

## INTRODUCTION

Published reports have questioned the benefit of serum HDL-cholesterol (HDL-C) raising and/or triglycerides (TG) lowering for patients at increased risk for cardiovascular (CV) events.

## METHODS

AIM-HIGH (NCT00120289) patient-level data, publicly available through NHLBI data repository, were reanalyzed to evaluate the effects of HDL-C raising and TG lowering treatment strategies (background statin ± extended-release niacin therapy) on major adverse cardiac events (MACE: a composite of myocardial infarction, stroke, and CV death) and all-cause mortality.

- Four groups, based on percent change from baseline to 6 months in HDL-C and TG due to antidyslipidemic therapy, were compared (Table 1). A percent change that exceeded total biological variation for each of the two analytes and average antidyslipidemic treatment effect was considered relevant and used to define groups.
- Time-to-first-event analyses were performed, with a multivariate analysis used to adjust for age, gender, body mass index (BMI), waist circumference, established cardiovascular disease (CVD), history of hypertension, diabetes, or metabolic syndrome, and estimated glomerular filtration rate [eGFR].

Table 1. Baseline Levels and Percent Change at 6 Month in HDL-C and TG by Group

| Groups by Percent Change in Lipids at 6 Months |                                        | Baseline (Mean±SD) |            | 6-Month Change from Baseline (Mean±SD) |        |
|------------------------------------------------|----------------------------------------|--------------------|------------|----------------------------------------|--------|
|                                                |                                        | HDL-C (mg/dL)      | TG (mg/dL) | HDL-C (%)                              | TG (%) |
| Group 1 (n=1007)                               | HDL-C raising >10%<br>TG lowering >25% | 35±6               | 192±70     | 35±19                                  | -45±13 |
| Group 2 (n=925)                                | HDL-C raising >10%<br>TG lowering <25% | 34±5               | 172±64     | 24±14                                  | 6±30   |
| Group 3 (n=292)                                | HDL-C raising <10%<br>TG lowering >25% | 35±5               | 200±68     | 1.5±7.4                                | -38±10 |
| Group 4 (n=948)                                | HDL-C raising <10%<br>TG lowering <25% | 36±5               | 176±62     | -0.9±8.6                               | 17±41  |

Table 2. Characteristics of the subjects at baseline.

|                           | Group 1 (N=1007) | Group 2 (N=925) | Group 3 (N=292) | Group 4 (N=948) |
|---------------------------|------------------|-----------------|-----------------|-----------------|
|                           | n (%)            |                 |                 |                 |
| Age ≥65 yr                | 508 (50)         | 403 (44)        | 132 (45)        | 407 (43)        |
| Men                       | 833 (83)         | 805 (87)        | 255 (87)        | 824 (87)        |
| BMI ≥30 kg/m <sup>2</sup> | 508 (50)         | 523 (57)        | 171 (59)        | 537 (57)        |
| WC ≥88 cm (women)         | 139 (80)         | 101 (84)        | 32 (86)         | 101 (81)        |
| WC ≥102 cm (men)          | 559 (67)         | 574 (71)        | 185 (73)        | 598 (73)        |
| Established CVD           | 965 (96)         | 898 (97)        | 286 (98)        | 917 (97)        |
| History of Hypertension   | 722 (72)         | 630 (68)        | 214 (73)        | 681 (72)        |
| History of Diabetes       | 333 (33)         | 308 (33)        | 104 (36)        | 303 (32)        |
| History of Metabolic Syn. | 825 (82)         | 726 (78)        | 250 (86)        | 763 (80)        |
| eGFR ≤60 mL/min           | 140 (14)         | 89 (9.62)       | 34 (12)         | 104 (11)        |

Abbreviations: BMI, Body Mass Index; CVD, Cardiovascular Disease; eGFR, Estimated Glomerular Filtration rate; WC, Waist Circumference.

Kaplan-Meier curves for MACE showed:

- a significant difference among the four groups overall (**p<0.05** by log-rank test) (Fig. 1) and in men (**p<0.05**) (Fig. 2B); and
- no difference among the four groups in women (Fig. 2A).

The risk of MACE was:

- unexpectedly increased in the group with the greatest drug response (Group 1) compared to that with the least (Group 4) overall (unadjusted HR 1.49; 95% CI 1.14 to 1.98, **p<0.01**);
- increased in Group 1 compared to Group 4 in men (unadjusted HR 1.57; 95% CI 1.17 to 2.11; **p<0.01**);
- not different among the four groups in women; and
- not different between Group 2 (predominantly HDL-C raising) or Group 3 (predominantly TG lowering) compared to Group 4 (least changes in HDL-C and TG) overall, in men, or in women.

