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Effects of fibrates on lipid profile: a meta-analysis of randomized controlled trials

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ABSTRACT

We conducted a meta-analysis to compare the lipid-lowering effects of fibratesLiterature was searched up to December 2024. Absolute changes in triglycerides (TG), LDL-cholesterol (LDL-C), apolipoprotein B (ApoB), and non-HDL cholesterol (non-HDL-C) were analyzed using both fixed and random effects models.

We included 63 randomized controlled trials. Compared to placebo, all fibrates significantly reduced TG levels. Fenofibrate and bezafibrate significantly reduced LDL-C (–15.12 and –15.04 mg/dL, respectively), while only fenofibrate significantly lowered ApoB (–24.88 mg/dL) and non-HDL-C (–46.38 mg/dL), followed by gemfibrozil and pemafibrate for non-HDL-C. In combination with statins, no fibrates significantly reduced LDL-C, while fenofibrate remained the only fibrate to significantly lower ApoB (–10.42 mg/dL) and non-HDL-C (–12.02 mg/dL).

Overall, we found that fibrates differ substantially in their lipid effects. Fenofibrate shows the most consistent and comprehensive lipid-lowering profile.

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Keywords
Fibrates; Mixed dyslipidemia; Dyslipidemia; Fibrates; Lipid-lowering therapy

Background

Dyslipidemia is a major modifiable risk factor for cardiovascular disease and remains a leading target for both primary and secondary prevention strategies. While elevated low-density lipoprotein cholesterol (LDL-C) is the primary focus of lipid-lowering therapies, patients with dyslipidemia often present with a complex lipid profile that involves abnormalities in multiple lipid parameters. These may include elevated triglycerides (TG), low levels of high-density lipoprotein cholesterol (HDL-C), and increased concentrations of apolipoprotein B (ApoB) [1, 2], each of which is independently associated with increased cardiovascular risk.

In clinical practice, this multifaceted dyslipidemic profile is particularly common in patients with metabolic syndrome, type 2 diabetes mellitus, and obesity [3-5]. In these populations, isolated LDL-C lowering may be insufficient to achieve optimal cardiovascular protection. Consequently, there is growing recognition of the need for comprehensive lipid management that targets a broader range of lipid abnormalities. This has led to increasing use of combination therapies that go beyond statin monotherapy [5, 6].

Statins, or HMG-CoA reductase inhibitors, are the cornerstone of lipid-lowering treatment and are highly effective in reducing LDL-C and cardiovascular events. However, their effect on triglyceride levels is moderate and variable, and they have minimal or no impact on HDL-C or ApoB in many patients. Fibrates, are a class of lipid-modifying agents that act primarily as peroxisome proliferator-activated receptor alpha (PPARα) agonists. They are particularly effective in lowering triglyceride levels and, to a lesser extent, in raising HDL-C [7]. Some fibrates also modestly reduce LDL-C and ApoB levels [7, 8]. Because of their complementary lipid effects, fibrates are often considered as add-on therapy to statins in patients with mixed dyslipidemia, especially when elevated triglycerides and low HDL-C persist despite statin use [9].

Despite their shared pharmacologic class, fibrates differ significantly in their pharmacokinetics, receptor selectivity, potency, and lipid-lowering profiles [10, 11]. Moreover, their interaction profiles with statins are not uniform, which has implications for both efficacy and safety, particularly in the context of combination therapy [12].

Despite compelling evidence for the utility of fibrates, comparisons among individual agents in randomized clinical trials remain scarce. Absent such direct comparisons, it is unclear whether observed differences are due to pharmacodynamic distinctions or co-

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hort selection biases. Given these differences, therapeutic decisions involving fibrates – whether as monotherapy or in combination with statins – should not treat the class as homogenous. Instead, clinicians should consider the specific pharmacological and clinical characteristics of each molecule. A nuanced understanding of these differences is crucial for optimizing lipid management strategies in patients with complex dyslipidemia, especially those with residual lipid abnormalities despite statin therapy [13].

In this context, the present meta-analysis examined 63 randomized controlled trials comparing fibrates versus placebo, or fibrate-plus-statin versus statin alone. Our goal was to quantify and contrast the magnitude of lipid changes – specifically TG, LDL-C, ApoB, and non-HDL-cholesterol (non-HDL-C – across different fibrates, both as monotherapy and combination therapy.

Methods

We conducted a meta-analysis according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [14].

Search Strategy and Information Sources

PubMed, EMBASE, Web of Science were searched from inception to December 2024. Details of searching strategies are shown in the **Supplementary material**.

Study Selection and Eligibility Criteria

Inclusion criteria were:

1) randomized controlled trials (RCTs) in humans, parallel design, phase II, III, or IV;
2) English language and full text available;
3) comparing the effect of fibrates both alone versus placebo and on top of statins versus statins;
4) reporting the absolute effects on TG, LDL-C, ApoB, or non-HDL-C levels.

Data extraction and synthesis

Two independent investigators extracted the data using a predefined data collection form including the first author; year of publication; the number of participants and their main characteristics (e.g. sex, mean age); intervention duration; treatment (name and dosage) and control; mean or median values and variance (standard deviation [SD], standard error [SE], interquartile range [IQR], 95% confidence interval [95%CI], the minimum and maximum values [range]) both at baseline and follow-up or absolute change for TG, LDL-C, ApoB, and non-HDL-C concentrations. The between-group (treatment vs. placebo) absolute mean differences in TG, LDL-C, ApoB, and non-HDL-C levels, along with their 95% confidence intervals, were calculated for each fibrate. All lipid values were expressed in mg/dL; when reported in mmol/L, they were converted using standard factors: values for TG were divided by 0.0113, while LDL-C, ApoB, and non-HDL-C were converted using a factor of 0.0259.

All data were presented as mean and SD. We converted SE, IQR, 95%CI, and range to SD by using formulas recommended by the Cochrane Handbook [15]. Since the within-group absolute mean difference was computed by subtracting the baseline level from the follow-up level, 0.5 was used as the correlation coefficient to calculate pooled SD within groups [16]. For trials that reported variances at baseline but without any information for variances at follow-up, the variances at baseline were also used for follow-up. Multiple intervention groups were combined into a single intervention group when they were compared to only one control group in the trial. Pooled estimates were assessed by using both the fixed-effects and the random-effects models. The generic inverse variance method was used to balance the heterogeneity between studies, and the restricted maximum likelihood estimator was used to estimate the between-study variance [17]. When significant heterogeneity was discovered (as determined by Cochrane's Q test and the I^2 statistic [18], $p<0.05$), the results from the random-effects model were presented.

All tests were considered statistically significant for p-value less than 0.05. The analyses and the corresponding graphical visualization of forest plots were conducted using R (version 4.3.2.).

Results

The flow chart indicating the procedure of literature searching and study screening is shown in **Supplementary Figure 1**. A total of 33,333 subjects from 63 RCTs were included in our meta-analysis (9 RCTs for bezafibrate, 3 RCTs for ciprofibrate, 3 RCTs for clofibrate, 19 RCTs for fenofibrate, 23 RCTs for gemfibrozil, 6 RCTs for pemafibrate, **Table 1**).

