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In Reply Whether slower reading contributes to Scantron filling speed is difficult to establish unless the same children are assessed on both tasks, which as far as I know has not been tested. While filling Scantron forms requires motor actions that reading does not, visual scanning is required to identify the circled answers and locate the corresponding answer bubbles. This engages oculomotor and visual skills in common with reading (eg, saccades,[1,2] accommodation, near vision). Therefore, reading-associated factors may be associated with performance on both tasks. The Brief Report by Kelly et al[3] specifically states that none of the children were enrolled in school reading intervention programs. If Drs Kelly and Birch believe that Scantron filling is independent from reading, then this exclusion may not have been necessary.

Regarding masking, I acknowledge that my phrasing at the beginning of paragraph 4 of my Invited Commentary[4] may have been ambiguous, but the end of the same paragraph recommends "careful masking of the study purpose from the participants and the parents/caregivers, as well as masking the participant's visual status from the researchers collecting data."[4(p942)] Without further study, we can only guess at the magnitude of any such psychosocial influences. In contrast with what Drs Kelly and Birch stated in their Letter, I would not presume that these unconscious influences can explain all of their results. As mentioned in my commentary,[4] it is entirely possible for some children to respond differently, adding unnecessary variability.

Drs Kelly and Birch may have misread my next point. The issue is not that the children's habitual corrections were used, but rather that their report "does not state whether the correction was up-to-date or appropriate for their refractive errors."[4(p942)] Because no refractive data were provided, readers like myself do not know whether uncorrected refractive errors may have been associated with the measured visuomotor performance. The same issue also occurs in Drs Kelly and Birch's previous articles[1,2] examining reading speed. In the so-called real world, prescribing practices for older children with previous amblyopia can vary, and the lack of reported refractive information might limit the clinical interpretation and utility of results.

In the original manuscript sent to me for comment, Drs Kelly and Birch concluded the abstract by stating that children with abnormal binocular vision history may require academic accommodations. This was amended in the final version, but I had overlooked the change. I note however that the published report still states that their findings "may aid in developing new guidelines in academic accommodations,"[3(p940)] and that a previous editorial by Drs Kelly and Birch appears to support such academic policies.[5]

Personally, I think academic accommodations can help children with substantial visual or visuomotor deficits, if these cannot be ameliorated by treatments. Before jumping to policy recommendations, we may also need to reconcile current findings with previous population-level evidence, which did not show definitive and substantial associations between amblyopia and academic success.[6] This may be because academic success is multifactorial, requiring more than just fast reading and Scantron filling. I thank Drs Kelly and Birch for providing this opportunity to clarify my comments.

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Published Online: March 7, 2019. doi:10.1001/jamaophthalmol.2019.0136

Conflict of Interest Disclosures: None reported.

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Implications of Birdshot-Like Uveitis on the Pathogenesis of Birdshot Chorioretinopathy

To the Editor The recent article by Acaba-Berrocal et al[1] presents a case of birdshot-like chorioretinopathy in a patient who was HLA-A29–negative and received treatment with a checkpoint-blockade agent for malignant melanoma. This case is of considerable interest with implications for the immunopathogenesis of birdshot chorioretinopathy (BCR).

In most, if not all, patients with BCR, HLA-A29 is found; however, HLA-A29 only confers risk, in that most white individuals who are HLA-A29–positive do not develop BCR. Increased risk is also conferred by killer-cell immunoglobulin-like receptor genes and the HLA-B44 subtype that interacts with killer-cell immunoglobulin-like receptors,[2] suggesting the possibility of either an infectious or neoplastic trigger. We believe the inciting event may be the presence of skin cancers or precancerous lesions, which are highly prevalent in middle-aged white individuals, the population in which BCR is almost exclusively found. There is also a rare association of BCR with ocular melanoma, further supporting a role for neoplasia inciting the disease.[3] In the case presented by Acaba-Berrocal et al,[1] we propose that immune activation through release of inhibition of the programmed cell death protein 1 checkpoint pathway in a patient treated for cutaneous melanoma mimics the altered immune reactivity to neoplastic changes in the skin (whether manifest or microscopic) in a subset of individuals who are HLA-A29–positive and develop BCR.

