A Roadmap for the Medical Management of Glaucoma

Ben Gaddie, OD, FAAO
Eric Schmidt, OD, FAAO

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Disclosure Slide for Dr Eric Schmidt

- Dr Schmidt is an advisor or consultant for the following:
  - Allergan
  - Tarsus
  - Eyenovia
  - Trukera
  - Thea Pharmaceuticals
  - Topcon
  - BSL
  - Sight Science
  - Avellino Labs
  - Visus
  - Sydnexis
  - Harrow Pharmaceuticals

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Ian Ben Gaddie, O.D., F.A.A.O. has the following relationships to disclose

- Topcon- Advisor
- Tarsus - Advisor, speakers bureau
- B+L - Advisor , speakers bureau
- Orasis - Advisor
- Any potential conflicts have been mitigated

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To Treat or Not To Treat, That Is The Question!

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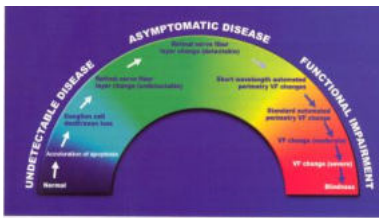

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A Review Of Risk Factors

- FINDACAR
  - Family history
  - IOP
  - Nearsightedness
  - Diabetes/Vascular disease
  - Age
  - Corneal thickness
  - Asymmetry
  - Race

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Glaucoma Risk Factors

- FINDACAR
- The more risk factors one has, the more likely one is to develop glaucoma
- The more risk factors one has, the lower the IOP target should be

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How Can We Make A Difficult Decision Less Difficult?

- Get Data
- What Data?
  - OCT
  - VF
  - FP
  - IOP
  - IOP
  - Pachymetry
  - Fam Hx
  - IOP

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Diagnosis In The Glaucoma Suspect —When To Treat?

- Glaucoma suspects can be (broadly) categorized into two groups:
  1. Ocular hypertensive subjects with risk factors for the future development of glaucoma
     - These patients are addressed by OHTS data and who to treat
  2. Subjects with questionable glaucomatous findings that cannot definitely be distinguished from normal
     - e.g., suspicious appearance of optic disk, RNFL, GCA or VF and
     - IOP that is 21 mmHg or lower

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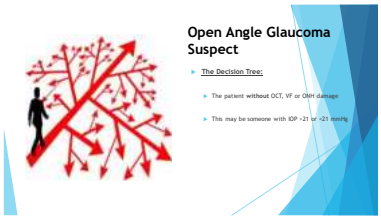

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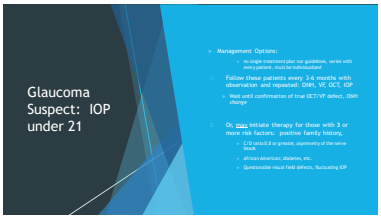

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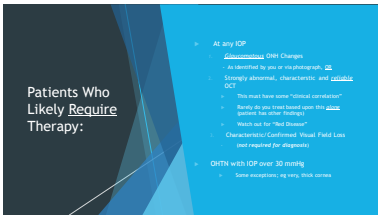

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Ocular Hypertension

- When do you treat – sometime, all the never, never?
- Can OH progress to glaucoma if it is treated?
- What are the downsides to therapy?
- When not treat everyone w elevated IOP?

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Ocular Hypertension

- Definition of ocular hypertension
  - IOP 21 mm Hg or higher
    - Based upon Armaly statistical definition of OHTN
    - Not based upon clinical findings
  - Visual Fields Full
  - Optic nerve considered Full
    - This part of definition is changing with OCT use allowing subtle optic nerve/RNFL changes to be detected
- Consider therapy based upon risk of developing glaucoma over lifetime
  - Concept of risk assessment
- Therapy is often considered optional since true damage is not present
- Still not clear if early therapy (before damage) altern long-term outcome
  - OHTS IS was meant to answer this question

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The Swinging Pendulum of Therapy for Ocular Hypertension

- 1960s IOP > 21 mm Hg Treat
- 1970s IOP > 21 mm Hg No Tx
  - Decade of Ocular Hypertension
- 1980s IOP > 21 mm Hg Tx/No Tx
  - 1982 Quigley paper field loss late sign OAG
  - Concept of risk factor analysis
- 1990s IOP > 21 mm Hg Tx/No Tx
  - Earlier therapy once latanoprost introduced

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Ocular Hypertension

- Many years ago, everyone with elevated IOP was treated
- Recognition that about 1% per year convert from OHTN to glaucoma
- Those with greater risk are more likely to convert
  - thinner cornea, African American, larger cupping
- Led to the concept of risk assessment
- OHTS provided information on when to treat
  - European Glaucoma Prevention Study (EGPS) also provided risk information

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Treating ocular hypertension Risk assessment

