

# Low LDL and HDL Correlated with Increased Likelihood of Myocardial Infarction and Coronary Artery Disease

Team A: Kersten Bartelt, RN; Alex Piff

Team B: Sam Butler, MD; Eric Barkley

Last updated 08 August 2024 • Check for updates at [EpicResearch.org](https://EpicResearch.org)

## Key Findings:

- Patients with an average LDL below 90 mg/dL have an increased likelihood of being diagnosed with a myocardial infarction (MI) compared to those with an average LDL of 100-109 mg/dL.
- Patients prescribed statins whose average LDL is below 80 mg/dL have an increased likelihood of coronary artery disease (CAD), while those without a lipid-lowering medication prescribed have an increased risk when their LDL is below 100 mg/dL.
- All studied patients, regardless of statin use, have an increased likelihood of an MI or a CAD diagnosis when their average HDL is less than 50 mg/dL, compared to patients with a higher average HDL level.

High cholesterol levels are known to increase the risk of adverse cardiovascular outcomes,<sup>1</sup> but the relationship between adverse cardiovascular outcomes and low cholesterol levels has not been well studied. LDL and HDL measure components of a patient's cholesterol levels. This study explores the relationship between LDL and HDL levels and adverse cardiovascular outcomes.

We studied patients aged 18 and older with at least five years of cholesterol readings and calculated a weighted average of both their LDL and HDL levels. We analyzed the likelihood of myocardial infarction (MI) or coronary artery disease (CAD) diagnosis following the last cholesterol reading. We adjusted for patient age, sex, race, ethnicity, BMI, history of hypertension, history of diabetes, previous care, and Social Vulnerability Index quartile. We studied patients treated with statins separately from patients not prescribed lipid-lowering medications.

Among patients prescribed statins, those with an average LDL less than 80 mg/dL generally had an increased likelihood of experiencing an MI or CAD compared to those with an average LDL of 100 mg/dL, as seen in Figure 1. In alignment with previous studies,<sup>1</sup> an elevated LDL was correlated with an increased likelihood of MI or CAD diagnosis.

