Ocular Manifestations of GLP-1/GLP-1+GIP Drugs

Julie Rodman OD, MSc, FAAO

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Rodman Disclosures

- Visionix
- iCare
- Apellis
- Astellas
- LKC
- Notal Vision
- Alcon
- LENZ

All relationships have been mitigated

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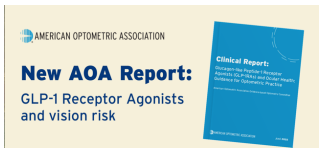
Learning Objectives

- Describe pharmacology and indications of GLP-1 drugs
- Recognize ocular effects: DR, NAION, glaucoma and others!
- Review studies….at least a few!
- Implement screening and triage strategies
- Counsel patients on vision red flags

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The numbers!

- In 2025, 12% of the U.S. adult population was actively taking GLP-1s for chronic diseases or weight loss.
  - Equates to 31 million people

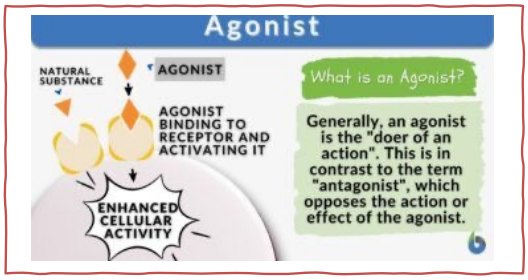


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Let's learn the terms.....

- **GLP-1 and GIP RAs**
  Glucagon-like Peptide-1 and glucose-dependent insulinotropic polypeptide (gastric inhibitory polypeptide)
- **Receptor Agonist (RAs)**
  A substance that binds to a specific receptor in the body and activates it, causing a response

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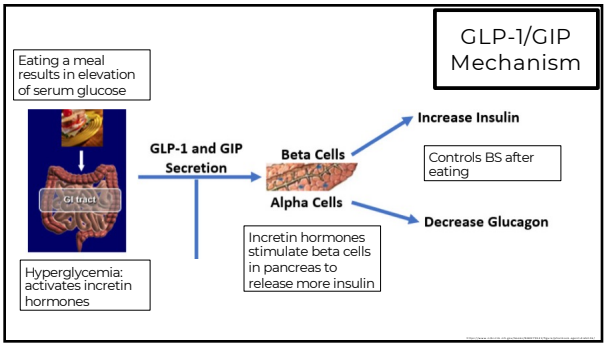
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GLP-1 and GIP

- **GLP-1/GIP hormones**:
  - We naturally have GLP-1 in our bodies
    - GLP-1 is an **incretin hormone** made in the gut after you eat
      - Helps your body manage blood sugar and digestion.
    - The GLP-1 drugs mimic this natural hormone but have a longer effect in the body



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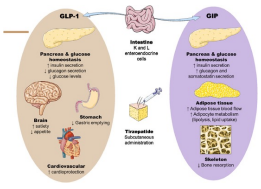
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Clinical Pearl:
Currently no “GIP only” drugs

When GIP is combined with GLP-1 activity, it enhances weight loss and metabolic benefits.

GLP-1 + GIP dual agonists activate both GLP-1 and GIP receptors

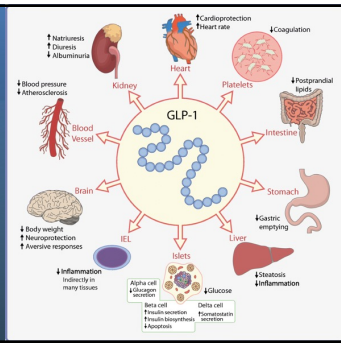
Stronger effect on BS control and weight loss compared to GLP-1 alone.



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Besides decreasing serum glucose, incretin hormones affect multiple body systems

Reduction in major adverse cardiovascular events (MACE)



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Evidence based guidelines: Diabetes

- Recommend GLP-1 receptor agonists and dual GIP/GLP-1 agonists as important glucose-lowering options for **adults with type 2 diabetes who do not meet individualized A1c goals with lifestyle treatment and/or metformin.**

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Evidence based guidelines: Diabetes

Support GLP-1 receptor agonists and dual GIP/GLP-1 agonists as **potential initial therapy**—independent of metformin use or baseline HbA1c—for adults with type 2 diabetes and certain **coexisting conditions**, particularly established atherosclerotic cardiovascular disease, heart failure, chronic kidney disease, or obesity/overweight when weight reduction is a treatment priority.

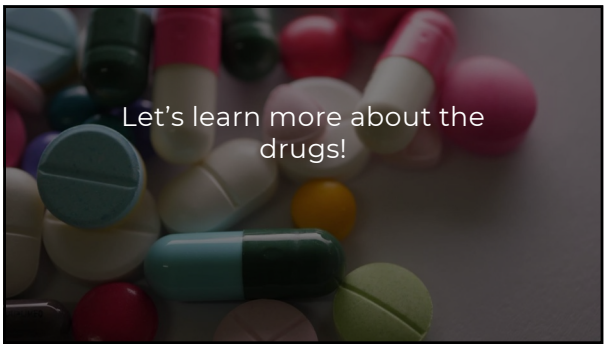
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Evidence based guidelines: Obesity

For chronic weight management, these medications may be indicated for adults with:

Obesity: BMI ≥30 kg/m²; or
Overweight: BMI ≥27 kg/m² plus at least one weight-related condition, such as hypertension, dyslipidemia, obstructive sleep apnea, or type 2 diabetes.

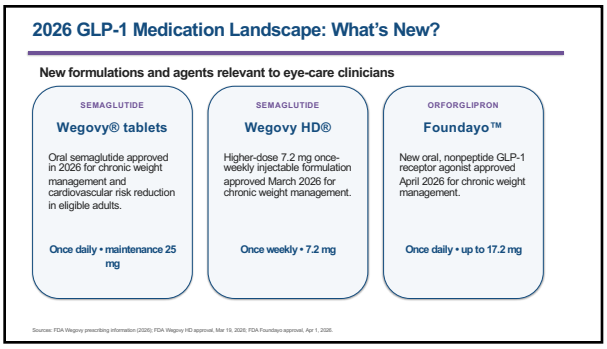
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Generic name	Brand name	FDA approval year	Typical dosing	Main FDA-approved indications
Exenatide	Byetta	2005	Twice daily injection	Type 2 diabetes
Exenatide ER	Bydureon BCise	2012	Once weekly injection	Type 2 diabetes
Liraglutide	Victoza	2010	Once daily injection	Type 2 diabetes; cardiovascular risk reduction
Liraglutide	Saxenda	2014	Once daily injection (up to 3 mg)	Chronic weight management / obesity
Lixisenatide	Adlyxin	2016	Once daily injection	Type 2 diabetes
Dulaglutide	Trulicity	2014	Once weekly injection	Type 2 diabetes; cardiovascular risk reduction
Semaglutide (injectable)	**Ozempic**	**2017**	**Once weekly injection**	**Type 2 diabetes; cardiovascular and kidney risk reduction**
Semaglutide (oral)	**Rybelsus**	**2019**	**Once daily oral tablet**	**Type 2 diabetes**
Semaglutide (high-dose injectable)	**Wegovy**	**2021**	**Once weekly injection (up to 2.4 mg)**	**Chronic weight management; reduction of major cardiovascular events in obesity/overweight**
Tirzepatide (dual GIP/GLP-1)	**Mounjaro**	**2022**	**Once weekly injection**	**Type 2 diabetes**
Tirzepatide (dual GIP/GLP-1)	**Zepbound**	**2023**	**Once weekly injection**	**Chronic weight management; obstructive sleep apnea associated with obesity**
Semaglutide (oral obesity version)	**Wegovy**	**2025**	**Once daily oral tablet**	**Chronic weight management**
Orforglipron	**Foundayo**	**2026**	**Once daily oral tablet**	**Obesity / chronic weight management**

