

## Ten Most Mis-interpreted Evidence in Myopia Management

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## Financial Disclosure

- I receive consulting fees from
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  - Essilor
  - No commercial interests

## Mis-interpretation 1. Heritability is pure evidence for genetic influence

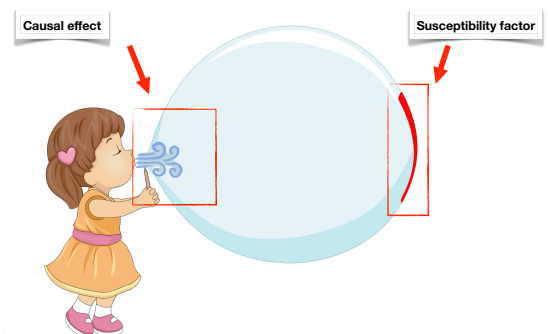
## Poll 1. Which of the following statement regarding the etiology of myopia is true?

- A. Myopia is mostly genetic, and the environmental factors only play minor role.
- B. The heritability is a reliable measure of the genetic influence of parental myopia.
- C. All myopia share similar etiology.
- D. Juvenile myopia is induced by abnormal visual experience, however with strong genetic predispositions.

## Common statement from parents:



## Juvenile Myopia = Visual Stress + Scleral Resistibility



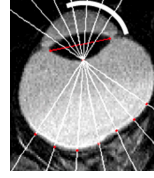
## Sources of genetic vs. environmental variances

- **Genetic source**
  - **Additive** - the sum of the effect of each allele
  - **Non-additive** - allele x allele interactions
- **Environmental source**
  - **Shared environmental factors**
  - **Unique environmental influences**

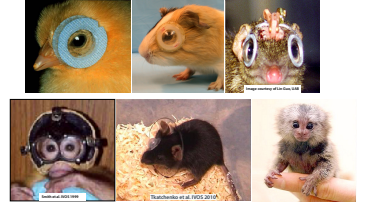
**Familial studies subject to high risk of confounding from shared environmental factors!**

## Evidence for causal inference of environmental factors

- **Rapid global increase of myopia incidence** - not explainable by rate of genetic changes
- **Lack of evidence for causal genes**
- **Local control of ocular growth**



Smith et al. Invest Ophthalmol Vis Sci. 2009;50(12):6857-66.



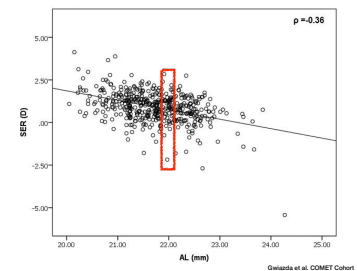
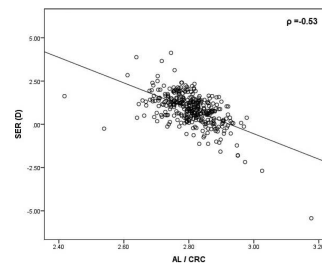
## Mis-interpretation 2. Axial length is closely associated with refractive error

## Mis-interpretation 3. Axial length is the most reliable predictor of myopia complications

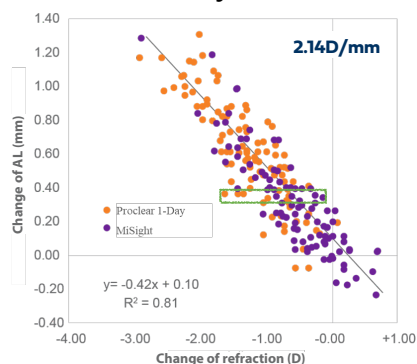
## Poll 2. Who has higher risk of myopia related complications?

- A -3D myope with AL of 24mm
- An emmetrope with AL of 25mm

## Statistically significant association $\neq$ predictive

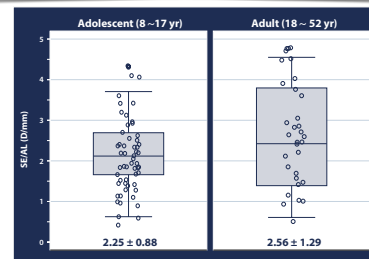


**The change of refraction is closely associated w. the change of AL**



**1mm AL elongation ≠ 3D myopia progression & its highly age-dependent**

**Age-related axial elongation:**  
4-8yr:  $0.3 \pm 0.17$ mm (n=243 eyes); 8-12yr:  $0.12 \pm 0.12$ mm (n=404 eyes)



**Misinterpretation 4. AL increase means  
myopia progression**

**Misinterpretation 5.**

**Relative change of AL provides  
reliably quantification of anti-myopia efficacy**

**Poll 3. T/F Any unit change of AL has the same impact on refractive change,  
implication on the myopia control efficacy, or the risk of complications.**