Cancer immunosurveillance could lead to initiation of BCR through antigenic mimicry involving presentation on HLA-A29 or loss of immunological tolerance. The situation is complex and multifactorial, as evidenced by the rarity of BCR even in middle-aged white people. For example, isolation of viral DNA from nonmelanoma skin cancers and their premalignant precursors suggests the potential of additional antigenic stimulation from highly immunogenic viral epitopes in a system adapted toward suppression of herpes-class viruses.[4]

While it has been suggested that patients with BCR may have a higher incidence of skin cancers, this association has not been well established. However, in some individuals, the inciting cancers may be successfully suppressed or eliminated by the mobilized immune system, resulting secondarily in the development of BCR in an autoimmunity-promoting milieu, without manifestation of clinically diagnosed skin cancer. This is congruent with recent observations that with cancer immunotherapy, the development of uveitis and vitiligo as adverse effects frequently signals successful tumor response.[5]

These observations support our proposal that immune surveillance and response to cutaneous neoplasia or ocular melanomas may contribute to the development of BCR. This explains, at least in part, why BCR is nearly exclusively found in middle-aged and older white individuals.

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Published Online: March 14, 2019. doi:10.1001/jamaophthalmol.2019.0214

Conflict of Interest Disclosures: None reported.

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In Reply We read with interest the letter from Sun et al regarding possible pathophysiologic implications of our article on birdshot-like chorioretinopathy associated with pembrolizumab treatment.[1] In the article, we observed a single patient who was treated for cutaneous melanoma with a checkpoint-inhibitor agent directed against the programmed cell death-1 receptor on T cells and soon thereafter developed a classic-appearing case of birdshot chorioretinopathy (BCR) in both eyes. Testing for HLA-A29 was negative. We speculated that this immunotherapy was associated with the development of clinical features of BCR.

Based on this case, Sun et al proposed a detailed theory that "immune surveillance and response to cutaneous neoplasia or ocular melanomas may contribute to the development of BCR." We were not aware of this association. Looking back over our 31 years of experience in a busy ocular oncology practice, which has involved treating several thousand patients with uveal melanoma, there has been no patient who clinically manifested BCR. Further, the association with cutaneous melanoma has not been verified. A PubMed search for "cutaneous melanoma and birdshot" yielded no reports. However, we agree with the authors that immune surveillance likely plays a role in BCR. In this case, the immunotherapy checkpoint inhibitor unleashed and activated T cells, which likely led to the development of this immune-mediated condition. The exact cascade of events remains unknown, to our knowledge.

Although many of the uveitides remain idiopathic or undifferentiated, we should always strive to find the underlying cause or causes. For example, tattoo-associated uveitis is a rare form of uveitis with clinical features that can mimic sarcoidosis. Whether tattoo-associated uveitis represents a distinct entity or a subset of cutaneous sarcoidosis remains unclear.[2] It is possible that the morphology of some of the uveitides may represent a final common pathway in the ocular inflammatory cascade, so that similar clinical findings may have multiple causes, including genetic predispositions and environmental exposure.

Understanding of the pathophysiology of BCR is limited by the rarity of the disease, paucity of histopathologic specimens, inconsistent descriptions of findings, limited understanding of genetic factors, and sometimes conflicting case definitions. The association of BCR with melanoma, as described by Pulido et al,[3] and the hypothesis of Sun et al that immune surveillance and response to cutaneous neoplasia or ocular melanomas may contribute to the development of BCR (which helps to explain why BCR is almost always found in white individuals who are middle-aged and older, rather than others) represent tantalizing clues toward unraveling the mysteries of this disease. Perhaps big data, such as that of the American Academy of Ophthalmology's Intelligent Research in Sight registry and the French national registry for rare diseases, by using feature-based rather than diagnosis-based data sets, will provide confirmation of the hypothesis of Sun et al.[4,5] We appreciate their interest in our findings and look forward to hearing more from their future research.

