Project Notes:

Project Title: OptiCare: A Mobile Application Diagnosing Ocular Diseases through Novel Point of Care Methods Utilizing Machine Learning TechnologyOptiCare: A Mobile Application Diagnosing Ocular Diseases through Novel Point of Care Methods Utilizing Machine Learning Technology
Name: **Isha Nagireddy**

Contents:

Please Read: The following project notes encompass the entire research process, from preliminary brainstorming to final results. Articles 1-3 are related to brainstorming potential project areas over the summer, and the rest of the articles are a combination of understanding the feasibility of using genetic information for the testing of glaucoma and cataracts, and research in the final idea, of using image data for the diagnosis of glaucoma and cataracts.

Knowledge Gaps:

This list provides a brief overview of the major knowledge gaps for this project, how they were resolved, and where to find the information.

Knowledge Gap	Resolved By	Information is located	Date resolved
Accessibility Issues With Eye Care	Research paper	https://www.aaojournal.org/article/S0161-6420(22)00529-2/fulltext	1/2/2024
Glaucoma basic information	Research paper/articles	https://www.nhs.uk/conditions/glaucoma https://www.aao.org/eye-health/diseases/what-is-glaucoma	12/24/2023
Cataracts basic information	Research paper/articles	https://www.hopkinsmedicine.org/health/conditions-and-diseases/cataracts https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/cataracts	1/5/2024
Diagnostic methods used in a point-of-care setting for glaucoma and cataracts	Research paper/articles	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2643302/	1/18/2023
The relationship between sound waves and intraocular pressure	Research paper	https://onlinelibrary.wiley.com/doi/full/10.1002/eng2.12355	1/26/2024

Diagnostics for cataracts and glaucoma through machine learning models	Research paper	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10217711/	11/15/2023
Mobile app development for the diagnosis of cataracts and glaucoma	Research paper	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10538832/	11/2/2023

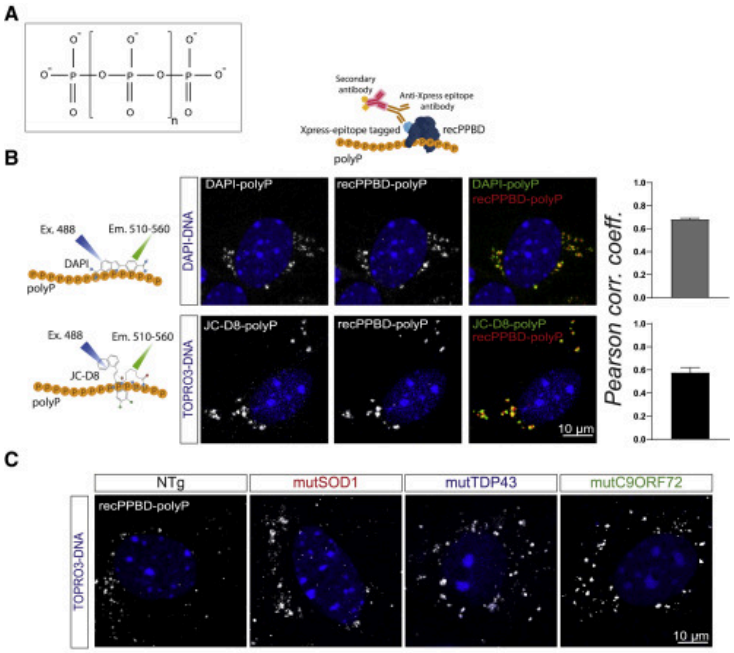
Literature Search Parameters:

These searches were performed between (8/15/2023) and 2/8/2024.
List of keywords and databases used during this project.

Database/search engine	**Keywords**	**Summary of search**
Google Search Engine	Glaucoma, cataracts, diagnoses	Research articles of the general paractice on how to diagnose glaucoma and cataracts.
PubMed	Sound waves, glaucoma	A novel relationship found that connects the reflection wave produced by sound waves to the internal pressure found in the eye.
NCBI	Glaucoma, cataracts, fundus imaging	Different diagnostic methods using fundus imagers and point of care fundus images were analyzed.

Article #1 Notes: Excessive release of inorganic polyphosphate by ALS/FTD astrocytes causes non-cell-autonomous toxicity to motoneurons

Source Title	Excessive release of inorganic polyphosphate by ALS/FTD astrocytes causes non-cell-autonomous toxicity to motoneurons
Source citation (APA Format)	Arredondo, C., Cefaliello, C., Dyrda, A., Jury, N., Martinez, P., Díaz, I., Amaro, A., Tran, H., Morales, D., Pertusa, M., Stoica, L., Fritz, E., Corvalán, D., Abarzúa, S., Méndez-Ruette, M., Fernández, P., Rojas, F., Kumar, M. S., Aguilar, R., … van Zundert, B. (2022). Excessive release of inorganic polyphosphate by ALS/FTD astrocytes causes non-cell-autonomous toxicity to motoneurons. Neuron, 110(10). https://doi.org/10.1016/j.neuron.2022.02.010
Original URL	https://www.cell.com/neuron/fulltext/S0896-6273(22)00148-9
Source type	Peer-reviewed journal article
Keywords	ALS, genes, gene motor neurons toxicity, polyP,
#Tags	N/A
Summary of key points + notes (include methodology)	Notes - Results - The polyP that was observed directly causes motor neuron death, and is released when ALS is present. “Interestingly, it has been shown that inorganic polyP is released from astrocytes (Angelova et al., 2018; Holmström et al., 2013), enhances neuronal excitability (Stotz et al., 2014), interacts with positively charged polyamines through molecular complementarity, and has a high affinity for glass (Kornberg et al., 1999). These findings, along with the longstanding difficulty in identifying toxic organic molecules within ALS-ACM (Mishra et al., 2020; our unpublished data), led us to hypothesize that excessive inorganic polyP is released by ALS/FTD astrocytes to induce neuronal hyperexcitability and subsequent MN death”. Staining- ● DAPI -> identify general DNA ● JC-D8 -> binding to polyP ● recPPBD -> detecting polyP Mice models - mutSOD1, mutTDP43, mutC9ORF72 Methods - 1. Confirmed staining methods would detect polyP. 2. Determined subcellular primary localization. 3. Compared polyP levels of non transgenic mice to mutant mice and found significantly more polyP in mutations.

	4. Synthetic polyP was created to recreate the effects. 5. To confirm that the polyP was causing the toxicity, polyP was reduced in mutSOD1 by transducing with AAV9 vectors carrying different versions of the yeast PPX1 gene, fused to GFP, and driven by a CMV promoter. It was confirmed polyP was causing significant MN death. 6. Methods to neutralize polyP were found, including pre-treatment with recPPX/PPase, CIP, etc.
Research Question/Problem/ Need	Is the harmful phenotype of Amyotrophic Lateral Sclerosis (ALS), the death of motor neurons, caused by excessive polyP?
Important Figures	 Cell imaging of polyP in different mice mutations.
VOCAB: (w/definition)	1. polyP - Polyphosphate (polyP) is a highly anionic inorganic polymer composed of phosphate monomers, connected by high-energy phosphoanhydride bonds. 2. DAPI - DAPI (4′,6-diamidino-2-phenylindole) is a blue-fluorescent DNA stain that exhibits ~20-fold enhancement of fluorescence upon binding to AT regions of dsDNA. 3. Staining - Staining is a technique used in microscopy to enhance contrast in a microscopic image. Stains and dyes are frequently used to highlight structures in microbes for viewing, often with the aid of different microscopes. 4. ALS - A disease affecting motor neurons of the spinal cord, which causes progressive weakness and atrophy of muscles.
Cited references to follow up on	1. High sensitivity, quantitative measurements of polyphosphate using a new DAPI-based approach. 2. Wild-type nonneuronal cells extend survival of SOD1 mutant motor neurons in ALS mice.

	3. Non-cell autonomous effect of glia on motor neurons in an embryonic stem cell-based ALS model. 4. Mutant SOD1-expressing astrocytes release toxic factors that trigger motoneuron death by inducing hyperexcitability.
Follow up Questions	1. Is polyP the only inorganic compound that is causing motor neuron death? What else is causing the phenotype of ALS? 2. Can this AAv9 vector that allows the scientists to reduce the amount of polyP in mice also be applied in humans? What further testing needs to be done in order for this to happen? 3. Is the gene knockout produced by the AAV9 vector permanent? How long does the gene knockout last? 4. Is there an exact value, or percentage, of deaths prevented when polyP is reduced? What will happen if polyP is completely removed?

Article #2 Notes: The depressive spectrum: diagnostic classification and course

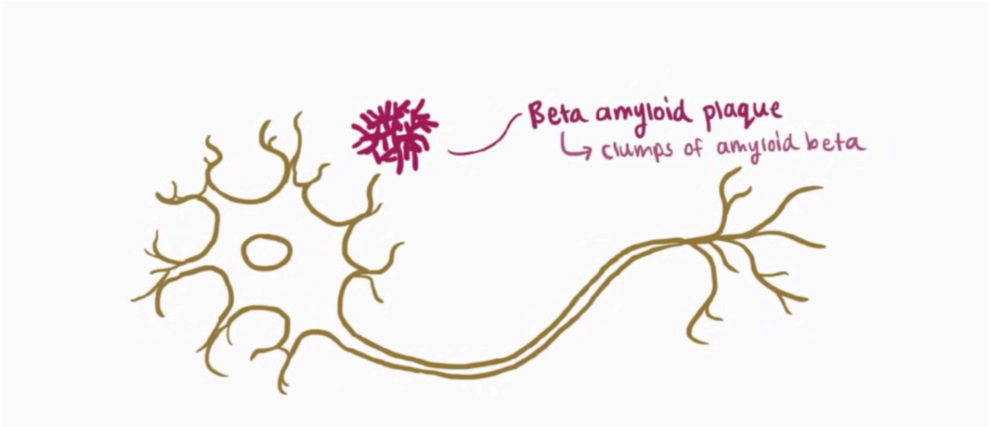
Source Title	The depressive spectrum: diagnostic classification and course
Source citation (APA Format)	Angst, J., & Merikangas, K. (1997). The Depressive Spectrum: Diagnostic Classification and course. Journal of Affective Disorders, 45(1–2), 31–40. https://doi.org/10.1016/s0165-0327(97)00057-8
Original URL	https://www.sciencedirect.com/science/article/pii/S0165032797000578?via%3Dihub
Source type	Peer-reviewed research paper
Keywords	Depression, classification, levels, spectrum, diagnostics
#Tags	N/A
Summary of key points + notes (include methodology)	Summary - The recent interest in mental disorders over the past few decades is because of the introduction of antidepressants, the development of long-term studies on these disorders, and the development of diagnostic tools. Numerous studies have been conducted to date, and many in particular, are related to the diagnostic methods of depression. However, these diagnostic methods seem to have some flaws: recent studies show that patients exemplifying signs of depressive symptoms, are not classified as depressed in some cases because they don't "surpass the diagnostic threshold". However, it is important to note that they still pose much harm to themselves.This study aims to broaden the range of depressive symptoms that are related to depressive disorders, and bring the idea that depression is a spectrum to light. This study was conducted in Switzerland on

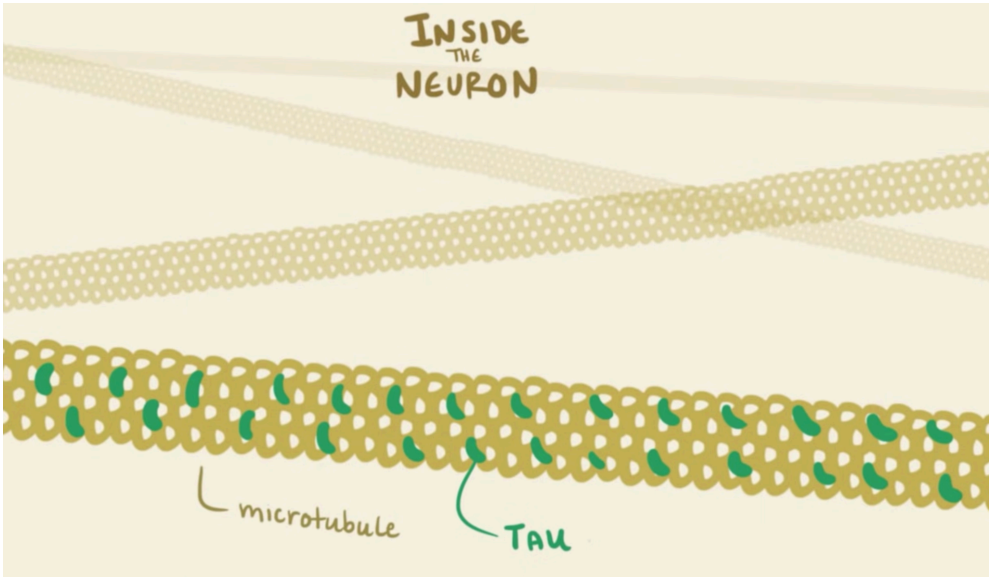
	young adults aged 18-19 years old. Through a series of individual interviews/check-ins. Signs of threshold depression (major depression and dysthymia), and sub-threshold depression (depression symptoms, minor depression, and recurrent brief depression) were analyzed. A main finding in the results was that the prevalence of sub-threshold depression was high in the community. In addition to this, sub-threshold depression was seen to indicate threshold depression in the past or future of an individual. As a result, it is important that we acknowledge the idea of minor depression, depression symptoms, and recurrent brief depression symptoms when diagnosing an individual with or without depression. Sub-threshold depression needs to be a part of the picture when diagnostic tools are created and utilized.
Research Question/Problem/ Need	Depression diagnosis should not be black-and-white, but rather address the spectrum and act upon it. Not all individuals are classified as depressed, but they still pose a harm to themselves..
Important Figures	Table 5. Subthreshold depression as antecedent of major depressive disorder[a] **Initial two interviews age 20–22** | **Follow-up three interviews age 28–35** **Major depression** | **Sub-threshold depression[b]** | ***n*** | **Major depressive disorder** | ***n*** | **%** No (*n*=387) | No | 267 | No | 221 | 82.4 No (*n*=387) | No | 267 | Yes | 46 | 17.2 No (*n*=387) | Yes | 110 | No | 78 | 70.9 No (*n*=387) | Yes | 110 | Yes | 32 | 29.1 Yes (*n*=50) | No | 32 | No | 20 | 62.5 Yes (*n*=50) | No | 32 | Yes | 12 | 37.5 Yes (*n*=50) | Yes | 18 | No | 8 | 44.4 Yes (*n*=50) | Yes | 18 | Yes | 10 | 55.6 Sub-threshold depression eventually turns into major depressive disorder.
VOCAB: (w/definition)	1. DSM - The Diagnostic and Statistical Manual of Mental Disorders (DSM) is the handbook used by healthcare professionals in the United States and much of the world as the authoritative guide to the diagnosis of mental disorders. 2. Sub-threshold depression - Subthreshold depression (also referred to as subsyndromal depression, subclinical depression, or mild depression) is an umbrella term that encompasses several conditions that do not meet criteria for a depressive disorder outlined by the past and current versions of nosological manuals. 3. Major depressive disorder - a mental health condition that causes a persistently low or depressed mood and a loss of interest in activities that once brought joy.

	4. Dysthymia - Dysthymia is a milder, but long-lasting form of depression. It's also called persistent depressive disorder.
Cited references to follow up on	1. The Zurich Study: a prospective epidemiological study of depressive, neurotic, and psychosomatic syndromes. IV: Recurrent and nonrecurrent brief depression 2. “Double depression”: superimposition of acute depressive episodes on chronic depressive disorders 3. Brief depression among patients in general practice. Prevalence and variation by recurrence and severity 4. Research diagnostic criteria: rationale and reliability
Follow up Questions	1. Is the DSM criteria used internationally for all mental health cases? If not, what other criteria systems are used? Are they better? 2. Is there a way sub-threshold depressed individuals can still be monitored even though they don’t have complete depression? 3. Can sub-threshold individuals take the same medicine as major depressive disorder individuals? What will happen if they do? 4. Can the diagnostic criteria be adapted for social media and technological platforms?

