



Analysis of Funding Source and Spin in the Reporting of Studies of Intravitreal Corticosteroid Therapy for Diabetic Macular Edema: A Systematic Review

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Purpose: This systematic review examined the relationship between industry funding and the presence of spin in high-impact studies evaluating intravitreal corticosteroid therapy for diabetic macular edema.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. MEDLINE and Embase were systematically searched from inception through July 16, 2018, for randomized controlled trials and meta-analyses investigating the treatment of patients with diabetic macular edema using intravitreal corticosteroid therapy. Only studies published in English journals with an impact factor greater than 2 as per the Clarivate Analytics 2017 Journal Citation Report were included. The authors independently assessed study quality, funding source and the presence of reporting bias using a standardized datasheet.

Results: Title and abstract screening were completed on 7158 unique hits and full-text review yielded 44 included studies. Overall, there was correspondence between the wording of abstract conclusions and study results in 41/44 (93%) articles. Correspondence between abstract conclusions and significance of main outcome was present in 14/14 (100%) industry-funded and 27/30 (90%) nonindustry-funded studies. The odds ratio of industry funding being associated with noncorrespondence was 0.27 (95% CI: 0.01–5.61, $p=0.54$). The most common reason for noncorrespondence was the failure to mention rates of steroid-related intraocular pressure elevation.

Conclusion: The results of this systematic review indicate that biased abstract outcome reporting is rare in published randomized controlled trials and meta-analyses of intravitreal corticosteroid therapy for diabetic macular edema. Biased reporting was not associated with the presence of industry funding or a conflict of interest.

Keywords: corticosteroids, diabetic retinopathy, intravitreal therapy, macular edema, systematic review

Introduction

Clinical research trials sponsored by the pharmaceutical industry have profound impacts on the practice of medicine.¹ The industry can support a number of trials at all stages of a product's life with significant financial investment assigned to the innovation.² Therefore, there is potential for considerable monetary loss if the results and conclusions of these trials are unfavourable for the sponsor.^{1,3} A number of systematic reviews have documented industry sponsorship of drug

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studies to be associated with findings favourable to the sponsor.^{4–8} More recently, a review written by the Cochrane Collaboration found there to be less correspondence between the results and conclusions of industry-funded studies when compared to non-industry-funded studies.¹

In an era of rapidly developing therapies, physicians often rely on the peer-reviewed literature – especially the abstracts of published studies – to remain well informed about their respective fields of practice. It is therefore of paramount importance to evaluate outcome reporting bias in study abstracts. This was assessed in the ophthalmic literature by Alasbali and colleagues, who found industry-funded studies on the ocular hypotensive efficacy of topical prostaglandin analogues to be more likely to report proindustry abstract conclusions, which often did not correspond with studies' results.⁹ Our group performed a similar analysis of randomized clinical trials on the efficacy of intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy for retinal vein occlusion published in high-impact journals and did not find industry-sponsorship to be associated with an increased rate of reporting bias.¹⁰ The focus on high-impact journals allowed the authors to capture journals that were most likely to be referred to by physicians, and the results of this study were reassuring given the rapid adoption of anti-VEGF therapy for a number of ocular conditions.

Treatment of diabetic macular edema (DME) remains controversial among vitreoretinal specialists.^{11,12} Given the increased recognition of the role of inflammation in the development of DME, intravitreal corticosteroid therapy has been shown to provide promising anatomical and visual benefits, especially when compared to laser therapy.^{13–15} Compared to anti-VEGF therapy, intraocular corticosteroids do carry class-specific risks such as cataract progression and ocular hypertension that theoretically could be downplayed in abstract presentation.¹⁵ The purpose of this study was to examine the relationship between industry funding and the presence of spin in high-impact studies assessing the efficacy and safety of intravitreal corticosteroid therapy for DME.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.¹⁶ Approval from an Institutional Review Board was not required for this study

as no human subjects were involved, and analysis was based upon information from published literature.

