

PROTECT Completed 3-Year Study Results: A Catenary-Curve Multifocal Contact Lens Reduces Pediatric Myopia Progression and Mitigates Common Risk Factors

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PURPOSE:

To identify predictors of pediatric myopia progression and assess how a catenary-curve multifocal contact lens mitigates their influence on refractive and axial progression.

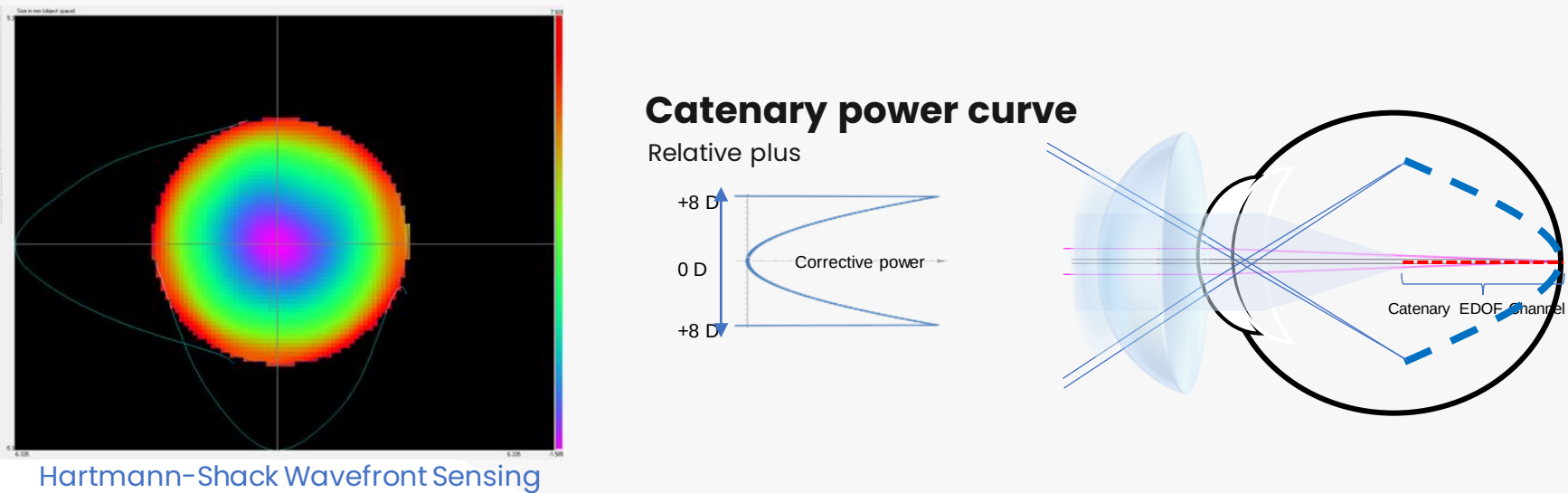


Figure 1. NVMF daily disposable soft contact lens with a distance-center aspheric multifocal optical power profile. **Left:** Wavefront measurement of NVMF, decomposed to power profile; 8 D of relative plus at 6 mm diameter **Right:** Schematic of the light rays passing through NVMF optic into the eye.

METHODS:

- PROgressive Myopia Treatment Evaluation for NaturalVue Multifocal Contact Lens Trial, PROTECT (NCT05159765) on pediatric myopes was a prospective, multi-center, double-blind, randomized controlled trial (vs. single vision and DyNaSynth™ synthetic control).
- 145 subjects randomized (2:1) to **Intervention Arm** (NVMF, Figure 1) or Control Arm (SVCL) in North America (U.S., Canada) and Asia (Hong Kong, Singapore), with 126 completed at 36 months planned follow-up.
- Active Control Arm (SVCL):** Single vision daily disposable lens with the same material as Intervention arm, with a cross-over at 24-month visit.
- Virtual Control Arm: DyNaSynth™** is designed to address the absence of an active control group at 36-month by providing a more robust estimate of the expected natural history trajectory, with less variability than would be expected from the relatively small control-group sample size in the study.
- DyNaSynth™ is a synthetic cohort of individual patient years that form a trajectory that is matched to the specific characteristics of the PROTECT Study Active Control subjects. DyNaSynth™ draws initially on actual data (control arm) collected from 50 different sources, and then assembled together with machine learning, entropy balancing, and then matching using known prognostic factors. Advantages of meta-analytic estimates and standard external controls include specific adjustments to subject and disease heterogeneity rather than pooling into a single point estimate, which does not offer minimum variance, best linear unbiased estimate (MVBLUE). DyNaSynth™ is currently endorsed for use in 4 ongoing FDA-approved clinical trials.
- Baseline age: 7 to 12 years old
- Baseline cycloplegic autorefraction: -0.75 D to -5.00 D
- Primary and Secondary Outcomes: Change of cycloplegic autorefraction [CSER] from baseline to 36-month and change of axial length [AXL] from baseline to 36-month.
- Outcome measures estimate applied specific statistical models:

Intervention arm & Active Control Arm: An outcome model via generalized linear mixed modeling (treatment, time, and treatment by time) with adjustments for age, sex, ethnicity, country, study site, and per-eye baseline value. A random intercept for subject handles within-person OD/OS correlation and repeated measures. This presentation focuses on the DyNaSynth™ Virtual Control arm for the treatment effect calculation.

Virtual Control (DyNaSynth™) arm: Matching to the baseline characteristics of the PROTECT SVCL subjects, preserving the heterogeneity/subject-level variations, with a method-of-moments comparison at each of the four-time observation waves (baseline, 12m, 24m, and 36m).

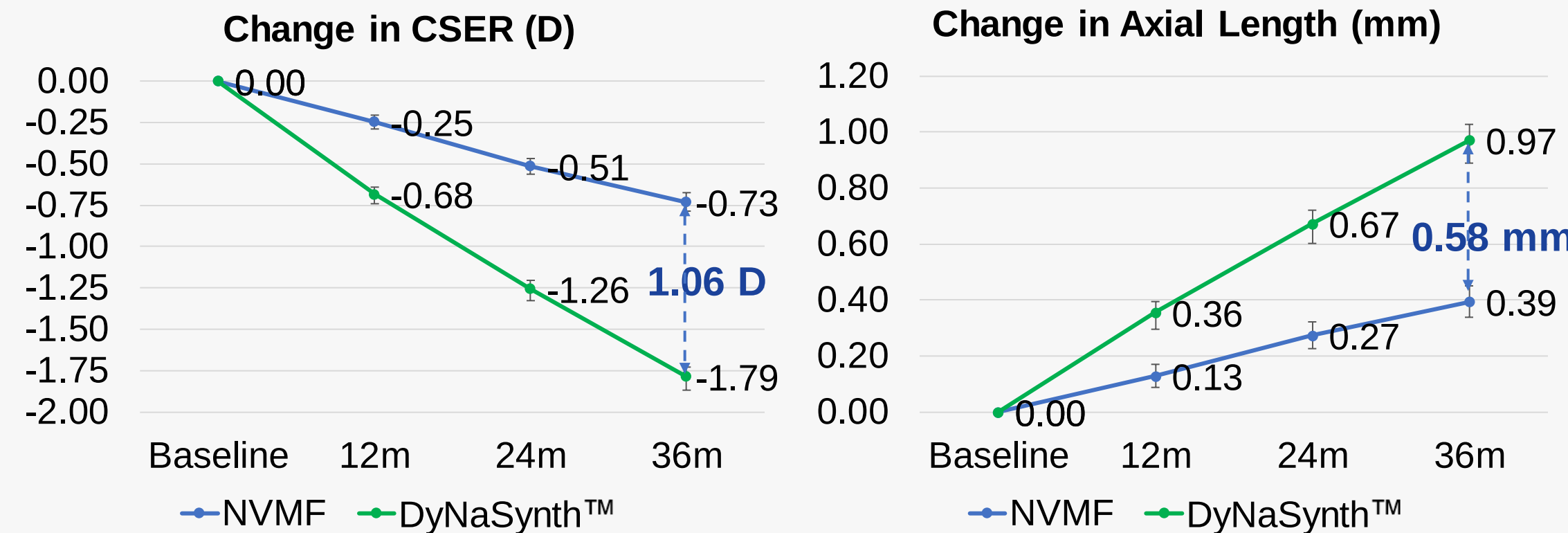


Figure 2. Refractive error (CSER) and axial length (AXL). Adjusted LS means, change from baseline. Error bars ±1 SE (Kenward-Roger 95% CI half-width ÷ 1.96). The DyNaSynth™ Control Group trajectory represents the expected natural-history progression in the absence of any myopia-control intervention.

