Exercise (Physical Activity) and Eye Disease

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Disclosure

- Key opinion leader and/or speaker for:
  - Visionix (Optovue)
  - Quidel
  - New World Medical
  - LKC Technologies
  - Allergan
  - Tarsus
  - Topcon
  - Thea

All financial relationships have been mitigated

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Ways to reach out

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Define terms

- **Exercise** – discretionary, voluntary activity that we do for health
- **Physical activity** - Physical activity is defined as any voluntary bodily movement produced by skeletal muscles that requires energy expenditure. Physical activity encompasses all activities, at any intensity, performed during any time of day or night. It includes both exercise and incidental activity integrated into daily routine.

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Opening Question

- How many of you do at least 150 minutes of physical activity per week?

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Physical activity reduces risk

- Cardiovascular disease 60%
- Diabetes 50%
- Obesity 50%
- Cancer
  - Colon 50%
  - Breast 25%
- Dementia 40%
  - Vascular
  - Alzheimer's 45%
  - Parkinson's
- Depression 25%
- ED 50%
- etc

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How can you add 5 years to your life?

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"There is diet, there is sleep, but the single most important intervention for your health is...EXERCISE" Ewan Ashley, MD, PhD Stanford Medicine

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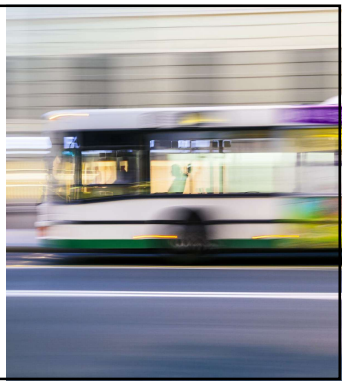
What allows him to make such a statement?

- 1958 London studies
  - Jerry Morris and Margaret Crawford
    - British Medical Journal
  - Bus conductors to drivers
  - Mail deliverers to administrators
- Plus thousands of other studies



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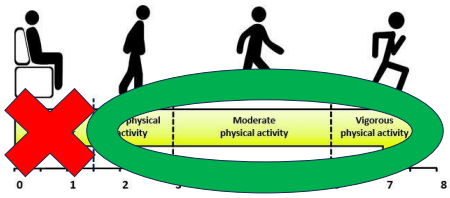
Conclusion

- Sitters die early
- Movers or standers live longer



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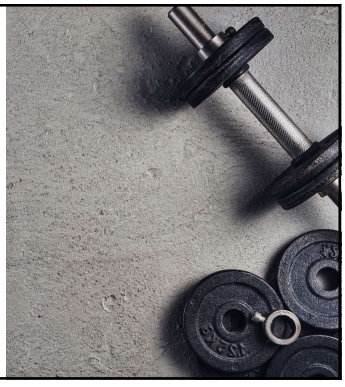
Why does physical activity work?

- The research is emerging
- Physical activity
  - Stresses the body
    - Muscle microtears
    - Mitochondria produce oxidation
    - Certain proteins/enzymes released
    - And at least a thousand of other reactions
  - For every one of these reactions, the body has an answer
    - Increased antioxidant enzyme activity
    - Stem cell release
    - Maintenance and repair
    - Overshoots



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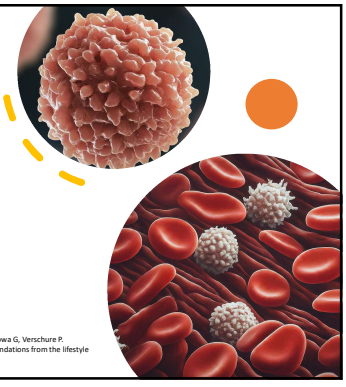
Exercise and stem cell release

- Adult stem cells
  - Found in many tissues throughout the body
    - Bone marrow is the main source of adult stem cells
  - Regenerative
- Exercise triggers a cascade of events that lead to the release of stem cells from the bone marrow



Vodovotz Y, Barnard N, Hu FB, Jakicic J, Lianov L, Loveland D, Buysse D, Szigethy E, Finkel T, Sowa G, Verschure P. Prioritized research for the prevention, treatment, and reversal of chronic disease: recommendations from the lifestyle medicine research summit. Frontiers in medicine. 2020 Dec 22;7:585744.

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What is the effect of exercise in the eye?

1) Increased antioxidant enzyme activity
2) Improves vascular endothelial function
3) Reduces retinal inflammation (except in extreme cases)
4) Increases expression of BDNF
5) Preserves retinal morphology and function
6) Temporarily increases choroidal thickness

Zhang Q, Jiang Y, Deng C, Wang J. Effects and potential mechanisms of exercise and physical activity on eye health and ocular diseases. Frontiers in Medicine. 2024 Mar 22;11:1353624.