Search Methods

Ovid Medline and Ovid Embase were searched from inception through July 16, 2018, for studies investigating the treatment of patients with diabetic macular edema with intravitreal corticosteroid therapy (ie, triamcinolone, fluocinolone, or dexamethasone) used in at least one of their treatment arms. The search strategy ([Appendix 1](#)) was designed to generate studies published in English journals with an IF greater than 2 as per the Clarivate Analytics 2017 Journal Citation Report.¹⁷ The inclusion of studies published in journals with IF greater than 2 is presumed to reflect studies more likely to be read by clinicians when browsing recent medical literature.

Study Selection

Search results were imported into DistillerSR (Evidence Partners; Ottawa, Canada) to manage all identified records. Title and abstract screening was completed to select for studies that were primary RCTs and meta-analyses. Full-text screening was then completed to select for studies that reported on main outcomes of visual acuity, retinal thickness, and/or complications. Studies that published secondary or sub-analyses on previously published RCTs were excluded. [Figure 1](#) outlines the flow of study selection as per the PRISMA statement.¹⁶

Data Collection and Analysis

Our methods of study evaluation and data extraction have been previously described.¹⁰ Study quality was assessed with the scoring scale utilized by Alasbali et al (2009) and is outlined in [Table 1](#).⁹ Correspondence between significance of the main outcome measure result and abstract conclusion was assessed by surveying whether the wording of the abstract conclusion matched the statistical analysis of the results as they pertained to the main outcome measure(s). Following independent data extraction, all discrepancies on the standardized data sheet were resolved by unanimous agreement amongst the authors (HN, AK, JS). One author (HN) also collected objective data on the included studies: sample size, source of funding (industry vs non-industry), whether the publication was authored by an industry employee as reported in the manuscript, and whether any of the co-authors had a potential conflict of interest (COI). The presence of a potential author COI was determined by assessing the study's disclosure statement and was defined as any