- A. True
- B. False

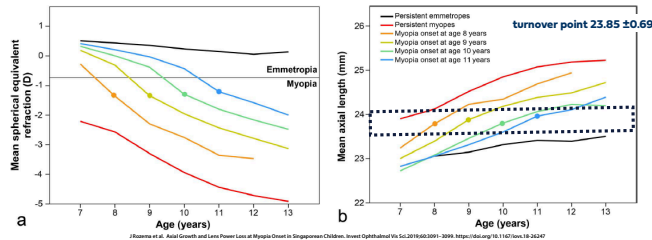
**Patient 1. 6YOAF, annual AL change 0.30 mm from 23.00mm**  
**Patient 2. 35YOCM, annual AL change 0.12mm from 26.50mm**

**Doctor's statement regarding myopia control efficacy:**

"The anti-myopia efficacies among various clinical trials are very comparable, and the relative change of AL is the best outcome measure".



### AL increase as combined product of physiological growth + visually driven elongation



Annual AL growth at age 8 (persistent emmetropes):  $0.12 \pm 0.24\text{mm}$   
 Annual AL growth at age 8 (myopia onset at age 10):  $0.35 \pm 0.20\text{mm}$

### Challenge in anti-myopia efficacy interpretation: confounding from physiological axial growth

AL(mm)	Hypothetical dataset		
	Baseline	Post-treatment	Change
Physiological growth	23.00	23.12	0.12
Control	23.00	23.50	0.50
Treatment	23.00	23.25	0.25

#### Anti-myopia efficacy:

- physiological growth not accounted for:  $\Delta 0.25\text{mm}$ ; 50%
- physiological growth accounted for:  $\Delta 0.13\text{mm}$ ; 67%

**The younger the subject cohort, the bigger the confounding!**

### Misinterpretation 6.

The anti-myopia efficacy of OrthoK is primarily attributable to the induced para-central corneal steepening & its impact on peripheral defocus

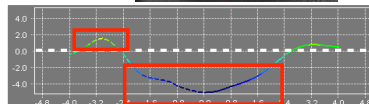
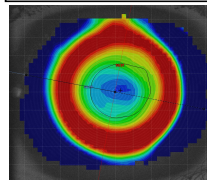
### Poll 4. Which of the following component(s) is(are) likely contributing to the myopia-controlling mechanism of OrthoK?

- The relatively myopic defocus imposed
- The higher order aberration imposed
- Clear uncorrected central vision during day time
- Free from spectacle correction hence positive behavioral modification
- All of the above

### Multifactorial Anti-Myopia Mechanisms of OrthoK

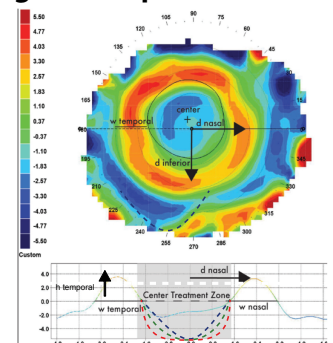
- Non-uniform (oblate) central flattening**
  - $\nabla$  + defocus;  $\nabla$  +SA, coma
  - Higher contribution to **central image quality**
- Significant paracentral steepening**
  - Higher contribution to **peripheral image quality**
- Behavioral benefit cannot be ignored**

Post-OrthoK Corneal Change



### Properties of competing defocus post-OrthoK

- Central flattening**
  - size of treatment area
  - asphericity
  - non-uniformity
- Paracentral steepening**
  - location (d)
  - width (w)
  - magnitude (h)

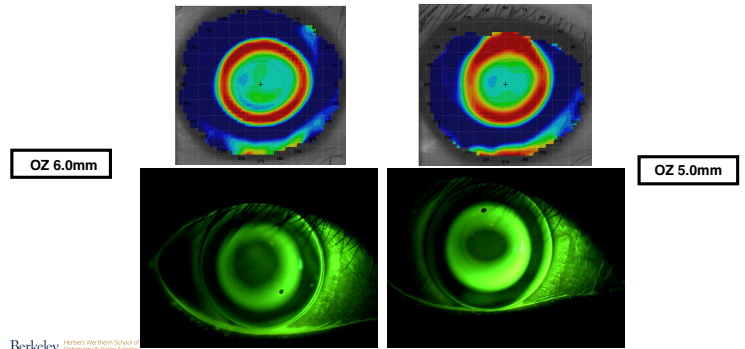




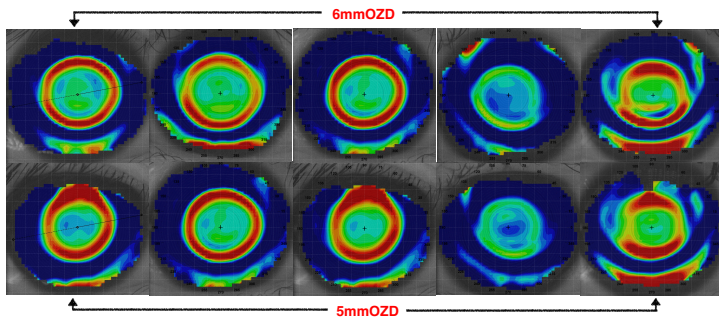
### Misinterpretation 7.