- Consider number of risks individual has that increases chance for
  - Conversion of ocular hypertension to the development of glaucomatous damage
  - Based upon evidence
- Studies include Ocular Hypertension Treatment Study (OHTS) and European Glaucoma Prevention Study (EGPS)
- If we are going to treat ocular hypertension, at what risk level?
  - 10% vs. 15% vs. 20%
  - Begin prophylactic therapy
- Uses concept from Framingham Heart Study

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OHTS – The Nitty Gritty

- The most predictive factors for conversion:
  - Older age
    - 22% increase/ decade
  - Larger horizontal and vertical C/D
    - 32% increase/0.1 larger
  - Higher baseline IOP
    - 10% increase/ mm Hg
  - Thinner corneas
    - 71% increase in risk/ 40 microns thinner

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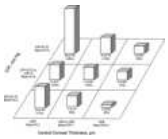
Risk Assessment

- Risk Level Low < 5%
  - Monitor
- Risk Level Moderate 5-15%
  - Consider Therapy
  - Discuss with patient
- Risk Level High >15%
  - Treat



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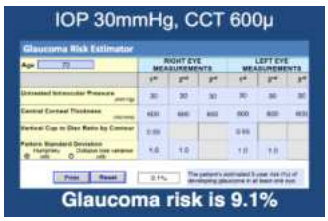

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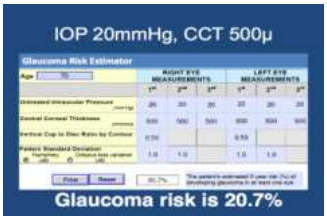

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iPhone Risk Calculator

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Risks

- OHTS
  - IOP
  - Corneal thickness
  - Cup/Disc ratio
  - VF status
- Other risks
  - Family history
  - Race including Hispanic

- Newer risks
  - Alcohol use
  - Cigarette smoking
  - Diabetes?
  - Age at menopause
  - Ovarian surgery
  - Physical activity
  - Metabolic diseases
    - Hypertension, cholesterol, Cardiopulmonary diseases
  - Sleep apnea

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Ocular Hypertension

- Treat when risk is significant but….
- Need to include patient in discussion about therapy
- Some patients would like OHTN to be treated when risk is present while others would rather not be treated
- Glaucoma is a slow- moving disease so can monitor those with OHTN safely without therapy
- Still not clear how soon therapy should be initiated

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Making the Diagnosis and Starting Therapy

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OGS E-Journal January 2008

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Glaucoma Clinical Trials: Study Design

Trial	N	Dx	Randomization	Follow-Up
OHTS[1] (NEJ)	1636 pts	OHT	Medical Tx vs observation	5 years
EMGT[2] (NEJ)	255 pts	OAG	Tx (ALT + betaxolol) vs observation	4-9 years
CNTGS[3] (GRF)	140 eyes	NTG	Medical Tx and/or surgery vs observation	7 years
CIGTS[4] (NEJ)	607 pts	OAG	Medical Tx vs surgery	4 + years
AGIS[5] (NEJ)	738 eyes	OAG	ALT vs surgery	8 years

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IOP in Clinical Trials

Study	IOP Reduction	%Progression
• OHTS*	20%	9.5%/4.5%
• EMGT*	25%**	62%/45%
• CNTGS	30%	35%/12%
• AGIS		<18; No progression
• CIGTS (meds)	38%	no progression
• CIGTS (surg)	45%	no progression

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Advanced Glaucoma Intervention Study (AGIS)

- Long-term study with follow-up of patients with advanced glaucoma
  - exhausted all medical options
  - follow-up 7 years
  - 249 whites/ 332 black patients
- Results initially published July 1998 Ophthalmology
  - Therapeutic options and success vary w race
  - ALT Vs. Trabeculectomy as first procedure

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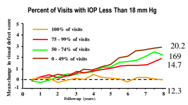
AGIS 7
Sustained IOP below 18 mm Hg:
Positive Correlation with Stability of Visual Field



AGIS Investigators, 2000, Am. J. Ophthalmol., 130, 429-440

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Glaucoma Clinical Trials: Summary of Implications

- Treat newly diagnosed glaucoma[1,2]
  - Patients with early glaucoma should be treated to reach low pressures that reduce the risk of progression
  - Both medical treatment and surgery effectively reduce IOP and risk of progression
- IOP needs to be consistently low[3]
  - IOP fluctuation over long time periods increases risk of VF loss in glaucoma
  - Results show that to be effective, patients need lower IOP
    - Not just most of the time
    - Need it lower consistently, all the time
- When pressures are low enough, patients on average have much lower risk of progression[2]

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Determining the Target IOP

- 1. Estimating the amount of glaucoma damage.
  - This is based upon both structural functional assessment.
- 2. Estimating the damaging IOP
  - One should make the best clinical assessment possible as to what the likely IOP was at which damage has already occurred. In some instances, multiple IOP measurements may help determine a baseline IOP and hence influence the initial determination of the target IOP

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Determining the Target IOP

- 3. Estimate the patient's life expectancy.
  - In general, the longer the patient's life expectancy, the lower the target IOP will need to be. Actuarial tables can be helpful, keeping in mind that any give patient may live much longer or shorter than the mean. When in doubt, err on the side of estimating a longer life expectancy. Nevertheless, on average, 40 year olds and 90 year olds may be treated differently.

