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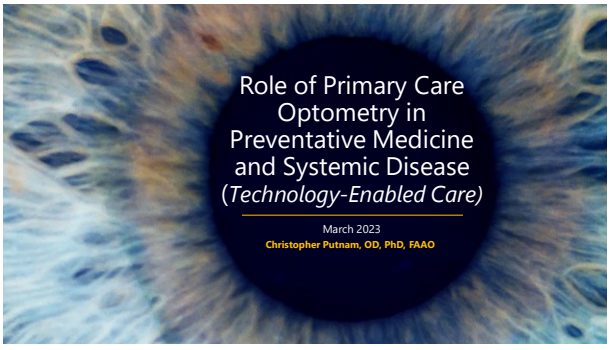
Role of Primary Care Optometry in Preventative Medicine and Systemic Disease
(*Technology-Enabled Care*)
March 2023
Christopher Putnam, OD, PhD, FAAO

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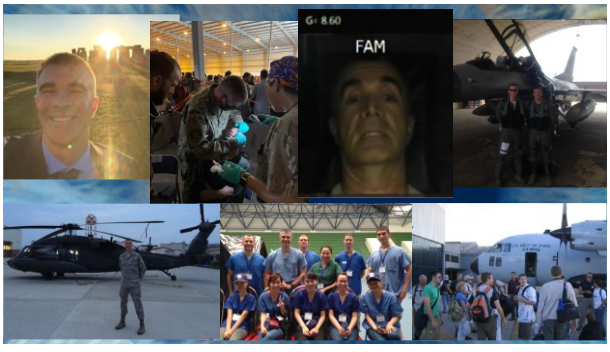

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Financial Disclosures

- None

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Retinal age gap as a predictive biomarker for mortality risk

Br J Ophthal (2022) doi: 10.1136/bjophthalmol-2021-319807

Methods

19,200 fundus images from participants without prior medical history at the baseline examination were used to validate the DL model for age prediction using cross-validation. 35,913 participants with mortality data were used to investigate the association between retinal age gap and mortality

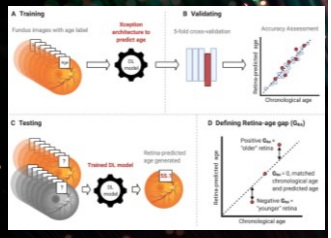
Results

The DL model achieved a strong correlation of 0.81 between retinal age and chronological age with overall error of 3.5yrs

- Regression models showed each 1-yr increase in the retinal age gap was associated with:
  - ***2% increase in risk of all-cause mortality***
  - ***3% increase in risk of cause-specific mortality***
- ***No significant association was between retinal age gap and cardiovascular- or cancer-related mortality***

Conclusions

- Findings indicate that retinal age gap may be aging biomarker that is closely related to risk of mortality
- ***Potential of retinal image as a screening tool for risk stratification and delivery of tailored interventions***



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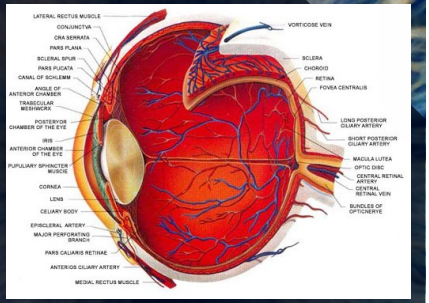
Ocular Anatomy and Physiology is…



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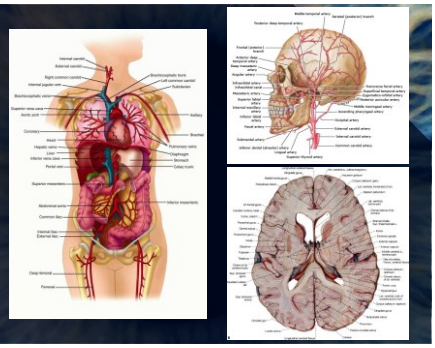
...Systemic Anatomy and Physiology



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Ocular Physiology + Systemic Disease

- Retina is a ***highly metabolic neural tissue*** with a ***microvascular supply*** originating at the internal common carotid artery
  - Only currently *in vivo* view of neurological and circulatory systems (to my knowledge)
- Systemic vascular, collagen vascular, neurological and autoimmune changes that manifest as retinal dysfunction can ***precede clinical symptoms by months to years***
- Although the diversity of systemic disease is broad, shared characteristics with the eye include:
  - ***Inflammation***
  - ***Oxidative Stress***
  - ***Mitochondrial dysfunction***

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Systemic Diagnosis and Mangement

- **Vasculopathies**
- Neurodegenerative
- Autoimmune
- Collagen Vascular Disease

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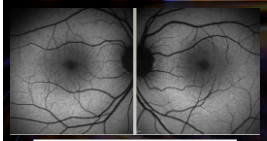
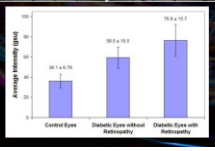
Vasculopathies

Diabetes Mellitus



- Worldwide prevalence is estimated at 483M
  - ~50% of diabetics are undiagnosed
- Estimated 5M diabetes related deaths in 2019
  - ~50% were < 60 years old

Retinal flavoprotein FAF as a measure of retinal health
Transactions of the Am Ophthal Society (2018) 106:215



- ***6-hour transient hyperglycemia results in significant 6-day increase in mitochrondrial ROS*** that is the underlying cause of diabetic retinopathy
- FAF imaging of retinal flavoproteins can detect *in vivo* mitochondrial ROS
- Zeiss FF4 fundus camera using 467nm excitation and 535nm emission filters with electron-multiplying, charge-coupled device (EMCCD)

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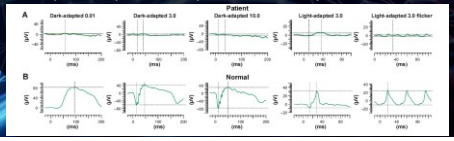
Vasculopathies

Diabetes Mellitus

Screening for DR using new mydriasis-free, full-field flicker ERG recording
Scientific Reports Volume 6, Article number: 36591 (2016)

Study aimed to determine whether a small, hand-held, mydriasis-free, full-field flicker ERG device called RETeval can be used to screen for DR. Study recorded full-field flicker ERGs with this device from ***48 normal eyes and 118 eyes with different severities of DR***. System delivered a constant flash retinal luminance by adjusting the flash luminance that compensated for changes in the pupil size.

Results showed that there were ***significant correlations between the severity of DR and the implicit times (r=0.55)*** and when the implicit time was used for the index, the ***area under the ROC curve was 0.84 for the detection of DR and was 0.89 for the detection of DR requiring ophthalmic treatments***. Results suggest that implicit times of the flicker ERGs recorded by the small, mydriasis-free ERG system can be used as an adjunctive tool to screen for DR.



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Vasculopathies

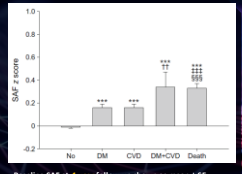
Diabetes Mellitus

Skin autofluorescence predicts incident DMII, CVD and mortality in the general population
Diabetologia (2019) 62:269-280

Methods
- 72,880 participants who underwent baseline investigations had validated baseline skin AF values available and were not known to have diabetes or CVD
- Participants were diagnosed with incident DMII by a fasting blood glucose ≥126mg/dL or HbA1c ≥ 6.5% at follow-up.
- Participants were diagnosed as having incident CVD (MI, coronary interventions, CVA, TIA, intermittent claudication or vascular surgery)

Results
After a median follow-up of 4 years, 1056 participants (1.4%) developed DMII 2, 1258 individuals (1.7%) were diagnosed with CVD while 928 (1.3%) had died.
- Baseline skin AF was elevated in participants with incident DMII, CVD and those who had died compared with individuals who survived and remained free of the two diseases
- ***Skin AF predicted the development of DMII, CVD and mortality independent of metabolic syndrome, glucose and HbA1c.***

Conclusions/interpretation
Non-invasive skin AF measurement shows clinical value for screening for future risk of DMII, CVD and mortality independent of glycemic measures and metabolic syndrome



Baseline SAF at *4-year* follow-up shown as mean ± SE
No DMII/CVD: 69,749 **DM:** 977 **CVD:** 1171
DM+CVD: 55 **Death:** 928

***p < 0.001 vs no type 2 diabetes/CVD group;
††p < 0.005 (women only) vs DM group;
‡‡‡p < 0.001 vs DM group;
§§§p < 0.001 vs CVD group

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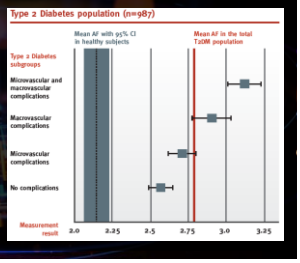
Vasculopathies

