J Appl Biomed
DOI: 10.32725/jab.2026.010
journal homepage: http://jab.zsf.jcu.cz

Journal of Applied Biomedicine

Authors' response to the Letter to the Editor

Five-year outcomes of posterior chamber phakic implantable collamer lens implantation in high myopia, keratoconus, and post-keratoplasty eyes

Iveta Nemcova [1, 2] *, Jiri Pasta [1, 2], Katerina Hladikova [1, 2], Martin Komarc [2, 3], Darina Pospisilova [1], Jan Havlik [1], Jan Tesar [1, 2], Vladimir Kratky [2, 4], Martin Sin [1, 2]

[1] *Military University Hospital Prague, Department of Ophthalmology, Prague, Czech Republic*
[2] *Charles University, 1st Faculty of Medicine, Prague, Czech Republic*
[3] *Charles University, Faculty of Physical Education and Sport, Department of Methodology, Prague, Czech Republic*
[4] *Queen's University, Kingston Health Sciences Centre, Kingston, Canada*

We thank the author (Tahavvori, 2026) for his careful reading of our article Nemcova et al. (2026) and for raising important questions regarding inter-eye dependency, incomplete follow-up, and the calculation of physiologically corrected endothelial cell loss (EC loss). We welcome the opportunity to clarify these methodological aspects and have conducted additional statistical analyses to determine whether the issues raised materially affect the findings and conclusions of our study.

Inter-eye dependency and statistical analysis

We agree that measurements obtained from fellow eyes of the same patient cannot be assumed to be completely independent. We would nevertheless like to clarify the rationale underlying the originally published analytical approach.

The eye was selected as the primary unit of analysis because the intervention was performed at the eye level and all clinical outcomes were measured separately for each eye. For the principal endothelial outcome, we considered the longitudinal dependency of repeated measurements within the same eye to be the dominant source of correlation. This dependency was explicitly addressed in the original linear mixed-effects model by modelling repeated observations within each eye.

Given the limited sample of 30 eyes from 18 patients, we initially selected a parsimonious model and did not include an additional patient-level random effect. Model specification inevitably requires a balance between adequately representing the dependency structure and avoiding unstable estimation of an overly complex covariance structure, particularly when the number of higher-level units is small. Thus, the original approach did not arise from an assumption that fellow eyes are biologically unrelated. Rather, it reflected a modelling decision that prioritised longitudinal dependency within each eye and model parsimony in a small dataset (McNeish and Stapleton, 2016).

We nevertheless acknowledge that the original model did not explicitly account for residual correlation between fellow eyes and that the patient level should ideally have been included or examined in a sensitivity analysis. We appreciate the author drawing attention to this issue.

We therefore reanalysed the longitudinal outcomes using linear mixed-effects models in which repeated observations were nested within eyes, and eyes were nested within patients. A patient-specific random intercept was included to account for correlation between fellow eyes, while the repeated-measures component accounted for longitudinal dependency within each eye (Ying et al., 2021). This allowed us to assess whether the simpler specification used in the original article materially affected the results.

The reanalysis confirmed that the principal findings concerning endothelial cell density remained unchanged. The comparisons yielded $P = 0.004$ for baseline versus 1 year, $P = 0.254$ for 1 versus 2 years, and $P < 0.001$ for 2 versus 5 years. All three comparisons therefore retained the same statistical interpretation as in the original analysis.

The analyses of the other longitudinal outcomes were repeated using the same hierarchical framework. Pearson correlations were reassessed using standard errors clustered at the patient level. The correlation coefficients and their directions remained unchanged, as the clustering adjustment affected the estimated uncertainty rather than the observed associations. Although some *P* values changed slightly, every correlation discussed in the original article retained its classification as statistically significant or nonsignificant.

The table on the following page shows the principal differences between the originally reported and patient-clustered longitudinal analyses.

*** Corresponding author:** Iveta Němcová, Military University Hospital Prague, Department of Ophthalmology, U Vojenské nemocnice 1200, Prague 6, Czech Republic; e-mail: Iveta.nemcova@uvn.cz
http://doi.org/10.32725/jab.2026.010
Submitted: 2026-10-08 • Accepted: 2026-10-30 • Prepublished online: 2026-11-03
J Appl Biomed 24/x: xxx–xxx • EISSN 1214-0287 • ISSN 1214-021X
© 2026 The Authors. Published by University of South Bohemia in České Budějovice, Faculty of Health and Social Sciences.
This is an open access article under the CC BY-NC-ND license.