Article #3 Notes: Alzheimer's disease - plaques, tangles, causes, symptoms & pathology

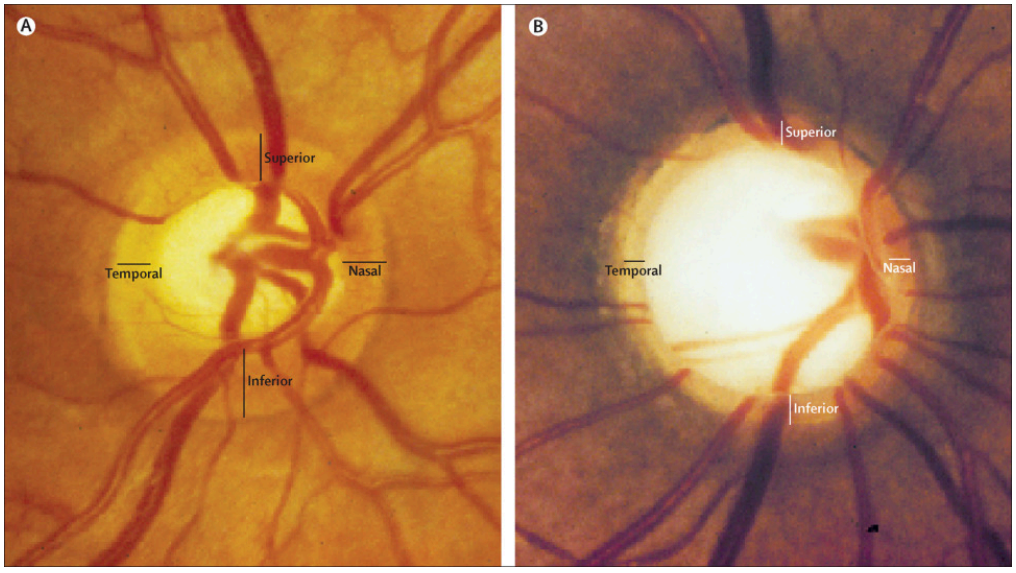
Source Title	Alzheimer's disease - plaques, tangles, causes, symptoms & pathology
Source citation (APA Format)	YouTube. (2016). YouTube. Retrieved October 17, 2023, from https://www.youtube.com/watch?v=v5gdH_Hydes.
Original URL	https://www.youtube.com/watch?v=v5gdH_Hydes
Source type	YouTube Video
Keywords	Alzheimer’s, dementia, APOE, genes, symptoms, phenotype
#Tags	N/A
Summary of key points + notes (include methodology)	Notes - 1. Alzheimer’s is a form of dementia 2. Amyloid precursor protein (APP) helps neurons grow and repair 3. After APP is used and recycled, alpha secretase and gamma secretase help chop it up

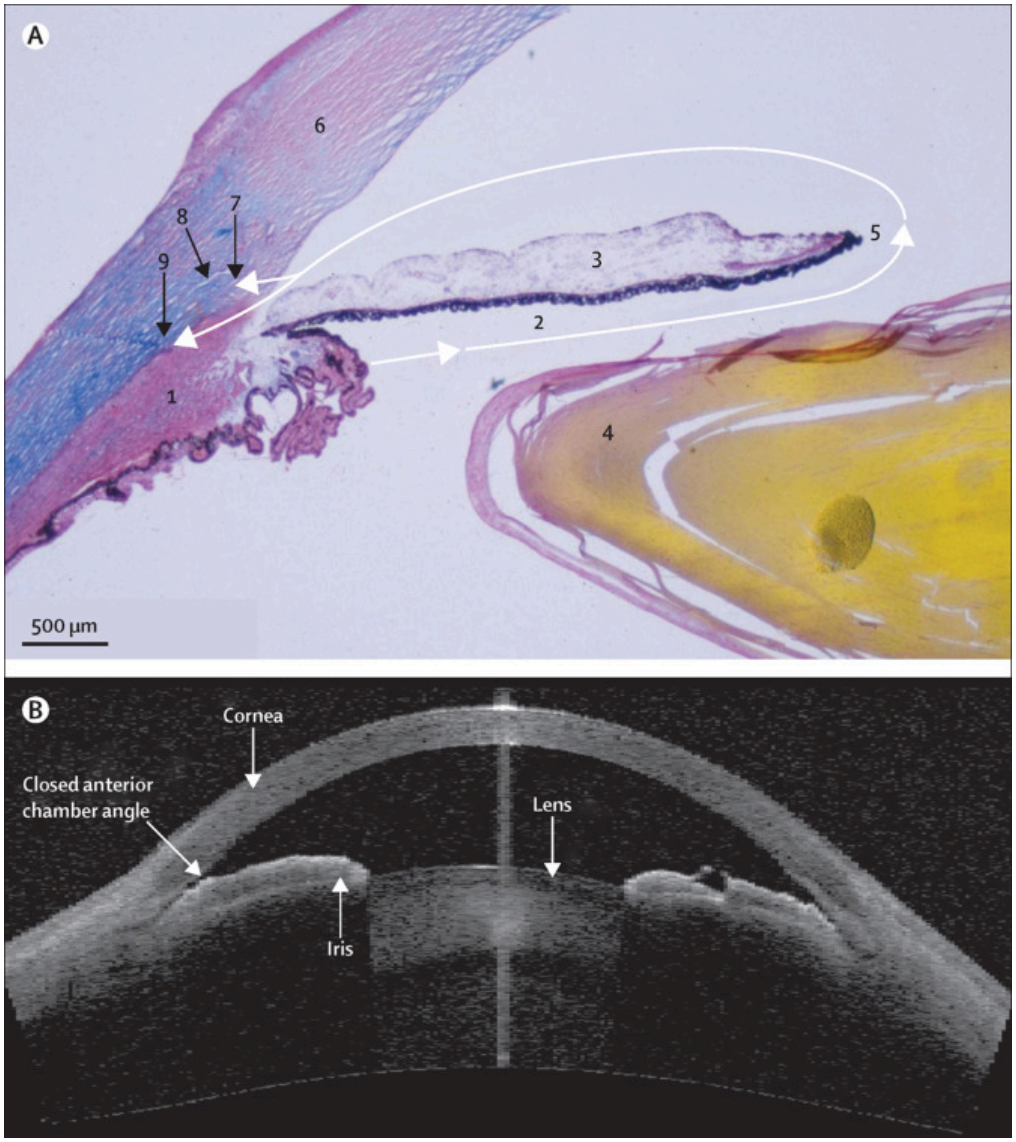
	4. If beta secretase helps slice up APP with gamma secretase, monomer is formed and not able to be recycled 5. This forms plaque plaque build up gets in between neurons 6. This disturbs signals between neurons and brain signals get messed up 7. Tau is a protein that helps keep microtubules functioning and together 8. Kinase sends phosphate groups to tau and makes the protein change shape 9. This makes tau clump up with itself and tangle, and causes apoptosis 10. When this happens at a cellular level, the brian shrinks 11. There are two forms of Alzheimer's: a. Sporadic - genetic + environmental risk factors (90% of cases) i. Effects people of higher age ii. Increased risk is connected with APOE e4 gene iii. APOE helps break down amyloid, but e4 variant is ineffective b. Familial - gene inherited that causes speed up of disease, early on-set i. Mutation of PSEN1/2: causes different location where secretase chops up APP ii. Down syndrome, extra copy of chromosome 21, causes extra APP gene and therefore increased expression of APP and plaque buildup 12. Symptoms of Alzhimer's are unrecognizable at first 13. Then leads to loss of short term memory 14. Then loose motor skills 15. Then loose long term memory and become bed-ridden 16. Diagnosis is very tough and can only be 100% certain of Alzheimer's by performing a brain autopsy after death 17. No medications currently exist that halt the progression of Alzheimer's
Research Question/Problem/ Need	Alzheimer's disease is a common form of dementia that still remains largely unknown. As a result, there are no medications and effective forms of treatment to prevent this disease.
Important Figures	 Visualization of beta amyloid plaque build-up between neurons.

	 A visual diagram of how tau proteins hold together microtubules.
VOCAB: (w/definition)	1. Tau - Tau protein (named after the Greek letter for "t") is a microtubule-associated protein that is concerned with axoplasmic transport in normal neurons. 2. APP - The APP gene provides instructions for making a protein called amyloid precursor protein. 3. PSEN 1- The PSEN1 gene provides instructions for making a protein called presenilin 1. 4. PSEN 2 - The PSEN2 gene provides instructions for making a protein called presenilin 2. 5. APOE - The APOE gene provides instructions for making a protein called apolipoprotein E. 6. Microtubules - Microtubules are polymers of tubulin that form part of the cytoskeleton and provide structure and shape to eukaryotic cells.
Cited references to follow up on	1. Vascular dementia - https://www.youtube.com/watch?v=5_RwXXhdpSg 2. Parkinson's disease - https://www.youtube.com/watch?v=8rLVU51Oeh0 3. APOE4 | APOE4 versus APOE3 - https://www.youtube.com/watch?v=ncXdFPuayKs 4. Understanding Dementia (Alzheimer's & Vascular & Frontotemporal & Lewy Body Dementia) - https://www.youtube.com/watch?v=gKZhp2JNYyI
Follow up Questions	1. If dementia is not a disease, what is it classified as? 2. Is it possible to remove the plaque build-up? How fast does this build-up occur? 3. What other genes are related to Alzheimer's other than APOE? 4. How are missense variants in APOE studied? Is what we know about gene relationships with Alzheimer's true for all races?

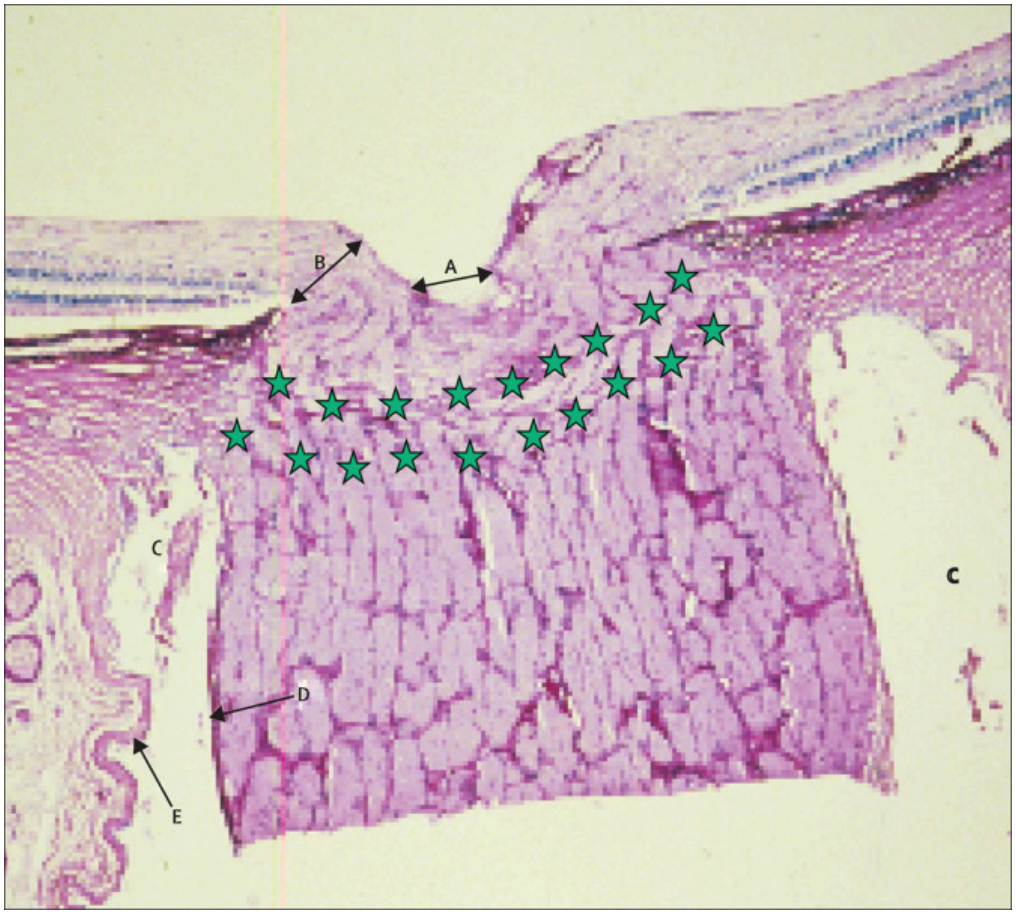
Article #4 Notes: Glaucoma

Source Title	Glaucoma
Source citation (APA Format)	Jonas, J. B., Aung, T., Bourne, R. R., Bron, A. M., Ritch, R., & Panda-Jonas, S. (2017). Glaucoma. The Lancet, 390(10108), 2183–2193. https://doi.org/10.1016/S0140-6736(17)31469-1
Original URL	https://www.sciencedirect.com/science/article/pii/S0140673617314691?via%3Dihub
Source type	Peer-reviewed journal article
Keywords	Glaucoma, diagnosis, symptoms, epidemiology
#Tags	N/A
Summary of key points + notes (include methodology)	Notes - ● Glaucoma contains numerous different sub-diseases that vary in symptoms, causes, etc ● Glaucoma has become one of the most frequent causes of blindness worldwide ● The primary risk factor of glaucoma is the increase of intraocular pressure in the eye ● Glaucoma has numerous different features: ○ Loss of retinal ganglion cells ○ Thinning of the nerve retinal fibre layer ○ Cupping of the optic disc ● Glaucoma can be split into subsections: open-angle and closure-angle glaucoma. ● The progression of glaucoma is mainly characterized by the increase of intraocular pressure in the eye. Oftentimes, this can be painless. ● An increase in intraocular pressure is a common risk factor in glaucoma patients but is not always present ● Early detection of glaucoma is hard due to a lack of pain and the slow pace of progression. However, it is vital to halt severe vision loss ● Of the 32.4 million blind people, 2.1 million of them were blind due to glaucoma in 2010 ● Glaucoma is heavily related to age because as an individual grows older, their intraocular pressure also increases ● Glaucoma was more prevalent in higher-class elder populations than in younger populations ● Primary open-angle glaucoma was highest in Africa ● Primary course angle glaucoma was most common in Asia ● Primary angle closure angle glaucoma is thought to have a worse prognosis because more people go blind to this versus pen-angle glaucoma ● Primary open-angle glaucoma is the most common type of glaucoma

	• Normal pressure glaucoma occurs when the IOP of the eye doesn't increase but glaucoma is still present due to damage to the optic nerve • Common to all forms of glaucoma is the enlargement of the optic disc • Glaucoma is related to genetic factors as well, with CDKN2B-AS1, CAV1 and CAV2, TMCO1, ABCA1, AFAP1, GAS7, TXNRD2, ATXN2 being common gene variants. • There are currently 8 gene loci that are related to glaucoma • Even though it is understood that genetics plays a role in glaucoma, the exact relations are yet to be found • 50-90% of people with glaucoma remain undiagnosed in developing countries • It is not logically feasible for everyone to be thoroughly screened for glaucoma, so it is important to screen people specifically of high-risk • Glaucoma is often identified late due to a lack of visual cues of the disease until later stages. The only way to diagnose glaucoma early is through constant monitoring of IOP levels and observations of the optic disc/nerves • Tonometry is an essential part of diagnosis as it helps identify and monitor IOP levels • The treatment of open-angle glaucoma mainly targets decreasing the intraocular pressure buildup in the eye • Medicine takes the form of eye drops in most cases • If there are severe cases of glaucoma, surgery may be required
Research Question/Problem/ Need	Glaucoma is an ocular disease that is a leading cause of blindness in the world.
Important Figures	 Regular versus glaucotamic optic discs



An eye with a healthy retinal nerve fibre layer and an eye with glaucoma's retinal nerve fibre layer.

	 An image of the healthy optic nerve head.
VOCAB: (w/definition)	1. Intraocular pressure (IOP) - Intraocular pressure (IOP) is the fluid pressure of the eye. 2. Retinal nerve fibre layer - The retinal nerve fibre layer (RNFL) is formed by retinal ganglion cell axons, which collect the visual impulses that begin with the rods and cones. 3. Optic disc - The raised disk on the retina at the point of entry of the optic nerve, lacking visual receptors and so creating a blind spot. 4. Tonometer - An instrument for measuring the pressure in a part of the body, such as the eyeball (to test for glaucoma) or a blood vessel.
Cited references to follow up on	1. HA Quigley, J Katz, RJ Derick, D Gilbert, A Sommer An evaluation of optic disc and nerve fiber layer examinations in monitoring progression of early glaucoma damage Ophthalmology, 99 (1992), pp. 19-28 2. M Kim, TW Kim, KH Park, JM Kim Risk factors for primary open-angle glaucoma in South Korea: the Namil study Jpn J Ophthalmol, 56 (2012), pp. 324-329
Follow up Questions	1. Is there a threshold intraocular pressure value that indicates glaucoma? Does this threshold fluctuate by person? 2. If someone has normal pressure glaucoma, are fundus images the best way to diagnose this individual?

	3. Are there point of care methods that allow for the diagnosis/suspicion of glaucoma to identify high risk individuals?

Article #5 Notes: Access to Eye Care in the United States: Evidence-Informed Decision-Making Is Key to Improving Access for Underserved Populations

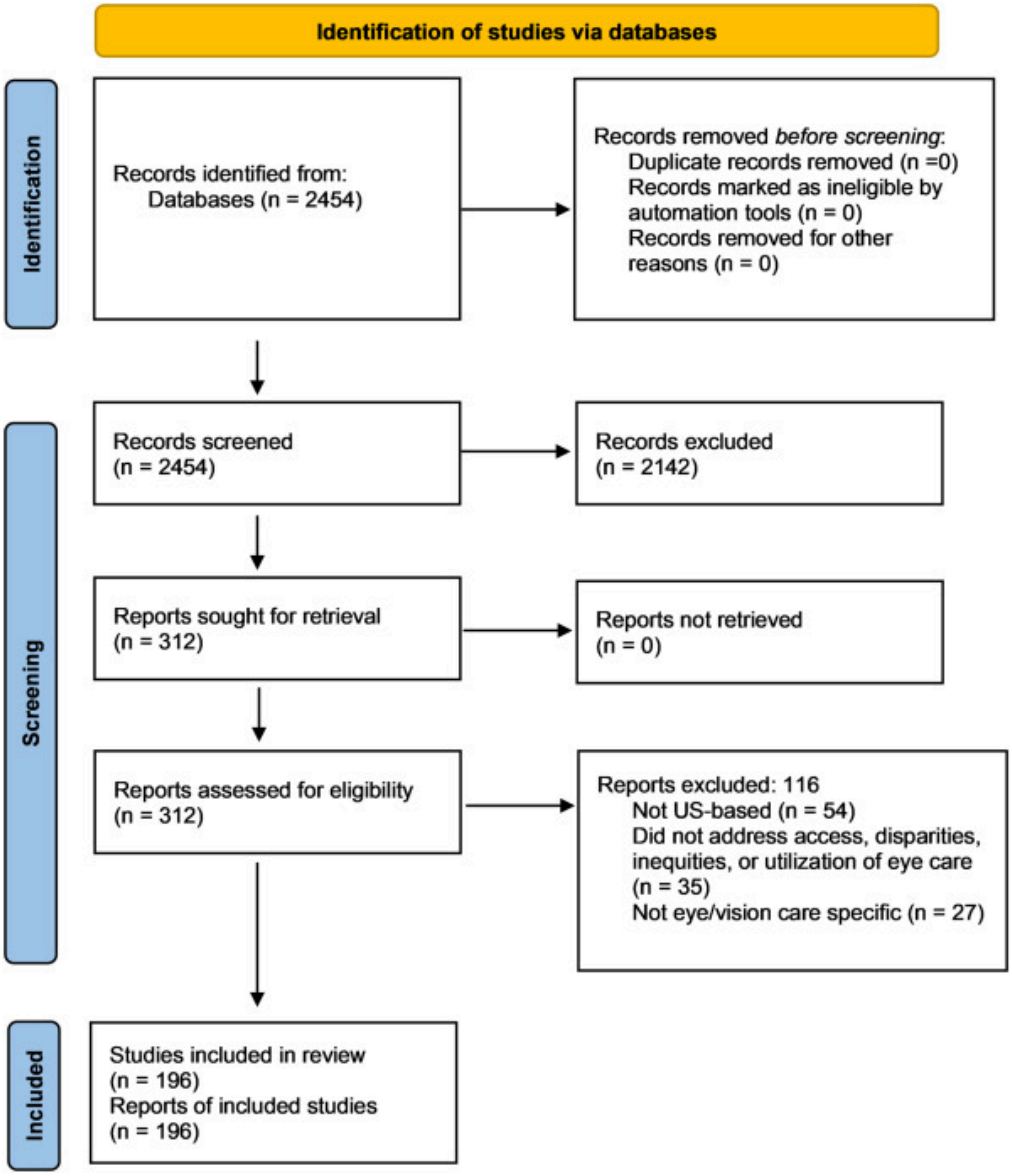
Source Title	Access to Eye Care in the United States: Evidence-Informed Decision-Making Is Key to Improving Access for Underserved Populations
Source citation (APA Format)	Ervin, A.-M., Solomon, S. D., & Shoge, R. Y. (2022). Access to eye care in the united states: Evidence-informed decision-making is key to improving access for underserved populations. Ophthalmology, 129(10), 1079–1080. https://doi.org/10.1016/j.ophtha.2022.07.011
Original URL	https://www.aaojournal.org/article/S0161-6420(22)00529-2/fulltext
Source type	Peer-reviewed research paper
Keywords	Eye care, ophthalmology, barriers, inequities, accessibility
#Tags	N/A
Summary of key points + notes (include methodology)	● Disparities in eye care are common despite current efforts ● Numerous factors influence an individual's use of eye care including geographic location, income, race, and ethnicity ● There are three main barriers to access: ○ Economic inequities - Lack of insurance plans, being uninsured, lack of transportation, cost of eyeglasses, and cost of vision-screening methods are known factors that influence an individual's decision to go to an ophthalmologist ○ Limited or no access to local eye care providers - Rural areas lack eye care providers and individuals are often forced to travel long distances for eye appointments. In many areas, there are simply no options for eye care. ○ Health literacy - There is a large lack of knowledge about eye diseases and also language barriers that can affect an individual's decision to get their eyes checked out. ● There are numerous recommendations to improve access to eye care: ○ Expanding Medicare and Medicaid - By increasing these programs, there will be an increase in eye-dilation tests being taken ○ State sponsors health insurance for children ○ School-based health centers and vision screenings ○ Federally funded community health centers

	○ Teleophthalmology - The idea of performing and monitoring eye health virtually over a call/meeting ○ Improving patient education
Research Question/Problem/ Need	There is a lack of accessibility to eye care in rural areas of the United States, leading to preventable vision loss problems.
Important Figures	*No figures were present in this paper
VOCAB: (w/definition)	1. Teleophthalmology - Teleophthalmology is the integration of electronic information and medical technology through digital medical equipment and telecommunications technology. 2. Medicare/Medicaid - Medicare is federal health insurance for people 65 or older, and some people under 65 with certain disabilities or conditions. 3. Dilated-eye exam - Dilating your pupil lets more light into your eye — just like opening a door lets light into a dark room. Dilation helps your eye doctor check for many common eye problems, including diabetic retinopathy, glaucoma, and age-related macular degeneration (AMD).
Cited references to follow up on	1. Chen E.M.v Armstrong G.W. Cox J.T. et al. Association of the affordable care act Medicaid expansion with dilated eye examinations among the United States population with diabetes. Ophthalmology. 2020; 127: 920-928 2. Solomon S.D. Shoge R.Y. Ervin et al. Improving access to eye care: a systematic review of the literature. Ophthalmology. 2022; 129: e114-e126
Follow up Questions	1. Based on Article #1 and Article #2, it is clear that eye testing for all is not a feasible solution due to high costs and lack of accessibility. Is it possible to create a point-of-care system where people with suspected glaucoma are then referred for further treatment? 2. Most of the policies for improvement in this paper are related to social changes or public policy. What improvements can be made in the scientific realm to improve accessibility to eye care? How can current diagnostic methods be simplified?