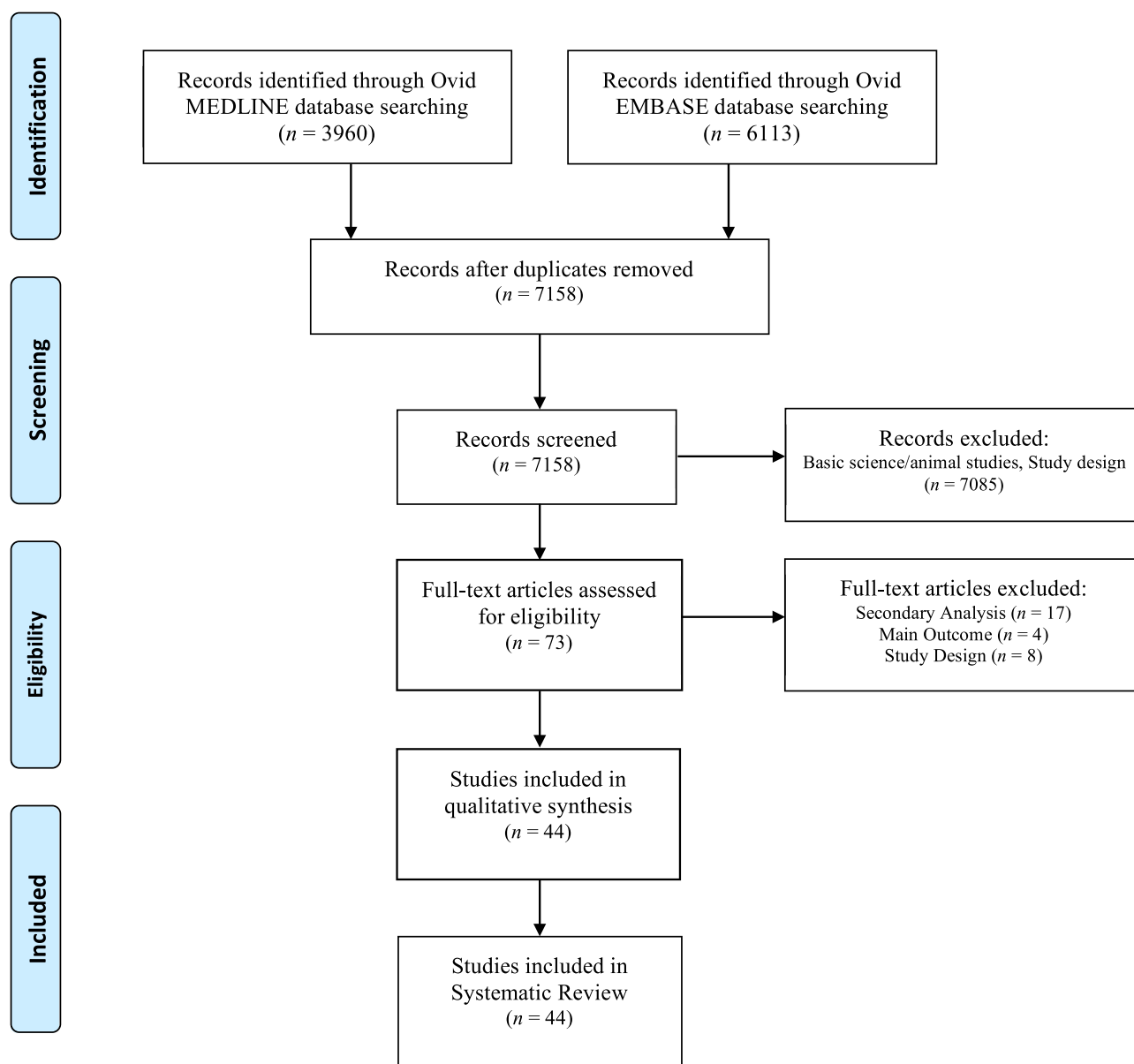


Figure 1 Selection of randomized clinical trials and meta-analyses.

previous relationship between a co-author and the company that manufactured the drug intervention(s) being studied. Corresponding authors of the included studies were contacted if any of the objective information was not evident as part of the published article.

The primary outcome of the present study was the association between funding source and the correspondence between the studies' abstract conclusion and statistical significance of their main outcome, expressed as an odds ratio. Exploratory secondary analyses were also performed to determine any associations between our variables of interest, including study sample size, journal impact factor and the presence of any COI. Statistical analysis included the Fisher

exact test for categorical data, and the Mann–Whitney *U*-test/ Kruskal–Wallis test or Student's *t*-test/one-way ANOVA for numerical data, as appropriate. A *p*-value < 0.05 was considered statistically significant. All data were extracted and stored in Microsoft Excel software (Microsoft; Redmond, WA). Statistical analysis was performed using SPSS (IBM Corp; Armonk, New York; software version 22).

Results

The original search of both databases yielded 10,073 articles, reduced to 7158 following the removal of duplicates. After title and abstract screening, the full texts of 73 articles were completed. Twenty-nine articles were then excluded due to

Table 1 Criteria Utilized for Grading of Study Quality⁹

Quality Score	Criteria
I: Meta-analysis (To assign this level, all of the following criteria must be met).	<ol style="list-style-type: none"> 1. The paper reports a comprehensive search for evidence. 2. The authors avoid bias in selecting articles for inclusion. 3. The authors assess each article for validity. 4. The paper reports clear conclusions that are supported by the data and appropriate analysis.
I: Large RCT (To assign this level, all of the following criteria must be met).	<ol style="list-style-type: none"> 1. Patients were randomly allocated to treatment groups. 2. Follow-up was at least 80% complete. 3. Both the patients and the investigators were blind to the treatment the patient received. 4. Patients were analyzed in the treatment groups to which they were assigned. 5. The sample size was large enough to detect the outcome of interest.
2: RCT	RCT or overview that did not meet level I

Abbreviation: RCT, randomized controlled trial.

being a secondary analysis (n=17), analysis of a main outcome not relevant to the present study (n=4), or inadequate study design (n=8). Therefore, 44 (41 RCTs and 3 meta-analyses) publications were included in the present analysis (Figure 1).^{18–61} Of these 44 studies, 36 (82%) were of higher impact factor (IF \geq 3), and 31 (70%) were assigned a study quality score of 2. Fourteen (32%) received industry funding, five (11%) had an author who was an industry employee, and 17 (39%) had an author(s) with a potential COI. Table 2 outlines characteristics of the included studies.

