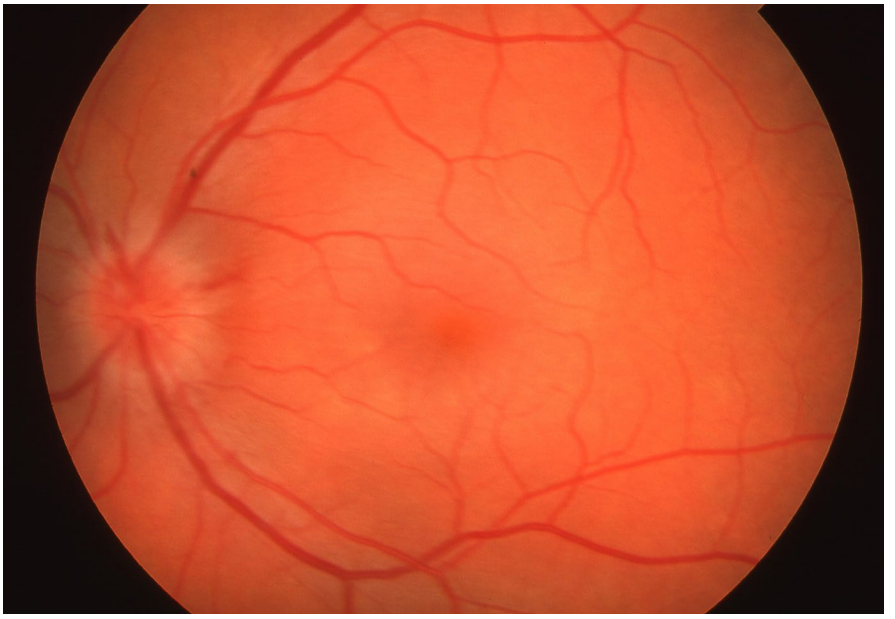


POSTERIOR UVEITIS. *Fundus photo of a 37-year-old patient with mild vitritis, optic disc hyperemia and edema, and several peripapillary nerve fiber layer hemorrhages.*

UVEITIS

Short-Term Use of Immunosuppressants Not Linked to Mortality, Suggests Study

TAKING IMMUNOSUPPRESSANTS FOR a relatively short time in order to treat an inflammatory eye disease is not linked to an increase in mortality and cancer-related mortality, according to researchers from Mass Eye and Ear, in Boston, and the University of Pittsburgh.[1]

The study in *Ophthalmology* and its companion study in *BMJ Oncology*[2] "provide strong reassurance that it is very unlikely that the immunosuppressive agents most commonly used for ocular inflammatory diseases increase the risk of death or cancer for our patients," said lead author John H. Kempen, MD, PhD, MPH, at Schepens Eye Research Institute of Mass Eye and Ear.

Methodology. For the retrospective cohort study in *Ophthalmology*, the scientists analyzed data on 15,938 people who were treated at ocular inflammatory disease subspecialty centers in 12 states, tracking them for about 10 years to assess overall or cancer-related mortality. All patients were enrolled in the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) study and had taken one or more immunosuppressants for a year or less to treat eye conditions. The commonly used immunosuppressant drugs fell into four classes: tumor necrosis factor inhibitors, antimetabolites, calcineurin inhibitors, and alkylating agents. The scientists also drew data from each state's cancer registry.

For their investigation, the researchers compared individuals with noninfectious ocular inflammatory diseases taking immunosuppressants to people with noninfectious ocular inflammatory diseases who did not take immunosuppressants. They also compared the two groups to individuals in the general U.S. population.

Results. They reported no evidence of excess risk of cancer in patients who took immunosuppressants on a short-term basis (median 0.54 to 1.47 years)—regardless of dose size—over a long-term follow-up (median of 10 years). Of the 15,938 patients on immunosuppressive drugs, "we observed 1,970 deaths, 435 due to cancer," and both groups of participants had similar mortality risk to the U.S. population, the authors wrote.