Article #6 Notes: Improving Access to Eye Care

Source Title	Imrpoving Access to Eye Care
Source citation (APA Format)	Solomon, S. D., Shoge, R. Y., Ervin, A. M., Contreras, M., Harewood, J., Aguwa, U. T., & Olivier, M. M. G. (2022). Improving access to eye care. Ophthalmology, 129(10), e114–e126. https://doi.org/10.1016/j.ophtha.2022.07.012
Original URL	https://www.aaojournal.org/article/S0161-6420(22)00530-9/fulltext
Source type	Peer-reviewed research journal

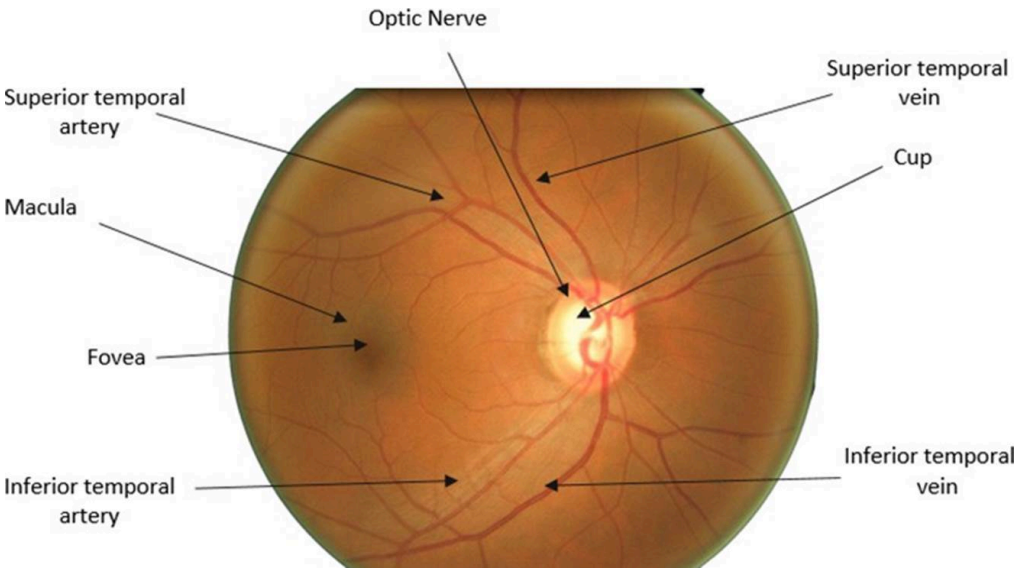
Keywords	Disparities in eye care, barriers and facilitators to access, utilization, compliance and adherence, recommendations to improve access
#Tags	N/A
Summary of key points + notes (include methodology)	● There are major inequities in health care, especially in eye care ● Eye care negatively numerous disease proccesses including glaucoma, cataracts, diabetic retinopathy, and also interventions such as surgical treatment and prescription of glasses ● A systemic review of all existing literature, around 2500 reports, addressing barriers and facilitators to health care, access, and disparitites in eye care, were taken into consideration ● The most common barriers of eye care were insurance, language, education, and transportaiton ● Having eye care was mainly related to having coverage, recommendations from primary care professionals and improved health status ● Populations that expeirence significant barriers to eye care include elderly patients, transgender communities, and those with cognitice impairment/low socioeconomic status. Females also have less access to eye care. ● Around 8 million adults with refractive errors, poor vision, could not afford to purchase glasses to fix their vision ● 67% of people reported costs as the reason they do not want a prescription or utilize eye care ● Programs such as the Affordable Care Act have potential of making eye care more accessible ● Telemedicine is also a potential solution, however there are some limitations due to patient education.
Research Question/Problem/ Need	Access to eye care is often difficult for numerous populations and groups. This leads to avoidable vision loss and even blindness.

Important Figures	 How the studies included in the literature review were chosen.
VOCAB: (w/definition)	1. Refractive errors - Refractive errors are a type of vision problem that makes it hard to see clearly. 2. Telemedicine - The remote diagnosis and treatment of patients by means of telecommunications technology.
Cited references to follow up on	1. Egunsola O. Dowsett L.E. Diaz R. et al. Diabetic retinopathy screening: a systematic review of qualitative literature. Can J Diabetes. 2021; 45: 725-733 2. Hark L.A. Radakrishnan A. Madhava M. et al. Awareness of ocular diagnosis, transportation means, and barriers to ophthalmology follow-up in the Philadelphia telemedicine glaucoma detection and follow-up Study. J Health Care Poor Underserved. 2018; 29: 1400-1415
Follow up Questions	1. Where do patients struggle the most with telecommunciation?

	2. What is the current form of telemedicine? Is this usually done over the phone or in a meeting-like setting? How can this setting be better orrganized to improve patient education and become a reliable source of diagnosis/suspect?

Article #7 Notes: Image-based Glaucoma Classification using Fundus Images and Deep Learning

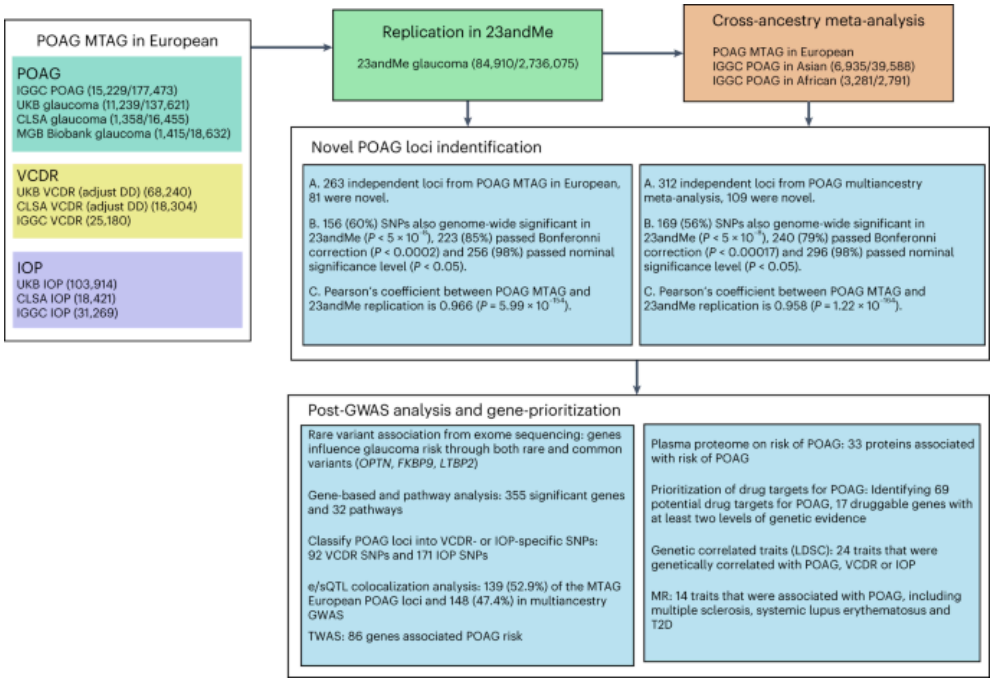
Source Title	Image-based Glaucoma Clasification using Fundus Images and Deep Learning
Source citation (APA Format)	Sandoval-Cuellar, H. J. (2021). Image-based glaucoma classification using fundus images and deep learning [Revista Mexicana de Ingeniería Biomédica]. https://doi.org/10.17488/RMIB.42.3.2
Original URL	https://www.rmib.mx/index.php/rmib/article/view/1188
Source type	Peer-reviewed research paper
Keywords	Deep Learning, Glaucoma diagnosis, Image-based classification, Convolutional Neural Networks
#Tags	N/A
Summary of key points + notes (include methodology)	1. WHO states that glaucoma is the second leading cause of blindness. An early diagnosis of glaucoma in individuals is neccesary to prevent severe vision loss. 2. In a normal eye, aqueous humor drains out of the eye through the trabecular meshwork, but in glaucoma this pathway is blocked causing a build-up of intraocular pressure 3. There are numerous different types of glaucoma such as open-angle, closed-angle, secondary, normal-tension, pigementary, etc 4. In most cases, treatment right after an early diagnosis can help prevent severe vision loss 5. A 6 layer CNN model was created for the detection of glaucoma based on fundus images 6. The methodology was as follows: a. Preprocessing - The colored images were turned to black and white on the grayscale b. Cropping - Images were cropped to reduce computing time of the entire image and rather focus on the region of interest 7. Binary cross entropy was used as a loss function 8. Different learning rates were tried for the model and 0.0001 performed the best, yielding an accuracy of 91.02%.
Research Question/Problem/ Need	Can fundus images of the eye be used to aid in the diagnosis of glaucoma?

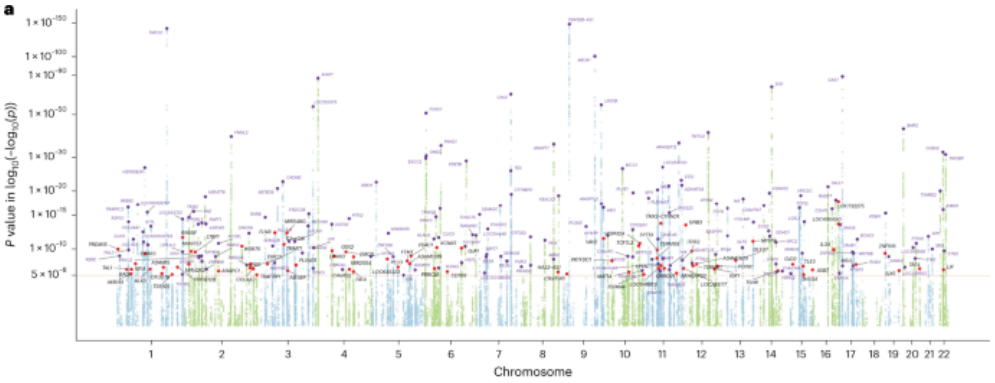
Important Figures	 An example of a fundus image taken of an eye.
VOCAB: (w/definition)	1. Convolutional Neural Networks (CNN) - A convolutional neural network is a type of artificial neural network used primarily for image recognition and processing, due to its ability to recognize patterns in images. 2. Learning rate - In machine learning and statistics, the learning rate is a tuning parameter in an optimization algorithm that determines the step size at each iteration while moving toward a minimum of a loss function. 3. Trabecular meshwork - The trabecular meshwork is a group of tiny canals through which most of the fluid in the eye drains. 4. Aqueous humor - Aqueous humor is the clear liquid inside the front part of the eye. It nourishes the eye and keeps it inflated.
Cited references to follow up on	1. Raghavendra U, Fujita H, Bhandary SV, Gudigar A, et al. Deep convolution neural network for accurate diagnosis of glaucoma using digital fundus images. Inf Sci [Internet]. 2018;441:41-49. Available from: https://doi.org/10.1016/j.ins.2018.01.051 2. Yin F, Liu J, Wong DWJ, Tan NM, et al. Automated segmentation of optic disc and optic cup in fundus images for glaucoma diagnosis. In: 2012 25th IEEE International Symposium on Computer-Based Medical Systems (CBMS). Rome: IEEE. 2012:1-6. Available from: https://doi.org/10.1109/CBMS.2012.6266344
Follow up Questions	1. These fundus images were quality taken photos from the ophthalmologist, how will fundus images taken from an iPhone camera perform with this model? 2. Is dilation required for fundus images or can they be taken with an un-dilated eye?

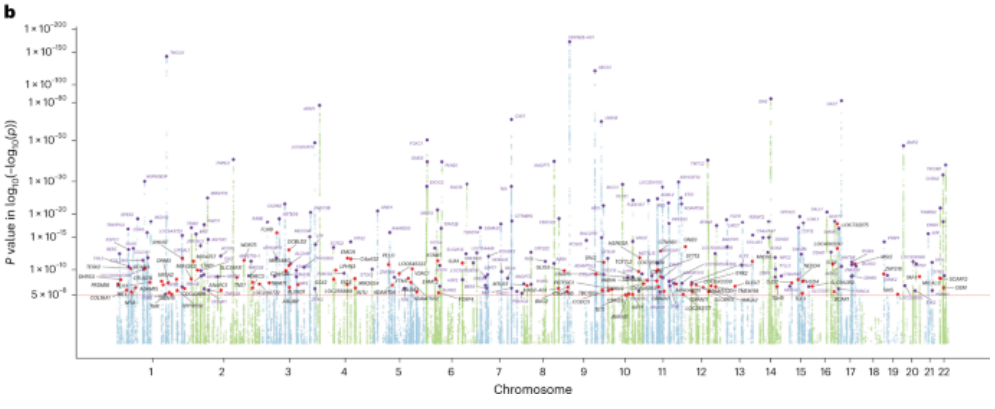
Article #8 Notes: Large-scale multitrait genome-wide association analyses identify hundreds of glaucoma risk loci

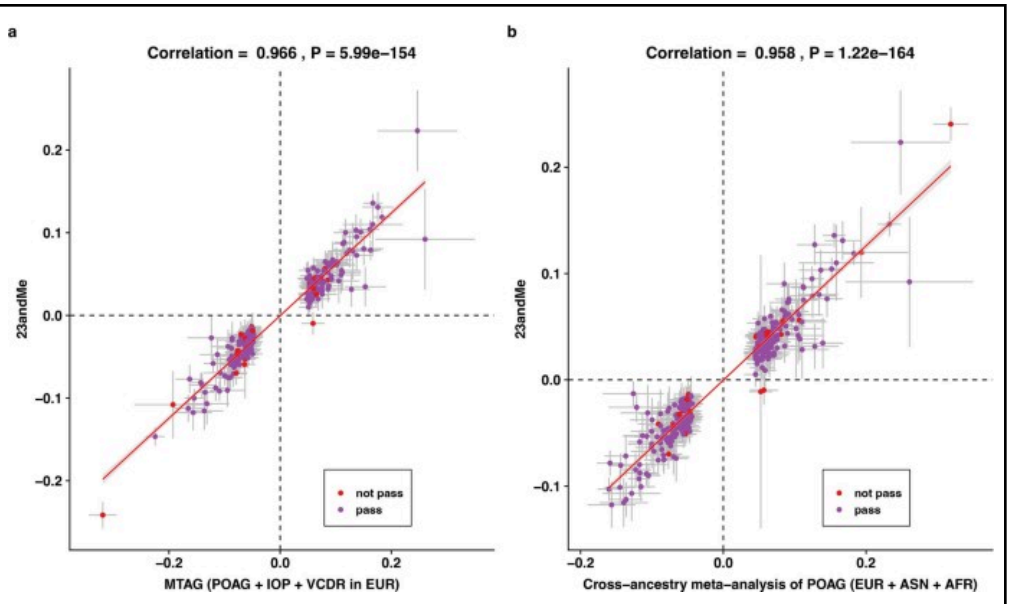
Source Title	Large-scale multitrait genome-wide association analyses identify hundreds of glaucoma risk loci
Source citation (APA Format)	Han, X., Gharahkhani, P., Hamel, A. R., Ong, J. S., Rentería, M. E., Mehta, P., Dong, X., Pasutto, F., Hammond, C., Young, T. L., Hysi, P., Lotery, A. J., Jorgenson, E., Choquet, H., Hauser, M., Cooke Bailey, J. N., Nakazawa, T., Akiyama, M., Shiga, Y., … MacGregor, S. (2023, June 29). Large-scale multitrait genome-wide association analyses identify hundreds of glaucoma risk loci. Nature News. https://www.nature.com/articles/s41588-023-01428-5
Original URL	https://www.nature.com/articles/s41588-023-01428-5
Source type	Peer-reviewed journal article
Keywords	N/A
#Tags	#genomics #glaucoma #analysis #genes #23andMe #data
Summary of key points + notes (include methodology)	● Glaucoma is a leading cause of irreversible blindness and is highly heritable. Understanding glaucoma risk loci will help us better understand the heritability of glaucoma. ● ~100 loci have already been found. Another 263 were found through this study. ● A large-scale multi-trait analysis was created to find more loci. ● P-values of specific loci show high statistical significance.
Research Question/Problem/ Need	Glaucoma is a leading cause of irreversible blindness, and is highly heritable. Much of glaucoma heritability and its two associated traits (intraocular pressure, and optic nerve head excavation damage) remains unexplained.