Figure 1 summarizes the lipid effects of different fibrates compared to placebo, without concomitant statin treatment. With the exception of clofibrate, fibrates significantly reduced TG levels (**Figure 1A**), with the greatest reduction observed for pemafibrate (–123.91 mg/dL [-196.60; -51.22]), followed by gemfibrozil (–93.22 mg/dL [-112.76; -73.69]), ciprofibrate (–75.05 mg/dL [-113.96; -36.14]), bezafibrate (–65.87 mg/dL [-95.25; -36.48]), and fenofibrate (–64.81 mg/dL [-83.90; -45.71]) (**Figure 1A**).

For LDL-C, significant reductions were observed with fenofibrate (–15.12 mg/dL [-29.89; -0.34]) and bezafibrate (–15.04 mg/dL [-21.92; -8.16]). All other fibrates showed no significant effect (**Figure 1B**).

Regarding ApoB, fenofibrate showed the most marked reduction (–24.88 mg/dL [-38.73; -11.03]), followed by bezafibrate (–20.81 mg/dL [-33.85; -7.78]), and gemfibrozil (–12.01 mg/dL [-18.16; -5.86]), while other fibrates had non-significant effects (**Figure 1C**).

In the case of non-HDL-C, only three fibrates had enough RCTs to assess a pooled effect, and all demonstrated significant reductions versus placebo: fenofibrate (–46.38 mg/dL [-61.50; -31.26]), gemfibrozil (–33.89 mg/dL [-36.02; -31.75]), and pemafibrate (–17.40 mg/dL [-23.86; -10.95]) (**Figure 1D**).

Figure 2 shows the effects of fibrates on top of statin therapy. This evaluation was possible only for fenofibrate and gemfibrozil, as they were the only fibrates with more than one eligible trial. In both cases, a significant reduction in TG levels was observed, with decreases of –59.09 mg/dL [-78.99; -39.20] and –44.68 mg/dL [-63.64; -25.72], respectively (**Figure 2A**). When considered on top of statin therapy, no fibrate class significantly reduced LDL-C levels. On the contrary, pemafibrate was associated with a significant increase (+9.68 mg/dL [8.48; 10.89]) (**Figure 2B**). Fenofibrate remained the only fibrate associated with a significant reduction in ApoB levels (–10.42 mg/dL [-15.17; -5.67]) (**Figure 2C**) and with a modest reduction in non-HDL-C (–12.02 mg/dL [-15.17; -5.67]), with no consistent effect observed for the other fibrates (**Figure 2D**).

Discussions

This meta-analysis of 63 randomized controlled trials including over 33,000 participants provides compelling evidence that fibrates exert heterogeneous effects on lipid parameters, with significant differences among individual agents.

While all fibrates significantly reduced TG levels, fenofibrate and

Table 1 | Characteristics of included trials.

No	Trial name	Year	Experimental group	Control group	Number of participants
Bezafibrate					
1	Niort et al (1988)[s1]	1988	Bezafibrate 400 mg/day	Placebo	24
2	Jones et al (1990)[s2]	1990	Bezafibrate 600 mg/day	Placebo	37
3	Winocour et al (1990)[s3]	1990	Bezafibrate 400 mg/day	Placebo	36
4	Niort et al (1993)[s4]	1993	Bezafibrate 400 mg/day	Placebo	32
5	Walzl et al (1993)[s5]	1993	Bezafibrate 400 mg/day	Placebo	40
6	Stewart et al (1995)[s6]	1995	Bezafibrate 400 mg/day	Placebo	22
7	SENDCAP[s7]	1998	Bezafibrate 400 mg/day	Placebo	128
8	Ogawa et al (2000)[s8]	2000	Bezafibrate 400 mg/day	Placebo	342
9	Leon-Martinez et al (2020)[s9]	2020	Bezafibrate 400 mg/day + Berberine 500 mg/day	Berberine 500 mg/day	20
Ciprofibrate					
1	Illingworth et al (1982)[s13]	1982	Ciprofibrate 50 or 100 mg/day	Placebo	20
2	Kontopoulos et al (1996)[s14]	1996	Ciprofibrate 100 mg/day + Simvastatin 20 mg/day	Simvastatin 20 mg/day	40
3	Bermudez-Pirela et al (2007)[15]	2007	Ciprofibrate 100 mg/day	Placebo	75
Clofibrate					
1	Cole et al (1971)[s10]	1971	Clofibrate 0.25 g/day	Placebo	119
2	Dujovne et al (1976)[s11]	1976	Clofibrate 2 g/day	Placebo	19
3	Miettinen et al (1980)[s12]	1980	Clofibrate 1.5 g/day or + Probucol 1-2 g/day	Placebo or + Probucol 1-2 g/day	100
Fenofibrate					
1	Mellies et al (1987)[s16]	1987	Fenofibrate 300 mg/day	Placebo	33
2	Athyros et al (2002)[s17]	2002	Fenofibrate 200 mg/day + Atorvastatin 20 mg/day	Atorvastatin 20 mg/day	80
3	Playford et al (2002)[s18]	2002	Fenofibrate 200 mg/day	Placebo	35
4	Cavallero et al (2003)[s19]	2003	Fenofibrate 200 mg/day	Placebo	28
5	Playford et al (2003)[s20]	2003	Fenofibrate 200 mg/day	Placebo	35
6	Vakkilainen et al (2003)[s21]	2003	Fenofibrate 200 mg/day	Placebo	405
7	Derosa et al (2004)[s22]	2004	Fenofibrate 200 mg/day + Fluvastatin 80 mg/day	Fluvastatin 80 mg/day	48
8	Athyros et al (2005)[s23]	2005	Fenofibrate 200 mg/day + Atorvastatin 20 mg/day	Atorvastatin 20 mg/day	200
9	Okopien et al (2005)[s24]	2005	Fenofibrate 267 mg/day	Placebo	34
10	Keech et al (2005)[s25]	2005	Fenofibrate 200 mg/day	Placebo	9795
11	Davidson et al (2009)[s26]	2009	Fenofibrate 145 mg/day + Atorvastatin 40 mg/day	Atorvastatin 40 mg/day	137
12	Derosa et al (2009)[s27]	2009	Fenofibrate 145 mg/day + Simvastatin 40 mg/day	Simvastatin 40 mg/day	153
13	Farnier et al (2010)[s28]	2010	Fenofibrate 160 mg/day + Pravastatin 40 mg/day	Pravastatin 40 mg/day	239
14	Miyazaki et al (2010)[s29]	2010	Fenofibrate 300 mg/day	Placebo	44
15	Krysiak et al (2011)[s30]	2011	Fenofibrate 200 mg/day alone or + Simvastatin 40 mg/day	Placebo or + Simvastatin 40 mg/day	190
16	Lella et al (2013)[s31]	2013	Fenofibrate 145 mg/day + Atorvastatin 10 mg/day	Atorvastatin 10 mg/day	58

