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Non-Statin Lipid-Lowering Therapy Prescribing Trends Among US patients with Dyslipidemia: 2016-2026

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Abstract

Non-statin lipid-lowering therapy (LLT) remains underutilized despite expanding cardiovascular outcomes evidence and guideline recommendations. Using Epic Cosmos, a federated electronic health record network, we characterized non-statin LLT prescribing trends from 2016 to 2026 among patients diagnosed with dyslipidemia (ICD-10 E78.x). While the dyslipidemia population in Epic Cosmos expanded from 9.2 to 33.6 million patients over the decade, prescriptions of non-statin LLT grew nearly 13-fold, from 172,248 to 2,172,506 patients per quarter. Ezetimibe remained the dominant non-statin LLT, accounting for 77% of non-statin prescriptions in Q1 2026. PCSK9 inhibitor use reached 489,269 patients but represented only 1.5% of the dyslipidemia population. Despite overall growth, 15.8 million patients (47.0%) remained without any LLT in Q1 2026. Sustained implementation of the 2026 ACC/AHA Dyslipidemia Guidelines and continued real-world monitoring are essential to improve uptake.

Introduction

Cardiovascular disease remains the leading cause of morbidity and mortality in the United States, for which lowering of atherogenic lipoproteins such as low-density lipoprotein (LDL) is key.[2]. While statins form the cornerstone of lipid-lowering therapy (LLT), non-statin agents including ezetimibe, PCSK9 inhibitors, bempedoic acid, and icosapent ethyl have demonstrated benefit for cardiovascular outcomes and are recommended by contemporary dyslipidemia guidelines, particularly for individuals failing to reach their recommended lipid goals [2–8]. However, real-world prescribing patterns for these agents remain incompletely characterized. These agents differ substantially in mechanism, route of administration, magnitude of LDL-C reduction, cardiovascular outcomes evidence, and cost, making characterization of their individual prescribing trajectories clinically informative. Using Epic Cosmos, a federated electronic health record network encompassing more than 280 million US patients, we sought to characterize non-statin LLT prescribing trends from 2016 through 2026 among patients with diagnosed dyslipidemia, spanning the 2018 ACC/AHA Blood Cholesterol Guideline, the 2022 ACC Expert Consensus Decision Pathway, and the 2026 ACC/AHA Dyslipidemia Guideline.

Methods

We conducted a cross-sectional trend analysis using Epic Cosmos, a federated electronic health record network comprising over 300 million patients across > 1,600 U.S. health systems, encompassing academic medical centers, community hospitals, and outpatient practices. We identified all patients with an active ICD-10 diagnosis of dyslipidemia (E78.x). Included patients were required to have an active clinical encounter during the extraction window. Among these patients, we extracted active prescription counts of statins, ezetimibe, evolocumab, alirocumab, icosapent ethyl, bempedoic acid, and inclisiran quarterly from Q1 2016 through Q1 2026. Patients receiving combination therapy, including those prescribed a fixed-dose statin-ezetimibe combination, were counted within each respective drug class independently. Data was extracted and analyzed using Epic Cosmos aggregate query tools. Figures were generated in R 4.4.2. This analysis used deidentified aggregate data and did not require institutional review board approval.

Results

The population of patients with an active encounter and a diagnosis of dyslipidemia expanded from 9.2 million in Q1 2016 to 33.6 million in Q1 2026. Over this period, non-statin LLT prescribing grew nearly 13-fold, from 172,248 to 2,172,506 patients per quarter (Fig. 1, Panel B). Despite this substantial growth, 15.8 million patients (47.0%) with dyslipidemia remained without any LLT in Q1 2026, compared with 5.1 million (55.5%) in Q1 2016, representing an absolute increase of 10.7 million untreated patients over the decade, as population growth consistently outpaced prescribing expansion, and as definitions of dyslipidemia has changed over time, resulting in a large group of individuals being classified as having dyslipidemia. (Table 1; Fig. 1, Panel A).

