td>Linolenic Omega-3</td>
<td>600 mg</td>
<td>170 mg</td>
<td>0</td>
<td>446 mg</td>
<td>419 mg</td>
</tr>
<tr>
<td>Linoleic Omega-6</td>
<td>2351 mg</td>
<td>900 mg</td>
<td>560 mg</td>
<td>4199 mg</td>
<td>3565 mg</td>
</tr>
<tr>
<td>DHA/ARA</td>
<td>-</td>
<td>60 mg/60 mg</td>
<td>0</td>
<td>51 mg/103 mg</td>
<td>81.6 mg/81.6 mg</td>
</tr>
</tbody>
</table>

The modular special formula has a relatively low-fat percentage, but with a higher amount of linolenic fatty acids with 600 mg. It provided 21 calories per ounce.

*Monogen, Alimentum, and Neocate Infant have been reformulated to add DHA/ARA

**LCT: Long-chain triglycerides**

**MCT: Medium-chain triglycerides**

**DHA: Docosahexaenoic acid**

**ARA: Arachidonic acid**

Objective/Purpose: The objective of our studies was to investigate the physiologic effect, particularly cardioprotective impact, of PA in animal models and human subjects.

Methods: Three animal studies were performed to investigate the effect of dietary PA on lipid/glucose metabolism, atherosclerotic development, and satiety. Furthermore, we are currently performing a randomized, double-blinded, crossover, placebo-controlled clinical trial on supplementation with PA concentrate oil (Clinical-Trials.gov Identifier: NCT03372733) to investigate its effect on cardiometabolic biomarkers.

Results: In type II diabetic mouse models that were orally administered PA for 4 week, PA improved insulin resistance and lipid profile through regulating lipogenic and inflammatory genes. In diet-induced atherosclerotic LDLR-KO mice that were fed Western diet supplemented with PA concentrate for 12 weeks, dietary PA, but not oleic-rich olive oil, reduced atherosclerosis. These favorable changes were associated with improvement of lipid and glucose metabolism, and favorable changes in regulatory genes involved in lipid metabolism and inflammation. Furthermore, oral administration of PA also caused dose-dependently increased satiety in SD rats compared with C16:0 or C18:1, possibly due to an increase production of satiety hormones.

Conclusions: In summary, the American Heart Association and Dietary Guidelines for Americans have long advised the replacement of saturated fatty acids with unsaturated fatty acids including MUFAs, but a more detailed understanding on the effect of various types of dietary MUFAs on CVD risk is needed. Our pre-clinical trials suggest that enrichment of dietary PA may have beneficial and perhaps unique effects on CVD risk factors, and thus could lead to new dietary recommendations and improvements in the formulation of MUFA supplements.
Effects of Conjugated Linoleic Acid (CLA) on HDL-C and Triglyceride levels in Subjects with and without the Metabolic Syndrome: A Systematic Review and Meta-analysis

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: CLA supplementation has been widely used by the general population as a weight reduction agent. In-vitro and animal studies have reported beneficial metabolic effects including cholesterol and triglyceride lowering effects, as well as anti-atherogenic actions potentially via PPARy-activation. However, findings in humans have been mixed, with some studies even reporting harmful effects.

Objective/Purpose: The aim of the present systematic review and meta-analysis is to evaluate the available evidence of the effects of CLA on relevant aspects of the lipoprotein profile in terms of metabolic syndrome, such as HDL-C and triglyceride levels.

Methods: We conducted a systematic literature search to identify studies up to December 2017. Only randomized controlled trials (RCTs) of t10-c12 CLA isomer or mix 50:50 CLA t10-c12 and c9-t11 compared to placebo on healthy subjects or with components of the metabolic syndrome were selected. The quality of individual studies was assessed using the Cochrane’s Risk of Bias tool. When appropriate, results were pooled to obtain weighted mean differences (WMDs) with 95% CI. Small study effects were assessed in funnel plots, and heterogeneity was further explored in subgroup analysis.

Results: A total of 17 RCTs were included in the qualitative review, which identified between study differences in type of participants, length and dose of intervention, and study quality. Meta-analysis of 13 studies showed that CLA was associated with a small reduction in HDL-C levels (-2.06 mg/dL, 95%CI -3.74, -0.39, p=0.016) and an increase in triglyceride levels (7.54 mg/dL, 95% CI 1.20, 13.88, p=0.020). Subgroup analysis indicated that the differences were largely driven by interventions with higher CLA doses (> 4g/day). Sensitivity analysis removing studies with high risk of bias still showed a statistically significant decrease in HDL-C levels while the effects on triglycerides was no longer seen.

Conclusions: Our systematic review and meta-analysis concluded that there is no beneficial effects of CLA on HDL-C and triglycerides levels, in contrast with the previously mentioned findings from mechanistic studies. However, our unexpected adverse outcomes should be interpreted with caution given the heterogeneity in study design and quality of the available evidence, suggesting the need for properly designed large randomized trials.

Lipid Effects of Dietary Education as a Function of Age and Gender

Debra Ann Friedrich, DNP, FNP-BC, CLS, FNLA, Paul Ziajka, MD, PhD, Bernice Boivin, RDN, Nancy Smith, MS, RDN, LDN, CD, (Bradenton, FL)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Evidence demonstrates that multiple Medical Nutritional Therapy (MNT) sessions by a registered dietician are clinically effective and cost beneficial in patients with dyslipidemia and cardiometabolic risk factors. However, data related to the lipid response stratified by age and gender is not clearly defined and will be the focus of the study.

Objective/Purpose: The purpose of the study was to retrospectively examine the lipid response of dietary education provided by a registered or licensed Dietician in or upon a referral from a lipid clinic stratified by age and gender.

Methods: Retrospective data was collected to examine both gender differences and age (<40 young adults) versus (>70 geriatrics) on the normalization components of the lipid panel in patients after receiving dietary education. Pre-education baseline lipids and follow-up post-education lipids were reviewed.

Results: There were no statistically significant changes in patient weight for the entire population or in any age or gender subset for either dietary education focusing on LDL-C or triglyceride reduction. For the entire LDL-C population (all ages and genders) LDL-C was reduced 13.8% (p<.000001). For the entire triglyceride population (all ages and genders) triglycerides were reduced 26.2% (p=.001). There were no statistically significant difference with respect to LDL-C or triglyceride lowering based on gender. LDL-C lowering based on age showed a non-statistically significant trend with the elderly achieving a greater reduction than younger age groups.

Conclusions: All patients achieved LDL-C lowering after referral to a registered dietician. However, patients over the age of 76 showed the greatest reduction in LDL-C with dietary education. Medical Nutritional Therapy should be considered first line in our elderly patients not at LDL-C goal.
Lifestyle intervention improve the weight and exercise patterns of geriatric depressed patients

Francisco Eduardo Ramirez, MD, (Weimar, CA)

Lead Author’s Financial Disclosures: None. Study Funding: None.

Background/Synopsis: Depressed individuals may lack motivation to take care of their health.

Objective/Purpose: We explore the effect that a medical residential lifestyle intervention have on these patients regarding weight and exercise patterns.

Methods: The retrospective intervention took place in Weimar, CA of 18 days. Patients were evaluated by a board certified physicians, some came with the diagnosis of depression, some were diagnosed with depression at the program. This comprehensive lifestyle intervention program included a whole foods plant-based diet, exercise, water, sunlight, temperance/moderation, fresh air, rest/sleep, and emotional, relational support. A baseline measurement of weight and various markers was done including miles walked was captured, at the end the of the program the same evaluation was repeated.

Results: In 12 years of patients data, n=107 patients were geriatric and have the diagnosis of major depression at baseline, from those 107, n=96 had the before and end data complete and were used for this study.

Average age was 66.7 SD 8.6. At the beginning their weight in pounds listed as mean, St Dev, mode, median was (164.3, 38.5, 158, 157.7). Using the baseline values of Body Mass Index, 23% were overweight and 23% were obese. At the end, the mean, St Dev, mode and median values were (159.6, 36.2, 146, 155). Regarding their exercise patterns at baseline the mean, St Dev, mode, median, minimum, maximum miles that they were walking per day was (.5, .9, 0, 0, 0, 4), their end walking values listed in the same order were (3, 1.9, 4, 3, 0.25, 9).