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Caveat

- Knowledge on the precise molecular events occurring within the retina during exercise is still incomplete

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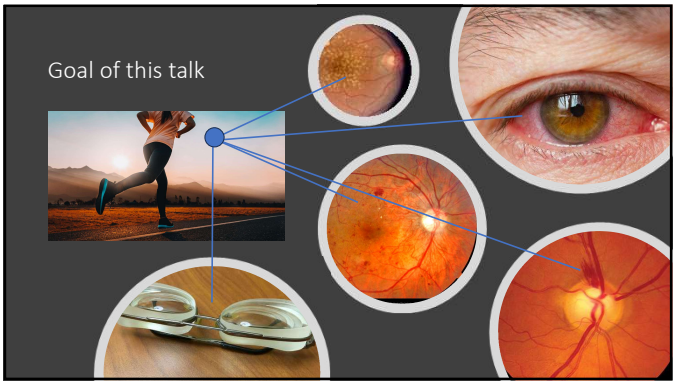
Goal of this talk



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Dry Eye

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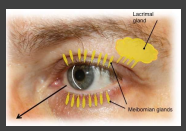
Dry Eye and Ocular Surface Disease



- Exercise causes enhanced circulation to the lacrimal and meibomian glands
  - boost tear production
  - stabilize tear osmolarity
  - reduce tear film cytokines
  - improve tear film stability

- Dartt DA. Neural regulation of lacrimal gland secretory processes: relevance in dry eye diseases. Prog Retin Eye Res. 2009;28(3):155-177.
- Vera J, Jimenez R, Madinabeitia I, Masiulis N, Cardenas D. A maximal incremental effort alters tear osmolarity depending on the fitness level in military helicopter pilots. Ocul Surf. 2017;15(4):795-801.
- Li H, Li F, Zhou R, Gao K, Liang L, Zhang X. Aerobic exercise increases tear secretion and decreases inflammatory cytokines in healthy subjects. Asia Pac J Ophthalmol. 2020;9(5):404-411.
- Sun C, Chen X, Huang Y, et al. Effects of aerobic exercise on tear secretion and tear film stability in dry eye patients. BMC Ophthalmol. 2022;22(1):9.

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"My eyes hurt"

- Regular exercise reduces pain perception
- Modulated by the central nervous system
- May contribute to alleviating dry eye symptoms

Lima LV, Abner TS, Sluka KA. Does exercise increase or decrease pain? Central mechanisms underlying these two phenomena. J Physiol. 2017;595(13):4141-4150.

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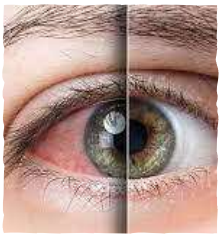
Dry Eye



- Long-term exposure to physical activity or exercise programs was associated with **relief** of dry-eye associated symptoms and a trend to increased tear break-up time.

Navarro-Lopez S, Moya-Ramón M, Gallar J, Carracedo G, Aracil-Marco A. Effects of physical activity/exercise on tear film characteristics and dry eye associated symptoms: A literature review. Contact Lens and Anterior Eye. 2023 May 10:101854.

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Dry Eye and OSD Exercise Tips

- Stay hydrated: Dehydration is a major trigger for dry eye symptoms, especially during physical activity.
  - Prioritize water and electrolytes
- Use lubricating eye drops:
  - Pre- and post-exercise drops help maintain moisture and protect the eye surface from further irritation due to increased airflow and potential dryness.
- Wear protective eyewear:
  - This is essential for shielding eyes from environmental factors like wind, dust, and sun, all of which can aggravate dry eye.

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Myopia

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Myopia

- Outdoor Activity and Myopia Prevention
- Reduced Risk of Myopia Progression
- Indirect Benefits of Exercise

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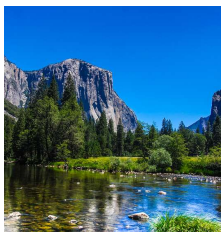
Myopia

- Outdoor Activity and Myopia Prevention
  - **Time Spent Outdoors:** Studies show that spending more time outdoors, particularly in childhood, is associated with a reduced risk of developing myopia.
  - The protective effect of outdoor time was related to the duration of **exposure and light intensity.**

Lingham, G., Yazar, S., Lucas, R.M. *et al.* Time spent outdoors in childhood is associated with reduced risk of myopia as an adult. *Sci Rep* **11**, 6337 (2021).

He X, Sankaridurg P, Wang J, Chen J, Naduvilath T, He M, Zhu Z, Li W, Morgan IG, Xiong S, Zhu J, Zou H, Rose KA, Zhang B, Weng R, Resnikoff S, Xu X. Time Outdoors in Reducing Myopia: A School-Based Cluster Randomized Trial with Objective Monitoring of Outdoor Time and Light Intensity. Ophthalmology. 2022 Nov;129(11):1245-1254.