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Determining the Target IOP

- 4. Consideration of the other risk factors for progression.
  - Other proposed risk factors include severe damage in the other eye, family history of blindness from glaucoma, etc.
- 5. Guesstimate the Rate of Progression (RoP) of glaucoma damage, either disc and/or fileds, based upon the assessment of damage already occurred vs time

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IOP Often Not Lowered to Recommended Target Pressures

- Review of 395 POAG patient charts in 6 managed care plans
  - IOP often inadequately controlled
    - Mild glaucoma
      - 52.4% of visits IOP >20 mm Hg
      - 21.1% of visits IOP >24 mm Hg
    - Moderate to severe glaucoma
      - 65.3% of visits IOP >17 mm Hg
      - 30.4% of visits IOP >21 mm Hg

Fremont AM et al. *Arch Ophthalmol*. 2003;121:777-783.

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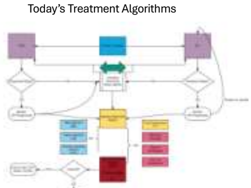
Today's Treatment Algorithms



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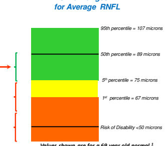
OCT and Progression Range

- *Just like perimetry, the average patient can lose a third of his/her RNFL or neuro-retinal rim and still be inside the OCT normal range.*
- *Normal person losses 2um/decade due to aging*



Values shown are for a 69 year old normal.[1]

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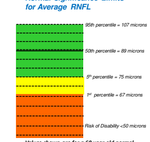
SDOCT measurements are highly reproducible.

2-4 Steps in Range

- *We can measure multiple steps of statistically significant change while a glaucoma suspect still is in the green normal range.*



Values shown are for a 69 year old normal.

- *Leung et al. Ophthalmology 2009;116:1257*
- *Roh et al. Ophthalmology 2013;120:969*
- *Wong et al.* Optom Vis Sci 2014;92
- Matlatch et al, IOVS Sep 2014 .

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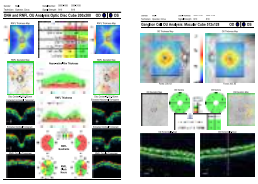

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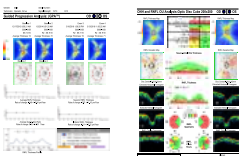

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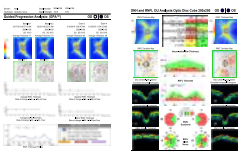

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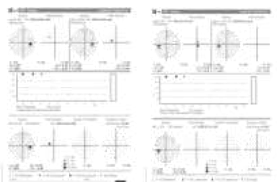

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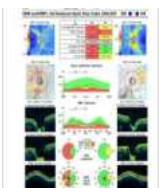

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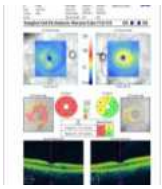

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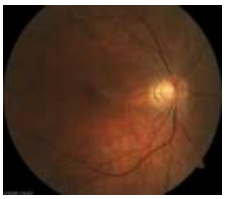

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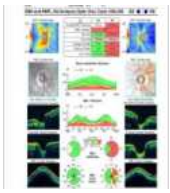

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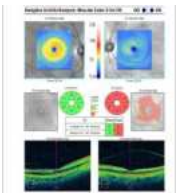

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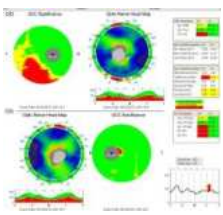

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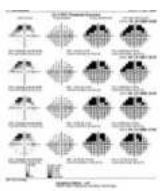

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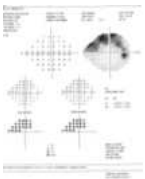

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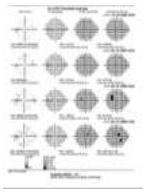

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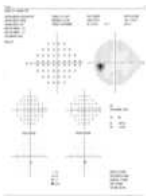

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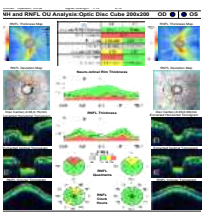

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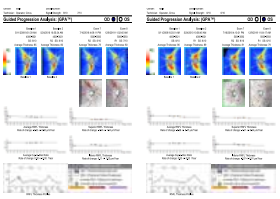

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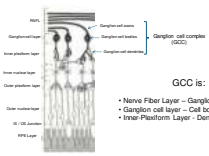
Retinal Ganglion Cells extend through three retinal layers



GCC is:

- Nerve Fiber Layer – Ganglion cell axons
- Ganglion cell layer – Cell bodies
- Inner Plexiform Layer - Dendrites

