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**Overlap of genetic loci for central serous chorioretinopathy with age-related macular degeneration (vol. 141, pg. 499, 2023)**

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**Citation**

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**In Reply** We thank Asensio-Sánchez for sharing his thoughts and appreciate the opportunity to respond to the comments. Asensio-Sánchez has accurately interpreted that this is the first time in the Diabetes Prevention Program Outcomes Study that age-related macular degeneration (AMD) assessment was performed; therefore, one cannot hypothesize on the prevalence or stage of AMD before the images were acquired.<sup>1</sup> The prevalence reported is for the current visit and does not account for previous time points. At the current visit, AMD was identified in 479 participants (30.0%) with early-stage AMD in 229 (14.4%), intermediate AMD in 218 (13.7%), and advanced AMD in 32 (2.0%). Breakdown by treatment arms is given in Figure 2.

We concur with the authors' comment on the crossover effect of metformin, which has also been discussed in detail in the article. We have carefully evaluated this potential confounder across all analysis. First, out-of-study metformin usage was collected from patients to the best possible extent and reported in the study. The mean number of years of any metformin use was 3.59 in the lifestyle arm and 4.35 in the placebo arm compared with 14.67 in the metformin arm. Although participants in the lifestyle and placebo arms also had taken metformin, the number of years exposed was significantly lower than the metformin arm.<sup>2</sup> Second, as shown in Table 2, the analysis for association of metformin with AMD was performed irrespective of the original study arm, which led to the study conclusions. Third, we classified the study population into those who had never used metformin and those who had used metformin, irrespective of number of years. As reported, the prevalence of AMD was 33.5% and 28.8%, respectively, further confirming the lack of association. Additionally, we analyzed the association between the type of metformin use (in-study vs out-of-study) and stage of AMD and found no association, as shown in Supplement 1.

Known risk factors for AMD, including age, sex, race, smoking status, BMI, and education level, were available and included.<sup>3,4</sup> Medical history, family history, and genetic information were not included in the analysis. However, despite these limitations, the power of these analyses lies in the randomization of the cohort, intent-to-treat strategy, and the differences in the metformin usage in the different treatment arms over the long-term follow-up. The masked gradings for the different stages of AMD by a reading center is another strength. We acknowledge that these findings are different from other studies while also similar to others, reflecting the different methodologies and different data sets used to analyze the association of AMD and metformin use. The answer to this question lies in the prospective evaluation of metformin in a randomized clinical trial.

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**Conflict of Interest Disclosures:** None reported.

1. Domalpally A, Whittier SA, Pan Q, et al; Diabetes Prevention Program Research (DPPPOS) Group. Association of metformin with the development of age-related macular degeneration. *JAMA Ophthalmol*. 2023;141(2):140-147. doi:10.1001/jamaophthalmol.2022.5567
2. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. *Lancet Diabetes Endocrinol*. 2015;3(11):866-875. doi:10.1016/S2213-8587(15)00291-0
3. Chakravarthy U, Wong TY, Fletcher A, et al. Clinical risk factors for age-related macular degeneration: a systematic review and meta-analysis. *BMC Ophthalmol*. 2010;10:31. doi:10.1186/1471-2415-10-31
4. Age-Related Eye Disease Study Research Group. Risk factors associated with age-related macular degeneration. a case-control study in the age-related eye disease study: Age-Related Eye Disease Study Report Number 3. *Ophthalmology*. 2000;107(12):2224-2232. doi:10.1016/S0161-6420(00)00409-7

## CORRECTION

**Errors in Abstract and Key Points:** The Original Investigation titled "Pulsed Oral Azithromycin vs 6-Week Oral Doxycycline for Moderate to Severe Meibomian Gland Dysfunction: A Randomized Clinical Trial,"<sup>1</sup> published on March 23, 2023, was corrected to fix errors in the Abstract and Key Points. The Objective in the Abstract was changed from "To determine if the AEs of a 3-week course of oral azithromycin were equivalent to the AEs of a 6-week course of oral doxycycline." to "To determine if the effects of a 3-week course of oral azithromycin were equivalent to a 6-week course of oral doxycycline." The Question in the Key Points was changed from "Are the adverse effects of a 3-week course of weekly oral azithromycin equivalent to that of the 6-week course of oral doxycycline in treating moderate to severe meibomian gland dysfunction (MGD)?" to "Are the effects of a 3-week course of weekly oral azithromycin equivalent to that of the 6-week course of oral doxycycline in treating moderate to severe meibomian gland dysfunction (MGD)?"

This article was corrected online. The article was previously corrected on May 4, 2023.

1. Upaphong P, Tangmonkongvoragul C, Phinyo P. Pulsed oral azithromycin vs 6-week oral doxycycline for moderate to severe meibomian gland dysfunction: a randomized clinical trial. *JAMA Ophthalmol*. Published online March 23, 2023. doi:10.1001/jamaophthalmol.2023.0302

**Error in Author Affiliations:** The Original Investigation "Overlap of Genetic Loci for Central Serous Chorioretinopathy With Age-Related Macular Degeneration,"<sup>1</sup> that was published online April 20, 2023, included errors in the affiliations for some of the authors in the byline. The affiliations for the following authors were corrected: Drs Abner, van Dijk, Palta, Esko, and Boon. This article was corrected online.

1. Rämö JT, Abner E, van Dijk EHC, et al; FinnGen Study; Estonian Biobank Research Team. Overlap of genetic loci for central serous chorioretinopathy with age-related macular degeneration. *JAMA Ophthalmol*. Published online April 20, 2023. doi:10.1001/jamaophthalmol.2023.0706

**Error in Author Name:** The Clinical Challenge titled "Red Eye and Choroidal Detachment in an Older Woman,"<sup>1</sup> published on May 18, 2023, was corrected to delete the corresponding author's middle initial. The article was corrected online.

1. Jadhav S, Padmalakshmi K, Bhende M. Red eye and choroidal detachment in an older woman. *JAMA Ophthalmol*. Published online May 18, 2023. doi:10.1001/jamaophthalmol.2023.1513

**Error in Conflict of Interest Disclosures:** The Invited Commentary "Optical Coherence Tomography Angiography, Artificial Intelligence, and the Missing Capillaries,"<sup>1</sup> that was published online May 25, 2023, included errors in the Conflict of Interest Disclosures section. The authors received support for this article from a National Institutes of Health grant. This article was corrected online.

1. Kashani AH, Liu TYA, Jones C. Optical coherence tomography angiography, artificial intelligence, and the missing capillaries. *JAMA Ophthalmol*. Published online May 25, 2023. doi:10.1001/jamaophthalmol.2023.1829