

Appendix 1 (as submitted by the authors): Information loss associated with data aggregation - an example

Consider a 60 year old non-diabetic white male with CHD and low HDL cholesterol. The patient has high LDL cholesterol but is intolerant to statins, so you consider adding a fibrate to his treatment. A recently published meta-analysis(1) concluded that *“Increasing HDL levels via pharmacological manipulation beyond optimal lipid lowering therapy for secondary prevention is not beneficial.”* Thus, deferring fibrates would seem to be the logical recommendation. However, a closer look may lead to a different conclusion. The FIELD study(2), which was included in the meta-analysis, did not demonstrate reduced cardiovascular mortality among fibrate-treated participants, however it did find a significant reduction in the rate of non-fatal myocardial infarction and coronary revascularization in those patients. The meta-analysis’s “bottom line” may thus be misleading. Moreover, the VA-HIT study(3) (also included in the meta-analysis) found that gemfibrozil treatment resulted in reduced rate of coronary death. Of note, these trials were also conducted on different populations, which may have contributed to their different conclusions. The VA-HIT study participants were all men, mostly (75%) non-diabetic and all had known CHD. The FIELD study had 63% male participants, only included diabetics and had a relatively low rate (22%) of CHD. Overall, our patient seems more similar to the VA-HIT trial population than to that of the FIELD study. This, in our opinion, may suggest that for our particular patient, the former is more relevant than the latter or the meta-analysis that includes both.

References:

- (1) Kaur N, Pandey A, Negi H, Shafiq N, Reddy S, Kaur H, et al. Effect of HDL-Raising Drugs on Cardiovascular Outcomes: A Systematic Review and Meta-Regression. *PLOS One*. 2014;9(4):e94585.
- (2) Keech A, Simes RJ, Barter P, Best J, Scott R, Taskinen MR, et al. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. *Lancet*. 2005 Nov 26;366(9500):1849–61.
- (3) Rubins HB, Robins SJ, Collins D, Fye CL, Anderson JW, Elam MB, et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. *N Engl J Med*. 1999 Aug 5;341(6):410–8.