**OrthoK treatment has high specificity, and the back surface lens design determines anti-myopia dosage.**

### Myopia-control optimized OK design?



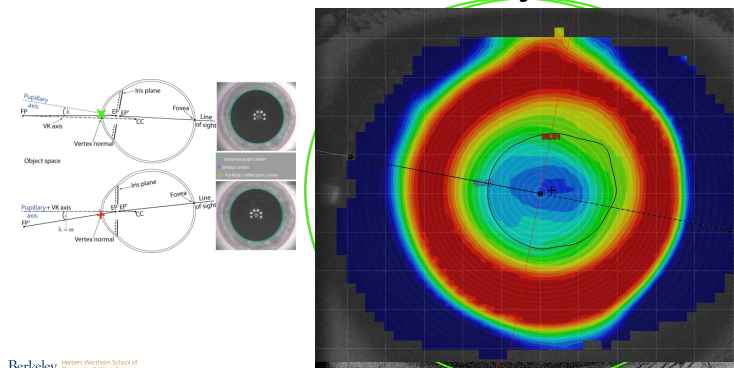
### OK design diff $\neq$ diff induced on corneal surface



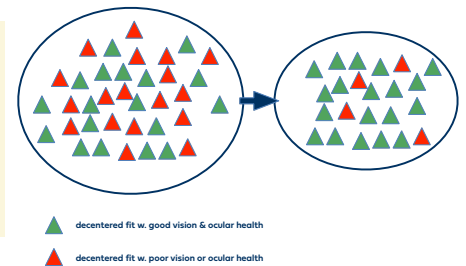
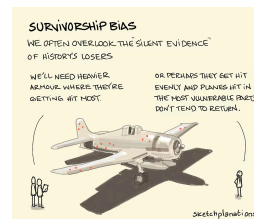
### Misinterpretation 8.

**Decentered OrthoK treatment appears to provide better anti-myopia efficacy.**

### Lens Decentration is NOT a Binary Outcome!

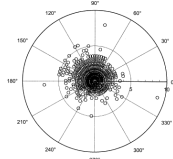


### Survivor Bias in Retrospective Studies



## Impact of Lens Decentration has multiple components

- **Confounding from angle kappa**
- **Direction of decentration**
  - superior & nasal less visually detrimental
  - significant difference in imposed retinal blur profile
- **Magnitude of decentration**
  - reference point: pupil center? visual axis?



Huether et al. Journal of Refractive Surgery • Vol. 34, No. 12, 2018

## Misinterpretation 9.

**Reduced outdoor exposure, not intensity of near work, is the primary cause of myopia**

## Close Correlation btw Time Spent Outdoor vs. Intensity of Near Work



**Both variables collected by questionnaires are not reliable & do not reflect patterns of exposure**

## Misinterpretation 10.

**Impact of outdoor exposure or near work is linear and the measurements of both in clinical studies are highly reliable.**

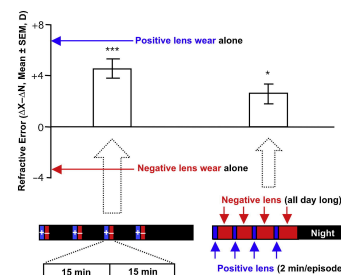
## Doctor's statement about outdoor times



"It does not matter how your child takes the outdoor break as long as there is sufficient time for it!"

## Outdoor break is more effective right after sustained near work

- **Compensation to defocus depends on**
  - duration
  - frequency
- **Integration of competing defocus**
  - non-linear on the temporal or spatial scale
  - bias towards "+"
- **Anti-myopia dosage**
  - sign
  - magnitude
  - spatial location
  - duration



## Summary

- **Myopia detection/monitor**
  - **visual experience causal**, genetic influence as susceptibility factor
  - all **juvenile myopia are axial**, regardless of the AL
  - **longitudinal change** should be the key measures, rather than cross-sectional comparison
  - no simple correlation from **unit change in AL to RE**
  - anti-myopia **efficacies across trials** dependent on age, rate of progression etc.
- **Myopia control**
  - **multifactorial mechanisms** involved, need better quantification of anti-myopia dosage
  - **time outdoor & near work intensity** closely correlated, currently lacking reliable measure of either
  - **nonlinear integration** of outdoor exposure/ "•" defocus

The eye sees only what the mind is prepared to comprehend.

— **Henri Bergson**