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The Medications: GLP-1 **Semaglutide**

Brand Names:

- **Ozempic**: Type 2 DM (injectable: once weekly)
- **Rybelsus**: Type 2 DM (oral: once daily)
- **Wegovy**: Weight management (injectable: once weekly) and oral once weekly (25mg)
- **Wegovy HD**: Weight management (injectable: once weekly 7.2mg)



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The Medications: Dual Agonist: **Tirzepatide**

The only available GLP-1+GIP (dual agonist) drug

- Marketed as Mounjaro for type 2 diabetes
- Marketed as Zepbound for weight loss and OSA

Both are once weekly injections



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The Medications: GLP-1: **Orforglipron**

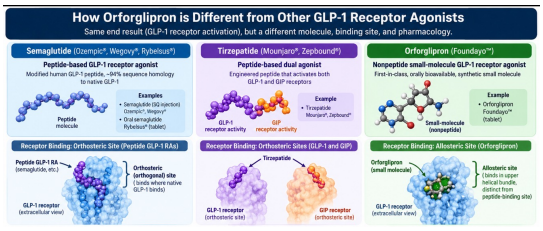
Brand name:

- Marketed as Foundayo for obesity/chronic weight management

Once daily oral tablet



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Orforglipron works on the same GLP-1 receptor as drugs like semaglutide, but it is built differently and interacts with the receptor differently.

Think of the GLP-1 receptor like a **door with different parts of the lock**:

- **Semaglutide and other peptide GLP-1 drugs** → are large, peptide molecules that interact primarily with the receptor's usual binding region.
- **Orforglipron** → is a much smaller, nonpeptide molecule that can enter the receptor and bind to a **different region (an allosteric site)**.

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Systemic and Ocular Risks of GLP-1RAs

System	Risk	Notes
GI	Nausea, vomiting, diarrhea, constipation	Common; mitigated with slow titration
Pancreatic	Acute pancreatitis	Rare; avoid in patients with a history of pancreatitis
Gallbladder	Cholelithiasis, cholecystitis	Especially with rapid weight loss
Retinal	Worsening diabetic retinopathy	Linked with semaglutide
Optic Nerve	NAION	Very rare but under active investigation
Renal	Acute kidney injury	Usually secondary to dehydration
Thyroid	Medullary thyroid carcinoma (MTC)	Contraindicated in multiple endocrine neoplasia type 2 (MEN-2)/MTC history
Glycemic	Hypoglycemia (with insulin/SUs)	Rare with monotherapy
GI Motility	Gastroparesis exacerbation	Contraindicated in severe cases
Psychiatric	Suicidal ideation	Under review (FDA, EMA, 2025)

https://www.aoa.org/AOA/Documents/Practice%20Management/Clinical%20Guidelines/AOA%20GLP-1_EBO_clinical-report.pdf

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Why Eye Care Should Care!!

- Explosive adoption in diabetes and obesity
- Visual complaints → urgent eye visits
- Emerging ocular signals



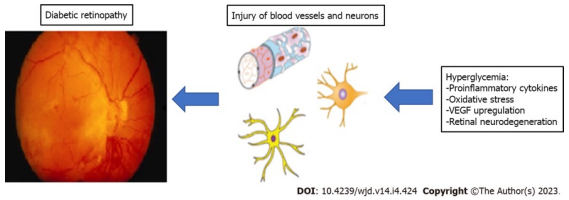
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Reported Ocular Effects

- **Diabetic retinopathy**
- NAION
- Idiopathic Intracranial Hypertension
- Glaucoma / IOP changes
- Other: refractive shifts, anti-inflammatory?
- Age Related Macular Degeneration
- Periorbital changes

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DR: Pathophysiology



DOI: 10.4239/wjd.v14.i4.424 Copyright ©The Author(s) 2023.

We need to avoid hyperglycemia!

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DR Trials

Trial	Drug	DR Findings
LEADER	Liraglutide (Victoza)	**No significant increase or decrease** in DR events overall
SUSTAIN 6	Semaglutide (inj)	⚠ **Increased risk** of diabetic retinopathy complications
PIONEER 6	Semaglutide (oral)	**No increase** in retinopathy events observed
REWIND	Dulaglutide (Trulicity)	**No significant effect** on DR progression; **substudy** looked at DR

https://www.aoa.org/AOA/Documents/Practice%20Management/Clinical%20Guidelines/AOA%20GLP-1_EBO_clinical-report.pdf

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SUSTAIN 6

Finding:

- 76 participants (3.0%) in semaglutide group vs 31 (1.8%) in placebo had **diabetic retinopathy complications**

Hazard ratio: 1.76 (significant)

Important Caveat: This effect was **mostly in patients with pre-existing DR (severe NPDR/PDR)**

EARLY WORSENING

SUSTAIN-6 (Marso, NEJM 2016)
Retinal photocoag, intravitreal therapy, vitreous hemorrhage all higher

A **hazard ratio** compares the **risk (hazard)** of an event happening at any time point in one group **relative to another group**.

HR = 1	No difference in risk between the two groups
HR > 1	**Higher risk** of the event in the treatment group
HR < 1	**Lower risk** of the event in the treatment group

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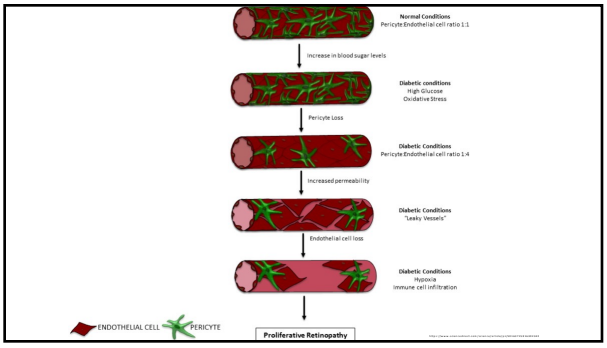
Why does it happen?