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No	Trial name	Year	Experimental group	Control group	Number of participants
17	La Fountaine et al (2019)[s32]	2019	Fenofibrate 145 mg/day	Placebo	16
18	Ihm et al (2020)[s33]	2020	Fenofibrate 160 mg/day + Pitavastatin 2 mg/day	Pitavastatin 2 mg/day	347
19	Park et al (2021)[s34]	2021	Fenofibrate 178.8 mg/day + Atorvastatin 10 or 20 or Rosuvastatin 10 mg/day	Atorvastatin 10 or 20 or Rosuvastatin 10 mg/day	127
Gemfibrozil					
1	HHS[s35]	1987	Gemfibrozil 1200 mg/day	Placebo	4081
2	Andersen et al (1990)[s36]	1990	Gemfibrozil 1200 mg/day	Placebo	43
3	Tsai et al (1992)[s37]	1992	Gemfibrozil 1200 mg/day	Placebo	12
4	Lahdenpera et al (1993)[s38]	1993	Gemfibrozil 1200 mg/day	Placebo	16
5	Wiklund et al (1993)[s39]	1993	Gemfibrozil 1200 mg/day alone or + Pravastatin 40 mg	Placebo or + Pravastatin 40 mg	266
6	Vinik et al (1993)[s40]	1993	Gemfibrozil 1200 mg/day	Placebo	442
7	Vuorinen-Markkola et al (1993)[s41]	1993	Gemfibrozil 1200 mg/day	Placebo	20
8	Knipscheer et al (1994)[s42]	1994	Gemfibrozil 1200 mg/day	Placebo	33
9	Avellone et al (1995)[s43]	1995	Gemfibrozil 1200 mg/day	Placebo	20
10	Kahri et al (1995)[s44]	1995	Gemfibrozil 1200 mg/day	Placebo	20
11	Smit et al (1995)[s45]	1995	Gemfibrozil 1200 mg/day + Fluvastatin 40 mg/day	Fluvastatin 40 mg/day	14
12	Vanhanen et al (1995)[s46]	1995	Gemfibrozil 1200 mg/day alone or + Pravastatin 40 mg/day	Placebo or + Pravastatin 40 mg/day	38
13	Sane et al (1995)[s47]	1995	Gemfibrozil 1200 mg/day	Placebo	20
14	Schaefe et al (1996)[s48]	1996	Gemfibrozil 1200 mg/day	Placebo	229
15	LOCAT[s49]	1997	Gemfibrozil 1200 mg/day	Placebo	395
16	Yoshida et al (1998)[s50]	1998	Gemfibrozil 900 mg/day	Placebo	19
17	VA-HIT[s51]	1999	Gemfibrozil 1200 mg/day	Placebo	2531
18	Avogaro et al (1999)[s52]	1999	Gemfibrozil 1200 mg/day	Placebo	217
19	Mussoni et al (2000)[s53]	2000	Gemfibrozil 1200 mg/day	Placebo	53
20	Dumont et al (2001)[s54]	2001	Gemfibrozil 1200 mg/day	Placebo	64
21	Bosse et al (2002)[s55]	2002	Gemfibrozil 1200 mg/day	Placebo	65
22	Miller et al (2002)[s56]	2002	Gemfibrozil 1200 mg/day	Placebo	37
23	Martínez et al (2003)[s57]	2003	Gemfibrozil 1200 mg/day	Placebo	70
Pemafibrate					
1	Ishibashi et al (2016)[s58]	2016	Pemafibrate 0.05 or 0.1 or 0.2 or 0.4 mg/day	Placebo	178
2	Arai et al (2017)[s59]	2017	Pemafibrate 0.1 or 0.2 or 0.4 mg/day + Pitavastatin or Pemafibrate 0.2 or 0.4 mg/day + Any statins	Pitavastatin or Any statins	593
3	Arai et al (2018)[s60]	2018	Pemafibrate 0.1 or 0.2 or 0.4 mg/day	Placebo	166
4	Matsuba et al (2018)[s61]	2018	Pemafibrate 0.4 mg/day	Placebo	18
5	Nakajima et al (2021)[s62]	2021	Pemafibrate 0.4 mg/day	Placebo	118
6	PROMINENT[s63]	2022	Pemafibrate 0.4 mg/day + Any statins	Placebo + Any statins	10497

*The references for each trial can be found in the supplementary file.

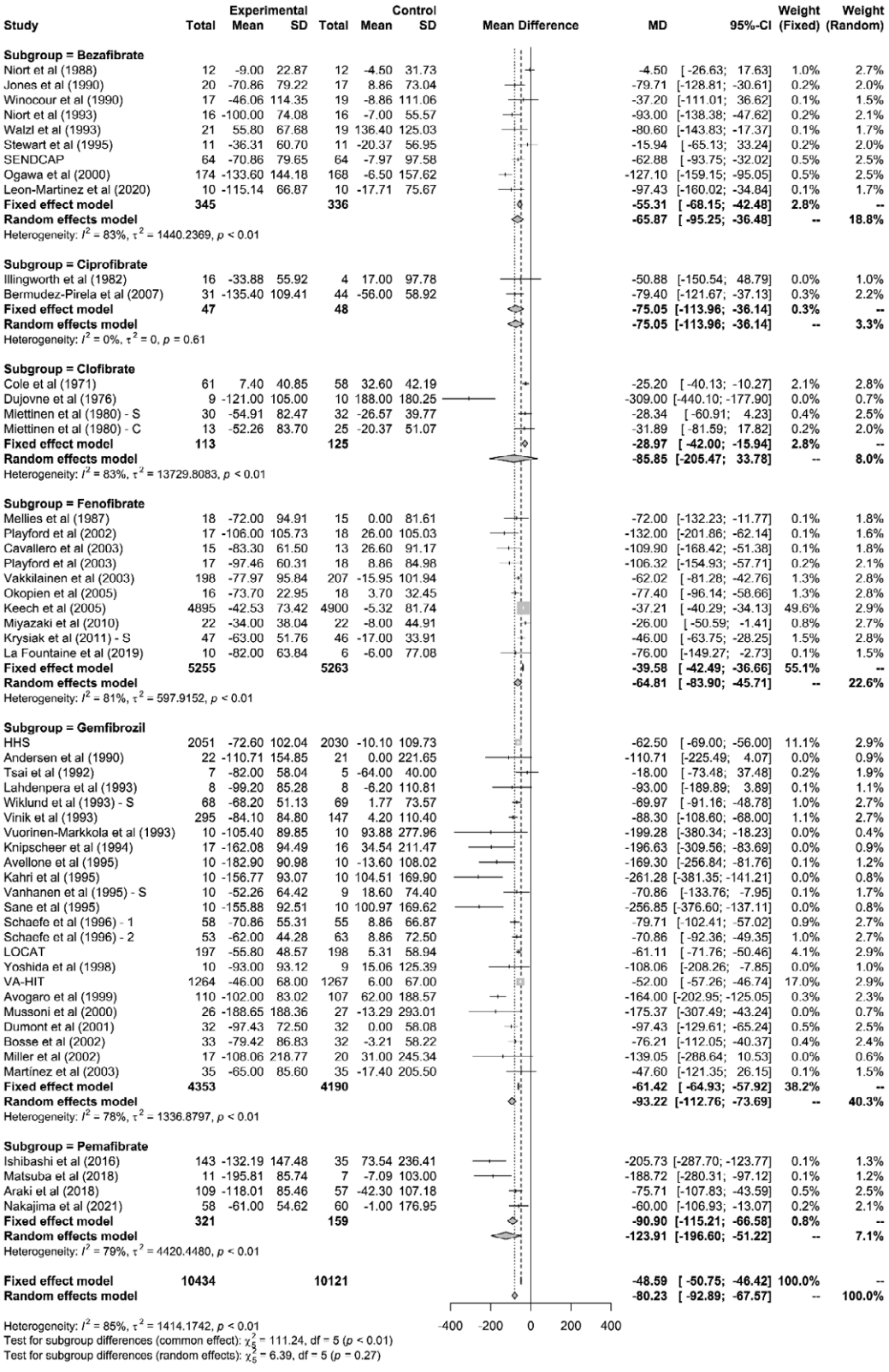

Figure 1A | Lipid-lowering effects of fibrates compared to placebo. Panel A: effects on triglycerides (TG); Panel B: effects on low-density lipoprotein cholesterol (LDL-C); Panel C: effects on apolipoprotein B (ApoB); Panel D: effects on non-high-density lipoprotein cholesterol (non-HDL-C). Effects on triglycerides (TG).