Conclusions: This short-term lifestyle intervention program of change in diet, exercise and other health components was able help patients improve their wait and increase their physical activity. The long-term effects of this lifestyle intervention needs to be studied.

Omega-3 Fatty Acids

Prevalence of Diabetes Mellitus with REDUCE-IT-Like Indications: Ramifications for Residual Risk and Potential Risk Reduction

John R. Nelson, MD, Lihong He, PhD, Michael Dansinger, MD, (Fresno, CA)

Lead Author’s Financial Disclosures: Advisory Board: Amgen, Amarin. Stock: Amgen, Amarin, Pfizer. Speaker for Amgen, Amarin, Regeneron, Boehringer Ingelheim, Boston Heart Diagnostics.

Study Funding: Boston Heart Diagnostics.

Background/Synopsis: The Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT) demonstrated that 4 grams of prescription eicosapentaenoic acid (EPA) significantly reduced cardiovascular disease (CVD) events including CVD deaths when added to statin therapy in subjects with LDL-c >40-100 mg/dL, and triglycerides 150-499 mg/dL, and with either known CVD aged >45 years, or diabetes mellitus aged >50 years plus at least one additional risk stratum criterion.

Objective/Purpose: This study determined the prevalence of four risk stratum criteria (age > 55 years for males or > 65 years for females, HDL-c <40mg/dL in males or <50 mg/dL in females, hsCRP > 3.0 mg/L, or stage 3 chronic kidney disease) in individuals with type 2 diabetes who met the REDUCE-IT criteria for LDL-c and triglycerides. We also tested the hypotheses that serum levels of EPA and the ratio of EPA to arachidonic acid (EPA/AA) progressively decreased according to the number of risk stratum criteria met.

Methods: We used de-identified data from the laboratory information system of Boston Heart Diagnostics to calculate the prevalence of REDUCE-IT-Like criteria and serum EPA and EPA/AA levels from blood specimens received during a 5-year period from August 2014 through September 2018.

Results: Among patients with type 2 diabetes aged >50 years who met the REDUCE-IT criteria for LDL-c and triglycerides (n=11,646), 96.87% met at least one risk stratum criterion (76.42% for age, 70.73% for HDL-c, 35.56% for hsCRP, 20.56% for stage 3 kidney disease). This included 72.53% who met two risk criteria, 19.18% who met three risk criteria, and 4.94% who met four risk criteria. The median serum levels for patients with 1, 2, 3, and 4 risk stratum criteria were, respectively, 26.6, 23.4, 20.9, 20.5 mcg/dL for EPA, and 0.086, 0.080, 0.074, 0.071 for EPA/AA ratio (p<0.0001 for trends).

Conclusions: This study shows that there is a substantial burden of residual risk and opportunity for CVD risk reduction among patients aged >50 years with type 2 diabetes who meet the REDUCE-IT criteria for LDL-c, and triglycerides, since 96.87% met at least 1 risk stratum criterion. The median serum EPA level and EPA/AA ratio progressively decreased with additional risk stratum criteria suggesting potential greater benefits of EPA supplementation with each additional risk criterion present.

Comparison of EPA and DHA-Rich Fish Oils on NMR Lipoprotein Metabolism in Adults

Marcelo Amar, MD, Zhihong Yang, PhD, Maureen Sampson, Alexander Sorokin, MD, Michael Stagliano, NP, Alan Remaley, MD, PhD, (Bethesda, MD)
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Eicosapentaenoic Acid, Unlike Arachidonic Acid, Maintains Normal Membrane Structure and Cholesterol Distribution Under Conditions of Hyperglycemia

Samuel Sherratt, CR, BS, R. Mason, PhD, (Beverly, MA)

Lead Author’s Financial Disclosures: None.

Study Funding: This study was conducted with financial support from Amarin Pharma, Inc.

Background/Synopsis: Highly purified, prescription eicosapentaenoic acid (EPA) reduced cardiovascular events in the REDUCE-IT study population, including in patients with diabetes. During hyperglycemia, there is abnormal membrane cholesterol aggregation which has been linked to oxidative stress and plaque instability. Due to its chemical structure, EPA at a pharmacologic dose may preserve normal cholesterol distribution as compared to arachidonic acid (AA), an omega-6 fatty acid (FA).

Objective/Purpose: To compare the effects of EPA and AA on membrane structure and cholesterol crystalline domain formation under conditions of hyperglycemia and oxidative stress.

Methods: Membrane vesicles were prepared from di-oleoylphosphatidylcholine (DLPC) at a cholesterol-to-phospholipid mole ratio of 0.6:1 and treated with pharmacologic levels of EPA and AA at a 1:30 FA to phospholipid mole ratio under conditions of hyperglycemia (200 mg/dL). Changes in membrane lipid organization and width were measured using small angle X-ray diffraction approaches and correlated with lipid hydroperoxide formation. Cholesterol domains were identified in experimental samples by the presence of diffraction peaks corresponding to a unit cell periodicity or width of 34 A.

Results: Membranes containing EPA had a membrane structure characterized by normal width of 55 A and cholesterol distribution under conditions of hyperglycemia. By contrast, AA containing samples yielded diffraction patterns consistent with a biaxial membrane structure containing prominent cholesterol crystalline domains and phospholipid-enriched membrane bilayer domains with unit cell periodicities of 34 A and 54 A, respectively. The width of 34 A corresponds to free cholesterol in an immiscible bilayer structure within the membrane. Unlike AA, EPA also inhibited lipid peroxide formation compared to vehicle.

Conclusions: EPA preserved normal membrane structure and cholesterol distribution while reducing lipid oxidation under conditions of hyperglycemia in a manner that was not reproduced with AA. These data indicate physico-chemical differences between these long chain FAs and support a potential benefit for EPA in reducing atherosclerotic cholesterol domain formation and associated pathology at pharmacologic levels.

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Acute Effects of Curcuminoids, EPA (Omega - 3), Astaxanthin and GLA On Cardiovascular Health

Divya Birudaraju, MD, Lavanya Cherukuri, MD, April Kinninger, MPH, Ryan Pozon, MD, Chandana Shekar, MD, Kashif Shaikh, MD, Sajad Hamal, MS, Ferdinand Flores, BSN, Sion Roy, MD, Matthew Budoff, MD, (Torrance, CA)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: We completed a prospective, randomized clinical trial to assess the efficacy of Curcuminoids, EPA (Omega-3), Astaxanthin and GLA (CEAG) for improving cardiovascular health (blood pressure, inflammation and endothelial reactivity) over a 4-week intervention period in individuals with Pre-Hypertension.
Objective/Purpose: We also assess the role of CEAG [Quell Gel] administration supplements in improving vascular health in Pre-hypertensive individuals and in those at risk for becoming hypertensive and other markers of cardiovascular function and cardiovascular disease risk factors.

Methods: We performed a double-blinded, placebo controlled, randomized clinical trial to investigate the blood pressure effects of CEAG [Quell Gel] tablets of 80 individuals (30 men and 50 women). The mean age of participants were 48.8 +/- 16.0 years. Participants were enrolled and randomized to CEAG or placebo over 4 weeks. The demographics of both groups are shown in Table 1. Paired and Independent T tests were used to analyze the mean differences between and within groups. Repeated Measures ANOVA with Pairwise comparisons using Tukey’s test was used to analyze the effect of CEAG on BP changes among genders in both groups.

Results: The primary endpoint of the study was reduction in BP at 4 weeks. There was significant reduction in mean SBP at 4 weeks in CEAG group compared to baseline [mean+/-SD 4.7 +/- 6.8 (p=0.002)], (Table 2). The effect was greater among females where reduction in mean systolic BP (SBP) at 4 weeks in the twenty-four female CEAG group was 5.0 mm Hg (P= 0.007), as compared to a slight decrease of 1.0 mm Hg in the female placebo group. (Table 3).