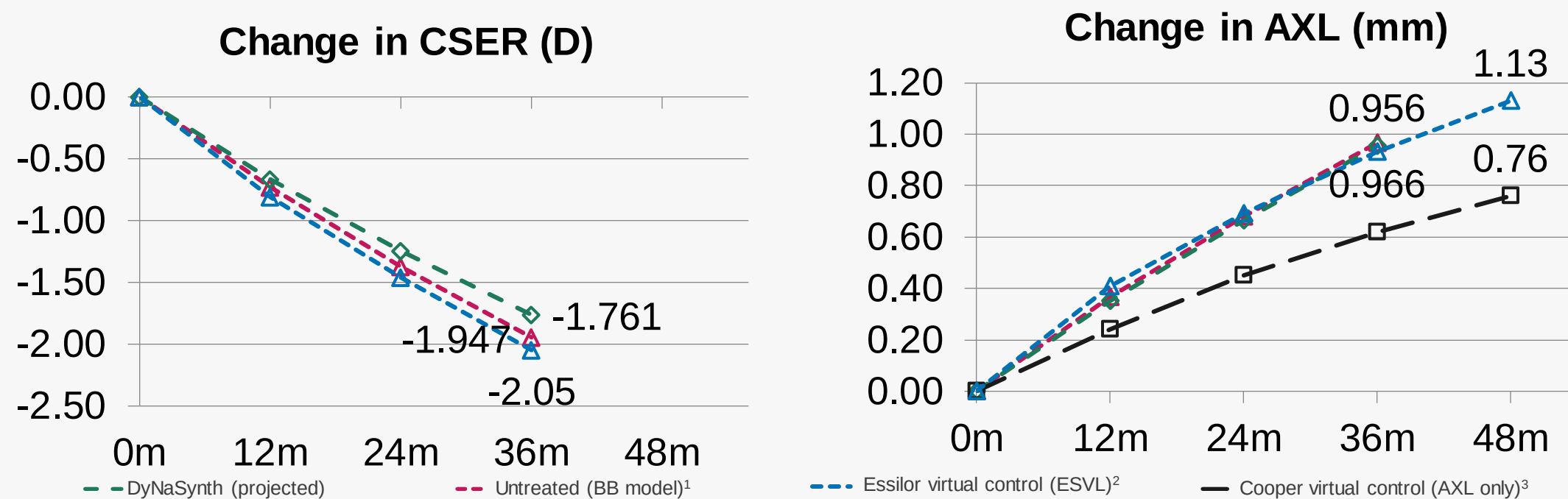


Figure 3. DyNaSynth™ Synthetic Control Compared to Published Virtual Control Groups
1. 15%/yr in AL (Shamp, Brennan, Bullimore et al, IOVS 2022;63:A0111), plotted to each chart's endpoint. <https://bullers2020.com/s/Axial-Elongation-and-Myopia-Progression-with-Age.xlsx>
2. Essilor virtual control (ESVL), the 2-year Wenzhou SVL control (Bao, JAMA Ophthalmol 2022;140:472-478) extrapolated at 9.7%/yr in SER (Smotherman, IOVS 2023;64:811); starting age 8-13, 100% Chinese
3. Cooper virtual control based on MiSight 36M Data (Chamberlain, Ophthalmic Physiol Opt 2024;44:199-205), starting age 8-12, ~22% Asian.

RESULTS (Treatment Effect):

- The synthetic control trajectory model developed from the PROTECT study was verified against published virtual control group models of myopia progression, demonstrating a high degree of concordance between the modeled trajectories. The differences may be explained by the proportion of Asian subjects in these models.
- 36m Adjusted LS Mean (95% CI) CSER progression was -1.79 (-1.95,-1.62) D vs -0.73 (-0.84,-0.62) D (NVMF), a difference of 1.06 D;
- 36m adjusted LS Mean (95% CI) AXL progression was 0.971 (0.90,1.04) mm (Control) vs 0.39 (0.35,0.44) mm (NVMF), a difference of 0.58 mm.

METHODS (Risk Factor Mitigation):

- Risk factors evaluated in this study: Baseline CSER, AXL, age and pupil size, age of onset, family history, and lifestyle factors were obtained and evaluated.
- Statistical method: Machine Learning methods were used to identify unique trajectories of change over the baseline and 24-month outcomes in the Active Control (Natural History) and Intervention arms, with gradient boosting methods employed to identify and rank the most powerful factors, and the degree to which the contact lens intervention could reduce the impact of these underlying risk factors.

CONCLUSIONS:

- NVMF significantly reduced CSER and AXL progression by an average of 1.06 D and 0.58 mm in 3 years of treatment.
- Natural history indicates myopia progression occurs most rapidly in children with early age of onset, genetic risks, and lifestyle. These factors had a relatively minor influence on the subjects wearing the NVMF lenses.
- NVMF buffered/mitigated the influence of both modifiable and immutable risk factors known to portend myopia progression, resulting in a consistent and robust treatment outcomes across a broad range of age and other risk factors.