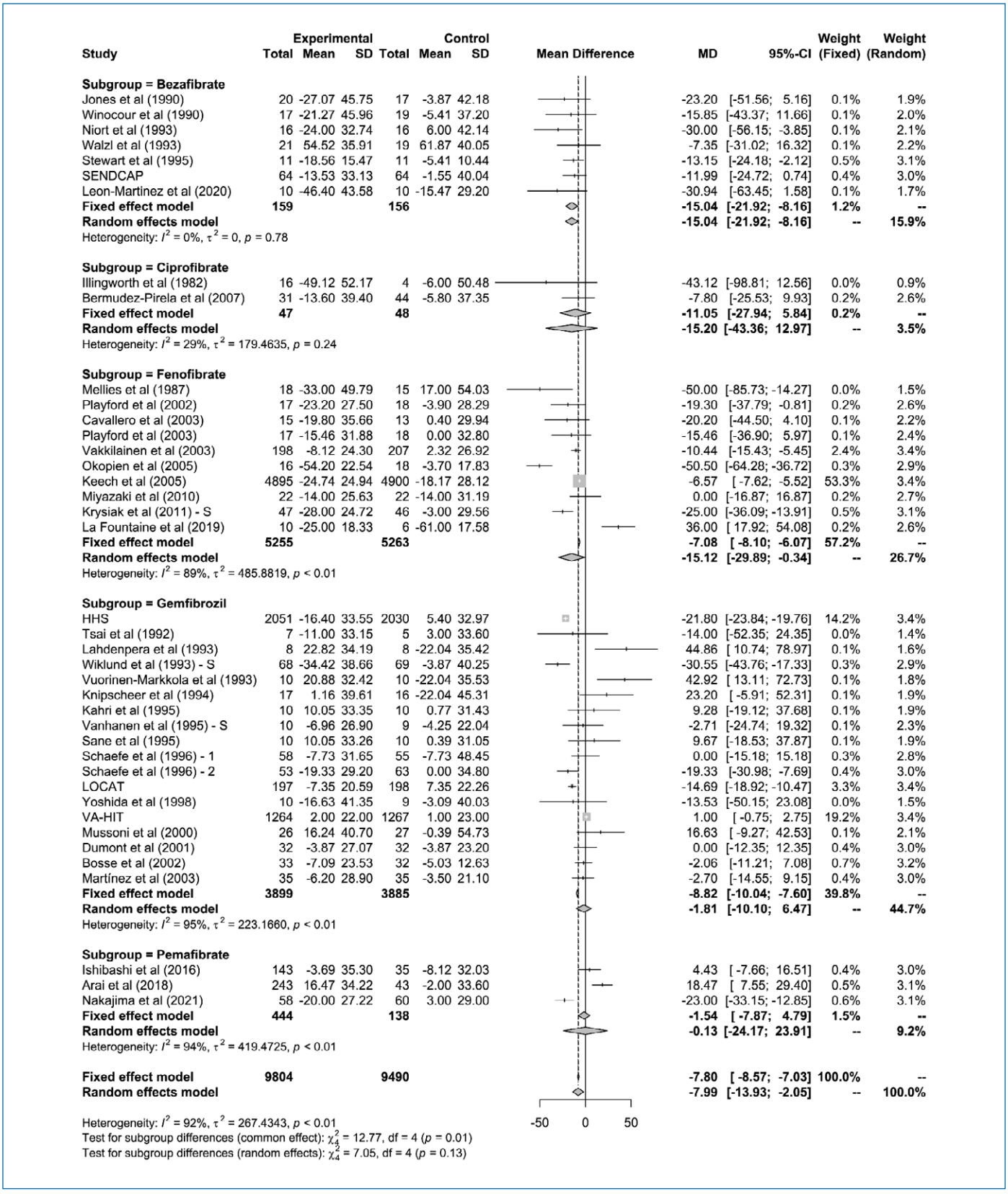

Figure 1B | Effects on low-density lipoprotein cholesterol (LDL-C).

