National Eye Institute
Research Today...Vision Tomorrow

Eliminating Blindness & Improving Quality of Life Through Vision Research

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Prevent Blindness: Focus on Eye Health National Summit
July 14, 2021

Why Does Our Work Matter?

- **Impact on quality of life**: blindness is among conditions that Americans fear most, work that matters
  - Daily living: driving, recognizing people, reading
  - How we experience the world, link to emotion
  - Risk of isolation, depression, acceleration of dementia
- **Impact on science**: enormous, broad
  - NEI: 8 Nobel Prize winners (initially Hubel & Wiesel)
  - Many seminal innovations occurred first in eye & visual system → accessible setting for generalizable research


Research

JAMA Ophthalmology | Original Investigation

Public Attitudes About Eye and Vision Health

Adrienne W. Scott, MD; Neil M. Bressler, MD; Suzanne Ffolkes, BA, MA; John S. Wittenborn, BS; James Jorkasky, MBA


The Worst That Could Happen? Going Blind, People Say

134

Paul Rogers

1. Where Have We Been (in past 5 years)?

Eye & Vision Research: A Window to Innovation…

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Example #1: Ocular Imaging

- OCT: revolution in research & clinical care, **qualitative to quantitative**
- Ex: guide to personalized anti-VEGF therapy for AMD → savings of $2.2B/$9B for patients/government
- High-speed Fourier-domain OCT → to 3D volumetric imaging
- **OCT Angiography**: noninvasively detect flow & motion, capillary-level resolution, potential to generalize across other fields (structure & function)