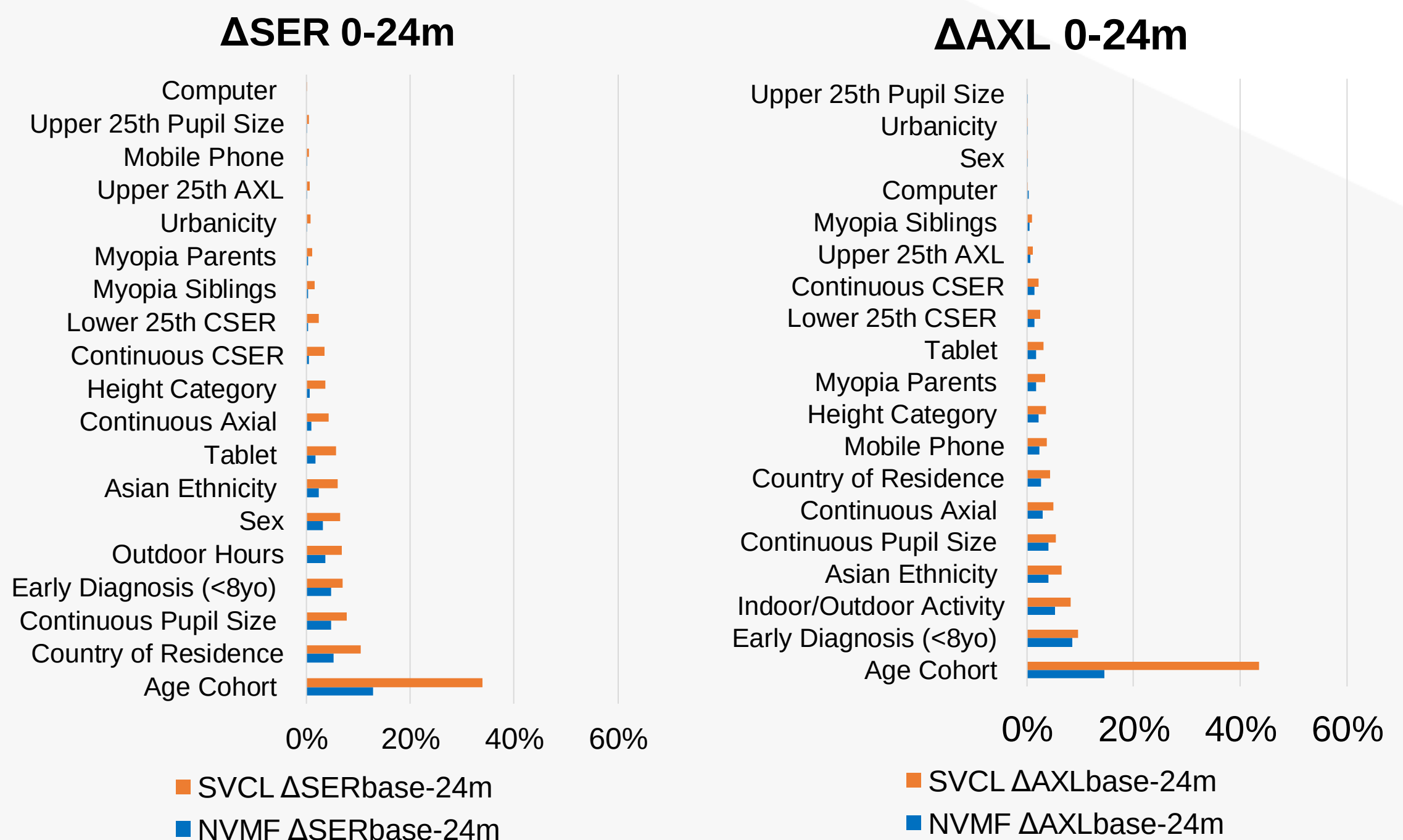


Figure 4. GLMM for heterogeneous treatment effects risk factors

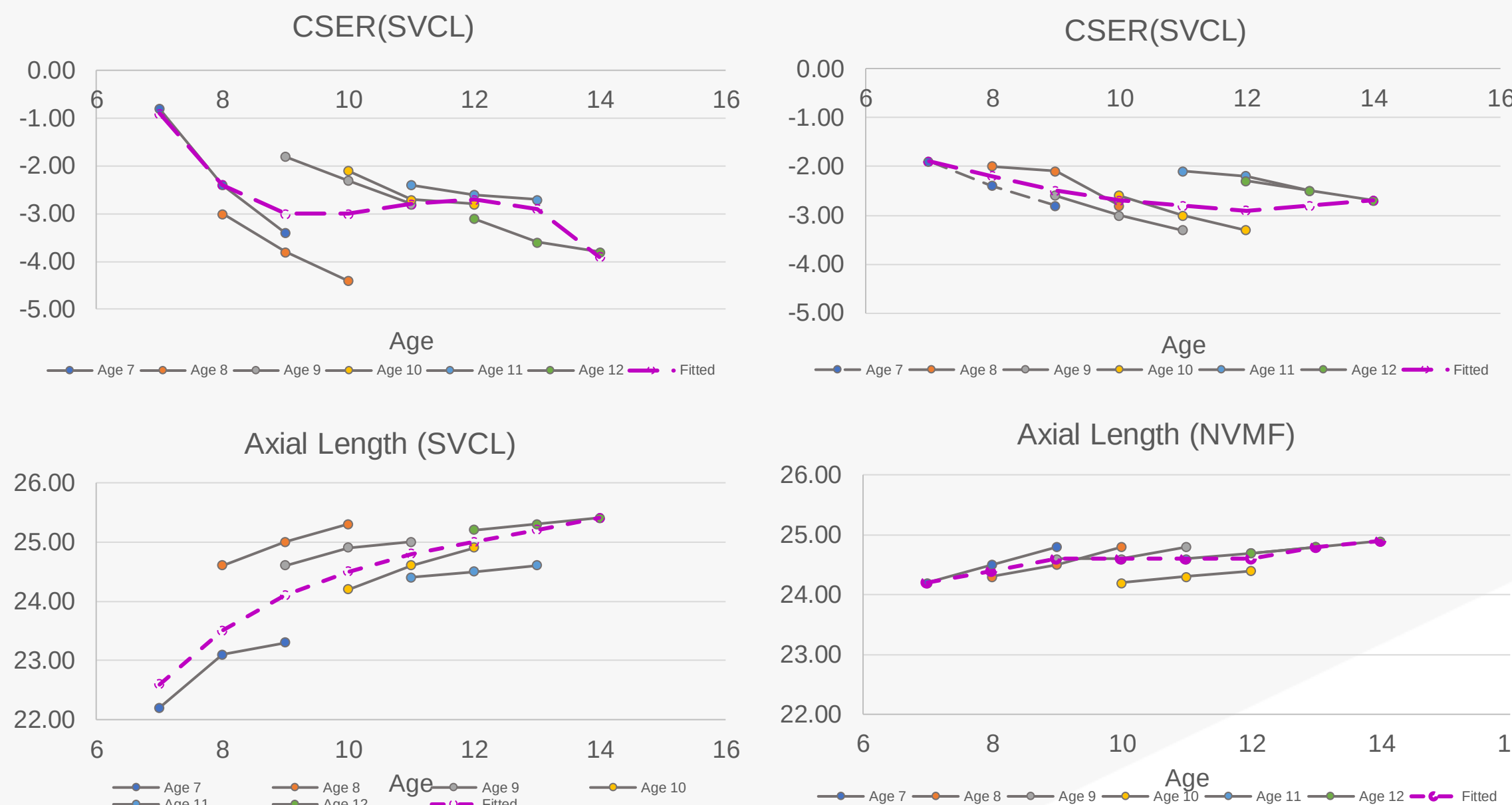


Figure 5. Refractive error (CSER) and axial length (AXL) by age at observation, stratified by baseline age cohort

RESULTS (Risk Factor Mitigation):

- CSER progression risk factors (Figure 3):
 - Control (= natural history), the top risk factor was age
 - NVMF: minimized the total impacts by 58%, and 63% of the age impact.
- AXL progression risk factors (Figure 3):
 - Control (= natural history), top risk factor was age
 - NVMF: minimized the total impacts of the above by 45%, and 66% of the age impact.
- Wearing NVMF showed a slower progression of CSER and AXL, and the magnitude was similar across age (Figure 4), suggesting that age of initiation did not alter treatment outcomes.

**US: NaturalVue® (etafilcon A) Multifocal 1 Day Disposable Soft Contact Lenses are indicated for daily wear for the correction of refractive ametropia (myopia and hyperopia), and/or presbyopia in normal eyes. OUS: indicated for daily wear for the correction of refractive ametropia (myopia and hyperopia), and/or presbyopia, and myopia progression control in normal eyes.