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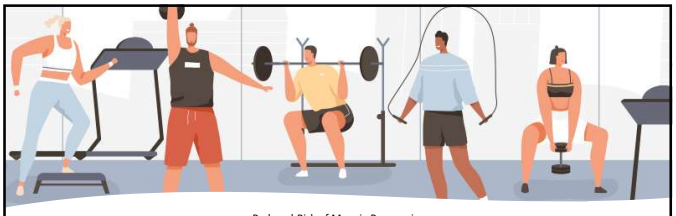

Myopia

- Reduced Risk of Myopia Progression
  - Exercise and General Physical Activity: Regular physical exercise may contribute to overall health, including ocular health. Although the direct effect of exercise on slowing myopia progression is still under study, exercise promotes better blood circulation, which benefits eye health and may indirectly influence myopia progression.
  - A consistent **relationship between more physical activity and less myopia was observed.**

Suhr Thykjær, A., Lundberg, K. and Grauslund, J. (2017), Physical activity in relation to development and progression of myopia – a systematic review. Acta Ophthalmol, 95: 651-659.

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Myopia

- Indirect Benefits of Exercise
  - Reduced Screen Time: Engaging in physical activities naturally limits the time spent on screens and near-vision tasks, which are linked to myopia progression.
  - **Increased digital screen time, near work, and limited outdoor activities were found to be associated with the onset and progression of myopia**, and could potentially be aggravated during and beyond the **COVID-19** pandemic outbreak period.

Wong CW, Tsai A, Jonas JB, Ohno-Matsui K, Chen J, Ang M, Ting DSW. Digital Screen Time During the COVID-19 Pandemic: Risk for a Further Myopia Boom? Am J Ophthalmol. 2021 Mar;223:333-337.

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Myopia Exercise Tips

- **20-20-20** Rule: This is a popular and effective method.
  - Every **20** minutes, take a **20**-second break to look at something **20** feet away. This helps to relax the eye muscles and reduce strain from prolonged near work.
- Outdoor Time: Spending time outdoors, particularly in natural light, has been shown to be beneficial in slowing the progression of myopia, especially in children.
  - Encourage at least **1-2 hours** of outdoor activity daily.

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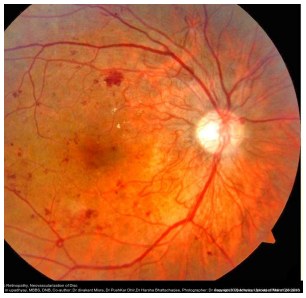
Diabetic Retinopathy



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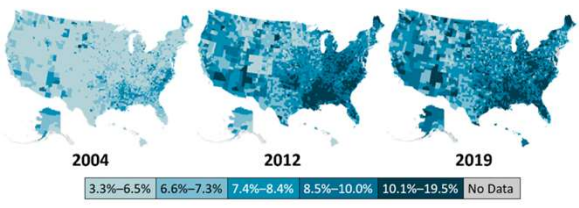
County-Level Distribution of Diagnosed Diabetes Prevalence Among US Adults Aged 20 Years or Older, 2004, 2012, and 2019



United States Diabetes Surveillance System and Behavioral Risk Factor Surveillance System, Centers for Disease Control and Prevention

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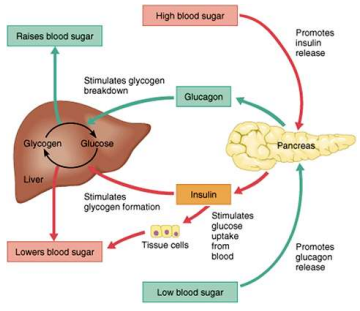
How does the body regulate glucose?



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What is the role of muscle mass?

- Muscle mass reduces your risk of Type 2 diabetes.
  - Relative muscle mass and the risk of incident type 2 diabetes: A cohort study, Sungwoo Hong et al., PLoS One. 2017; 12(11): e0188650.
- Why?
  - exercise increases the delivery of glucose to our muscle cells
- Resistance training has been shown to be particularly beneficial for T2D
  - A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes, Castaneda C. et al., Diabetes Care. 2002 Dec;25(12):2335-41.

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Interval vs Continuous in Type 1

Exercise induced hypoglycemia may reduce exercise adherence

- Randomized Crossover
- **Men showed a higher rate of blood glucose reductions** immediately after and 20 minutes after continuous **aerobic** exercise, as well as immediately after **interval** exercise
- **Women showed reduced blood glucose values only after continuous exercise**
- Conclusion: **Men may become hypoglycemic with either type of exercise while women are more likely to become hypoglycemic with continuous.**

de Sá Martins TB, Gomes OV, Soltani P, Oliveira TH, de Brito-Gomes JL. Sex-Related Glycemic and Cardiovascular Responses After Continuous and Interval Aerobic Sessions in Patients With Type 1 Diabetes: A Randomized Crossover Study. The American Journal of Cardiology. 2024 Oct 1;228:48-55.