Table 1

Non-statin Lipid-Lowering Therapy Prescribing Among US Dyslipidemia Patients, Q1 2016 and Q1 2026

Category / Agent	Q1 2016 Patients	Q1 2016% of Dyslipidemia	Q1 2026 Patients	Q1 2026% of Dyslipidemia	Q1 2026% of Non-Statin	Change Q1 2016 to Q1 2026
Section A. Overall Treatment Landscape						
Total Dyslipidemia Population	9,188,799	—	33,645,904	—	—	+ 24,457,105 (+ 266%)
Any Lipid-Lowering Therapy	4,088,509	44.5%	17,839,483	53.0%	—	+ 13,750,974
No Lipid-Lowering Therapy	5,100,290	55.5%	15,806,421	47.0%	—	+ 10,706,131
Statins (any)	4,032,948	43.9%	17,081,407	50.8%	—	+ 13,048,459
Section B. Individual Non-Statin Agent Prescribing						
Any Non-Statin LLT (deduplicated)	172,248	1.87%	2,172,506	6.46%	**100%**	**+ 2,000,258 (+ 1,161%; 12.6×)**
Ezetimibe	163,294	1.78%	1,668,653	4.96%	**76.8%**	+ 1,505,359 (+ 922%)
PCSK9 Inhibitors Combined	4,131	< 0.1%	489,269	1.45%	22.5%	+ 485,138 (+ 11,744%)
Evolocumab	2,062	< 0.1%	433,100	1.29%	19.9%	+ 431,038 (+ 20,904%)
Alirocumab	2,069	< 0.1%	56,169	0.17%	2.6%	+ 54,100 (+ 2,615%)
Icosapent Ethyl	6,663	< 0.1%	193,943	0.58%	8.9%	+ 187,280 (+ 2,811%)
Bempedoic Acid	0	—	62,992	0.19%	2.9%	New agent (FDA Feb 2020)
Inclisiran	0	—	14,682	0.04%	0.7%	New agent (FDA Dec 2021)

Category / Agent	Q1 2016 Patients	Q1 2016% of Dyslipidemia□	Q1 2026 Patients	Q1 2026% of Dyslipidemia□	Q1 2026% of Non-Statin□	Change Q1 2016 to Q1 2026
Section A. Overall Treatment Landscape						
Footnotes						
□ *Denominator: total patients with an active E78.x dyslipidemia diagnosis and at least one clinical encounter during each quarter in Epic Cosmos.*						
□ *Denominator: deduplicated Any Non-Statin LLT count in Q1 2026 (2,172,506 patients). Individual agent percentages may sum to more than 100% because patients on multiple non-statin agents appear once in the deduplicated total but in each relevant agent row.*						
□ *Any Non-Statin LLT: deduplicated count of patients with at least one active non-statin prescription per quarter.*						
□ *Ezetimibe includes patients prescribed the bempedoic acid/ezetimibe fixed-dose combination (28,379 patients in Q1 2026).*						
□ *Bempedoic Acid includes bempedoic acid monotherapy and bempedoic acid/ezetimibe fixed-dose combination (28,379 patients in Q1 2026).*						
□ *Agent not approved in Q1 2016. FDA approvals: bempedoic acid February 2020; inclisiran December 2021.*						
LLT = lipid-lowering therapy. PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor. Data source: Epic Cosmos. April 1–7 2026 partial quarter excluded..						

Ezetimibe remained the most widely prescribed non-statin agent, growing from 163,294 to 1,668,653 patients per quarter (+ 922%) and accounting for 77% of all non-statin prescriptions in Q1 2026 (Fig. 2).

Among PCSK9 inhibitors, evolocumab prescribing demonstrated sustained growth from 2,062 to 433,100 patients per quarter (+ 20,904%) in the years following FOURIER (2017) and VESALIUS-CV (2025). Alirocumab demonstrated a distinct trajectory, rising to a peak of 55,191 patients in Q3 2023, following ODYSSEY OUTCOMES (2018), before declining to a trough of 45,433 in Q3 2024 and recovering to 56,169 patients in Q1 2026. Combined PCSK9 inhibitor prescriptions reached 489,269 patients in Q1 2026, representing 1.5% of the dyslipidemia population (Fig. 2).

Icosapent ethyl prescriptions grew from 6,663 to 193,943 patients per quarter, with growth accelerating following REDUCE-IT and subsequent FDA approval in 2019, followed by attenuation after 2022 [7] Bempedoic acid prescriptions showed the most pronounced post-approval growth inflection among newer agents, with prescribing accelerating following the CLEAR OUTCOMES trial in March 2023 and reaching 62,992 patients per quarter by Q1 2026, a figure that includes patients prescribed the bempedoic acid/ezetimibe fixed-dose combination.[8] Prescriptions of inclisiran, approved in December 2021, reached only 14,682 patients per quarter by Q1 2026. (Fig. 2).

