

One-year changes in lipid-based cardiometabolic risk markers following resmetirom initiation: a real-world analysis

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BACKGROUND

- Metabolic dysfunction–associated steatohepatitis (MASH) is a progressive liver disease associated with profound disturbances in hepatic lipid metabolism and is closely linked with obesity, type 2 diabetes, dyslipidaemia, and other cardiometabolic risk factors^{1,2}
- Cardiovascular disease (CVD) is the leading cause of mortality in patients with MASH,³ and many patients require concomitant lipid-lowering therapy, including statins, as part of routine clinical management⁴
- Resmetirom is an oral thyroid hormone receptor β agonist that received accelerated approval in the United States (US) in March 2024 for the treatment of adults with noncirrhotic MASH with moderate to advanced fibrosis (consistent with stages F2-F3)⁵
- In phase 3 clinical studies, decreases in multiple lipids and lipoproteins were observed in patients treated with resmetirom^{6,7}; however, evidence characterising these changes in real-world clinical practice remains limited

OBJECTIVE

- To provide post-approval real-world evidence on 1-year lipid outcomes following resmetirom initiation using 2 large US real-world data sources

METHODS

Study design and data source

- This observational, retrospective cohort study used de-identified electronic health record (EHR) data from Truveta (30 health systems in the US) and Trio Health (US RWD platform)

Study population

- Adults aged ≥ 18 years initiating resmetirom on or after March 14, 2024, were included and followed through June 3, 2026 (Truveta), or January 23, 2026 (Trio Health)
- Patients were required to have had ≥ 1 healthcare interaction during the 1-year period prior to index date (date of earliest observed resmetirom prescription fill)
- Patients were excluded if they had coding consistent with other non–metabolic dysfunction–associated steatotic liver disease/MASH chronic liver disease etiologies or advanced liver disease during the 1 year before index
- Patients were required to have at least 1 year of observed follow-up

Baseline characteristics

- Sociodemographic and clinical characteristics are reported based on the most recent available value on the index date or during the 365 days preceding the index date

Outcomes

- Among patients with both baseline (closest value within ≤ 365 days before the index date) and 1-year after resmetirom initiation (value closest to 1-year post index ± 90 days) lipid measurements, changes in low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides (TG), and TG/HDL-C ratio were evaluated
 - Variables are summarised using means (SD), changes were assessed using paired t tests, and analyses are descriptive with nominal P values
 - LDL-C threshold category shift (<1.81 mmol/L or <2.59 mmol/L among patients above each threshold at baseline) was assessed
- Analyses were conducted independently within each data source and stratified according to concomitant statin use

RESULTS

Patient characteristics

- A total of 3853 patients (Truveta, $n = 2241$; Trio Health, $n = 1612$) met the eligibility criteria; mean (SD) age was 58.5 (12.7) and 58.4 (12.5), 62.4% and 61.2% were female, 77.2% and 68.0% were White, and 14.0% and 7.0% were Hispanic in the Truveta and Trio Health datasets, respectively (**TABLE 1**)
- In the Truveta and Trio Health datasets, respectively, 56.3% and 36.7% of patients received concomitant statin therapy during resmetirom treatment (**TABLE 1**)
- Patients receiving concomitant statins had a higher prevalence of type 2 diabetes, hypertension, and dyslipidaemia, and more CVD risk factors than those not receiving concomitant statins (**TABLE 1**)

