CLOSER LOOK

Mary Tyler Moore Vision Fall Workshop 2025

November 4, 2025; Ann Arbor, MI; Conference Highlights – Draft

Executive Highlights

- **The Mary Tyler Moore Vision Initiative (MTM Vision) hosted its fourth annual Fall Symposium on Curing Vision Loss from Diabetes in Ann Arbor, just around the corner from the University of Michigan.** The convening of global experts from academia and industry and people living with diabetes reviewed the progress made by the MTM Vision and partners towards accelerating development of new ways to prevent and cure vision loss from diabetic retinal disease (DRD). The organization was founded by Dr. S. Robert Levine in honor of his late wife, Mary Tyler Moore, who suffered greatly from eye complications from T1D. The MTM Vision aims to establish new indications and therapeutic targets for treatments in DRD, as well as inform new regulatory pathways for drug approvals. This annual conference offered an intimate look at the research landscape in eye health today, with many Q&A sessions volleying between presenters and audience members – in fact, some questions for panelists were answered by members of the audience, allowing for a rich discussion that allowed all 195 attendees to walk away smarter about eye health.
- **Dr. Levine, along with MTM Vision Scientific Co-Director Dr. Jennifer Sun (Joslin Diabetes Center) and MTM Vision Biorepository Director Dr. Patrice Fort (University of Michigan) provided important updates to the MTM Vision work in the past year.** Dr. Levine called on attendees to harness their "collective genius" through collaboration and open inquiry. Dr. Sun stressed the importance of establishing measurable clinical endpoints to guide therapeutics development and regulatory approval, noting that two multicenter studies are now ready to launch to validate new biomarkers and measures of visual function. Dr. Fort rounded out the session with updates on the MTM Vision Biorepository, which has amassed nearly 80 paired ocular samples now undergoing proteomic and RNA sequencing analyses. By integrating these molecular data with imaging modalities like OCT and fundus photography, researchers are gaining novel insights into disease mechanisms. The Biorepository's new web portal will also accelerate global data sharing, advancing the Initiative's mission to turn scientific discovery into real-world impact for patients.
- **Dr. George King (Joslin Diabetes Center) highlighted the Joslin 50-Year Medalist Study,** which includes over 1,000 individuals with T1D for more than five decades. Strikingly, only half have developed retinopathy and just 12% kidney disease, suggesting innate protective factors. Through organ donations and multi-omic analyses of more than 100 ocular tissues, his team identified retinol-binding protein 3 (RBP3) as one such factor, with its higher levels strongly linked to reduced risk of PDR and diabetic macular edema**.**
- **Speakers also highlighted the acceleration of translational research, AI innovation, and emerging therapeutics in DRD.** Drs. Lloyd Paul Aiello (Joslin Diabetes Center), Fabio Baschiera (BI), and Leo Kim (Massachusetts Eye and Ear) highlighted the need for validated biomarkers and more predictive endpoints to guide the next generation of therapies, which are complemented by industry initiatives from Boehringer - Ingelheim to expand data-driven and accessible treatments. Meanwhile, a session led by Mr. Ali Tafreshi (Topcon Healthcare) and Dr. Brian Athey (University of Michigan) underscored that the tools for AI-driven eye care already exist, but progress depends on breaking data silos and building the infrastructure for "transparent" AI.

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1. Power of longitudinal data: Dr. George King shares insights from 50-year Medalist program

Inspired by early mentors who urged him to uncover the elusive "Factor X" driving severe diabetic eye disease, Dr. George King (Joslin Diabetes Center) explained how he and his colleagues were among the first to identify and validate vascular endothelial growth factor (VEGF) as a central mediator of proliferative diabetic retinopathy (PDR) in the mid-1990s. This discovery, based on analyses of over 200 vitreous samples, underscored the critical role of direct study of human ocular tissues in advancing translational research.