Correspondence Between Main Outcome Measure and Abstract Conclusion

Statistically significant main outcome measures were present in 26 of 44 (59%) of the included studies. There was correspondence between wording of abstract conclusions and study results in 41 of 44 (93%) articles. Reasons for non-correspondence included the failure to mention high rates of steroid-related intraocular pressure (IOP) elevation

(n=2)^{41,42} and the implication of safety despite a case of endophthalmitis in a small sample (n=1) (Table 2).⁵²

Funding

Among the 14 studies that received industry funding, two were funded by Alimera Sciences, Inc.,^{27,30} eight studies by Allergan, Inc.,^{18–22,24,54,55} three by both Allergan, Inc. and Genentech, Inc.,^{23,26,48} and one study was funded by Bausch & Lomb, Inc.²⁸ Eighteen studies received funding from a nonindustry sponsor.

Comparing Industry-Funded versus Nonindustry-Funded Studies

A statistically significant main outcome measure was reported in 8 of 14 (57%) industry-funded studies and in 18 of 30 (60%) nonindustry-funded studies (p=1.00, Fisher exact test). Correspondence between abstract conclusions and significance of main outcome was present in 14 of 14 (100%) industry-funded and 27 of 30 (90%) nonindustry-funded studies. The odds ratio of industry funding being associated with noncorrespondence was 0.27 (95% CI: 0.01 to 5.61, p=0.54). Industry-funded studies had significantly greater sample sizes (p=0.01), but similar mean study quality (p=0.50) and journal impact factor (p=0.14) when compared to the nonindustry-funded studies. These data are summarized in Table 3.

Comparing Higher-Impact versus Lower-Impact Publications

When publications were stratified by journal IF into a “high-impact” group (n = 36) with IF \geq 3 and a “low-impact” group (n=8) with IF<3, statistically significant main outcome measures were reported in 21 of 36 (58%) high-impact publications and in 5 of 8 (63%) of low-impact publications (p=1.00). Correspondence between abstract conclusions and significance of the main outcome was present in 33 of 36 (92%) high-impact publications and in 8 of 8 (100%) of low-impact publications (p=1.00). When comparing high-impact and low-impact publications there were no significant differences in rates of significant main outcome measures (p=1.00), rates of industry funding (p=1.00), rates of author COI (p=0.76), sample size (p=0.87), or study quality (p=0.68). These data are summarized in Table 4.

Comparing COI-Present versus COI-Absent Publications

After compiling responses from corresponding authors with published disclosures, 17 studies had a COI, 22 had no COI

Table 2 Summary of Full-Text Study Assessments

Article	Impact Factor	Study Quality	Sample Size	Interventions	MOM(s)	MOM (p<0.05)?	Correspondence?	Any COI	Industry Author	Industry Sponsor	Sponsor	Comments
HIGHER-IMPACT JOURNALS (Impact Factor ≥ 3.0)												
Heng et al (2016) ¹⁸	3.806	2	80	Macular Laser \pm IV DEX Implant	BCVA	No	Yes	COI Present	No	Yes	Allergan	Small sample size
Shah et al (2016) ¹⁹	3.7	2	50	IVB vs IV DEX implant	BCVA and CST	Yes	Yes	COI Present	No	Yes	Allergan	Failed to mention steroid-related IOP elevation rate. Small sample size
Maturi et al (2015) ²⁰	3.7	2	40	IVB \pm IV DEX Implant	BCVA and CST	Yes	Yes	COI Present	No	Yes	Allergan	Small sample size
Gillies et al (2014) ²¹	8.2	2	88	IV DEX Implant vs IVB	BCVA	No	Yes	COI Not Present	No	Yes	Allergan	Failed to mention steroid-related IOP elevation rate. Small sample size
Callanan et al (2013) ²²	8.2	2	253	Laser \pm IV DEX Implant	BCVA	No	Yes	COI Present	Yes	Yes	Allergan	-
Elman et al (2010) ²³	8.2	2	854	Laser \pm IVR or IVT	BCVA	No	Yes	COI Present	No	Yes	Genentech, Allergan	-
Ip et al (2008) ²⁴	8.2	2	840	IVT vs Focal/Grid Laser	BCVA	Yes	Yes	COI Present	No	Yes	Allergan	-
Chew et al (2007) ²⁵	8.2	2	129	STT \pm Focal Laser	BCVA and CST	No	Yes	COI Present	No	No	Soley Non-Industry	-
Googe et al (2011) ²⁶	3.7	2	345	IVR vs IVT	BCVA and CST	Yes	Yes	COI Present	No	Yes	Genentech, Allergan	-
Campochiaro et al (2012) ²⁷	8.2	1	953	Fluocinolone Vitreous Inserts	BCVA	Yes	Yes	COI Present	Yes	Yes	Alimera Sciences	-
Pearson et al (2011) ²⁸	8.2	1	196	IV Fluocinolone Implant	BCVA	Yes	Yes	COI Present	Yes	Yes	Bausch & Lomb	-
Eibendary et al (2011) ²⁹	3.7	2	32	IV Diclofenac vs IVT	VA, CMT, IOP	No	Yes	COI Not Present	No	No	None	Small sample size

