Original Article

# Retrospective study of changes in ocular coherence tomography characteristics after failed macular hole surgery and outcomes of fluid-gas exchange for persistent macular hole

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**Purpose:** The aim is to study the changes in ocular coherence tomography (OCT) parameters of large (≥400 μ) full-thickness macular holes (FTMHs) after a failed surgery and evaluate the outcome of fluid-gas exchange (FGE) in the treatment of persistent macular hole and role of OCT in predicting outcome after the secondary intervention. **Methods:** Changes occurring in the OCT parameters of FTMH after a failed vitrectomy were evaluated. FGE was done in an operating room with three pars plana sclerostomy ports. The anatomical and functional outcomes of FGE for these persistent macular holes were also assessed. Anatomical closure was defined as the flattening of the hole with resolution of subretinal cuff of fluid. Anatomical success after FGE was defined as flattening of macular hole with the resolution of subretinal cuff of fluid and neurosensory retina completely covering the fovea. Functional success was defined as an improvement of at least one line of best-corrected visual acuity (BCVA). **Results:** Twenty-eight eyes (28 patients) were included in the study. After the failed vitrectomy, OCT showed an increase in the base diameter, opening diameter, and height of the hole. After the secondary procedure, anatomical closure was achieved in 89.3% eyes. Mean BCVA improved from logMAR 0.88 ± 0.24 (20/152) to logMAR 0.66 ± 0.24 (20/91) ($P < 0.001$). Eight (28.6%) patients achieved final BCVA ≥20/60. Functional success was obtained in 19 patients (67.9%). There was no association between anatomical success after FGE and any of the pre-FGE OCT parameters or indices. **Conclusion:** Unsuccessful surgery causes swelling of the outer and middle retinal layers with retraction of inner layers of the retina. Performing FGE while visualizing the retina is a good option for the treatment of large persistent macular holes as it causes complete drying of the macula, better success rates, and a reduced complication rate. Pre-FGE OCT does not help in predicting the outcome of FGE for persistent macular hole.

**Key words:** Failed surgery, fluid-gas exchange, ocular coherence tomography, persistent macular hole

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The first effective treatment of macular hole, in the form of vitrectomy, was introduced by Kelly and Wendel in 1991.[1] Macular hole surgery has undergone immense technological refinements since then. With an overall anatomical success rate of 93%–98%, it is regarded as the most successful surgeries in the vitreoretinal subspecialty.[2-6] However, there are few patients, especially those with large and chronic macular holes, in whom the surgery fails to close the hole.[7-11]

One study showed that there is an increase in both the macular hole diameter and surrounding fluid cuff after the failed surgery.[12] The treatment of persistent macular hole still remains a dilemma. Some studies have shown that "fluid-gas exchange (FGE)" can be used for the treatment of persistent macular holes.[13-19] However, all these studies included mostly small and Stage III macular holes. The number of patients with large macular holes in these studies was minimal.

We present a detailed account of changes occurring in ocular coherence tomography (OCT) parameters of large full-thickness macular hole (FTMH) after unsuccessful vitrectomy, anatomical and visual outcome of FGE, and role of OCT in predicting outcome after the secondary intervention.

## Methods

In this retrospective analysis, we reviewed the records of all the patients who underwent vitrectomy for large idiopathic FTMH (i.e., minimum diameter [MD] >400 μ) between January 2013 and December 2016. The patients in whom the macular hole failed to close underwent secondary FGE within 1 month of the primary surgery.

The data obtained included age, gender, intraocular pressure (IOP), and best-corrected visual acuity (BCVA) before the vitrectomy, after the vitrectomy (i.e., before FGE), and finally, after the FGE procedure. The Snellen visual acuity was converted into logarithm of the minimum angle

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of resolution, i.e., logMAR for statistical analysis. Various macular hole parameters, i.e., base diameter (BD), MD, opening diameter (OD), height, and nasal and temporal arm length were measured with the help of a Heidelberg Spectralis Spectral-Domain Optical Coherence Tomography (Heidelberg Engineering, Heidelberg, Germany) using high-definition 5-line raster scan passing through the fovea, before and after each intervention. OD, MD, and BD were measured at the level of the inner opening of macular hole, at the level of the minimum extent of macular hole, and at the level of retinal pigment epithelium (RPE), respectively. Height was defined as the maximum distance from RPE to the innermost aspect of the hole. Nasal and temporal arm length was defined as the distance from RPE to the level of minimum extent of the hole nasally and temporally, respectively. Hole forming factor (HFF) was calculated as the ratio of the sum of nasal arm length and temporal arm length to BD. Macular hole index (MHI) was calculated the ratio between maximum height and BD. Tractional hole index (THI) was calculated as the ratio between maximal height and MD.[4,20-24]