Diabetes Mellitus

Diagnoptics *Advanced glycation end-products (AGE) reader*



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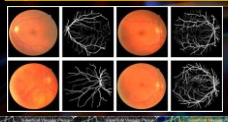
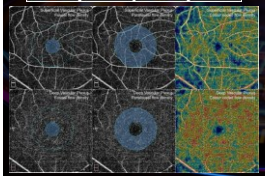
Vasculopathies

Hypertension





- US prevalence is estimated at 116M (~45% of adults)
  - ***Leading modifiable risk factor for cardiovascular disease and premature death***
- ***Clinically-evident hypertensive retinopathy signs typically develop late in the disease***
- High-resolution retinal microvascular imaging
  - Lumen caliber changes
- Retinal capillary rarefaction and flowrate
  - Density relative to normative database

Hypertensive retinopathy identification through retinal fundus image using back-propagation neural network.
Journal of Physics: Conference Series (2018) 978(1):012106

Systemic hypertension associated retinal microvascular changes can be detected with OCTA
Scientific Reports (2020) 10: 9580

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Systemic Diagnosis and Mangement

- Vasculopathies
- **Neurodegenerative**
- Autoimmune
- Collagen Vascular Disease

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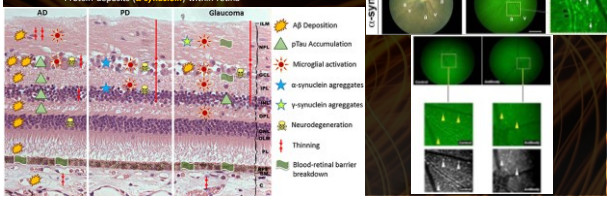
Neurodegenerative disease
Parkinson's disease

- Motor disorders associated with degeneration of dopaminergic neurons in the substantia nigra associated with high levels of ***α-synuclein***
  - Abnormalities in visual function have been reported in PD and LBD patients correlated with changes in retinal tissue to include:
    - Retinal thickness decrease
    - Inner retinal involvement
    - Protein deposits (***α-synuclein***) within retina



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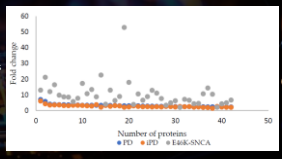
Neurodegenerative disease
Parkinson's disease

Tear Proteins as Possible Biomarkers for Parkinson's Disease
IOVS (2018) 59:4909

Methods
Tear samples from 60 diagnosed PD patients of varying severity and 30 matched non-PD controls were collected and pooled from both eyes for analysis. α-synuclein and MMP9 were measured using a human magnetic luminex assay kit while lactoferrin was measured using a human lactoferrin ELISA kit. Oligomeric α-synuclein was measured using a human α-synuclein oligo ELISA kit.

Results
Total α-synuclein decreased significantly in PD patients relative to healthy controls However, ***oligomeric α-synuclein increased significantly in PD patients*** relative to healthy controls
- Neither MMP9 or LF varied significantly between PD and controls

Conclusions
- ***Total tear α-synuclein and oligomeric synuclein may have potential to discriminate between tears of PD patients and healthy controls***
- ***Elevations in oligomeric α-synuclein are found in early, intermediate and late-stage PD***



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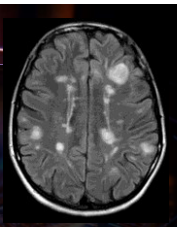
Neurodegenerative disease
Multiple Sclerosis

- Autoimmune disease represented by axon demyelination, disruption of inflammatory homeostasis and neuronal death
  - ***Cerebral pathology may mirror ocular manifestations***
  - ***Disease progression governed by the slow, subclinical injury accumulation of neuroaxonal structures***
- MRI is pivotal in clinical management/diagnosis of MS
  - Several limitations:
    - Low sensitivity of conventional MRI in grey-matter involvement
    - Diffuse damage in white matter
    - Conventional MRI shows limited associations with clinical status
- Etiology remains unclear with no definitive cure
  - MS cases (within United States) are more frequent above the 37th parallel than below
    - ***Above – 125 case per 100,000***
    - ***Below – 65 cases per 100,000***

Risk is defined AFTER the age of 15



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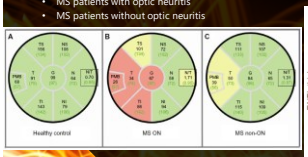
Neurodegenerative disease

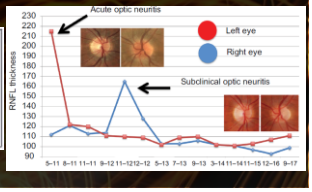
Multiple Sclerosis

Retinal imaging with OCT: Biomarker in MS?

Eye and Brain (2018) 8:701–706

- Associated with RNFL thinning and neuronal degeneration
- OCT imaging has demonstrated a significant differences of average and temporal RNFL thickness was found in:
  - MS patients with optic neuritis
  - MS patients without optic neuritis





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Neurodegenerative disease

Multiple Sclerosis

Retinal asymmetry in multiple sclerosis

Brain (2021) 144(1):224-235

Abstract

Feasibility of OCT measures of retinal asymmetry as a diagnostic test for MS across 72,120 subjects for inter-eye percentage difference (IEPD) and inter-eye absolute difference (IEAD) were calculated for the macular GCC, ganglion cell inner plexiform layer (GCIPL) complex and ganglion cell complex.

- ***OCT macular GCC inter-eye difference may be considered as supportive MS diagnostic criteria in a young patient without relevant co-morbidity***
- ***Does not allow separation of multiple sclerosis from neuromyelitis optica***

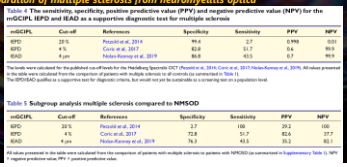

Table 4 The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the mGCIPL, IEPD and IEAD as a supportive diagnostic test for multiple sclerosis

mGCIPL	Cut-off	References	Specificity	Sensitivity	PPV	NPV
IEPD	28 %	Petzold et al., 2014	99.4	2.7	0.998	0.01
IEPD	4 %	Cruz et al., 2017	82.8	51.7	0.6	99.9
IEAD	4 µm	Nolan-Kenney et al., 2019	86.8	43.5	0.7	99.9

The levels were calculated for the published cut-off levels for the Heidelberg Spectralis OCT (Petzold et al., 2014; Cruz et al., 2017; Nolan-Kenney et al., 2019). All values presented in this table were calculated from the comparison of patients with multiple sclerosis to all controls (as summarized in Table 1).
The IEPD/IEAD qualifies as a supportive test for diagnostic criteria, but would not yet be sustainable as a screening test on a population level.

Table 5 Subgroup analysis multiple sclerosis compared to NMSOD

mGCIPL	Cut-off	References	Specificity	Sensitivity	PPV	NPV
IEPD	28 %	Petzold et al., 2014	2.7	100	29.2	100
IEPD	4 %	Cruz et al., 2017	72.8	51.7	82.6	37.7
IEAD	4 µm	Nolan-Kenney et al., 2019	76.3	43.5	35.2	82.1

All values presented in the table were calculated from the comparison of patients with multiple sclerosis to patients with NMOSD (as summarized in Supplementary Table 1). NPV = negative predictive value; PPV = positive predictive value.

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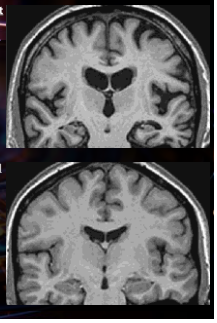
Neurodegenerative disease

Alzheimer's disease

- AD is characterized by an insidious onset of cognitive decline with deficits in episodic memory:
  - Forgetting recent personal and family events
  - Losing items around the house
  - Repetitive questioning
- As the disease progresses, other deficits gradually arise including:
  - Aphasia (language)
  - Apraxia (motor)
  - Agnosia (recognition)
  - Visuospatial difficulties
  - Executive dysfunction
- Clinical diagnosis is made using McKhann (1984) criteria:
  - Definite AD (established by postmortem or biopsy),
  - Probable AD
  - Possible AD (other cognitive syndromes equally likely)

*****Average AD survival is typically 8-12 years from symptom onset*****



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Neurodegenerative disease

Alzheimer's disease

Associations between recent and established ophthalmic conditions and risk of AD

Alzheimer's and Dementia (2019) 15:34-41

Glaucoma 5-yr HR:

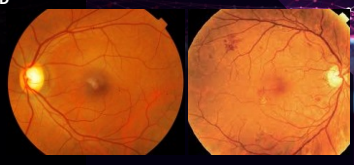
Recent	1.46
Established	0.87

AMD 5-yr HR:

Recent	1.20
Established	1.50

DR 5-yr HR:

Recent	1.50
Established	1.50



***Glaucoma, AMD and DR are associated with increased AD risk**

Shared characteristics:

1) *Progressive neurodegeneration*
2) *Chronic microvascular insults*
3) *Protracted oxidative stress*

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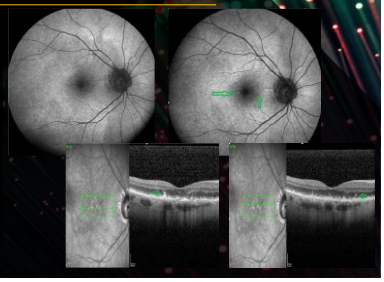
Clinical Retinal Imaging

Alzheimer's disease (AD)

Retinal amyloid pathology and proof-of-concept imaging trial in Alzheimer's disease

JCI Insights (2017) 2(16)

- Curcumin is a lipophilic polyphenol derived from turmeric and a fluorophore with a high affinity to A_β
- Aβ in AMD Lesions isolated in patient diagnosed with Alzheimer's Disease in 4 separate studies since 2017
- High bioavailability, proprietary blend used in conjunction with cSLO:
  - *100% sensitivity*
  - *81% specificity*
- ***Retinal Aβ load was strongly correlated with brain amyloid plaque burden confirmed through PET imaging***



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Specific Retinal Biomarkers of Alzheimer's Disease

Peripheral Retinal Imaging Biomarkers for Alzheimer's Disease: A Pilot Study

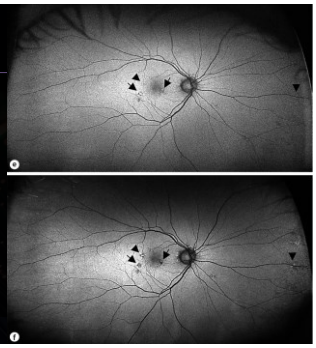
Ophthalmic Research (2018) 24.5

Results:

- Baseline analysis showed a significantly higher prevalence of peripheral hard drusen in AD subjects (25%) vs. control subjects (4%)
- Marked increase in drusen number at the 2-year follow-up in AD subjects vs. control subjects

Conclusions:

- ***UWF retinal imaging revealed a significant association between AD and peripheral hard drusen formation beyond the posterior pole at baseline and over 2-year progression***



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Systemic Diagnosis and Mangement

- Vasculopathies
- Neurodegenerative
- **Autoimmune**
- Collagen Vascular Disease

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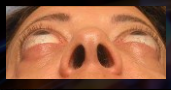
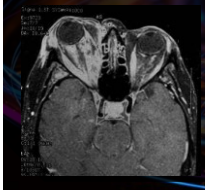
Automimmune disease

Grave's disease





- Hyperthyroidism caused by thyroid-stimulating antibodies to the TSH receptor
- Most commonly affects females ages 30-50
  - ***8X more common in women*** than men and risk increases if other family members affected
- Other system conditions linked to Graves:
  - RA
  - SLE
  - Celiac
  - Addison's disease (hypocortisolism)

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Automimmune disease

Grave's disease –> Thyroid Eye Disease

Selenium supplementation for patients with Graves' hyperthyroidism (the GRASS trial): Randomized controlled trial.
Trials (2013) *14*, 1-10.

Methods:
- Randomized, blinded, multicenter clinical trial including patients ≥18 years old with diagnosis of active Graves' hyperthyroidism within the last 2 months
- 452 participants, randomized (1:1) to two tablets of 100 µg selenium once daily for the 24 to 30 months intervention period versus placebo
- Primary outcome is the proportion of anti-thyroid drug treatment failure at 24 to 30 months

Results:
- Both FT4 and FT3 decreased more in the selenium group than the control
- Anti-TSH receptor antibody level was significantly lower in selenium group ($p = 0.04$).
- Normal anti-TSH receptor antibody levels at 6 months were also significantly higher in the selenium group (19.0 vs. 0 %, $p = 0.016$).
- Kaplan-Meier survival curve showed ***selenium group had a significantly higher rate of remission than controls***

Conclusions:
- ***Selenium supplementation @ 100ug BID x 6 months can enhance the effect of antithyroid drugs in patients with Graves' disease***


TRIALS

STUDY PROTOCOL Open Access

Selenium supplementation for patients with Graves' hyperthyroidism (the GRASS trial): study protocol for a randomized controlled trial

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Automimmune disease

Grave's disease –> Thyroid Eye Disease

***In vivo* confocal microscopy assessment of MG microstructure in patients with Graves' orbitopathy**

BMC Ophthal. (2021) 21:261

Methods

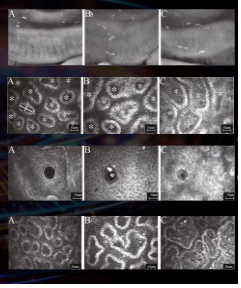
Forty patients (80 eyes) with GO (34 with active GO, 46 with inactive GO) and 31 age- and sex-matched control participants (62 eyes) were enrolled. A complete ophthalmic examination was then performed including external eye, ocular surface and MGs including *in vivo* confocal ophthalmoscopy

Results

All confocal microscopy assessments of MGs significantly differed among groups (all $P = 0.000$). Compared to controls, GO groups showed significant differences in all measures ($P<0.05$). Eyes with active GO had higher degrees of acinar irregularity and inhomogeneity, while eyes with inactive GO had higher degrees of secretion reflectivity and fibrosis (all $P<0.05$).

Conclusions

IVCM effectively revealed microstructural changes of MGs in eyes with GO and provided strong evidence for the roles of obstruction and inflammation in the ocular surface disease process. Furthermore, it ***revealed discernible patterns of MG abnormalities in eyes with active GO and inactive GO, which are not easily distinguishable by clinical examinations***.



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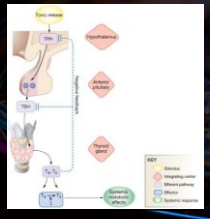
Automimmune disease

Thyroid Eye Disease… just when it seemed easy

Thyroid

- Largest endocrine gland
- Controlled by hypothalamus and pituitary
- Primary function is T4, T3 and calcitonin production



Thyroid Panel Test (Standard vs. Full)

- T3 (Free T3)
- T4 (Free T4)
- TSH
- T7 [(T4 * T3 Uptake)/100]
- TPO (thyroid peroxidase antibodies)*
- Tg (thyroglobulin antibodies)*
- TR (thyroid antibodies)*

- **Thyroid Eye Disease**
- **~80%** = autoimmune hyperthyroid disorder
  - Graves' disease
- **~10%** = autoimmune hypothyroidism
  - Hashimoto's thyroiditis, atrophic thyroiditis or Hashitoxicosis
- **~10%** = normal thyroid function
  - Euthyroid Graves' disease
    - Some euthyroid Graves' disease never develop thyroid dysfunction

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Automimmune disease

Grave's disease –> Thyroid Eye Disease

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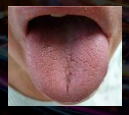
Automimmune disease

Sjogren's disease



- 2nd most common chronic autoimmune rheumatic disease and associated with a high burden of illness.
- Common clinical manifestations include xerostomia and keratoconjunctivitis sicca also ***including the development of non-Hodgkin's lymphomas***
- Diagnosis requires objective evidence of dry eyes and/or objective evidence of dry mouth associated with autoimmunity
- Sjo® Test as clinical point-of-care testing for KCS or recalcitrant DES in patients meeting the demographic

Prevalence of primary Sjögren's syndrome in a US population-based cohort.
Arthritis care & research (2017) 69(10:1612-1616
- Female (~85%)
- 65±15 years old
- Symptoms duration of 10±8 years

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Autoimmune disease

Prevalence of Autoimmune Disease in POAG

Prevalence of Autoimmune Diseases in Patients with Primary Open-Angle Glaucoma Undergoing Ophthalmic Surgeries
Ophthalmology Glaucoma (2022) 5(2):128-136

Results
172 patients with POAG and 179 controls were included
- Overall prevalence of AiD
  - ***17% in the POAG group vs. 10% in the controls***
  - 6.4% of POAG patients and 3.4% of controls had >1 AiD
  - Most prevalent AiD in POAG group were ***RA (4.6%)*** and ***psoriasis (4.1%)*** which were also the most common in controls (2.8%)
  - AiD was associated with 2.62X increased odds of POAG relative to controls

Demographic and Ophthalmic Information	*POAG (n = 62)*	*Controls (n = 97)*	*p-value*
Age (years)	74.56 ± 7.97	70.92 ± 11.14	**0.027**
Gender (% male)	45%	38%	0.38
Race (% Caucasian)	60%	81%	**0.003**
BMI (kg/m²)	27.38 ± 4.48	27.62 ± 5.48	0.773
Type 2 Diabetes (%)	37%	25%	0.096
BCVA (LogMAR)	0.36 ± 0.41	0.66 ± 0.87	**0.012**
HVF MD (decibels)	-11.06 ± 8.00	—	—
IOP (mmHg)	15.90 ± 4.50	15.42 ± 2.89	0.414
Cup to Disc Ratio	0.76 ± 0.15	0.33 ± 0.13	**< 0.0001**
Any history of systemic steroid use (%)	18%	14%	0.413
Any history of inhaled steroid use (%)	10%	20%	0.168
Autoimmune disease (%)	27%	9%	**0.003**