Outcome and comparison	Originally reported *P*	Patient-clustered analysis *P*	Change in statistical interpretation
MRSE: baseline vs 1 year	<0.001	<0.001	No
MRSE: 1 vs 2 years	0.244	0.309	No
MRSE: 2 vs 5 years	0.029	0.022	No
Cylinder: baseline vs 1 year	**0.062**	**0.035**	**Yes**
Cylinder: 1 vs 2 years	0.085	0.062	No
Cylinder: 2 vs 5 years	0.779	0.761	No
CDVA: baseline vs 1 year	<0.001	<0.001	No
CDVA: 1 vs 2 years	**0.033**	**0.060**	**Yes**
CDVA: 2 vs 5 years	0.103	0.154	No
UDVA: 1 vs 2 years	**0.100**	**0.025**	**Yes**
UDVA: 2 vs 5 years	**0.040**	**0.082**	**Yes**
IOP: baseline vs 1 year	0.279	0.238	No
IOP: baseline vs 5 years	0.005	0.002	No
ECD: baseline vs 1 year	0.004	0.004	No
ECD: 1 vs 2 years	0.282	0.254	No
ECD: 2 vs 5 years	<0.001	<0.001	No

Several *P* values for secondary outcomes crossed the conventional 0.05 threshold after the additional clustering was taken into account. These changes are consistent with the expected effect of modelling an additional source of dependency: the observed means, mean differences, and directions of the effects remained unchanged, whereas their standard errors and, consequently, some *P* values close to 0.05 changed.

Specifically, the baseline-to-1-year change in cylinder became statistically significant, the 1-to-2-year change in CDVA became nonsignificant, and the statistical interpretations of the two longitudinal UDVA comparisons were reversed. These were secondary outcomes, and the original discussion did not rely on these borderline comparisons to support the principal clinical conclusion. Their updated interpretation would be that cylinder showed a small early change followed by stability, whereas UDVA differed between years 1 and 2 but not between years 2 and 5.

Most importantly, none of these changes concerned the principal endothelial outcome. The pattern of endothelial cell loss (EC loss), the significance of its longitudinal changes, and the significance classifications of its reported associations with the clinical predictors remained unchanged after the dependency of fellow eyes was explicitly taken into account.

Incomplete follow-up and differing denominators

We agree that the visit-specific denominators and reasons for missing measurements should have been described more clearly.

The denominators differed because not every outcome was available for every eye at every visit. For the refractive outcomes, measurements were available for 30 eyes at baseline, 29 eyes at 1 year, and 26 eyes at both 2 and 5 years. For endothelial cell density, measurements were available for 30 eyes at baseline and 1 year, and for 26 eyes at 2 and 5 years. Missing follow-up data were due either to patients not attending their scheduled follow-up visits or to individual measurements being unavailable.

In the additional analyses, all available observations were retained in the linear mixed-effects models. An eye was therefore not excluded merely because one of its follow-up measurements was unavailable, and missing observations were neither replaced by zero nor imputed using a single estimated value. Each eye contributed all available information up to its last observed measurement.

Likelihood-based mixed-effects estimation is particularly appropriate for unbalanced longitudinal data because it does not require every eye to have a complete set of observations. Under the assumption that the probability of a missing measurement can be explained by observed information included in the analysis – that is, the missing-at-random assumption – the approach provides valid estimates without listwise exclusion of incomplete cases.

We recognise that no statistical model can entirely exclude bias if missingness is related to an unobserved clinical outcome. The limited sample and incomplete follow-up should therefore be considered when interpreting the precision of the estimates. Nevertheless, the mixed-effects approach made the most complete use of the available longitudinal information and avoided restricting the analysis to eyes with complete data at all time points.

Physiologically corrected endothelial cell loss

We agree that the values reported in Table 6 are inconsistent with the stated physiological EC loss of 0.6% per year. This resulted from a calculation and transcription error: 0.30 and 0.60 percentage points were subtracted at 1 and 2 years, respectively, instead of the intended 0.60 and 1.20 percentage points.

The correct calculations are:

- at 1 year: 4.12% – 0.60% = 3.52%
- at 2 years: 5.63% – 1.20% = 4.43%
- at 5 years: 14.41% – 3.00% = 11.41%

Accordingly, the physiologically corrected EC losses should be 3.52%, 4.43%, and 11.41% at 1, 2, and 5 years, respectively. We apologise for this error and appreciate the opportunity to correct it.