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Macular Vulnerability Zone

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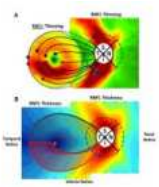

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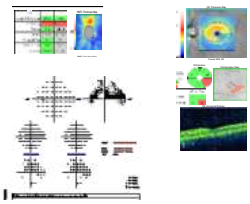

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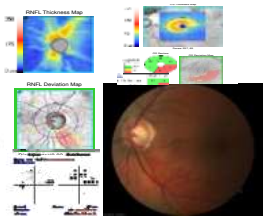

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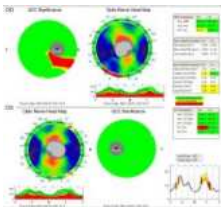

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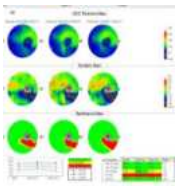

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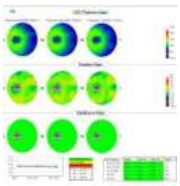

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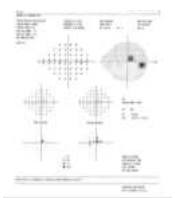

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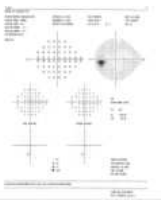

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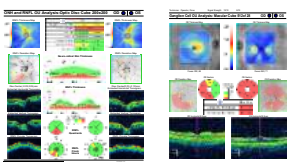

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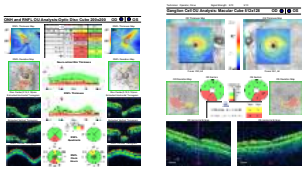

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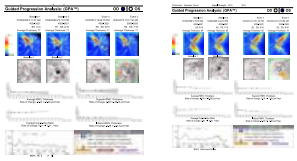

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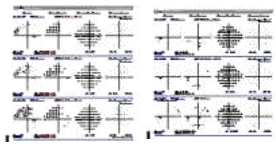

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Glaucoma Treatment Universe 2024

- Prostaglandins
- Alpha agonists
- Rho-kinase Inhibitors
- Beta-blockers
- Carbonic Anhydrase Inhibitors
- Combo Agents
- SLT
- MIGS
- Glaucoma Surgery
- How Do You Know Which Category To Choose???

85

What Are You Trying To Achieve?

- Optimal IOP Reduction
- Minimal Side Effects
- Rigid Compliance
- Anything Else?

86

PGA

- QHS dosing
- Long duration of action
- Flatten diurnal curve
- Effective on trough and peak IOP
- No systemic side effects
- Little tachyphylaxis

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Prostaglandins

- All decrease IOP by increasing uveoscleral outflow
- All are effective at squashing the diurnal curve
- They have either no effect or a positive effect on retinal perfusion
- Some affect nitric oxide at the optic disk
- Some have BAK, others don't
- But does 1 work better than the others?
- Is there really any reason to not start with a PGA?

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XLT Study - Parrish, Palmberg, et. al. (AJO, May 2003, Vol. 135, No.5)

- Multicenter study to compare IOP lowering efficacy of Bimatoprost vs Latanoprost vs Travaprost
- Also compared safety profiles of the 3 drugs
- Conclusions: All 3 drugs were comparable in their ability to lower IOP at all time periods.
  - Latanoprost exhibited greater ocular tolerability

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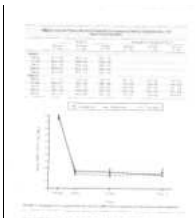

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Vyzulta – A different kind of PGA

- Reduces IOP by 32%
- 1.2mm HG lower than latanoprost
- Preserves VF better by 10%
- No loss of effect while sleeping
- Improved side effect profile
- Releases nitric oxide at the trabecular meshwork level

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- Effect of latanoprostene bunod on Optic Nerve Head Flow
  - Samaha, Diaconu et al, IOVS, Feb 2022, Vol 9, Iss 2 pp172-176
  - Purpose was to evaluate effect of latanoprostene bunod on optic nerve blood volume and O2 saturation - *IN HEALTHY SUBJECTS*
  - Measurements were taken before initiating therapy and then 7 days after QD therapy of both Latanoprost and latanoprostene bunod

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- ONH saturated O2 levels were 4% higher with Vyzulta than latanoprost
- ONH blood volume was way higher with Vyzulta
  - 66% higher at Hr 1, 45% higher at Hr 2
- What is the clinical significance of this?

93

Are generics really as good as branded products?

What about when it comes to prostaglandins?

94

94

But really… Is There Anything New??

Iyuzeh-
(latanoprost 0.005%)

Thea Pharmaceuticals

Let's talk about this…

95

- Does that sound familiar?
- Monoprost (in Europe) - the market leader in PGA in Europe
- This actually is PRESERVATIVE FREE latanoprost!!
- Single dose container
- But does it really work??