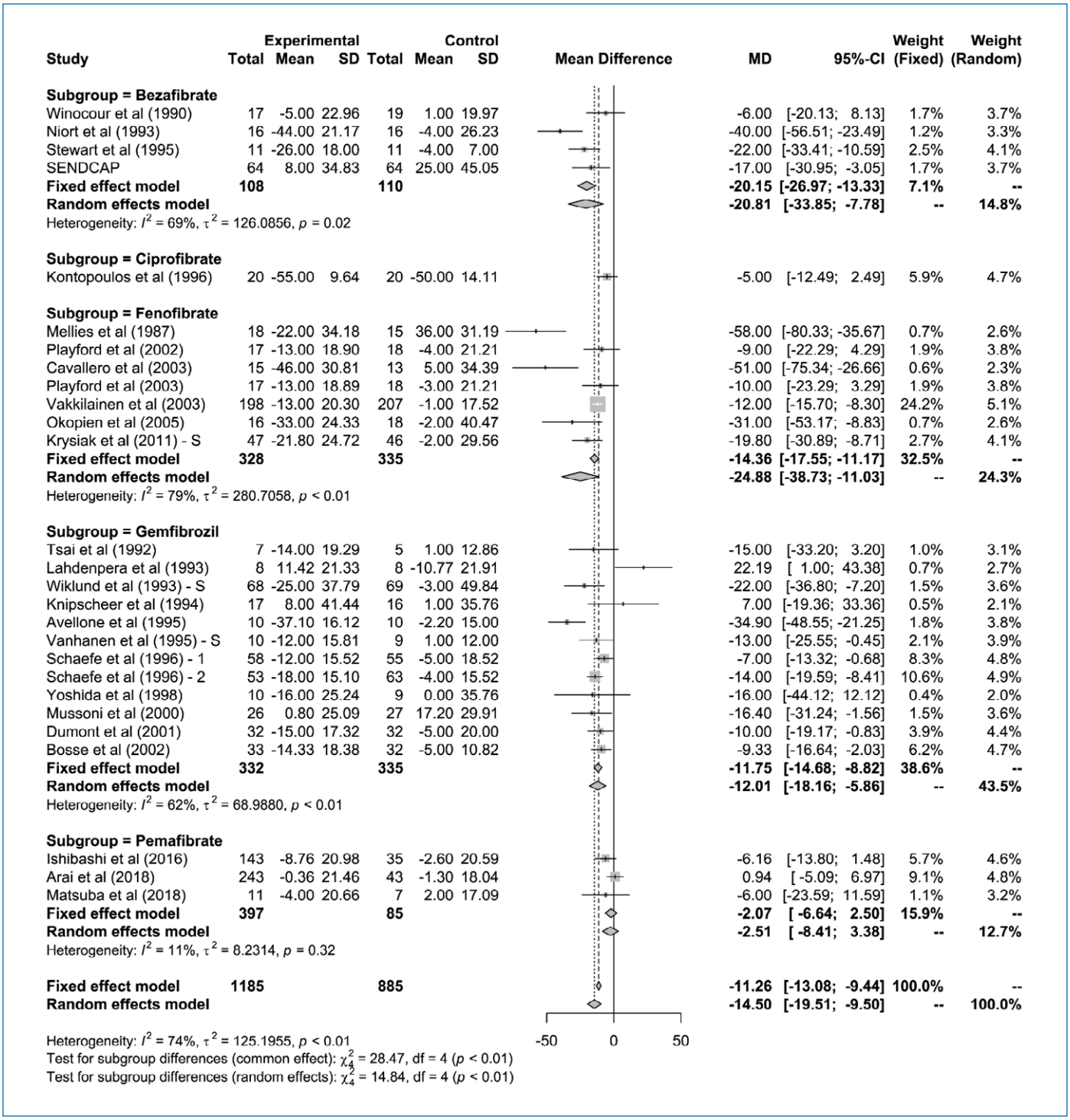

Figure 1C | Effects on apolipoprotein B (ApoB).

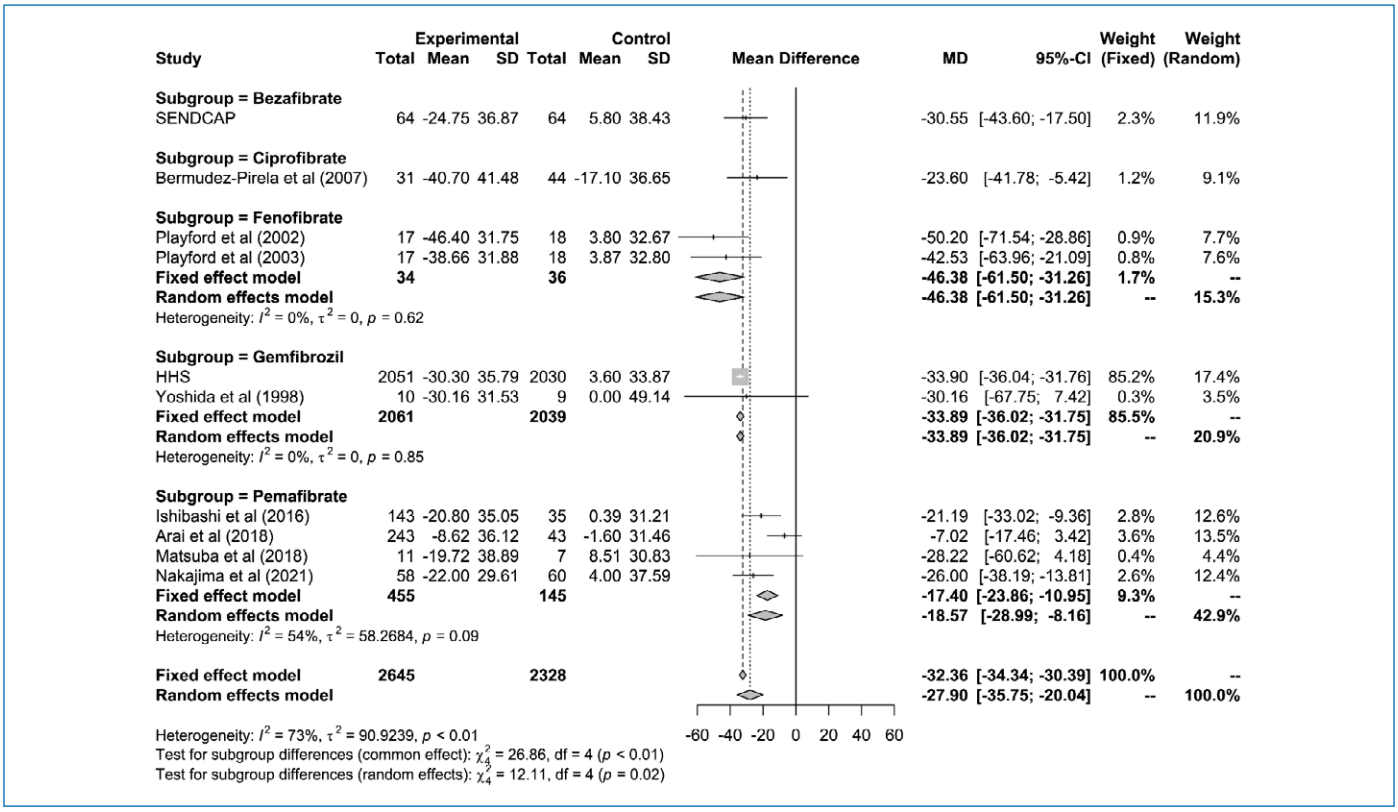

Figure 1D | Effects on non-high-density lipoprotein cholesterol (non-HDL-C).