Important Figures





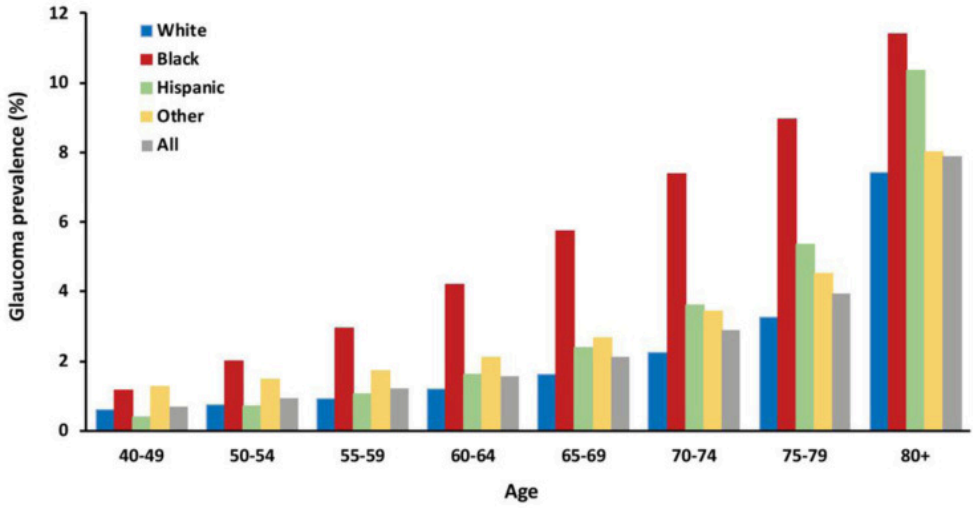


	
VOCAB: (w/definition)	1. Loci - A locus, as related to genomics, is a physical site or location within a genome. 2. Glaucoma - A locus, as related to genomics, is a physical site or location within a genome. 3. Intraocular pressure - A locus, as related to genomics, is a physical site or location within a genome. 4. Optic nerve head excavation damage - Optic nerve head excavation damage.
Cited references to follow up on	1. Wang, K., Gaitsch, H., Poon, H., Cox, N. J. & Rzhetsky, A. Classification of common human diseases derived from shared genetic and environmental determinants. Nat. Genet. 49, 1319–1325 (2017). 2. Craig, J. E. et al. Multitrait analysis of glaucoma identifies new risk loci and enables polygenic prediction of disease susceptibility and progression. Nat. Genet. 52, 160–166 (2020).
Follow up Questions	1. Does p-value correspond to causation or correlation? Just because certain gene locus areas show up in glaucoma, does this mean they don't show up in other conditions or general conditions?

Article #9 Notes: Racial Disparitites in Glaucoma: From Epidemiology to Pathopysiology

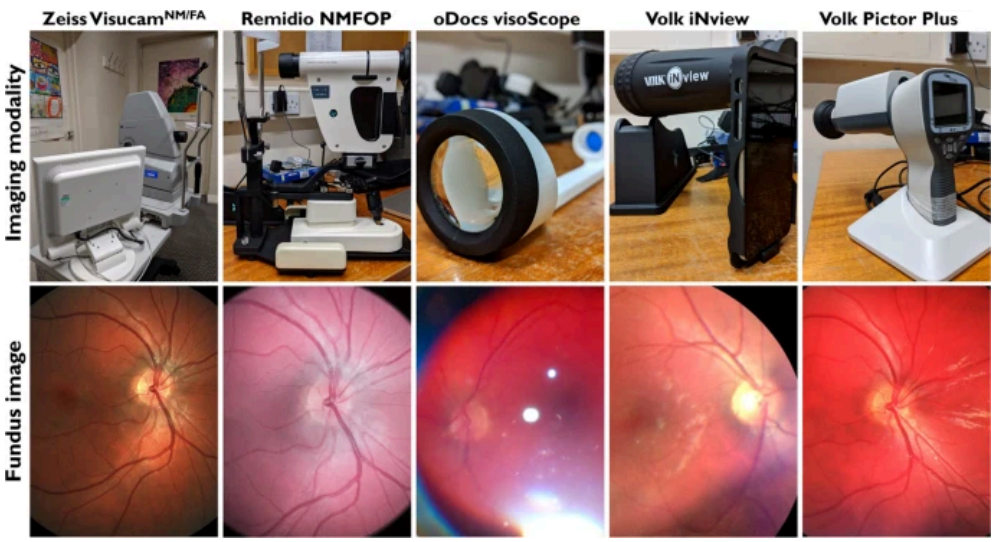
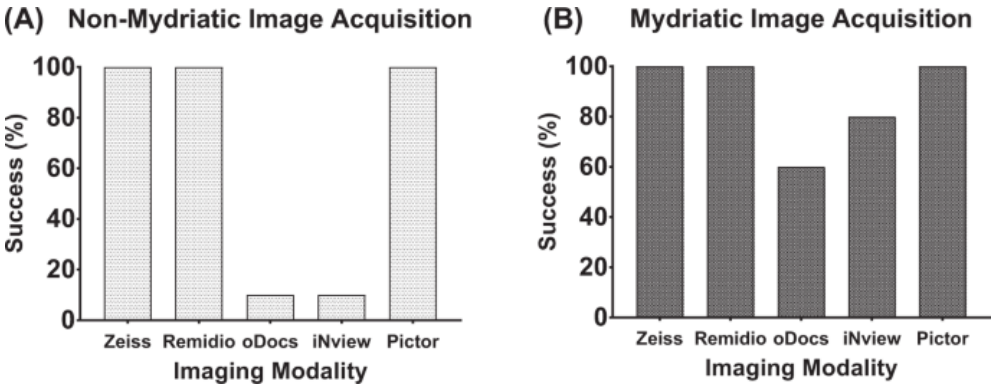
Source Title	Racial Disparities in Glaucoma: From Epidemiology to Pathopysiology

Source citation (APA Format)	Siegfried, C. J., & Shui, Y.-B. (2022). Racial disparities in glaucoma: From epidemiology to pathophysiology. Missouri medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9312450/
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9312450/
Source type	Peer-Reviewed Research Paper
Keywords	Racial disparities, race, ethnicity, Glaucoma, GWAS
#Tags	#Glaucoma, #Race, #Ethnicity, #African Americans
Summary of key points + notes (include methodology)	● Individuals with African and Latinx backgrounds have a higher prevalence, earlier onset, and more rapid progression of open angle glaucoma and blindness ● Memebrs of minority groups are likely to get less quality treatment even after factoring in the effects of income levels, insurance status, and education ● Glaucoma is a optic neuropathy disease that leads to serious vision loss ● Medical and surgical treatments lead to better outcomes, however there is no cure for Glaucoma ● Cost, access, and health literacy issues also add to disparities ● Black patients are at more risk for surgical failure ● African Americans are six times more likely to have Glaucoma than Europeans. The disease progress quicker and also shows signs up to 10 years early. ● There have been many variants found that are related to Glaucoma, however, this is usually done on European data and does not transfer smoothly to African Americans. ● GWAS study data can be complemented with gene expression data and protein transcritional data if there any missing gaps in knowledge ● Important racial disparities in diseases in Glaucoma can be uncovered by looking at other diseases and the cause of racial disparities there ● Oxidative stress contributes to Glaucoma ● Gene expression data can hold information about ATP synthesis, ROS production, and antioxidant defense mechanisms in TM cells
Research Question/Problem/ Need	Racial disparities in the healthcare system, and with the disease Glaucoma in particular, lead to worse results for minorities.

Important Figures	
VOCAB: (w/definition)	1. ATP synthesis - This involves the transfer of electrons from the intermembrane space, through the inner membrane, back to the matrix (CliffNotes). 2. ROS production - The production of by-products of normal cell activity (NIH). 3. Antioxidant defense mechanisms - A system that protects an organism against the damaging effects of oxidation (Collins Dictionary). 4. TM cells - The primary cell type that occupy and form the proximal portion of the conventional outflow pathway (NIH).
Cited references to follow up on	1. Murakami Y, Lee BW, Duncan M, et al. Racial and ethnic disparities in adherence to glaucoma follow-up visits in a county hospital population. Arch Ophthalmol. 2011;129(7):872–8. 2. Kosoko-Lasaki O, Gong G, Haynatzki G, Wilson MR. Race, ethnicity and prevalence of primary open-angle glaucoma. J Natl Med Assoc. 2006;98(10):1626–9.
Follow up Questions	1. There are different forms of Glaucoma. Does race just affect POAG or these other types of Glaucoma as well? 2. What caused there to be an imbalance of genetic data in the first place? African Americans are more populous in the US than some other minorities, but still have some of the worst polygenic risk score models.

Article #10 Notes: Feasibility and clinical utility of handheld fundus cameras for retinal imaging

Source Title	Feasibility and clinical utility of handheld fundus cameras for retinal imaging
Source citation (APA Format)	Das, S., Kuht, H. J., De Silva, I., Deol, S. S., Osman, L., Burns, J., Sarvananthan, N., Sarodia, U., Kapoor, B., Islam, T., Sampath, R., Poyser, A., Konidaris, V., Anzidei, R., Proudlock, F. A., & Thomas, M. G. (2023). Feasibility and clinical utility of handheld fundus cameras for retinal imaging. Eye, 37(2), 274–279. https://doi.org/10.1038/s41433-021-01926-y
Original URL	https://www.nature.com/articles/s41433-021-01926-y#change-history
Source type	Peer-Reviewed Research Paper
Keywords	Fundus imagers, glaucoma, point of care, eye care, testing
#Tags	N/A
Summary of key points + notes (include methodology)	● Handheld fundus imagers are cheap options to table-top fundus imagers found at the ophthalmologist ● Four different handheld fundus images were tested on a population without known eye diseases: ○ Remidio Non-Mydriatic Fundus on Phone - This is a small system used with the help of a smartphone to capture images of the fundus with a field view of 40º. This costed around 4600 pounds. ○ Volk Pictor Plus - This was another fundus imager that also had a field view of 40º. This one costed around 4400 pounds. ○ Volk iNview - A fundus camera attached to an iPod or iPhone 6 with a field view of 50º. This cost around 700 pounds. ○ oDocs visoScope - a 3D printed fundus imager with a field view of 45º. This cost around 260 pounds. ○ Zeiss Visucam - this is a table-mounted fundus imager and was used as the control or “gold standard” for this study ● Zeiss, Remidio, and Pictor all performed well in both mydriatic and non-mydriatic settings but the oDocs and iNview didn’t perform as well (10%). However, all performed well in mydriatic settings.
Research Question/Problem/ Need	Table-top fundus imagers are bulky and expensive. Are hand-held fundus imagers on the market a viable replacement to table-top fundus imagers?

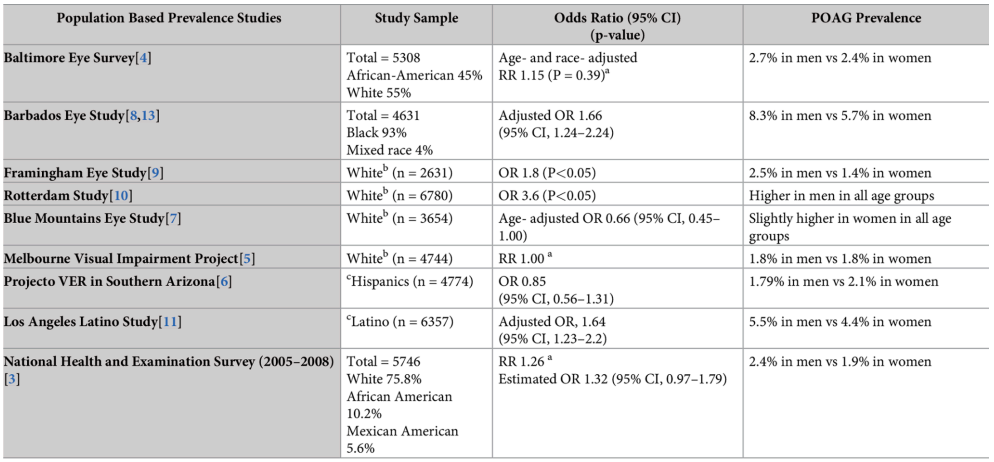
Important Figures	 The different hand-held fundus imagers and the pictures they took below.  The success rate of different fundus imagers given mydriatic versus non-mydriatic environments.
VOCAB: (w/definition)	1. Mydriatic - Excessive or prolonged dilatation of the pupil of the eye. 2. Fundus - The fundus of the eye is the interior surface of the eye opposite the lens and includes the retina, optic disc, macula, fovea, and posterior pole.
Cited references to follow up on	1. Sachdeva V, Vasseneix C, Hage R, Bidot S, Clough LC, Wright DW, et al. Optic nerve head edema among patients presenting to the emergency department. Neurology. 2018;90:e373–9. 2. Gulshan V, Peng L, Coram M, Stumpe MC, Wu D, Narayanaswamy A, et al. Development and validation of a deep learning algorithm for the detection of diabetic retinopathy in retinal fundus photographs. JAMA. 2016;316:2402–10.

Follow up Questions	1. Are these the minimum price possible for fundus imagers? These high prices are oftentimes still out of the budget of people living in rural areas. 2. Mydriatic environments are not always available, especially in a point-of-care setting due to the idea that dilation drops cannot be taken over the counter. How can non-mydriatic photos be more successful?

Article #11 Notes: Primary Open-Angle African American Glaucoma Genetics (POAGG) Study: gender and risk of POAG in African Americans

Source Title	Primary Open-Angle African American Glaucoma Genetics (POAGG) Study: gender and risk of POAG in African Americans
Source citation (APA Format)	Khachatryan, N., Pistilli, M., Maguire, M. G., Salowe, R. J., Fertig, R. M., Moore, T., Gudiseva, H. V., Chavali, V. R., Collins, D. W., Daniel, E., Murphy, W., Henderer, J. D., Lehman, A., Cui, Q., Addis, V., Sankar, P. S., Miller-Ellis, E. G., & O'Brien, J. M. (2019). Primary open-angle African American Glaucoma Genetics (POAAGG) study: Gender and risk of Poag in African Americans. PLOS ONE, 14(8). https://doi.org/10.1371/journal.pone.0218804
Original URL	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0218804
Source type	Peer-reviewed research paper
Keywords	Glaucoma, African Americans, Risk score
#Tags	#Glaucoma, #African Americans, #Polygenic risk score
Summary of key points + notes (include methodology)	Notes ● Glaucoma is the leading cause of irreversible vision loss worldwide ● POAG is the most common form of Glaucoma and accounts for 74% of cases ● More than 44 million people are affected by POAG, and this was estimated to grow to 58 million by 2020, currently it is around 60 million people ● Most scientists agree that race plays a large role in Glaucoma as it is 4 to 5 times more prevalent in African Americans than Europeans ● Participants had met the following criteria: ○ Aged 35 years and older ○ Self-identified as Black ○ Had a coexisting history of ocular trauma, non-glaucomatous optic disc neuropathy, inflammatory eye diseases, or other forms of

	Glaucoma were excluded. Only people with POAG were observed.
	• Patients diagnosed as cases had the following criteria:
	  ○ An open iridocorneal angle
	  ○ Glaucomatous optic nerve findings in one or both eyes
	• Control patients had to satisfy the following criteria:
	  ○ No high myopia
	  ○ Abnormal visual field
	  ○ Intraocular pressure
	• The relationship between POAG and phenotypic features such as gender, age, diabetes, hypertension, body mass index, and smoking status were observed
	• The relationship between race, gender, and POAG was analyzed

Research Question/Problem/ Need	Scientific controversy surrounds the idea of racial and gender disparities in the risk of African Americans versus Europeans obtaining Glaucoma.
Important Figures	

Population Based Prevalence Studies	Study Sample	Odds Ratio (95% CI) (p-value)	POAG Prevalence
Baltimore Eye Survey[4]	Total = 5308 African-American 45% White 55%	Age- and race- adjusted RR 1.15 (P = 0.39)[a]	2.7% in men vs 2.4% in women
Barbados Eye Study[8,13]	Total = 4631 Black 93% Mixed race 4%	Adjusted OR 1.66 (95% CI, 1.24–2.24)	8.3% in men vs 5.7% in women
Framingham Eye Study[9]	White[b] (n = 2631)	OR 1.8 (P<0.05)	2.5% in men vs 1.4% in women
Rotterdam Study[10]	White[b] (n = 6780)	OR 3.6 (P<0.05)	Higher in men in all age groups
Blue Mountains Eye Study[7]	White[b] (n = 3654)	Age- adjusted OR 0.66 (95% CI, 0.45–1.00)	Slightly higher in women in all age groups
Melbourne Visual Impairment Project[5]	White[b] (n = 4744)	RR 1.00 [a]	1.8% in men vs 1.8% in women
Projecto VER in Southern Arizona[6]	[c]Hispanics (n = 4774)	OR 0.85 (95% CI, 0.56–1.31)	1.79% in men vs 2.1% in women
Los Angeles Latino Study[11]	[c]Latino (n = 6357)	Adjusted OR, 1.64 (95% CI, 1.23–2.2)	5.5% in men vs 4.4% in women
National Health and Examination Survey (2005–2008) [3]	Total = 5746 White 75.8% African American 10.2% Mexican American 5.6%	RR 1.26 [a] Estimated OR 1.32 (95% CI, 0.97–1.79)	2.4% in men vs 1.9% in women

[a] We estimated risk ratio (RR), which for rare disease such as POAG is close to OR

[b] Predominantly white population, with other racial groups <5%

[c] Hispanics or Latino population only

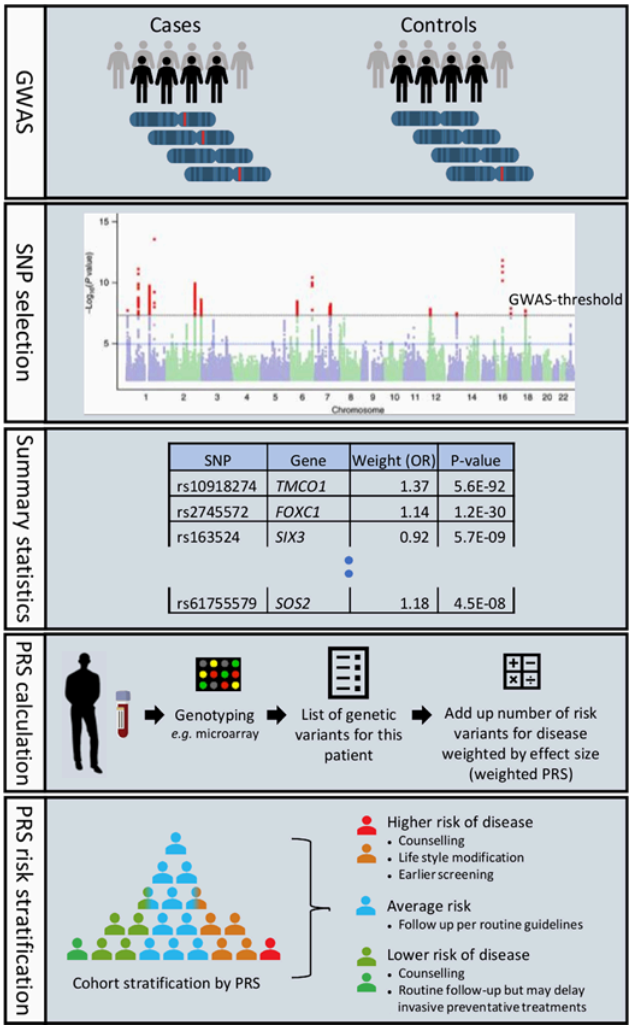
https://doi.org/10.1371/journal.pone.0218804.t003

VOCAB: (w/definition)	1. Iridicorneal angle - The structure responsible for the outflow of aqueous humor from the anterior chamber of the eye (NIH). 2. Intraocular pressure - The pressure or force inside your eyes. 3. Myopia - A defect of the eye that causes light to focus in front of the retina instead of directly on it resulting in nearsightedness.
Cited references to follow up on	1. Gupta P, Zhao D, Guallar E, Ko F, Boland MV, et al. (2016) Prevalence of Glaucoma in the United States: The 2005–2008 National Health and Nutrition Examination Survey. Invest Ophthalmol Vis Sci 57: 2905–2913. Pmid:27168366 2. Weih LM, Nanjan M, McCarty CA, Taylor HR (2001) Prevalence and predictors of open-angle glaucoma: results from the visual impairment project. Ophthalmology 108: 1966–1972. pmid:11713063

Follow up Questions	1. While there doesn't seem to be that much of a difference, it does seem like women are slightly less likely to have Glaucoma than men in some races. Is there a reason for this? 2. How does specific phenotypic data that was collected for this study relate to Glaucoma (hypertension, BMI, etc)? How do scientists choose features?