(Continued)

Table 2 (Continued).

Article	Impact Factor	Study Quality	Sample Size	Interventions	MOM(s)	MOM (p<0.05)?	Correspondence?	Any COI	Industry Author	Industry Sponsor	Sponsor	Comments
Campochiaro et al (2011) ³⁰	8.2	1	953	Low vs High dose Fluocinolone IV Implant	BCVA	Yes	Yes	COI Present	Yes	Yes	Alimera Sciences	-
Gillies et al (2011) ³¹	8.2	1	84	Laser ± IVT	BCVA	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Takata et al (2010) ³²	3.7	2	24	IV vs ST infusion of Triamcinolone	BCVA, CMT, IOP	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Mirshahi et al (2010) ³³	3.7	2	36	PRP and MPC ± IVT	BCVA, CMT	No	Yes	No Disclosure Provided	No	No	None	Small sample size
Gillies et al (2010) ³⁴	3.38	1	81	IVT	BCVA	No	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Soheilian et al (2009) ³⁵	8.2	1	150	IVB ± IVT vs Macular Laser	BCVA	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	-
Maia et al (2009) ³⁶	5.052	2	44	Laser ± IVT	BCVA, CMT, TMV	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Hauser et al (2008) ³⁷	3.7	2	42	IVT	BCVA, CMT, IOP, Cataract	No	Yes	COI Not Present	No	No	None	Small sample size
Ockrim et al (2008) ³⁸	3.806	2	88	IVT vs Laser	BCVA	No	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Paccola et al (2008) ³⁹	3.806	2	26	IVT vs IVB	BCVA and CMT	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Failed to mention steroid-related IOP elevation rate, Small sample size
Soheilian et al (2007) ⁴⁰	3.7	1	103	IVB ± IVT vs Macular Laser	BCVA	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	-

Lam et al (2007) ^{a,1}	8.2	2	111	IVT vs Grid Laser	BCVA, CFT	No	No	No Disclosure Provided	No	No	Soley Non-Industry	Laser alone had similar BCVA and CFT outcomes at final follow up: Failure to mention steroid-related IOP elevation rate
Lam et al (2007) ^{b,2}	3.806	2	63	IVT	BCVA, CFT, IOP	Yes	No	COI Not Present	No	No	Soley Non-Industry	Failed to mention high rates of steroid-related IOP elevations. Small sample size
Audren et al (2006) ⁴³	5.052	2	32	IVT	CMT	No	Yes	No Disclosure Provided	No	No	None	Failed to mention high rates of steroid-related IOP elevations. Small sample size
Bonini-Filho et al (2005) ⁴⁴	3.38	2	28	STT vs IVT	BCVA, CMT, IOP, Lens Status	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Spandau et al (2005) ⁴⁵	3.806	2	27	IVT	BCVA, IOP	Yes	Yes	COI Not Present	No	No	None	Small sample size
Cardillo et al (2005) ⁴⁶	8.2	2	24	IVT vs STT	BCVA, CMT	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Tunc et al (2005) ⁴⁷	8.2	2	60	Focal Laser ± STT	BCVA	Yes	Yes	COI Not Present	No	No	None	Small sample size
Maturi et al (2018) ⁴⁸	5.6	2	129	IVR ± IV DEX Implant	BCVA	No	Yes	COI Present	No	Yes	Genentech, Allergan	-
Sarao et al (2017) ⁴⁹	3.157	2	42	PRN vs Single IV DEX Implant	BCVA	Yes	Yes	COI Present	No	No	None	Small sample size
Isaac et al (2012) ⁵⁰	3.157	1	22	IVT vs IVB	CFT	Yes	Yes	No Disclosure Provided	No	No	None	Small sample size
Kim et al (2008) ^{a,51}	3.7	2	33	IVT	BCVA	No	Yes	No Disclosure Provided	No	No	Soley Non-Industry	Failed to mention high rates of steroid-related IOP elevations. Small sample size

