Motivation: Predicting the subject-specific future outcome of a disease under treatment is essential in precision medicine.

Aim: Predict future visual acuity outcomes of patients under treatment from early time-points combining longitudinal spectral domain optical coherence tomography (SD-OCT) images and ETDRS Best-Corrected Visual Acuity (BCVA) scores.

Methodology:
- Assumption: visual acuity and its development is affected by three major factors: (1) amount of fluid in retina, (2) reversible damage and (3) irreversible damage.
- Population-wide BCVA trajectories are modeled as a function of time and fluid volume using Mixed-effects regression [1]. Using random slope and intercept per subject allows to model deviation from population-wide BCVA trajectory accounting for variance in reversible and irreversible damage (random intercept) and speed of recovery (random slope).
- IRF and SRF volume in central millimeter are obtained from automatic segmentations in fovea aligned OCT volumes [2].
- BCVA trajectories for an unobserved subject are predicted from population-wide model and initial subject observations by estimating random intercept/slope and BCVA trajectory for the subject using Best Linear Unbiased Predictor (BLUP) [1].

Results - Model fit:
- Training and Validation Set: 194 patients with macular edema secondary to central retinal vein occlusion.
- Retinal SD-OCT baseline scan + 12 monthly follow-up scans from two vendors (Heidelberg Spectralis, Zeiss Cirrus), 2,433 scans overall.
- ETDRS BCVA acquired at each visit.
- Treatment and follow-up are based on three month induction phase with monthly ranibizumab injections, followed by a PRN (pro re nata = per need) regimen.

Models:
- Two models were fitted to BCVA scores, one incorporating IRF and SRF volume, as well as a quadratic time term ($T^2$), and a baseline model assuming linear trajectories based on BCVA only ($T$).

Results:
- Morphology:
  - IRF and SRF volume factors were significant (p<0.0001).
  - An increase of IRF / SRF volume by 1000 µm³ cause a mean decrease (SD) in BCVA of 0.0409 (0.00021) / 0.0258 (0.0033) letters.

- Target variable: median BCVA month 10 to 12
- Performance measures:
  - Mean absolute error (MAE) in letters.
  - Predicted R²

Results - Prediction:
- Validation:
  - 5-fold cross validation setup.
  - BCVA population models $\text{bcva}$ and $\text{bcva+oct}$ are computed from training fold.
  - For each subject in test fold random factors and BCVA trajectories are predicted for an increasing amount of time-points.
- Target variable: median BCVA month 10 to 12
- Performance measures:
  - Mean absolute error (MAE) in letters.
  - Predicted R²

Conclusions:
- We propose a method to predict future visual acuity development and outcome under treatment combining knowledge from a population-wide model and patient specific information from initial visits.
- Longitudinal mixed-effects model allows to model the population-wide trend of BCVA development, and the patient-wise deviation from the general trend according to the various disease progression stages at first visit and differing response to treatment. Furthermore, the model allows to estimate the influence of intraretinal and subretinal fluid on BCVA.
- Incorporating intraretinal and subretinal fluid into the model from automatic segmentations in SD-OCT images improves model accuracy and prediction performance.

References:
[1] Wolf-Dieter Vogl, Sebastian M. Waldstein, Bianca S. Gerendas, Thomas Schlegl, Jing Wu, Dominika Podkowski, Ursula Schmidt-Erfurth, and Georg Lang, Computational Imaging Research Lab (CIR), Department of Biomedical Imaging and Image-guided Therapy, Vienna Reading Center, Department of Ophthalmology and Optometry, Christian Doppler Laboratory for Ophthalmic Image Analysis (OPTIMA), Medical University of Vienna, Austria.