During the primary surgery, phacoemulsification, intraocular lens implantation, 25-gauge (G) pars plana vitrectomy (PPV), and internal limiting membrane (ILM) peeling (at least 2-disc areas from the edges of the hole) were done in all the patients. Fluid-air exchange (FAE) was done multiple times at the end of the surgery, to ensure that the macula becomes completely "dry." The inverted ILM flap technique was not used in any of the patients. ILM was stained using a 0.05% solution of Heavy Brilliant Blue G dye (HBBG; Ocublue plus, Aurolab, India mixed with 10% dextrose in 1:2 proportions) in all the patients.[25] Tamponade was given with either 20% sulfur hexafluoride (SF6) or 18% perfluoropropane (C3F8), according to surgeon's preference. A prone position for 5–7 days was advised to the patients.

Postoperative visits were scheduled at day 1, 2 weeks, 1 month, 3 months, and 6 months. Additional follow-ups were scheduled, in case of any complication (s). At each follow-up visit, BCVA, IOP, and OCT images were recorded. Anatomic closure was defined, on the basis of OCT, as the flattening of the hole with resolution of subretinal cuff of fluid.[26] The surgery was deemed as anatomical failure if the neurosensory retina (NSR) around the macular hole did not attach to the underlying RPE, and "intraretinal cysts" were present at the edges of the hole. Type 1 anatomical closure was defined as the flattening of macular hole with resolution of subretinal cuff of fluid and NSR completely covering the fovea. Type 2 anatomical closure was defined when the whole rim of NSR around the macular hole was attached to the underlying RPE, the absence of any "intraretinal cysts" at the edge of the hole, but the absence of NSR above the fovea. Type 2 anatomical closure was not considered as anatomical failure of the primary surgery, and no further intervention was done.

The secondary procedure, i.e., FGE was done under all aseptic precautions in an operating room. Three 25 G standard PPV sclerostomy ports were made under local anesthesia. HBBG was used to check if adequate ILM peeling was done during primary surgery. As adequate ILM peeling was done during the primary surgery, additional ILM peeling was not needed in any of the cases. FAE was done multiple times to ensure that the macula becomes completely "dry." Finally, FGE was done with either 20% SF6 or 18% C3F8. Patients were again instructed to maintain a face-down position for 5–7 days. Postoperative visits were scheduled at day 1, 2 weeks, 1 month, 3 months, and 6 months. The patients included a minimum follow-up of 6 months.

The outcomes of the secondary intervention were assessed after 6 months of the intervention. Anatomical success of FGE was defined as Type 1 anatomical closure. Type 2 anatomical closure was also defined as anatomical failure in case of FGE. Functional success was defined as an improvement of at least one line of BCVA.

### Statistical analysis

Statistical analysis was performed with STATA statistical software, version 14.1 (StataCorp, College Station, Texas, USA). Descriptive variables were expressed as mean (±standard deviation) or median (range). Student's *t*-test or Mann–Whitney U-test was used to find the difference between two continuous variables. Paired *t*-test or Wilcoxon signed-rank test was used to find the difference between preintervention and postintervention continuous variables. To find the factors that associated with outcome, multivariate analyses were used. $P < 0.05$ was considered to be statistically significant.

## Results

Twenty-eight patients with mean age of 61.7 ± 5.6 years (range, 50–71 years) were included in the study [Fig. 1]. The mean MD and BD of the treatment-naïve FTMH were 670.0 ± 148.0 μ and 1234.9 ± 264.8 μ, respectively. After the failed vitrectomy, an increase in the mean values of BD, height (H), and OD of the macular hole was seen [Table 1 and Figs. 2-4].