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Physical activity = lower risk of Diabetic Retinopathy

- In Type 1
  - Along with lipid levels
- In Type 2
  - Impact is more pronounced in **vision threatening DR**
  - Improves lipid profile, BMI and blood pressure

Ren C, Liu W, Li J, Cao Y, Xu J, Lu P. Physical activity and risk of diabetic retinopathy: a systematic review and meta-analysis. Acta diabetologica. 2019 Aug 1;56:823-37.

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Physical Activity

- Data from 1,814 patients with type 2 diabetes without DR were obtained from a Japanese diabetes registry at Tenri Hospital, Nara, Japan.
- **Higher PA levels are independently associated with a lower incidence of DR in Japanese patients with type 2 diabetes.**

Kuwata H, Okamura S, Hayashino Y, Tsujii S, Ishii H, Diabetes Distress and Care Registry at Tenri Study Group. Higher levels of physical activity are independently associated with a lower incidence of diabetic retinopathy in Japanese patients with type 2 diabetes: A prospective cohort study, Diabetes Distress and Care Registry at Tenri (DDCRT15). PloS one. 2017 Mar 3;12(3):e0172890.

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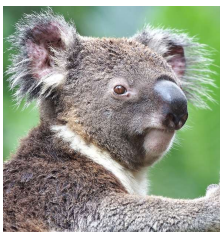
Physical Activity helps

- Nine thousand and eighteen working-aged diabetic patients were enrolled from the baseline of the 45 and Up Study from New South Wales, Australia.
- Self-reported PA collected by questionnaire at baseline in 2006 was graded into low (<5 sessions/week), medium (≥5–14), and high (≥14) levels.
- **Higher PA level was independently associated with a lower risk of DR progression** among working-aged diabetic populations in this large cohort study. (Males)

Yan X, Han X, Wu C, Shang X, Zhang L, He M. Effect of physical activity on reducing the risk of diabetic retinopathy progression: 10-year prospective findings from the 45 and Up Study. PLoS One. 2021 Jan 14;16(1):e0239214.



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Diabetic Retinopathy Exercise Tips

- Prioritize blood sugar control
  - Monitor levels, increase gradually to reduce BS dips
- Proper footwear
  - Peripheral neuropathy issues – custom fitting
- Cardio and Strength training
  - Yoga and Tai Chi
- Use caution within 1 week of intravitreal injections
  - Slightly increased risk of vitreous hemorrhage, endophthalmitis

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Case

- 92 Y/O W/F
- Type 2 Diabetes x 15 years
- Last HbA1c 7.3
- Entering Va 20/30 and 20/50 ph to 20/25 and 20/30
- Previous cataract surgery
- Moderate NPDR OU

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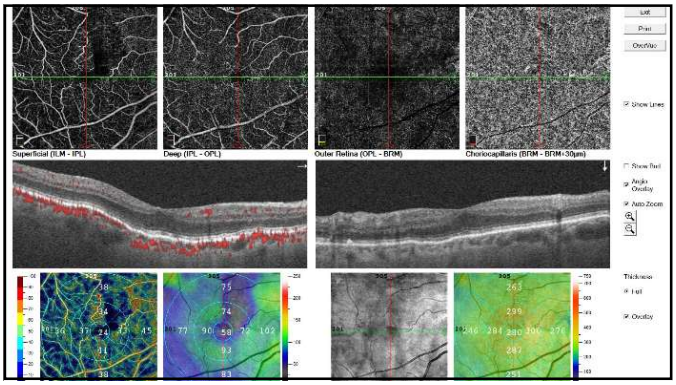

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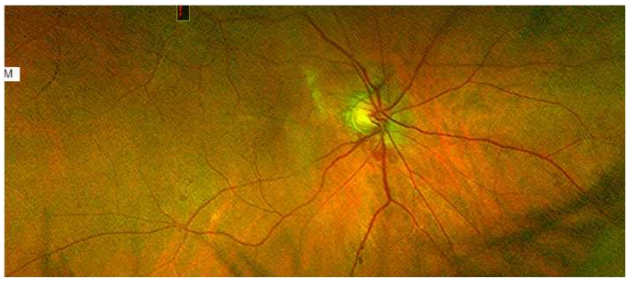

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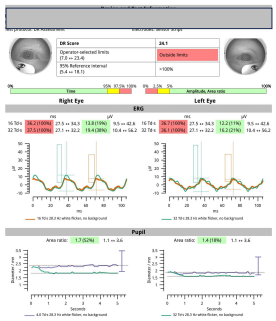
6 months ago



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Treatment

Began supplement	Increased exercise	Increased Metformin

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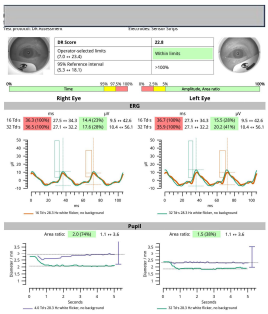
Now



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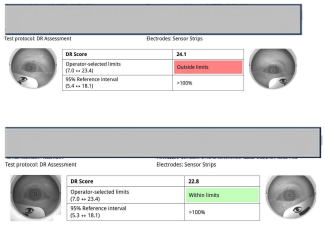
DR Score