Conclusions: Systolic BP were robustly reduced by CEAG in all subjects, but specifically noted in females over 4 weeks. In pre-hypertensive and metabolic syndrome patients, lowering inflammation has been shown to substantially reduce the risk of developing cardiovascular diseases. Such observations highlight the importance and growing need for accessible and effective anti-inflammatory interventions.

Other

Awareness of Risk factors decrease CVD*

Erum Sohail Jiva, ARNP, (Ocala, FL)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Adequate awareness of risk factors and lifestyle modification may help to reduce rate of cardiovascular disease (CVD) who are at high risk and decrease the long-term complications in those who already have CVD. There is limited data on implementation of series of educational sessions in community wellness center or churches to increase access to health care and increase awareness regarding preventive care. Lack of time during primary care visit and lack of access due to cultural factors hinders preventive care.

Objective/Purpose: We aimed to conduct multiple educational sessions to increase awareness regarding modifiable risk factors in small community church so that we can decrease rate of CVD.

Table 1 Baseline Characteristics among Participants

<table>
<thead>
<tr>
<th></th>
<th>Placebo n=40</th>
<th>Active n=38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs. (mean +/- SD)</td>
<td>45.3 ± 17.2</td>
<td>52.2 ± 14.0</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>26 (65)</td>
<td>24 (63.2)</td>
</tr>
<tr>
<td>Hispanics, n (%)</td>
<td>25 (62.5)</td>
<td>25 (62.5)</td>
</tr>
<tr>
<td>Never Smoked, n (%)</td>
<td>31 (77.5)</td>
<td>28 (73.6)</td>
</tr>
<tr>
<td>Body Mass Index, (kg/m^2) (mean +/- SD)</td>
<td>30.2 ± 5.9</td>
<td>29.8 ± 5.3</td>
</tr>
</tbody>
</table>

Table 2 BP reduction stratified by placebo and active treatment (* data present by mean ± SD and P value comes from paired and Independent t test)

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Group</th>
<th>Baseline</th>
<th>4 weeks</th>
<th>Difference within Group mean ± SD</th>
<th>Difference Between Groups mean ± SD</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>Active</td>
<td>129.6 ± 5.8</td>
<td>124.9 ± 8.7</td>
<td>4.6 ± 7.1</td>
<td>4.7 ± 6.8</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>127.4 ± 6.3</td>
<td>127.5 ± 7.2</td>
<td>0.1 ± 5.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>Active</td>
<td>70.8 ± 4.3</td>
<td>73.5 ± 5.9</td>
<td>2.9 ± 6.8</td>
<td>1.7 ± 7.1</td>
<td>0.287</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>72.6 ± 5.0</td>
<td>73.7 ± 6.3</td>
<td>1.2 ± 7.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Repeated Measures of ANOVA on differences between active and placebo stratified by gender.

<table>
<thead>
<tr>
<th>Group</th>
<th>Active</th>
<th>Placebo</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>Baseline SBP</td>
<td>128.3 ± 5.6</td>
<td>129.0 ± 6.6</td>
</tr>
<tr>
<td></td>
<td>4 weeks SBP</td>
<td>123.3 ± 8.7</td>
<td>128.0 ± 6.8</td>
</tr>
<tr>
<td></td>
<td>Baseline DBP</td>
<td>71.7 ± 5.1</td>
<td>71.8 ± 4.6</td>
</tr>
<tr>
<td></td>
<td>4 weeks DBP</td>
<td>72.9 ± 5.9</td>
<td>73.8 ± 5.9</td>
</tr>
<tr>
<td>Men</td>
<td>Baseline SBP</td>
<td>132.6 ± 5.4</td>
<td>129.0 ± 5.5</td>
</tr>
<tr>
<td></td>
<td>4 weeks SBP</td>
<td>129.3 ± 6.6</td>
<td>127.0 ± 6.9</td>
</tr>
<tr>
<td></td>
<td>Baseline DBP</td>
<td>73.2 ± 3.6</td>
<td>76.6 ± 5.1</td>
</tr>
<tr>
<td></td>
<td>4 Weeks DBP</td>
<td>76.4 ± 5.5</td>
<td>72.5 ± 5.3</td>
</tr>
</tbody>
</table>
**Methods:** This was a community-based Quasi-experimental study conducted in small community church among randomly selected adults (>18 years). Data on sociodemographic characteristics and risk factors collected. Also, knowledge about risk factors of CVD types, their risk factors and warning signs for CVD events (stroke and heart attack) were acquired using a Heart Disease questionnaire before and after educational sessions. The questionnaire was found to have good internal consistency, determined through calculation of Cronbach’s alpha scores of 0.697, and 0.533 for the pre-and post tests, respectively.

**Results:** There was a statistically significant increase in patient CVD knowledge mean scores of 1,813 points, from a pre-test score of 5,703 (SD = 2,514) to a post-test score of 7.444 (SD = 1,108) following the educational intervention (t (33) = 5.740, p < .001). The educational intervention was found to be equally effective for both male and females, with mean score of 1,965 for females and 1.765 for male (t (33) = 5.82, p = .525). Along with change in knowledge, change in participant’s attitude and behavior is noticed. The majority (83%) of participants claimed the

### Table 1.1 Project Demographic & Clinical Characteristic Information

<table>
<thead>
<tr>
<th>Please answer the following question</th>
<th>True/False</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Demographic Information:</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
</tr>
<tr>
<td>Highest level of education</td>
<td></td>
</tr>
<tr>
<td>Form of health insurance</td>
<td></td>
</tr>
<tr>
<td>Common reason to see Primary Care Provider</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
</tr>
<tr>
<td>How many times a week you exercise</td>
<td></td>
</tr>
<tr>
<td>How many times a week you eat fast food</td>
<td></td>
</tr>
<tr>
<td>Family history of heart disease</td>
<td></td>
</tr>
</tbody>
</table>

### Table 1.2 Participants Medical Status: CVD Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Frequency (%) (n=36)</th>
<th>Results (%) (n=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>45%</td>
<td>42%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>50%</td>
<td>55%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>60%</td>
<td>67%</td>
</tr>
<tr>
<td>Obesity</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>History of CVD</td>
<td>38%</td>
<td>35%</td>
</tr>
<tr>
<td>Chronic use of medications for any of the above conditions</td>
<td>52%</td>
<td>55%</td>
</tr>
</tbody>
</table>

### Health Disease Questionnaire: Project Pre-Education Heart Disease Questionnaire

| Questions True/False |
|----------------------|------------------|
| Please respond True/False to the following questions below: | |
| Polyunsaturated fats are healthier for the heart then saturated fats. | |
| Women are less likely to get heart disease after menopause than before | |
| Having had chicken pox increases the risk of getting heart disease | |
| Eating a lot of red meat increases heart disease risk | |
| Most people can tell whether or not they have high blood pressure | |
| Trans-fats are healthier for the heart than most other kinds of fats | |
| The most important cause of heart attack is stress | |
| Walking and gardening are considered types of exercise that can lower heart disease risk | |
| Most of the cholesterol in an egg is in the white part of the egg | |
| Smokers are more likely to die of lung cancer than heart disease | |
| Taking an aspirin each day decreases the risk of getting heart disease. | |
| Dietary fiber lowers blood cholesterol. | |
| Heart disease is the leading cause of death in the United States. | |
| The healthiest exercise for the heart involves rapid breathing for a sustained period of time. | |
| Turning pale or gray is a symptom of having a heart attack. | |
| A healthy person's pulse should return to normal within 15 minutes after exercise. | |
| Sudden trouble seeing in one eye is a common symptom of having a heart attack. | |
| Cardiopulmonary resuscitation (CPR) helps to clear clogged blood vessels. | |
| HDL refers to “good” cholesterol, and LDL refers to “bad” cholesterol. | |
| Atrial fibrillation is a procedure where hardened arteries are opened to increase blood flow. | |
| Feeling weak, lightheaded, or faint is a common symptom of having a heart attack. | |
| Taller people are more at risk for getting heart disease. | |
| “High” blood pressure is defined as 110/80 (systolic/diastolic) or higher. | |
| Most women are more likely to die from breast cancer than heart disease. | |
| Margarine with liquid safflower oil is healthier than margarine with hydrogenated soy oil. | |
| People who have diabetes are at higher risk of getting heart disease. | |
| Men and women experience many of the same symptoms of a heart attack. | |
Eating a high fiber diet increases the risk of getting heart disease
Heart disease is better defined as a short-term illness than a chronic, long-term illness.
Many vegetables are high in cholesterol.