After FGE, 17 patients (60.7%) achieved Type 1 anatomical closure, 8 patients (28.6%) achieved Type 2 anatomical closure, while 3 patients (10.7%) did not achieve any anatomical closure. Mean BCVA improved from logMAR 0.88 ± 0.24 (Snellen equivalent 20/152) to logMAR 0.66 ± 0.24 (Snellen equivalent 20/91) after FGE ($P < 0.001$) [Table 2]. Mean BCVA in patients achieving anatomical success was logMAR 0.58 ± 0.23 (Snellen equivalent 20/78). Overall, BCVA improved in 19 patients (67.9%) and remained same in 8 patients (28.6%). One patient, in whom anatomical closure could not be achieved, had a decrease in BCVA. Eight patients (28.6%) achieved final BCVA ≥20/60 [Table 2].

None of the eyes developed any complications such as retinal holes, retinal detachment, fibrinous exudates, or endophthalmitis.

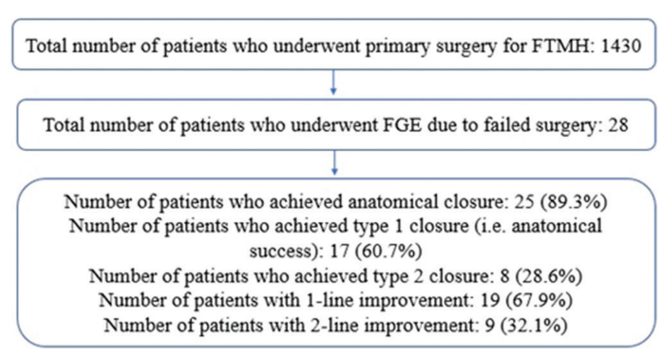


**Figure 1:** Flowchart representing the number of patients undergoing the primary and the secondary procedures

**Table 1: Change in mean values of best-corrected visual acuity and various macular hole ocular coherence tomography parameters after the macular hole failed to close after vitrectomy**

| | Before vitrectomy | After vitrectomy | Percentage change | *P* |
|---|---|---|---|---|
| Mean BCVA | LogMAR: 0.82±0.23 (Snellen equivalent: 20/132) | LogMAR: 0.88±0.24 (Snellen equivalent: 20/151) | +7.3 | 0.134 |
| Mean minimum diameter | 669.96±147.96 μ (443-1110 μ) | 657.04±206.40 μ (174-1178 μ) | −1.9 | 0.709 |
| Mean base diameter | 1234.86±264.77 μ (709-1848 μ) | 1370.68±420.50 μ (796-2711 μ) | +11.0 | 0.147 |
| Mean height | 457.96±82.51 μ (332-710 μ) | 586.64±158.70 μ (352-1076 μ) | +28.1 | <0.001 |
| Mean opening diameter | 903.71±255.24 μ (180-1413 μ) | 1072.18±240.73 μ (710-1693 μ) | +18.6 | 0.009 |

LogMAR: Logarithm of the minimum angle of resolution, BCVA: Best-corrected visual acuity

**Table 2: Functional outcome in patients who achieved Type 1 anatomical closure, Type 2 anatomical closure, and no anatomical closure after fluid-gas exchange**

| | Anatomical success (Type 1 anatomical closure) | Anatomical failure | | Total |
|---|---|---|---|---|
| | | Type 2 anatomical closure | No anatomical closure | |
| Number of patients (%) | 17 patients (60.7) | 8 (28.6) | 3 (10.7) | 28 |
| Final mean BCVA (logMAR) | 0.58±0.23 (Snellen equivalent: 20/78) | 0.70±0.16 (Snellen equivalent: 20/100) | 1.03±0.05 (Snellen equivalent: 20/214) | 0.66±0.24 (Snellen equivalent: 20/91) |
| Functional success (one-line improvement in BCVA) (%) | 16/17 (94.1) | 3/8 (37.5) | 0 | 19/28 (67.9) |
| Two-line improvement in BCVA (%) | 9/17 (52.9) | 0 | 0 | 9/28 (32.1) |
| Three-line improvement in BCVA (%) | 7/17 (41.2) | 0 | 0 | 7/28 (25.0) |
| No change in BCVA (%) | 1/17 (5.9) | 5/8 (62.5) | 2/3 (66.7) | 8/28 (28.6) |
| Decrease in BCVA (%) | 0 | 0 | 1/3 (33.3) | 1/28 (3.6) |