- **The Joslin 50-Year Medalist Study,** which includes over 1,000 individuals with T1D over more than 50 years' duration, has become a cornerstone of this translational work. Despite decades of T1D, only about 50% of Medalists develop DR and just 12% develop kidney disease; these rates are much lower than the general T1D population. Notably, those with minimal or no DR tend to stabilize within the first 20 years of diabetes, suggesting the presence of protective factors. Dr. King stressed the incredible impact that these participants have had on our collective understanding of diabetes, noting his close relationship with all one thousand ("they each have my personal cell phone number").
- **Through partnerships with the National Disease Research Interchange (NDRI),** over 600 Medalists have consented to organ donation, with more than 100 tissues procured to date. Ocular studies have included proteomic, metabolomic, and epigenetic (DNA methylation) analyses of the retina, aqueous humor, or vitreous. These investigations have led to the identification of retinol-binding protein 3 (RBP3) as a protective factor against DR. RBP3 exhibits a strong inverse correlation with DR severity across T1D and T2D cohorts (n=205). Reduced vitreous RBP3 levels are associated with proliferative DR and diabetic macular edema (DME), whereas higher concentrations seemingly confer protection against both complications.

2. Updates on the MTM Vision: Progress towards a world without vision loss from DRD

Throughout the symposium, Dr. S. Robert Levine (MTM Vision), Dr. Jennifer Sun (Joslin Diabetes Center), and Dr. Patrice Fort (University of Michigan) each shared updates on the progress made by MTM Vision since the last symposium. Dr. Levine framed the initiative as both a personal and professional commitment, reflecting on the legacy of his love for his late wife, Mary Tyler Moore. He emphasized that the symposium's purpose was to foster open dialogue and stimulate new collaborations that would translate scientific knowledge into tangible clinical benefits. Dr. Sun expanded on this by sharing the importance of a fundamental understanding of DRD and the necessity of defining measurable outcomes to enable effective therapies development. She highlighted significant progress in clinical research, including the initiation of multicenter studies aimed at validating new endpoints for regulatory approval. Dr. Fort complemented these perspectives by detailing the ongoing work of the MTM Vision Biorepository, explaining how the systematic collection of ocular samples is already revealing critical insights into the disease's molecular mechanisms.

- **Dr. Levine began his remarks by contextualizing the symposium's work** within a promise he made to Mary. His vow to "love, honor, support, and protect" her has now become a guiding principle for his professional legacy: preventing the vision loss caused by diabetic retinal disease. Dr. Levine's remarks were punctuated by a call for collaboration, urging participants to ask themselves, "What are we missing?" and recognizing the "collective genius" of those gathered to address this pressing issue. He framed the symposium not only as an opportunity to share knowledge but as a moment to ignite new partnerships and strategies that could accelerate meaningful progress in the fight against DRD.

- **Dr. Sun emphasized the necessity of a clear, foundational understanding of DRD** in order to develop effective therapies, reiterating that one cannot solve a problem without first defining it. She discussed the importance of defining success through measurable clinical endpoints, which are essential for both research and regulatory approval. She reported significant progress on multiple fronts, including the submission of several papers to peer-reviewed journals and the presentation of research findings at key conferences. Moreover, Dr. Sun highlighted the launch of two multicenter clinical studies within the DRCR Retina Network-Protocol AR, which aims to study retinal function in people with diabetes, and Protocol AS, which focuses on patients treated for DME. These studies aim to validate new endpoints for regulatory approval which, in turn will accelerate the development of new therapies.
- **Dr. Fort provided a comprehensive overview of the status of and progress on the MTM Vision Biorepository**, a critical resource in the effort to better understand the pathophysiology of DRD and identify new therapeutic targets. He detailed the ongoing collection of ocular samples, which now includes 79 ocular pairs. These samples are being analyzed through proteomics and RNA sequencing, providing a detailed snapshot of molecular changes throughout the continuum of DRD. Dr. Fort highlighted how the integration of clinical imaging data, such as fundus photography, optical coherence tomography (OCT), and whole-mount staining, is enabling researchers to zoom in on specific regions of the retina and assess how disease features like microaneurysms and retinal nonperfusion affect retinal structures. Furthermore, he announced the recent launch of the MTM Vision Biorepository's Web Portal, which will facilitate real-time access to sample data, clinical histories, and phenotypic information for global collaborators. He reinforced the idea that collaboration, rather than competition, is essential to overcoming the challenges in DRD research and ultimately improving patient care.

3. Translating science to clinical care

In a series of short seminars, Drs. Lloyd Paul Aiello (Joslin Diabetes Center), Fabio Baschiera (Boehringer Ingelheim), Leo Kim (Massachusetts Eye and Ear), and Remko Bakker (Boehringer Ingelheim) presented updates on several preclinical and clinical studies and shared best practices for translating this information into clinical practice.