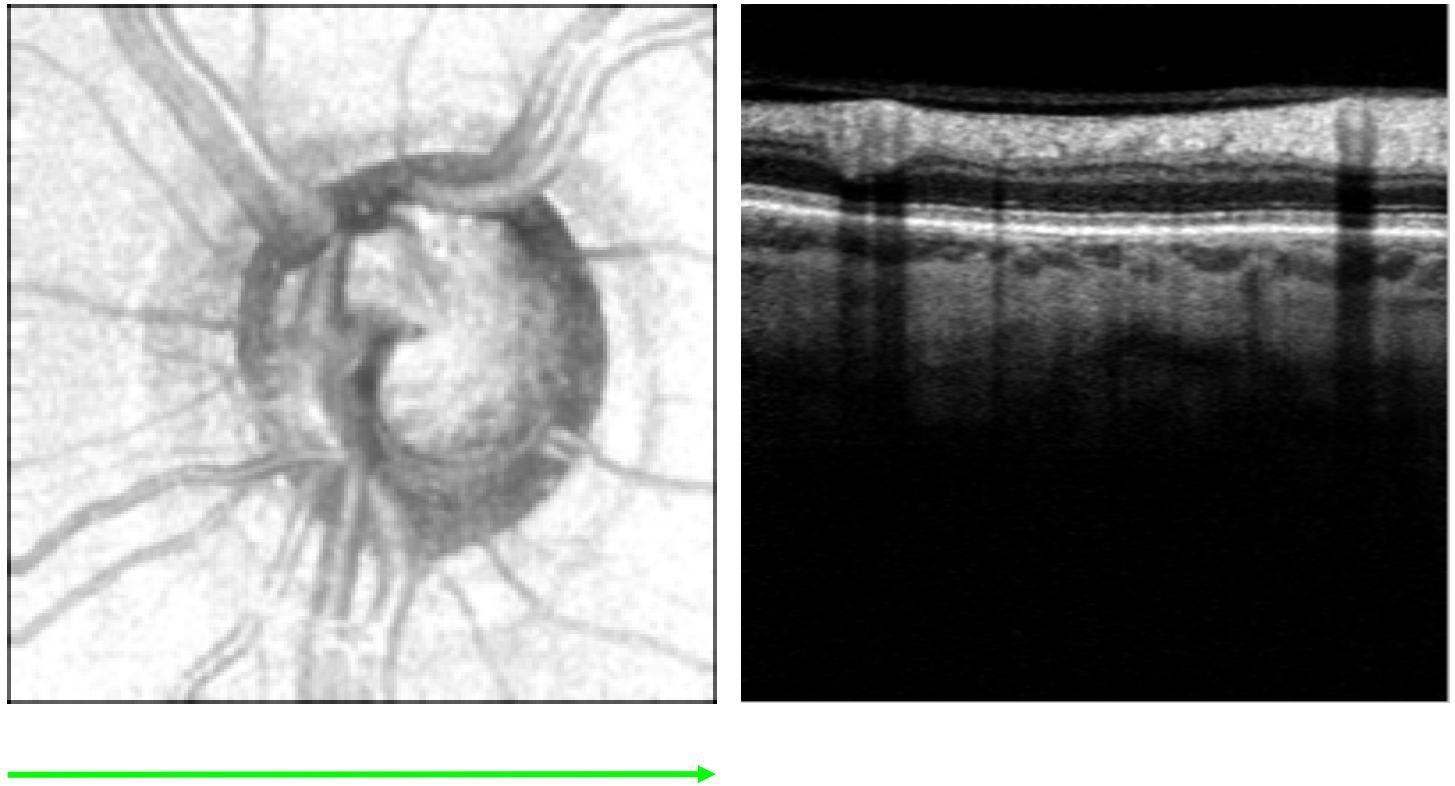


Image and video courtesy of David Huang, MD, PhD, and Yali Jia, PhD (OHSU Casey Eye Institute)

Windsor MD et al. *Am J Ophthalmol* 2018; 185:115-22
Hormel TT, et al. *Prof Retin Eye Res* 2021 Mar 22:10965

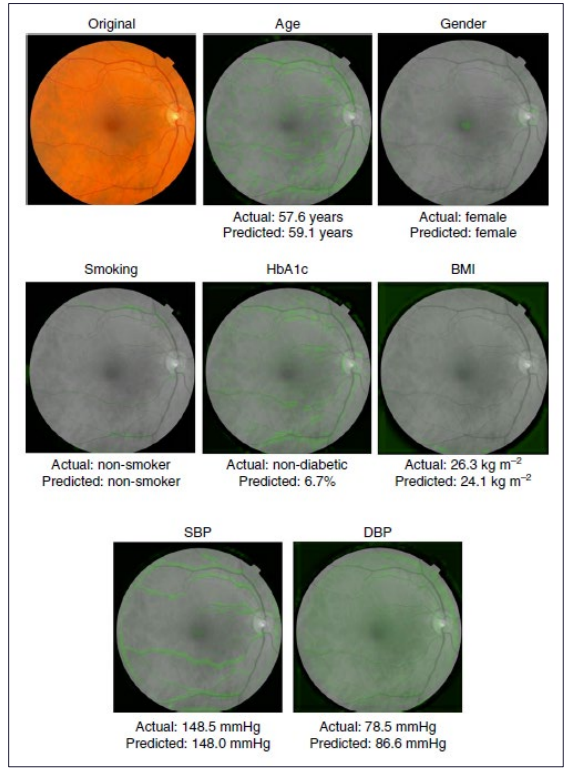
Example #2: Gene Therapy

- Infants with Leber Congenital Amaurosis (20 years ago): "we can provide supportive care as your child loses vision"
- **First FDA-approved gene therapy for an inherited disease** → utility of precision medicine (RPE65 mutation)
- Regenerative medicine: advancing treatment using gene editing, cell reprogramming, cell-based therapies (Audacious Goals Initiative)

Video courtesy of Jean Bennett, MD, PhD (University of Pennsylvania)
Russell S, Bennet J, Wellman JA, et al. *Lancet* 2017;390:849-60.