BCVA: Best-corrected visual acuity, LogMAR: Logarithm of the minimum angle of resolution

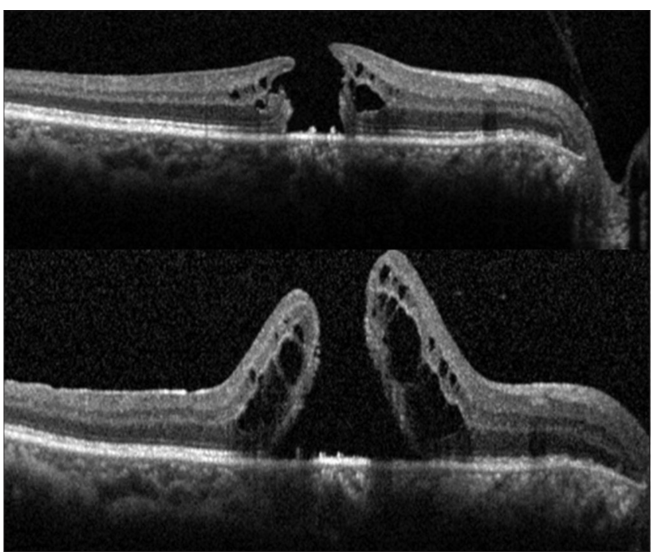

**Figure 2:** Ocular coherence tomography images showing preoperative (above) and postoperative (below) configuration of macular hole in patient number 10 (base diameter increased from 771 to 1771; minimum diameter decreased from 596 to 542; and opening diameter increased from 398 to 820)

There was no association between the anatomical success, i.e., Type 1 closure after the secondary procedure and the macular hole parameters and indices such as MD, BD, MHI, THI, or HFF of the persistent macular hole [Table 3].

## Discussion

Introduction of ILM peeling as a surgical step in macular hole surgery has resulted in tremendous rise in anatomical success rates.[2-6] However, 20%–60% large FTMHs fail to achieve anatomical closure.[7-11] Due to the low incidence of surgical failure, changes occurring in the configuration of a macular hole after failed surgery and treatment of persistent macular holes have not been adequately studied.

Leonard *et al*. studied the changes occurring in the configuration of a macular hole after failed vitrectomy with the help of fundus photographs. He noted that there was an increase in the macular hole diameter and the surrounding fluid cuff.[12] We went a step ahead and measured the changes occurring in various OCT parameters of FTMH. We found that there was a statistically significant increase in the mean height and mean OD of the hole after the failed vitrectomy. Furthermore, there was an increase in mean BD, but this increase did not reach statistical significance. These findings can be explained on the basis of the "hydration theory."[27-29] Newly formed postvitrectomy aqueous humor gains access to the macular hole and are absorbed by the various retinal layers.[28,29] The inner retinal layers at either edge of the hole absorb the fluid and get retracted away from each other, thereby

**Table 3: Multivariate analysis to find the risk factors associated with unsuccessful outcome after FGE**

| Factors | Outcome (mean±SD) | | Unadjusted | | Adjusted |
|---|---|---|---|---|---|
| | Unsuccessful | Successful | OR (95% CI) | *P* | *P* |
| BD | 1416.09±351.84 | 1326.00±445.52 | 1.00 (0.99–1.00) | 0.554 | 0.763 |
| MD | 741.36±195.05 | 574.43±207.21 | 1.00 (0.99–1.01) | 0.058 | 0.960 |
| Height | 613.00±189.31 | 608.33±162.38 | 1.00 (0.99–1.00) | 0.940 | 0.210 |
| OD | 1106.82±225.29 | 1030.43±239.48 | 1.00 (0.99–1.00) | 0.381 | 0.536 |
| MHI | 0.44±0.11 | 0.48±0.11 | 0.03 (0.00–39.77) | 0.346 | 0.192 |
| THI | 0.87±0.31 | 1.21±0.60 | 0.14 (0.01–1.61) | 0.115 | 0.411 |
| HFF | 0.58±0.14 | 0.71±0.15 | 0.00 (0.00–0.81) | 0.044 | 0.409 |