Conclusions
- ***Higher prevalence of AiD was found in POAG patients compared with control patients undergoing ophthalmic surgery***
- ***Presence of AiD was associated with increased risk for POAG after adjusting for covariates***

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Systemic Diagnosis and Mangement

- Vasculopathies
- Neurodegenerative
- Autoimmune
- **Collagen Vascular Disease**

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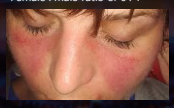
Collagen Vascular Disease
Systemic Lupus Erythematosus

- US prevalence of ~250 per 100,000
- Female : Male ratio of 6 : 1



Orbit	Myositis/ proptosis/ ptosis
Eyelids	Discoid rash
Anterior segment:- • Cornea • Episclera/sclera • Iris/ciliary body	• KCS / SPK / PUK • Chemosis/ scleritis/ episcleritis • Uveitis (uncommon)
Posterior segment:- • Retina • Choroid	• CWS/ HE / hemes/ vascular tortuosity/ pigmentary changes • Choroidalischemia
Neuro-ophthalmological	Optic neuritis/ optic neuropathy/ INO / EOM dysfunction/ diplopia

Condition	**Differentiating** Characteristics
Bechet's disease	• H/O genital or oral ulcers
Sarcoidosis	• Uveitis common
Lyme disease	• Annular skin lesions • Endemic area
HTN retinopathy	• A/V nicking • Copper wire vessels
DR	• H/O elevated A,C
Polyarteritis nodosa	• More common in males • ANCA negative
Syphilis	• Uveitis common • Uniform retinal inflammation

- ***KCS is most common ophthalmic manifestation***
  - ***Most develop secondary Sjogren's syndrome***

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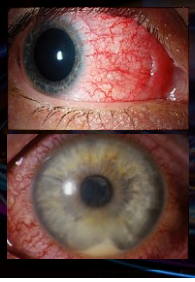
Collagen Vascular Disease
Rheumatoid arthritis



- Annual U.S. incidence of ~50 per 100,000 individuals
- Onset is most frequent ages 40-50 and ***women are affecting 2.5X more frequently than men***
- Early diagnosis and treatment can substantially slow progression of joint damage in up to 90% of patients
  - ***KCS is most common ophthalmic manifestation***
- Current understanding of disease is a combination of genetic and environmental factors
  - Elevated ESR and CRP (non-specific)
  - Elevated RF and anti-CCP (not definitive)
- Three phases of progression
  - Initiation phase due to non-specific inflammation
  - Amplification phase due to T-cell activation
  - Chronic inflammatory phase with tissue injury resulting from the ***cytokines, IL–1, TNF-α and IL–6***

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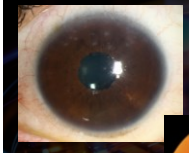
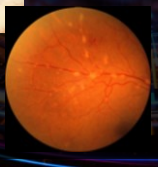
Collagen Vascular Disease
Sarcoidosis





- Annual U.S. incidence
  - 8 per 100,000 in Caucasians
  - ***18 per 100,00 in African Americans***
- More common in women 20-40
- 30-40% have ocular presentation as initial symptoms
  - ***Bilateral uveitis (most common)***
  - KCS
  - Choroidal granulomas
  - Periphlebitis
  - Perivascular exudates (candle-wax drippings)
- Systemic testing
  - Chest x-ray or CT (hilar lymphadenopathy)
  - Elevated ACE and lysozyme

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What is the role of primary care optometry in autoimmune and collagen vascular disease management?

Every primary care OD's bad penny…

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What is the role of primary care optometry in autoimmune and collagen vascular disease management?

Every primary care OD's bad penny…

Idiopathic anterior uveitis

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Autoimmune and Collagen Vascular Disease

Clinical Decision Making

Patterns of Laboratory Testing Among Uveitis Specialists

Am J Ophthal (2016) 170:161-167

- 13 patient scenarios were evaluated by 11 specialists
- Mean number of tests was 5.47±2.71
  - Average cost of testing per provider was ***$282.80***
  - Most tests within each scenario were ordered by ***less than 50% of respondents***
  - Only ***1 test (ANA)*** in a single scenario (unilateral scleritis) yielded ***universal consensus***
  - ***No relationship*** between years in-practice and # of tests ordered was found

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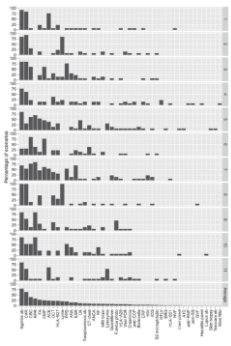
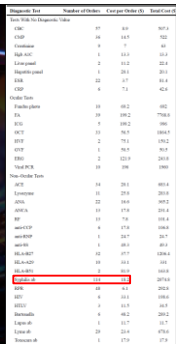


Top 13 tests ordered:

1) Syphilis Ab [79.7%]
2) Chest x-ray [63.6%]
3) CBC [39.8%]
4) RPR [33.6%]
5) ***FA*** [27.3%]
6) CMP [25.2%]
7) ACE [23.8%]
8) ***OCT*** [23.1%]
9) HLA-B27 [22.4%]
10) Lyme titer [20.3%]
11) PPD [19.6%]
12) ANA [15.9%]
13) ESR [15.9%]



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Autoimmune and Collagen Vascular Disease

Clinical Decision Making

Referral Patterns of Uveitis in Tertiary Eye Care

Archives of Ophthalmology (May 1996)

- Much of ordered uveitis lab and imaging is ***low-yield***
  - ***Of 1237 patients, only 17% were given a definitive diagnosis on initial presentation***
    - Remaining 83% of patients received confirmed or strongly suspected diagnoses made during longitudinal follow-up based on repeated clinical and laboratory evaluations

Uveitis and Systemic Disease

British Journal of Ophthalmology (March 1992)

- In most cases, systemic disease was not suspected prior to ocular involvement and ***recognized only after subsequent diagnostic procedures***
  - Of 865 patients, 73% were given a specific diagnosis for intraocular inflammation
    - 26% of all cases identified a causal systemic disease
    - 23% of all cases identified a presumed systemic disease

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What does this mean clinically?

Bayesian Calculators

- Pause for a quick homage to my graduate advisor:
  - Dr. Carl Bassi (UM-SL)

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Development and validation of Bayesian network for differential diagnosis of anterior uveitis
Eye (2016) 30(6): 865-872

- 11 most common etiologies were reviewed using Bayes theorem of conditioned probability
  - Idiopathic ankylosing spondylitis
  - Inflammatory bowel disease
  - Posner-Schlossman
  - Fuchs' heterochromic cyclitis
  - Psoriatic arthritis
  - Sarcoidosis
  - Bechet's
  - Juvenile idiopathic arthritis
  - Reactive arthritis
  - Tuberculosis
- 2954 case of anterior uveitis diagnosed at Moorfield's Eye Hospital
  - 200 randomly selected case and diagnostics were evaluated using a retrospective validation
  - Epidemiology, clinical signs/symptoms & lab results were entered into the algorithm
  - Results were compared to senior clinician diagnosis ***(gold standard)***

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Development and validation of Bayesian network for differential diagnosis of anterior uveitis
Eye (2016) 30(6): 865-872

Pre-test probability or $p(A)$ = uveitis diagnosis according to population average
Pre-test probability or $p(B)$ = RA diagnosis according to population average
Pre-test probability or $p(B|A)$ = RA diagnosis when uveitis present

$$p(A|B) = \frac{p(B|A) \cdot p(A)}{p(B)}$$

$$\text{Positive likelihood ratio} = \frac{\text{Sensitivity}}{1 - \text{Specificity}}$$

$$\text{Negative likelihood ratio} = \frac{1 - \text{Sensitivity}}{\text{Specificity}}$$

Post-test probability or $p(A|B)$= uveitis etiology average given identifying characteristic (e.g. RA)
Post-test probability = (pre-test probability) * (Likelihood ratio)

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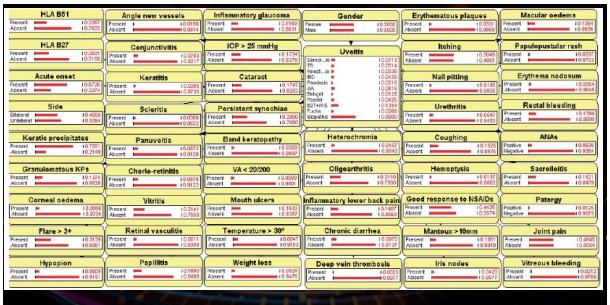