Example #3: Artificial Intelligence

- **First FDA-cleared autonomous AI system in any medical field** (Abramoff et al, NPJ Digit Med 2018)
- Knowledge discovery regarding systemic health (Poplin et al, Nat Biomed Eng 2018)
- Prediction of AMD progression (Yim et al, Nat Med 2020)



2. What is unique about this point in time?

Opportunities and mission…

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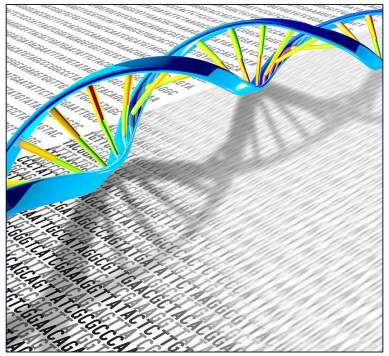
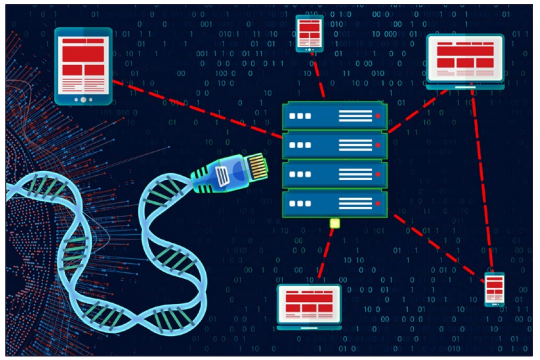
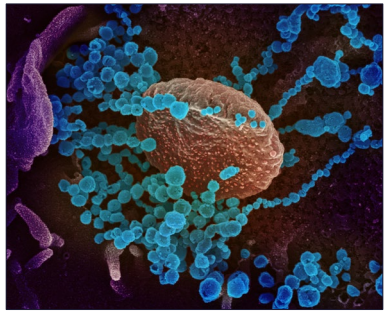
Current Climate: 2021

- Advances in **science, technology, computing**
  - **Unprecedented opportunities** for knowledge discovery, clinical translation, public health
- COVID-19 pandemic: exposed underlying health **disparities & inequities**
- Increasing recognition: scientific advances must be accessible to **entire population**
- Importance of **effective communication** of scientific findings to public







Revised NEI Mission Statement: First Since 1968

The mission of the National Eye Institute is to eliminate vision loss and improve quality of life through vision research. To achieve this mission, NEI provides leadership to:

- Drive innovative research to understand the eye and visual system, prevent and treat vision diseases, and expand opportunities for people who are blind or require vision rehabilitation
- Foster collaboration in vision research and clinical care to develop new ideas and share knowledge across other fields
- Recruit, inspire, and train a talented and diverse new generation of individuals to expand and strengthen the vision workforce
- Educate health care providers, scientists, policymakers, and the public about advances in vision research and their impact on health and quality of life.