Discussion

These findings from the largest cohort of patients with dyslipidemia in the US characterize a decade of substantial growth in non-statin LLT prescribing. Despite this expansion, 15.8 million patients (47.0%) with diagnosed dyslipidemia remained without any LLT as of Q1 2026, consistent with prior population-based analysis (albeit with different inclusion criteria than the present study) identifying fewer than 40% of eligible US adults receiving LLT across complementary data sources.[1] A recent analysis using national pharmacy dispensing data documented growth in non-statin LLT prescribing from 2019 to 2024 but was limited by the absence of a patient-level denominator, precluding treatment gap quantification, and did not capture inclisiran prescribing. [10]

The most consistent temporal acceleration in prescribing across all non-statin classes occurred during the period following the 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies.[3] The persistent predominance of ezetimibe prescribing, accounting for 77% of all non-statin prescriptions in Q1 2026, despite a decade of newer agents with greater LDL-C lowering, likely reflects its oral formulation, established safety profile and tolerability, generic status, low cost, and guideline endorsement as a first-line non-statin. [2, 3]. The transient decline in alirocumab prescribing in 2023–2024 temporally coincided with Sanofi's discontinuation of the 75 mg dose formulation in 2023, possibly reflecting formulary dynamics, given similar guideline recommendations for both agents. [2, 5, 6] The 2026 ACC/AHA Dyslipidemia Guidelines further position ezetimibe and PCSK9 inhibitors as co-equal options in very high-risk patients, potentially expanding future utilization, given the now lower recommended LDL goals [2]. The attenuation of icosapent ethyl’s prescribing growth occurred amid ongoing debate regarding the cardiovascular outcomes evidence base for omega-3 fatty acids, including concerns surrounding the mineral oil placebo used in REDUCE-IT and neutral findings from STRENGTH, which evaluated a pharmacologically distinct omega-3 formulation (high-dose EPA + DHA vs EPA alone). The limited uptake of inclisiran may reflect limited prescriber familiarity, formulary restrictions, payer coverage challenges in the post-approval period, and current lack of cardiovascular outcome trials.

Several methodological considerations warrant emphasis in interpreting these findings. The E78.x cohort includes patients across the full cardiovascular risk spectrum. At present, the database does not allow for calculation of the PREVENT risk score or consistent information about coronary artery calcium scoring. Therefore, the proportion of patients not on LLT cannot be strictly interpreted as a treatment gap as the untreated group likely includes low-risk primary prevention individuals for whom lifestyle modification is sufficient. This population-level characterization is intended to document prescribing trajectories over time rather than to adjudicate treatment appropriateness at the individual patient level. Our study is also limited by its a cross-sectional design, which captures prescription volume but not LDL-C levels, adherence, or treatment duration. Demographic and insurance-based disparities in non-statin prescribing warrant further study.

These findings document a decade of substantial but uneven growth in non-statin lipid-lowering therapy prescribing across the US dyslipidemia population, with ezetimibe predominating and newer agents

remaining underutilized relative to their evidence base. Sustained implementation of the 2026 ACC/AHA Dyslipidemia Guidelines and continued real-world monitoring are essential to improve uptake.

Ethics Approval:

This study used de-identified aggregate data from Epic Cosmos and was determined to not require institutional review board approval. All analyses were performed at the aggregate level without access to individual patient records.

Declarations

Conflicts of Interest: F.Q. is supported by the National Institutes of Health T32 Training Grant (T32 HL125232, Multidisciplinary Training Program in Cardiovascular Epidemiology). E.S. receives funding from the Centers for Disease Control and Prevention (20042801-Sub01), the US Food and Drug Administration through the Yale-Mayo Clinic Center of Excellence in Regulatory Science and Innovation (CERSI; U01FD005938), the National Heart, Lung, and Blood Institute (R01HL151240), and the Patient-Centered Outcomes Research Institute (HM-2022C2-28354). D.L.J. is a part-time employee of the American Heart Association. J.M., S.P., and J.R.H. report no relevant funding or conflicts of interest.

Funding Declaration: None

Author Contribution

Jaideep Menda: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review and editing. Frank Qian: Methodology, Writing – review and editing. Donald M. Lloyd-Jones: Conceptualization, Writing – review and editing. Shan Parikh: Resources, Writing – review and editing. Erica Spatz: Conceptualization, Writing – review and editing. Jiun-Ruey Hu: Conceptualization, Methodology, Project administration, Supervision, Writing – review and editing.