Rapid reduction in HbA1C:

- Retinal blood vessel changes
- Hypoxia and inflammation

(Similar to what is seen with intensive insulin therapy)

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TABLE 2. HIGH-RISK CHARACTERISTICS IN CARDIOVASCULAR TRIALS AND META-ANALYSES[17]

Risk factors associated with negative eye outcomes:
Higher hemoglobin A1c at GLP-1/GIP agonist treatment baseline.
Insulin use at GLP-1/GIP agonist treatment baseline.
Magnitude of hemoglobin A1c reduction with GLP-1/GIP agonist treatment.
Speed of hemoglobin A1c reduction with GLP-1/GIP agonist treatment.
Longer duration of diabetes (>10 years).
Older patient age (>60 years).

Who is at risk?

https://www.reviewofoptometry.com/article/glp1-gip-receptor-agonists-and-diabetic-retinopathy-what-ods-should-know

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Clinical Pearl

The **long-term effect of GLP-1 agonists on diabetic retinopathy is generally positive**. In some cases, they have been associated with either **stabilization or improvement** of retinopathy over time, primarily due to the sustained improvement in blood sugar control and associated reductions in **inflammation** and **oxidative stress**.

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Home › BMC Ophthalmology › Article

Assessing the risk of diabetic retinopathy progression with GLP-1 receptor agonists: a systematic review and meta-analysis

Systematic Review | Open access | Published: 30 June 2026
Volume 26, article number 583 (2026) Cite this article

2026 Meta-analysis: GLP-1 RAs and Diabetic Retinopathy

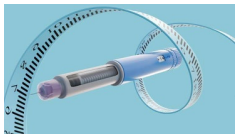
- 11 studies included
- Overall DR progression: **RR 1.07 (95% CI 0.90–1.28)**
- No statistically significant class-wide increase in DR progression
- Semaglutide remains the agent with the most inconsistent findings
- SUSTAIN-6: **RR 1.76 (95% CI 1.11–2.79)**
- Rapid glycemic improvement and pre-existing DR remain important clinical considerations

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2026 Update: Semaglutide, DR and NAION

Diabetic retinopathy

- FDA labeling continues to warn about diabetic retinopathy complications.
- Risk was greatest among patients with pre-existing diabetic retinopathy.
- Rapid improvement in glucose control can produce transient worsening of DR.
- 2026 labeling includes DR data from semaglutide tablets as well as established injectable data.



Clinical message: focus on baseline ocular risk, agent/formulation/dose, and speed of HbA1c reduction—not simply "GLP-1 = eye risk."

Sources: FDA Wegovy 2026 label; 2026 systematic review/meta-analysis of semaglutide and NAION; 2026 ocular-safety review.

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Practical DR Management

- Baseline exam (before starting or early on in usage)
  - Determine level of retinopathy
  - Moderate to severe NPDR more likely to progress to PDR within 1-2 years
    - Follow q3-4 months
- **Watch for worsening in the first 6–12 months**, especially if:
- Patient has existing DR or other discussed risk factors
- HbA1c drops rapidly (>1–2% in 3–6 months)
- Co-manage with ophthalmology for any moderate/severe DR.

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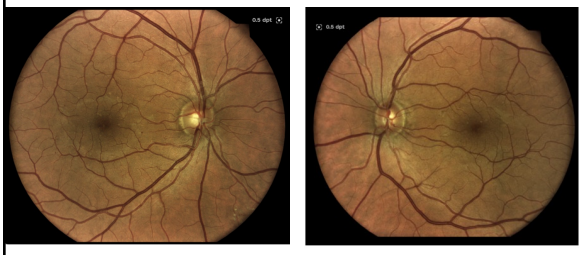
Case 1 — DR Early Worsening

- 58-year-old male
- **Type 2 diabetes** x 15 years
  - History of poorly controlled BS; HbA1c 10%
  - metformin and sulfonylurea
- Hypertension and Hyperlipidemia



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At presentation:

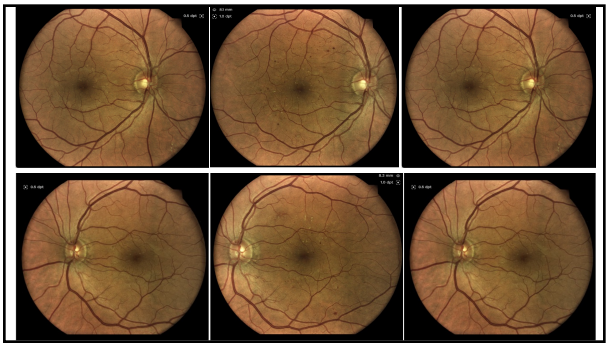


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Initiation of GLP-1

- Started on **liraglutide** to improve glycemic control and reduce weight.
  - His HbA1c dropped from **10% to 7.5%** within 3 months.
- 3 months after initiating liraglutide, the patient reported blurred vision and was found to have **progression of diabetic retinopathy.**

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Summary

- **Rapid glycemic improvement** after initiating a GLP-1 receptor agonist can lead to **worsening diabetic retinopathy**.
- ***Monitor retinal health*** *in patients starting GLP-1 therapy, especially for those with* ***pre-existing diabetic retinopathy***.

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Reported Ocular Effects

- Diabetic retinopathy
- **NAION**
- Idiopathic Intracranial Hypertension
- Glaucoma / IOP changes
- Other: refractive shifts, anti-inflammatory?
- Age Related Macular Degeneration
- Periorbital Changes

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Non-Arteritic Ischemic Optic Neuropathy

- **NAION** is the most common cause of **sudden, painless vision loss** in adults over 50
- Estimated US incidence 2.3-10.2 per 100,000 (W>B)

Semaglutide accounted for 86.5% of NAION cases among GLP-1 receptor agonists.

https://www.aoa.org/AOA/Documents/Practice%20Management/Clinical%20Guidelines/AOA%20GLP-1_EBO_clinical-report.pdf

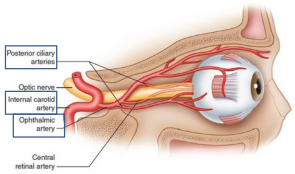
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Blood Supply to the ONH

Internal Carotid Artery

Ophthalmic Artery

Posterior Ciliary Artery



Circulation of the posterior ciliary artery is main source of blood supply to the ONH

Surface NFL: Supplied by retinal circulation

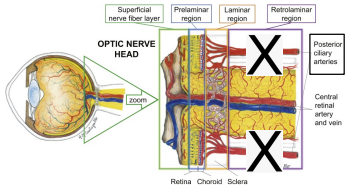
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Non-Arteritic Ischemic Optic Neuropathy

Internal Carotid Artery

Ophthalmic Artery

Posterior Ciliary Artery



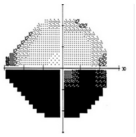
Caused by transient hypoperfusion or infarct within retrolaminar portion of ONH; supplied by the PCA

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What will patient's report (NAION)?