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Iyuzeh – Phase 3 data

- Compared to Xalatan (Switch Study)
- Stable POAG pxs on Xalatan
- 8 day washout period
- 3 months on Iyuzeh
- IOP reduction was 4-8mm Hg on Xalatan
- IOP reduction was 3-8mm Hg on Iyuzeh
- Baseline IOP was 19mmHG!!

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Iyuzeh – Phase 3 data-Adverse Effects

- Xalatan group
  - Hyperemia – 31%
  - Eye Irritation – 34%
- Iyuzeh Group
  - Hyperemia – 34%
  - Eye Irritation – 19%
- ZERO reports of SPK

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- European data – Higher baseline IOP (24mm Hg)
  - IOP lowered to 15.5mm Hg
  - Same rate of adverse effects
- Bachrach data (2021 AGS)
  - 12 week trial comparing to Xalatan
  - Similar IOP reduction (as measured by ability to get IOP <18mm Hg)
  - 2% experienced redness or ocular irritation
  - 0% SPK

  Fewer ocular side effects (13.9% vs 22.5%)
- PAGST study
  - 93% tolerated drop
  - ATT usage decreased 24%

99

#What's The Big Deal??

- OSD is an epidemic in glaucoma
- Will this improve compliance?
- Will this cost $1M??
- Is it better than what we have?

100

Are we going to see a trend towards Preservative free glaucoma drops??

101

Beta-blockers

- 40 year history of successfully lowering IOP
- Reduces aqueous humor formation
- Adrenergic agonists
- Lowers IOP 22-28%
- Ocularly well tolerated

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Beta-blocker side effects

- Cardiac problems
  - Bradycardia
  - Hypotension
  - Exercise intolerance
  - Heart block
- Respiratory problems
  - Bronchospasm
  - Status asthmaticus

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Beta-blocker side effects

- CNS
  - Often overlooked
  - ACID
    - Anxiety
    - Confusion
    - Impotence
    - Depression
  - General decreased affect
- Diabetic problems
  - Decreased sense of caloric need due to depressed adrenergic surge

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Beta-blocker side effects

- 22% of pxs have contraindication to or significant side effect from beta-blocker
- Question, query and query some more!
- Be specific
- Remember the dose relationship so:
  - ½% rather than 1%
  - QD rather than BID
- They are real (may be anecdotal)
- IS THERE REALLY ANY REASON TO USE A BETA-BLOCKER??

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Rhopressa (netarsudil) -MOA

Works at the cellular level within the trabecular meshwork

ROCK inhibitors improve outflow by relaxing contraction and stress fibers at the t.m.

106

What Do We Know About Rhopessa (netarsudil 0.02%)

- Rhopressa QD is non-inferior to timolol 0.5% BID in lowering IOP
- Expected IOP reduction 3.7 -7.0mm Hg
- Rhopressa seems to better at lowering IOP (as compared to itself) in pressures < 25mm Hg
- IOP lowering effect is maintained over 12 months
- Was given a broad label by FDA

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Rhopressa – Adverse Effects

- Generally well tolerated
- Conjunctival hyperemia - 53%
  - Did not worsen with time
  - Mild-36.8%, moderate - 10.5%, severe -0.6%
  - D/C rate due to redness – 3%
- Corneal verticillata - 18%
- Conjunctival hemorrhage - 15%
  - All are transient and considered mild

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What's to like about Rhopressa?

- New MOA so… it is absolutely different
- It should be additive
- Definitely works better at lower IOP
- What about side effects?

109

M.O.S.T. Study

- Real World Open Label Phase 4 Study
- ASCRS 2020
- To determine efficacy of Rhopressa as an adjunct med
- Investigator's Choice – Rhopressa + any other agent
- 24.4% African-American participants

110

M.O.S.T. Results

Rhopressa + PGA - IOP 21.1> 16.9 mmHg (20% reduction)

Rhopressa + 2 meds – 20.6 > 16.6 mmHg (20% reduction)

Notice the low baseline IOP

111

More M.O.S.T. Results

- % of pxs less than < 18mm Hg
  - <18mm -72.7 % (from 34.4%)
  - <17mm- 65% (from 25.2%)
  - <15mm -40.6% (from 15.9%)
  - <14mm- 30.1% (from 11.3%)
- 2/3 of all patients achieved IOP < 17mm Hg

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M.O.S.T. Tolerability rates

Hyperemia – 20.* %

D/C rate – hyperemia 3.4%

Tolerability rating

67.8-73.1% good or decent (physician response)

65-78%good or decent (Patient response)

113

Roclatan – Alcon

- Fixed Combination drug – Rhopressa + latanoprost
- QD dosing
- "Quadruple acting" MOA – (adds increased uveoscleral outflow)
- IOP lowering better than either of its components
- Potential to be very effective – lowered IOP an additional 2-3 mm compared to Rhopressa (and other PGAs)

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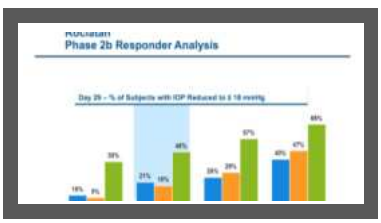