BD: Base diameter, MD: Minimum diameter, OD: Opening diameter, MHI: Macular hole index, THI: Tractional hole index, HFF: Hole forming factor, SD: Standard deviation, OR: Odds ratio, CI: Confidence interval

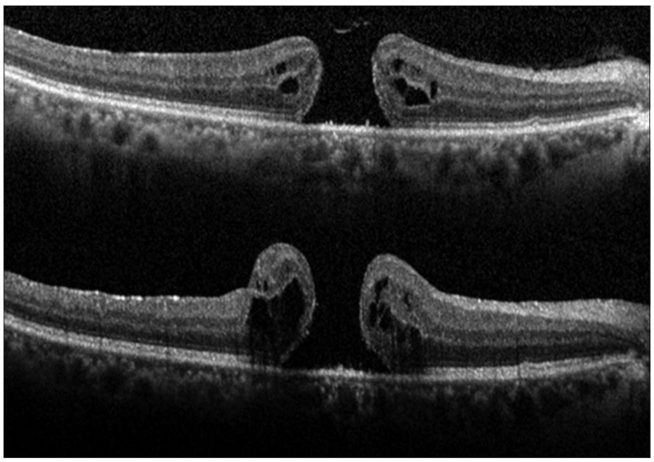

**Figure 3:** Ocular coherence tomography images showing preoperative (above) and postoperative (below) configuration of macular hole in patient number 14 (base diameter increased from 1159 to 1466; minimum diameter decreased from 665 to 680; and opening diameter increased from 410 to 584)

increasing the OD and the height of the hole. The swelling of the middle and outer retinal layers causes an increase in BD of the hole.[27]

After the secondary intervention in this study, anatomical closure was achieved in around 90% of the persistent macular holes. Type 1 anatomical closure was achieved in around 60% of the patients, while around 30% patients achieved Type 2 closure. BCVA increased by at least one line in more than two-third of the patients and at least two lines in around one-third of the patients. BCVA in about 50% of the patients who achieved Type 1 closure improved to ≥ 20/60. FGE makes the macula "dry" and provides adequate tamponade to halt the access of fluid to the various retinal layers. RPE pumps then drive the fluid out of the swollen macula.[13-19] Comparison of other studies evaluating the treatment of persistent macular holes by FGE is given in Table 4. The largest study till date was conducted by Rao *et al*. and included 23 patients with Stage IV macular hole. In their study, <50% patients achieved Type 1 closure.[13] The other two studies performed by Iwase and Sugiyama and Imai *et al*. included only two and one patient, respectively, with Stage IV macular hole. The size of FTMH included in their study was much smaller than those included in this study (this study – 0.45 disc diameter,

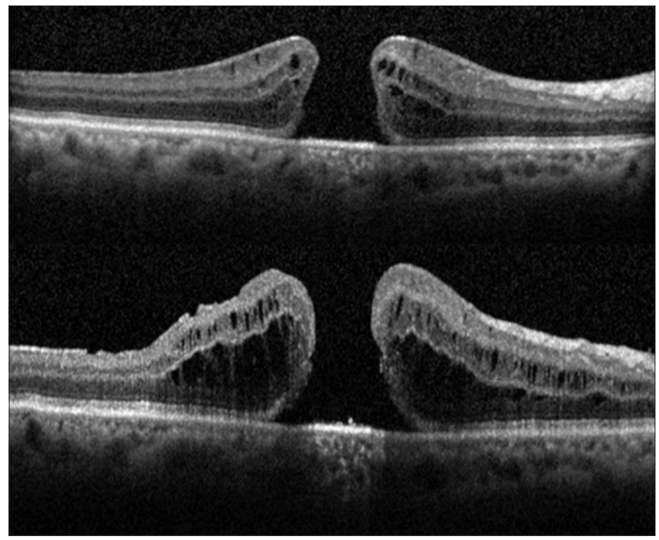

**Figure 4:** Ocular coherence tomography images showing preoperative (above) and postoperative (below) configuration of macular hole in patient number 19 (base diameter increased from 1301 to 1631; minimum diameter decreased from 689 to 644; and opening diameter increased from 480 to 654)

Iwase and Sugiyama – 0.37 disc diameter, and Imai *et al.* –0.29 disc diameter).[14,16] We had a lower anatomical success rate compared to these studies mainly because of the larger size of the holes included in this study.