- Acute (sudden), painless vision loss
  - -Initially unilateral, may become bilateral
- Visual field loss: Altitudinal (half) or central -Inferior most common





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Clinical Signs (NAION):



- (+)APD
- VA varies widely; 20/200 or better
- Dyschromatopsia (correlates with vision)

- <u>Acute</u>: Optic Disc Edema:
  (Diffuse or Segmental)
  Hyperemic but not pallid (AAION)
  Peripapillary Splinter Hemorrhages



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What would put a patient at risk?

- Patient's medical history
- Patient's ocular history
- Medications

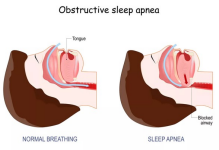
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Patient's **Medical** History

What would increase the risk of Optic Neuropathy?

❖Sleep Apnea

-BP drops as night: leads to exaggerated hypoxic episodes
-May result in chronic inflammation, oxidative stress and dysregulation of blood flow
-Could cause optic nerve edema and ischemia due to compromise of blood supply feeding the ONH



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Patient's **Medical** History

❖Nocturnal Hypotension

-Patients taking antihypertensive medications may be at increased risk, as such medications significantly lower nighttime systolic blood pressure, causing a larger percent difference between daytime and nighttime blood pressure when compared to normal diurnal blood pressure variations

❖Vasculopathic Risk Factors

-High blood pressure (50%)
-Diabetes (25%)
-Smoking
-Anemia
-Kidney disease

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Patient's **Ocular** History

What would increase the risk of Optic Neuropathy?

❖Structurally small disc

-Structural crowding---leads to ischemia
-Disc at risk

❖Optic Disc Drusen

-Contributes to the "crowded" optic nerve in discs with small cup to disc ratios.



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Patient's Ocular History: Medications??

Interferons:
- Group of glycoproteins with complex antiviral, antitumor, and antiangiogenic activities
- It has been hypothesized that interferon alpha might cause an NAION by depositing immune complexes in the optic disc circulation that leads to ischemia

Sildenafil:
- Treatment for erectile dysfunction (ED)
- Inhibits phophodiesterase type 5 (PDE5), an enzyme that regulates blood flow in the penis
- Can cause systemic hypotension

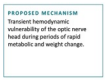
Amiodarone:
- Association underdetermined

Semaglutide/Tirzepatide:
- Though direct causation is not yet established, **several mechanisms are being proposed** to explain how semaglutide could elevate the risk of NAION in susceptible individuals

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Semaglutides: Pathophysiology

Mechanism	Description
Rapid glycemic control	Impairs autoregulation of optic nerve perfusion
Dehydration/volume depletion	GI side effects may lower blood volume and perfusion; reduces ONH perfusion
Shared comorbidities	Diabetes, hypertension may elevate baseline NAION risk



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And the studies....

Meta-Analysis > Graefes Arch Clin Exp Ophthalmol. 2026 Sep;264(9):2611-2621. doi: 10.1007/s00417-026-07291-4. Epub 2026 May 27.

Semaglutide and risk of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) in type 2 diabetes mellitus: A systematic review and meta-analysis

Stamatios Lampsas [1], Chryssa Agapitou [1], Evangelos Oikonomou [2], Gerasimos Siasos [2 3], Panagiotis Theodossiadis [1], Georgios Tsivgoulis [4], Vaia Lambadiari [5], Irini Chatziralli [6]

Affiliations + expand
PMID: 42201355 DOI: 10.1007/s00417-026-07291-4

One 2026 meta-analysis of 12 studies involving **14.3 million+ participants** with T2D reported:
- Semaglutide vs non-GLP-1 therapies:
  - **1-year HR 3.36** (95% CI 1.44–7.84)
  - **2-year HR 2.37** (95% CI 1.46–3.85)
  - 3-year sensitivity analysis: **HR 2.37** (95% CI 1.45–3.87)

But the heterogeneity was extremely high for the 1-year analysis (**I^2 = 97%**).

Conclusion: This meta-analysis indicates a significant association between semaglutide use and NAION in patients with T2DM compared to non-GLP-1RAs, with this association remaining significant even after 5-years of semaglutide use.

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And the studies....

> Front Pharmacol. 2026 Jun 2:17:1808359. doi: 10.3389/fphar.2026.1808359. eCollection 2026.

Ocular disorders during treatment with GLP-1 receptor agonists: a systematic review and meta-analysis of observational studies

Antonietta Arturiello [# 1 2], Valerio Liguori [# 1 2], Cecilia Cagnotta [1 2], Ciro Pentella [1 2], Cristina Scavone [1 2 3], Annalisa Capuano [1 2], Barbara Rinaldi [1]

Affiliations + expand
PMID: 42311413 PMCID: PMC13269103 DOI: 10.3389/fphar.2026.1808359

Another 2026 systematic review/meta-analysis of observational studies found:
- **NAION:** RR **1.01** (95% CI 0.42–1.64)
- **Glaucoma:** HR **0.84** (95% CI 0.71–1.00)
- **New-onset/progression of retinopathy:** HR **0.96** (95% CI 0.85–1.08)
- Another retinopathy progression analysis: HR **0.97** (95% CI 0.83–1.14)
- NAION heterogeneity: **I^2 = 89%**.

Conclusion: Even if no difference was observed between GLP-1 RAs and other antidiabetic medications for all safety outcomes evaluated, it is optimal to monitor the administration of these molecules.

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And the studies....

Meta-Analysis > Ophthalmology. 2026 Jun;133(6):709-810.
doi: 10.1016/j.ophtha.2026.02.013. Epub 2026 Feb 13.

Semaglutide and the Risk of Nonarteritic Ischemic Optic Neuropathy: A Systematic Review and Certainty of Evidence Meta-Analysis

Abdelaziz Abdelaal [1], Hashem Abu Serhan [2], Mustafa Alsaadi [2], Luke Yelds [3], Eric D Gaier [3], Abdelrahman M Elhusseiny [4]

Affiliations + expand

PMID: 41692115 DOI: 10.1016/j.ophtha.2026.02.013

And a separate 2026 evidence-certainty meta-analysis concluded that the overall observational evidence **does not demonstrate a consistent increase in NAION**, with substantial heterogeneity and low/very-low certainty. For T2D specifically, its pooled adjusted HR was **1.70 (95% CI 1.10–2.64)**, while obesity/overweight studies showed HR **0.47 (95% CI 0.19–1.13)**.