Ethics Approval: This study used de-identified aggregate data from Epic Cosmos and was determined to not require institutional review board approval. All analyses were performed at the aggregate level without access to individual patient records.

Consent to Participate: Not applicable. This study used de-identified aggregate electronic health record data; individual patient consent was not required.

Data Availability Statement

The data underlying this study were obtained from Epic Cosmos under a data use agreement and are not publicly available. Aggregated de-identified data may be made available upon reasonable request to the corresponding author, subject to data use agreement restrictions.

Declaration of Generative AI and AI-Assisted Technologies in the Manuscript Preparation Process

During the preparation of this work, the authors used Claude (Anthropic) to assist with troubleshooting code for figure generation. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Figures

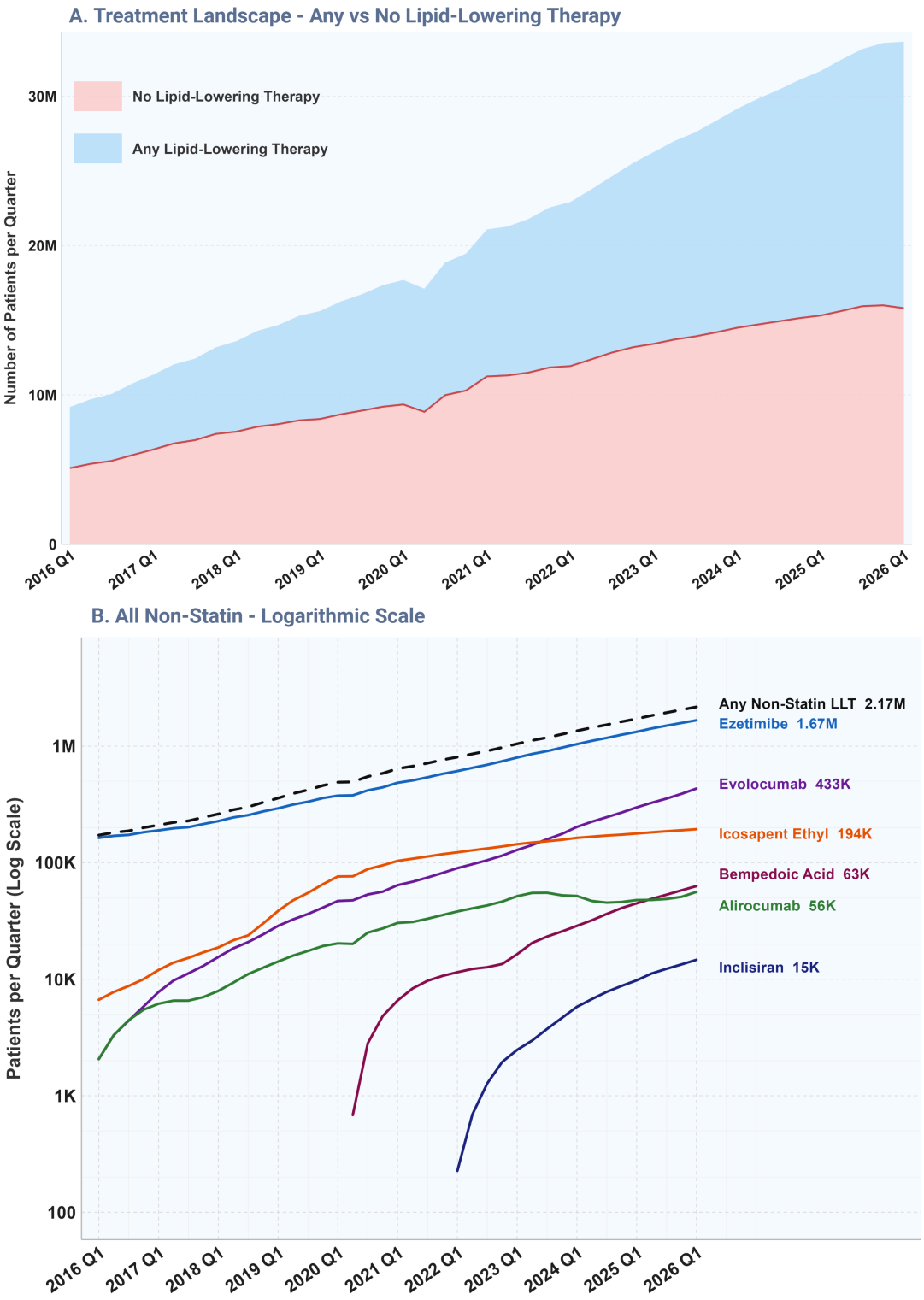

Figure 1

Treatment patterns and non-statin lipid-lowering therapy use over time.
A: Treatment landscape of patients receiving any lipid-lowering therapy versus no lipid-lowering therapy.
B: Temporal trends in the use of individual non-statin lipid-lowering therapies.