TABLE 1. Baseline demographic and clinical characteristics overall and by statin use in the Truveta and Trio Health databases						
	Truveta			Trio Health		
Characteristic	Overall N = 2241	Statin n = 1261	No statin n = 980	Overall n = 1612	Statin n = 591	No statin n = 1021
Age at index, mean (SD), years	58.5 (12.7)	61.2 (11.3)	55.1 (13.5)	58.4 (12.5)	60.8 (10.7)	57.1 (13.2)
Female	1399 (62.4)*	755 (59.9)	644 (65.7)	986 (61.2)	353 (59.7)	633 (62.0)
BMI						
<25 kg/m ²	70 (3.1)	43 (3.4)	27 (2.8)	33 (2.0)	8 (1.4)	25 (2.4)
25 to <30 kg/m ²	313 (14.0)	174 (13.8)	139 (14.2)	152 (9.4)	65 (11.0)	87 (8.5)
≥ 30 kg/m ²	1112 (49.6)	631 (50.0)	481 (49.1)	560 (34.7)	211 (35.7)	349 (34.2)
Missing	746 (33.3)	413 (32.8)	333 (34.0)	867 (53.8)	307 (51.9)	560 (54.8)
Type 2 diabetes	1266 (56.5)	836 (66.3)	430 (43.9)	750 (46.5)	381 (64.5)	369 (36.1)
Obesity	1299 (58.0)	731 (58.0)	568 (58.0)	775 (48.1)	295 (49.9)	480 (47.7)
Hypertension	1337 (59.7)	807 (64.0)	530 (54.1)	996 (61.8)	447 (75.6)	549 (53.8)
Dyslipidaemia	1655 (73.9)	1159 (91.9)	496 (50.6)	1056 (65.5)	519 (87.8)	537 (52.6)
Number of CVD risk factors						
0	180 (8.0)	46 (3.6)	134 (13.7)	213 (13.2)	15 (2.5)	198 (19.4)
1-2	873 (39.0)	429 (34.0)	444 (45.3)	774 (48.0)	242 (40.9)	532 (52.1)
3-4	1188 (53.0)	786 (62.3)	402 (41.0)	625 (38.8)	334 (56.5)	291 (28.5)
Baseline CVD ^b	334 (14.9)	240 (19.0)	94 (9.6)	217 (13.5)	105 (17.8)	112 (11.1)
Observed follow-up, mean (SD), days	523.2 (110.5)	524.6 (111.7)	521.4 (108.9)	461.1 (65.0)	463.2 (65.4)	459.9 (64.7)
Data are n (%) unless otherwise stated.						
*Missing data for 1 patient.						
^b CVD includes myocardial infarction, stroke, transient ischaemic attack, unstable angina, peripheral artery disease, coronary artery disease, and coronary revascularisation.						
BMI, body mass index; CVD, cardiovascular disease.						

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DISCLOSURES

WA reports speaking/consulting roles with: Madrigal Pharmaceuticals, Inc., 89Bio, Echoscans, GlaxoSmithKline (GSK), Goldman Sachs, Inventiva, Janssen, Kudu Spectrum, Novo Nordisk, and UCB. QMUL has received completed or active grants from Gilead, GSK, and MSD.
CMP, ST, YK, DW, FL, and JO are employees and shareholders of Madrigal Pharmaceuticals, Inc. IM is an employee of Trio Health Inc. WA reports speaking/teaching/consulting/advisory roles with Madrigal Pharmaceuticals, Inc., 89Bio, Boehringer Ingelheim, Cima, Echoscans, Fibronectics, Gilead, Intercept, Ipsen, Novo Nordisk, and Perspectum; and has received grant/research support/research funding from Madrigal Pharmaceuticals, Inc., 89Bio, Akero, Arbutus, AstraZeneca, Boehringer Ingelheim, Boston Pharma, Concept, Eli Lilly, Galectin, Gilead, GSK, Inventiva, Ipsen, Merck, Novo Nordisk, Perspectum, Pfizer, and Regeneron.

RESULTS

Changes in lipid parameters

- Statistically significant reductions in mean LDL-C, TC, and TG were observed across both real-world data sources, regardless of concomitant statin use (**TABLE 2**)
 - LDL-C reductions (10.9%-11.1%) were smaller than those previously reported in the MAESTRO-NASH trial (13.7%-19.5%), potentially reflecting the lower baseline LDL-C levels in this real-world population (2.39 mmol/L in Truveta, 2.43 mmol/L in Trio Health vs ~ 2.66 - 2.76 mmol/L in MAESTRO-NASH)⁶
- TG/HDL-C ratio improved consistently following resmetirom initiation, irrespective of concomitant statin use (**TABLE 2**)
 - Reductions were statistically significant across all groups except for the Trio Health cohort not receiving concomitant statins
- Small increases in HDL-C were observed after resmetirom initiation; increases were statistically significant in the Truveta dataset but not in the Trio Health dataset (**TABLE 2**)
- The magnitude of lipid improvements was generally similar, and in some cases numerically greater, among patients receiving concomitant statins than among those not receiving statins
 - Comparisons between statin subgroups were descriptive only; no formal between-group statistical comparisons were performed
- Patient-level changes in lipid parameters showed substantial interindividual variability, with broadly similar response patterns regardless of concomitant statin use (**FIGURE 1**)