Conclusion: Across observational studies comparing semaglutide with non-GLP-1 RA therapies, pooled adjusted evidence does not demonstrate a consistent overall increase in NAION risk. However, estimates are limited by substantial heterogeneity, residual confounding, outcome misclassification, and fragility, resulting in low to very low certainty. Apparent indication-based differences should be interpreted cautiously and may reflect underlying disease-related risk rather than a drug-specific effect. Causality cannot be established, and further well-designed studies with standardized NAION ascertainment are needed.

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OD Management

- Counsel patients with disc-at-risk anatomy and vasculopathic risk factors.
- Any new monocular visual loss on therapy warrants urgent evaluation.
- Do not withhold semaglutide on NAION risk alone- the propensity-matched data do not support it.



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2026 Update: Semaglutide, DR and NAION



NAION

- NAION remains a rare but vision-threatening event under investigation.
- Recent reviews find the most consistent signal with higher-exposure subcutaneous semaglutide.
- Evidence is observational and heterogeneous; causality has not been established.
- Current evidence does not support class-wide prescribing restrictions.

Clinical message: focus on baseline ocular risk, agent/formulation/dose, and speed of HbA1c reduction—not simply "GLP-1 = eye risk."

Sources: FDA Wegovy 2026 label; 2026 systematic review/meta-analysis of semaglutide and NAION; 2026 ocular-safety review.

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Case: NAION

- 47-year-old Caucasian female
- Body Mass Index (BMI) of 27.92; no known personal history of diabetes, hypertension, or ischemic heart disease

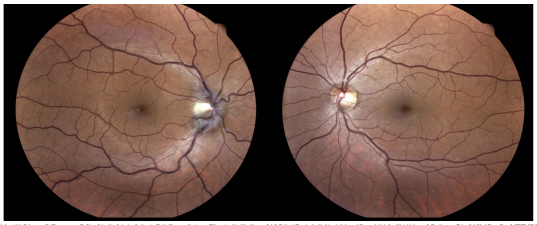
✅ BMI range: 18.5 – 24.9 kg/m²

- CC: 1-year history of progressive and severe visual acuity decline OD.
  - Started one month after initiating therapy with liraglutide for weight loss.
  - Dosage gradually increased every 10 days from 0.6 mg/day to 2.4 mg/day. After the onset of visual acuity decline, the patient underwent ophthalmological evaluation.

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Case: NAION

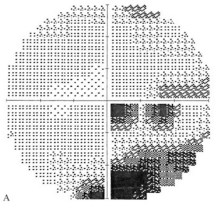
- BCVA: 20/40 OD, 20/20 OS
- Fundus exam: ONH swelling OD, vascular tortuosity



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Case: NAION

- 30-degree standard VF: **One month after the beginning of liraglutide therapy**:



Deep defect in the inferior hemifield, particularly in the inferotemporal quadrant, with partial involvement of the central field was detected, mean deviation (MD) of −6.87 dB

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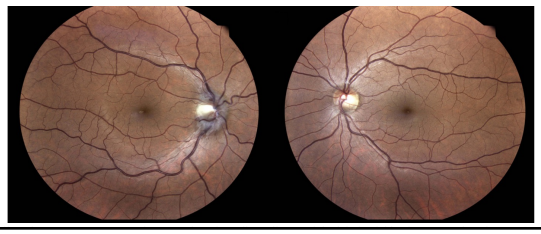
Case: NAION

- Oral corticosteroids (25 mg/day prednisone) initiated
  - Discontinued after one month due to poor glycemic control (blood glucose 135 mg/dL).
- Treatment was switched after four months from liraglutide to semaglutide (due to inadequate effect)
- The therapy began with 0.25 mg once weekly for one month, then increased to 0.50 mg weekly for additional 3 months.
- After an additional 8 months:
  - Patient's vision continued to decline, he discontinued weight loss therapy and presented to eye dr.

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Case: Sequelae

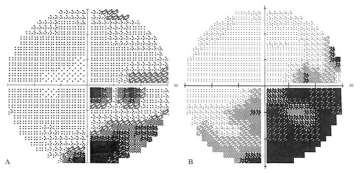
- BCVA: **20/400 OD**, 20/20 OS
- Fundus exam: ONH edema, prominent vascular tortuosity



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Case: Sequelae

- Eight months after the beginning of systemic therapy: lower altitudinal defect, with a deep scotoma in the inferotemporal quadrant, diffuse involvement of the inferonasal quadrant and extension into the central field, MD of –12.11 dB



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Pearls

- Remember your NAION risk factors
- Be familiar with presenting signs of disease
- Coach patients properly
- Co-manage!

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Reported Ocular Effects

- Diabetic retinopathy
- NAION
- **Idiopathic Intracranial Hypertension**
- Glaucoma / IOP changes
- Other: refractive shifts, anti-inflammatory?
- Age Related Macular Degeneration
- Periorbital changes

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Idiopathic Intracranial Hypertension

Definition: Idiopathic Intracranial Hypertension (IIH) is a condition of elevated intracranial pressure in the absence of an identifiable intracranial mass, structural abnormality, or hydrocephalus, with normal cerebrospinal fluid (CSF) composition and no other neurological causes.



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Idiopathic Intracranial Hypertension

12-week trial

Original Investigation

GLP-1 Receptor Agonists in Idiopathic Intracranial Hypertension

Georgios S. Sioutas, MD[1]; William Mualem, MD[1]; John Reavey-Cantwell, MD, MBA, MS[1] ; et al

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Key Points

Question Does glucagon-like peptide 1 receptor agonist (GLP-1 RA) therapy improve the management of idiopathic intracranial hypertension (IIH) compared with conventional therapies?

Findings In this cohort study using data from the TriNetX US Collaborative Network and involving 1110 propensity score–matched patients with IIH, GLP-1 RA therapy was associated with significantly lower medication use, fewer symptoms and signs, and reduced need for procedural interventions over a 1-year follow-up period.

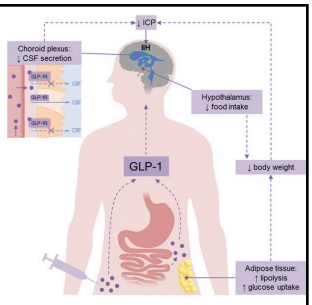
Meaning GLP-1 RA therapy may offer an alternative management strategy for IIH, warranting further prospective evaluation.

Conclusions and Relevance GLP-1 RA therapy in IIH is associated with significant reductions in medication use, symptoms/signs, and procedural interventions, suggesting its potential as a management strategy. Further prospective studies are warranted to confirm these findings.