Article #12 Notes: Risk Stratification and Clinical Utility of Polygenic Risk Scores in Ophthalmology

Source Title	Risk Stratification and Clinical Utility of Polygenic Risk Scores in Ophthalmology
Source citation (APA Format)	Qassim, A., Souzeau, E., Hollitt, G., Hassall, M. M., Siggs, O. M., & Craig, J. E. (2021). Risk stratification and clinical utility of polygenic risk scores in ophthalmology. Translational Vision Science & Technology, 10(6), 14. https://doi.org/10.1167/tvst.10.6.14
Original URL	https://tvst.arvojournals.org/article.aspx?articleid=2772583
Source type	Peer-reviewed research paper
Keywords	Polygenic risk scores, risk prediction, common complex disease, GWAS
#Tags	#polygenic risk scores, #GWAS #Glaucoma #predisposition
Summary of key points + notes (include methodology)	Notes ● Over the years, GWAS studies have become more popular because due to the increase in accessibility (prices, quality, etc) ● SNPs with frequency of 1% are associated with traits in a GWAS ● Monogenic diseases are diseases that altered by a change in jsut one gene. While these variants are rare, they are very powerful. ● On the other hand, complex diseases are diseases that have hundreds or thousands of variants contributing to form a phenotype ● In order to find all these variants, large GWAS studies employing numerous people must be connected ● "A PRS is a quantitative probabilistic summary of an individuals likelihood of obtaining a disease". ● SNPs that have a genome-wide significance threshold of 5 x 10^-8 and is adjusted through Bonferri correction are used for studies ● SNPs with a large LD are not counted towards a study ● AUC is a common measure to understand the accuracy and performance of PRS models ● Glaucoma is the leading cause of irreversible blindness and affects over 64

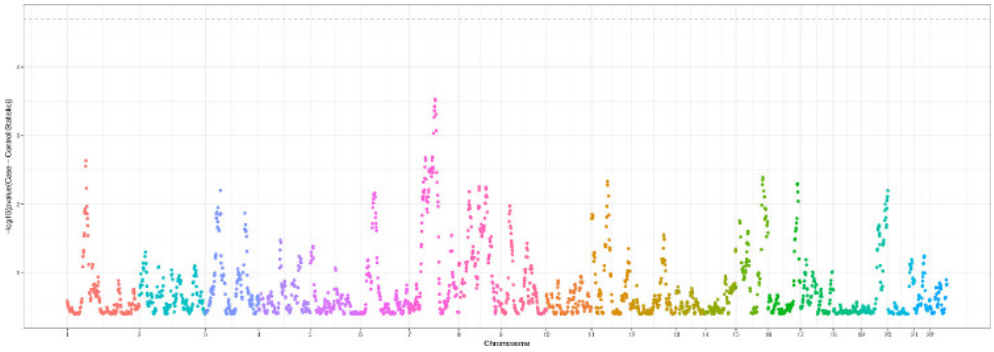
	million people worldwide • In the past, studies were often limited by smaller samples and therefore a smaller number of SNPs being observed. Nw, as data from large GWAS studies are more accessible, more can be done with the data • When models created on Europeans were transferrde to South Asians and Africans, they performed poorly because of didfferences in genetics in these ethnicities. Therefore, in the future GWAS studies specific to certain ehtnicities, not just Europeans, needs to be studied • MYOC is one gene that is highly correlated to Glaucoma • Using low-risk interventions such as genotyping to target high-risk individuals will improve the cost-beenfit ratio • The main disadvantage with GWAS studies currently is the fact that they have only really targetted European populations. As a result, polygenic risk scores generated for other ethnicities using this data is inaccurate and causes medical disparitites
Research Question/Problem/ Need	Scientific controversy surrounds the idea of racial and gender disparities in the risk of African Americans versus Europeans obtaining Glaucoma.
Important Figures	

	The entire process of creating polygenic risks scores all the way from creating a GWAS study, to validating the model.
VOCAB: (w/definition)	Bonferri correction - The p-value of each test must be equal to its alpha divided by the number of tests performed. Monogenic diseases - A disease caused by the inheritance of a single gene mutation. This is rarer, but this mutation is also more powerful.
Cited references to follow up on	1. Wiggs JL, Pasquale LR. Genetics of glaucoma. Hum Mol Genet. 2017; 26(R1): R21–R27. 2. Khera AV, Chaffin M, Aragam KG, et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. Nat Genet. 2018; 50(9): 1219–1224. 3. Chatterjee N, Shi J, García-Closas M. Developing and evaluating polygenic risk prediction models for stratified disease prevention. Nat Rev Genet. 2016; 17(7): 392–406.
Follow up Questions	● For a disease that has a well amount of documented causal SNP, how does the sum of risk alleles model compare against a machine learning model and deep learning model? If deep learning model improves complexity and captures more parts of the data (gene-gene expression and epistasis), then why is this technique less adopted for polygenic risk scores? ● Is there a uniform set of rules that are set in stone for quality controlling target and base data before use or does this depend on the study? If it depends ont the study, what is making te data/results uniform and comparable across studies?

Article #13 Notes: The Role of Genetic Ancestry as a Risk Factor for Primary Open-angle Glaucoma in African Americans

Source Title	The Role of Genetic Ancestry as a Risk Factor for Primary Open-angle Glaucoma
Source citation (APA Format)	Cole, B. S., Gudiseva, H. V., Pistilli, M., Salowe, R., McHugh, C. P., Zody, M. C., Chavali, V. R., Ying, G. S., Moore, J. H., & O'Brien, J. M. (2021). The role of genetic ancestry as a risk factor for primary open-angle glaucoma in African Americans. Investigative Opthalmology & Visual Science, 62(2), 28. https://doi.org/10.1167/iovs.62.2.28
Original URL	https://iovs.arvojournals.org/article.aspx?articleid=2772307

Source type	Peer-Reviewed Research Journal
Keywords	Ancestry, Glaucoma, primary open-angle glaucoma, African Americans, genetics
#Tags	#Glaucoma, #Genetic risk score #Poredisposition models
Summary of key points + notes (include methodology)	Notes ● Primary open-angle Glaucoma (POAG) is a major neurodegenerative disorder that causes vision loss ● African Americans are 4 to 5 times more likely to be diagnosed with POAG than Europeans ● POAG is linked heavily to genetics, but little is known about the specifics. Of what is known, most are related to Europeans and Asians. ● Since most data from Europeans and Asians doesn't transfer to Africans, it can be concluded that different ethnic groups have different variants related to POAG ● Different ancestries affect disease prevalence due to linkage disequilibrium, allele frequency, copy number of variants, and allelic architecture ● This study was conducted over 5 years and genetic information was obtained through array-based genotyping. Phenotype data was collected from clinical validation ● Subjects were ages 35 and older and self-identified as Black ● Samples were collected through blood ● Array content contained 5000 SNP from prior GWAS on POAG and other past studies ● There was a heavy emphasis on quality control, and variants would be removed if they had any of the following properties: ○ If they discordant genders ○ Outlying heterozygosity ○ Atleast 3% missing genotype cells ○ Identical to already existing samples ○ Missing data ○ Significant evidence of differential call rate between cases and controls ○ Deviation from Hardy-Weinberg equilibrium with significance level at a P value of less than 0.00001 ○ Minor allele frequency less than 0.01 (rare variants) ● A polygenic risk score model was created using 23 SNP discovered from previous related studies and the sum of risk alleles mathematical model ● A multivariable risk model was created using logistic regression and the factors of age, gender, polygenic risk score, and ancestry
Research Question/Problem/ Need	Little is known about the genetic makeup of Glaucoma in African Americans.

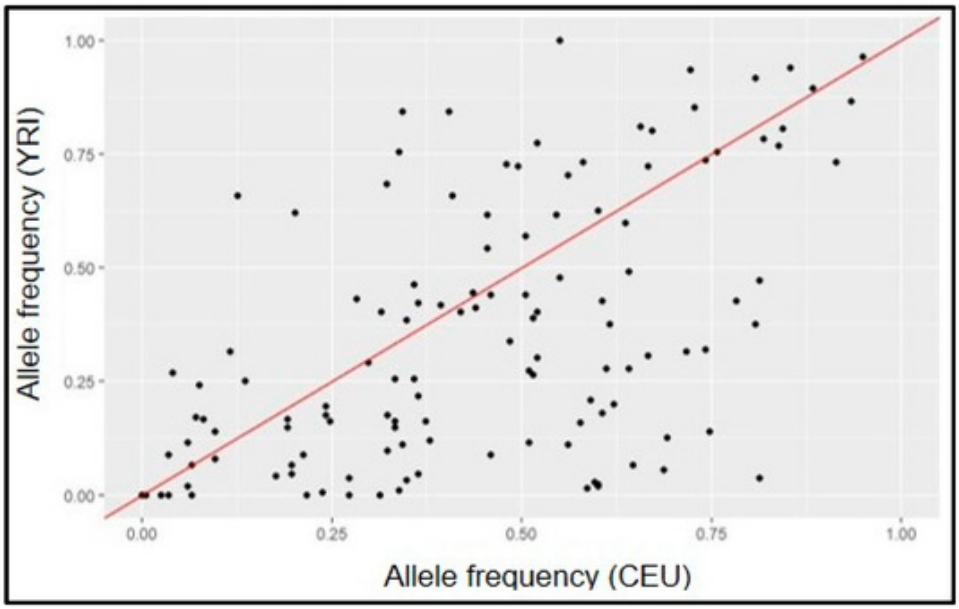
Important Figures	 A Manhattan plot showing the causal SNP related to Glaucoma in African Americans based on previous studies. No individual variant reached significance, therefore multiple variants need to be taken into consideration to create a PRS model.
VOCAB: (w/definition)	1. Discordant genders - A discrepancy or misalignment between sex observed at birth and individual gender identity 2. Outlying heterozygosity - An unusual number of traits that have different alleles 3. Call rate - the proportion of individuals in the study for which the corresponding SNP information is not missing 4. Hardy-Weinberg equilibrium - a principle stating that te genetic variation in a population will stay the same from one generation to the next
Cited references to follow up on	1. Kapetanakis VV, Chan MP, Foster PJ, Cook DG, Owen CG, Rudnicka AR.. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. Br J Ophthalmol. 2016; 100: 86–93 2. eprah E, Xu H, Tekola-Ayele F, Royal CD.. Genome-wide association studies in Africans and African Americans: expanding the framework of the genomics of human traits and disease
Follow up Questions	1. What was the accuracy or area under the curve of the model for the polygenic risk score and multivariable model? 2. How can you use data collected later on as the study continues to observe the individuals lives in the multivariable model? What features would be of interest?

Article #14 Notes: Diversity in Polygenic Risk of Primary Open-Angle Glaucoma

Source Title	Diversity in Polygenic Risk of Primary Open-Angle Glaucoma

Source citation (APA Format)	Cooke Bailey, J. N., Funk, K. L., Cruz, L. A., Waksmunski, A. R., Kinzy, T. G., Wiggs, J. L., & Hauser, M. A. (2022). Diversity in polygenic risk of primary open-angle glaucoma. Genes, 14(1), 111. https://doi.org/10.3390/genes14010111
Original URL	https://www.mdpi.com/2073-4425/14/1/111
Source type	Peer-Reviewed Research Journal
Keywords	Glaucoma, polygenic risk score, genetic risk score, diversity, glaucoma genetics
#Tags	#Glaucoma, #Polygenic risk scores, #GWAS, #Diversity
Summary of key points + notes (include methodology)	Notes ● Glaucoma is the leading cause of irreversible blindness worldwide ● Primary-open angle Glaucoma (POAG) is most prevalent in people of African ancestry ● Even though Africans are most likely to have this disease they are underrepresented in genetic models for POAG ● Thousands of loci are related to diseases. However, some have very little effect and therefore looking at single loci would not provide much analysis of disease risk. ● To calculate disease risk, polygenic risk score models were created in which numerous causal SNP were added together ● GRS (genetic risk score)- add causal SNP that show a statistical significance at the genome level ● PRS (polygenic risk score)- shows promise for predicting the genetic risk for complex diseases by including genome-wide variants and specific risk variants ● GRS and PRS can help precision medicine and identify personalized medicine plans for disease management and high-risk individuals ● MYOC is a gene that causes the early-onset of Glaucoma ● Glaucoma caused by MYOC is rarer than Glaucoma caused by a combination of multiple risk variants. As a result PRS can be potentially effective model for this disease. ● Currently, there needs to be more work done on identifying genetic variants that cause Glaucoma as not much is known at this point ● Concerns with polygenic risk scores and limtationns (plus personal responses) ○ Individual variants often have a smaller affect than socioeconomic demographic factors and the environment ■ Even though the environment does play a factor in disease prediction and diagnosis, this doesn't mean genes don't play a key factor as stated by multiple other sources. ○ The sensitivity of these tests doesn't correspond to the cost-effectiveness ■ Genetic tests are getting cheaper by the day with some even being as low as $100. As the prices become lower, our information on risk variants continues to grow. We need to contribute to research for this to happen. ○ Each proposed test needs validation in a clinical setting.

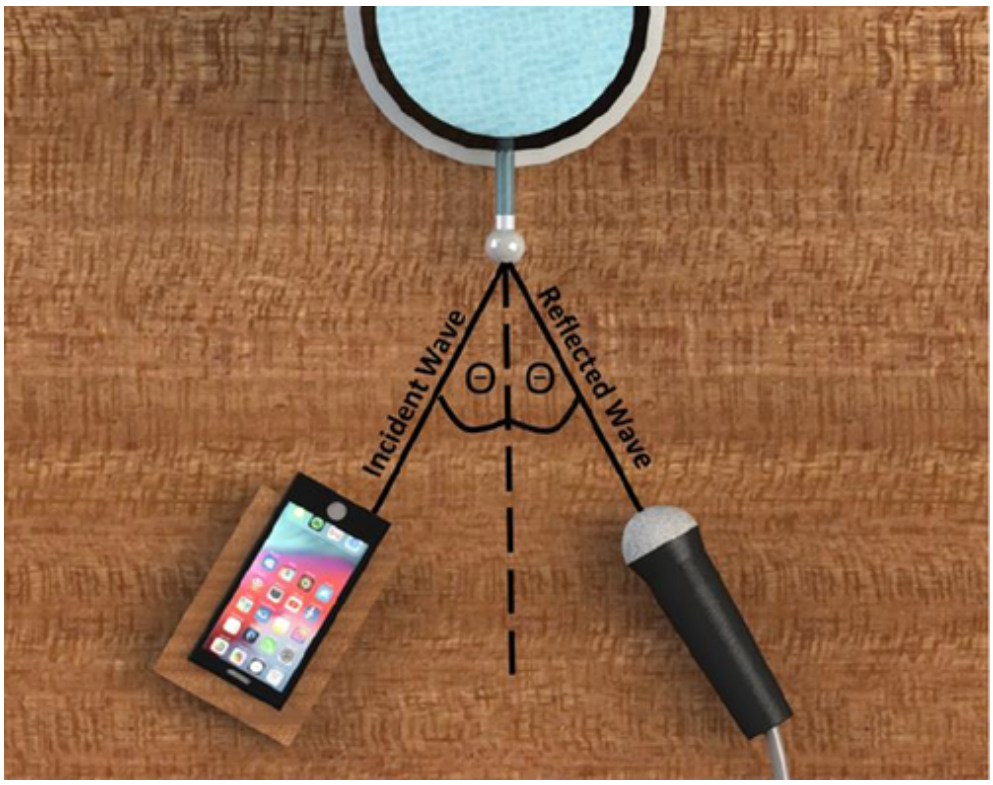
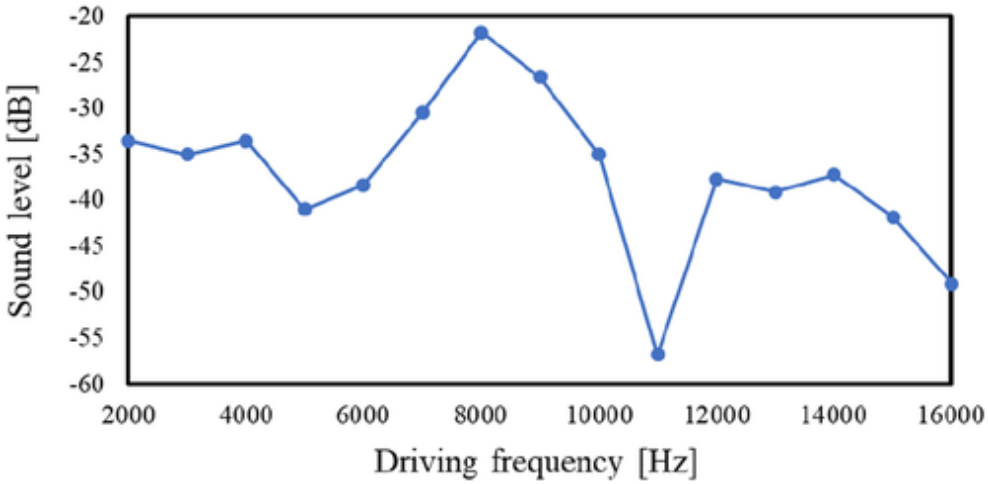
	■ Going to a clinical setting off of suspicion of disease risk is often not an option for many individuals due to high healthcare costs. As a result, a cheap at-home genetic test that hints to genetic risk would help individuals feel more comfortable reaching out to healthcare after getting confirmation and going off of more than a nudge. ● Due to GWAS studies occurring 80% of the time on European populations, creating a PGS model for African Americans based on majority of existing data will be inaccurate ● There is limited cross-ancestry variation because of the differences in linkage-disequillibrium and allele frequency in Africans Americans versus Europeans ● One genetic variant found, rs59892895*C, was found in a descent amount of people of African descent and related to POAG, but found in less than 0.1% of Asians and European genomes ● Based on current risk variants found in majority European and Asian populations, an African American polygenic risk score model constantly underperforms ● Polygenic risk scores can help immensely with Glaucoma prevention. With previous models that have been created, the top 5% of high scores were more than 50% likely to get Glaucoma than the bottom 95% ● There needs to be more work done to increase diversity study in GWAS for POAG ● Based on prior studies and evidence, it is clear that there are no "one size fits all" models that can detect POAF for all ethnicities ● Early intervention with POAG can help reduce vision loss. ● It makes sense for POAG early diagnosis to be a priority for African Americans since they are the most likely to have POAG ● more GWAS studies must be conducted on Africans to gain more insight into causal SNP for their specific ethnicity and gene pool
Research Question/Problem/ Need	Currently, polygenic risk scores for African Americans are inaccurate due to the lack of GWAS studies focused on Africans.