TABLE 2. Mean changes in lipid parameters overall and stratified by concomitant statin use

	n (%) with both measurements	Baseline mean (SD)	Follow-up mean (SD)	Mean change (SD)	Mean % change
Truveta					
Statin (n = 1261)					
LDL-C, mmol/L	333 (26.4)	2.18 (1.00)	1.77 (0.86)	-0.40 (0.93)	-11.0 (46.0)
HDL-C, mmol/L	331 (26.2)	1.16 (0.32)	1.19 (0.31)	0.03 (0.25)	5.4 (23.4)
TC, mmol/L	338 (26.8)	4.14 (1.21)	3.55 (1.06)	-0.59 (1.08)	-11.7 (22.5)
TG, mmol/L	341 (27)	1.98 (1.40)	1.42 (0.87)	-0.57 (1.09)	-20.5 (36.9)
TG/HDL-C ratio	330 (26.2)	4.5 (5.1)	3.1 (2.6)	-1.5 (3.8)	-19.5 (47.1)
No statin (n = 980)					
LDL-C, mmol/L	213 (21.7)	2.71 (0.82)	2.32 (0.78)	-0.39 (0.73)	-11.4 (26.8)
HDL-C, mmol/L	218 (22.2)	1.22 (0.30)	1.26 (0.28)	0.04 (0.22)	5.6 (20.5)
TC, mmol/L	218 (22.2)	4.68 (0.92)	4.19 (0.92)	-0.49 (0.90)	-9.0 (18.0)
TG, mmol/L	220 (22.4)	1.77 (0.87)	1.41 (0.72)	-0.36 (0.80)	-12.5 (41.0)
TG/HDL-C ratio	212 (21.6)	3.7 (2.4)	2.8 (1.7)	-0.9 (2.1)	-13.2 (47.9)
Trio Health					
Statin (n = 591)					
LDL-C, mmol/L	127 (21)	2.27 (1.02)	1.79 (0.82)	-0.48 (0.98)	-10.6 (60.7)
HDL-C, mmol/L	139 (24)	1.15 (0.34)	1.19 (0.32)	0.03 (0.22)	5.0 (20.4)
TC, mmol/L	168 (28)	4.18 (1.15)	3.69 (1.01)	-0.5 (1.1)	-9.1 (23.8)
TG, mmol/L	167 (28)	2.04 (1.19)	1.58 (1.01)	-0.46 (0.83)	-19.0 (32.4)
TG/HDL-C ratio	137 (23)	4.7 (4.3)	3.5 (3.2)	-1.2 (2.6)	-19.3 (36.6)
No statin (n = 1021)					
LDL-C, mmol/L	107 (10)	2.63 (0.82)	2.22 (0.76)	-0.4 (0.72)	-11.1 (29.0)
HDL-C, mmol/L	133 (13)	1.21 (0.43)	1.24 (0.43)	0.03 (0.36)	5.7 (38.2)
TC, mmol/L	164 (16)	4.62 (1.08)	4.09 (1.18)	-0.53 (0.89)	-10.3 (18.5)
TG, mmol/L	165 (16)	1.95 (1.22)	1.68 (1.75)	-0.27 (1.18)	-11.3 (39.4)
TG/HDL-C ratio	130 (13)	4.3 (3.3)	3.8 (5.2)	-0.5 (3.5)	-11.9 (43.2)

Bold values indicate $P < 0.05$ from paired t test.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

Shift into lower LDL-C threshold categories

- Among patients with elevated baseline LDL-C, a substantial proportion shifted into lower guideline-defined LDL-C threshold categories 1 year after resmetirom initiation (**TABLE 3**)
 - Among patients with baseline LDL-C ≥ 1.81 mmol/L, 32.9% (Truveta) and 34.3% (Trio Health) shifted to LDL-C <1.81 mmol/L after 1 year
 - Among patients with baseline LDL-C ≥ 2.59 mmol/L, 56.3% (Truveta) and 61.6% (Trio Health) shifted to LDL-C <2.59 mmol/L after 1 year
- Similar patterns were observed regardless of concomitant statin use