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Pearls

- **GLP-1 RAs reduce intracranial pressure primarily by decreasing the production of CSF in the choroid plexus.**
  - Direct treatment for raised brain pressure
  - Disease modifying approach through driving weight loss in IIH.



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Reported Ocular Effects

- Diabetic retinopathy
- NAION
- Idiopathic Intracranial Hypertension
- **Glaucoma / IOP changes**
- Other: refractive shifts, anti-inflammatory?
- Age Related Macular Degeneration
- Periorbital changes

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Glaucoma/Ocular Hypertension

Question:

In people with or without Type 2 Diabetes Mellitus , does use of GLP-1 receptor agonists affect the incidence (risk) of developing glaucoma, compared to non-use or to other antihyperglycemic agents?

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There are actually **three separate questions** emerging:

1. Do GLP-1 RAs increase glaucoma risk?
Current evidence does **not** support that. The newer observational studies generally show either no association or a lower observed incidence of POAG/OHTN.

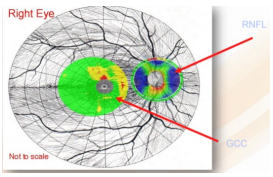
2. Do GLP-1 RAs lower IOP?
Not convincingly. The IOP study found only a very small reduction, and that association disappeared after multivariable adjustment.

3. Could GLP-1 drugs have neuroprotective effects in glaucoma?
This is probably the **most interesting research question**, but it remains investigational. GLP-1 receptors are present in ocular tissues, and preclinical work has suggested potential neuroprotective, anti-inflammatory, and mitochondrial effects. The clinical observational data are now beginning to generate a signal, but they don't establish that GLP-1 therapy prevents glaucoma or slows glaucomatous progression.

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Pathophysiology: Why Might GLP-1 RAs Be Protective

Glaucoma is neuro-degenerative disease involving progressive loss of retinal ganglion cells and optic nerve damage



GLP-1 RAs located on RGCs and directly protect them from death and injury

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GLP-1 Receptor Agonists & Glaucoma: Emerging Evidence

- Recent observational studies **do not demonstrate increased risk of POAG or ocular hypertension**
- Some large database studies suggest **lower incidence of POAG/OHTN** among GLP-1 RA users
- Tirzepatide has been associated with **lower incident POAG compared with GLP-1 RAs** in two 2026 retrospective studies
- Small reductions in IOP have been reported, but **no convincing independent IOP-lowering effect**
- Possible mechanisms include **GLP-1 receptor–mediated neuroprotection, reduced neuroinflammation, and metabolic effects**
- **Causality has not been established**
- Prospective studies with standardized **IOP, RNFL/GCC, visual field, and glaucoma progression endpoints** are needed

Bottom line: *Current evidence does not suggest that GLP-1 therapy increases glaucoma risk; emerging observational data raise the possibility of a protective association, but this remains investigational.*

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Take home message

- This raises the possibility that GLP-1 RAs may one day be explored as a neuroprotective agent in glaucoma.
- Current evidence suggests that **GLP-1 receptor agonists are not associated with increased risk of glaucoma—in fact, several large studies point to a **protective effect**, especially with long-term use.

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Reported Ocular Effects

- Diabetic retinopathy
- NAION
- Idiopathic Intracranial Hypertension
- Glaucoma / IOP changes
- **Other: refractive shifts, anti-inflammatory?**
- Age Related Macular Degeneration
- Periorbital changes

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Transient Refractive Shifts: Blood Glucose, Not GLP-1 Agents

- While GLP-1 and GIP receptor agonists don't inherently shift refractive state, they **can rapidly lower blood glucose and HbA1c**.
  - This may provoke **transient refractive changes**, particularly in **patients with long-standing poorly controlled diabetes**
  - During the **initial phase** of treatment, when glucose drops are most pronounced

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Case: Transient Refractive Shift

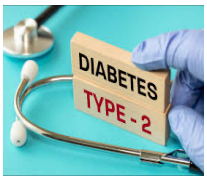
- A 56-year-old male presented for evaluation of bilateral blurry vision that started 1 week prior
- He stated that if he adjusted his head to look through the bifocal portion of his glasses, this improved his vision.
- LEE: 1 year prior; unremarkable



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Case Details

- POH:
  - Myopia OU
  - Presbyopia OU
  - Mild cataracts
- PMH:
  - Sleep apnea
  - Type 2 DM
    - HbA1C 8% and BS 130;
      - Achieved with semaglutide
    - One-year prior 12%, 162
      - Metformin 1000mg bid



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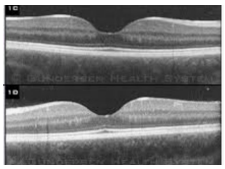
Exam Findings

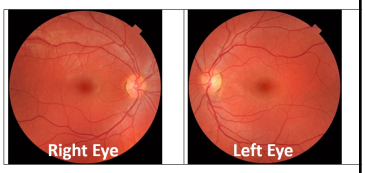
- BCVA OD 20/250 PH 20/25-, OS 20/125 PH 20/25-
  - Lensometry: -0.50 DS OD, pl-0.50x012 DS OS
  - Manifest refraction: +2.25-0.25x165 DS OD 20/20
    +2.00-0.50x100 DS OS 20/20

Remainder of ocular examination unremarkable

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OCT and fundus appearance normal





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8/2023	• OD -0.50 DS • OS -0.75-0.50x100	20/20 20/20	Glucose: 128 A1C 8.0%
8/2024	• OD -0.50 DS • OS -1.00-0.50x100	20/20 20/20	Glucose: 192 A1C 8.1%

Patient was sent to PCP. Semaglutide was initiated

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12/2024	• OD +2.25DS • OS +2.00-0.50x100 Blurry vision	20/20 20/20	Glucose: 163 A1C 7.0%
3 weeks later	• OD+0.25-0.25x100 • OS pl-0.50x100	20/20 20/20	Glucose: 103 A1C 7.0%
1 month later	• OD -0.75DS • OS pl-0.50x100	20/20 20/20	Glucose: 103 A1C 7.2%

Medication indirectly brought rx back to baseline:
BS normalization

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Management

- Investigation for other causes of hyperopic shift with corneal topography, optical coherence tomography, complete eye exam, ocular ultrasound or imaging if needed
- If all other causes ruled out; better glycemic control (in conjunction with primary care provider)
- Close follow-up
- Defer dispensing final rx until refraction and BS have normalized

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Reported Ocular Effects

- Diabetic retinopathy
- NAION
- Idiopathic Intracranial Hypertension
- Glaucoma / IOP changes
- **Other: refractive shifts, anti-inflammatory?**
- Age Related Macular Degeneration
- Periorbital changes

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Anti-Inflammatory-Uveitis??