- Improved from **24.1 to 22.8**



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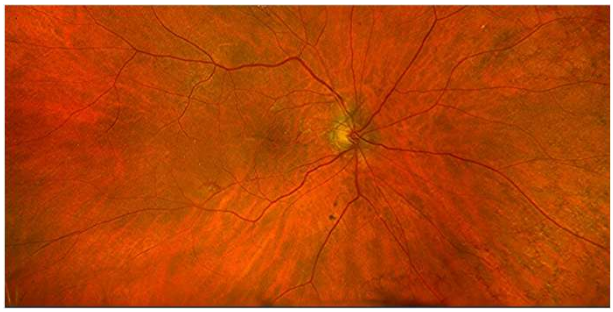

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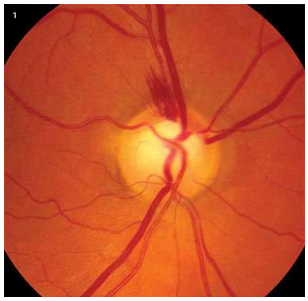
Glaucoma

- Data supporting the idea that physical activity may protect against glaucoma damage comes from
  1) Studies showing IOP reduction with physical activity
  2) Cross sectional analysis showing less physical activity
  3) Intriguing animal models



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Exercise and IOP

- 20 **healthy volunteers** with average age of 25 years old. The volunteers exercised with a **stationary bike to 70% of heart rate reserve**
- Exercise significantly decreased intraocular pressure (**1.7**mmHg)
- Small increase in anterior chamber depth

The short-term influence of exercise on axial length and intraocular pressure, Read SA; Collins MJ, Eye, 2011; 25: 767-774

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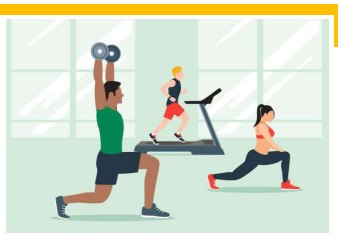
Exercise and IOP

- Prospective non-randomized study in **45-healthy** (non-glaucoma) volunteers who were entering a **6-week exercise program**, consisting of aerobic activities and weight training, three days a week
- Individuals enrolled in the exercise program saw a reduction in average IOP of **−2.18** ± 2.25 mmHg ($p < 0.001$) at the end of the 6-week period
- Suggest that **regular exercise can lower IOP by clinically meaningful levels**



Effects of regular exercise on intraocular pressure, Yeak Dieu Siang J; Mohamed MNAB; Mohd Ramli NB et al., European Journal of Ophthalmology, 2022; 32: 2265-2273

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Exercise and IOP

- The authors measured intraocular pressure before and five minutes after **aerobic** activity
- Seven groups of participants ranging from normotensives that exercise regularly; normotensives treated in the right eye with timolol, latanoprost, or brimonidine; and glaucoma patients treated with beta-blockers, prostaglandin analogs, or combined ocular hypotensive treatment
- Found a **2-3** mmHg reduction in all groups
- Suggests that **exercise has an additive effect** of lowering intraocular pressure **regardless of the class of ocular hypotensive medication, or the number of medications**

Aerobic exercise and intraocular pressure in normotensive and glaucoma patients, Natsis K; Asouhidou I; Nousios G *et al.*, BMC Ophthalmology, 2009; 9: 6

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Exercise and IOP

- Regular exercise, both short- and long-term, helps maintain IOP within normal limits and couild be recommended for patients with POAG

Kumar A, et al. From bench to behaviour: the role of lifestyle factors on IOP, neuroprotection, and disease progression in glaucoma. Clin Exp Ophthalmol. 2023;51:380394.

Ma QY, Zhou J, Xue YX, et al. Analysis of aerobic exercise influence on intraocular pressure and ocular perfusion pressure in patients with primary open-angle glaucoma: a randomized clinical trial. Indian J Ophthalmol. 2022 Dec;70(12):4228-4234.

Seo JH, Lee Y. Association of exercise intensity with the prevalence of glaucoma and intraocular pressure in men: a study based on the Korea National Health and Nutrition Examination Survey. J Clin Med. 2022 Aug 12;11(16):4725.

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Glaucoma patients exercise **less** than age matched controls

- Ramulu PY, Maul E, Hochberg C, Chan ES, Ferrucci L, Friedman DS. Real-world assessment of physical activity in glaucoma using an accelerometer. Ophthalmology. 2012 Jun 1;119(6):1159-66.
- Rockwood K, Song X, Mitnitski A. Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. Cmaj. 2011 May 17;183(8):E487-94.

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Glaucoma patients exercise **less** during evening hours

- Yuan Y, Hu W, Zhang X, Borchert G, Wang W, Zhu Z, He M. Daily Patterns of Accelerometer-Measured Movement Behaviors in Glaucoma Patients: Insights From UK Biobank Participants. The Asia-Pacific Journal of Ophthalmology. 2022 May 19:10-97.