At odds with transplant literature. The International Agency for Research on Cancer (IARC) has designated certain immunosuppressants as carcinogenic to humans, including azathioprine, cyclosporine, and cyclophosphamide.[1] However, the designation draws heavily from studies involving transplant patients undergoing lifelong immune suppression. Because of the comparatively short length of treatment in these studies, the researchers said that their findings do not apply to patients in the transplant setting.

The study evidence supports the safety of systemic therapy for treatment of noninfectious intermediate, posterior, and panuveitis, said Dr. Kempen.

—Miriam Karmel

1 Kempen JH et al. *Ophthalmology*. 2023;130(12):1258-1268.
2 Buchanich JM et al. *BMJ Oncology*. 2023;2:e000037.

Relevant financial disclosures: Dr. Kempen—Betaliq: EO; Gilead: C; Tarsier Pharma: EO.

DEIA

Barriers to DR Screening

FOOD INSECURITY. HOUSING CHAL-lenges. Mental health concerns. These are some of the self-reported barriers to regular vision screenings for diabetic retinopathy (DR) among adults with diabetes, said Stanford researchers.[1]

About the study. Previous studies have examined some of the socioeconomic factors associated with disparities in diabetic eye care, but the authors wanted to deepen their understanding of the social determinants of health that stand between patients and getting regular DR screenings, said corresponding author Sophia Y. Wang, MD, MS.

The findings will enable experts "to find ways to help people with diabetes receive the eye care they need," she said.

The retrospective cross-sectional study included data from people ages 18 and up with type 2 diabetes who participated in the All of Us Research Program, a national multicenter cohort of individuals who contributed their electronic health records and survey data between May 2018 and July 2022.

"The program places special emphasis on including participants who are traditionally underrepresented in medical research. Participants share their electronic health records and are invited to complete surveys and self-report many social factors that affect their health and medical care," Dr. Wang said.

Findings. Of the 11,551 study participants, 7,983 (69%) reported visiting an eye care practitioner within the previous year. The study found that compared with patients who were financially stable, individuals with food and housing insecurity were less likely to see an eye care provider.

Individuals who reported "fair" mental health were less likely to visit an eye care professional than those who reported "good" mental health.

Dr. Wang said the authors also looked at practitioner concordance, "when a provider understands or shares the same race or ethnicity or gender or religion or language or other identifying factors and beliefs." She and colleagues reported that participants who placed more importance on practitioner concordance were less likely to see an eye care practitioner.

"Practitioner concordance is clearly important to individuals most at risk, which highlights the need for diversity within the provider workforce to ensure their care," she said.

The researchers also found that with every 10-year increase in age, participants were more likely to visit an eye care practitioner. Factors such as higher income and educational level were also independently associated with a greater likelihood of receiving eye care in the past year. Hispanic and non-Hispanic Black participants were found to be less likely to have received eye care compared with non-Hispanic White participants in unadjusted models.

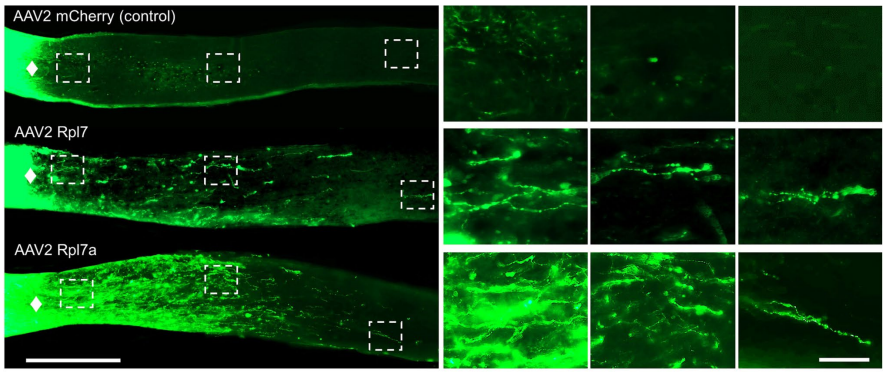
Limitations. Not all participants completed the surveys or answered the question on eye care utilization, leading to possible selection bias. The survey neither distinguished between optometrist and ophthalmologist visits nor noted if dilation occurred.