## Likelihood of MI and CAD by LDL Among Statin-Treated Patients

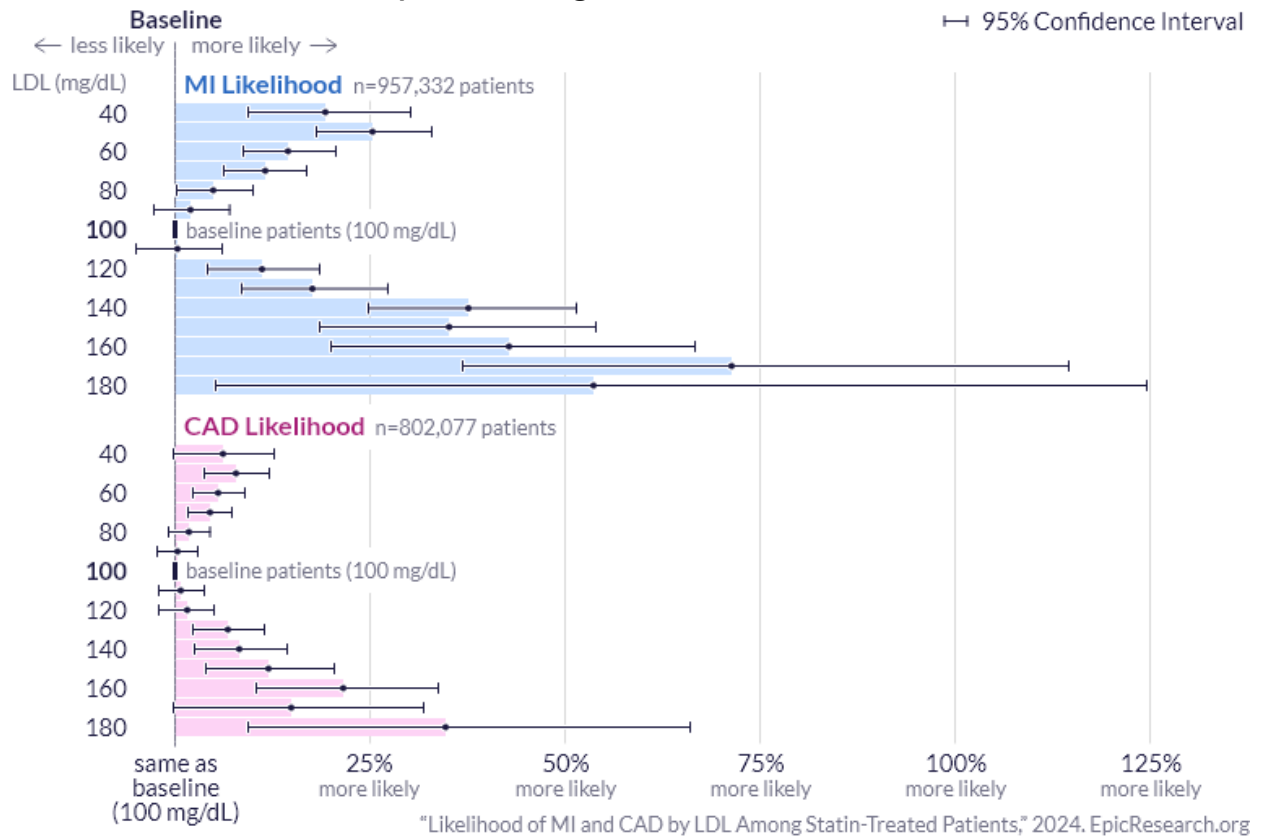
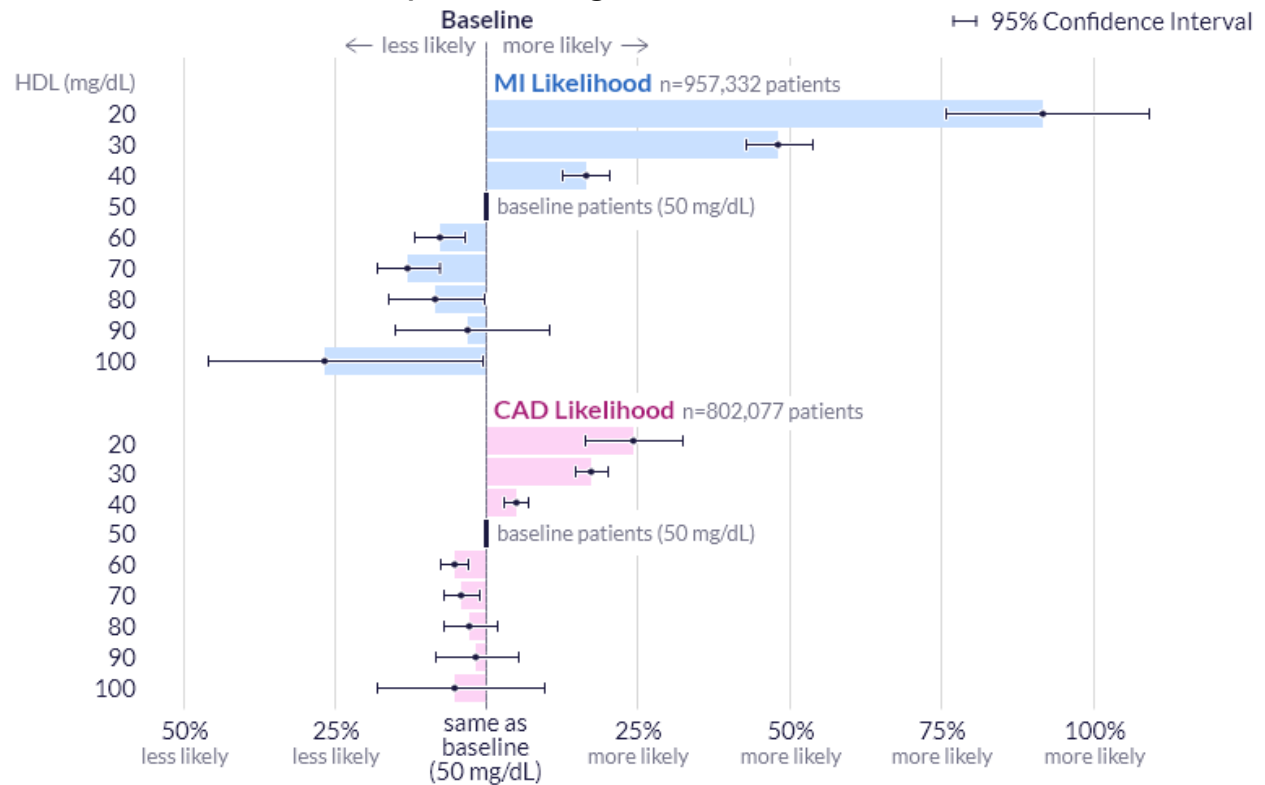