JAMA Ophthalmology

Original Investigation 2025 in *JAMA Ophthalmology*

Glucagon-Like Peptide-1 Receptor Agonists and Risk of Uveitis

Nitesh Mohan, BS[1,2,3]; Sunil K. Srivastava, MD[1,4]; Matthew J. Schulgit, BS[1,2,3]; et al

84

Key Points

Question Is the use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) associated with a reduced risk of developing non-infectious uveitis?

People prescribed GLP-1RAs had about a **52% lower risk of uveitis** than controls (**risk ratio 0.48**).

Lower risk in patients with and without diabetes

Compared with **metformin** and **insulin**, GLP-1RAs appeared more protective. Compared with **SGLT2 inhibitors**, however, GLP-1RAs had a **slightly higher** uveitis risk. SGLT2 inhibitors also showed reduced risk overall.

The authors suggested GLP-1 medications may have **anti-inflammatory effects beyond blood sugar control**, which could potentially reduce the risk of inflammatory eye disease.

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Published May 4, 2026

Long-term Uveitis Risk of GLP-1 Users Impacts Women More than Men

A recent study over a five-year follow-up period suggests potential sex-related differences in condition susceptibility, which may reflect underlying differences in immune-mediated responses to therapy.

Researchers looked at adults age 40+ with type 2 diabetes who were taking GLP-1 medications to see whether men and women developed **uveitis** at different rates over time.



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Main Findings

At **1 year**, men and women had **similar uveitis risk**; men showed a slightly lower risk, but it wasn't statistically significant.

At **3 years and 5 years**, **men had a significantly lower risk** of developing uveitis compared with women.

The study suggests **women taking GLP-1 drugs may have greater long-term susceptibility** to uveitis.

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Why?

Possible explanation:
The researchers think **sex-related immune differences** may influence how GLP-1 therapies interact with inflammation pathways. They also noted that previous research already shows **women generally develop uveitis more often than men**, so GLP-1 use may reflect or amplify that pattern.



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Conclusions and Relevance:



• This cohort study found that GLP-1RA prescriptions were associated with a lower risk of uveitis compared with controls. These findings suggest potential anti-inflammatory benefits beyond glycemic control, warranting further investigation into their role in ocular inflammatory diseases.

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Reported Ocular Effects

- Diabetic retinopathy
- NAION
- Idiopathic Intracranial Hypertension
- Glaucoma / IOP changes
- Other: refractive shifts, anti-inflammatory?
- **Age Related Macular Degeneration**
- Periorbital changes

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Summary Points

GLP-1 RA → AMD
- 🟢 **Dry/nonexudative AMD:** emerging evidence of a *possible protective association*
- 🟡 **Progression of AMD:** some observational evidence suggesting reduced progression
- 🟡 **Neovascular AMD:** evidence is inconsistent/mostly neutral
- 🔴 **Proof of prevention or treatment: none yet**
- 🔬 **Prospective randomized studies:** needed

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Summary Points

GLP-1RA users had a **lower incidence of nonexudative (dry) AMD** than non-users.
Among patients who already had early or intermediate AMD, GLP-1RA use was associated with a **lower risk of progression to advanced AMD**.

Proposed Mechanisms:
Anti-inflammatory effects
Neuroprotective effects
Promotion of retinal neuronal survival

These mechanisms could potentially slow retinal degeneration and AMD progression.

92

Exudative AMD: Is there a risk?

Comment > JAMA Ophthalmol. 2025 Jul 1;143(7):587-594.
doi: 10.1001/jamaophthalmol.2025.1455.

Glucagon-Like Peptide-1 Receptor Agonists and Risk of Neovascular Age-Related Macular Degeneration

Reut Shor [1], Andrew Mihalache [2], Atefeh Noori [3], Renana Shor [4], Radha P Kohly [1], Marko M Popovic [1], Rajeev H Muni [1, 5]

Affiliations + expand
PMID: 40471562 PMCID: PMC12142475 (available on 2026-06-05)
DOI: 10.1001/jamaophthalmol.2025.1455

A very large **2026 semaglutide-specific study** looked specifically at **neovascular AMD** in 227,971 new semaglutide users with T2DM. It found **no evidence that semaglutide either increased or decreased NVAMD risk** compared with other GLP-1 RAs or non-GLP-1 medications.

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Summary Statement: AMD

Studies show that patients without any AMD could be protected from developing dry AMD if they take GLP-1 drugs for either diabetes or weight loss; however, there is still no conclusive indication that treatment is beneficial or harmful with regards to wet AMD.



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Reported Ocular Effects

- Diabetic retinopathy
- NAION
- Idiopathic Intracranial Hypertension
- Glaucoma / IOP changes
- Other: refractive shifts, anti-inflammatory?
- Age Related Macular Degeneration
- **Periorbital changes**

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(*Ophthalmic Plast Reconstr Surg* 2025;XX:00–00)

ORIGINAL INVESTIGATION

Periorbital Changes Following Glucagon-Like Peptide-1 Receptor Agonist Use: A Retrospective Cohort Study of Oculofacial Complications and Interventions

Persiana S. Saffari, M.D., M.S., Natalia Davila, B.S.*,†, Tejus Pradeep, M.D.*, Brian Wong, M.D.†, and Wendy W. Lee, M.D., M.S.**

**Division of Ophthalmic Plastic and Reconstructive Surgery, Bascom Palmer Eye Institute, University of Miami, Miami, Florida, U.S.A.; and †Division of Oculoplastics, University of Texas Medical Branch, Galveston, Texas, U.S.A.*

Compared people using **GLP-1 receptor agonists** with similar people who were not using them. They looked for periorbital changes including:
- **Brow ptosis** → eyebrows sitting lower
- **Dermatochalasis** → excess/loose upper eyelid skin
- **Blepharoptosis** → droopy upper eyelids
- **Entropion / ectropion** → eyelids turning inward or outward
- Cosmetic or corrective procedures:
  - Botox use
  - eyelid procedures
  - facial interventions

They analyzed separate groups with **obesity** and **type 2 diabetes**

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TABLE 2. Rate of eyelid, brow, and skin pathologies and repairs in patients with T2DM who have used GLP-1RA and those with T2DM who are GLP-1RA naive between April 28, 2005, and December 31, 2024

