Sulaica et al raise 3 relevant issues related to our analysis: (1) clinical presentation with (un)stable plaque; (2) timing of aspirin discontinuation; and (3) sex differences in safety and efficacy.

Sulaica et al state that the lack of difference in ischemic outcomes may partially be explained by including patients with low-risk coronary artery disease (CAD) and that extrapolation to patients with non-ST-segment elevation myocardial infarction should be done with caution. While it is not simple to define high-risk CAD, we acknowledge that the trials included heterogeneous populations of patients with CAD at varying risk. However, they were not at low risk. In the RE-DUAL PCI trial, for instance, more than 60% of the trial population had at least 1 complex factor, involving either clinical factors (acute coronary syndrome [ACS], renal impairment, or low left ventricular ejection fraction) or procedural factors (multivessel disease, bifurcation lesions, or unprotected left main). In the other included trials, most patients were older, had median CHA2DS2-VASc scores of around 4, and frequently presented with ACS, including non-ST-segment elevation myocardial infarction. When looking at ischemic outcomes, subgroup analyses from the PIONEER AF-PCI,3 RE-DUAL PCI,2 and AUGUSTUS4 trials found no interaction between treatment effects and type of index event for ischemic outcomes. While underpowered and thus exploratory in nature, combining the individual patient data would permit exploration of subgroups of high-risk patients with CAD. However, there would have to be a substantial increase in CAD risk (and thus ischemic risk reduction) to counterbalance the important increased bleeding risk with aspirin.

We agree that it is important to acknowledge that, in all the included trials, aspirin was discontinued at least a few days after the index procedure and/or ACS event. We are currently exploring the timing of bleeding and ischemic events to further delineate the optimal duration of aspirin for a given patient. This would allow for more personalized antithrombotic strategies instead of a one-size-fits-most approach.

Finally, we agree with Sulaica et al that female patients are underrepresented (20% to 29%) in the included trial populations. This is a valuable observation, particularly given that female sex is an important risk factor for bleeding. Promoting enrollment in randomized clinical trials to reflect the population as a whole (whether it is sex, race/ethnicity, age, socioeconomic status, or other factors) is a desirable goal. Subgroup analyses of sex from all the available trials did not demonstrate heterogeneity of the aspirin effect in terms of bleeding or ischemic events.2-5 As such, we believe that the observed decreases in bleeding warrant dropping aspirin in both women and men.

Ralf E. Harksamp, MD, PhD
John H. Alexander, MD, MHS
Renato D. Lopes, MD, PhD

Author Affiliations: Duke Clinical Research Institute, Durham, North Carolina (Harksamp, Alexander, Lopes); Amsterdam UMC, Academic Medical Center, Amsterdam, the Netherlands (Harksamp).

Corresponding Author: Renato D. Lopes, MD, PhD, Duke Clinical Research Institute, 200 W Morris St, Durham, NC 27701 (renato.lopes@duke.edu).

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CORRECTION

Errors in Table 1 and Figures 2 and 3: The Original Investigation titled “Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83 000 Individuals in 21 Randomized Clinical Trials: a Meta-analysis,” published August 2019, contained errors in Table 1 and Figures 2 and 3. In Table 1, the study period of the Vitamin D in Isolated Systolic Hypertension (VITDISH) study by Witham et al was stated as 2009 to 2001, but this should have been 2009 to 2011. The study period of Vitamin D and Omega-3 Trial (VITAL) study by Manson et al was reported as 2011 to 2014, but this should have been 2011 to 2017. There are also several errors in Figure 2. With respect to the major adverse cardiovascular events (MACE) outcome, the total number of populations in the study by Jiang et al are given as 18 106 in the vitamin D group and 18 176 in the placebo group; these values should be 18 176 and 18 106, respectively. Per resulting recalculation, the upper bound of the 95% CI of the Jackson et al study decreased by 0.01 (from 0.96 to 1.07). In addition, in the same section, the total population for the MACE outcome was reported incorrectly as 39 528 and 39 583 in the vitamin D and placebo groups, respectively; the numbers should instead be 39 598 and 39 513, respectively. In addition, in the MACE portion of Figure 2, several statistical phrases were incorrect, including a 95% CI reported as 0.95 to 1.06 (corrected to 0.95-1.05), a P value stated as .85 (corrected to .93), and an R2 statistic stated as 11% (corrected to 8%).

In the all-cause mortality section of Figure 2, event numbers for the Lehouck et al study are listed as 8 events in the group receiving vitamin D and 0 in those receiving placebo; there should have been reported 9 and 6 events, respectively. With regard to the all-cause mortality values for the study by Jackson et al, the total population numbers were listed as 18 178 and 18 176 for the vitamin D and placebo groups, respectively, but these should have been 18 176 and 18 106, respectively. This change means that the associated 95% CI has been corrected from 0.92 to 1.04 to 0.91 to 1.03. Finally, in Figure 2, the hazard ratio (95% CI) for the cardiovascular mortality subtotal was given as 0.98 (0.90-1.07); this should instead have been 0.98 (0.90-1.07). In Figure 3, there are 2 further errors. With respect to the myocardial infarction outcome, the relative ratio (95% CI) for the Prince et al study is listed as 0.87 (0.31-3.83); it should instead have been stated as 0.67 (0.31-3.93). Finally, the 95% CI of the subtotal in the myocardial infarction section of Figure 3 was stated as 0.03 to 1.08; it should have been 0.93 to 1.08. These errors have been corrected.