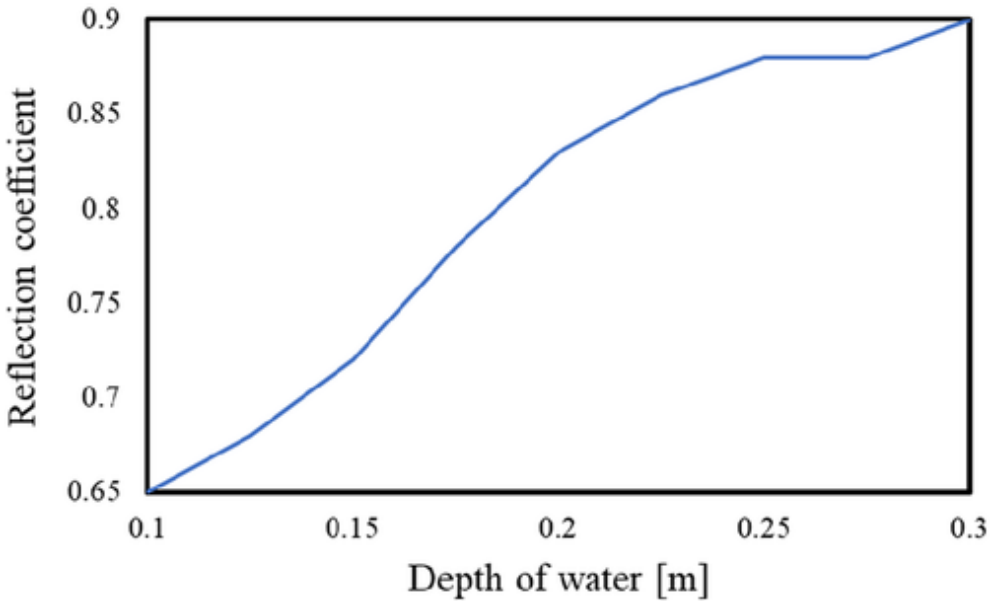
Important Figures	 This graph displays the allele frequency of certain variants in different ethnicities. Not all ethnicities have the same allele frequency and therefore polygenic risk scores built for one ethnicity cannot be easily transferred to another ethnicity.
VOCAB: (w/definition)	1. Linkage disequilibrium - 2. Minor allele frequency -
Cited references to follow up on	1. Siggs, O.M.; Qassim, A.; Han, X.; Marshall, H.N.; Mullany, S.; He, W.; Souzeau, E.; Galanopoulos, A.; Agar, A.; Landers, J.; et al. Association of High Polygenic Risk with Visual Field Worsening Despite Treatment in Early Primary Open-Angle Glaucoma. JAMA Ophthalmol. 2022, 10, e224688. 2. Buniello, A.; MacArthur, J.A.L.; Cerezo, M.; Harris, L.W.; Hayhurst, J.; Malangone, C.; McMahon, A.; Morales, J.; Mountjoy, E.; Sollis, E.; et al. The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays, and summary statistics 2019. Nucleic Acids Res. 2019, 47, D1005–D1012.
Follow up Questions	1. Even though it is true that the majority of genetics is currently Eurocentric, can we work with the 20% of GWAS studies that have been conducted on minorities to improve PRS scores? 2. It makes sense that PGS models built using European data don't perform that well on African Americans. Has anyone tried using solely African-American GWAS data? Even though there isn't as much, will it prevent the overshadowing of variants?

Article #15 Notes: Testing the viability of measuring intraocular pressure using soundwaves from a smartphone

Source Title	Testing the viability of measuring intraocular pressure using soundwaves from a smartphone
Source citation (APA Format)	Soanes, M., Essa, K., & Butt, H. (2021). Testing the viability of measuring intraocular pressure using soundwaves from a smartphone. Engineering Reports, 3(7), e12355. https://doi.org/10.1002/eng2.12355
Original URL	https://onlinelibrary.wiley.com/doi/full/10.1002/eng2.12355
Source type	Peer-reviewed research aper
Keywords	Sound waves, intraocular pressure, smartphone
#Tags	N/A
Summary of key points + notes (include methodology)	● It is hard to identify the subpopulation that is at high risk for glaucoma. Therefore, measuring IOP over time would help keep track of an individual's risk and potentially provide early diagnosis. ● This method is not used for the direct diagnosis of glaucoma, but rather as a tool to measure risk level ● There are numerous risk factors of glaucoma including an inflated intraocular pressure, intracranial pressure, and cerebrospinal fluid pressure ● Intracranial pressure plays a significant role in post-laminar neural tissue failure ● A healthy value of IOP is between 10 and 20 mmHg in most individuals ● Ocular hypertension, elevated IOP levels, are most common in the older population ● Glaucoma is a ideas that affects the optic nerve. 64.3 million people worldwide suffered from glaucoma in 2013. ● The gold standard for measuring IOP is applanation tonometry called Goldmann. The IOP is taken by measuring the force required to applanate the eye, which is equal to the pressure inside the eye times the area of the applanated surface ● Sometimes if an individual has a thin central corneal thickness, then the reading of the tonometer will be lower than it is. A workaround to this is using the Perkins tonometer, however these are much more expensive than Goldmann tonometers. ● Air-puff tonometry is another form of tonometry for no-contact use. However, this form of tonometry is known to be inaccurate and often gives higher readings than what is the truth. In addition to this, patients think it is uncomfortable. ● Novel tonometry methods using ultrasounds are also being studied, but are not practical in a point-of-care system due to the machinery required ● A model eye was constructed based on average eye measurements ● Using COSMOL technology, a relationship between intraocular pressure and the reflection coefficient was proven

	• An experimental setup was created in which sound waves were sent to the eye model. A portion of the sound waves was absorbed by the eye, and the remaining portion was reflected at the same angle as a microphone. The microphone captured the number of decibels returned using oscilloscope technology. • First, the resonance frequency and optimal frequency were found. Resonance frequency refers to the frequency in which the most sound waves are being absorbed by the eye model. This frequency will be avoided because the number of decibels returned in the reflection wave will be very small and there will be little variance. • The optimal frequency is the frequency at which the least amount of sound waves are absorbed by the model eye. This is the best-case scenario because the reflection wave will be higher and more variance based on the internal pressure of the eye model can be observed. • Reflection coefficients at different frequencies were observed by keeping the internal pressure of the eye model the same, only changing the Hz of the sound wave, and measuring the reflection wave • The resonance frequency was 11,000 Hz and the optimal frequency was 8000 Hz. • After, the relationship between internal pressure and reflection coefficient was observed by varying the water pressure applied to the eye at 8000 Hz. • There was a clear increase in decibels being returned by the reflection wave the higher the water pressure is applied on the eye model Reflection coefficient = average sound level of reflected wave / sound level of incident wave • This system has the potential to be used as at-home testing given more research related to how eye geometry effects the reflection coefficient
Research Question/Problem/ Need	How can intraocular pressure be measured at home using cheap equipment?

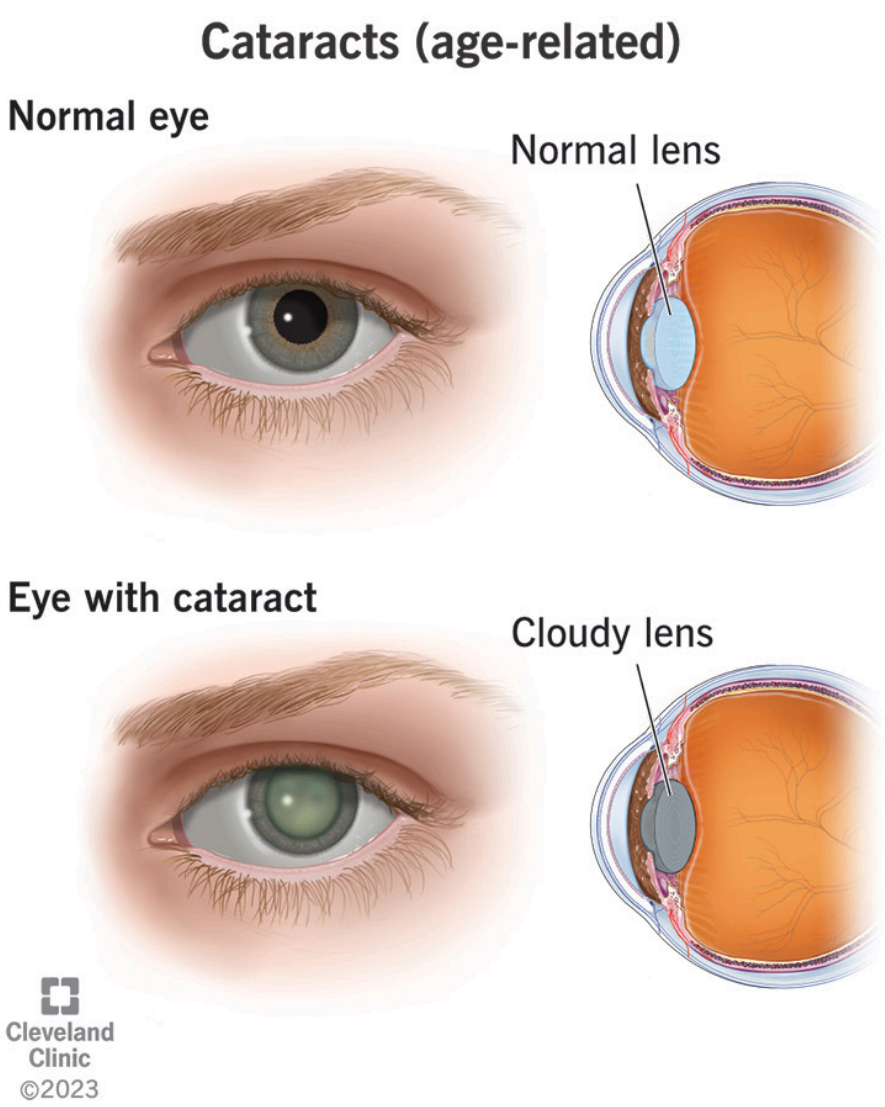
Important Figures	 The experimental setup for this study.  Identifying the resonance frequency and optimal frequency for testing.

	 The reflection coefficient in relation to the depth of water, and therefore internal pressure, of the eye at 8000 Hz.
VOCAB: (w/definition)	1. Resonance frequency - Resonant frequency is the natural frequency where a medium vibrates at the highest amplitude. 2. Optimal frequency - Optimal frequency is achieved when the least number of decibels is absorbed by the eye model. 3. Ocular hypertension - Ocular hypertension is a condition that occurs when pressure within the eye increases without affecting a person's vision or damaging their eye anatomy.
Cited references to follow up on	1. Wang YX, Xu L, Wei WB, Jonas JB. Intraocular pressure and its normal range adjusted for ocular and systemic parameters. The Beijing Eye Study 2011. 2018; 13(5). 2. Tham Y-C, Li X, Wong TY, Quigley HA, Aung T, Cheng C-Y. Global prevalence of Glaucoma and projections of Glaucoma burden through 2040. Ophthalmology, ISSN: 1549-4713. 2014; 121(11): 2081-2090.
Follow up Questions	1. In addition to the eye's geometry, will the material also be a changing factor that alters the optimal frequency and relationship between internal pressure and reflection coefficient? How can the material of a real eye be reproduced to further confirm this relationship? 2. How can the change

Article #16 Notes: Cataracts: Signs, Symptom & Treatment Options

Source Title	Cataracts: Signs, Symptoms, & Treatment Options
Source citation (APA Format)	Cataracts: Signs, symptoms & treatment. (n.d.). Cleveland Clinic. Retrieved February 9, 2024, from https://my.clevelandclinic.org/health/diseases/8589-cataracts-age-related
Original URL	https://my.clevelandclinic.org/health/diseases/8589-cataracts-age-related
Source type	Article
Keywords	Cataracts, symptoms, signs, diagnosis
#Tags	N/A
Summary of key points + notes (include methodology)	● Cataracts are cloudy areas that form around the lens of the eye ● The lens is made out of crystallins and as an individual gets older, these proteins being to break down and form cloudy patches ● Cataracts is very common in the elderly population ● Cataracts is like you are looking out of dirty window ● There are numerous types of cataracts: ○ Pediatric cataracts - This affects babies and children. Babies can be born with cataracts or may form after birth. ○ Traumatic cataracts - This type of cataract is formed when something hurts the individual's eye. ○ Secondary cataracts - These are a type of cataracts that form on top of the lens and are called posterior capsular opacification. ● The eye lens starts to break down around 40 and symptoms of cataracts won't be noticeable until age 60 or older ● About 17% of the people around the world have cataracts, with people in middle-income and low-income regions suffering the most due to lack of eye care resources and more risk factors. ● In the US, almost 1 in 5 people ages 65 to 74 have cataracts in their vision. 50% of people over 80 years old had or currently have cataracts. ● There are numerous symptoms of cataracts: ○ Cloudy or blurry vision ○ Changes in the way color is seen ○ Sensitivity to brightness ○ Glare ○ Difficult seeing at night ○ Changes in vision prescription ○ Double vision ● There are multiple risk factors for cataracts:

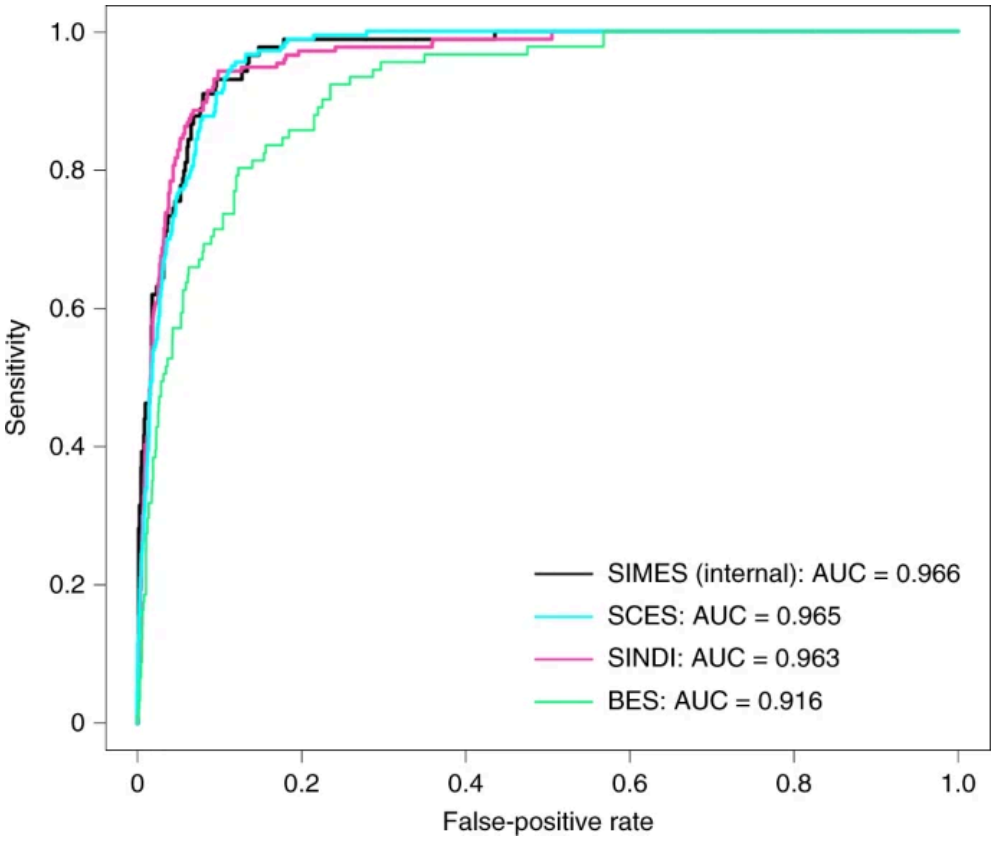
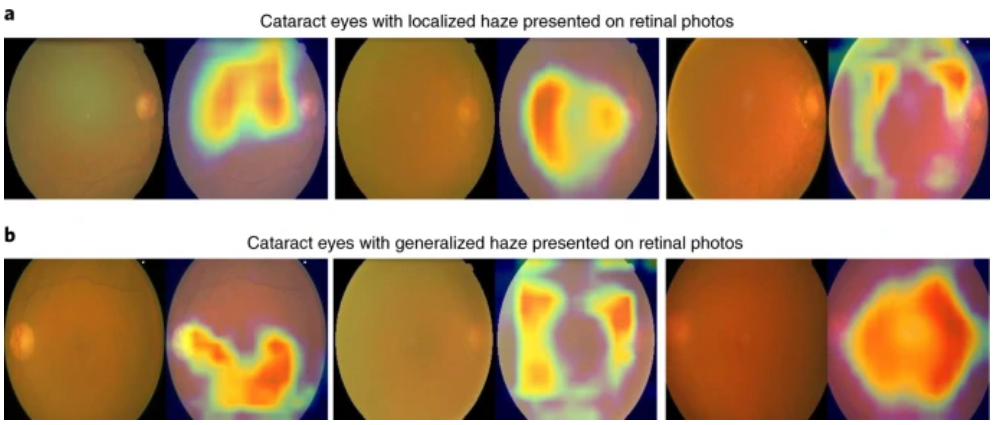
	○ Environmental factors - air pollution, tobacco smoke, alcohol, industrial chemicals, pesticides, long-term exposure to UV-light, and History of radiation therapy ○ Medical risk factors - having diabetes or high blood sugar, having eye surgeries for glaucoma or other diseases, using corticosteroids, having eye diseases such as retina pigmentosa and uveitis ○ Genetic risk factors - If people in our family such as parents or siblings have cataracts, you may be more likely to develop cataracts as well. ● Cataracts can be diagnosed with a slit lamp test or a visual acuity test ● Cataract surgery is the main treatment option for removing cataracts
Research Question/Problem/ Need	What is cataracts?