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But there is a problem here

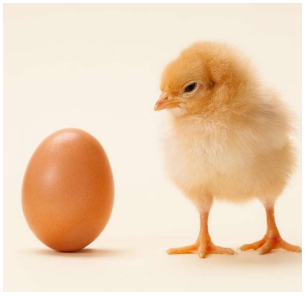
- It is unclear whether physical activity patterns influenced the onset and progression of glaucoma

Or

- Glaucoma damage led to activity restriction

Or

- Both



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Glaucoma Mouse Model 1

- Exercise in middle-aged mice, in the form of daily swimming, robustly protected RGCs against age-related functional loss and signs of stress after an acute injury (**50mmHg for 30 minutes)**
- Effect was so potent that **exercised 12-month-old mice responded to injury in a similar manner to young nonexercised 3-month-old mice**
- **Exercise can reverse negative impacts of aging in RGCs and modify their response to injury**

- Chrysostomou V, Kezic JM, Trounce IA, Crowston JG. Forced exercise protects the aged optic nerve against intraocular pressure injury. Neurobiology of Aging. 2014 Jul 1;35(7):1722-5.

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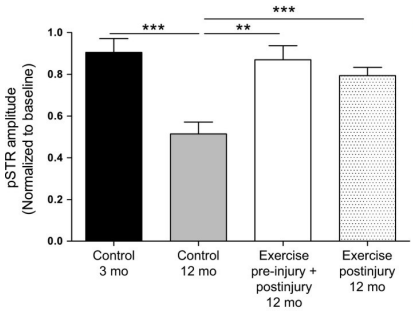

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Glaucoma Mouse Model 2

- Exercise initiated 24 h postinjury protects RGCs against age-related functional loss. Exercise prevents inner retinal synaptic loss after injury
- Exercise prevents inner retinal synaptic loss after injury
- Exercise reduces synaptic complement deposition after injury
- **Exercise reduces RGC loss after injury**
- Exercise maintains retinal brain derived neurotrophic factor (BDNF) levels postinjury
- **BDNF signalling is critical for functional protection conferred by exercise**

Chrysostomou V, Galic S, van Wijngaarden P, Trounce IA, Steinberg GR, Crowston JG. Exercise reverses age-related vulnerability of the retina to injury by preventing complement-mediated synapse elimination via a BDNF-dependent pathway. Aging Cell. 2016 Dec;15(6):1082-91.

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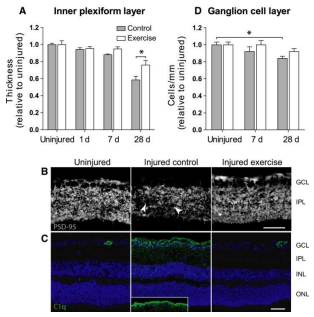

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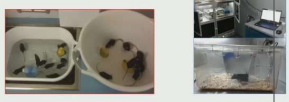
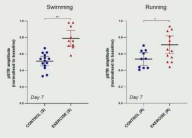
Methods: Swimming vs running



Forced (swimming)

Voluntary (running)

Results: Improved functional recovery all around



Both forms of exercise protected against functional loss

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Glaucoma Exercise Tips

- Discuss proper breathing with strength training
  - Valsava maneuver
- Avoid head down yoga poses
- Avoid contact sports
  - Boxing, karate sparring, rugby
- Beta blockers
  - Exercise fatigue
- Normal tension glaucoma
  - Prioritize aerobic exercise

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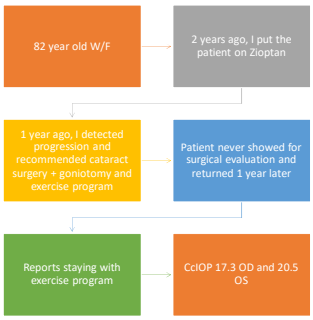
Case



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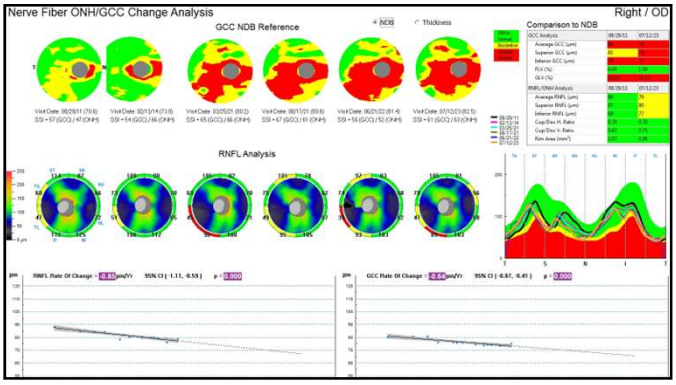