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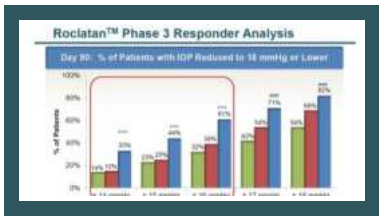

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Newest Rocklatan Data

1400 pxs

Rocklatan vs Rhopressa vs Latanoprost

60% achieved >30% reduction in IOP	1/3 achieved > 40% reduction in IOP	CIGTS showed 36% drop to STOP VFQ progression	75% achieved <18mm Hg	1/3 achieved 16mm or less	On average 1.2 mm lower IOP than either latanoprost or Rhopressa

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Newest side effect data

- No tachyphylaxis at 12 months
- No unexpected A.E.
- Very few serious A.E.- majority are mild
- 58% hyperemia but 5% d/c rate
- 20% Instillation pain – 0% d/c
- 10% subconj heme – 0% d/c

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Adrenergic Agonists

- Dual mechanism of action
  1. Reduce aqueous production
  2. Enhance outflow mechanisms
- 22-28% IOP reduction
- Short duration of action
- TID dosage
- Avoid in kids

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Mechanism of Action of Brimonidine-PURITE®

- Complements PGAs because it decreases aqueous production
- Complements timolol because it increases uveoscleral outflow

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Brimonidine side effects

- 10-20%
  - Hyperemia
  - Allergic conjunctivitis
  - Ocular pruritis
- 5-9%
  - burning sensation,
  - conjunctival folliculosis,
  - ocular allergic reaction,
  - oral dryness,
  - visual disturbance

- Do these worsen with time?
- How do you know if the drops are the culprit?

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Alphagan systemic side effects

- Dry mouth (~20%)
- Fatigue (1-2%)
- Drowsiness
- Decreased BP

- This drug can cross blood-brain barrier, esp in older and younger pxs

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Brimonidine questions

- What is the correct dosage?
- Which of the 3 products should be prescribed?
- Can it be used as stand alone therapy?
- Effect on diurnal curve?

- What Happens If Hypersensitivity To 0.2% Brimonidine Occurs?

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Let's talk (quickly) about combo drops!

- What are their advantages?
- What about their side effects?
- Are they twice as good as their individual components?

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Dry Eye and Glaucoma

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Considerations on Glaucoma and Dry Eye

- Same age range as chronic dry eye
- Preservatives in PGAs and also combo medications
  - QD vs. BID vs.. TID etc
- Preservative Free Glaucoma Medications
  - Effect of preservative on hydrolyzation of drug
- Blepharitis/PGA's

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Preservatives in Glaucoma Medications

- BAK ranges depending on agent
- At once/day PGA BAK seems innocuous
- Adjunct drugs containing BAK
  - Beta Blockers, CAI's, Brimonidine, RhoKinase
- Mostly BAK; others such as Sofzia and "P" for Alphagan P

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OSD and Glaucoma

- Strategies
  - Go with non preserved PGA
  - Consider SLT
    - Single treatment can last 5 years
  - Consider Durysta
  - Consider Cat Sx +MIGS when appropriate
  - Avoid multiple time/day drugs w BAK
  - Treat OSD/Blepharitis in addition to glaucoma
    - Medications
    - MGD procedures (IPL/Lipiflow/Tear Care etc)
    - Amniotic membranes

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Non Preserved PGA's

- Zioptan (Tafluprost) Thea
- Iuezah (Latanoprost) Thea

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100% perfluorohexyloctane
NO INACTIVE INGREDIENTS

- Wafer free
- Preservative free
- Steroid free

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Miebo Phase 3 Program

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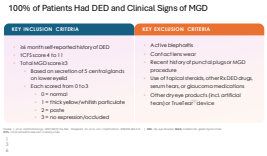

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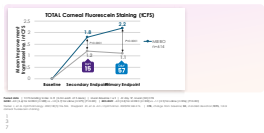

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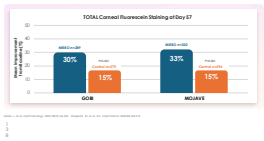

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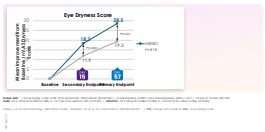

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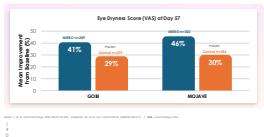

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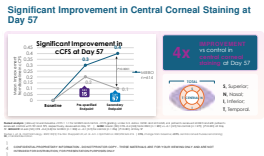

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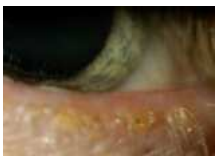

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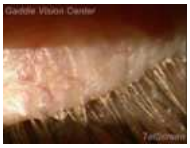

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Lid Margin Erythema Scale Used in Saturn-1

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Erythema Cure and Response

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And Now It's Time To Talk About Compliance!!!!!