3. Where are we heading?

NEI Strategic Plan 2021: Vision for the Future…

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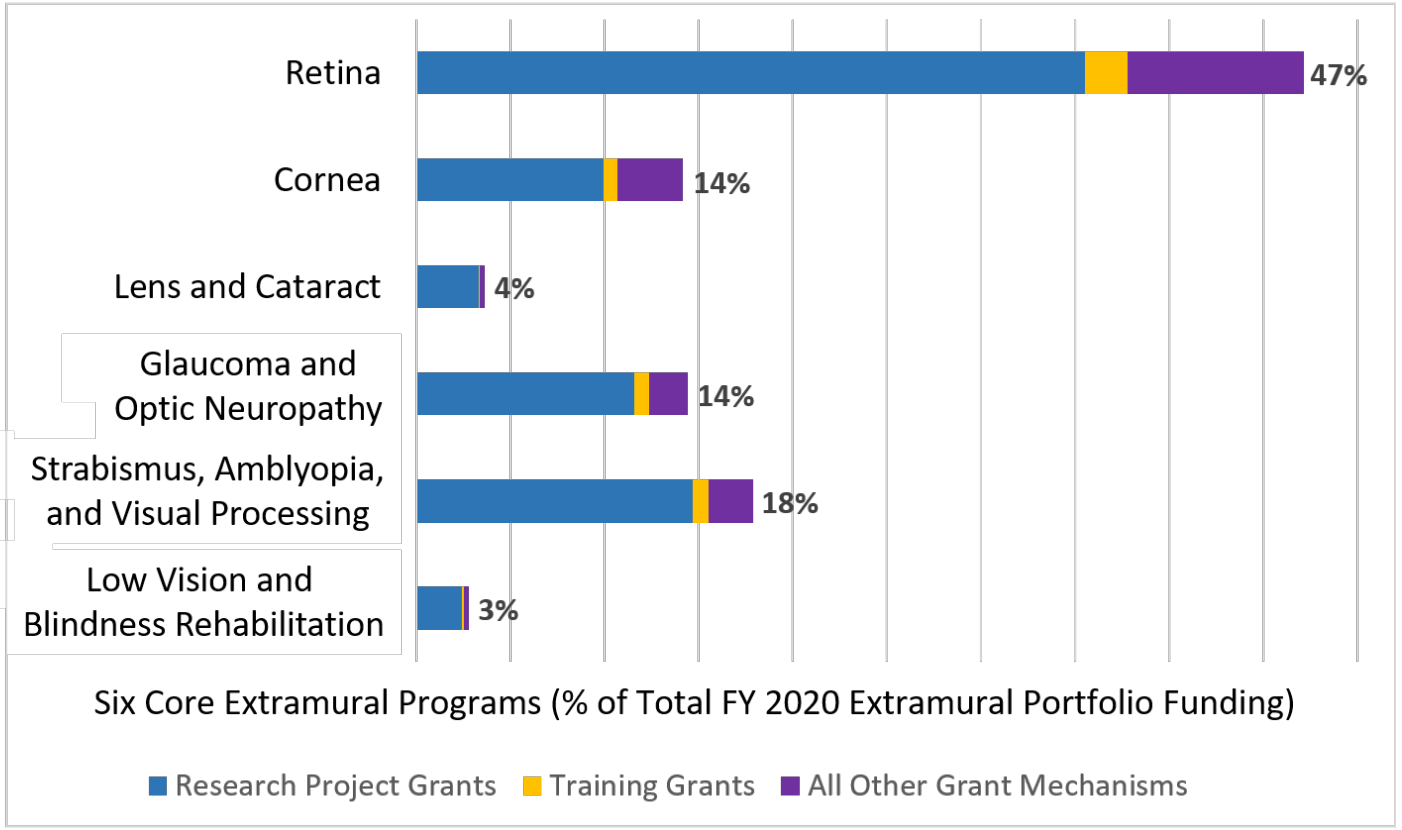
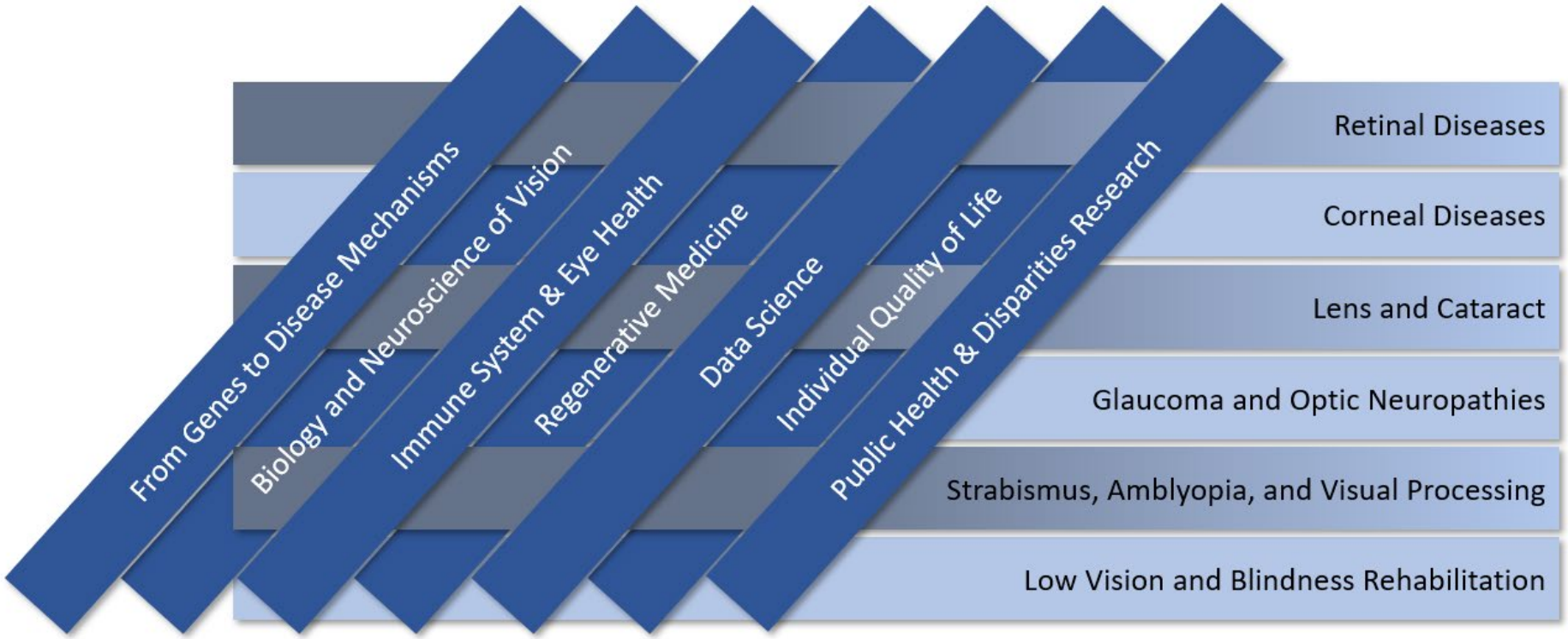
What's Here Now: Core NEI Programs

