VISION ACADEMY VIEWPOINT

The Vision Academy is a partnership between Bayer and ophthalmic specialists, established with the aim of addressing key clinical challenges in the field of retinal diseases: www.visionacademy.org.

A Novel Tool to Assess the Quality of RWE to Guide the Management of Retinal Disease

Background

Although randomized controlled trials (RCTs) are designed to generate robust data, their tightly controlled experimental designs and rigorous participant selection criteria present difficulties when extrapolating the relevance of the data to the real-world setting.[1] For this reason, real-world evidence (RWE) is increasingly important; it complements RCTs in informing regulatory decisions and contributing to the development of clinical guidelines and clinical trial designs.[2] RWE studies can capture information not possible with RCTs, such as longitudinal safety, adherence, and outcomes data, and additional endpoints in patients that more reliably reflect the general population.

However, RWE may lack standardization, as data are often compiled from multiple sources using varying data collection methods, and reflect heterogeneous patient populations which can lead to biases.[3]

There is therefore a need for global consensus among the ophthalmic community on how to assess the quality of RWE to ensure that clinical decision-making in neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), and retinal vein occlusion (RVO) is based on the highest-quality evidence.

This Vision Academy Viewpoint describes a retinal disease-specific data quality assessment tool, adapted from the Good ReseArch for Comparative Effectiveness (GRACE) checklist (with permission) to ensure relevance to the ophthalmic community.[4]

Developed by the Real-World Evidence Steering Committee in May 2021

Viewpoint

- The GRACE checklist is a previously published,[5] extensively validated, RWE quality checklist that was adapted, with permission from the original authors, to be made specific to retinal disease
- The resulting tool consists of a series of Yes/No questions that should be answered when considering a RWE study. These quality assessment questions evaluate the strength of ophthalmic RWE and are organized into four categories: treatment details, outcome measures, study population, and controlling for bias
- If the majority of the checklist responses are marked as 'Yes', the RWE is likely to be of a high quality and can be relied upon to inform clinical decision-making

December 2024 | MA-PFM-OPHT-ALL-0374-1

Code: VA_016

Retinal disease-specific tool to evaluate the quality of RWE

	Quality assessment question	Retinal disease-specific considerations	Checklist
Treatment details	Were important details of treatment exposure adequately recorded for the study purpose in the data source(s)?	• Important details should include the treatment name, dose, strategy/regimen (e.g. treat-and-extend), and duration	**YES** **NO**
Outcome measures	Were the primary outcomes adequately recorded for the study purpose (can the primary outcome adequately address the research question)?	• Change in visual acuity from baseline as a measure of treatment effectiveness is an example of an appropriate use of outcomes	**YES** **NO**
	Was the primary outcome measured objectively, and adjudicated/validated where required?	• Objective methods to measure outcomes include use of ETDRS (Early Treatment Diabetic Retinopathy Study) letters to measure visual acuity and independent adjudication of optical coherence tomography images	**YES** **NO**
	Were outcomes measured or identified in an equivalent manner between treatment groups?	• Wherever possible, outcomes should be measured using the same method, such as using either ETDRS letters or logMAR uniformly with or without correction to measure visual acuity • Use of different methods may be necessary in some cases, e.g. if optical coherence tomography equipment varies across treatment sites	**YES** **NO**
Study population	Was the study population relevant to the research question and clinical practice?	• To ensure results are translatable, the study population should be reflective of patients seen in clinical practice (e.g. inclusive of both treatment-experienced and treatment-naïve patients) • Injection frequency, duration of prior therapies, and response should be reported for treatment-experienced patients	**YES** **NO**
	If one or more comparison groups were used, were they concurrent comparators? If not, did the authors justify the use of historical comparison group(s)?	• Use of historical comparison groups is often not justified • Due to significant changes in the management of retinal disease over time, the use of historical comparators may significantly reduce the quality of the data	**YES** **NO**
Controlling for bias	Were important covariates, confounding, and effect-modifying variables taken into account in the design and/or analysis?	• Appropriate statistical adjustments should be carried out to minimize the risk of bias from confounding factors that may affect outcomes between treatment groups • Potential confounding variables in retinal disease include age, gender, concomitant conditions and treatments, smoking status, baseline visual acuity, and bilateral involvement • DME-specific variables that may affect outcomes include diabetes disease characteristics (e.g. glycemia), blood pressure, and macular edema characteristics (e.g. macular thickness) • nAMD-specific variables that may affect outcomes include polypoidal choroidal vasculopathy and duration of visual symptoms • RVO-specific variables that may affect outcomes include duration of macular edema and resulting photoreceptor damage	**YES** **NO**
	Were any meaningful analyses conducted to test key assumptions on which primary results are based?	• Sensitivity, subgroup, or stratified analyses may improve the robustness of the findings	**YES** **NO**

Table adapted from Finger RP *et al. Acta Ophthalmol* 2020 [epub ahead of print]. DOI: 10.1111/aos.14698.

Further considerations

The retinal disease-specific tool described here can be used to facilitate individual assessments of RWE quality to inform clinical practice. However, although this tool has been adapted from the GRACE guidelines (which have been extensively validated), validation of the revised tool through a robust method such as a Delphi consensus would be beneficial to confirm its utility.

References

1. Mehta H, Tufail A, Daien V *et al.* Real-world outcomes in patients with neovascular age-related macular degeneration treated with intravitreal vascular endothelial growth factor inhibitors. *Prog Retin Eye Res* 2018; 65: 127–146.
2. US Food and Drug Administration. Real-world evidence. Available at: https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence. Accessed January 2021.
3. Garrison LP, Jr., Neumann PJ, Erickson P *et al.* Using real-world data for coverage and payment decisions: the ISPOR Real-World Data Task Force report. *Value Health* 2007; 10 (5): 326–335.
4. Finger RP, Daien V, Talks JS *et al.* A novel tool to assess the quality of RWE to guide the management of retinal disease. *Acta Ophthalmol* 2020 [epub ahead of print].
5. Dreyer NA, Bryant A and Velentgas P. The GRACE checklist: a validated assessment tool for high quality observational studies of comparative effectiveness. *J Manag Care Spec Pharm* 2016; 22 (10): 1107–1113.

Vision Academy Viewpoints are intended to raise awareness of a clinical challenge within ophthalmology and provide an expert opinion to engage in further discussion.
They can be downloaded from https://www.visionacademy.org/resource-zone/resources/all
The Vision Academy is sponsored by Bayer. This document was prepared by the Real-World Evidence Steering Committee, all of whom are members of the Vision Academy.
Always refer to local treatment guidelines and relevant prescribing information.
The views represented in this document do not necessarily reflect those of Bayer.
December 2024 | MA-PFM-OPHT-ALL-0374-1

Code: VA_016