TABLE 3. Changes in LDL-C threshold categories and LDL-C levels from baseline to 12 months, overall and by concomitant statin use

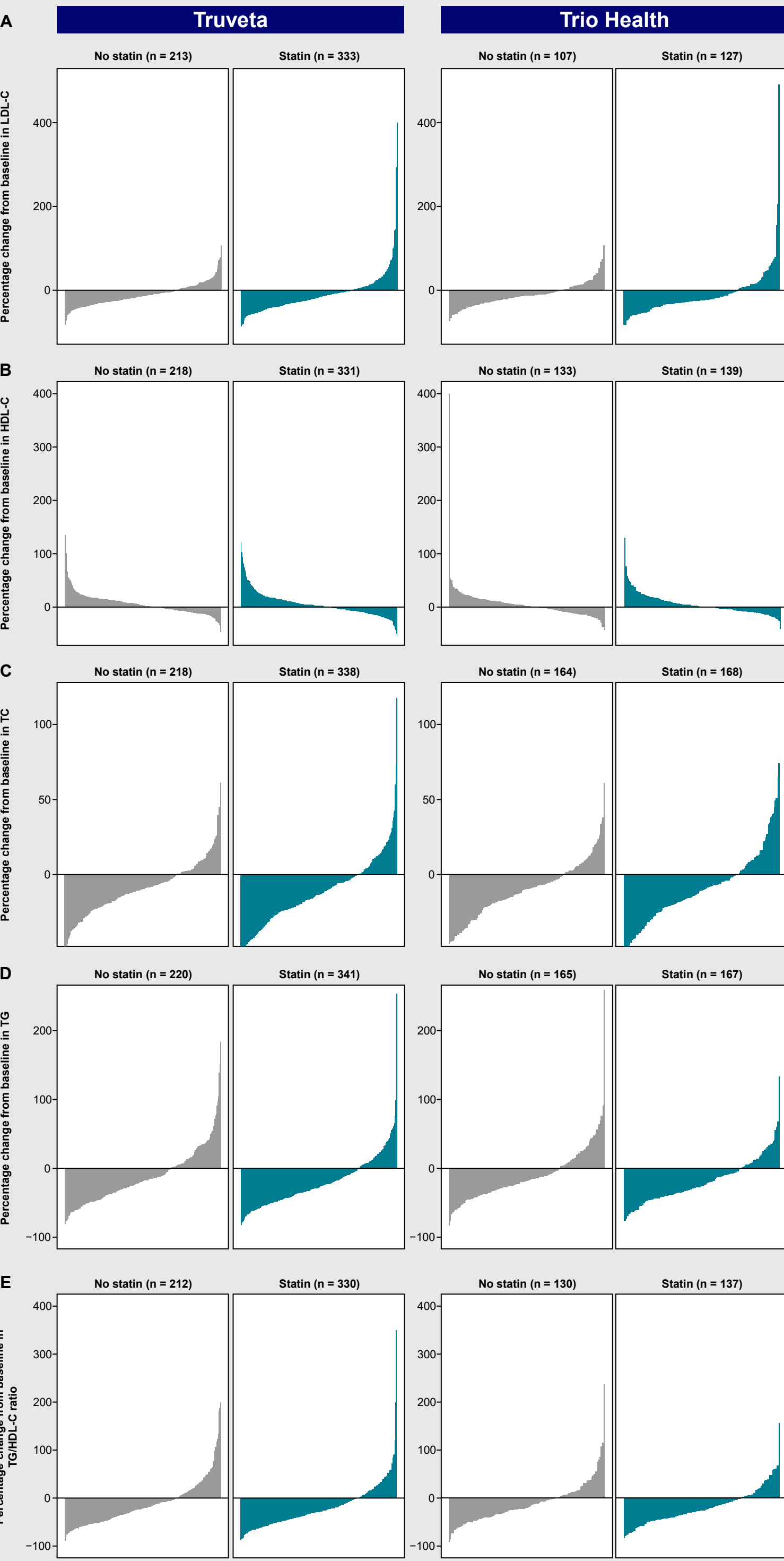
Group		n with both measurements	LDL-C ≥ 1.81 mmol/L at baseline, n (%)	LDL-C ≥ 1.81 mmol/L at 1 year, n (%)	n who shifted from LDL-C ≥ 1.81 to <1.81 mmol/L, n (%)	Among patients who crossed threshold			
						Baseline mean (SD)	Follow-up mean (SD)	Baseline median (IQR)	Follow-up median (IQR)
Truveta	Overall	546	389 (71.2)	291 (53.3)	128 (32.9)	2.55 (0.78)	1.41 (0.30)	2.30 (1.99, 2.82)	1.49 (1.24, 1.64)
	Statin	333	202 (60.7)	139 (41.7)	86 (42.6)	2.57 (0.83)	1.38 (0.32)	2.25 (1.98, 2.89)	1.45 (1.19, 1.64)
	No statin	213	187 (87.8)	152 (71.4)	42 (22.5)	2.50 (0.68)	1.50 (0.21)	2.35 (2.12, 2.73)	1.55 (1.40, 1.84)
Trio Health	Overall	234	174 (74.4)	125 (53.4)	60 (34.5)	2.45 (0.67)	1.34 (0.29)	2.20 (1.99, 2.68)	1.44 (1.18, 1.55)
	Statin	127	83 (65.4)	53 (41.7)	38 (45.8)	2.45 (0.73)	1.31 (0.3)	2.17 (1.99, 2.63)	1.36 (1.16, 1.50)
	No statin	107	91 (85)	72 (67.3)	22 (24.2)	2.47 (0.57)	1.39 (0.27)	2.39 (2.11, 2.86)	1.47 (1.26, 1.58)
Group		n with both measurements	LDL-C ≥ 2.59 mmol/L at baseline, n (%)	LDL-C ≥ 2.59 mmol/L at 1 year, n (%)	n who shifted from LDL-C ≥ 2.59 to <2.59 mmol/L, n (%)	Among patients who crossed threshold			
						Baseline mean (SD)	Follow-up mean (SD)	Baseline median (IQR)	Follow-up median (IQR)
Truveta	Overall	546	206 (37.7)	118 (21.6)	116 (56.3)	3.27 (0.62)	1.90 (0.48)	3.13 (2.84, 3.52)	1.99 (1.57, 2.28)
	Statin	333	89 (26.7)	47 (14.1)	58 (65.2)	3.38 (0.72)	1.75 (0.51)	3.22 (2.85, 3.65)	1.72 (1.51, 2.19)
