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Semaglutide and Risk of Non-arteritic Anterior Ischemic Optic Neuropathy: Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202530110

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 March 2025 and was last updated on 25 March 2025.

INTRODUCTION

Review question / Objective What is the risk of non-arteritic anterior ischemic optic neuropathy in patients receiving semaglutide?

Condition being studied Semaglutide, a GLP-1 receptor agonist used for diabetes and obesity, has recently been linked to rare but serious ocular events. Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in adults, and concerns have emerged about its potential association with semaglutide use.

METHODS

Search strategy A comprehensive search of PubMed and Embase will be conducted on March 26, 2025, using the keywords "semaglutide" and "NAION," with no restrictions on language or publication date. An updated search may be

performed prior to manuscript submission to ensure inclusion of the most recent studies. A comprehensive search of PubMed and Embase will be conducted on March 26, 2025, using the keywords "semaglutide" and "NAION," with no restrictions on language or publication date. An updated search may be performed prior to manuscript submission to ensure inclusion of the most recent studies. A comprehensive search of PubMed and Embase will be conducted on March 26, 2025, using the keywords "semaglutide" and "NAION," with no restrictions on language or publication date. Updated search may be necessary before the manuscript submission.

Participant or population The population of interest includes individuals with (1) type 2 diabetes (T2D) or (2) obesity or overweight.

Intervention Semaglutide.

Comparator Active comparator or non-user group.

Study designs to be included Cohort studies.

Eligibility criteria For studies with overlapping populations from the same data source, only the one with the longer inclusion period is retained. When studies included multiple drug comparisons, we will extract only the results related to sodium-glucose cotransporter 2 (SGLT2) inhibitors, as these comparisons typically involve more homogeneous populations.

Information sources Pubmed and Embase.

Main outcome(s) NAION, as reported by hazard ratio between semaglutide and comparator group.

Quality assessment / Risk of bias analysis The risk of bias in cohort studies will be assessed using the Newcastle Ottawa Scales.

Strategy of data synthesis Mantel-Haenszel Hazard Ratio (MH-HR) for time-to-event variables will be calculated and displayed as forest plots, using random-effect models.

Subgroup analysis T2D and obesity or overweight.

Sensitivity analysis None.

Country(ies) involved Taiwan.

Keywords semaglutide, non-arteritic anterior ischemic optic neuropathy, cohort studies.

Contributions of each author

Author 1 - Eugene Yu-Chuan Kang. Author 2 - Shih-Chieh Shao.