Is More Better? Association of Cholesterol-Lowering Therapy Class With Outcomes in Patients With Abdominal Aortic Aneurysms, A TriNetX Cohort Study

Asad Siddiqui BA, Firas Batrash BA, Devan Girish, Harish Karthikeyan BA, Mahmoud Kutmah BA, Amani Raheel MD, Jamal Malik DO

University of Missouri Kansas City School of Medicine

March 7, 2026

Disclosure

Nothing to disclose

UMKC

Background

High-dose statin therapy is associated with reduced AAA growth and improved clinical outcomes. (Skovbo et al., 2025)

- ❖Prospective cohort of 998 men with small (30–55 mm) screening-detected AAAs

❖Higher statin intensity associated with lower risk of repair, rupture, and death

- ❖Dose-dependent effect
- ❖Each increase in statin dose associated with slower AAA growth (~0.22 mm/year reduction)

UMKC

Common HLD Adjuncts

- **Combination therapy represents a promising approach to enhance LDL reduction and reduce ASCVD risk.**

Ezetimibe + Statin (Valvukis 2018)	**Fibrate + Statin** (ACCORD Lipid Trial)
Ezetimibe added to statin therapy provides significant additional LDL-C reduction (25% further lowering)	**Fibrates + simvastatin did not significantly reduce fatal cardiovascular events, nonfatal myocardial infarction, or nonfatal stroke compared with simvastatin alone.**

Purpose

- To evaluate whether combination lipid-lowering therapy (dual-modality treatment targeting hyperlipidemia) is associated with improved clinical outcomes in patients with abdominal aortic aneurysm (AAA) compared to statin monotherapy following AAA diagnosis.

- Relative to statin therapy alone, is there a synergistic effect between two lipid-lowering modalities that results in meaningful risk reduction?
  - aneurysm-related progression
  - need for repair
  - AAA rupture
  - mortality

UMKC

Methods

- Using **TriNetX**, we identified **adults** (≥18 years) with a diagnosis of AAA, without rupture
  - Started on a HLD lowering agent within 6 months of dx
- **Exposure Groups:** Patients stratified by cholesterol-lowering therapy within 6 months of AAA diagnosis, using ICD-10, CPT & RxNorm.
  - Statin monotherapy (n=63,226)
  - Statin + Ezetimibe based therapy (n=2,664)
  - Statin + Fibrate therapy (n=1,760)

UMKC

Methods, continued

- Outcomes included: 5 years mortality, MACE (major adverse cardiac events), rupture, and repair
- Patients were 1:1 propensity matched: Age, Sex, HTN, Smoking History, HLD, Diabetes, BMI > 30, CKD, CAD, and on antiplatelet therapy
- **Statistical Analysis:** Adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated; statistical significance defined as $p < 0.05$

Demographic Data

Fibrate + Statin Cohort

Characteristic	Statin (n = 1749)	Fibrate + Statin (n = 1749)	P-value
Age, mean (SD)	70.4 (8.9)	70.4 (9.1)	0.823
White, n (%)	1463 (83.6%)	1456 (83.2%)	0.75
Male, n (%)	1402 (80.2%)	1407 (80.4%)	[illegible]

Ezetimibe + Statin Cohort

Characteristic	Statin (n = 2646)	Ezetimibe + Statin (n = 2646)	P-value
Age, mean (SD)	72.6 (8.6)	72.5 (8.6)	0.696
White, n (%)	2098 (79.3%)	2078 (78.5%)	0.5
Male, n (%)	2003 (75.7%)	1979 (74.8%)	0.445

UMKC

Outcomes

Fibrate + Statin Cohort

Outcomes (5yr)	**OR**	**95% CI**
Mortality	1.033	(0.866, 1.231)
Rupture	0.575	(0.350, 1.146)
MACE	1.071	(0.926, 1.239)
Repair	1.082	(0.835, 1.401)

Ezetimibe + Statin Cohort

Outcomes (5yr)	**OR**	**95% CI**
Mortality	1.574	(0.837, 1.815)
Rupture	1.332	(0.880, 2.010)
MACE	1.226	(0.901, 1.378)
Repair	1.184	(0.958, 1.464)

No statistically significant results noted in either cohort

Discussion

- **No significant improvement with dual therapy:** In patients with AAA, combination lipid-lowering therapy (statin + ezetimibe or statin + fibrate) was not associated with significantly improved outcomes compared with statin monotherapy.
- **Consistent with fibrate literature:** Prior studies have shown limited cardiovascular benefit from adding fibrates to statins, supporting the lack of additional outcome benefit observed in our analysis.
- **Ezetimibe benefits may not translate to AAA:** Although ezetimibe–statin therapy improves LDL-C reduction and ASCVD outcomes, these effects may not significantly impact AAA-related disease progression or outcomes.

UMKC

Limitations

Observational Retrospective Design	Database Constraints	Limited clinical granularity due to lack of stratification of aneurysm size

Conclusion

- **Statin monotherapy demonstrated similar AAA-related outcomes compared with dual lipid-lowering therapy** (statin + ezetimibe or statin + fibrate) in this retrospective cohort.
- **Additional lipid-lowering beyond statin therapy was not associated with significant improvement in AAA outcomes** despite evidence of cardiovascular benefit in other ASCVD populations.
- **These findings suggest the benefit of combination lipid therapy in AAA may be limited**, highlighting the need for further prospective studies to better define optimal medical management in this population.

UMKC

Citations

1. Dawson, J. A., Choke, E., Loftus, I. M., Cockerill, G. W., & Thompson, M. M. (2011). A randomised placebo-controlled double-blind trial to evaluate lipid-lowering pharmacotherapy on proteolysis and inflammation in abdominal aortic aneurysms. *European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery*, *41*(1), 28–35. https://doi.org/10.1016/j.ejvs.2010.08.023
2. Ginsberg, H. N., Elam, M. B., Lovato, L. C., Crouse, J. R., Leiter, L. A., Linz, P., Friedewald, W. T., Buse, J. B., Gerstein, H. C., Probstfield, J., Grimm, R. H., Ismail-Beigi, F., Bigger, J. T., Goff, D. C., Cushman, W. C., Simons-Morton, D. G., & Byington, R. P. (2010). Effects of combination lipid therapy in type 2 diabetes mellitus. *New England Journal of Medicine*, *362*(17), 1563–1574. https://doi.org/10.1056/NEJMoa1001282
3. Skovbo, J. S., Obel, L. M., Diederichsen, A. C. P., Steffensen, F. H., Frost, L., Lambrechtsen, J., Busk, M., Urbonaviciene, G., Egstrup, K., Dahl, M., Karon, M., Rasmussen, L. M., Hallas, J., & Lindholt, J. S. (2025). Association of Statin Treatment and Dose With the Clinical Course of Small Abdominal Aortic Aneurysms in Men: A 5-Year Prospective Cohort Study From 2 Population-Based Screening Trials. *Circulation*, *152*(6), 384–396. https://doi.org/10.1161/CIRCULATIONAHA.125.07454
4. Vavlukis, M., & Vavlukis, A. (2018). Adding ezetimibe to statin therapy: latest evidence and clinical implications. *Drugs in context*, *7*, 212534. https://doi.org/10.7573/dic.212534

UMKC

Thanks

- Dr. Jamal Malik, UHTMC Vascular Surgery, UMKC Assistant Professor
- Dr. Amani Raheel PGY3, UMKC General Surgery

Contact Information

Asad Siddiqui M3, UMKC School of Medicine, ahsh3r@umsystem.edu