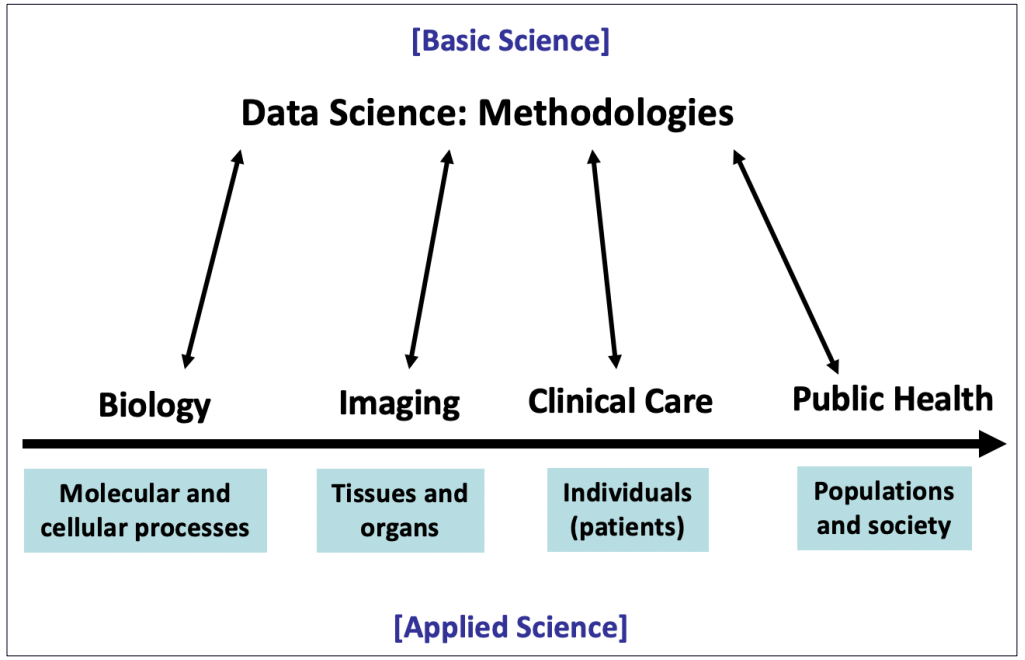


What's New: Cross-Cutting Areas of Emphasis



Area #1: Data Science (Big Data, AI)

