Men Experience Greater LDL Reductions Than Women Across Multiple Lipid-Lowering Medications, with the Largest Gap for PCSK9 Inhibitors

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Key Findings:

- Across all lipid-lowering drug classes, men had a 4.5-percentage point greater reduction in LDL than women.
- By drug class, the male-female gap in LDL lowering was 7.3 percentage points for PCSK9 inhibitors, 5.8 percentage points for selective cholesterol absorption inhibitors, and 4.0 percentage points for statins.

Cholesterol-lowering medications are a common treatment for patients with hyperlipidemia (high cholesterol). Prior research into some of these treatments has shown sex-based differences in their effectiveness, with a smaller LDL response among women than men taking PCSK9 inhibitors.[1] Prior research has also found that LDL reductions reduce major cardiovascular events, supporting LDL as a valid surrogate for cardiovascular benefit.[2] Current U.S. guidelines recommend type of LDL-lowering therapy based on the percentage reduction required, determined by baseline LDL level and overall cardiovascular risk, regardless of sex.[3]

We studied more than 1 million patients aged 20 years and older who initiated a lipid-lowering medication between January 1, 2016, and August 1, 2025. We accounted for patient demographics, comorbidities, use of other lipid-lowering medications in the past or concurrently, BMI, smoking status, rurality, and social vulnerability. The dosage of the medications prescribed was not accounted for.

Across all cholesterol-lowering medications, men experienced larger LDL reductions than women after starting therapy, as seen in Figure 1. The difference was consistent across every drug class, suggesting a systematic sex-based disparity in response rather than an isolated effect of any single treatment. The gap was most pronounced for PCSK9 inhibitors, where men showed a 7.3-percentage point greater decrease in LDL, and remained notable for statins and cholesterol absorption inhibitors, both showing about a 4–6 percentage point larger decline in men. Even among classes less directly associated with LDL lowering (such as fibric acid derivatives, bile acid sequestrants, and omega-3 fatty acid agents) men continued to demonstrate modestly greater reductions. Only the combination of ACLY plus cholesterol absorption inhibitor showed no meaningful difference between sexes.

Disparity in LDL Reduction Between Sexes by Lipid-Lowering Medication

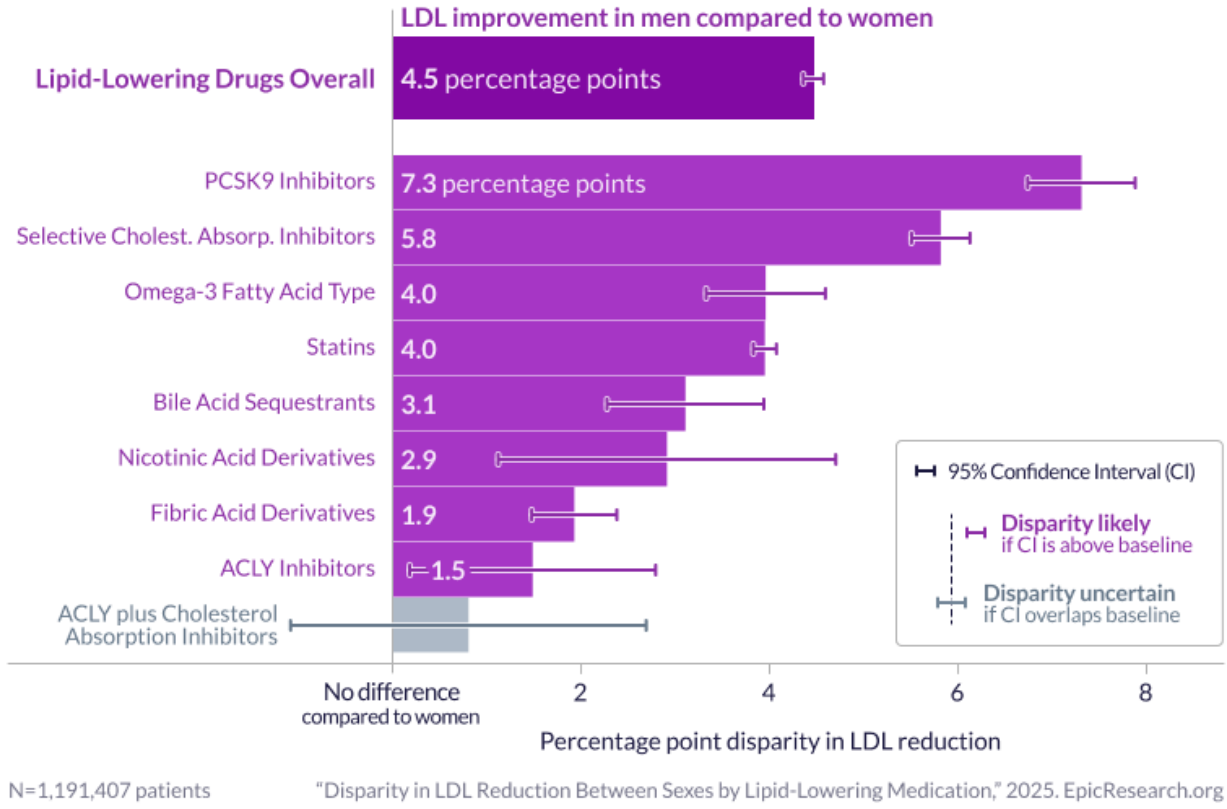

Figure 1. The difference in LDL change between the sexes by which lipid-lowering medication was prescribed.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 42,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. 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 Brian Olson.