Bayesian inference mode using only population averages and zero clinical data

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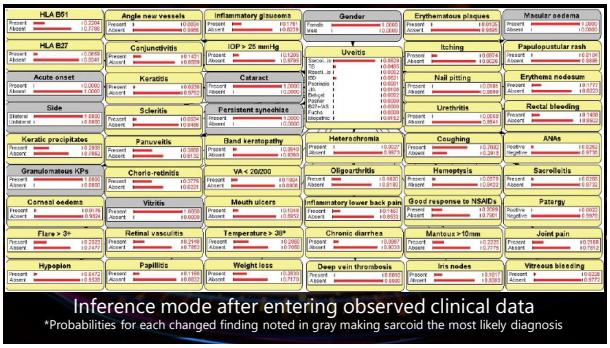

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Table 3 Comparison between clinical diagnosis and automated diagnosis by Bayesian belief network in 10 typical cases of anterior uveitis

Case	Age	Sex	Chronicity	Laterality	Findings	Clinical diagnosis	Predicted probability (%)									
							Idiopathic	B27+/AS	Sarcoidosis	JIA	TB	IBD	Posner	Fuchs	RA	PA	Behçet
1	63	Female	Chronic	Bilateral	Granulomatous KPs, vitritis, cataract, synechiae, CMO	Sarcoidosis	2	0	96	1	5	6	0	0	0	0	0
2	28	Male	Acute	Unilateral	Flare 4+, synechiae, back pain, HLA-B27+	Ankylosing spondylitis	0	97	0	2	0	0	0	0	0	0	0
3	41	Female	Acute	Unilateral	Flare 4+, hypopion, panuveitis, vasculitis, VA < 20/200, B51+	Behçet's disease	1	0	0	0	0	0	0	0	0	0	99
4	57	Female	Acute	Unilateral	Posterior synechiae, B27+, chronic diarrhea and rectal bleeding	IBD	28	9	0	0	1	59	0	0	2	1	0
5	36	Male	Chronic	Unilateral	Stellate KPs, glaucoma, cataract	Fuch's	17	0	1	10	1	5	0	63	0	5	0
6	14	Male	Chronic	Bilateral	Fine KPs, Flare 3+, vitritis, glaucoma, cataract, synechiae, VA < 20/200, arthritis	JIA	11	0	22	52	0	1	0	0	1	0	14
7	55	Female	Acute	Unilateral	Glaucoma, IOP 42 mm Hg	Posner	25	1	0	0	1	1	69	1	0	1	0
8	58	Female	Acute	Bilateral	Skin plaques, itching, nail pitting	Psoriasic arthritis	3	0	0	0	0	0	0	0	0	97	0
9	17	Male	Acute	Bilateral	Vitritis, urethritis, joint pain	Reactive arthritis	10	0	0	0	0	0	0	80	0	0	0
10	50	Female	Chronic	Unilateral	Granulomatous KPs, Vitritis, CMO, positive PPD	TB	4	0	31	0	59	6	0	0	0	0	0

Abbreviations: AS, ankylosing spondylitis; IBD, inflammatory bowel disease; JIA, juvenile idiopathic arthritis; KPs, keratic precipitates; PA, psoriasic arthritis; RA, reactive arthritis; TB, tuberculosis.

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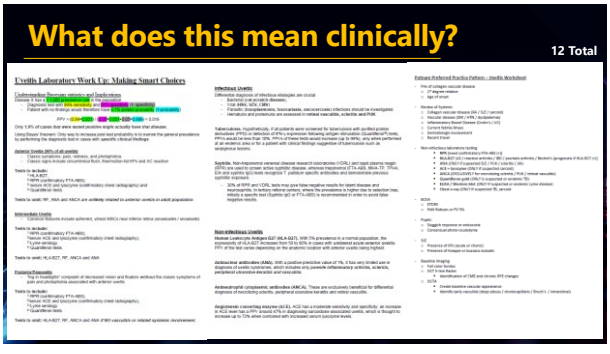

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Clinical Diagnostic Testing

- Point-of-Care
- Retinal Imaging

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Clinical Diagnostic Imaging

Point-of-Care

- **Osmolarity System (TearLab)** [Class I CLIA]
  - Measurement of tear film osmolality
  - ***Non-differential KCS marker***
- **Lactoferrin (Advanced Tear Diagnostics)** [Class II CLIA]
  - Protein produced by the acinar cells of the lacrimal gland
  - ***Differential KCS marker***
- **IgE (Advanced Tear Diagnostics)** [Class II CLIA]
  - ***Presence of ocular allergen***
- **InflammaDry (RPS)** [Class I CLIA]
  - ***Detection of inflammatory marker MMP-9***
  - Qualitative marker
- **AdenoPlus® (RPS)** [Class II CLIA]
  - FDA-approved with CLIA-waiver
  - ***In vivo* detection of adenoviral antigen**
- **Sjo® Test**
  - **RF and ANA**
  - **SS-A and SS-B with immune markers PSP-1, CA-6 and SP-1**

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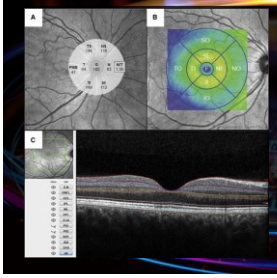
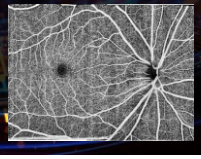
Clinical Diagnostic Imaging

Retinal Imaging



- ***Sensitivity vs. Specificity***
- **They're here....**
  - ***Normative databases***
  - ***Commercial AI***
  - ***Deep learning***



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What can be done to bridge the gap from ocular management to systemic management?

If only there were a ubiquitous device with a widely-used platform that could make evidence-based research accessible to clinicians…

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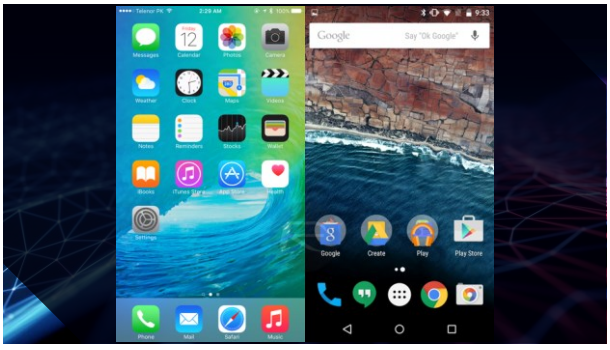

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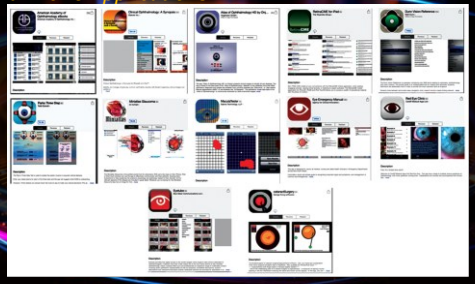
Clinical Biomarkers of Retinal Injury

Smart Phone Applications



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Preventative Medicine + Systemic Disease Smartphone Applications

- *OHTS + EMGT Calculators**
- ASCVD Calculator
- Retinal Risk Calculator
- *Cradle*
- *StrabPix*
- *Aberrometry*
- *Periocular melanoma*
- MS Monitoring
- ASD Screening
- *mTBI (Concussion)*
- *NITBUT Screening*
- DryEyeRhythm
- *Myopic Progression*
- *Smart Optometry*
- *Epocrates*
- *Doc in a Box DDx Calculator*
- *Austere Retinal Imaging*

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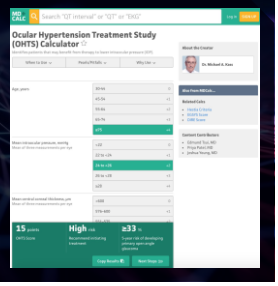
Clinical Systemic Disease Management

Smart Phone Applications – POAG Risk

- MDCalculator
  - OHTS calculator
    - Age
    - Mean IOP
    - Mean CCT
    - Mean vertical C/D ratio
    - Mean SITA Standard 30-2 or 24-2 PSD
  - Recommendation for observation vs treatment
  - Estimated 5-year risk of developing POAG
    - Provides supporting references

CAVEAT: OHTS IOPS inclusion criteria
- ***24 – 32 mmHG in one eye***
- ***21 – 32 mmHg in other eye***



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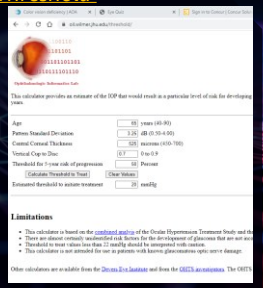
Clinical Systemic Disease Management

Smart Phone Applications – IOP Threshold

- Ophthalmic Informatics Lab
  - OHTS + EMGT calculator
    - Age
    - SITA Standard 30-2 or 24-2 PSD in dB
    - CCT
    - Vertical C/D ratio
    - Estimated 5-year risk of progression
  - Estimated Threshold to Initiate Treatment



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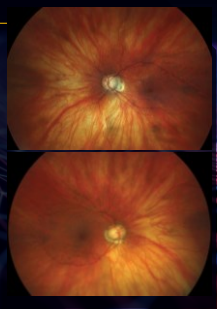
Clinical Systemic Disease Management

Smart Phone Applications

Degree of Myopia and Glaucoma Risk: Dose-Response Meta-Analysis

Am J Ophthalmol (2022) 235:107-119



Results

24 studies in 11 countries (514,265 individuals) made up the meta-analyses.