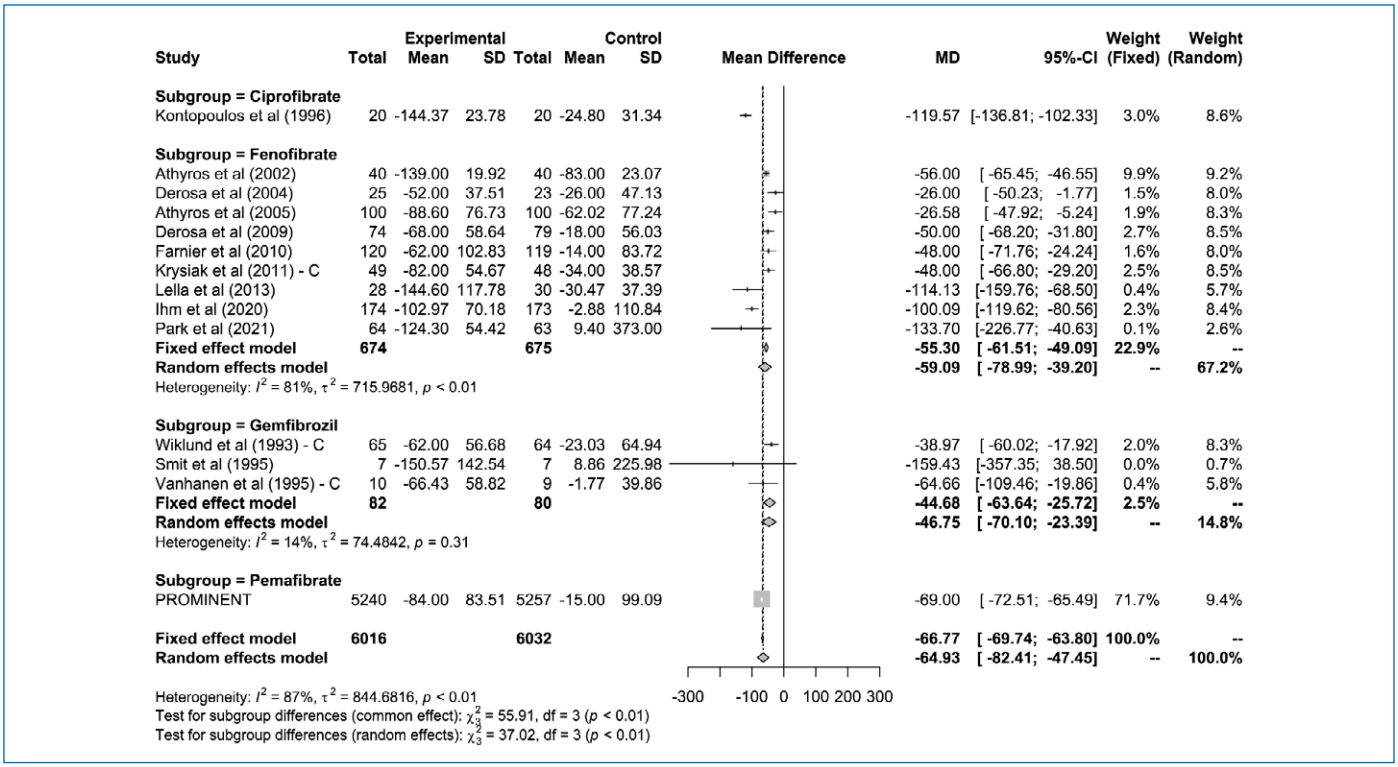

Figure 2A | Lipid-modifying effects of fibrates added to statin therapy. Panel A: effects on triglycerides (TG); panel B: effects on low-density lipoprotein cholesterol (LDL-C); panel C: effects on apolipoprotein B (ApoB); Panel D: effects on non-high-density lipoprotein cholesterol (non-HDL-C). Effects on triglycerides (TG).

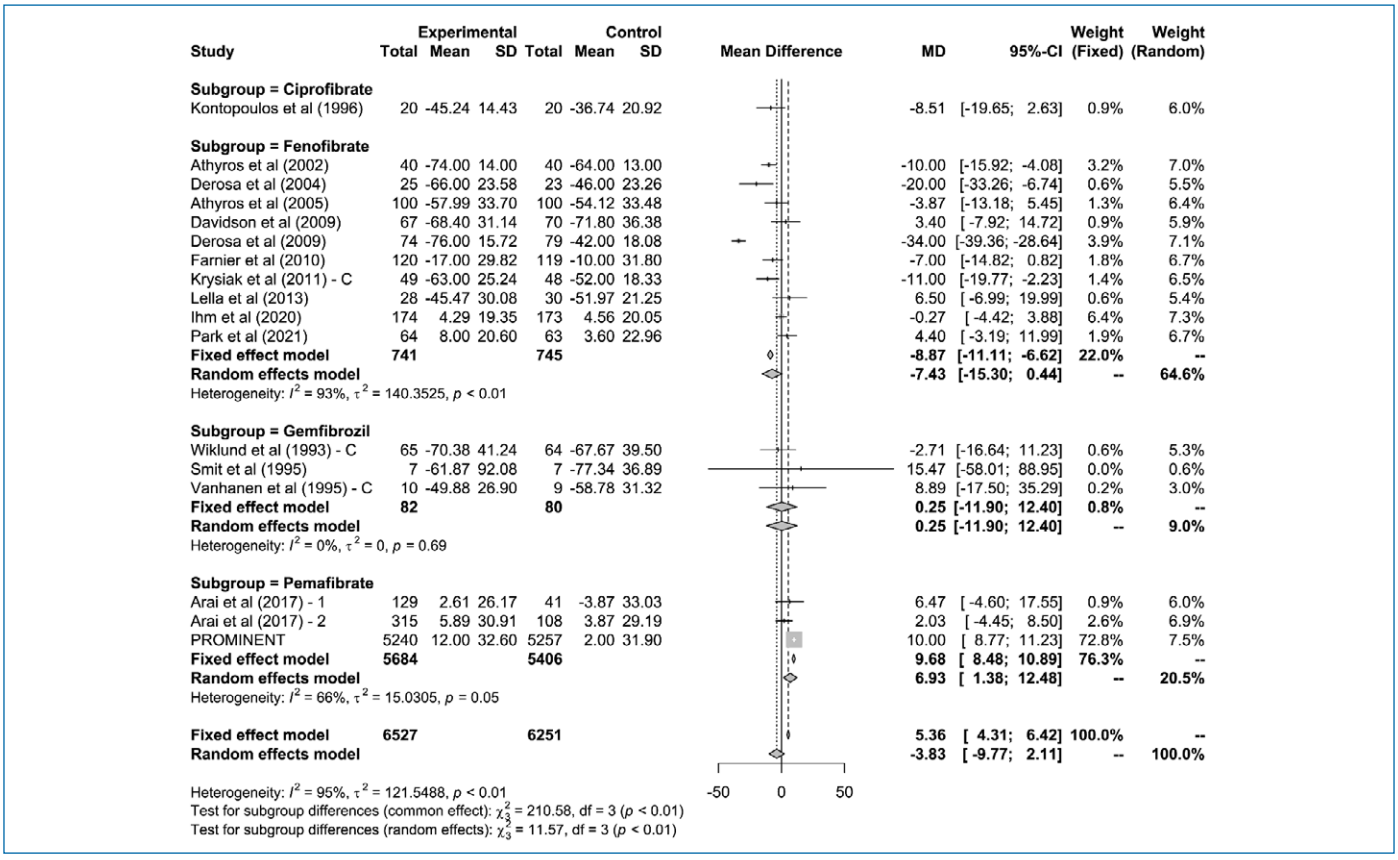

Figure 2B | Effects on low-density lipoprotein cholesterol (LDL-C).