This correction changes the descriptive estimates at 1 and 2 years but does not affect the statistical analyses of the longitudinal endothelial cell density (ECD) measurements. Those analyses were based on the observed ECD values rather than on the subsequently calculated physiologically corrected percentages. The associated *P* values and statistical conclusions therefore remain unchanged.

Moreover, the corrected 5-year estimate of 11.41%, which is particularly relevant to the long-term assessment of endothelial safety, was reported correctly and remains unchanged.

To avoid implying direct causation, these values are more appropriately described as the estimated EC loss remaining after subtraction of the assumed physiological decline, rather than as EC loss directly caused by the implanted lens.

Clinical interpretation and endothelial preservation

The primary aim of our research was to evaluate the long-term outcomes of phakic intraocular lenses (pIOLs) implanted at the Department of Ophthalmology, Military University Hospital Prague, over approximately 20 years, with particular emphasis on their different long-term risk profiles and implications for postoperative follow-up.

Although iris-fixated phakic intraocular lenses (IF pIOLs) are now implanted less frequently, many patients with these lenses continue to require long-term monitoring, and some may eventually need additional surgical interventions or lens explantation. In contrast, posterior chamber implantable collamer lenses (ICLs) with a central port are widely used in contemporary refractive surgery. As patients may receive subsequent ophthalmic care at different centres, understanding the specific long-term risks associated with each lens type remains clinically relevant.

Our intention in discussing the results of our previously published IF pIOL study alongside the present V4c ICL cohort (Nemcova et al., 2021, 2026) was to provide a broader clinical perspective rather than to perform a direct statistical comparison between two independent, nonconcurrent cohorts. Importantly, the cohorts were comparable in several key baseline characteristics, particularly age and degree of myopia. In both studies, patient selection followed established indication criteria specific to the implanted lens type, including the relevant anatomical requirements. We acknowledge that differences in lens-specific eligibility criteria, the inclusion of selected eyes with corneal pathology in the V4c ICL cohort, follow-up duration, and surgical era limit direct comparative conclusions. Nevertheless, the similarity in major demographic and refractive characteristics, together with the experience gained at the same surgical centre, provides a meaningful clinical context for interpreting the different long-term safety profiles of these lens designs.

We acknowledge the limitations associated with the relatively small and heterogeneous V4c ICL cohort, as already stated in our original publication. The inclusion of eyes with stable keratoconus and previous penetrating keratoplasty (PKP) was intentional, reflecting the clinical practice of specialised corneal and refractive surgery centres, where ICL implantation may offer visual and refractive benefits in carefully selected patients. These indications are relatively uncommon, and long-term evidence remains limited. We therefore considered it valuable to report our clinical observations, including endothelial outcomes, while recognising that the very small subgroup sizes do not allow reliable subgroup-specific conclusions.

We appreciate the reference to Jadidi et al. (2019), which illustrates the potential value of evaluating specific anatomical subgroups. However, their study focused on eyes with low vault, whereas our study included patients with stable keratoconus and previous PKP, representing different clinical circumstances. We agree that larger studies with adequately sized and more homogeneous subgroups would be valuable. In our cohort, descriptive reporting of these uncommon indications was considered more appropriate than separate statistical analyses.

We also recognise that the single-centre, single-surgeon design limits the generalisability of our findings. At the same time, the fact that all procedures were performed by the same surgeon reduced variability related to surgical technique and experience. Long-term follow-up data of this nature remain difficult to obtain, particularly in refractive surgery patients who may subsequently attend different centres.

Importantly, lower baseline ECD does not necessarily imply a faster rate of postoperative EC loss. Although greater EC loss was observed more frequently in eyes with keratoconus or previous PKP in our cohort, the small number of such eyes prevents us from attributing this finding directly to the underlying corneal diagnosis.

Other factors, including anterior segment anatomy, may contribute to the observed differences. In particular, the eligibility criteria for eyes following PKP allowed a narrower preoperative anterior chamber angle, and our analysis identified an association between anterior chamber angle and postoperative EC loss. These findings underline the importance of considering individual anatomical characteristics when interpreting endothelial outcomes, rather than attributing endothelial loss solely to the presence of corneal pathology.