- **Dr. Aiello discussed ongoing efforts to establish retinal nonperfusion (RNP)** as a validated endpoint in diabetic retinopathy (DR) research and clinical trials. RNP is a key pathological hallmark and early driver of DR, closely linked to both disease progression and visual dysfunction. Analyses from the Protocol AA longitudinal observational study (n=367) demonstrated that eyes exhibiting fluorescein angiography-defined peripheral nonperfusion (FA-PPL) had a 1.7-fold increased risk of DR worsening over four years, consistent across all DR severity subgroups.
    - **Moreover, more severe baseline lesions** on ultra-widefield fluorescein angiography (UWF-FA) were strongly predictive of disease progression, with risks increasing by up to 90% depending on lesion type. Lesion types included hemorrhages/microaneurysms (H/MA), intraretinal microvascular abnormalities (IRMA), and neovascularization elsewhere (NVE). RNP severity also correlated with retinal ischemia and elevated VEGF activity. Dr. Aiello emphasized that establishing RNP as a primary clinical endpoint will require alignment among scientific, clinical, and regulatory stakeholders, including clear definitions of clinically meaningful change and demonstration of superior predictive value for visual outcomes relative to current standards. Collectively, these data position RNP as a promising biomarker for identifying early disease progression and guiding future DR therapies.
- **Dr. Baschiera (Boehringer Ingelheim), presenting on behalf of his former colleague Dr. Kai Riecke (Bayer), reflected on the value of learning from negative studies in drug development,** noting that roughly 80% of programs fail at the proof-of-concept stage. While prior trials (such as PANORAMA) demonstrated the success of intravitreal aflibercept in preventing progression from severe non-proliferative diabetic retinopathy (NPDR) to more advanced stages, subsequent findings from DRCR Protocol W revealed that, despite a significant reduction in the risk of PDR and center-involved diabetic macular edema (CI-DME), long-term visual acuity outcomes did not differ from placebo after four years. Regulatory agencies have consistently emphasized best-corrected visual acuity (BCVA) as the preferred functional endpoint, underscoring the challenge of using vision-threatening complications (VTC) as a consistent metric. Dr.

Baschiera stressed that there is currently a lack of global consensus on efficacy endpoints for DR trials or early endpoints that translate to or are predictive of long-term vision.

- **Dr. Kim, the recipient of the Research to Prevent Blindness / Mary Tyler Moore Vision Initiative 2024 Physician-Scientist Award, shared updates on his recent research**. His research focuses on the molecular mechanisms underlying proliferative diabetic retinopathy (PDR), with particular emphasis on the transcription factor RUNX1 as a mediator of pathological ocular angiogenesis. Using patient-derived fibrovascular membranes (FVMs) obtained through surgical dissection, endothelial cells were isolated via magnetic bead separation and subjected to next-generation sequencing and bioinformatic gene ontology analyses. This approach identified a 25-fold increase in RUNX1 expression in endothelial cells from PDR samples compared with nondiabetic post-mortem retinal tissue, in which RUNX1 was absent.
    - RUNX1 is known to regulate cell cycle progression, differentiation, and self-renewal in hematopoietic (blood cell forming) and vascular systems – which could promote neovascularization and hence vision loss. Functional studies have indeed demonstrated that RUNX1 knockdown reduces neovascularization in a retinopathy model. In contrast, anti-VEGF therapy, while widely used in PDR management, may disrupt physiological revascularization without fully preventing disease progression.
    - Collectively, these findings position RUNX1 as a novel and potentially targetable driver of pathological angiogenesis in diabetic retinopathy. Future work aims to develop an mRNA-encoded therapeutic, RUNX1-Trap, designed to bind RUNX1, prevent its nuclear translocation, and suppress RUNX1-mediated transcriptional activity, offering a new avenue for treating PDR beyond VEGF inhibition.
- **Dr. Bakker emphasized BI's commitment to improving patient access to new and effective treatments,** particularly in ophthalmology. A major goal is to reduce treatment burden and enhancing durability. Dr. Bakker highlighted the company's growing emphasis on **computational innovation and multi-modal data integration** to enable **target discovery and biomarker identification**. Collaborations with institutions like MTM Vision, which provide robust datasets and a culture of data sharing, are therefore central to BI's mission of translating scientific insight into tangible patient benefit.