References

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2. Silverman MG, Ference BA, Im K, et al. Association between lowering LDL-C and cardiovascular risk reduction among different therapeutic interventions: A systematic review and meta-analysis. JAMA. 2016;316(12):1289. doi:10.1001/jama.2016.13985
3. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: Executive summary: A report of the American college of cardiology/American heart association task force on clinical practice guidelines. Circulation. 2019;139(25). doi:10.1161/cir.0000000000000624

Data Definitions

Term	Definition
Study period	1/1/2016 to 8/1/2025
Study population: inclusion	Patients who: • Were at least 20 years old • Have a hyperlipidemia diagnosis: A billing, encounter, or problem list diagnosis with ICD-10-CM code E78.2, E78.3, E78.4, or E78.5 • Have been prescribed a **lipid-lowering medication** • Have at least one **LDL** lab result from six months prior to through the day of initiating their **exposure** medication that has a value >=100 mg/dl • Have at least one **LDL** reading between 60 and 120 days after initiating their **exposure** medication • Have an evaluated sex of male or female
Study population: exclusion	**Pregnancy** between a year prior to initiating the **exposure** medication through 120 days after initiating the **exposure** medication
Exposure	Type of **lipid-lowering medication**
LDL	A lab result mapped to LOINC code 13457-7, 2089-1, or 18262-6 Results greater than 300 or less than 50 were ignored
Outcomes	Percentage change in LDL was calculated using the formula: Percentage change in LDL = (Average LDL reading 60–120-day after treatment start - Most recent pre-treatment LDL) / Most recent pre-treatment LDL
Confounders	Diagnosis of familial hypercholesterolemia: A billing, encounter, or problem list diagnosis with ICD-10-CM code E78.01 Diabetes: A billing, encounter, or problem list diagnosis with ICD-10-CM code E08*-E13* Hypertension: A billing, encounter, or problem list diagnosis with ICD-10-CM code I10-I16*, I1A* CKD: A billing, encounter, or problem list diagnosis with ICD-10-CM code N18* CVD: A billing, encounter, or problem list diagnosis with ICD-10-CM code I20*-I26*, I30*-I39*, I40*-I49*, I51*, or I70*-I79* Other **lipid-lowering medications** in the six months prior to index Other **lipid-lowering medications** between index and 120 days after BMI classification Race and ethnicity History of smoking Age • 20-34 • 35-64 • 65-74 • 75+ RUCA Social Vulnerability Index quintile
Race and ethnicity	Patients were classified by self-reported race and ethnicity mapped to standards as Hispanic, multiracial, White, Black, Asian, other, or unknown

Lipid-lowering medication	Prescription of one of the following medications identified by pharmaceutical subclass: • ACLY inhibitors: Antihyperlipidemic - ATP-Citrate Lyase (ACLY) Inhibitor • Bile acid sequestrants: Antihyperlipidemic - Bile Acid Sequestrants • Fibric acid derivatives: Antihyperlipidemic - Fibric Acid Derivatives • Nicotinic acid derivatives: Antihyperlipidemic - Nicotinic Acid Derivatives • Omega-3 fatty acid type: Antihyperlipidemic - Omega-3 Fatty Acid Type • PCSK9 inhibitors: Antihyperlipidemic - PCSK9 Inhibitors • Selective cholesterol absorption inhibitors: Antihyperlipidemic - Selective Cholesterol Absorption Inhibitor • ACLY and cholesterol absorption inhibitors: Antihyperlipidemic-ATP-Citrate Lyase and Cholesterol Absorption Inhib • Statins: "Antihyperlipidemic – HMG CoA Reductase Inhibitors (statins)"; "Antihyperlipidemic HMG CoA Reduct Inhib and Calcium Channel Blocker"; "Antihyperlipidemic-HMG CoA Reductase Inhibitor-Aspirin,Buffered Comb."; or "Antihyperlipidemic-HMG CoA Reduct Inhib and Cholesterol Absorp Inhibit"
Model specifications	Linear Regression

Table 1. Disparity in LDL Reduction Between Sexes by Lipid-Lowering Medication

Row Title	Odds Ratio	Lower CI	Upper CI
Lipid-lowering Drugs Overall	-4.5%	-4.6%	-4.4%
PCSK9 Inhibitors	-7.3%	-7.9%	-6.7%
Selective Cholest. Absorp. Inhibitors	-5.8%	-6.1%	-5.5%
Omega-3 Fatty Acid Type	-4.0%	-4.6%	-3.3%
Statins	-4.0%	-4.1%	-3.8%
Bile Acid Sequestrants	-3.1%	-3.9%	-2.3%
Nicotinic Acid Derivatives	-2.9%	-4.7%	-1.1%
Fibric Acid Derivatives	-1.9%	-2.4%	-1.5%
ACLY Inhibitors	-1.5%	-2.8%	-0.2%
ACLY Plus Cholesterol Absorption Inhibitors	-0.8%	-2.7%	1.1%