Talk show in particular was helpful in facilitating their understanding of CVD risk factors, and 67.3% of participants claimed that hands on sessions like yoga classes and cooking challenge provided good insight and helpful in making lifestyle changes to reduce risk of CVD.

Conclusions: There exists a significant gap in population awareness about risk factor modification can decreases rate of CVD. Treating cause of the cause is challenging due to lack of access to preventive care. Conducting educational sessions in community wellness center or churches can increase awareness regarding prevention and decrease rate of CVD in community.

Key words: Cardiovascular Disease, Risk factors, Prevention

Project Evaluation Form:

Evaluation form
For the following questions, please circle the response that matches the extent to which you agree or disagree with the following statements.

1. The educational sessions were very informative

<table>
<thead>
<tr>
<th>Don't agree</th>
<th>Somewhat agree</th>
<th>Agree</th>
<th>Strongly agree</th>
<th>Comments</th>
</tr>
</thead>
</table>

2. The objectives of session were cleared

<table>
<thead>
<tr>
<th>Don't agree</th>
<th>Somewhat agree</th>
<th>Agree</th>
<th>Strongly agree</th>
<th>Comments</th>
</tr>
</thead>
</table>

3. All sessions were clear in language and easily understandable

<table>
<thead>
<tr>
<th>Don't agree</th>
<th>Somewhat agree</th>
<th>Agree</th>
<th>Strongly agree</th>
<th>Comments</th>
</tr>
</thead>
</table>

4. Timing of each session was appropriate

<table>
<thead>
<tr>
<th>Don't agree</th>
<th>Somewhat agree</th>
<th>Agree</th>
<th>Strongly agree</th>
<th>Comments</th>
</tr>
</thead>
</table>

5. Educational material provided was helpful

<table>
<thead>
<tr>
<th>Don't agree</th>
<th>Somewhat agree</th>
<th>Agree</th>
<th>Strongly agree</th>
<th>Comments</th>
</tr>
</thead>
</table>

Suggestions for future sessions

Update on dyslipidemia patterns in Chilean adult population: Findings from the 2016-2017 National Health Survey

Paulina Mendoza, MD,
Guadalupe Echeverria, MSc, (Santiago, Chile)

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Cardiovascular diseases (CVD) are the leading cause of death worldwide. Their most common pathological basis is atherosclerosis, which has a multifactorial etiology including dyslipidemia as one of the main risk factors. Thus, nationwide prevalence assessment of dyslipidemia is a fundamental strategy for public health policymaking in both primary and secondary CVD prevention.

Objective/Purpose: To determine the prevalence of different dyslipidemic patterns in Chilean adult population.

Methods: The 2016-2017 National Health Survey (2016-2017 NHS) is a cross-sectional household survey performed in non-institutionalized adults aged ≥18 years. Complex design random selection was used in a nationally representative sample, which included administrative regions and urban/rural locations. In a randomly selected subsample of this survey, fasting total cholesterol, HDL cholesterol, and triglycerides were directly measured, whereas LDL cholesterol and non HDL cholesterol were calculated.

Results: The subsample included 3,399 subjects with valid measurements of blood lipids. National weighted prevalences of high total cholesterol (>200 mg/dl), high LDL cholesterol (>130 mg/dl), high non HDL cholesterol (>160 mg/dl), hypertriglyceridemia (>150 mg/dl) and low HDL cholesterol (<40 mg/dl in males and <50 mg/dl in females) were 27.4%, 18.8%, 21.6% 34.7%, and 47.2%, respectively. Dyslipidemias were more prevalent in older age groups and at lower socioeconomic levels. 38.8% of Chilean adults had at least two lipid abnormalities (high LDL cholesterol, high triglycerides, or low HDL cholesterol) and 13% (1.2 million subjects) exhibited alterations in all three lipid measurements. Thus, achievement of recommended levels of these lipids -as indicated above- reached only 32.0% of the overall population.

Conclusions: Some form of lipid abnormality affects two out of three adults in Chile. Low HDL cholesterol, high non HDL cholesterol and triglycerides, and mixed dyslipidemias were very frequent even at higher prevalences than LDL hypercholesterolemia. This pattern of atherogenic dyslipidemia is consistent with a high prevalence of sedentarism, overweight, obesity and metabolic syndrome in Chile. Rather than focusing exclusively on coverage for LDL cholesterol lowering drug therapy, these findings call for action highlighting the need of population wide as well as more comprehensive lipid-based preventive strategies.
Serving the Underserved: Are We Overlooking HoFH Patients?

Linda C. Hemphill, MD, FNLA, Anne Goldberg, MD, FNLA, FACP, G. Hovingh, MD, PhD, MBA, Jerome Cohen, MD, FNLA, FACC, Dean Karalis, MD, FACC, FNLA, (Boston, MA)

Lead Author’s Financial Disclosures: Amgen (consulting fee), Regeneron (consulting fee), IONIS (research funding), Regeneron/Sanofi (research funding).

Study Funding: Supported in part by Aegerion, Inc. and REGENXBIO Inc.

Background/Synopsis: The National Lipid Association (NLA) Health Quality & Research Committee identified the need to conduct a survey to better understand the diagnosis and treatment of patients with familial hypercholesterolemia (HoFH) among primary care professionals. It is estimated that up to 300,000 Americans have HoFH and are usually seen first by primary care providers. These patients develop atherosclerotic vascular disease at an early age and most remain undiagnosed and undertreated.

Objective/Purpose: To evaluate the knowledge of primary care providers in the diagnosis and treatment of HoFH.

Methods: An electronic survey was sent out in June and July of 2018 to 14,904 medical professionals licensed in the United States who treat patients with elevated LDL-C levels. 504 healthcare providers completed the survey.

Results: Most respondents were physicians (85%) and the majority (88%) did not consider themselves lipid specialists. Most respondents (69%) treat patients with LDL-C > 400 mg/dL, and 53% identified such patients as having HoFH. 82% of the respondents would use a risk calculator to assess cardiovascular risk in such a patient. Regarding treatment, 80% would treat with a high-intensity statin, 60% would add a PCSK9 inhibitor, and only 13% would consider LDL apheresis. Approximately 2/3 of respondents do not have access to an LDL apheresis center. Over half of respondents (63%) would refer to a lipid specialist; 14% as their 1st choice, 22% as their 2nd choice and 27% as their last choice. 37% do not have access to a lipid specialist. Most respondents would start lipid lowering medications in a patient with HoFH after the age of 18. Only 24% would treat males and 20% female HoFH patients at a younger age.

Conclusions: Many primary care providers do not adequately treat HoFH and do not have access to a lipid specialist. There is a need to provide more education to primary care providers and to ensure them greater access to lipid specialists.

Virtual Patient Simulation Improves Clinical Decision-Making in Dyslipidemia: Success of Online CME

Jelena Spyropoulos, PhD, Piyali Shin, (New York, NY)

Lead Author’s Financial Disclosures: None.

Study Funding: The funding for the educational activity was provided by an independent educational grant from Sanofi US and Regeneron Pharmaceuticals and Amgen.

Background/Synopsis: Patients with dyslipidemia are at high risk for cardiovascular (CV) events. However, many patients are not optimally managed, leaving them vulnerable to CV events.

Objective/Purpose: This study was conducted to determine if an online continuing medical education (CME) intervention could improve the performance of cardiologists and primary care physicians (PCPs) in managing patients with dyslipidemia.

Methods: The CME intervention comprised two cases presented in a virtual patient simulation (VPS) platform that allows learners to order lab tests, make diagnoses, and prescribe treatments in a manner matching the scope and depth of actual practice. Learners’ clinical decisions were analyzed using a sophisticated decision engine. Tailored clinical guidance (CG), based on current evidence and expert recommendation, was provided following each decision and learners were then given the opportunity to modify their decisions. Decisions were collected post-CG and compared with each user’s baseline (pre-CG) decisions using a 2-tailed paired t-test to determine P values.