(Continued)

Table 2 (Continued).

Article	Impact Factor	Study Quality	Sample Size	Interventions	MOM(s)	MOM (p<0.05)?	Correspondence?	Any COI	Industry Author	Industry Sponsor	Sponsor	Comments
Sutter et al (2004) ⁵²	8.2	I	69	IVT	BCVA	Yes	No	COI Present	No	No	Soley Non-Industry	Infectious endophthalmitis developed in one IVT eye. Small sample size
Yilmaz et al (2009) ⁵³	8.2	I	293	IVT vs STT	BCVA	No	Yes	COI Not Present	No	No	None	Meta-Analysis
LOWER-IMPACT JOURNALS (Impact Factor ≥ 2.0 and < 3.0)												
Callanan et al (2017) ⁵⁴	2.349	2	363	IV DEX implant vs IVR	BCVA	Yes	Yes	COI Present	Yes	Yes	Allergan	-
Ramu et al (2015) ⁵⁵	2.275	2	100	PRN vs fixed dosing IV DEX Implant	BCVA	No	Yes	COI Present	No	Yes	Allergan	-
Kriechbaum et al (2014) ⁵⁶	2.275	2	30	IVB vs IVT	BCVA and CST	Yes	Yes	COI Present	No	No	None	Small sample size
Zhang et al (2013) ⁵⁷	2.238	I	434	IVT vs IVB	BCVA and CMT	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Meta-Analysis
Doi et al (2012) ⁵⁸	2.349	2	40	PPV vs IVT	BCVA and CMT	Yes	Yes	COI Not Present	No	No	Soley Non-Industry	Small sample size
Ahmadi et al (2008) ⁵⁹	2.349	I	115	IVB ± IVT	CMT	No	Yes	COI Not Present	No	No	Soley Non-Industry	-
Qi et al (2012) ⁶⁰	2.238	I	172	IVT vs STT	BCVA, CMT, IOP	No	Yes	COI Not Present	No	No	None	Meta-Analysis
Kim et al (2008) ⁶¹	2.68	2	46	STT	VA+CMT +DR progression	Yes	Yes	COI Not Present	No	No	None	Small sample size

Abbreviations: MOM, main outcome measure; COI, conflict of interest; IV DEX, intravitreal dexamethasone; IVB, intravitreal bevacizumab; IVR, intravitreal ranibizumab; IVT, intravitreal triamcinolone; STT, subtenon triamcinolone; PRP, panretinal photocoagulation; MPC, macular photocoagulation; PRN, pro re nata; BCVA, best corrected visual acuity; CST, central sub-foveal thickness; CMT, central macular thickness; IOP, intraocular pressure; TMV, total macular volume; CFT, central foveal thickness.

Table 3 Summary of Studies Investigating Steroid Therapy for Diabetic Macular Edema, Based on Funding Status

Outcome Studied	Industry-Funded (n=14)	Nonindustry-Funded (n=30)	p-value
Correspondence of main outcome and conclusions	14 (100%)	27 (90%)	0.54*
Statistically significant (p<0.05) main outcome	8 (57%)	18 (60%)	1.00*
Sample size, mean \pm SD (95% CI)	374.6 \pm 360.0 (278.4–470.8)	82.7 \pm 88.3 (66.6–98.8)	0.01 [†]
Study quality, mean \pm SD (95% CI)	1.79 \pm 0.43 (1.68–1.90)	1.67 \pm 0.48 (1.58–1.76)	0.50 [‡]
Journal impact factor, mean \pm SD (95% CI)	5.90 \pm 2.51 (5.23–6.57)	4.68 \pm 2.27 (4.27–5.09)	0.14 [‡]

Notes: *Fisher exact test; [†]Student's t-test; [‡]Mann–Whitney U-test.