4. Building the infrastructure for AI-driven eye care

In a forward-looking session, Mr. Ali Tafreshi (Topcon Healthcare) and Dr. Brian Athey (University of Michigan) outlined a pragmatic roadmap for integrating AI and advanced imaging into everyday clinical care. Their central message was clear: the technology and data signals already exist, but the infrastructure and interoperability that make those tools usable at scale are still catching up. Both speakers stressed that progress will depend on increased collaboration between players in the care continuum, and that AI offers significant potential to streamline imaging, accelerate clinical trials, and bridge basic science and patient care. In the Q&A, they shared that the main limitation on the use of AI is the speed at which the humans moderating (i.e. checking) AI can work.

- **Breaking data silos for greater interoperability.** Mr. Tafreshi emphasized that AI in ophthalmology, and healthcare more broadly, is often trapped in isolated data silos. He advocated for open, interoperable platforms that allow device makers, AI engineers, EHRs, clinicians, and researchers to securely share and build upon one another's work. He predicted that "democratizing data" would spur faster innovation in hardware and software and help build accessible, large-scale datasets for use across the continuum of care, ultimately lowering healthcare costs.
- **The potential of AI in patient screening and drug discovery.** Mr. Tafreshi shared results from a pilot project using Topcon's OCT screening platform, which analyzed nearly one million scans from over 375,000 patients and identified tens of thousands with undiagnosed disease biomarkers. From this pool, the AI-enabled platform refined a subset of 50,000 patients and pinpointed 3,000 potential trial candidates, compressing what traditionally takes months into hours. This approach, he suggested, could transform diabetic retinopathy screening and clinical trial recruitment by cutting costs and improving participant diversity. While the system currently stops short of managing downstream follow-up, future AI models could be designed to handle referrals and trial logistics. Both speakers agreed that closer coordination among industry, academia, and

government will be essential to accelerate these timelines. On the research front, Dr. Athey added that quantum computing may help overcome bottlenecks in drug discovery by rapidly exploring biological pathways and molecular interactions.

- **Stitching together longitudinal data.** Dr. Athey took a systems-level view to describe how AI must integrate across data types (genomics to phenomics, imaging to clinical notes). With today's computational power, he argued, clinicians can generate longitudinal multi-omics datasets that map disease trajectories over time. The key is developing the agents that compile datasets and the "federated systems" that preserve privacy but enable collaboration. When this infrastructure works, it enables widespread use of technologies like digital twins and broader use of real-world evidence in clinical research. Both speakers reiterated throughout the session that "transparent AI" will be essential to connect discovery research with clinical medicine.

Mr. Tafreshi later said:

The call to action is clear: imaging device companies must not lock data behind proprietary formats. To accelerate research and clinical innovation, device manufacturers should adopt open, standards-based approaches that allow imaging data to be seamlessly integrated, shared, and studied. Only by removing today's technical and commercial barriers can we build the large, diverse data repositories required for meaningful advances in healthcare. Topcon is now the first OCT company to lead this effort, advancing open data standards and interoperable imaging through the Institute for Digital Health (IDHea). This marks the beginning of a new era, one in which imaging data serves not just devices, but patients, clinicians, and scientific discovery worldwide.

5. Advances and obstacles in optic nerve regeneration

Dr. Leonard Levin (McGill University, Canada) detailed biological and translational hurdles of regenerating the optic nerve and their relevance to restoring vision in diabetic retinal disease (DRD). In this afternoon session moderated by Dr. Thomas Gardner (University of Michigan), Dr. Levin discussed how we can learn from advances in retinal ganglion cell (RGC) regeneration and stem cell technology with respect to eventual restoration of functional vision for people with end-stage diabetic eye disease.

- **Dr. Levin first outlined four requirements for optic nerve regeneration:** (i) keeping RGCs alive; (ii) extending injured axons; (iii) ensuring those axons reach the correct targets; and (iv) re-establishing precise synaptic connectivity in both the retina and the lateral geniculate nucleus (LGN). Multiple regenerative strategies are being studied to address these steps, and he said that several recent laboratory studies have shown promise. Dr. Levin also highlighted the emergence of "optic nerve on a chip" systems that allow human-relevant modeling of axonal injury and repair to inform preclinical work, and how ARPA-H–funded research into whole-eye transplantation could be a potential long-term solution.
- **However, he cautioned that these biological advances must be reconciled with the realities of DR.** In end-stage DR, extensive vascular damage and fibrosis further complicateretinal restoration. Dr. Levin concluded that lessons from optic nerve regeneration will be critical for informing future approaches in restoring functional vision in end-stage DR.