Results: Significant absolute improvements were observed after clinical guidance:

Case 1 (n=248 cardiologists; n=596 PCPs):
- Diagnose dyslipidemia: 27% improvement among cardiologists (16% pre-CG vs 42% post-CG; P<.001) and 29% improvement among PCPs (16% pre-CG vs 45% post-CG; P<.001)
- Order eGFR testing: 10% improvement among cardiologists (41% pre-CG vs 51% post-CG; P=.01) and 11% improvement among PCPs (35% pre-CG vs 46% post-CG; P<.001)
- Appropriately order ezetimibe: 17% improvement among cardiologists (16% pre-CG vs 33% post-CG; P=.01) and 21% improvement among PCPs (9% pre-CG vs 30% post-CG; P<.001)

Case 2 (n=141 cardiologists; n=509 PCPs):
- Diagnose CAD: 33% improvement among cardiologists (3% pre-CG vs 39% post-CG; P=.004) and 48% improvement among PCPs (9% pre-CG vs 57% post-CG; P<.001)
- Order patient education and counseling: 14% improvement among cardiologists (42% pre-CG vs 56% post-CG; P=.004)
Methods: Total of 8 randomized trials having ≥ 200 patients with at least ≥ 1-year follow-up period were selected using PubMed, Medline, EMBASE, and the CENTRAL (Inception-30 November 2018) evaluating n-3 FAs supplementation in patients with IHD (excluded trials with fish advice alone). The primary outcome was major adverse cardiovascular events (MACE) (composite of myocardial infarction (MI), stroke, CV mortality and coronary revascularization (CR)). The secondary outcomes were components of the MACE and all-cause mortality. The outcomes were estimated as relative risk (RR) with 95% confidence interval (CI) using a random effects model.

Results: In analysis of 23,383 patients with IHD (mean age of 57 ± 7 years and mean follow-up of 31 ± 17 months), use of n-3 FAs did not result in significant reduction of MACE (RR: 0.93; 95% CI, 0.84-1.04; P = 0.22) as compared to the control group (Figure 1). In contrast, n-3 FAs significantly lowered CV mortality (RR: 0.79; 95% CI, 0.65-0.96; P = 0.02) in patients with IHD. There was no significant reduction in terms of MI (RR: 0.87; 95% CI, 0.67-1.12; P = 0.27), all-cause mortality (RR: 0.97; 95% CI, 0.80-1.18; P = 0.75), stroke (RR: 0.72; 95% CI, 0.10-4.95; P = 0.74), and CR (RR: 0.99; 95% CI, 0.92-1.06; P = 0.69) with the n-3 FA use.

Conclusions: Use of n-3 FAs led to improved CV mortality in patients with IHD, however, it failed to reduce the overall MACE.

Pathophysiology of Atherosclerosis

Effects of Marine Omega-3 Fatty Acids on Cardiovascular Outcomes in Patients with Ischemic Heart Disease: A Meta-Analysis*

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Previous meta-analyses had not addressed the impact of marine omega-3 fatty acids (n-3 FAs) specifically in the ischemic heart disease (IHD) patients. The role of n-3 FAs in the IHD population remains uncertain.

Objective/Purpose: To investigate the effects of n-3 FAs on cardiovascular (CV) outcomes in the IHD patients.

Methods: Total of 8 randomized trials having ≥ 200 patients with at least ≥ 1-year follow-up period were selected using PubMed, Medline, EMBASE, and the CENTRAL (Inception-30 November 2018) evaluating n-3 FAs supplementation in patients with IHD (excluded trials with fish advice alone). The primary outcome was major adverse cardiovascular events (MACE) (composite of myocardial infarction (MI), stroke, CV mortality and coronary revascularization (CR)). The secondary outcomes were components of the MACE and all-cause mortality. The outcomes were estimated as relative risk (RR) with 95% confidence interval (CI) using a random effects model.

Results: In analysis of 23,383 patients with IHD (mean age of 57 ± 7 years and mean follow-up of 31 ± 17 months), use of n-3 FAs did not result in significant reduction of MACE (RR: 0.93; 95% CI, 0.84-1.04; P = 0.22) as compared to the control group (Figure 1). In contrast, n-3 FAs significantly lowered CV mortality (RR: 0.79; 95% CI, 0.65-0.96; P = 0.02) in patients with IHD. There was no significant reduction in terms of MI (RR: 0.87; 95% CI, 0.67-1.12; P = 0.27), all-cause mortality (RR: 0.97; 95% CI, 0.80-1.18; P = 0.75), stroke (RR: 0.72; 95% CI, 0.10-4.95; P = 0.74), and CR (RR: 0.99; 95% CI, 0.92-1.06; P = 0.69) with the n-3 FA use.

Conclusions: Use of n-3 FAs led to improved CV mortality in patients with IHD, however, it failed to reduce the overall MACE.

Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Elevated lipid levels are associated with cardiovascular diseases such as atherosclerosis and myocardial infarction.

Objective/Purpose: We explore the effect of intensive lifestyle interventions on lipids.

Methods: The intervention took place in Weimar CA. Retrospective data from 11 years of patients that finished the intervention was used. The 18-day medical holistic intervention administered during the program changed patient lifestyle habits in the areas of sleep, physical activity, plant-based diet, hydration, sun exposure, self-control, addictions, respiration, mental health, spirituality and relationships among others applied by health
professionals including board certified physicians. An education component was included to train the patients to continue with the change long term.

A retrospective paired-samples t-test was conducted to compare serum glucose, total cholesterol, HDL, and LDL levels before and after the residential intervention program.

All values are reported as mg/dl.

**Results**: Baseline total cholesterol dropped from group mean 213.3 (SD: 45.77) to 187.0 (SD: 37.79) mg/dL; t(396) = 18.4 p<0.001; Serum fasting glucose dropped from mean 104.9 (SD: 35.53) to 99.21 (SD: 29.76) mg/dL; t(396) = 3.5 p<0.001. Serum HDL cholesterol changed from 49.53 (SD: 15.67) to 47.56 (SD: 13.96) mg/dL; t (396) = 5.1 p<0.001.

Serum LDL cholesterol decreased from mean 128.3 (SD: 15.67) to 47.56 (SD: 13.96) mg/dL; t(396) = 3.5 p<0.001. Serum HDL cholesterol changed from 49.53 (SD: 15.67) to 47.56 (SD: 13.96) mg/dL; t (396) = 5.1 p<0.001.

Chol/HDL ratio was reduced from an average of 4.751 (SD: 40.03) to 107.3 (SD: 31.32) mg/dL; t (396) = 17.2 p<0.001.

**Conclusions**: The intervention was effective reflected in the results of the 5 categories measured. The biggest t-values were found in total serum cholesterol levels (t = 18.411) and LDL levels (t = 17.260). Long term study is planning to see if the changes continue.

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Final Report of the OSLER-1 Study: Long-Term Evolocumab for the Treatment of Hypercholesterolemia

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**Lead Author’s Financial Disclosures**: employment (significant): Jacksonville Center for Clinical Research, a company that has received research funds and consulting fees from Amgen, Pfizer, Regeneron, Sanofi, and The Medicines Company.

**Study Funding**: Amgen.

**Background/Synopsis**: Evolocumab and other monoclonal antibodies against PCSK9 reduced major adverse CV outcomes in clinical trials of patients with CV disease treated up to a median of 2.8 years.

**Objective/Purpose**: OSLER-1 evaluated long-term evolocumab treatment in a diverse population of hypercholesterolemic patients now exposed for up to 5 years (year 1 standard of care [SOC] controlled, years 2-5 open label).

**Methods**: OSLER-1 enrolled patients who completed 1 of 5 double-blind, controlled studies of evolocumab, and randomized patients 2:1 to open-label evolocumab 420 mg monthly + SOC; n=882) versus SOC alone (n=442) for 1 year followed by extended, monthly evolocumab + SOC for all. Here we report lipid effects and safety of evolocumab, including anti-drug antibodies (ADA), over the 5-year study. Updated final efficacy and safety data, including neurocognitive and muscle events, and new-onset diabetes, await final patient visits (June 2018) and will be available for presentation at AHA.