	No statin	213	117 (54.9)	71 (33.3)	58 (49.6)	3.15 (0.49)	2.04 (0.40)	3.12 (2.84, 3.36)	2.15 (1.86, 2.34)
Trio Health	Overall	234	100 (42.7)	54 (23.1)	62 (62)	3.27 (0.72)	1.94 (0.53)	3.03 (2.75, 3.55)	2.11 (1.50, 2.37)
	Statin	127	42 (33.1)	20 (15.7)	31 (73.8)	3.39 (0.87)	1.81 (0.57)	3.05 (2.78, 3.62)	1.97 (1.28, 2.29)
	No statin	107	58 (54.2)	34 (31.8)	31 (53.4)	3.16 (0.52)	2.07 (0.46)	2.92 (2.75, 3.41)	2.22 (1.95, 2.39)

Follow-up window: 9-15 months post-index date.
*Denominator is patients with baseline LDL-C at or above the respective threshold. Change is from baseline to 1 year.
LDL-C, low-density lipoprotein cholesterol.

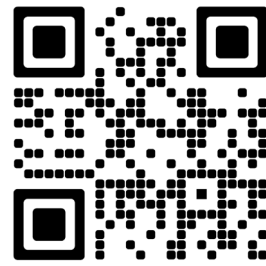
CONCLUSIONS

- Improvements in lipid parameters observed with resmetirom treatment in clinical trials were reproduced 1 year after treatment initiation across 2 independent real-world data sources, irrespective of concomitant statin therapy
- A substantial proportion of patients shifted into lower LDL-C threshold categories 1 year after resmetirom initiation
- As a retrospective real-world database study, the analysis is limited by potential missing or inaccurate data and incomplete capture of patients' healthcare journeys by the structured data format of the EHR

FIGURE 1. Patient-level percentage change in (A) LDL-C, (B) HDL-C, (C) TC, (D) TG, and (E) TG/HDL-C ratio from baseline to 1-year follow-up, by concomitant statin use



HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.



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