Pooled OR with OAG:

- Low 1.50
- Moderate 1.69
- ***Moderate-to-high 2.27***
- ***High myopia 4.14***

- Pooled OR (per SE 1D change) was 1.21

- ***OAG risk accelerated at around –6 D, and further accelerated from –8 D, showing a non-linear concave upward slope***

Conclusions

- ***For each 1Dincrease in myopia, the risk of OAG increases by ~20%***
- ***Risk increases steeply in high-degree myopia***

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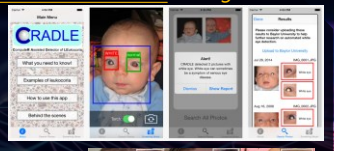
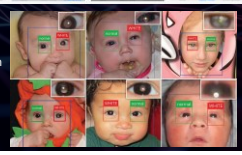
Clinical Systemic Disease Management

Smart Phone Applications - Leukocoria Screening

- **Cradle**
  - Leukocoria screener
    - Congenital cataracts
    - Coats disease
    - Retinoblastoma
    - ROP
    - Toxocariasis
    - Retrolental fibroplasia
  - 50K images incorporated
  - Mean detection ~1.3 years prior to diagnosis
  - False positive rate: ~1%
  - Database is heavily weighted with Caucasian children





Evaluation of a free public smartphone application to detect leukocoria in high-risk children aged 1 to 6 years.

J Aapos Ophthal & Strab (2019) *56*(4), 229-232

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Clinical Systemic Disease Management

Smart Phone Applications – Strabismus Screening

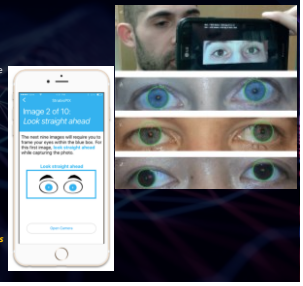
Validation of StrabisPIX, a mobile application for home measurement of ocular alignment

Trans Vision Science & Tech. (2019) *8*(2), 9-9.

Methods:
In this cross-sectional study, 30 strabismus patients aged ≥2 years were evaluated. Participants received standardized instructions and used StrabisPIX to obtain images as prompted. During the same visit, standard clinical images with a professional camera were taken. All 60 image sets were evaluated by three observers.

Results:
Clinic photographs had significantly higher acceptability for horizontal versions (81% vs. 67%), vertical versions (76% vs. 60%), and head posture (93% vs. 81%). **StrabisPIX had significantly higher detection of alignment abnormalities (89% vs. 77% for clinical photos).** Interrater and intrarater agreements were moderate to high (κ = 0.44–1.00) for all parameters except pupil abnormality.

Conclusions:
Overall, ***StrabisPIX images had similar quality and were as useful as images obtained in the clinic in detecting abnormalities.***



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Clinical Systemic Disease Management

Smart Phone Applications - Aberrometry

Evaluation of the SVOne: a handheld, smartphone-based autorefractor

Optometry and Vision Science (2015) 92(12): 1133

Methods
Refractive error was assessed both with and without cycloplegia in 50 visually normal, young adults using the five techniques described above. Further, to assess repeatability of the instruments, the entire procedure was repeated in a subgroup of 10 subjects.

Results
No significant difference was observed between the mean values of SE for the different techniques. Retinoscopy and subjective refraction showed the best repeatability for pre-cycloplegic and post-cycloplegic measurements, respectively. High and significant linear correlations were observed between the subjective findings and the other four techniques.

Conclusions
SVOne handheld aberrometer provides measurements of refractive error in normal, young individuals that are not significantly different from other subjective and objective procedures

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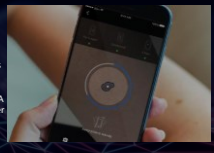
Clinical Systemic Disease Management

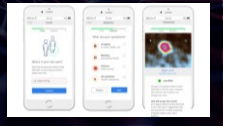
Smart Phone Applications – Periocular Melanoma

Accuracy of a smartphone application for triage of skin lesions based on machine learning algorithms

J European Acad Derm and Venereology (2020), 34(3), 648-655.



Methods
The algorithm is trained on 131,873 images taken by 31,449 users in multiple countries between and rated for risk by dermatologists. To evaluate the sensitivity of the algorithm we use 285 histopathologically validated skin cancer cases (138 malignant melanomas), from two previously published clinical studies (195 cases) and from the SA user database (90 cases). We calculate the specificity on a separate set from the SA user database containing 6000 clinically validated benign cases.



Results
The algorithm scored a 95.1% (95% CI, 91.9% - 97.3%) sensitivity in detecting (pre) malignant conditions (93% for malignant melanoma and 97% for keratinocyte carcinomas and precursors). This level of sensitivity was achieved with a 78.3% (95% CI, 77.2%–79.3%) specificity.

Conclusions
This SA provides a ***high sensitivity to detect skin cancer***, however there is still room for improvement in terms of specificity. Future studies are needed to assess the impact of the SA on health systems and its users.

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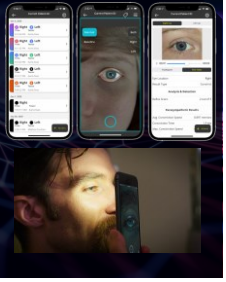
Clinical Systemic Disease Management

Smart Phone Applications – Concussion Screening

Utility of pupillary light reflex metrics as a physiologic biomarker for adolescent sport-related concussion

JAMA ophthalmology (2021)*138*(11), 1135-1141.



DESIGN, SETTING, AND PARTICIPANTS
Prospective cohort of adolescent athletes between ages 12 and 18 years were enrolled in a study within a specialty concussion program and private suburban high school and included healthy control individuals (n = 134) and athletes with a diagnosis of sport-related concussion (n = 98).

RESULTS
Pupillary light reflex metrics of 134 healthy control individuals and 98 athletes with concussion were obtained a median of 12.0 days following injury (interquartile range [IQR], 5.0-18.0 days). Eight of 9 metrics were significantly greater among athletes with concussion after Bonferroni correction: ***maximum pupil diameter, minimum pupil diameter, percentage constriction; average constriction velocity, peak constriction velocity, average dilation velocity, peak dilation velocity*** and ***T75***. In exploratory analyses, sex-based differences were observed, with girls with concussion exhibiting longer T75. Among healthy control individuals, diminished PLR metrics were observed after exercise.

CONCLUSIONS AND RELEVANCE
These findings suggest that enhancement of PLR metrics characterize acute adolescent concussion, while exercise produced smaller pupil sizes and overall slowing of PLR metrics, presumably associated with fatigue. ***Quantifiable measures of the PLR may serve in the future as objective physiologic biomarkers for concussion in the adolescent athlete.***

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Clinical Systemic Disease Management

Smart Phone Applications - NITBUT Screening

Reliability and clinical applicability of a novel tear film imaging tool

Clin Exp Ophthalmol (2021) **259:** 1935–1943

METHODS

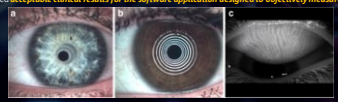
A total of 264 videos of TBUT were randomly selected and analyzed by three different examiners: two masked observers and a third investigator using the automatic software application. Subjective evaluation was conducted only once on an online software designed for this protocol where videos were presented in random masked order. Automatic evaluation based on color and texture analysis was performed by (1) automatic localization of sequences of interest, (2) extraction of the region of interest within each frame, and (3) automatic TBUT measurement from evolution curves in the region of interest as time elapsed from the beginning of the sequence of interest until the curve exceeds a threshold.

RESULTS

Substantial correlation was observed among the examiners (intraclass correlation coefficient, 0.752). There was a ***statistical difference between observer 1 and 2 evaluations*** (*t* test, *P* < .001), whereas data provided by the ***software showed no significant differences from those of the observers*** (*t* test, *P* ≥ .26). Similar results to the whole data set analysis were obtained when the sample was reassessed only considering mean BUT values ≤15 seconds.

CONCLUSIONS

The present pilot study showed ***acceptable clinical results for the software application designed to objectively measure the TBUT***



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Clinical Systemic Disease Management

Smart Phone Applications – Pediatric Myopic Progression

Myopia: Should We Treat It Like a Disease? The research is mounting...