Important Figures	 The visual difference between an individual with and without cataracts.
VOCAB: (w/definition)	1. Radiation therapy - The treatment of disease, especially cancer, using X-rays or similar forms of radiation. 2. Corticosteroids - Corticosteroids, often known as steroids, are an anti-inflammatory medicine. 3. Retina pigmentosa - Retinitis pigmentosa (RP) is a group of rare eye diseases that affect the retina (the light-sensitive layer of tissue in the back of the eye). RP makes cells in the retina break down slowly over time, causing vision loss. 4. Uveitis - Uveitis is a form of eye inflammation. It affects the middle layer of tissue in the eye wall (uvea). Uveitis (u-vee-I-tis) warning signs often come on suddenly and get worse quickly. They include eye redness, pain and blurred vision.

Cited references to follow up on	1. What is an ophthalmologist? Definition & types. (n.d.). Cleveland Clinic. Retrieved February 9, 2024, from https://my.clevelandclinic.org/health/articles/22159-ophthalmologist 2. Posterior capsular opacification (Secondary cataract): Symptoms & treatment. (n.d.). Cleveland Clinic. Retrieved February 9, 2024, from https://my.clevelandclinic.org/health/diseases/24737-posterior-capsular-opacification
Follow up Questions	1. How can cataracts be prevented even as an individual grows older? 2. What are the benefits to cataract surgery? Can this surgery also prevent other eye diseases and if so, how?

Article #17 Notes: Detecting visually significant cataract using retinal photograph-based deep-learning

Source Title	Detecting visually significant cataract using retinal photograph-based deep-learning
Source citation (APA Format)	Tham, Y.-C., Goh, J. H. L., Anees, A., Lei, X., Rim, T. H., Chee, M.-L., Wang, Y. X., Jonas, J. B., Thakur, S., Teo, Z. L., Cheung, N., Hamzah, H., Tan, G. S. W., Husain, R., Sabanayagam, C., Wang, J. J., Chen, Q., Lu, Z., Keenan, T. D., … Cheng, C.-Y. (2022). Author Correction: Detecting visually significant cataract using retinal photograph-based deep learning. Nature Aging, 2(6), 562–562. https://doi.org/10.1038/s43587-022-00245-5
Original URL	https://www.nature.com/articles/s43587-022-00171-6#change-history
Source type	Technical Report
Keywords	Cataracts, imaging, deep learning, diagnosis
#Tags	N/A
Summary of key points + notes (include methodology)	• Age-related cataracts are the leading cause of visual impairment among older adults • Many cases of cataracts remain undiagnosed due to limited accesibility to cataract screening • The normal diagnosis of cataracts depends on the slit-lamo bionicroscopy operated by trained professionals • This paper proposes a novel machine learning method to diagnose cataracts based on fundus images of the eye
Research Question/Problem/	Can cataracts be diagnosed through imagle classification machine learning models?

Need	
Important Figures	 The area under the curve of the created machine learning algorithm.  How the machine learning algorithm analyzes fundus images of the eye for classification.
VOCAB: (w/definition)	1. Saliency maps - In computer vision, a saliency map is an image that highlights the region on which people's eyes focus first. The goal of a saliency map is to reflect the degree of importance of a pixel to the human visual system.

Cited references to follow up on	1. Adelson, J. D. et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Global Health https://doi.org/10.1016/S2214-109X(20)30489-7 (2020). 2. Chua, J. et al. Prevalence, risk factors, and impact of undiagnosed visually significant cataract: the Singapore epidemiology of eye diseases study. PLoS ONE 12, e0170804 (2017).
Follow up Questions	1. Can diagnosis be done on normal images of the eye taken by an individual without fundus imagers? 2. If so, will these images procude less accurate diagnoses?

Article #18 Notes: SNVformer: An Attention-based Deep Neural Network for GWAS Data

Source Title	An Attention-based Deep Neural Network for GWAS Data
Source citation (APA Format)	Elmes, K., Benavides-Prado, D., Tan, N. Ö., Nguyen, T. B., Sumpter, N., Leask, M., Witbrock, M., & Gavryushkin, A. (2022). SNVFORMER: An Attention-Based Deep Neural Network for GWAS Data. https://doi.org/10.1101/2022.07.07.499217
Original URL	https://www.biorxiv.org/content/10.1101/2022.07.07.499217v2
Source type	Peer-reviewed Research article
Keywords	Deep learning, Neural networks, GWAS, genetics, polygenic risk score
#Tags	#GWAS, #Deep learning, #SNVFormer, #Attention
Summary of key points + notes (include methodology)	Notes ● GWAS data is often used to create polygenic risk scores, but the models are limited due to their simplicity. They are often just linear models of genetic effects ● This study focuses on the prediction of gout, a form of arthritis ● Few studies in the past have tried detecting/predicting gout through genotype data ● Predicitions are limited by two factors: heritability and genetic effects of the phenotype ● Due to these limitations, simple mathematical linear models are often created for polygenic risk scores, but this does not model gene-gene interactions (epistasis)

	● If a trait is epistatic, then identifying the variants that lead to this is an important step when generating PGS scores ● This study will input SNVs into a complex Transformer model for prediction ● AlphaFold-2 is a previous model utilizing Transformer technology in a genetic context ● However, AlphaFold-2 is limited because it can only take small genetic sequences at a time. ● This study aims to create a Transformer model that takes GWAS data as input and can model gene-gene interactions and multidimensional phenotypes ● The key piece of technology in Transformer models is Attention. Attention assigns a score to every token in a sequence representing its relationship with the other tokens. In other words, Attention technology allows the machine to consider the context of a sequence. ● The following steps were taken to conduct the study: ○ 870,000 SNV data was collected and another 90 million were imputed per individual ○ Extracted a sequence of SNV for a specific sequence in the genome ○ Translated each SNV to an integer based on a table of values ○ Each SNV is separated into two components, its position in the genome and its major/minor alleles ● Individuals in the study self-reported about their phenotype ● SNVs with a minimum allele frequency of 10^-4 were taken into consideration with the Hardy-Weiberg having a threshold of 10^-6 ● In addition to genotype information, age, gender, and sex also featured ● AUROC value of 0.84 achieved, which is already much better than many generated linear models ● The accuracy increased from 0.64 to 0.84 with the addition of phenotypic data of age and sex ● In the future, other encodings for the SNVs can be observed ● Attention-based token relevancy scores can be analyzed to further determine which specific SNV supports the phenotype prediction.
Research Question/Problem/ Need	Polygenic risk score models are often created through simplistic linear systems, which leads to the ignorance of gene-gene interactions and epistasis.

Important Figures

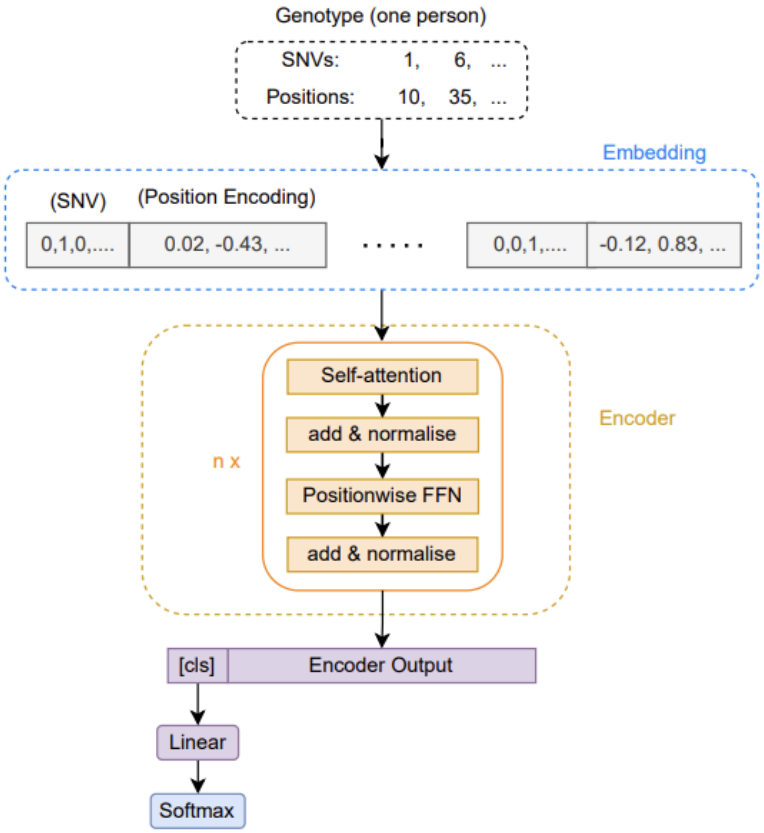


Figure 2: Architecture of SNVformer. Input (genotype) is shown at the top, followed by the embedding, network's layers, and output at the bottom.

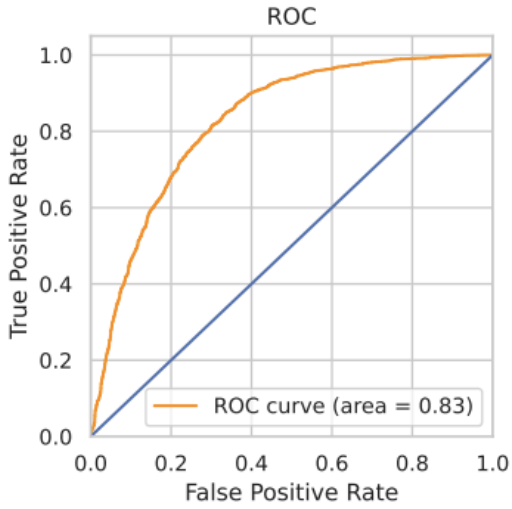


Figure 4: ROC curve when trainied on 66k genotyped SNVs combined with Age, Sex, and BMI.

Table 1: SNV encoding. Homozygous alleles are encoded as 'X', heterozygous as 'X,Y', I encodes unique sequences.

'nan' : 00	'ins' : 01	'del' : 02	'G' : 03
'A' : 04	'C' : 05	'T' : 06	'CI' : 07
'GI' : 08	'TI' : 09	'AI' : 10	'G,A' : 11
'A,G' : 12	'G,C' : 13	'C,T' : 14	'G,T' : 15
'C,G' : 16	'T,C' : 17	'A,ins' : 18	'A,C' : 19
'CI,del' : 20	'G,ins' : 21	'GI,del' : 22	'T,G' : 23
'C,A' : 24	'TI,del' : 25	'A,T' : 26	'C,ins' : 27
'T,ins' : 28	'AI,del' : 29	'T,A' : 30	'AI,ins' : 31

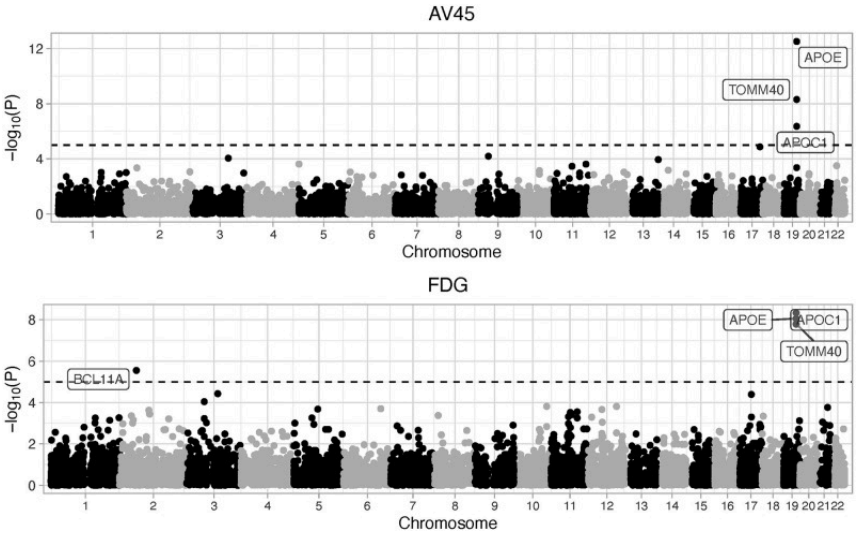
VOCAB: (w/definition)

1. Embeddings - This represents real-world objects or ideas in a form that the computer can understand and interpret.
2. SNV - A variation of a single nucleotide ina population's genome. This is slightly different than SNPs because SNVs are rarer.
3. AUROC - This means area under the receiving operating characteristic and is a performance metric to evaluate models.

Cited references to follow up on	1. Beltagy, I., Peters, M. E., and Cohan, A. Longformer: The Long-Document transformer. April 2020. 2. Ji, Y., Zhou, Z., Liu, H., and Davuluri, R. V. DNABERT: pre-trained bidirectional encoder representations from transformers model for DNA-language in genome. Bioinformatics, February 2021. 3. Cahyawijaya, S., Yu, T., Liu, Z., Mak, T. T. W., Zhou, X., and others. SNP2Vec: Scalable Self-Supervised Pre-Training for Genome-Wide association study. arXiv preprint arXiv, 2022
Follow up Questions	1. I wonder how well the model will do without the genotype information and solely the phenotypic information (age and sex)? 2. How will this model do in comparison with other basic machine learning models implemented for polygenic risk scores such as Logistic Regression or Naive Bayes?

Article #19 Notes: Explainable deep transfer learning model for disease risk prediction using high-dimensional genomic data

Source Title	Explainable deep transfer learning model for disease risk prediction using high-dimensional genomic data
Source citation (APA Format)	Liu, L., Meng, Q., Weng, C., Lu, Q., Wang, T., & Wen, Y. (2022). Explainable deep transfer learning model for disease risk prediction using high-dimensional genomic data. PLOS Computational Biology, 18(7). https://doi.org/10.1371/journal.pcbi.1010328
Original URL	https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1010328
Source type	Peer-reviewed research paper
Keywords	Deep learning, genetic risk score, PRS, genomics
#Tags	#deep learning, #machine learning, #GWAS, #genomic data
Summary of key points + notes (include methodology)	Notes ● An accurate polygenic risk score is needed in order to improve polygenic risk scores ● At its simplest form, polygenic risk scores are calculated as the sum of risk alleles ● With these simple models, oftentimes complex factors such as epistasis are

	lost ● Feature selection in the current linear models help reduce noise, but can also limit prediction power because pre-selected features and performance were two separate parts and not the same goal ● The goal for feature selection is to choose genetic variants ● After this study created a deep learning model for polygenic risk scores there were numerous benefits: ○ The model streamlines dimension reduction and the modeling process. As a result, there is a smaller chance that important predictors and variant will be overlooked, and accuracy will be improved. ○ This model structure is very flexible and can encompass various model assumptions ● The paper took the following steps to look into feature selection and a prediction models utilizing deep learning: ○ Feature selection: the input is genetic variants categorized into specific groups and weight is calulacted ○ Prediction model: Genetic variants are groped into regions again and a model is created based on weights given to the top features in the feature importance model. Previous githhub work: https://github.com/YaluWen/EDNN
Research Question/Problem/ Need	Currently, ploygenic risk score models are simple and unadvanced. Through the use of deep learning, previousdata that w
Important Figures	 Finding the causal SNP using the feature selection method proposed in this study.
VOCAB: (w/definition)	1. AV45 - An amyloid biomarker that is seen in Alzheimer's 2. FDG - a positron-emitting radiotracer used with positron tomography 9PET)to diagnose and monitor various conditions.

Cited references to follow up on	1. Nolte IM, van der Most PJ, Alizadeh BZ, de Bakker PI, Boezen HM, Bruinenberg M, et al. Missing heritability: is the gap closing? An analysis of 32 complex traits in the Lifelines Cohort Study. Eur J Hum Genet. 2017;25(7):877–885. doi: 10.1038/ejhg.2017.50 2. Hai Y, Wen Y. A Bayesian linear mixed model for prediction of complex traits. Bioinformatics. 2020;36:5415–23. doi: 10.1093/bioinformatics/btaa1023 3. Lu Q, Wen Y. Multi-kernel linear mixed model with adaptive lasso for prediction analysis on high-dimensional multi-omics data. Bioinformatics. 2020;36(6):1785–1794. doi: 10.1093/bioinformatics/btz822 4. 18. Eraslan G, Avsec Z, Gagneur J, Theis FJ. Deep learning: new computational modelling techniques for genomics. Nat Rev Genet. 2019;20(7):389–403. doi: 10.1038/s41576-019-0122-6
Follow up Questions	1. Are there any limitations to using deep learning? In whichways if any does linear programming perform bet? 2. What is the exact matrix/complex input to the machine learning models?