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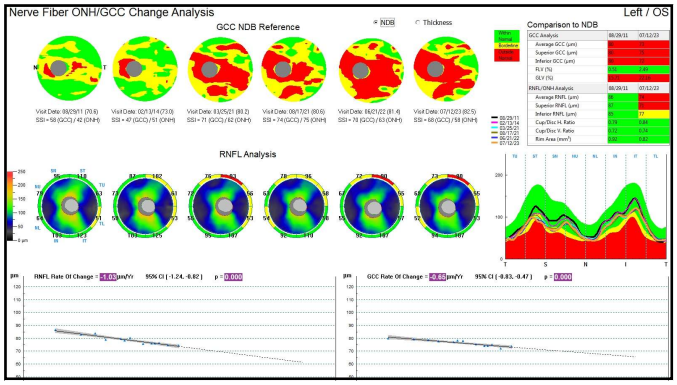

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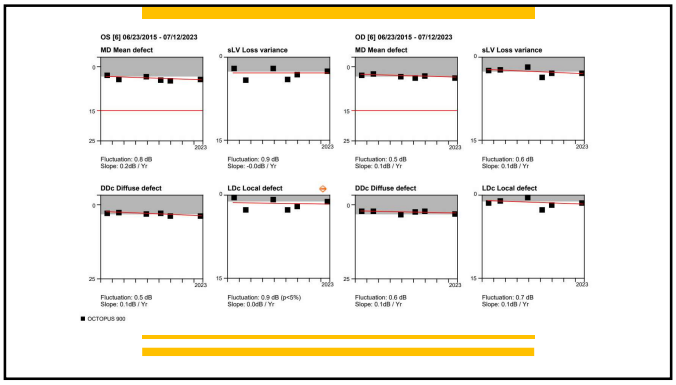

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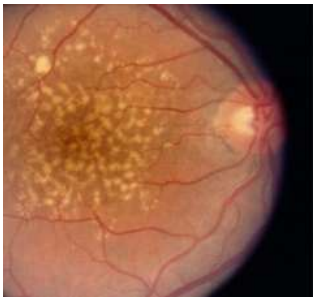
AMD



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AMD

- Decreased physical activity was associated with an increase in early pathogenic features, or "precursors" of AMD
- A physically active, heart-healthy lifestyle prevents the earliest manifestation of AMD
- **more physical activity significantly reduced the odds for having precursors of AMD**
- **a physically active lifestyle reduces the risk of developing the earliest stages of AMD also in genetically predisposed people**
- Munch IC, Linneberg A, Larsen M. Precursors of age-related macular degeneration: associations with physical activity, obesity, and serum lipids in the inter99 eye study. Investigative ophthalmology & visual science. 2013 Jun 1;54(6):3932-40.

64

AMD

- Exercise has been shown to **reduce the severity of AMD**, with higher levels of vigorous exercise in **middle-aged adults**
- Williams PT. Prospective study of incident age-related macular degeneration in relation to vigorous physical activity during a 7-year follow-up. Investigative ophthalmology & visual science. 2009 Jan 1;50(1):101-6.

65

AMD

- Exercise has been shown to **reduce the severity of AMD** with moderate exercise in people **over 75** associated with a lower incidence rate of AMD
- Gopinath B, Liew G, Burlutsky G, Mitchell P. Physical activity and the 15-year incidence of age-related macular degeneration. Investigative ophthalmology & visual science. 2014 Dec 1;55(12):7799-803.

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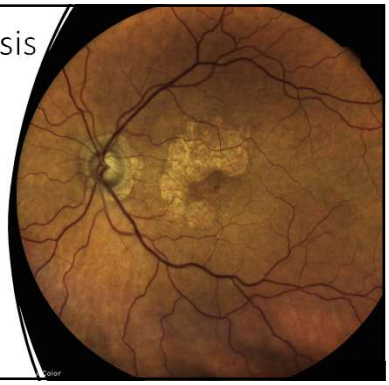
AMD – meta analysis



- Physical activity is associated with lower odds of early and late AMD in white populations.
- The effect was stronger in late AMD

McGuinness MB, Le J, Mitchell P, Gopinath B, Cerin E, Saksens NTM, Schick T, Hoyng CB, Guymer RH, Finger RP. Physical Activity and Age-related Macular Degeneration: A Systematic Literature Review and Meta-analysis. Am J Ophthalmol. 2017 Aug;180:29-38. doi: 10.1016/j.ajo.2017.05.016. Epub 2017 May 24.

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AMD Mouse Model 1

- **voluntary exercise** provides protection to the retina against photo-oxidative damage with both functional, morphological and histological improvements
- **reduces photoreceptor cell death and inflammation**
- voluntary exercise may confer retinal protection against degeneration
- **supporting the potential use of exercise as a non-pharmacological intervention to slow the progression of retinal degenerations and AMD**
- Chu-Tan JA, Cioanca AV, Wooff Y, Kirkby M, Ellis M, Gulati P, Karl T, Boatright JH, Bales K, Nickerson J, Natoli R. Voluntary exercise modulates pathways associated with amelioration of retinal degenerative diseases. Frontiers in Physiology. 2023 Mar 10;14:372.