Rev Optom (2020) 157(10):32-38

- In 2015, the WHO and Brien Holden Vision Institute gathered for a global scientific summit on myopia.
- Current models project that by 2050, myopia and high myopia will reach epidemic proportions affecting 52% and 10% of the world's population, respectively.
- Based on these projections, the WHO identified the increase in myopia as the number one health threat facing vision worldwide, in part because of its association with ***myopic macular degeneration, cataracts and glaucoma.***

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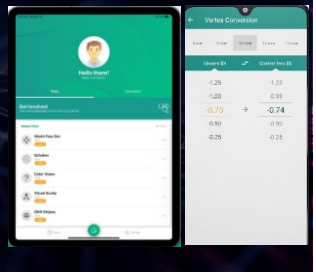
Clinical Systemic Disease Management

Smart Phone Applications – Austere Toolkit

Smart Optometry Pro

15 application-based tests
- VA (x2)
- CS
- Color vision
- Amsler grid
- Accommodation
- ***Aniseikonia***
- ***Duochrome***
- ***Cobalt blue filter***
- Hirschberg
- Maze
- MEM retinoscopy
- ***OKN***
- ***Red desaturation***
- ***Schober***
- Worth 4-dot

Calculators
- Vertex correction
- VA conversion



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Clinical Systemic Disease Management

Smart Phone Applications – Drug Interactions / Contraindications

Mobile Medical Applications for Dosage Recommendation, Drug Adverse Reaction and Drug Interaction: Review and Comparison

Therapuetic Innov & Reg Sci (2018) 51(4)

Results

8 mobile medical apps were included and used to compare their features and functionalities. The 4 apps that scored the highest (14/17 points) are: Lexicomp®, ***Epocrates®***, Micromedex®, and Drugs.com®. Lexicomp and Micromedex do not provide the image of the drug and have an access subscription fee. Epocrates does not provide interaction classification and clinical teaching advice and occupies a large space in the memory to be installed. Meanwhile, My Blue Book® scored the lowest (9/17 points) because certain features such as toxicology information, drug interaction, clinical teaching advice, contraindicated drug and black box warning were not included.

Conclusion

Based on the features assessment criteria of each mobile medical application, Lexicomp, Epocrates, Micromedex, and Drugs.com are the apps that scored the highest. ***Epocrates® and Micromedex are useful for checking drug interactions***. In addition, some of the apps have additional features for the DoReADI criteria, for example, dose calculator and interaction classification.

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Clinical Systemic Disease Management

Smart Phone Applications – Doc in a Box

- **Smartphone-based AI in primary care medicine**

How accurate are digital symptom assessment apps for suggesting conditions and urgency advice: Clinical vignettes comparison to GPs

BMJ Open (2020) 10:e040269

Intervention/comparator

For eight apps and seven general practitioners (GPs): breadth of coverage and condition-suggestion and urgency advice accuracy measured against the vignettes' gold-standard.

Results

Condition-suggestion coverage was highly variable, with some apps not offering a suggestion for many users; in alphabetical order, ***Ada: 99.0%***; Babylon: 51.5%; Buoy: 88.5%; K Health: 74.5%; Mediktor: 80.5%; Symptomate: 61.5%; YourMD: 64.5%; WebMD: 93.0%. ***Top-3 suggestion accuracy*** was GPs (average): 82.1%±5.2%, ***Ada: 70.5%***; Babylon: 32.0%, Buoy: 43.0%, K Health: 36.0%, Mediktor: 36.0%, Symptomate: 27.5%; WebMD: 35.5%; YourMD: 23.5%. For ***safe urgency advice***, tested GPs had an average of 97.0%±2.5%. For the vignettes with advice provided, only three apps had safety performance within 1 SD of the ***GPs—Ada: 97.0%***; Babylon: 95.1%; Symptomate: 97.8%.

Conclusions

The safety of digital symptom assessment apps relies on coverage, accuracy and safety. While ***no digital tool outperformed GPs, some came close, and the nature of iterative improvements to software offers scalable improvements to care***.

ada

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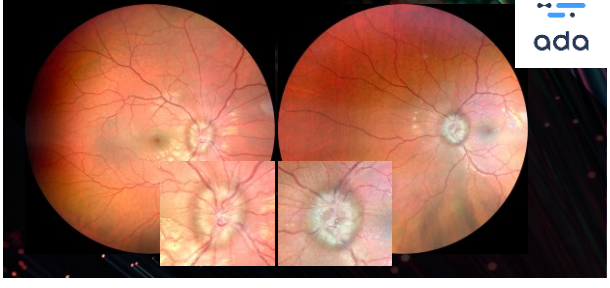
Clinical Systemic Disease Management

Smart Phone Applications – Case Report



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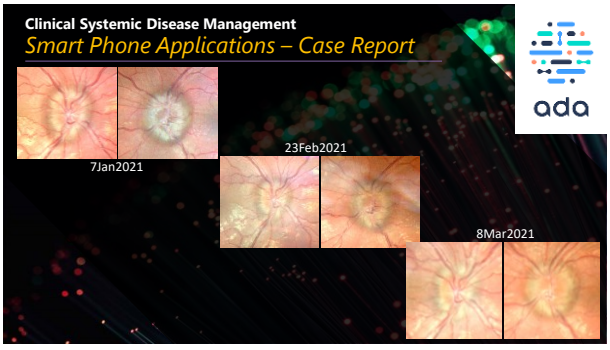
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Smart Phone Applications – Case Report
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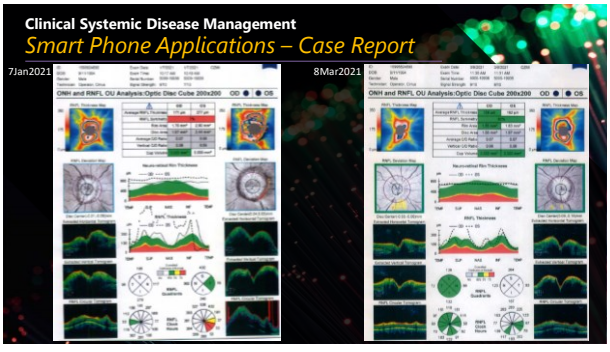
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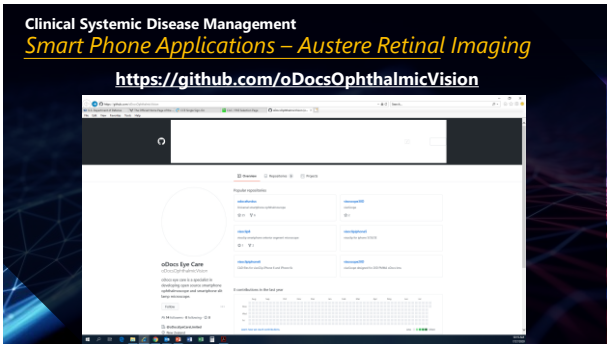
Clinical Systemic Disease Management
Smart Phone Applications – Austere Retinal Imaging
https://github.com/oDocsOphthalmicVision

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Clinical Systemic Disease Management

Smart Phone Applications – Austere Retinal Imaging

https://github.com/oDocsOphthalmicVision

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Opportunity and Limitations

- What's now?
- What's next?

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What's now?

Timolol eyedrops in the treatment of acute migraine attacks: Randomized cross-over study

JAMA Neurology (2018) 75(8):1024-1025

University of Missouri-Kansas School of Medicine reported the first small, placebo-controlled, cross-over study of topical β-blockers for acute migraine.

- Initial enrollment of 26 established migraine patients
  - ***78% of migraines had a severity of none or mild at two hours on timolol 0.5% compared to 57% with placebo.***
- Subject-rated overall effectiveness of timolol 0.5% was 2.4 out of 4 compared to 1.4 with placebo. Notably ***40% patients found β-blockers very effective while only 1 of placebo patients did***
- Vital component: ***Instillation OU at the first sign of an aura or migraine and a second set within 15 minutes***

Topical Beta Blockers for the Treatment of Acute Migraines in 2019

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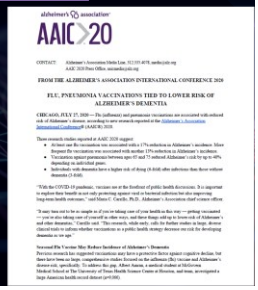
What's now?