Article #20 Notes: A Generalized Method for the Creation and Evaluation of Polygenic Scores: Details for Each Report

Source Title	A Generalized Method for the Creation and Evaluation of Polygenic Scores: Details for
Source citation (APA Format)	CE - 2022 appendix to White Paper 23-21 - PGS methods. (n.d.). https://permalinks.23andme.com/pdf/23_21-PRSMethodologyAppendix_2022.pdf
Original URL	https://permalinks.23andme.com/pdf/23_21-PRSMethodologyAppendix_2022.pdf
Source type	White Paper Report
Keywords	Glaucoma, GWAS, polygenic risk score, race
#Tags	#Glaucoma, #Polygenic risk score, #PRS, GWAS
Summary of key points + notes (include methodology)	● In this white paper report, the cases were defined as people who had experiences Glaucoma related illness in the past, and the controls were people who didn't ● The PRS model was trained and used a group of causal SNP selected meta-analysis of GWASs that were conducted about numerous ethnic groups including African Americans, East Asians, South Asians, and

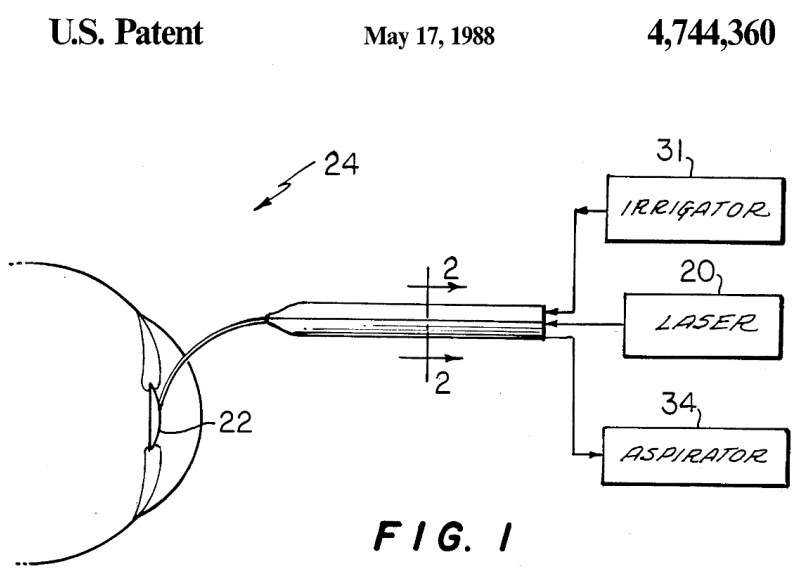
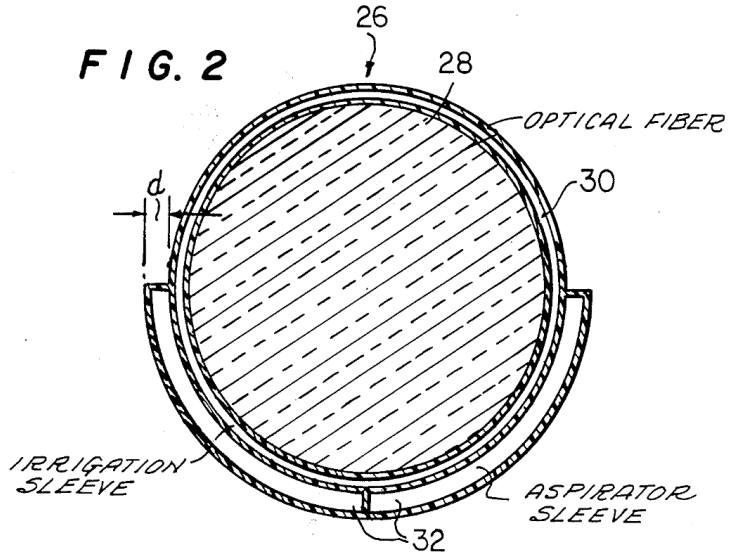
	Latinos ● Additional features in the model include sex and age ● While the paper was done on multiple ethnic groups the sizes of training and validation sets were not equal with one another at all. As a result, some of the risk variants from a minority of a lower sample might have their unique variants shadowed and not show up as holding to much weight in the polygenic risk score model. This can also be seen in the table in the important figures section ● The AUC of the 23AndMe glaucoma study on Europeans was 0.6171, while it was 0.5823 for African Americans
Research Question/Problem/ Need	Glaucoma is a leading cause of vision loss that needs to cand can be prevented with the early detection and help of polygenic rsk score model.
Important Figures	**Table 5-2:** Glaucoma participant cohort descriptives (see table below)
VOCAB: (w/definition)	1. GWAS - GWAS stand for Genome Wide Assocoation study and it is the collection of genotyping information from a sample of people 2. Platform - The platforms determines where an individuals genome was sequenced and using which specific technology. 3. Prevalence - Prevalence in disease prediction is the number of people are are infected by a disease at a certain period in time
Cited references to follow up on	*These aren't cited directly, but these diseases are alo mentioned in other parts of the white paper and it would be useful to see how other models with simiailri databases and algorithms perform as well in order to learn the technique behind creating a PRS 1. PRS model for Depression

Sample use	Platform	Ancestry group	N	Age mean (SD)	Sex (% female)	Glaucoma prevalence (%)
GWAS	V2 to V5	European	2,454,498	50.6 (16.7)	57.68%	3.80%
GWAS	V2 to V4	East/Southeast Asian	23,916	42.4 (13.6)	60.73%	2.78%
GWAS	V2 to V5	Hispanic/Latino	435,234	41.5 (14.5)	58.58%	2.74%
GWAS	V2 to V4	South Asian	7,189	44.3 (12.6)	34.58%	3.07%
GWAS	V2 to V4	Sub-Saharan African/African American	32,048	49.2 (15.3)	58.84%	5.60%
Training trans-ancestral models	V5	European, Hispanic/Latino	2,568,772	47.3 (16.4)	58.84%	3.27%
Testing	V5	European	232,661	48.9 (16.6)	58.71%	3.4%
Testing	V5	East/Southeast Asian	115,960	38.0 (13.1)	61.09%	2.3%
Testing	V5	Hispanic/Latino	44,906	40.3 (14.1)	59.27%	2.43%
Testing	V5	Northern African/Western Asian	25,207	42.5 (15.1)	45.48%	2.01%
Testing	V5	South Asian	31,270	39.8 (13.0)	42.83%	2.31%
Testing	V5	Sub-Saharan African/African American	72,054	41.8 (14.8)	60.55%	3.68%

	2. PRS model for Gout 3. PRS model for Insomnia
Follow up Questions	1. Has 23andMe looked into implementing multiple different PRS models for different ethnicities rather than just combining all the ethnicities and data into one large model? Would this potentially eliminate the problem of strong genetic variants overshadowing quieter in models? 2. Other than data avaiavability and access, what are some other major drawbacks for creating polygenic risk score models?

Patent #1 Notes: Apparatus for ablating and removing cataract lenses

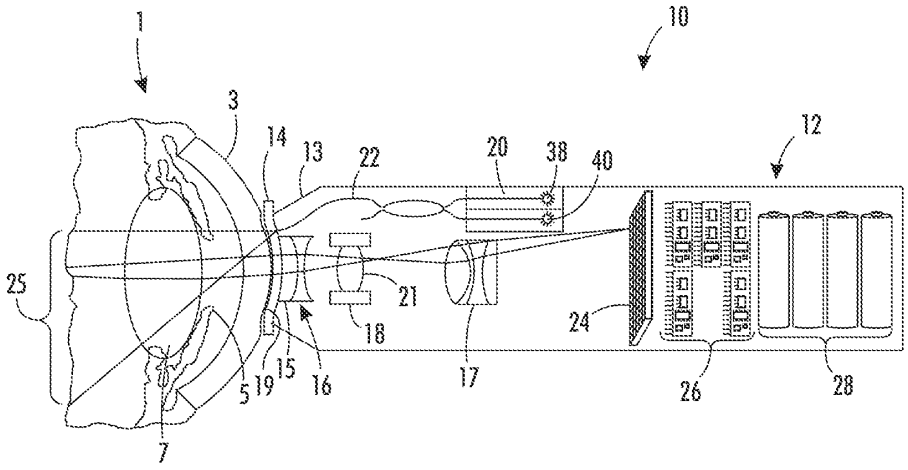
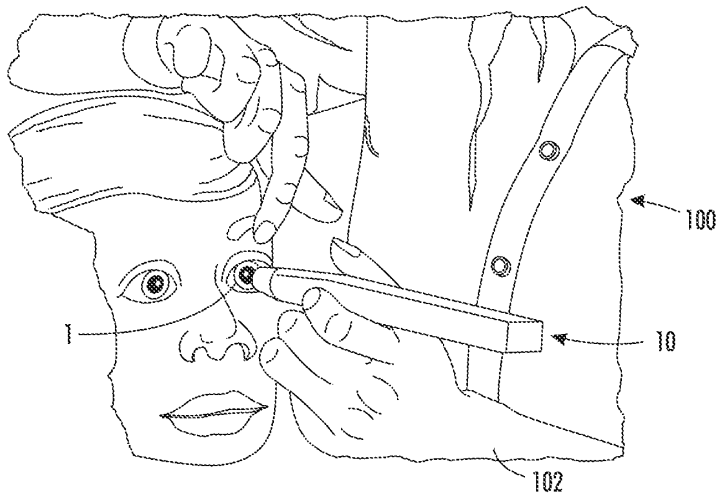
Source Title	Apparatus for ablating and removing cataract lenses
Source citation (APA Format)	Bath, P. E. (1988). Apparatus for ablating and removing cataract lenses (United States Patent US4744360A). https://patents.google.com/patent/US4744360A/en
Original URL	https://patents.google.com/patent/US4744360A/en
Source type	Patent
Keywords	Cataracts, treatment, lens removal
#Tags	N/A
Summary of key points + notes (include methodology)	● Laser radiation is now a commonly used surgery tehcnique in ocular related problems ● Optical fibers are commonly used for medical and other application to transmit coherent radiation from a laser to some other location ● In this method, an apparatus with coherent radiation is transmitted with an opticla fiber and then positioned inside the crystalline lens where cataracts occurs ● The radiation disintegerates the crystalline material in the lens and can then be taken out of the eye
Research Question/Problem/ Need	How can cataract surgery be performed in a more non-invasive and smoother method using laser radiation and optical fibers?

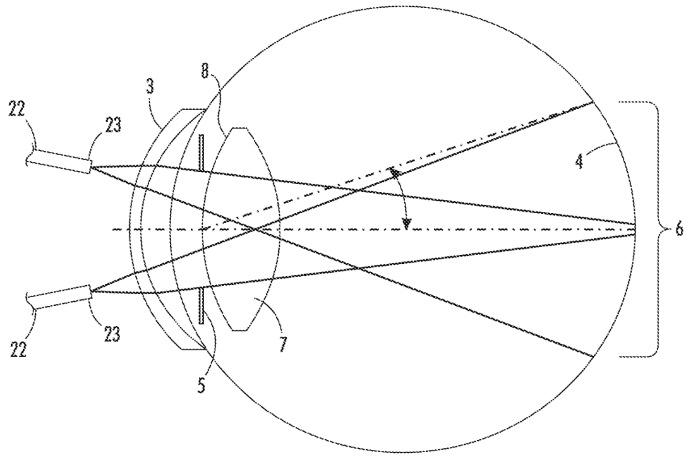
Important Figures	 FIG. 1  FIG. 2 How tis surgical proccess and technique can take place.
VOCAB: (w/definition)	1. Laser radiation - Laser is an acronym for "Light Amplification by Stimulated Emission of Radiation" and relates to the way of radiation generation. The laser is a relatively recent invention. It was for the first time realized in 1960 with a synthetic ruby crystal. 2. Optical fibers - Fiber optics, or optical fiber, refers to the technology that

	transmits information as light pulses along a glass or plastic fiber. A fiber optic cable can contain a varying number of glass fibers, from a few up to a couple hundred. Another glass layer called cladding surrounds the glass fiber core.
Cited references to follow up on	There were no cited references for this patent application.
Follow up Questions	1. This seems liek a viable solution for cataracts that forms within the crystalline lens, but what about the form of cataracts that forms right on top of the lens? Would this still be a viable solution, and if so, how can it be modified to remove this form of cataracts? 2. How does this method of cataracts surgery perform when compared to other methods? Is it easier, quicker, or more efficient in some other manner?

Patent #2 Notes: Portable Fundus Camera

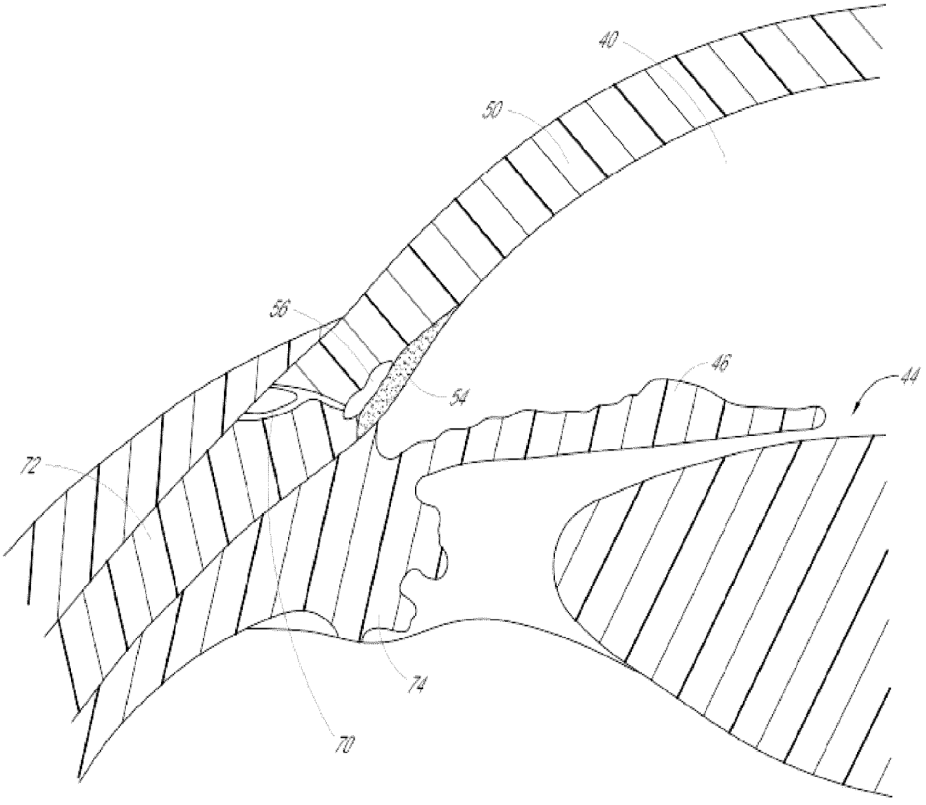
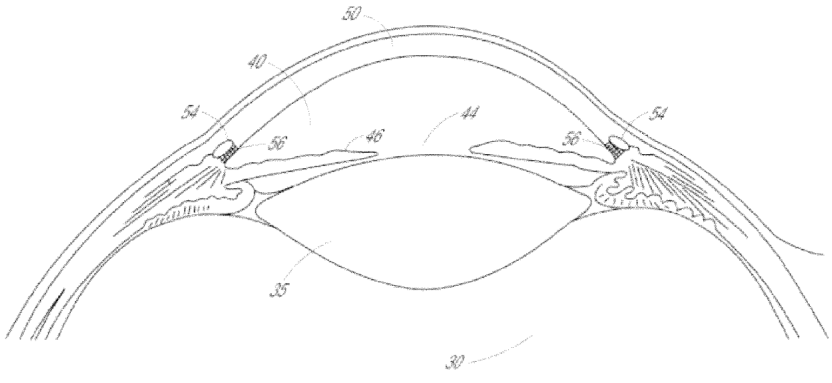
Source Title	Portable Fundus Camera
Source citation (APA Format)	IGNATOVICH, F. V., Kleinman, D. M., Cotton, C. T., & Blalock, T. (2014). Portable fundus camera (United States Patent US8836778B2). https://patents.google.com/patent/US8836778B2/en
Original URL	https://patents.google.com/patent/US8836778B2/en
Source type	Patent
Keywords	Fundus imagining, glaucoma
#Tags	N/A
Summary of key points + notes (include methodology)	● Fundus systems are only available in high-end high-overhead ophthalmologist offices ● Patients that rely on general hospitals and physicians have no access to test for glaucoma and other ocular diseases ● Ocular diseases are directly proportional to age, and as baby boomers continue to age, this will become a major issue in the following years ● Ultrasound imaging is a way in which diagnosis methods are emergeing, however this remains s system that isunaccesible to people in remote or rural areas ● This patent describes the model for a hand-held fundus imager that is

	attached to an iPhone or Android and takes quality fundus images, that of which is comparable to fundus images taken by the table-top imagers
Research Question/Problem/ Need	Table-top fundus imagers are blky and inaccessible to the general population.
Important Figures	  How the fundus imager works with a patient demonstration.

	 FIG. 5 How the fundus imager takes a picture of the eye.
VOCAB: (w/definition)	3. Fundus - The fundus of the eye is the interior surface of the eye opposite the lens and includes the retina, optic disc, macula, fovea, and posterior pole. 4. Ophthalmology - The branch of medicine concerned with the diagnosis and treatment of disorders of the eye.
Cited references to follow up on	1. C.Gliss et al., "Toward a miniaturized fundus camera," Journal of Biomedical Optics, 9(1), 126-131 (Jan./Feb. 2004). EFS file name: 20130430-13-512336-IDS-NPL-Cite4. 2. E.Dehoog et al., "Fundus Camera Systems: a comparative analysis," Appl. Opt. Jan. 10, 2009; 48(2): 221-228, US. EFS file name: 20130430-13-512336-IDS-NPL-Cite1.
Follow up Questions	3. This fundus imager seems to have some technology inside of it that operates how it performs. How much does this technology add to the cost? What is the benefit of this technology given fundus imagers on the market that don't incorporate this form of technology also exist? 4. What is the angle view of this fundus imager? What have patients that have used this in past stated in terms of comfortability?

Patent #3 Notes: Composition and Method for Treating Glaucoma

Source Title	Composition and Method for Treating Glaucoma
Source citation (APA Format)	US Patent Application for Compositions and Methods for Treating Glaucoma Patent Application (Application #20170368024 Issued December 28, 2017) - Justia Patents Search. https://patents.justia.com/patent/20170368024. Accessed 15 Dec. 2023.
Original URL	https://patents.justia.com/patent/20170368024
Source type	Patent
Keywords	Glaucoma, treatment
#Tags	#disease treatment, #Glaucoma
Summary of key points + notes (include methodology)	Notes ● This patent provides multiple potential treatments to combat against Glaucoma: ○ Method #1 is related to lowering intraocular pressure with the use of a reasonable dosage of ascorbic acid conjugate or nucleic acids ○ A pharmaceutical option was also given which consisted of tyrosine, L-DOPA, and ascorbic acid. ○ In another option, the composition includes a nucleic acid that codes an enzyme ○ Method #2 is related to administering trabecular meshwork cells onto a trabecular meshowrk of an eye ● An example is given as part of the patient that explains the treatment of Glaucoma using Ascorbic Acid linked to Tyrosine with a 75 year old patient
Research Question/Problem/ Need	Glaucoma is a leading cause of blindness that does not have a cure and very limited treatments.

Important Figures	 Fig. 1B  Images of the eye and highlighting different parts.
VOCAB: (w/definition)	1. Tyrosine - Tyrosine is a nonessential amino acid the body makes from another amino acid called phenylalanine.

	2. L-DOPA - Levodopa is the precursor to dopamine. 3. Enzyme - Enzymes are proteins that help speed up metabolism, or the chemical reactions in our bodies. 4. Conjugate ascorbic acid - The conjugate of ascorbic acid is L-ascorbic acid. It has a role as a coenzyme.
Cited references to follow up on	No cited references were seen in the patent.
Follow up Questions	5. Are chemical and biological treatments the only treatments that have made substantial improvement for a person with Glaucoma? Have any exercises, physical therapy, or other forms of treatment helped before? 6. When is the proposed solutions most affective for a person who is likely to inherit Glaucoma? How much more beneficial is it to take these medications earlier versus later?