Abbreviations: 95% CI, 95% confidence interval; SD, standard deviation.

Table 4 Summary of Studies Investigating Steroid Therapy for Diabetic Macular Edema, Based on Impact Factor

Outcome Studied	High-Impact (n=36)	Low-Impact (n=8)	p-value
Correspondence of main outcome and conclusions	33 (92%)	8 (100%)	1.00*
Statistically significant (p < 0.05) main outcome	21 (58%)	5 (63%)	1.00*
Industry funding	12 (33%)	2 (25%)	1.00*
Any author COI	14 (39%)	3 (38%)	0.76*
Sample size, mean \pm SD (95% CI)	178.4 \pm 270.3 (133.4–223.4)	162.5 \pm 154.1 (108.0–217.0)	0.87 [†]
Study quality, mean \pm SD (95% CI)	1.72 \pm 0.45 (1.64–1.80)	1.63 \pm 0.52 (1.45–1.81)	0.63 [‡]
Journal impact factor, mean \pm SD (95% CI)	5.67 \pm 2.21 (5.30–6.04)	2.34 \pm 0.14 (2.29–2.39)	<0.01 [‡]

Notes: *Fisher exact test; [†]Student's t-test; [‡]Mann–Whitney U-test.

Abbreviations: 95% CI, 95% confidence interval; SD, standard deviation.

and five did not have a disclosure statement. Correspondence between abstract conclusions and significance of main outcome was present in 16 of 17 (94%) studies with a COI, 21 of 22 (96%) studies without a COI and in four of five (80%) studies without a COI disclosure statement (p=0.48). Studies with a COI had a significantly greater mean sample size when compared to studies without a COI or a disclosure statement (p<0.01). There were no significant differences in rates of significant main outcome measures (p=0.25), study quality (p=0.61), or journal impact factor (p=0.61). These data are summarized in Table 5.

Discussion

This study aimed to examine whether the presence of industry funding affected the likelihood of biased outcome

reporting among studies of intravitreal corticosteroid therapy for DME. Overall, the results of the present study indicated that abstract outcome reporting corresponded with their statistical results for almost all of the included studies, and that funding source was not a predictor for biased reporting. Journal impact factor and the presence of a COI were not predictors of biased outcome reporting. Industry-funded studies and studies with a COI had greater samples sizes but were of similar impact and quality when compared to their counterparts.

The results of this study are reassuring given that biased outcome reporting has been identified in a number of published studies. In 2009, Berwanger et al published the results of a systematic survey of RCT abstract reporting in high-impact general medical journals and found that 29% of studies lacked a definition of the primary outcome and that half of the studies did not report on side effects or harms.⁶² In RCTs of wound treatments, Lockyer et al found that among studies of wound care treatment that did not have a statistically significant result, 71% had some form of biased reporting.⁶³ Among RCTs in oncology, Vera-Badillo et al found biased reporting of efficacy outcomes to be common in studies with a negative primary endpoint and that toxicity was underreported.⁶⁴ Recently, biased outcome reported has been shown to be prevalent among high-impact neurology journals.⁶⁵

Although biased outcome reporting has been identified as a concern in biomedical research, the role of industry sponsorship has been debated in the literature. Recently, a meta-analysis of “spin” in the medical literature found that clinical trials had the greatest variability in the prevalence of spin, with common practices being detracting from statistically nonsignificant results and inappropriately using causal language.⁶⁶ Although the industry sponsorship was hypothesized by the authors to be associated with spin, the results of this meta-analysis were inconclusive.⁶⁶ Published reviews have found that industry funding was not associated with biased reporting among oncology trials,⁶⁷ musculoskeletal studies,⁶⁸ general medical journals,⁶⁹ or in gastrointestinal research.⁷⁰