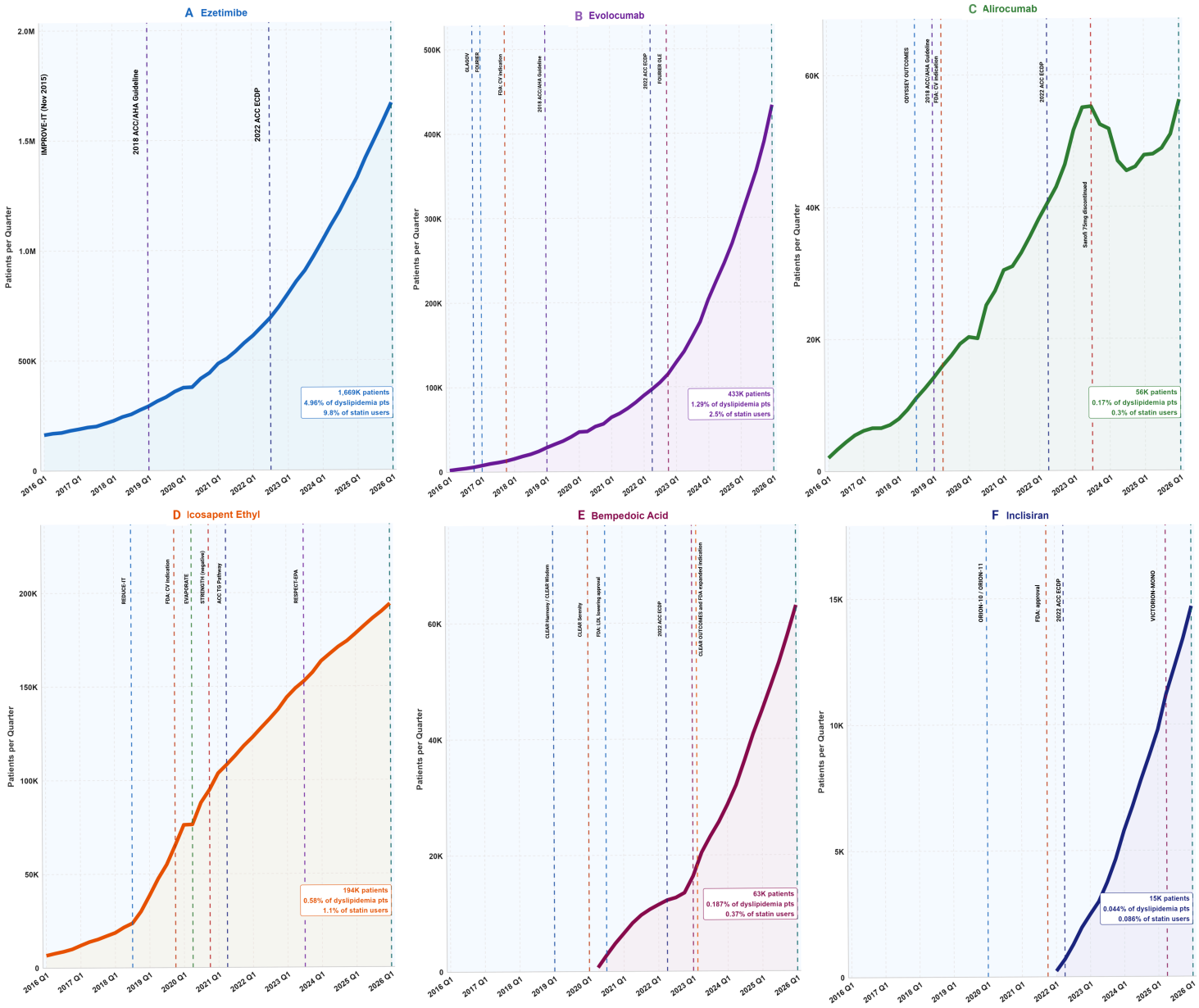

Figure 2

Temporal trends in individual non-statin lipid-lowering therapies in relation to major regulatory and guideline milestones.