2020 Alzheimer's Association International Conference

1) History of at least one flu vaccination was associated with a ***17% reduction*** in Alzheimer's incidence. More frequent flu vaccinations were associated with an ***additional 13% reduction*** in Alzheimer's incidence
2) Pneumonia vaccination between ages 65 and 75 reduced Alzheimer's risk by ***up to 40%*** depending on individual genes.
3) ***Individuals with dementia have a 6-fold mortality risk after infections than those without dementia (3-fold)***

Primary care optometry for patients 65+ and at-risk for dementia and Alzheimer's disease should include H/O:
- Pneumonia vaccination
- Influenza vaccination


alzheimer's association
AAIC 20

FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2020

FLU, PNEUMONIA VACCINATIONS TIED TO LOWER RISK OF ALZHEIMER'S DEMENTIA

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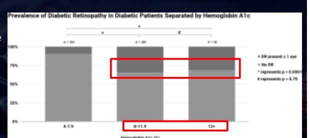
What's now?

15-Month Experience with Primary Care-based Telemedicine Screening Program for Diabetic Retinopathy
BMC Ophthal (2021) 21: 1-9

Methods:
Review of 15 months of data investigating how many patients were screened, how interpretable the photographs were, how often the photographs generated a diagnosis of DR based on the screening photo and how many patients followed-up for an exam in the office

Results:
689 digital retinal screening exams of DR patients were conducted. Among all of the screening exams, 52% triggered a request for a referral to ophthalmology.
- 33% of photos were uninterpretable
- 10% suspected to have alternate condition

Conclusions:
- ***~50% of the patients required a referral***
  - ***Only 9.5% of referrals actually received an eye exam***
- ***Identification of referral-warranted diabetic retinopathy and other ophthalmic conditions is not enough***



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What's now?

- IDx - DR
  - FDA approved in 2018 for AI recognition of DR (including CSME) in a primary care setting
  - Sensitivity = 87.4%
  - Specificity = 89.5%

Validation of automated screening for referable diabetic retinopathy with the IDx-DR device in the Hoorn Diabetes Care System.
Acta ophthalmologica (2018) 96(1):63-68.

Diagnostic accuracy of a device for the automated detection of diabetic retinopathy in a primary care setting.
Diabetes care (2019) 42(4):651-656.

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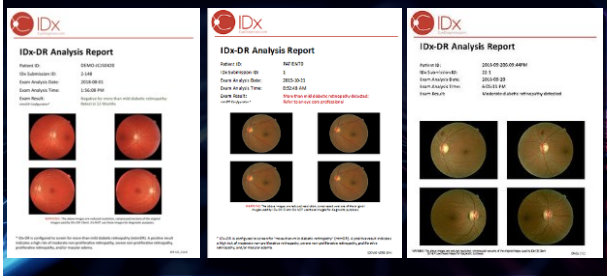
What's now?



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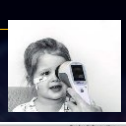
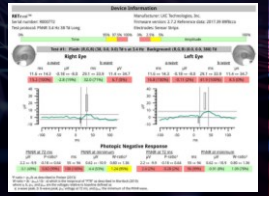
What's now?

Comparison of the handheld RETeval ERG system with a routine ERG system in healthy adults and in pediatric patients
Eye (2022) *35*(8):2180-2189




Methods
Cone and rod ERGs were recorded using a standard photic stimulator and the RETeval device. Both methods involve ***using skin electrodes, without mydriasis and under dark and light conditions***. Two groups of participants were recruited: 44 healthy adult subjects (mean=39 yrs) and 37 pediatric patients (mean=5 yrs)



Results
- ***Lack of absolute agreement in the measurements between the two devices, highlighting the need for device-specific reference data***
- Pediatric group showed high level of diagnostic agreement between both systems
- ***RETeval sensitivity = 1.0 and specificity = 0.91***

Conclusions
ERGs are similar between the two methodologies demonstrates that the RETeval device is a useful tool for assessing retinal function in children

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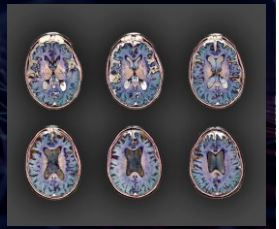
What's now? *(Update May 2023)*

Donanemab in Early Alzheimer's Disease
N Engl J Med (2021) 384:1691-1704



RESULTS
131 were assigned to receive donanemab and 126 to receive placebo. The baseline iADRS score was 106 in both groups. The

- ***Change from baseline in the iADRS score at 76 weeks was −6.86 with donanemab and −10.06 with placebo***
- ***Most secondary outcomes showed no substantial difference.***
- ***At 76 weeks, the reductions in the amyloid plaque level and the global tau load was greater with donanemab than with placebo***

CONCLUSIONS
In early AD, donanemab resulted in a better composite score for cognition and ADL than placebo at 76 weeks

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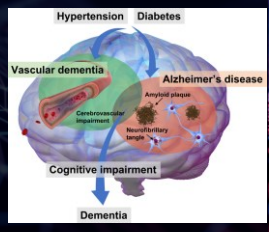
What's now?

Mechanisms Associated with Type 2 Diabetes as a Risk Factor for Alzheimer-Related Pathology
Mol Neurobio (2019) 56:5815-5834

Abstract
Evidence suggests dementia and pathology in AD are both dependent and independent of amyloid processing and can be induced by multiple 'hits' on vital neuronal functions

- ***T2D poses the most important risk factor for developing AD after aging and dysfunctional neuronal signaling is a major contributor in both diseases***
- ***Aβ42 induced a more severe, short-lasting deficits in memory and deregulation of proteins***
- ***Presence of Aβ on the T2D phenotype exacerbated and prolonged the memory deficits and induced more severe aberrant regulation of proteins associated with autophagy, inflammation and glucose uptake from the periphery***



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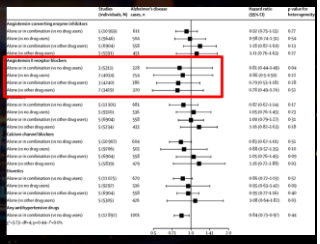
What's now?

Antihypertensive medications and risk for incident dementia and Alzheimer's disease: a meta-analysis of prospective cohort studies
Lancet Neurol (2020) 79(1):61-70

Methods
Meta-analysis included more than 2000 participants, dementia events over 5 years, measured blood pressure and verified use of AHMs. Assessed the association of incident dementia and clinical AD with use of 5 AHM classes, within strata of baseline high (SBP ≥140 mm Hg or DBP ≥90 mm Hg) and normal (SBP <140 mm Hg and DBP <90 mm Hg) blood pressure

Results
3728 dementia cases and 1741 AD diagnoses across cohorts of 7-22 years were analyzed. Those using any AHM had reduced risk for developing dementia ***(HR: 0.88)*** and AD ***(HR: 0.84)*** compared with those not using AHM.

Interpretation
Among people with hypertension, use of any AHM with efficacy to lower blood pressure may reduce the risk for dementia.



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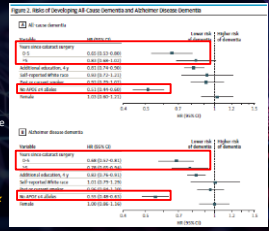
What's now?

Association between cataract extraction and development of dementia
JAMA Internal Medicine (2022) 182(2):134-141

RESULTS
- 3038 participants were included aged 74.4 (6.2) years; 1800 women (59%) and 1238 men (41%)
- Based on 23,554 person-years of follow-up, cataract extraction was associated with significantly reduced risk ***(HR: 0.71)*** of dementia after controlling for years of education, self-reported White race and smoking history and stratifying by apoE genotype, sex, and age group at cataract diagnosis
- Similar results were found with the development of Alzheimer disease dementia

CONCLUSIONS
- ***Cataract extraction was significantly associated with lower risk of dementia development***
- ***Cataract surgery may have clinical relevance in older adults at risk of developing dementia***



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Wrap-Up

- Preventive medicine and systemic disease diagnosis and management of vasculopathy, neurodegeneration, autoimmune and collagen vascular disease includes comprehensive eye exams, ancillary testing and high-resolution imaging
  - *This is what optometry does*
- Mitigation of systemic *microvascular insults*, *inflammation* and *oxidative stress* have direct benefits in both retinal and systemic health and function
- Smartphone-based apps have a force multiplying effect
  - *No replacement for a comprehensive exam but accurate, repeatable screening devices allow for population-level use*
- AI and Deep Learning algorithms are here to stay

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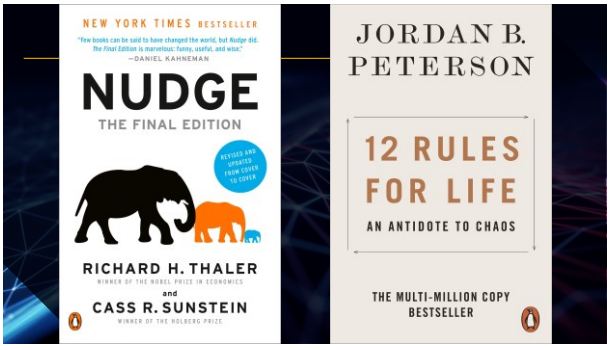

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Questions?

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