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AMD Exercise Tips

- UV protection
- Proper indoor lighting
- Caution with outdoor low illumination activities
- Caution in certain activities in moderate to severe AMD
  - Biking, mountainbiking
  - Trail running

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Case

- 80 Y/O W/F
- Dx with AMD 2013
- Used AREDS/AREDS2 "off and on"
- 6 months ago Adapt Dx Rod Intercept 13.2

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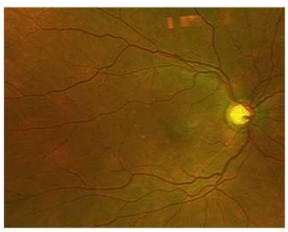
Optomaps



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And now...

- 6 months ago, began new supplement, reports excellent compliance
- Begins a consistent walking program
- Adapt Dx 12.1 (Baseline 13.2)

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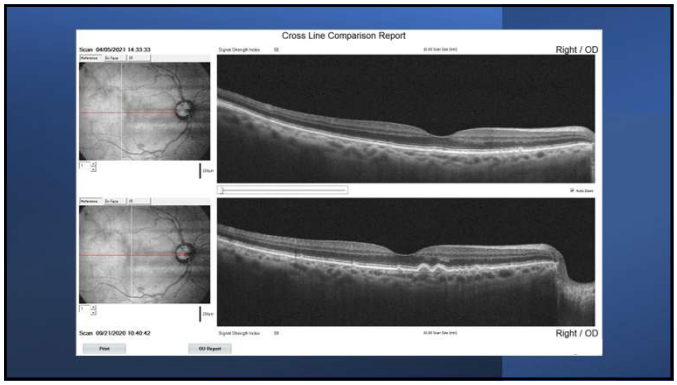

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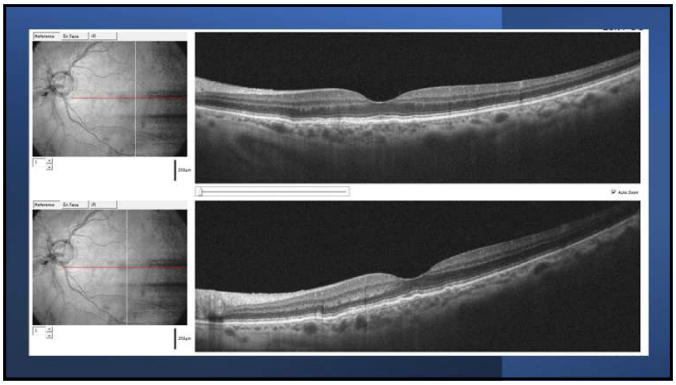

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Be this guy!

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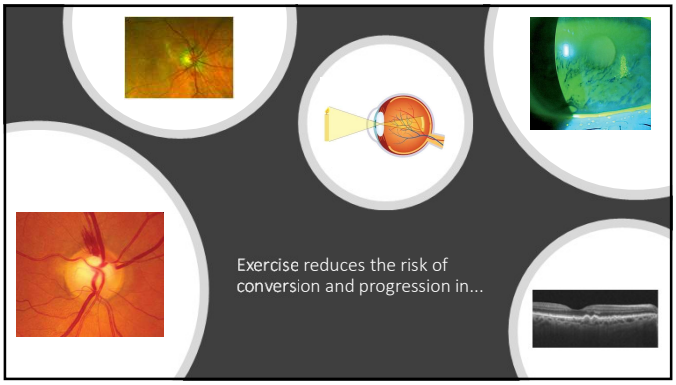

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Summary

THE BENEFITS OF EXERCISE ARE FAR-RANGING WITH INCREASING EVIDENCE DEMONSTRATING THE THERAPEUTIC EFFECTS OF EXERCISE IN THE CNS AND RETINA

IT IS REASONABLE TO SUGGEST INCREASED EXERCISE TO PATIENTS WITH DR, GLAUCOMA, AMD AND DRY EYE

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Thank You!!!

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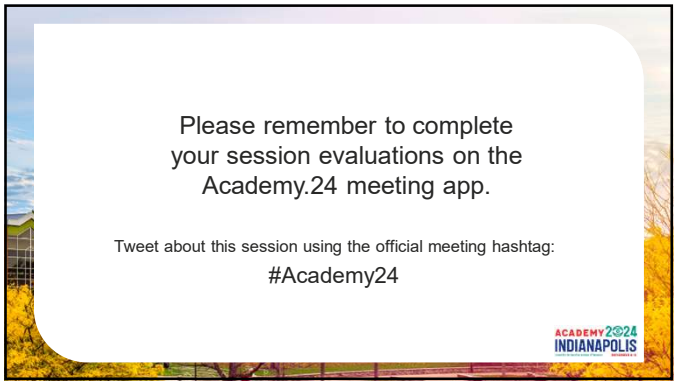
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