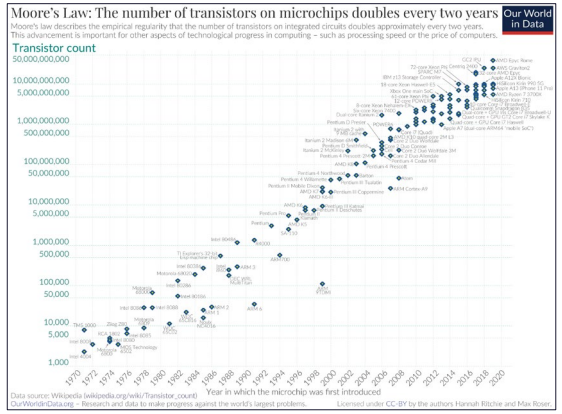
- **What's the 1 tool that every scientist & clinician uses?** Unprecedented access to large-scale data…
- **Biology**: Human Genome Project → genomics, proteomics, metabolomics, transcriptomics, etc.
- **Imaging**: noninvasive, raw structural & functional data (photo, OCT, visual fields, etc.)
- **Clinical**: EHRs, highly-structured exam, correlation with systemic health
- **Public health**: large-scale datasets, social determinants of health

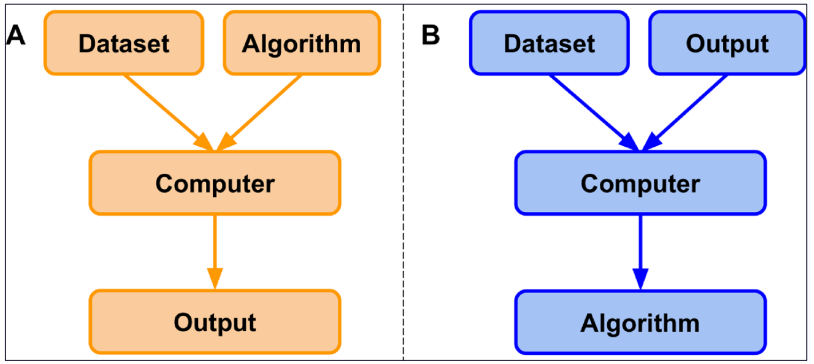


Shortliffe EH, Cimino JJ, Chiang MF. *Biomedical Informatics, 5th edition.* Springer; 2021.

New Analytic Methodologies

- Continuing exponential advances in computing power
- AI/ML methods: learn complex, latent relationships
  - Technologies of deep learning & convolutional neural networks: origins in systems neurobiology of vision
- Academic-industry collaborations
- **Need large, well-curated datasets**





https://en.wikipedia.org/wiki/Moore%27s_law

Choi RY, et al. *Trans Vis Sci Technol* 2020; 9:14.

Opportunity: Data Sharing & Harmonization

- Challenges in generalizability of AI study findings
  - Often homogeneous datasets from few centers
  - Real-world data is often lower quality
  - Heterogeneity among different imaging devices, different races, different populations
- Multiple small clinical trials that address similar problems: underpowered, unable to share data
- Opportunity for **cross-modality data analysis in vision** (e.g. imaging, EHR, genomics, metabolomics)
- **Need incentives for data sharing & collaboration**

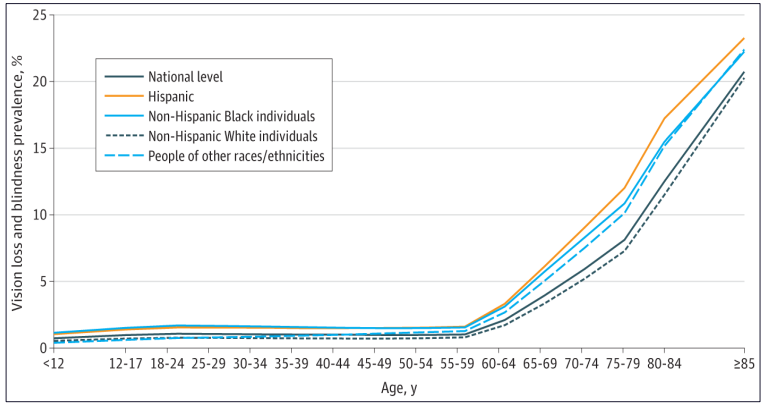
https://eyewire.news/articles/idx-and-topcon-sign-exclusive-ai-platform-agreement-for-the-u-s-market/
Work of Michael Abramoff, MD, PhD (University of Iowa)