Variable	GLP-1 RA use	GLP-1 RA naive	RR	95% CI	*p*
Blepharoptosis	2,233 (0.673%)	2,823 (0.850%)	−8.826	(−0.002, −0.001)	<0.001
Brow ptosis	465 (0.139%)	363 (0.109%)	3.553	(<0.001, <0.001)	<0.001
Dermatochalasis	2,029 (0.611%)	2,543 (0.764%)	−7.551	(−0.002, −0.001)	<0.001
Ectropion/entropion	882 (0.265%)	1,479 (0.443%)	−12.32	(<−0.002, <−0.002)	<0.001
Repair of blepharoptosis	366 (0.110%)	381 (0.114%)	−0.544	(>−0.001, <0.001)	0.587
Repair of brow ptosis	166 (0.050%)	143 (0.043%)	1.31	(>−0.001, <0.001)	0.190
Blepharoplasty	479 (0.144%)	478 (0.143%)	0.041	(>−0.001, <0.001)	0.967
Repair of Ectropion/entropion	233 (0.070%)	362 (0.108%)	−5.291	(>−0.001, <−0.001)	<0.001
Rhytidectomy	46 (0.0138%)	40 (0.0120%)	0.647	(>−0.001, <0.001)	0.518
Botulinum toxin A	3,451 (0.010%)	3,174 (0.009%)	3.420	(>0, <0.001)	0.001

CI, confidence interval; GLP-1RA, glucagon-like peptide-1 receptor agonists; RR, relative risk; T2DM, type 2 diabetes mellitus.

© 2025 The American Society of Ophthalmic Plastic and Reconstructive Surgery, Inc.

For patients with **type 2 diabetes using GLP-1 drugs**:
•More likely to develop **brow ptosis**
•More likely to receive **Botox treatments** afterward

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TABLE 4. Rate of eyelid, brow, and skin pathologies and repairs in patients with obesity who have used GLP-1RA and those with obesity who are GLP-1RA naive between June 4, 2021, and December 31, 2024

Variable	GLP-1 RA use	GLP-1 RA naive	RR	95% CI	*p*
Blepharoptosis	575 (0.214%)	542 (0.201%)	1.007	(>−0.001, <0.001)	0.314
Brow ptosis	166 (0.061%)	117 (0.043%)	2.917	(>0, <0.001)	0.004
Dermatochalasis	446 (0.165%)	347 (0.128%)	3.536	(>0, <0.001)	<0.001
Ectropion/entropion	114 (0.042%)	171 (0.063%)	−3.377	(>−0.001, <0)	0.001
Repair of blepharoptosis	113 (0.042%)	74 (0.027%)	2.854	(>0, <0.001)	0.004
Repair of brow ptosis	78 (0.029%)	42 (0.016%)	3.288	(>0, <0.001)	0.001
Blepharoplasty	197 (0.073%)	118 (0.044%)	4.458	(>0, <0.001)	<0.001
Repair of Ectropion/entropion	30 (0.011%)	54 (0.019%)	−2.619	(>−0.001, <0)	0.009
Rhytidectomy	25 (0.009%)	10 (0.003%)	2.536	(>0, <0.001)	0.011
Botulinum toxin A	3,992 (0.015%)	2,411 (0.009%)	19.876	(0.005, 0.006)	<0.001

CI, confidence interval; GLP-1RA, glucagon-like peptide-1 receptor agonists; RR, relative risk; T2DM, type 2 diabetes mellitus.

For patients with **obesity using GLP-1 drugs**:
•More likely to develop:
- **brow ptosis**
- **dermatochalasis (looser eyelid skin)**

•More likely to receive **Botox treatments** afterward

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Summary Points

The study did **not** prove the drug itself damages tissues around the eyes.

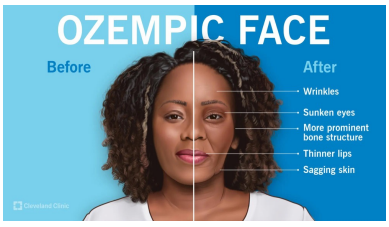
The leading explanation is:
- GLP-1 drugs → significant weight loss
- Rapid loss of facial fat volume
- Less support under the skin around the eyes
- Brow lowering, hollowing, loose skin, more visible aging changes

That aligns with the broader idea often called **"Ozempic face"**: facial volume loss after rapid weight reduction.

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What about Ozempic Face?

Aesthetic issues associated with rapid weight loss induced by these medications



https://health.clevelandclinic.org/ozempic-face

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And the others.....

AUG 20, 2025

Semaglutide May Be Associated With Increased Risk of Many Ocular Adverse Events



By Jason H Peragallo, MD

Comprehensive Ophthalmology, Neuro-Ophthalmology/Orbit, Retina/Vitreous

Significantly elevated odds of retinal detachment, retinal hemorrhage, retinal tear, vitreous detachment, vitreous hemorrhage, papilledema, macular edema and macular hole.

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Newer GLP-1 Agents: Ocular Safety Snapshot

What we know now — and what remains uncertain

Agent / formulation	Current ocular signal	What the evidence supports	Clinical point
Semaglutide injection (including Wegovy HD)	DR worsening; NAION signal under investigation	FDA labeling warns about DR complications, especially with pre-existing DR and rapid HbA1c improvement. Recent literature continues to report a possible NAION association, particularly with higher-exposure SC semaglutide.	Association ≠ causation. Monitor high-risk patients and counsel about sudden vision loss.
Semaglutide tablets (Wegovy tablets)	DR monitoring; NAION evidence limited	FDA labeling includes DR monitoring. Current evidence does not establish a class-wide NAION risk for oral semaglutide.	Watch for rapid glycemic improvement and baseline DR.
Tirzepatide (Mounjaro / Zepbound)	Retinal/NAION outcomes generally reassuring	A 2026 cohort study found lower risks of retinal complications, vision-saving interventions and NAION versus GLP-1 RAs without GIP activity; prospective confirmation is still needed.	Do not present this as proven protection.
Orforglipron (Foundayo)	DR monitoring; direct NAION signal not established	FDA labeling warns that rapid glucose improvement may temporarily worsen DR and recommends monitoring patients with a history of DR. Direct NAION evidence is currently unavailable.	New agent → formulation-specific postmarketing surveillance is important.

Sources: FDA 2026 prescribing information; FDA Foundayo label; 2026 ocular-safety review; 2026 tirzepatide ocular outcomes study.

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Practical Eye-Care Takeaways for Newer GLP-1 Therapies

- Ask which GLP-1/GIP agent, formulation, dose, and indication the patient is taking.
- Document baseline diabetic retinopathy status when clinically appropriate—especially before major glycemic intensification.
- Patients with established DR should be monitored for progression during periods of rapid glucose improvement.
- Sudden painless vision loss, new field loss, or optic-disc edema warrants urgent evaluation for NAION or another optic neuropathy.
- Do not assume that a newly approved formulation has the same ocular evidence base as an older formulation.
- Counsel patients that reported associations do not establish that the medication caused an ocular event.

Sources: FDA 2026 prescribing information; 2026 ocular-safety review; 2026 tirzepatide ocular outcomes study.

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Thank you!

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