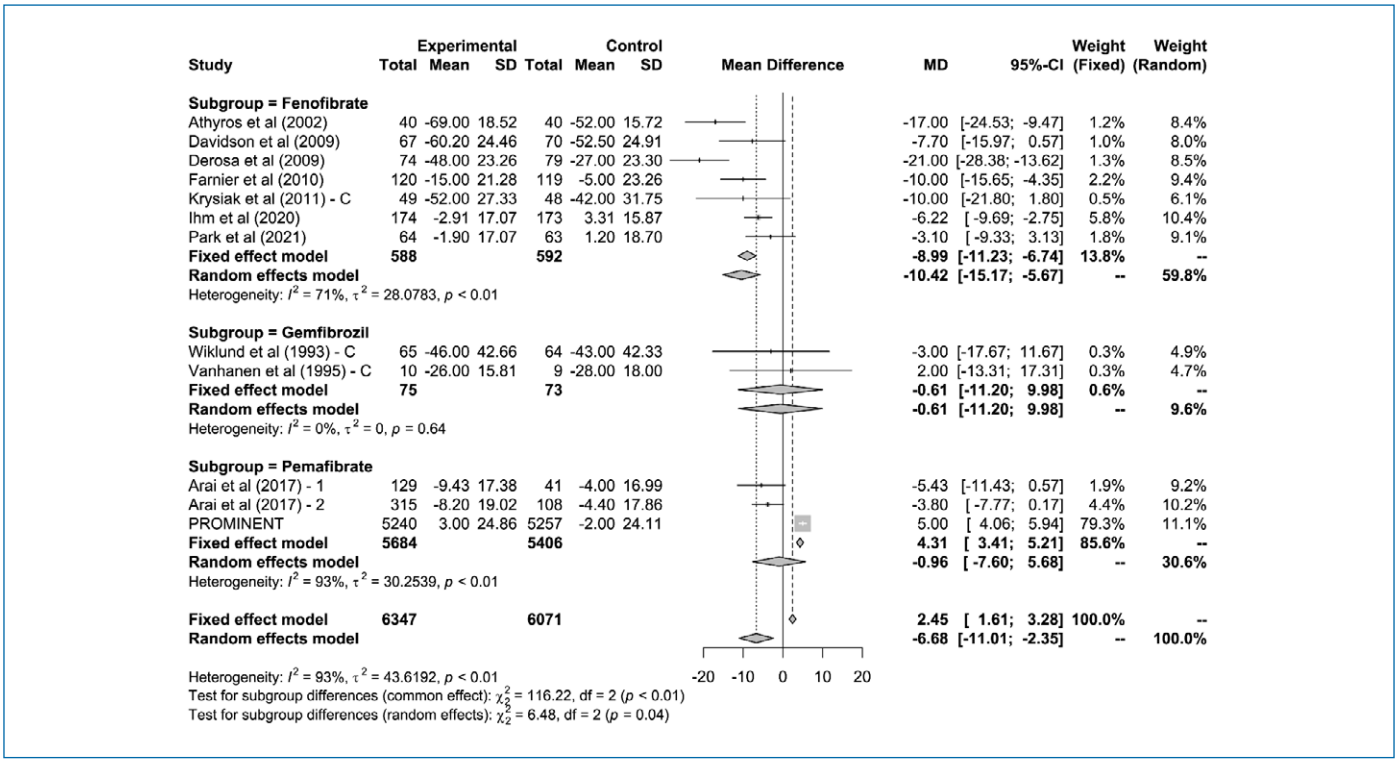

Figure 2C | Effects on apolipoprotein B (ApoB).

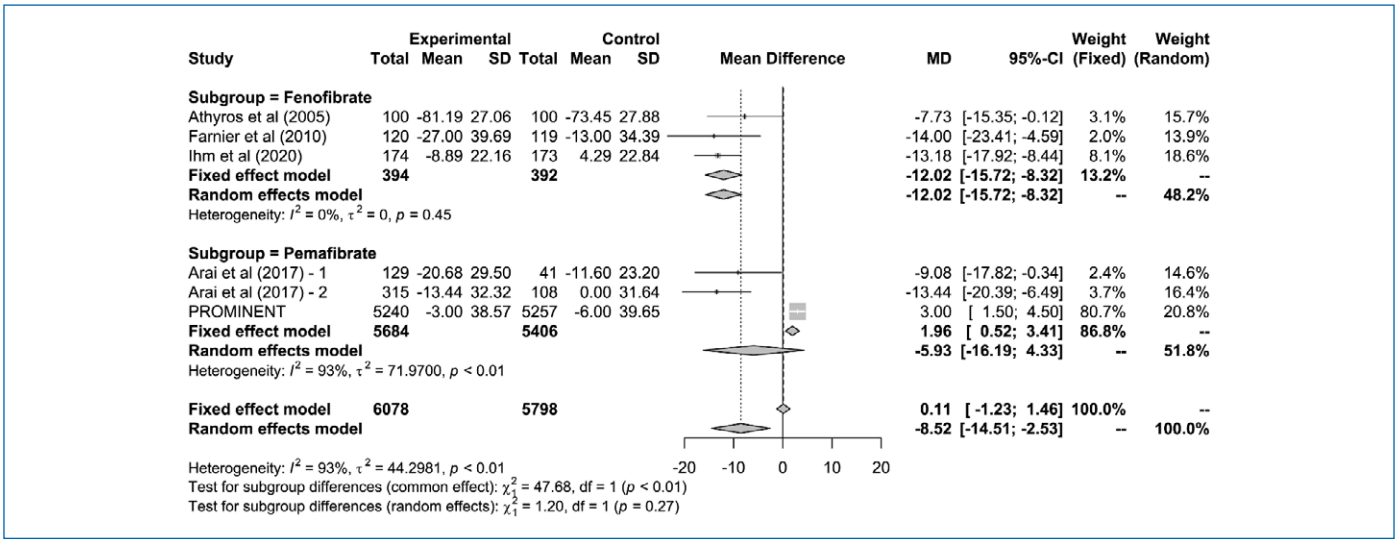

Figure 2D | Effects on non-high-density lipoprotein cholesterol (non-HDL-C).

bezafibrate consistently lowered both LDL-C and ApoB, but only fenofibrate confirmed these effects whether used as monotherapy or in combination with statins.

These findings support the hypothesis that not all fibrates are pharmacologically or clinically equivalent. Despite sharing the PPAR-α agonist mechanism, fibrates differ in their affinity for nuclear receptors, tissue-specific activity, and effects on lipid-modifying gene expression. Fenofibrate's capacity to reduce both ApoB and LDL-C suggests broader atherogenic lipoprotein modulation, which may underlie the subgroup benefits observed in large cardiovascular outcome trials such as FIELD and ACCORD-Lipid, particularly among patients with atherogenic dyslipidemia [19, 20].

Regarding pemafibrate, despite its favorable impact on TG levels, it failed to lower – and even increased – LDL-C levels in the statin-combination subgroup. These findings may in part explain the neutral results of the PROMINENT trial [21], where pemafibrate did not reduce major cardiovascular events in patients with type 2 diabetes and atherogenic dyslipidemia despite significant TG lowering. This reinforces the notion that reduction in TGs alone, without corresponding improvement in ApoB or LDL-C, may be insufficient to achieve cardiovascular risk reduction.

Interestingly, gemfibrozil showed moderate ApoB reduction but had no significant effect on LDL-C. Historical trials (HHS [22], VA-HIT [23]) showed cardiovascular benefit with gemfibrozil, but their results predate modern statin use and may reflect unique metabolic effects, including modulation of HDL particle functionality [24], which were not captured in our lipid-focused analysis. Gemfibrozil was shown to effectively reduce TG, ApoB, and non-HDL cholesterol, but its use in combination with statins is contraindicated, as leads to increased plasma levels of statins, raising the risk of severe myopathy and rhabdomyolysis [12].

Limitations

Several limitations of our analysis warrant mention. First, we included trials with varying durations, populations, and background therapies, which may contribute to heterogeneity. Second, few trials directly comparing fibrates were available; thus, comparisons among agents rely on indirect data. Third, our analysis focused on surrogate lipid markers rather than hard cardiovascular endpoints, though ApoB and LDL-C are well-validated biomarkers of risk. Finally, data on newer agents such as pemafibrate remain limited, and further investigation is needed to define their long-term clinical utility.