"By identifying the barriers, we can better target our interventions to increase delivery of care in the future," Dr. Wang said, adding that more research is required to explore the complex barriers that need to be addressed to promote health equity.

—Patricia Weiser, PharmD

1 Ravindranath R et al. *JAMA Ophthalmol.* 2023;141(12):1161-1171.

Relevant financial disclosures: Dr. Wang—National Eye Institute: S; National Institutes of Health: S; Research to Prevent Blindness: S.



OPTIC NERVE SECTIONS. *An image from the study indicates optic nerve crush sites two weeks after nerve crush, including (left to right) proximal, medial, and distal views.*

NEURO-OPHTHALMOLOGY

Targeting Ribosomal Proteins for Optic Nerve Repair

RESEARCHERS AT THE UNIVERSITY of Connecticut School of Medicine report that two ribosomal proteins associated with neurodevelopment and neurodegeneration—Rpl7 and Rpl7A—downregulate as the nervous system develops but can be altered to be expressed in adult nerve cells in a mouse model of optic nerve injury.

Their study, published in *Experimental Neurology*, goes on to describe that when bundles of retinal ganglion cells' axons were crushed (to model damage to the optic nerve), the neurons that the researchers had altered—using viral vectors to overexpress Rpl7 or Rpl7A—began to grow axons again after injury.[1] In other words, experimentally enhancing the levels of Rpl7 or Rpl7A in retinal ganglion cells in a mouse model promoted regeneration of damaged nerve cell axons after injury, said lead investigator Ephraim F. Trakhtenberg, PhD.

"We believe that experimental treatments targeting ribosomal proteins could tilt the balance toward the necessary levels of reactivation of axon growth mechanisms," said Dr. Trakhtenberg, noting that he and colleagues are continuing to work toward this goal.

Rationale. Dr. Trakhtenberg's team initially looked at a group of 80 ribosomal protein genes—all of which progressively become less active as nerve cells mature—but focused on Rpl7 and

Rpl7A because "Rpl7 was previously reported to be dysregulated in neurodegenerative diseases, and Rpl7A was selected as a control because of its relatedness to Rpl7," Dr. Trakhtenberg said. The researchers hypothesized that experimentally upregulating Rpl7 and Rpl7A into injured cells would fully reinstate their embryonic levels of expression and promote axon regeneration.

Of mice and humans. The research is early, and animal studies do not necessarily equate to similar results in humans. Jeffrey L. Goldberg, MD, PhD, at the Byers Eye Institute at Stanford University, in Stanford, California, who was not involved in the study, said, "Although the distance between mice and humans is large, the shared biology is significant. And vision loss in traumatic, ischemic, glaucomatous, and other optic neuropathies in our patients has more similarities than differences."

Looking ahead. More research is needed to explore the role of ribosomal proteins in the regeneration of other neuron types and to determine the mechanism by which Rpl7 and Rpl7A regulate axon regeneration and retinal ganglion cell survival, said Dr. Trakhtenberg. Researchers also need to assess whether regulation of multiple ribosomal subunits has an even greater impact on axon regeneration, he said, noting that the ultimate goal would be to study their findings in the human eye.

According to Dr. Goldberg, uncovering the molecular mechanisms that promote axon regeneration is critical for developing new therapies and has the potential to open up a whole new field of research into the role of ribosomal proteins, local protein translation, and cell signaling pathways with clinical impact. "With molecular or gene therapy, these data could be rapidly translatable to clinical testing," he said. —*Christos Evangelou, PhD*

1 Xing J et al. *Exp Neurol.* 2023;368:114510.

Relevant financial disclosures: Dr. Goldberg—None. Dr. Trakhtenberg—None.

See the financial disclosure key, page 10.

For full disclosures, including category descriptions, view this News in Review at aao.org/eyenet.