Figure 1. The likelihood of MI and CAD diagnosis by average LDL for patients prescribed a statin medication. The LDL values are grouped 30-39 mg/dL, 40-49 mg/dL, etc.

Next, we evaluated the likelihood of MI and CAD by average HDL level among patients prescribed statins. We found that an average HDL less than 50 mg/dL increased the likelihood of MI and CAD, as seen in Figure 2.

## Likelihood of MI and CAD by HDL Among Statin-Treated Patients



"Likelihood of MI and CAD by HDL Among Statin-Treated Patients," 2024. EpicResearch.org

Figure 2. The likelihood of MI and CAD diagnosis by average HDL for patients prescribed a statin medication. The HDL levels are grouped 20-29 mg/dL, 30-39 mg/dL, etc.

Patients with no lipid-lowering medication prescription generally had an increased likelihood of MI or CAD when their average LDL was less than 100 mg/dL compared to those with an average LDL of 100-109 mg/dL, as seen in Figure 3. Like the patients treated with statins, this population also had an increased likelihood of experiencing an MI or CAD with elevated LDL levels.

### Likelihood of MI and CAD by LDL Among Patients on No Lipid-Lowering Medications

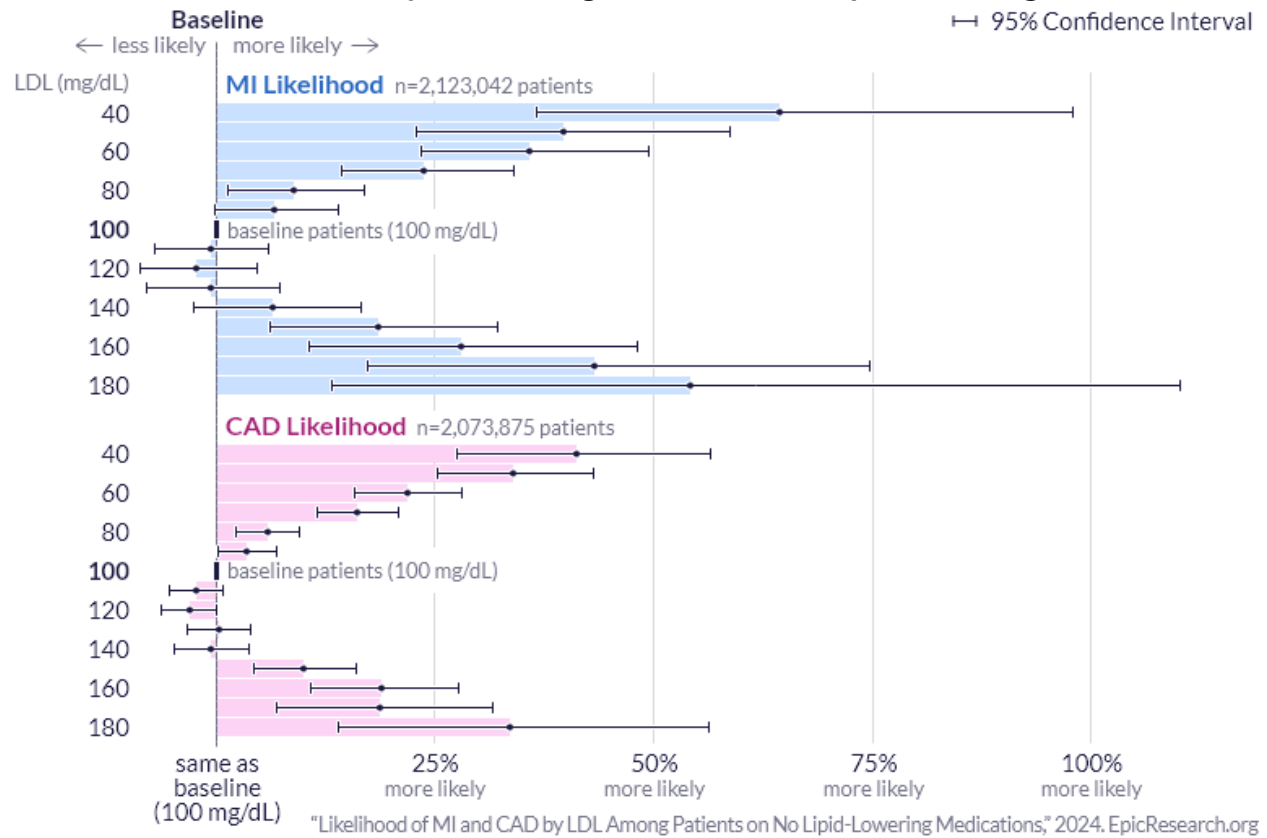
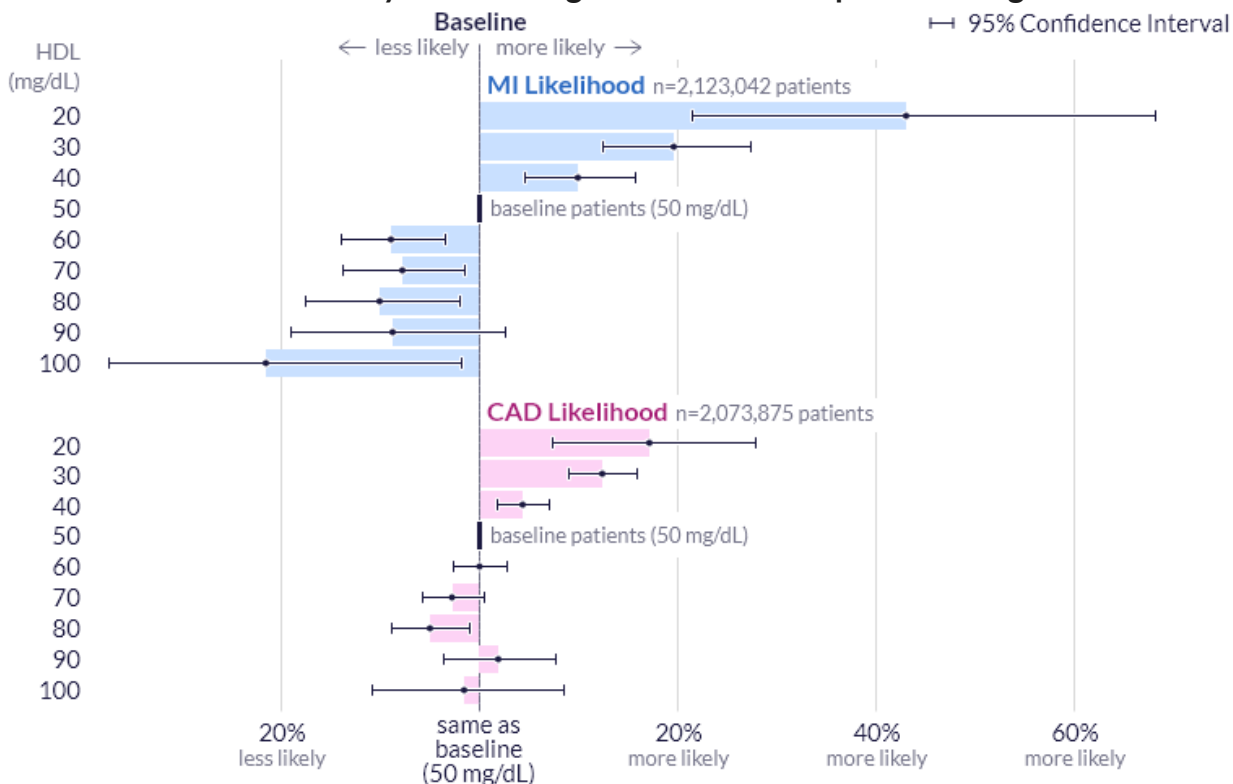


Figure 3. The likelihood of MI and CAD diagnosis by average LDL for patients without a lipid-lowering medication prescription. The LDL values are grouped 30-39 mg/dL, 40-49 mg/dL, etc.