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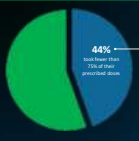
Adherence to IOP-Lowering Therapy Is Challenging

Over 3 months in a study of 196 patients with glaucoma taking an IOP-lowering medication in one or both eyes[1,2]:



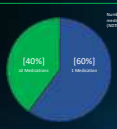
Despite instruction, free medication, once-daily administration, use of a dosing aid, and electronic monitoring of adherence

150

Individualizing the Target IOP

Target IOP should be individualized and updated as needed

- Periodically reassess the IOP target by comparing optic nerve status (optic disc appearance, quantitative assessments of disc and nerve fiber layer) and VF with previous examinations[3]
- Consider switching or adding medications if target is not yet achieved with initial therapy[4]
- Many patients require 2 or more medications to achieve target IOP[5]



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Adherence to IOP-Lowering Therapy Is a Complex, Multifaceted Problem[1,2]

Adherence includes both persistency and compliance issues[1]

Components of successful adherence[1]

- Successfully obtain medication
- Correctly instill drops into eye
- Use drops at appropriate times
- Use drops every day without gaps

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Compliance really is a hot topic

Dr David Friedman – OGF Educators Meeting 9/19

Looked at compliance studies in glaucoma- found that 70% compliance with medications was average

But is that good enough to preserve VF?

Friedman also showed that those who said they missed their drops some of the time, actually used their drops ~50% of the time.

That was much worse than those who say they never miss their drops

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Predictors of Poor Adherence – Friedman 2019

Gaps In Visits

Patients Don't Understand Severity Of Disease

Cost of Drops (25%)

Those who Travel A Lot

Younger Pxs and Very Old Pxs

African-Americans

Those In Poor Health
- These drop adherence to <60%

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Compliance, adherence and side effects of therapy

Compliance decreases the more bottles Rx'd

Robin – Each extra bottle used decreased compliance by 1/3

The more topical meds used the more ocular side effects occur

OSD in G pxs (way) higher than initially thought

60% of G pxs use ocular lubricants

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What are the biggest barriers to proper compliance?

1. Forgetfulness

2. Ability to put drops in

3. Unaware of the importance of the drops

Cost was not in the top 5!!!

156

Ways To Improve Compliance

See Pxs more frequently… especially early in treatment

Improve tracking system – better identify no shows

Call/email appointment reminders

Reminders to pxs to take their drops

Change Dr/Patient intervention

G pxs ask 3.2 questions at visit whereas in other chronic diseases pxs ask ~ 6 questions/visit

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Question Time

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MF

Drug Delivery Options

Is this where therapy is going?

159

Drug Delivery

- Why
  - Reduce need for patient to take their drops
  - Host of studies have shown majority of eydrops not taken
    - Leads to worsening of condition
- Different ways to get medication into eye
  - Inject into AC
  - Contact lens
  - Punctal plug
  - Mist spray/thicken drug increasing contact time
  - Reservoir tacked into trabeculum
- Types – temporary vs. semi-permanent vs. permanent
- What are the downsides?
  - Cost? Does procedure and implant outweigh cost of eyedrop?
  - Side effects of medication
  - Complications for placing medication into eye

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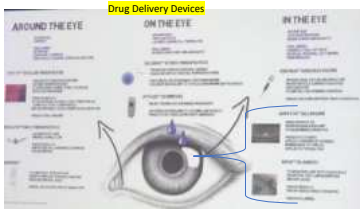
Drug Delivery Devices



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Drug Eluting Ocular Implants

- Unmet needs; Compliance, Compliance, Compliance!
  - forgetfulness, physical or cognitive disability
  - cost
  - side effects
- Locations;
  - Subconjunctiva, Lacrimal puncta
    - higher concentration, must cross ocular barrier; cornea, sclera
    - periocular side effects may be similar to topical application
  - Intraocular
    - lower quantity of drug required, higher concentration
    - at target tissues, fewer barriers, fewer periocular side effects
- Challenges – biocompatible device, sufficient drug content, constant drug release, ease of implantation

Seal JR, Robinson MR, Burke J, Bejanian M, Costa M, Attar M. J Ocul Pharmacol Ther. 2019;35:50-57

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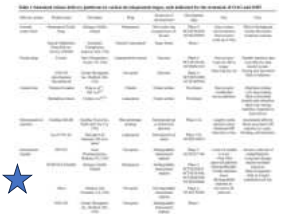

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Bimatoprost SR (Durysta)

- Allergan
- Sustained release bio erodible implant that lasts 4-6 months with similar efficacy to eyedrops
- Small dissolvable pellet is injected into the anterior chamber
  - Sits in/near the angle that resorbs over time
- Can be performed in the office
- Insert can be visualized in the inferior angle
- Ensures patient compliance

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When Should Patients Return?

Managing Glaucoma

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When Should Patients Return?