6. Natural history of DRD as an opportunity for learning

Dr. Marianne Laouri (BI) moderated a session with Dr. Baschiera and Prof. Aude Couturier (Universite of Paris, France) on recent work to gain consensus on useful endpoints, including incorporating visual function endpoints into longitudinal studies to the natural history of diabetic retinal disease.

- **Dr. Baschiera elaborated on the company's commitment** to cross-sector collaboration through initiatives such as the BRIDGE consortium, which unites 30 international clinicians and multiple stakeholders, including Retina International, MTM Vision, and several leading pharmaceutical firms. The consortium aims to define global standards for structural and functional endpoints in retinal diseases and generate consensus using published evidence. These biomarkers are critical to predicting disease progression and understanding the dissociation between structural improvements seen in anti-VEGF therapy and the functional vision outcomes observed in clinical practice. By integrating findings across studies and emphasizing the need for composite endpoints, BRIDGE aims to establish a more holistic and clinically meaningful framework for evaluating emerging retinal therapies.

- **Complementing these efforts,** Dr. Couturier presented the *EviRed* program designed to transform diabetic retinopathy (DR) classification through artificial intelligence. Conducted across 14 ophthalmology and 18 diabetology centers in France, including 3,075 patients, with a follow-up time of 1-4 years, and collecting more than 55,000 images, *EviRed* has combined multimodal imaging (color fundus photography, OCT, and OCT angiography) with systemic and clinical data to develop predictive algorithms for DR progression. Preliminary results indicate a significant decline in progression rates from non-proliferative to proliferative DR, reflecting advances in glycemic control, screening, and anti-VEGF therapies. The study's AI-driven tools have demonstrated high predictive accuracy, offering reliable biomarkers for clinical decision-making. Dr. Couturier further described the two-year extension of observation of a sub-group of the EVIRED cohort in which the investigators will add assessments of visual function using the same the devices as those called for in the MTM Vision – DRCR studies AR and AS described previously). The data collected will be an important early supplement to AR and AS data, and this collaboration between MTM Vision and EVIRED reinforces the power of working together toward shared goals of enhancing understanding of the natural history of DRD and validation of useful biomarkers and endpoints that can demonstrate progression/regression of disease and predict progression risk.

7. Importance of listening to and learning from community partners

To the gathering of predominantly academic and industry partners, Ms. Emily Coles used a breathing exercise to help the audience understand the psychological impact of eye exams and risk of vision threatening complications. Following the passionate retelling of her most recent eye exam, Ms. Coles joined a panel discussion about the value of community voices. The panel, which included Dr. Angela Elam (University of Michigan), Ms. Candyce Jenkins (Diabetic Mom Coach), and Mr. Adam Leone (University of Cincinnati College of Medicine) discussed barriers to better eye health. With both Ms. Coles and Ms. Jenkins living with T1D, patient voice was well-represented within the panel.

- **Mr. Leone, as part of his work as a dual degree MPH-MD student,** had tried to identify where the largest barriers to eye screening were. Given that over half of individuals with diabetes, who all have an elevated risk of eye complications, do not attend their yearly dilated eye exam, these findings offered widespread clinical potential. He found that common barriers include: (i) not knowing or having a relationship with a local ophthalmologist; (ii) difficulty or impossibility in securing transportation to the eye doctor; (iii) inability to take time off work to go to their screening; (iv) affordability issues; and (v) lack of referral by their PCP to go get screened. Most interestingly, Mr. Leone cited data indicating that 20% of individuals are diagnosed with DRD at the time of their diagnosis with T2D, meaning they were unable to be screened as they did not know they even had diabetes.
- **Dr. Elam said that one of the best ways to combat these barriers is community engagement and partnership;** while up to 94% of severe vision loss from diabetes can be prevented, at least 50% of individuals with diabetes are not receiving dilated eye exams as recommended. She cited community-led research as the gold standard in partnering with communities to identify and address the disparities that exist in our health system, including vision health and eye care. This commentary was echoed in a presentation from Dr. Chris German (Chair of MTM Vision's Lay Advisory Committee), who shared his experience over the last 37 years with T1D to help researchers understand the value of inclusive drug development. By sharing their stories, these speakers helped underline the value of understanding both the pathophysiology as well as impact to individuals who live with the disease.

--by Jeremy Alkire, Monica Oxenreiter, and Kelly Close