Within the ophthalmic literature, Alasbali et al investigated whether funding source was associated with biased abstract conclusions among studies of topical prostaglandins for intraocular pressure lowering.⁹ Their study found 62% of industry-funded articles to have an abstract conclusion that was not consistent with the results of the main outcome measure, while none of the non-industry-funded articles had noncorrespondence. Additionally, while only 24% of

Table 5 Summary of Studies Investigating Steroid Therapy for Diabetic Macular Edema, Based on Any Author COI

Outcome Studied	Author COI Present (n=17)	No Author COI (n=22)	No COI Disclosure (n=5)	p-value
Correspondence of main outcome and conclusions	16 (94%)	21 (96%)	4 (80%)	0.48*
Statistically significant ($p < 0.05$) main outcome	11 (65%)	14 (64%)	1 (20%)	0.25*
Sample size, mean \pm SD (95% CI)	319.2 \pm 347.7 (263.7–374.7)	93.8 \pm 98.8 (45.0–142.6)	46.8 \pm 36.3 (–55.5–149.1)	$<0.01^{\dagger}$
Study quality, mean \pm SD (95% CI)	1.76 \pm 0.44 (1.65–1.87)	1.64 \pm 0.49 (1.54–1.74)	1.80 \pm 0.45 (1.6–2.0)	0.61 ‡
Journal impact factor, mean \pm SD (95% CI)	5.66 \pm 2.58 (5.08–6.24)	4.68 \pm 2.30 (4.17–5.19)	4.76 \pm 2.05 (3.69–5.83)	0.61 ‡

Notes: *Fisher exact test; † One-way ANOVA; ‡ Kruskal–Wallis test.

Abbreviations: 95% CI, 95% confidence interval; SD, standard deviation.

the industry-funded studies had a statistically significant main outcome measure, 90% of the industry-funded studies had a proindustry abstract conclusion.⁹ These findings contrast those of the present study quite dramatically and may reflect differences in intervention efficacy (topical prostaglandins vs intravitreal corticosteroids) or differences in methodologies between the studies. Namely, the present study only included RCTs and meta-analyses published in relatively higher-impact journals, which may explain the difference in non-correspondence rates. Recently, our group published a study using a very similar methodology examining the effect of funding source on reporting bias in studies of intravitreal anti-VEGF therapy for retinal vein occlusion.¹⁰ Similar to the present study, rates of biased abstract reporting were low and were unaffected by funding source, reflecting no differences despite the increased risk profile of intraocular corticosteroids compared to intravitreal anti-VEGF therapy. Finally, the rigorousness of the peer-reviewed process between 2009 and 2019 may partly explain the difference in results. It is interesting to note that all 3 studies with non-correspondence were published prior to 2008.

Although the present study found an overall abstract conclusion and study results correspondence rate of 93%, it is important to note that only the primary outcome was evaluated. The most common primary outcomes among the included studies were visual acuity and retinal thickness. Adverse events, namely intraocular pressure elevation, were rarely reported as a primary outcome and are especially relevant in the context of intravitreal steroid therapy. This review identified seven studies that failed to mention the increased prevalence of steroid-related intraocular pressure elevations in their respective abstracts. If this adverse effect was included as reported as a primary outcome in these studies, the overall non-correspondence rate of the present review would have increased by roughly 11%. This highlights the importance of comprehensive outcome reporting to allow readers to fully understand and appreciate the risks and benefits of therapies they later offer to their patients.

The major limitation of the present study was its highly selective inclusion criteria. Unlike prior studies, the present study only included RCTs and meta-analyses that were published in journals with an impact factor greater than 2. RCTs and meta-analyses are considered to provide the highest level of evidence and are likely preferentially assessed by physicians. Although the present study may have excluded high-quality studies published in journals of lower impact, the authors feel that this analysis captured articles that would more likely be read by physicians when scanning the recent medical literature. Although the present study did not identify differences in the rates of noncorrespondence between the subgroups of journal impact factor, future studies may find it useful to examine biased reporting among studies published in lower-impact journals (impact factor <2). Nonetheless, it is reassuring to note that among these higher-impact publications of intravitreal corticosteroid therapy for DME, biased abstract reporting overall appears to be uncommon and unrelated to industry sponsorship or authorship, or to journal impact factor.

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Disclosure

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