Conclusions

This meta-analysis reveals significant heterogeneity in the lipid-modifying effects of fibrates. Fenofibrate demonstrates the most consistent and favorable profile, significantly reducing TG, LDL-C, and apoB levels both as monotherapy and in combination with statins. Gemfibrozil exerts a modest effect, primarily on apoB, however, its use cannot be considered in combination with statins. Pemafibrate, despite potent TG lowering, fails to improve – or may even worsen – LDL-related parameters. The findings of this meta-analysis underscore the importance of distinguishing between fibrates when considering adjunctive lipid-lowering therapy. These differences should guide the selection of fibrates in clinical practice, especially for patients with mixed dyslipidemia or residual risk despite statin therapy.

Conflict of Interest

Sining Xie, Federica Galimberti, Elena Olmastroni report no disclosures. Alberico L Catapano received research funding and/or honoraria for advisory boards, consultancy or speaker bureau from Amarin, Amgen, Amryt, AstraZeneca, Daiichi Sankyo, Esperion, Ionis Pharmaceutical, Medscape, Menarini, Merck, Novartis, Peer Voice, Pfizer, Recordati, Regeneron, Sandoz, Sanofi, The Corpus, Ultragenyx, Viatris. Manuela Casula received honoraria for speaker bureau from Sobi and Ultragenyx.

Author contributions

Sining Xie and Manuela Casula made the contributions to the concept and design. Sining Xie and Federica Galimberti were responsible for the acquisition, and interpretation of data. Sining Xie and Elena Olmastroni did the statistical analysis. Sining Xie and Elena Olmastroni prepared the draft of the manuscript. All authors contributed to the critical revision of the manuscript. Alberico L. Catapano provided overall supervision of the study.

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Supplementary material

Effects of fibrates on lipid profile: a meta-analysis of randomized controlled trials

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Search Strategy

Details of searching strategies:

PubMed

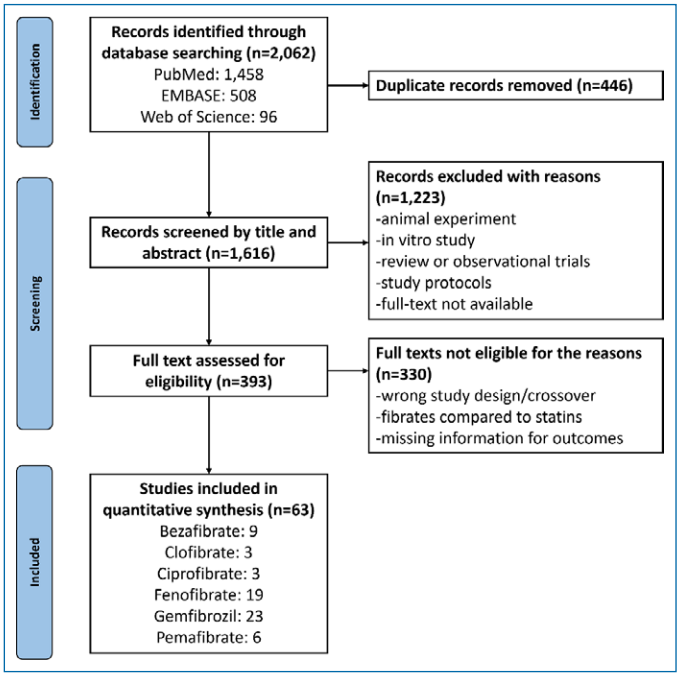
(Randomized controlled trial[pt] OR controlled clinical trial[pt] OR "randomized controlled trials as topic"[MeSH Terms] OR "random allocation"[MeSH Terms] OR "double-blind method"[MeSH Terms] OR "single-blind method"[MeSH Terms] OR randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]) OR "single blind procedure"[All Fields] OR "double blind procedure"[All Fields] OR (("random allocation"[MeSH Terms] OR ("random"[All Fields] AND "allocation"[All Fields]) OR "random allocation"[All Fields] OR "randomization"[All Fields]) AND controlled[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "trial"[All Fields])) OR ("controlled clinical trial"[Publication Type] OR "controlled clinical trials as topic"[MeSH Terms] OR "controlled clinical trial"[All Fields]) OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trials"[All Fields] OR "randomised controlled trials"[All Fields]) OR (randomly[All Fields] AND controlled[All Fields] AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "trial"[All Fields])) OR (randomly[All Fields] AND ("controlled clinical trial"[Publication Type] OR "controlled clinical trials as topic"[MeSH Terms] OR "controlled clinical trial"[All Fields])) OR "double-dummy trial"[All Fields] OR "double-masked trial"[All Fields]) AND ((("Fibric Acids"[Mesh]) OR ((((((((((Methyl-2-Phenoxypropanoic Acid Derivatives[Title/Abstract]) OR (Methyl 2 Phenoxypropanoic Acid Derivatives[Title/Abstract])) OR (Fibric Acid Derivatives[Title/Abstract])) OR (Acid Derivatives, Fibric[Title/Abstract])) OR (2-Phenoxy Isobutyric Acids[Title/Abstract])) OR (2 Phenoxy Isobutyric Acids[Title/Abstract])) OR (Isobutyric Acids, 2-Phenoxy[Title/Abstract])) OR (2-Phenoxy-2-Methylpropionic Acid Derivatives[Title/Abstract])) OR (2 Phenoxy 2 Methylpropionic Acid Derivatives[Title/Abstract])) OR (Fibrates[Title/Abstract])) OR (Fibrate[Title/Abstract] OR ("bezafibrate"[MeSH Terms] OR "bezafibrate"[All Fields] OR "gemfibrozil"[MeSH Terms] OR "gemfibrozil"[All Fields] OR "clofibrate"[MeSH Terms] OR "clofibrate"[All Fields] OR "clofibrates"[All Fields] OR "clofibric"[All Fields] OR "fenofibrate"[MeSH Terms] OR "fenofibrate"[All Fields] OR "procetofen"[All Fields] OR "procetofene"[All Fields] OR "ciprofibrate"[Supplementary Concept] OR "ciprofibrate"[All Fields] OR "fenofibrate"[MeSH Terms] OR "fenofibrate"[All Fields] OR "fenofibrates"[All Fields] OR "fenofibric"[All Fields] OR "r 2 3 benzoxazol 2 yl d4 3 4 methoxyphenoxy d7 propyl amino methyl phenoxy butanoic acid"[Supplementary Concept] OR "r 2 3 benzoxazol 2 yl d4 3 4 methoxyphenoxy d7 propyl amino methyl phenoxy butanoic acid"[All Fields] OR "pemafibrate"[All Fields])))))) AND (english[Lang]) NOT (meta-analysis[Filter] OR review[Filter] OR systematicreview[Filter]).

Embase

('gemfibrozil':ti OR 'fenofibrate':ti OR 'bezafibrate':ti OR 'clofibrate':ti OR 'ciprofibrate':ti OR 'pemafibrate':ti OR 'fenofibric acid':ti) AND [english]/lim NOT ('meta-analysis' OR 'review' OR 'commentary' OR 'editorial' OR 'protocol' OR 'cohort study' OR 'design') AND ('controlled clinical trial'/de OR 'randomized controlled trial'/de) AND 'article'/it

Web of Science

TS=(fenofibrate OR gemfibrozil OR bezafibrate OR clofibrate OR ciprofibrate OR pemafibrate OR renofibrate or fenofibric acid) AND TS=("randomized controlled trial" OR "controlled clinical trial").



Supplementary Figure 1 | Flow diagram of literature search and study selection.

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