**Results**: Of 1324 patients randomized to enter the OSLER-1 SOC-controlled period for 1 year, 1255 (mean age 57 years; 53% female) continued into the evolocumab + SOC period starting at year 2. Evolocumab reduced median LDL-C at years 1, 2, 3, 4, and 5 by 61% (N=818), 59% (N=1122), 59% (n=1059), 59% (n=1012), and 58% (n=870), respectively.

Adverse events (AE) were reported in 79%, 74%, 71%, 67%, and 65% of patients and serious AEs were reported in 7%, 7%, 8%, 7%, and 7% of patients each year (years 1 through 5). AEs leading to drug discontinuation occurred in 2.8%, 0.8%, 1.3%, 1.0% and 0.2% of patients each year (years 1-5). Two SOC and 2 evolocumab patients transiently tested positive for binding ADAs in Year 1, with no subsequent or new binding or neutralizing ADAs detected to date.

**Conclusions**: In OSLER-1, the longest duration study of a PCSK9 inhibitor to date, evolocumab consistently reduced LDL-C with no increase in AEs over time and no neutralizing antibodies.

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**Alirocumab Reduces Total Nonfatal Cardiovascular and Fatal Events in the ODYSSEY OUTCOMES Trial**

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Chern Eng Chiang, MD, PhD, Rafael Diaz, MD,
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Kenneth Mahaffey, MD, Angele Moryusef, MD,
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**Lead Author’s Financial Disclosures**: Employment, Regeneron Pharmaceuticals, Inc; Ownership interest: Regeneron Pharmaceuticals, Inc.

**Study Funding**: Sanofi & Regeneron Pharmaceuticals, Inc.

**Background/Synopsis**: In ODYSSEY OUTCOMES, first occurrence of coronary heart disease (CHD) death, myocardial infarction (MI), fatal/nonfatal ischemic stroke, or hospitalization for unstable angina (UA) was reduced from 1052 for placebo to 903 for alirocumab (hazard ratio [HR] 0.85; p=0.0003). However, this does not reflect the
Table 1:

<table>
<thead>
<tr>
<th>Death and total nonfatal CV events (n=5425)</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alirocumab : placebo HR for nonfatal events (n=2186 vs. n=2513)</td>
<td>0.87 (0.82−0.93)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alirocumab : placebo HR for fatal events (n=334 vs. n=392)</td>
<td>0.83 (0.71−0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Association between nonfatal and fatal events 2.04 (1.78−2.79)</td>
<td>–</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Frailty variance 0.94 (95% CI 0.80−0.97)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Death and total nonfatal CV events restricted to MI, stroke, or UA (n=2999)</td>
<td>0.84 (0.77−0.91)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alirocumab : placebo HR for nonfatal events (n=1034 vs. n=1239)</td>
<td>0.82 (0.68−0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>Alirocumab : placebo HR for fatal events (n=334 vs. n=392)</td>
<td>–</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Association between nonfatal and fatal events 3.29 (2.86−3.72)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Frailty variance 0.87 (95% CI 0.84−0.91)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Analysis of first event: death or nonfatal CV event (n=3064)</td>
<td>0.88 (0.82−0.94)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Alirocumab : placebo HR for first event (n=1437 vs. 1627)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

CI, confidence interval; CV, cardiovascular; HR, hazard ratio; UA, unstable angina.

full impact of treatment, as many patients had multiple events and non-CHD death and other nonfatal cardiovascular (CV) events were excluded.

Objective/Purpose: Here we describe effects of alirocumab on total (first and subsequent) nonfatal CV events and all-cause death by a model that accounts for the relationship between nonfatal and fatal events.

Methods: Patients with acute coronary syndrome (ACS) and LDL cholesterol ≥70 mg/dL, non-HDL cholesterol ≥100 mg/dL, or apolipoprotein B ≥80 mg/dL on maximum tolerated dose of atorvastatin or rosuvastatin were randomized 1:1 to treatment with alirocumab or placebo. The present analysis included all-cause death and total nonfatal CV events (MI, stroke, hospitalization for UA or heart failure, or ischemia-driven coronary revascularization). A sensitivity analysis restricted nonfatal events to MI, stroke, or UA. Total nonfatal and fatal event hazard functions were jointly estimated, linked by a shared frailty accounting for patient risk heterogeneity and correlated within-patient nonfatal events. The model also determines if nonfatal events are associated with an increased risk for death. Treatment effects were summarized by HRs and compared against the customary analysis of first nonfatal CV event or death.

Results: There were 5425 total deaths or nonfatal CV events, 77% greater than first events (3064). Alirocumab produced similar relative reductions in first and total events when compared with placebo. Importantly, there were 385 fewer total events with alirocumab versus 190 fewer first events. Nonfatal CV events were associated with a higher risk of death, and the frailty variance indicated substantial inter-patient heterogeneity in risk.

Conclusions: In patients with ACS, the total number of deaths and nonfatal CV events prevented with alirocumab was twice the number of first events prevented. Total event reduction may be a useful metric to gauge the efficacy of alirocumab after ACS.

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Efficacy and Safety of Triplet Therapy With Bempedoic Acid, Ezetimibe, and Atorvastatin in Patients with Hypercholesterolemia

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Lead Author’s Financial Disclosures: Esperion employee.

Study Funding: This clinical trial was funded by Esperion Therapeutics Inc.

Background/Synopsis: Patients with hypercholesterolemia often fail to achieve sufficient cholesterol reduction, despite the use of guideline-recommended lipid-lowering therapies at maximally tolerated doses. Bempedoic acid, an oral, first-in-class ATP-citrate lyase inhibitor, reduces low-density lipoprotein cholesterol (LDL-C) when administered alone or in combination with statins or ezetimibe.

Objective/Purpose: To evaluate the extent of LDL-C lowering achieved during triplet therapy with bempedoic acid, ezetimibe, and atorvastatin.

Methods: This phase 2, randomized, double-blind, placebo-controlled study enrolled adults with fasting LDL-C of 130 to 189 mg/dL following washout of lipid-lowering drugs and nutritional supplements. After completing a 6-week screening/washout period, eligible patients were randomized 2:1 to treatment with triplet therapy (bempedoic acid 180 mg, ezetimibe 10 mg, and atorvastatin 20 mg) or placebo once daily for 6 weeks. The primary endpoint was the percent change from baseline in LDL-C at week 6.

Results: Sixty-three patients were enrolled at 14 sites in the United States: 43 patients were randomized to triplet therapy and 20 patients to placebo. Mean baseline LDL-C concentrations were 154 and 156 mg/dL in patients receiving triplet therapy and placebo, respectively. At week 6, triplet therapy lowered LDL-C by 63.6% compared
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with a 3.1% lowering in the placebo group. LDL-C lowering with triple therapy was significantly greater than placebo (difference, -60.5% [95% confidence interval: -68.0% to -53.0%]; p<0.001). Significant reductions with triple therapy vs placebo (p<0.001 for all comparisons) were observed for non-high-density lipoprotein cholesterol (-60.0% vs -1.3%), total cholesterol (-47.1% vs -1.1%), apolipoprotein B (-53.5% vs 0.6%), high-sensitivity C-reactive protein (median, -47.7% vs -2.7%), and triglycerides (-27.4% vs 8.9%). No appreciable treatment effect on high-density lipoprotein cholesterol was observed. In the triple therapy group, 90.2% of patients achieved an LDL-C <70 mg/dL and 95.1% of patients had a reduction in LDL-C of >50% at week 6. No patients in the placebo group met either treatment goal. The majority of treatment-emergent adverse events were mild to moderate in severity; adverse event rates were comparable in the 2 treatment groups. No patients experienced clinically relevant aminotransferase or creatine kinase elevations.

Conclusions: Oral, once-daily, combination therapy with bempedoic acid 180 mg, ezetimibe 10 mg, and atorvastatin 20 mg lowered LDL-C by 64% and was well tolerated, with an adverse event profile similar to that of the placebo group. Most patients (>90%) who received triple therapy experienced >50% LDL-C lowering from baseline and achieved LDL-C <70 mg/dL.