- Baseline period – making the diagnosis whether it is OHTN or Glaucoma
  - Important to have good quality visual fields and OCT as therapy is initiated
  - If therapy is initiated, then see 2-6 weeks afterwards
    - Making sure the medication/procedure is tolerated and effective
    - Having only one post therapy IOP measurement can be misleading
    - If not at target IOP, see sooner
  - Follow up period is for first year
  - If the person has mild to moderate glaucoma, examine every three months
    - Fields and imaging done at 6, 12, 18, 24 months
    - If stable and good quality can reduce interval for both doing fields/imaging and when to examine patient
- Stable vs. Uncontrolled

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Ocular hypertension

- See on 6-month basis with imaging/fields done yearly
- May reevaluate over time

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When Should Patients Return?

- Is there a need to do visual fields after the initial assessment if the patient is stable?
  - If OCT is stable, why do a field?
- Which fields to do?
  - 24-2 vs. 24-2C vs. 10-2
  - SITA Standard vs. Fast vs. Faster
  - What about bundling fields
    - Do 2 SITA Faster fields at one visit separating by few minutes

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BG

Advancing Therapy

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BG

Dry Eye and Glaucoma

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Ocular Hypertension

- New risks are being discovered
  - Cigarette smoking
  - Alcohol
  - Time for menopause

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The Association of Female Reproductive Factors with Glaucoma and Related Traits

A Systematic Review

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Age at Menopause

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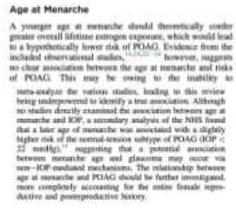

Age at Menarche

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Association between lifestyle habits and glaucoma incidence: a retrospective cohort study

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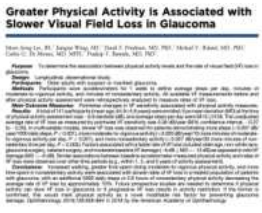

Greater Physical Activity Is Associated with Slower Visual Field Loss in Glaucoma

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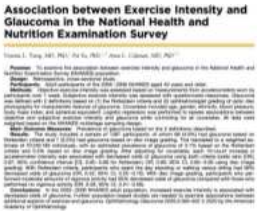

Association between Exercise Intensity and Glaucoma in the National Health and Nutrition Examination Survey

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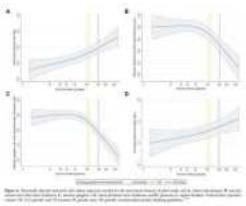

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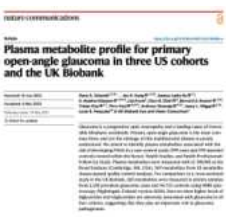

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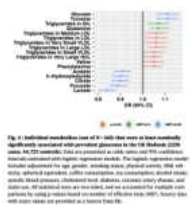

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Is Genetic Risk for Sleep Apnea Causally Linked With Glaucoma Susceptibility?

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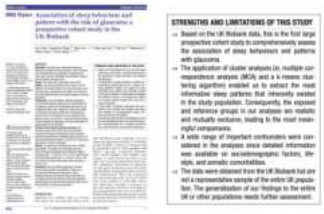

STRENGTHS AND LIMITATIONS OF THIS STUDY

201

BMC Medicine

Associations of sleep apnoea with glaucoma and age-related macular degeneration: an analysis in the United Kingdom Biobank and the Canadian Longitudinal Study on Aging

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Results: During the 9-year follow-up in the UK Biobank, glaucoma incidence rates per 1000 person-years were 2.46 and 1.04 for participants with and without sleep apnoea, and the AMD incidence rates per 1000 person-years were 3.27 and 1.41 for participants with and without sleep apnoea, respectively. Multivariable adjusted hazard ratios of glaucoma and AMD risk for sleep apnoea were 1.33 (95% confidence interval [CI] 1.10–1.60, P = 0.003) and 1.39 (95% CI 1.15–1.68, P < 0.001) relative to participants without sleep apnoea. In the CLSA cohort, disease information was collected through in-person interview questionnaires. During the 3-year follow-up, glaucoma incidence rates per 1000 person-years for those with and without sleep apnoea were 9.31 and 6.97, and the AMD incidence rates per 1000 person-years were 8.44 and 9.67, respectively. In the CLSA, similar associations were identified, with glaucoma and AMD odds ratios of 1.63 (95% CI 1.13–1.78) and 1.39 (95% CI 1.08–1.77), respectively, in participants with sleep apnoea compared to those without sleep apnoea (both P < 0.001).

Conclusions: In two large-scale prospective cohort studies, sleep apnoea is associated with a higher risk of both glaucoma and AMD. These findings indicate that patients with sleep apnoea might benefit from regular ophthalmologic examinations.

Keywords: Sleep apnoea, Glaucoma, Age-related macular degeneration, UK Biobank, CLSA, Cohort study

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Key Points

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Thank You!!!

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