Similar to patients prescribed statins, patients with no lipid-lowering medication and an average HDL less than 50 mg/dL had an increased likelihood of both CAD and MI, as seen in Figure 4.

## Likelihood of MI and CAD by HDL Among Patients on No Lipid-Lowering Medications



"Likelihood of MI and CAD by HDL Among Patients on No Lipid-Lowering Medications," 2024. EpicResearch.org

Figure 4. The likelihood of MI and CAD diagnosis by average HDL for patients without a lipid-lowering medication prescription. The HDL levels are grouped 20-29 mg/dL, 30-39 mg/dL, etc.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 256 million patient records from 1,500 hospitals and more than 34,100 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Aishwarya Shettigar and Brian Olson.

## References

1. Lower your LDL. www.heart.org. <https://www.heart.org/en/health-topics/cholesterol/hdl-good-ldl-bad-cholesterol-and-triglycerides/lower-your-ldl>. Accessed June 14, 2024.

## Data Definitions

Term	Definition
Study period	8/2/1999 – 4/2/2024
Study population	<p>Patients aged 18-89 with five years of <b>cholesterol readings</b> and at least one additional reading after that window.</p> <p>Analyzed patients in the two populations either had no documented <b>lipid-lowering medications</b> or were on <b>statin</b> medications and no other lipid-lowering medications throughout the five-year window.</p>

	<p>For patients given no lipid-lowering medications, we analyzed the five-year window after their initial cholesterol reading. For patients given statins, we analyzed the five-year window starting at their first cholesterol reading after the first documentation of the medication.</p> <p>Patients were excluded if they had a documented <b>lipid-lowering condition</b> prior to the end of the five-year window.</p>
<b>Cholesterol readings</b>	<p><b>Weighted average</b> cholesterol during the five-year window  HDL: LOINC code 2085-9 or 18263-4  LDL: LOINC code 13457-7, 18262-6, or 2089-1</p> <p>Lab values were required to be between 10 mg/dL and 1,000 mg/dL. The top and bottom 1% of labs by value per type were excluded.</p>
<b>Weighted average</b>	<p>Calculated based on time between readings.</p> <p>For example, if day 0 the LDL was 80 mg/dL and year two it was 90 mg/dL, the first two years would use a value of 80 while the next three years would use a value of 90. The formula would be <math>(80+80+90+90+90)/5</math>.</p>
<b>Lipid-lowering condition</b>	<p>Lipoprotein deficiency: ICD-10-CM code E78.6  Chylomicron retention disease: ICD-10-CM code E78.3  Malnutrition: ICD-10-CM code E4* or E64*  Malabsorption: ICD-10-CM code K90*  Hyperthyroidism: ICD-10-CM code E05*  Chronic hepatitis C: ICD-10-CM code B18.2  Blood cancer: ICD-10-CM code C81*, C85*, or C90*-C95*  Colon cancer: ICD-10-CM code C18*  Prostate cancer: ICD-10-CM code C61*  Crohn's disease: ICD-10-CM code K50*</p>
<b>Lipid-lowering medication</b>	<p>Statin medications: a pharmaceutical subclass of "Antihyperlipidemic - HMG CoA Reductase Inhibitors (statins)" or "Antihyperlipidemic - HMG CoA Reductase Inhibitor and Niacin Comb" or a generic name of rosuvastatin calcium, simvastatin, atorvastatin calcium, pravastatin sodium, niacin/lovastatin, lovastatin, or fluvastatin sodium.</p> <p>Other lipid lowering medications: a pharmaceutical subclass of "Antihyperlipidemic - Bile Acid Sequestrants," "Antihyperlipidemic - Fibric Acid Derivatives," "Antihyperlipidemic - Selective Cholesterol Absorption Inhibitor," "Antihyperlipidemic - PCSK9 Inhibitors," "Antihyperlipidemic - ATP-Citrate Lyase (ACLY) Inhibitor," or "Antihyperlipidemic - Omega-3 Fatty Acid Type" or a generic name of alirocumab, evolocumab, inclisiran sodium, bempedoic acid, icosapent ethyl, omega-3 acid ethyl esters, niacin, cholestyramine, cholestyramine (with sugar), cholestyramine/aspartame, or cholestyramine/saccharin sod</p>
<b>Exposures</b>	Weighted average of cholesterol readings over the five-year window
<b>Outcomes</b>	New onset of:

