# PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<u>see an example</u>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

## **ARTICLE DETAILS**

TITLE (PROVISIONAL)	Current treatments in Diabetic Macular Oedema: systematic review
	and meta-analysis
AUTHORS	Ford, John; Lois, Noemi; Royle, Pamela; Clar, Christine;
	Shyangdan, Deepson; Waugh, Norman

## **VERSION 1 - REVIEW**

REVIEWER	Dr Victoria Allgar Senior Lecturer in Medical Statistics. Hull and York Medical School, University of York, England.
	I have no conflicts of interest.
REVIEW RETURNED	20-Nov-2012

THE STUDY	Although there is a small section relating to the analysis appoach in the methodology, but it is qiute limited in detail. This needs to be expanded to include the rationale for the random effects models, Statistical heterogeneity etc This is discussed in places thoughout the results section, but would be better placed by a fuller decription in the methodology.
RESULTS & CONCLUSIONS	Overall the results of the meta analyese are clear. There is a large amount of discussion on the results of the individual studies. These could be removed to reduce the word count and length of the results section, and the focus be on the meta analysis specifically.
GENERAL COMMENTS	The paper needs a few sections moving about from results to methodology. The results section could be simplified to focus on the meta analysis.

REVIEWER	Sobha Sivaprasad
	Consultant in Medical Retina
	Moorfields Eye Hospital
	London
	United Kingdom
	I have participated in advisory boards of Allergan, Alimera Sciences, Novartis, Bayer and Pfizer. I have received travel grants and research grants from Allergan, Novartis, Bayer and Pfizer
REVIEW RETURNED	23-Dec-2012

GENERAL COMMENTS	In he section of evidence acquisition, please summarize it to a paragraph.
	There is also a repeat of diabetic macular oedema in search item

REVIEWER	Sven Crafoord
	Ass. professor
	MD. PhD.
	Senior consultant
	Dept. of Ophthalmology
	Örebro University Hospital, School of Health and Medical Sciences,
	Örebro University
	SE-701 85 Örebro, Sweden
	No conflict of interest or competing interests.
REVIEW RETURNED	15-Jan-2013

This is an extensive summory of current treatments in diabetic macular edema very much needed and surched for by treating doctors in ophthalmology. You are to be congratulated for putting all the energy in doing this metaanalysis and for describing all the defferent options so extensively.  The paper adresses a review of almost all current treatment options for a complex progressive and hard to treat disease. The method for doing this review is scientifically good. All the mentioned methods of treatment are well explained and discussed. Focus is on the anti-VEGF, laser and steroid treatments. A thorough description and discussion of costs and complications is also added. The only treatment alternatives I miss is vitreoretinal surgery. Some cases will do better after removal of posterior hyaloid and possibly ILM and I think you could add a few words concerning these results. Also
worth mentioning is medical treatment of elevated bloodpressure as a role in treating macular edema.

#### **VERSION 1 – AUTHOR RESPONSE**

Reviewer: Dr Victoria Allgar Senior Lecturer in Medical Statistics. Hull and York Medical School, University of York, England.

I have no conflicts of interest.

Although there is a small section relating to the analysis approach in the methodology, but it is quite limited in detail. This needs to be expanded to include the rationale for the random effects models, Statistical heterogeneity etc... This is discussed in places throughout the results section, but would be better placed by a fuller description in the methodology.

Overall the results of the meta analyse are clear. There is a large amount of discussion on the results of the individual studies. These could be removed to reduce the word count and length of the results section, and the focus be on the meta analysis specifically.

The paper needs a few sections moving about from results to methodology. The results section could be simplified to focus on the meta analysis.

Authors: Clearer discussion about the methods of the methodology added. We do not want to place too much weight on the meta-analysis since it does not include important studies and we do not want readers to be only concerned with the meta-analysis of a few of the included studies.

Reviewer: Sobha Sivaprasad

Consultant in Medical Retina Moorfields Eye Hospital London United Kingdom

I have participated in advisory boards of Allergan, Alimera Sciences, Novartis, Bayer and Pfizer. I have received travel grants and research grants from Allergan, Novartis, Bayer and Pfizer

In the section of evidence acquisition, please summarize it to a paragraph.

There is also a repeat of diabetic macular oedema in search item

Authors: This seems at odds with Dr Allgar's comments. We would prefer to leave the detailed description of the methods. Thank you for spotting the repetition of "diabetic macular oedema". One of these should read "diabetic macular edema". Text amended.

Reviewer: Sven Crafoord

Ass. professor MD. PhD.

Senior consultant

Dept. of Ophthalmology

Örebro University Hospital, School of Health and Medical Sciences, Örebro University

SE-701 85 Örebro, Sweden

No conflict of interest or competing interests.

#### Dear authors.

This is an extensive summary of current treatments in diabetic macular edema very much needed and searched for by treating doctors in ophthalmology. You are to be congratulated for putting all the energy in doing this metaanalysis and for describing all the different options so extensively. The paper addresses a review of almost all current treatment options for a complex progressive and hard to treat disease. The method for doing this review is scientifically good. All the mentioned methods of treatment are well explained and discussed. Focus is on the anti-VEGF, laser and steroid treatments. A thorough description and discussion of costs and complications is also added. The only treatment alternatives I miss is vitreoretinal surgery. Some cases will do better after removal of posterior hyaloid and possibly ILM and I think you could add a few words concerning these results. Also worth mentioning is medical treatment of elevated bloodpressure as a role in treating macular edema.

Authors: Thank you for these comments. The evidence base for intra-ocular drugs for DMO is changing rapidly and therefore our review only included drugs for DMO. We specifically excluded any surgical interventions or systemic treatments. We have amended the text to make this clearer. We accepted that vitreoretinal surgery may be an option and have amended the discussion to raise this issue. While not included in our search strategy, we have included some important and new systemic treatments in the "Other pertinent studies" section.