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Published Online: March 14, 2019. doi:10.1001/jamaophthalmol.2019.0220

Conflict of Interest Disclosures: Dr Dunn reports personal fees from AbbVie Inc outside the submitted work. No other disclosures were reported.

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Association of Cataract Surgery With Driving Safety and Falls

To the Editor Cataracts are a leading cause of reversible vision impairment worldwide, and age-associated decline in visual acuity has been associated with increased risk for car crashes and falls.[1] A recent, methodologically strong, population-based study[2] has found that the rate of serious car crashes decreased by 9% after cataract surgery. The researchers[2] evaluated 559 546 patients who had cataract surgery in at least 1 eye. The association between cataract surgery and crash involvement has been previously reported by Owsley et al.[1] This study found that patients with cataract who underwent cataract surgery experienced only half the crash risk compared with patients with similar conditions who did not undergo surgery. An Australian study[3] based on similar linked administrative data also found cataract surgery is effective in reducing car crashes. The reduction in crash risk associated with cataract surgery lends support for consideration of cataract surgery prioritization for drivers older than 65 years.

However, poor vision is only 1 of many risk factors for motor vehicle crashes and falls.[4] Other potential risk factors include visual processing speed, multiple comorbidities, polydrug use, cognitive status changes, reduced cognitive capacity, balance and gait impairments, functional impairments, and changes in neuromuscular function, motor function, reaction time, hearing, and physical activity levels.[3-5] Unfortunately, it was impossible to examine these factors through administrative health data sets. Even though the benefit of a population-based approach is that the crash involvement can be investigated with a sufficient sample size, a limitation of the current study[2] is that information gleaned from anonymous records does not extend far beyond the recording of surgeries, car crashes, and falls. The authors[2] mentioned that cataract surgery was not associated with a reduction in the subsequent risks of falls. Other important factors that might be useful to include and influence interpretation of the results would be the number of times a participant had fallen before the cataract surgery, since a previous fall is a known risk factor for recurrent falls. This information is not likely available in this data set. Therefore, it may be beneficial for the ophthalmology research community to think innovatively how these other individual patient-level data might be incorporated successfully into population-based data sets, to further the understanding of the association of cataract surgery with motor vehicle crash involvement by older adults.

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Published Online: March 28, 2019. doi:10.1001/jamaophthalmol.2019.0379

Conflict of Interest Disclosures: None reported.

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In Reply We thank Dr Desapriya for the letter regarding our article, "Association of Cataract Surgery With Traffic Crashes."[1] We agree in the value of population-based research in providing a comprehensive, longitudinal, patient-level, self-matched analysis of important clinical outcomes, such as traffic crashes and falls. We also agree that many factors beyond impaired vision can contribute to adverse incidents and cataract surgery can only improve vision, contrast sensitivity, and glare, but not other factors that contribute to these incidents.[2] The results also indicate that cataract surgery does not completely eliminate the risk of a traffic crash or fall.

We agree that limitations of administrative database research include a lack of detailed clinical information. In addition, administrative database research of emergency visits does not address near-miss events or fatal events. The reported secondary analysis of falls does not preclude visual impairment as a potential risk factor, and we acknowledge that more research is needed on a potential association.[3-5] One of the strongest risk factors for traffic crashes was a previous traffic crash; we did not formally evaluate risk factors for the secondary outcomes, although we would also presume that a previous fall is a risk factor for subsequent falls. We hope that continued research into important adverse events, in line with our medical research into drug toxicity and surgical complications, might help elucidate risk factors and preventive strategies to ultimately improve patient lives.