	<ul style="list-style-type: none"> <li>MI: ICD-10-CM code I21*</li> <li>CAD: ICD-10-CM code I24*-I25*</li> </ul>
<b>Confounders</b>	Age at end of window Sex Race and ethnicity Diabetes: ICD-10-CM code E10*-E11* Family history of CVD: ICD-10-CM code Z82.4* Hypertension: ICD-10-CM code I10* Smoking history as evidence by one of the following: <ul style="list-style-type: none"> <li>Smoking status of: <ul style="list-style-type: none"> <li>Current</li> <li>Current every day smoker</li> <li>Current some day smoker</li> <li>Every day</li> <li>Former</li> <li>Former smoker</li> <li>Heavy smoker</li> <li>Heavy tobacco smoker</li> <li>Light smoker</li> <li>Light tobacco smoker</li> <li>Some days</li> </ul> </li> <li>Documented packs per day &gt; 0</li> <li>Documented pack years &gt; 0</li> </ul>
<b>Model Specifications</b>	Cox PH for each population censoring at start/stop of meds, last encounter, onset of a <b>lipid-lowering condition</b> , or death

**Table 1: Likelihood of MI by LDL Among Statin-Treated Patients**

	LDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
MI	30	957,332	1.06	0.06	0.83	1.37
	40	957,332	1.19	0.19	1.09	1.30
	50	957,332	1.25	0.25	1.18	1.33
	60	957,332	1.15	0.15	1.09	1.21
	70	957,332	1.12	0.12	1.06	1.17
	80	957,332	1.05	0.05	1.00	1.10
	90	957,332	1.02	0.02	0.97	1.07
	<b>100</b>		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	110	957,332	1.00	0.00	0.95	1.06
	120	957,332	1.11	0.11	1.04	1.19
	130	957,332	1.18	0.18	1.09	1.27
	140	957,332	1.38	0.38	1.25	1.52
	150	957,332	1.35	0.35	1.18	1.54
	160	957,332	1.43	0.43	1.20	1.70
	170	957,332	1.72	0.72	1.37	2.15
180	957,332	1.54	0.54	1.05	2.25	

**Table 2: Likelihood of CAD by LDL Among Statin-Treated Patients**

	LDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
CAD	30	802,077	1.05	0.05	0.88	1.25
	40	802,077	1.06	0.06	1.00	1.13
	50	802,077	1.08	0.08	1.04	1.12
	60	802,077	1.06	0.06	1.02	1.09
	70	802,077	1.04	0.04	1.02	1.07
	80	802,077	1.02	0.02	0.99	1.04
	90	802,077	1.00	0.00	0.98	1.03
	<b>100</b>		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	110	802,077	1.01	0.01	0.98	1.04
	120	802,077	1.01	0.01	0.98	1.05
	130	802,077	1.07	0.07	1.02	1.12
	140	802,077	1.08	0.08	1.02	1.14
	150	802,077	1.12	0.12	1.04	1.20
	160	802,077	1.22	0.22	1.10	1.34
	170	802,077	1.15	0.15	1.00	1.32
180	802,077	1.35	0.35	1.09	1.66	

**Table 3: Likelihood of MI by HDL Among Statin-Treated Patients**

	HDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
MI	20	957,332	1.92	0.92	1.76	2.09
	30	957,332	1.48	0.48	1.43	1.54
	40	957,332	1.16	0.16	1.13	1.20
	<b>50</b>		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	60	957,332	0.92	-0.08	0.88	0.96
	70	957,332	0.87	-0.13	0.82	0.92
	80	957,332	0.91	-0.09	0.84	1.00
	90	957,332	0.97	-0.03	0.85	1.10
	100	957,332	0.73	-0.27	0.54	0.99