Opportunity: Imaging Standards

- **"Can't easily exchange data among imaging systems"**
- **Challenges for clinical care:**
  - Former institution maintains 2 image management systems concurrently because of interoperability challenges, lack of standards conformance
- **Enormous barriers to research involving images**:
  - Very difficult to obtain quantitative image metrics for research: biomedical informatics PhD student unable to obtain data (OCT, VF) after 1 year
  - IRIS Registry: customized interfaces to "pull" or "push" EHR data
  - Unable to include image data into large-scale datasets (e.g. IRIS, All of Us)

Area #2: Individual Quality of Life

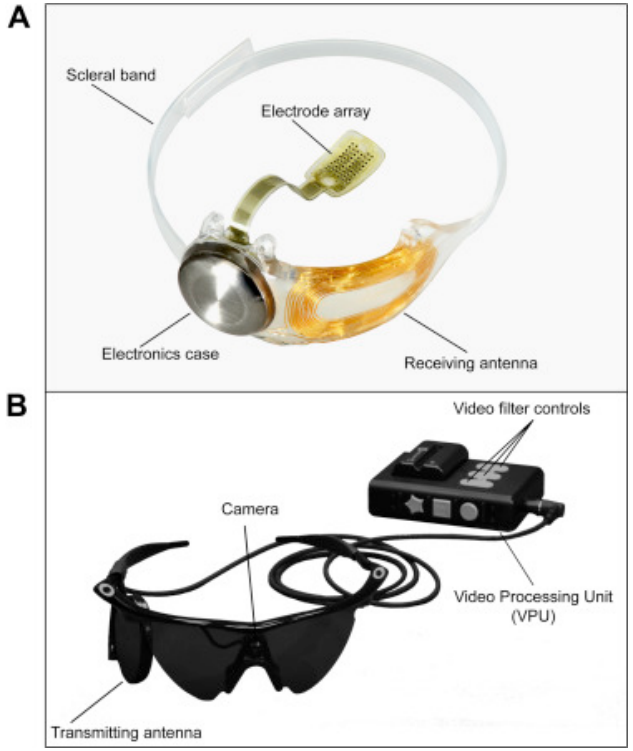
- NEI mission: "improve quality of life", "expand opportunities" for those with blindness or low vision
  - 7.1M Americans with low vision (≤20/40), 1.1M with blindness (≤20/200)
  - Globally: 250M with low vision or blindness
  - Increasing prevalence as population ages
- Increasing recognition of importance of incorporating patient perspectives in health-related quality of life assessments
  - Outcome measures for clinical trials, patient-reported outcomes



Flaxman AD, et al. *JAMA Ophthalmol* 2021 May 13:e210527.

Impact of Vision Rehabilitation

- **Examples of impact**: transportation, education, employment
- **Traditional**: magnifier, assistive technology (e.g. screen reader)
- **Emerging**: technology & innovation (e.g. retinal prosthetic…)
  - Video camera (eyeglasses) → processing → wireless transmission to implant array of electrodes → array stimulation on retina → visual perception
  - Drug delivery & bioelectronic implants (MEMS, nanotechnology)
  - Wearable electronics (data acquisition & analytics)
  - Bioengineered scaffolds (applications for cell-based therapies)
  - **Lessons: innovation across disciplines, real-world translation**



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Da Cruz L, et al. *Ophthalmology* 2016;123:2248-54.
Abiotic-Biotic Interfaces for Ophthalmology (http://ibt.usc.edu/symposium/), Jan 2021

Example: Retinal Prosthetic for Rehabilitation

- Retinitis pigmentosa: rare genetic condition with gradual loss of peripheral vision, night vision, and often blindness.
- **First FDA-approved implanted retinal prothesis system** for adults with advanced RP (Second Sight Medical Products, Argus II, Feb 2013)
- Device (video camera, eyeglasses with transmitter, video processing unit, artificial retina) replaces the function of degenerated cells in retina.

Video courtesy of Mark Humanyn, MD, PhD (USC) showing Lisa Kulik, who had not bowled since she lost her vision over 20 years ago. After receiving the Argus II implant, she has taken up the sport again.