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Lipid Lowering With Bempedoic Acid Added to Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor Therapy: A Randomized Controlled Trial

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Lead Author’s Financial Disclosures: None.

Study Funding: This clinical trial was funded by Esperion Therapeutics Inc.

Background/Synopsis: Combination therapy is often required to reach optimal lipid levels in patients with elevated low-density lipoprotein cholesterol (LDL-C) despite lipid-lowering monotherapy. Bempedoic acid, an oral, once daily, first-in-class inhibitor of ATP-citrate lyase, has been shown to provide additional LDL-C lowering when added to background treatment with a statin or ezetimibe.

Objective/Purpose: To assess the efficacy and safety of bempedoic acid added to stable proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor background therapy in patients with elevated LDL-C.

Methods: This phase 2, randomized, double-blind, placebo-controlled study consisted of 3 phases: a 1.5-month screening/washout period during which all lipid-modifying drugs and nutritional supplements were discontinued if applicable, a 3-month lipid stabilization period wherein patients initiated background therapy with subcutaneous evolocumab 420 mg/3.5 mL administered via the Pushtronex(R) system once monthly, and a 2-month double-blind treatment period. Patients were required to have LDL-C ≥160 mg/dL prior to initiating evolocumab and LDL-C ≥70 mg/dL prior to randomization. Eligible patients were randomized 1:1 to treatment with bempedoic acid 180 mg or placebo once daily added to background evolocumab for 2 months. The primary endpoint was the percent change from baseline in LDL-C at month 2.

Results: A total of 59 patients were randomized: 28 to bempedoic acid and 31 to placebo. Mean LDL-C at the end of the evolocumab-only lipid stabilization period was 103 mg/dL, and was similar in patients randomized to bempedoic acid or placebo. Two-month treatment with bempedoic acid lowered LDL-C by 27.5%, whereas LDL-C in the placebo group increased by 2.8% (placebo-corrected difference, -30.3%; p<0.001). With reference to the secondary endpoints, reduction in LDL-C of a similar magnitude was observed at month 1 of the treatment period. Patients in the bempedoic acid treatment group also experienced significant reductions compared with placebo in apolipoprotein B (-27.8% vs 2.7%; p<0.001), non-high-density lipoprotein cholesterol (-23.0% vs 1.3%; p<0.001), total cholesterol (-17.0% vs 0.6%; p<0.001), and high-sensitivity C-reactive protein (-34.4% vs -1.6%; p=0.029). Changes in lipoprotein(a), high-density lipoprotein cholesterol, and triglycerides were similar between treatment groups. Rates of treatment-emergent adverse events were similar in the bempedoic acid and placebo treatment groups.

Conclusions: Bempedoic acid provided significant additional lipid lowering throughout a 2-month treatment period when added to background PCSK9 inhibitor therapy, with a safety profile similar to that of placebo.

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Real-world health care costs incurred by early adopters of PCSK9 inhibitor therapy*

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Lead Author’s Financial Disclosures: None.

Study Funding: The project described was supported by Award Number Grant UL1TR002733 from the National Center For Advancing Translational Sciences. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Advancing Translational Sciences or the National Institutes of Health.

Background/Synopsis: Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) reduce atherogenic

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low density lipoprotein cholesterol (LDL-C) by an additional 60% beyond standard lipid-lowering therapies and result in a significant decrease in atherosclerotic cardiovascular disease (ASCVD) events. However, the initial annual cost of PCSK9i therapy in the United States exceeded $14,000, which has raised cost-effectiveness concerns. Published data from simulated models have estimated annual cost-effective prices to be $4,500-$10,000 to achieve a conventional quality-adjusted life-year threshold. However, real-world health care costs incurred by PCSK9i-treated individuals are needed to provide more precise estimates of cost-effectiveness.

**Objective/Purpose:** The goal of this study was to define the real-world economic impact of PCSK9i among early adopters.

**Methods:** The Truven Health MarketScan Commerical Claims and Encounters Database was queried for individuals continuously enrolled in a commercial health insurance plan for 12 months prior to and 12 months after PCSK9i initiation in 2015 or 2016. Presence (ASCVD+) or absence (ASCVD-) of prior ASCVD events for each participant was determined: ASCVD+ was defined as any claim for unstable angina (ICD-10 code I20.xx), myocardial infarction (I21.xx), or stroke (I63.xx), in the 12 months preceding the PCSK9i initiation period. Claims for pharmaceutical, inpatient, and outpatient health care were compared among 3 groups of individuals: 1) ASCVD- with use of PCSK9i, 2) ASCVD+ with use of PCSK9i, and 3) a comparison group (n=1,000) of ASCVD+ individuals who did not initiate PCSK9i.

**Results:** A total of 1,944 early PCSK9i adopters met inclusion criteria (ASCVD+, n=973; ASCVD-, n=971). Initiation of PCSK9i was associated with an average increase of $10,733 in total pharmaceutical (lipid lowering drug and otherwise) costs (Fig. 1A). Outpatient and inpatient costs (Figs. 1B, 1C) increased modestly (11% and 29%, respectively) among ASCVD- who initiated PCSK9i and markedly (104% and 292%, respectively) among ASCVD+ who did not initiate PCSK9i. Outpatient and inpatient costs decreased (-10% and -42%, respectively; combined mean reduction = $6,744) among ASCVD+ who initiated PCSK9i.

**Conclusions:** Among early adopters of PCSK9i therapy, outpatient and inpatient costs decreased among ASCVD+ but not ASCVD- individuals. Outpatient and inpatient costs were much higher in ASCVD+ individuals who did not start PCSK9i. These real-world results suggest that individuals with prior ASCVD events may benefit from greater cost-effectiveness of PCSK9i. A recognized limitation is that the association between PCSK9i initiation and costs may be subject to confounding factors. Further study may elucidate the mechanism of this difference, such as fewer ASCVD testing or revascularization procedures among PCSK9i-treated individuals.

**345 Determinants of response and tolerability of PCSK9 inhibitor therapy**

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Lead Author’s Financial Disclosures: None.

Study Funding: Unrestricted educational grant from Amgen to Professor T.J. Reynolds and investigators for audits of lipid clinic prescribing.

Background/Synopsis: PCSK9 inhibitor therapy is recommended for patients with genetic hyperlipidemias, established cardiovascular disease and those unable to tolerate current routine lipid-lowering therapies. Studies suggest that some patients cannot tolerate PCSK9 therapy but the characteristics of these patients are unclear.

Objective/Purpose: This audit of PCSK9 prescribing in a university hospital and 2 district general hospitals investigated the factors related to efficacy and tolerability of PCSK9 inhibitor therapy.

Methods: Data on patients attending lipid clinic services and prescribed PCSK9 was obtained following all prescriptions for this therapy followed up for up to 1 year. Other data gathered included demographics, co-morbidities, other drug therapies, pre- and post-treatment lipids, liver alanine transaminase function (ALT), creatine kinase (CK) and glycated haemoglobin (HbA1c). Concomitant drug therapies were classified by principal indication e.g. anti-thrombotic, anti-hypertensive, anti-depressant, analgesic, immunosuppressant, thyroid hormone or vitamin D supplementation. Data were analysed by multiple linear and logistic regression.

Results: Data was available for 132 patients, average age 61 (SD13) years, 54% male, 70% with familial hypercholesterolaemia, 71% intolerant to 2+statins, 40% with coronary heart disease and 16% with contra-indications to statin therapy. Diabetes was present in 12% and current smoking in 9%. Any statin therapy had been introduced in 47% and ezetimibe in 46% by time of PCSK9 prescription. Anti-depressants were prescribed in 5%, diabetes drugs in 13%, analgesics in 16% and vitamin D in 7%. Baseline lipid values were cholesterol 303mg/dl; triglycerides 212mg/dL; HDL-C 60mg/dl, LDL-C 206mg/dL and Lp(a) 212mg/dL; HDL-C 60mg/dl, LDL-C 206mg/dL and Lp(a) 117mg/dl (44% reduction; P<0.001) and Lp(a) 113nmol/L (39% reduction; p=0.003) and HbA1c 42(13)mmol/mol. Concomitant drug therapies were classified by principal indication e.g. anti-thrombotic, anti-hypertensive, anti-depressant, analgesic, immunosuppressant, thyroid hormone or vitamin D supplementation. Data were analysed by multiple linear and logistic regression.