**Table 4: Likelihood of CAD by HDL Among Statin-Treated Patients**

	HDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
CAD	20	802,077	1.24	0.24	1.16	1.32
	30	802,077	1.17	0.17	1.15	1.20

	40	802,077	1.05	0.05	1.03	1.07
	<b>50</b>		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	60	802,077	0.95	-0.05	0.92	0.97
	70	802,077	0.96	-0.04	0.93	0.99
	80	802,077	0.97	-0.03	0.93	1.02
	90	802,077	0.98	-0.02	0.91	1.05
	100	802,077	0.95	-0.05	0.82	1.09

**Table 5: Likelihood of MI by LDL Among Patients on No Lipid-Lowering Medications**

	LDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
MI	30	2,123,042	0.78	-0.22	0.42	1.44
	40	2,123,042	1.64	0.64	1.37	1.98
	50	2,123,042	1.40	0.40	1.23	1.59
	60	2,123,042	1.36	0.36	1.23	1.49
	70	2,123,042	1.24	0.24	1.14	1.34
	80	2,123,042	1.09	0.09	1.01	1.17
	90	2,123,042	1.07	0.07	1.00	1.14
	<b>100</b>		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	110	2,123,042	0.99	-0.01	0.93	1.06
	120	2,123,042	0.98	-0.02	0.91	1.05
	130	2,123,042	0.99	-0.01	0.92	1.07
	140	2,123,042	1.06	0.06	0.97	1.16
	150	2,123,042	1.18	0.18	1.06	1.32
	160	2,123,042	1.28	0.28	1.11	1.48
	170	2,123,042	1.43	0.43	1.17	1.75
180	2,123,042	1.54	0.54	1.13	2.10	

**Table 6: Likelihood of CAD by LDL Among Patients on No Lipid-Lowering Medications**

	LDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
CAD	30	2,073,875	0.98	-0.02	0.73	1.30
	40	2,073,875	1.41	0.41	1.27	1.57
	50	2,073,875	1.34	0.34	1.25	1.43
	60	2,073,875	1.22	0.22	1.16	1.28
	70	2,073,875	1.16	0.16	1.12	1.21
	80	2,073,875	1.06	0.06	1.02	1.10
	90	2,073,875	1.03	0.03	1.00	1.07
	<b>100</b>		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	110	2,073,875	0.98	-0.02	0.95	1.01

	120	2,073,875	0.97	-0.03	0.94	1.00
	130	2,073,875	1.00	0.00	0.97	1.04
	140	2,073,875	0.99	-0.01	0.95	1.04
	150	2,073,875	1.10	0.10	1.04	1.16
	160	2,073,875	1.19	0.19	1.11	1.28
	170	2,073,875	1.19	0.19	1.07	1.32
	180	2,073,875	1.33	0.33	1.14	1.56

**Table 7: Likelihood of MI by HDL Among Patients on No Lipid-Lowering Medications**

	HDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
MI	20	2,123,042	1.43	0.43	1.22	1.68
	30	2,123,042	1.20	0.20	1.12	1.27
	40	2,123,042	1.10	0.10	1.05	1.16
	50		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	60	2,123,042	0.91	-0.09	0.86	0.97
	70	2,123,042	0.92	-0.08	0.86	0.99
	80	2,123,042	0.90	-0.10	0.83	0.98
	90	2,123,042	0.91	-0.09	0.81	1.03
	100	2,123,042	0.78	-0.22	0.63	0.98

**Table 8: Likelihood of CAD by HDL Among Patients on No Lipid-Lowering Medications**

	HDL Value	Patient N	Ratio	Ratio-1	Low CI	High CI
CAD	20	2,073,875	1.17	0.17	1.07	1.28
	30	2,073,875	1.12	0.12	1.09	1.16
	40	2,073,875	1.04	0.04	1.02	1.07
	50		<b>1.00</b>	<b>0.00</b>	<b>1.00</b>	<b>1.00</b>
	60	2,073,875	1.00	0.00	0.97	1.03
	70	2,073,875	0.97	-0.03	0.94	1.01
	80	2,073,875	0.95	-0.05	0.91	0.99
	90	2,073,875	1.02	0.02	0.96	1.08
	100	2,073,875	0.98	-0.02	0.89	1.08