Significant risk factors for MACE included:

- men, age ≥65 years, eGFR ≤60 mL/min in the entire population (adjusted HR 1.47; 95% CI 1.10 to 1.94, **p<0.01**); and
- age ≥65 years, eGFR ≤60 mL/min in men (adjusted HR 1.51; 95% CI 1.12 to 2.03, **p<0.01**).

The risk of all-cause mortality was not different among the four groups (data not shown).

## RESULTS

Figure 1. Kaplan-Meier Curves for MACE by Group

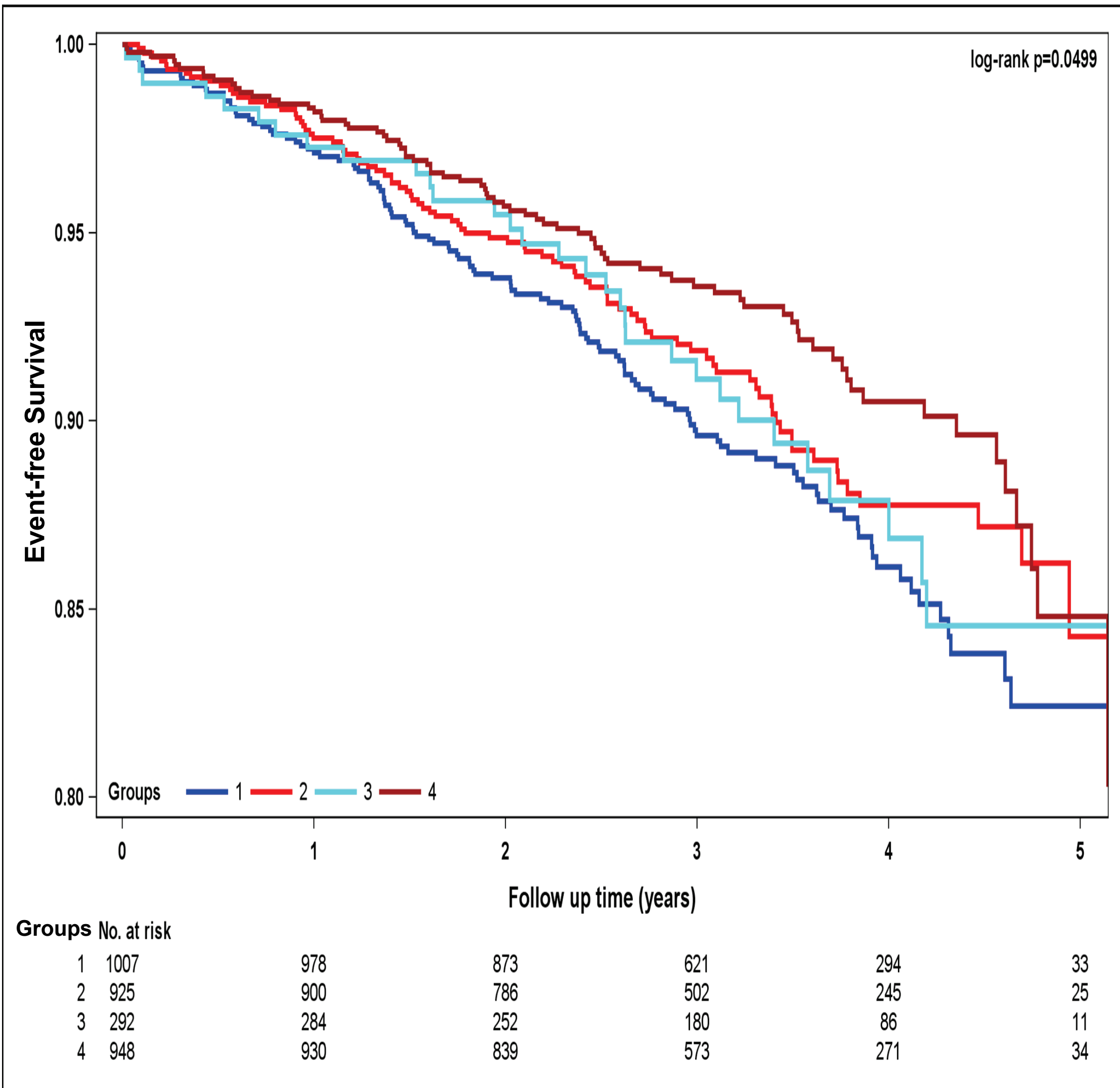
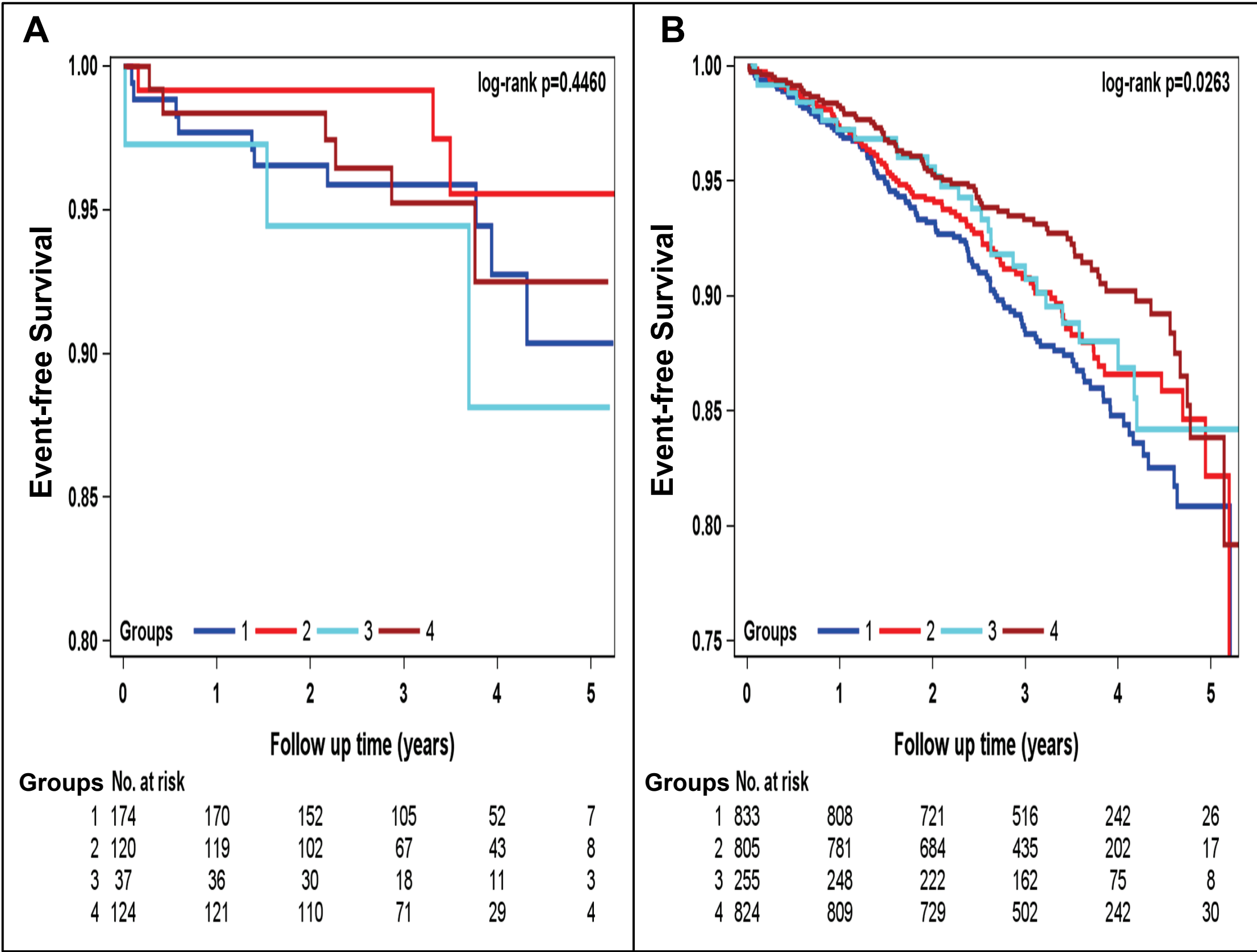


Figure 2. Kaplan-Meier Curves for MACE by Group in women (A) and men (B)



## CONCLUSION

- In response to background statin therapy with/without extended-release niacin, the group with both >10% increase in HDL-C and >25% decrease in TG (Group 1) showed an unexpected increase in MACE risk in these *post hoc* hypothesis-generating secondary analyses of the AIM-HIGH trial.
- Additional studies are needed to further define lipid thresholds associated with MACE, investigate potential mechanisms for our findings, and validate them in other populations.

DISCLOSURES:  
NONE

DISCLAIMER: The contents of this poster are solely the responsibility of the authors, and do not represent the official views of the NIH, the FDA, Howard University, or Ohio State University. These analyses were conducted on publicly available data from BioLINCC.