Among patients discontinuing PCSK9 therapy only the presence of concomitant analgesics (including for neuralgic and chronic pain) predicted outcome (β=2.23; p=0.01).

Conclusions: PCSK9 inhibitors in clinical practice show efficacy in line with clinical trial data and independent of baseline characteristics and indications. Discontinuation was seen in 11% of patients similar to that found in trials in statin-intolerant patients. The only predictor of likely discontinuation was the prescription of analgesia for neuralgic or chronic pain.

### Distribution of Apolipoprotein(a)-Containing Species in Human Plasma Assessed by Fast Protein Liquid Chromatography

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Lead Author’s Financial Disclosures: Research contract with Ionis.

Study Funding: Canadian Institutes for Health Research, natural Sciences and Engineering Research Council of Canada.

Background/Synopsis: Lipoprotein(a) (Lp(a)) consists of apolipoprotein(a) (apo(a)) covalently linked to lipoproteinB100 (apoB100) in a lipoprotein particle with similar lipid composition to LDL. Fundamental questions regarding the biogenesis and metabolism of Lp(a) remain unresolved, particularly the site of Lp(a) assembly and the nature of the apoB100-containing species involved.

Objective/Purpose: We aim to address reports of small amounts of apo(a) in plasma, kinetic data suggesting dissociation of apo(a) from Lp(a) with possible reassociation with triglyceride-rich lipoproteins (TRLs), and the appearance of Lp(a) in TRL-containing fractions in hypertriglyceridemic subjects.

Methods: We subjected fasting plasma from two individuals with high or low Lp(a) levels to fast protein liquid chromatography (FPLC) over a Superose 6 column to separate lipoprotein classes by size under native conditions.

Results: We found, using an apo(a)-specific ELISA, that Lp(a) eluted in a broad peak, centered approximately on the LDL-containing peak but also extending into the VLDL-size range; the latter characteristic was particularly evident for the subject with high Lp(a) levels. No apo(a) was detectable in later fractions where free apo(a) would be expected to elute. Addition of ε-aminocaproic acid (ε-ACA, a lysine analog) had no impact on the elution profile of apo(a), indicating a lack of non-covalent apo(a) complexes with apoB100-containing particles. We also supplemented the plasma with purified, recombinant 17-kringle apo(a) (17K). The majority of this material eluted in a pattern identical to Lp(a) itself, suggesting that the added apo(a) became associated with predominantly LDL-size particles. Western blot analysis of column fractions revealed that at least some of the added apo(a) was non-covalently associated with these particles. Interestingly, we achieved the same results as for 17K when we used an apo(a) variant lacking the strong lysine-binding sites in kringle K IV types 7 and 8 (17KALBS7,8), indicating that these interactions do not depend on these lysine binding sites, which are otherwise key for Lp(a) assembly. A small peak of apo(a) in fractions spanning a size range smaller than HDL was detected by ELISA, although this material was not observable on western blots. As before, addition of ε-ACA did not...
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Effects (Critical Role) of Nitrile and Nitrate determinants in Saliva and Plasma Correlating Cardio Metabolic factors

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Lead Author’s Financial Disclosures: None.

Study Funding: None.

Background/Synopsis: Endothelial nitric oxide (NO) bioavailability is a diagnostic marker and has been a major topic of research, which has clinical implications for monitoring cardiovascular disease (CVD) and metabolic syndrome that includes obesity, hypertension, hyperlipidemia and impaired glucose tolerance.

Objective/ Purpose: We hypothesized to assess the efficacy of inorganic nitrate-containing tablets (NO3) to elevate NO bioavailability.

Methods: 62 individuals (22 men and 40 women; the mean age of 60.4+9.0 years) with mean baseline systolic and diastolic Blood pressure (BP)>120 and 80 mg Hg respectively who were randomized to receive daily an 314 mg NO3 or NO3-free (placebo) tablets in a randomized double-blinded study for 12 weeks, with an interim visit at 2 weeks(Table 2) Inorganic NO3 tablets (Berkeley Life Tablet) consisted of nitrate-rich beetroot extract, thiamine nitrate, and potassium nitrate in the presence of ascorbic acid, to facilitate NO formation.

Results: At 12 weeks, the bio conversion of NO3 to NO2 after receiving placebo tablets, as compared to 435.0+297.93 (p<0.001) among the 30 participants that received the inorganic NO3 supplement. As predicted, plasma nitrate levels increased significantly more in the NO3 supplement group vs the placebo group (Table 1). (Table 1)

Conclusions: Inorganic NO3 supplementation demonstrated significant increase in NO. Inorganic NO3 supplementation has the potential to be used to complement antihypertensive and hyperlipidemic therapies, including plant-based dietary approaches, for improvement in vascular function.

**Table 1** Significant correlation of plasma and salivary nitrate and nitrite/Salivary strip Test (Berkeley Test Strip) _adjusted Values in active and placebo groups:

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>2 hours</th>
<th>P-value*</th>
<th>2 weeks</th>
<th>P-value*</th>
<th>12 weeks</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Plasma Nitrate</td>
<td>49.16±27.22</td>
<td>37.61±95.16</td>
<td>0.47</td>
<td>42.26±99.28</td>
<td>0.65</td>
<td>41.60±68.88</td>
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<tr>
<td></td>
<td>Plasma Nitrite</td>
<td>0.11±0.13</td>
<td>0.09±0.12</td>
<td>&lt;0.0001</td>
<td>0.12±0.22</td>
<td>&lt;0.0001</td>
<td>0.05±0.13</td>
</tr>
<tr>
<td>Salivary Nitrate</td>
<td>31.3455±275.3043</td>
<td>122.744±960.13</td>
<td>0.13</td>
<td>146.56±466.92</td>
<td>0.06</td>
<td>68.70±1503.39</td>
<td>0.881</td>
</tr>
<tr>
<td>Salivary Nitrite</td>
<td>150±277.98</td>
<td>119.43±651.37</td>
<td>0.744</td>
<td>160.59±841.32</td>
<td>0.30</td>
<td>143.39±362.90</td>
<td>0.865</td>
</tr>
<tr>
<td>Salivary Strip</td>
<td>20.00±64.51</td>
<td>110.00±131.24</td>
<td>&lt;0.0001</td>
<td>110.00±245.48</td>
<td>0.0006</td>
<td>110.00±161.28</td>
<td>0.0001</td>
</tr>
<tr>
<td>Active</td>
<td>Plasma Nitrate</td>
<td>39.75±26.52</td>
<td>167.67±107.27</td>
<td>0.016</td>
<td>232.54±139.11</td>
<td>0.00</td>
<td>190.06±170.37</td>
</tr>
<tr>
<td></td>
<td>Plasma Nitrate</td>
<td>0.07±0.22</td>
<td>0.20±0.36</td>
<td>&lt;0.0001</td>
<td>0.14±0.26</td>
<td>&lt;0.0001</td>
<td>0.16±0.42</td>
</tr>
<tr>
<td>Salivary Nitrate</td>
<td>27.75±286.01</td>
<td>2,177.62±4,352.13</td>
<td>&lt;0.0001</td>
<td>1,878.47±6,218.14</td>
<td>&lt;0.0001</td>
<td>1,516.65±3,625.42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Salivary Nitrite</td>
<td>19.09±670.04</td>
<td>1,315.93±1,801.33</td>
<td>0.0001</td>
<td>913±2260.06</td>
<td>&lt;0.001</td>
<td>970.24±1452.94</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Salivary Strip</td>
<td>20.00±53.36</td>
<td>435.00±332.24</td>
<td>&lt;0.0001</td>
<td>435.00±335.17</td>
<td>&lt;0.0001</td>
<td>435.00±297.93</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*data present by median ± SD and P-value comes from Wilcoxon Signed Rank test