Opportunity: Rehabilitation for Brain-Based Vision Impairment

- **Cerebral visual impairment (CVI)**: major cause of childhood blindness
  - Causes/associations: prematurity, perinatal brain damage, oxygen deprivation…
  - Visual acuity & field deficits, higher-order deficits (e.g. attention & recognition)
- Need understanding of **neural basis** (applications to TBI/stroke)
- Need **tools & guidelines** for diagnosis, classification (quantitative biomarkers), management
- Different rehabilitation needs of **brain-based vs. ocular impairment**
- Need interdisciplinary approach (structural & functional imaging, neuroscience & neural connections, PT/OT, educators)

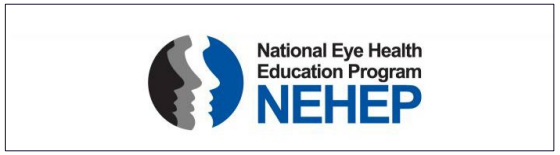
Opportunity: Addressing Quality of Life

- Society increasingly reliant on **computing & mobile devices with visual cues** → barriers from visual loss
- Need user-friendly innovations for accessibility
  - Example: mobile apps with cameras/sensors → computer vision or AI to identify objects in environment, non-visual outputs
- Need to understand factors associated with successful education & employment for visually impaired people → translate into best practices, develop new devices
- Need patient perspectives: update vision-related quality of life instruments & patient-reported outcomes

Video courtesy of Giovanni Fusco, PhD, and James Coughlan, PhD (Smith-Kettlewell Eye Research Institute)
Fusco G, et al. Comput Help People Spec Needs 2020;12376:485-94.

Area #3: Public Health & Disparities Research

- Visual loss & blindness: **leading causes in disability** in US
- Public health impact: **economic burden** to society from lost productivity & higher incidence of falls, accidents, depression
- Significant gaps in care for **high-risk groups** (e.g. elderly, children, women, rural & urban underserved communities)
- Coordination with NASEM report (vision health), Healthy People 2030 (promote prevention behaviors), USPSTF (evidence review for health care recommendations), NEHEP (promote eye health) → **how to make scientific advances accessible to entire population?**



Opportunity: Delivery & Access to Care

- **Telehealth**: remote delivery of care, disease surveillance, health promotion, population health
  - Trends: "real" to "virtual" (entertainment, communication…), accelerated adoption during COVID-19 pandemic
- Need to evaluate telehealth **efficacy, acceptability, cost-effectiveness** & develop new models for remote care
- Need to understand **social determinants** relevant to vision disease & eye care (e.g. education, employment, housing density, transportation…)
  - Impact on preventable vision loss (e.g. access to care, treatment compliance), **integration into electronic systems** for analysis

Collon S, … Myung D, et al. *Asia Pac J Ophthalmol* 2020;9:54-8.

Why Does Diversity Matter?

- "Recruit, inspire, and train a talented & diverse new generation to strengthen the vision workforce": cognitive & identity diversity
  - Benefits of **interdisciplinary research**: major innovations
  - Evidence that **teams with different kinds of thinkers outperform homogeneous groups**, including improved problem solving & innovation
  - May have stronger perspective on understanding role of **social determinants of health** & other factors in health outcomes
  - **Eye diseases often affect vulnerable populations disproportionately:** benefits of deeper familiarity with populations, improved trust
- NEI needs to **work with entire community** to address (academia, professional organizations, community workers, industry)

Ginther DK, et al. *Science* 2011; 333 (6045): 1015-9.
Page SE. *The Diversity Bonus: How Great Teams Pay Off in the Knowledge Economy*, 2017
Swartz TH et al. *J Infect Dis* 2019;220(220 Suppl 2):S33-S41.
Fairless EA, et al. *Ophthalmology*. 2021; S0161-6420 (21) 00012-9.

Concluding Thoughts

- **Work that matters**: transformative impact of **eliminating vision loss & improving quality of life**
- Many examples of innovation → **transformative impact of vision research on clinical care**, with benefits of interdisciplinary work
  - "Drive innovative research"
  - "Foster collaboration to develop new ideas & share knowledge across other fields"
  - "Recruit, inspire, and train a talented & diverse new generation"
- **NEI Strategic Plan**: excitement about future innovations