Regarding the expression "superior endothelial preservation" in our conclusion, we acknowledge that this wording may imply a level of comparative evidence that our study design cannot establish. Our conclusion was based on the observation that physiologically corrected EC loss was lower in the V4c ICL cohort than that reported in our previously published IF pIOL cohort. This was observed despite the inclusion of eyes with stable keratoconus and previous PKP, in which greater EC loss occurred more frequently. The inclusion of these clinically complex eyes may therefore have adversely affected the overall endothelial outcome of the V4c ICL cohort. We considered these observations suggestive of a more favourable endothelial safety profile of V4c ICLs. However, we agree that differences between independent historical cohorts cannot establish direct comparative superiority. We therefore recognise that our original wording was stronger than warranted by the study design and would more appropriately describe the findings as suggesting, rather than demonstrating, a potential advantage in endothelial preservation.

Overall conclusion

The additional statistical analyses demonstrate that explicitly accounting for the nesting of eyes within patients does not alter the conclusions concerning the principal endothelial outcome. All statistically significant and nonsignificant comparisons of ECD retained their original interpretation, as did the significance classifications of the reported correlations involving EC loss. The conclusions concerning MRSE and intraocular pressure also remained unchanged.

We acknowledge that the additional analysis resulted in changes to several P values for secondary outcomes, particularly those originally close to the conventional 0.05 threshold. These changes concern the estimated uncertainty of the secondary comparisons and do not represent reversals in the observed means or directions of the effects. They do not ma-

terially alter the principal clinical interpretation or the overall conclusions of the article. We also acknowledge the calculation error in the physiologically corrected EC loss at 1 and 2 years. The corrected values are 3.52% and 4.43%, respectively, while the 5-year value remains 11.41%. This numerical correction does not affect the underlying longitudinal ECD analysis or its statistical significance.

We recognise the limitations associated with the relatively small and heterogeneous cohort, the very small keratoconus and post-keratoplasty subgroups, and incomplete follow-up. We also acknowledge that the comparison with our previously published iris-fixated lens cohort is observational and does not establish direct comparative superiority of one lens design over another. Nevertheless, these limitations do not negate the observed long-term endothelial outcomes. The additional analyses support the stability of the principal statistical findings and reinforce the clinical relevance of long-term endothelial monitoring following phakic intraocular lens implantation.

We believe that the clarifications and additional analyses presented in this response address the methodological concerns raised in the Letter to the Editor and demonstrate the robustness of the principal findings. Should the Editor consider a formal correction necessary, we would of course be prepared to provide a concise correction limited to the affected descriptive values, secondary P values, and accompanying wording. The central findings concerning longitudinal EC loss and the main clinical interpretation of the study remain unchanged.

Ethical aspects and conflict of interest

The authors have no conflict of interest to declare.

References

McNeish DM, Stapleton LM (2016). The effect of small sample size on two-level model estimates: A review and illustration. Educ Psychol Rev 28(2): 295–314. DOI: 10.1007/s10648-014-9287-x.

Nemcova I, Pasta J, Hladikova K, Komarc M, Pospisilova D, Havlik J, et al. (2026). Five-year outcomes of posterior chamber phakic implantable collamer lens implantation in high myopia, keratoconus, and post-keratoplasty eyes. J Appl Biomed 24(2): 72–80. DOI: 10.32725/jab.2026.004.

Nemcova I, Pasta J, Hladikova K, Komarc M, Pospisilova D, Nemec P, Tesar J, et al. (2021). Myopic Correction with Iris-Fixated Phakic Intraocular Lenses: Twelve-Year Results. J Ophthalmol 2021: 7027793. DOI: 10.1155/2021/7027793.

Jadidi K, Mosavi SA, Nejat F, Mohammadi N, Aghamolaei H, Daryabari SH, Torabi H, Alishiri A (2019). Use of low-vault posterior chamber collagen copolymer phakic intraocular lenses for the correction of myopia: a 3-year follow-up. Graefes Arch Clin Exp Ophthalmol 257(7): 1555–1560. DOI: 10.1007/s00417-019-04336-9.

Tahavvori M (2026). Comment on “Five-year outcomes of posterior chamber phakic implantable collamer lens implantation in high myopia, keratoconus, and post-keratoplasty eyes”. J Appl Biomed 24(4): 101–102. DOI: 10.32725/jab.2026.009.

Ying GS, Maguire MG, Glynn RJ, Rosner B (2021). Tutorial on biostatistics: Longitudinal analysis of correlated continuous eye data. Ophthalmic Epidemiol 28(1): 3–20. DOI: 10.1080/09286586.2020.1786590.