FGE in the previous studies was performed as an office-based blind procedure and done on a slit lamp. On the other hand, we performed the procedure in the operating room and used a light probe to visualize the whole procedure. As a result, none of the patients in this study developed any of the severe complications such as retinal holes, retinal detachment, fibrinous exudates, or endophthalmitis. However, other authors have reported a high rate of such serious complications [Table 4].[13-15] We propose that the procedure should be performed in an operating room while visualizing the retina. This will not only ensure complete drying of the macula and better success rates but also a reduced rate of complications.

Previous studies have found that the macular holes "with a cuff of fluid" around the macular hole have a better chance of achieving anatomical success.[30,31] In this study, only the patients "with a cuff of fluid" around the macular

**Table 4: Previous studies evaluating the outcome of fluid-gas exchange in case of persistent macular hole (internal limiting membrane peeling done during primary surgery in all patients)**

| Author | Number of patients | Procedure of FGE | Anatomical outcome | Complications |
|---|---|---|---|---|
| Rao *et al.*[13] | 36 eyes<br>29 failed/7 reopened<br>13 Stage III, 23 Stage IV<br>Size NA<br>IOL status: NA | Gas (20% SF6 or 15% C3F8) injected into vitreous by syringe through 27 G needle, through inferior pars plana, Simultaneously, another 25 G needle inserted at another site in inferior pars plana to drain fluid. 4-8 mL of gas injected. Stopped when gas bubble started draining from fluid drainage syringe | Among Stage IV, Type 1 closure: 48% (*n*=11/23)<br>Type 2 closure: 35% (*n*=8/23)<br>No closure: 17% (*n*=4/23) | 2 eyes (6%) had RRD |
| Iwase *et al.* (2007)[15] | 7 eyes (all failed)<br>5 Stage III, 2 Stage IV<br>Size: 0.37±0.17 DD; (macular holes with duration >1 year and/or macular holes >0.5 DD were excluded)<br>All pseudophakic | Patient seated in front of slit lamp. 5 mL syringe, containing 20% SF6, connected to 27 G needle inserted into vitreous cavity through inferior sclera. 0.5 mL 20% SF6 injected and the same volume of fluid drained. Technique repeated 8-10 times | Anatomical closure: 7 eyes (100%); Type 1 and Type 2 not mentioned | Three eyes developed fibrinous exudate in anterior chamber |
| Imai *et al.*[14] | 5 eyes (all failed)<br>4 Stage III, 1 Stage IV<br>Size: 0.29 DD<br>All pseudophakic | Patient seated in front of slit lamp. FGE performed by one-syringe pumping technique. 10 mL syringe, containing 15% C3F8, connected to 26 G was inserted into vitreous cavity through inferior pars plana | Anatomical success: 5 eyes (100%)<br>U type closure in 2 eyes and V type closure in 3 eyes | Iris–lens adhesion in one case |

NA: Details not available, SF6: Sulfur hexafluoride, C3F8: Perfluoropropane, RRD: Rhegmatogenous retinal detachment, DD: Disc diameter, FGE: Fluid-gas exchange, IOL: Intraocular lens

hole were included in the study. We tried to find if there was any association between Type 1 anatomical closure and various macular hole and parameters of the persistent macular hole. However, there was no statistically significant association between Type 1 anatomical closure and either of the macular hole parameters or indices, after the secondary intervention.

The limitations of the study were those inherent with a retrospective study, lack of a control group, and the involvement of multiple surgeons. As only those patients who underwent a second surgery were included in the study, information on the patients who had failed primary surgery but declined subsequent surgery was not analyzed. The absence of information on these patients needs to be taken into account when interpreting the results. It is relevant to point out that no selection was made and all patients were advised further intervention. However, few patients declined any further intervention. Still, the results of the study are encouraging as a decent rate of anatomical closure, and visual recovery was achieved with minimum complication rate.

## Conclusion

Unsuccessful surgery causes swelling of the outer and middle retinal layers with retraction of inner layers of the retina. Performing FGE while visualizing the retina is a good option for the treatment of large persistent macular holes as it causes complete drying of the macula, better success rates, and a reduced complication rate. Pre-FGE OCT does not help in predicting the outcome of FGE for persistent macular hole.

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### Conflicts of interest

There are no conflicts of interest.

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