Asian *and* **Western** refractive centile curves from meta-analysis of population refraction data

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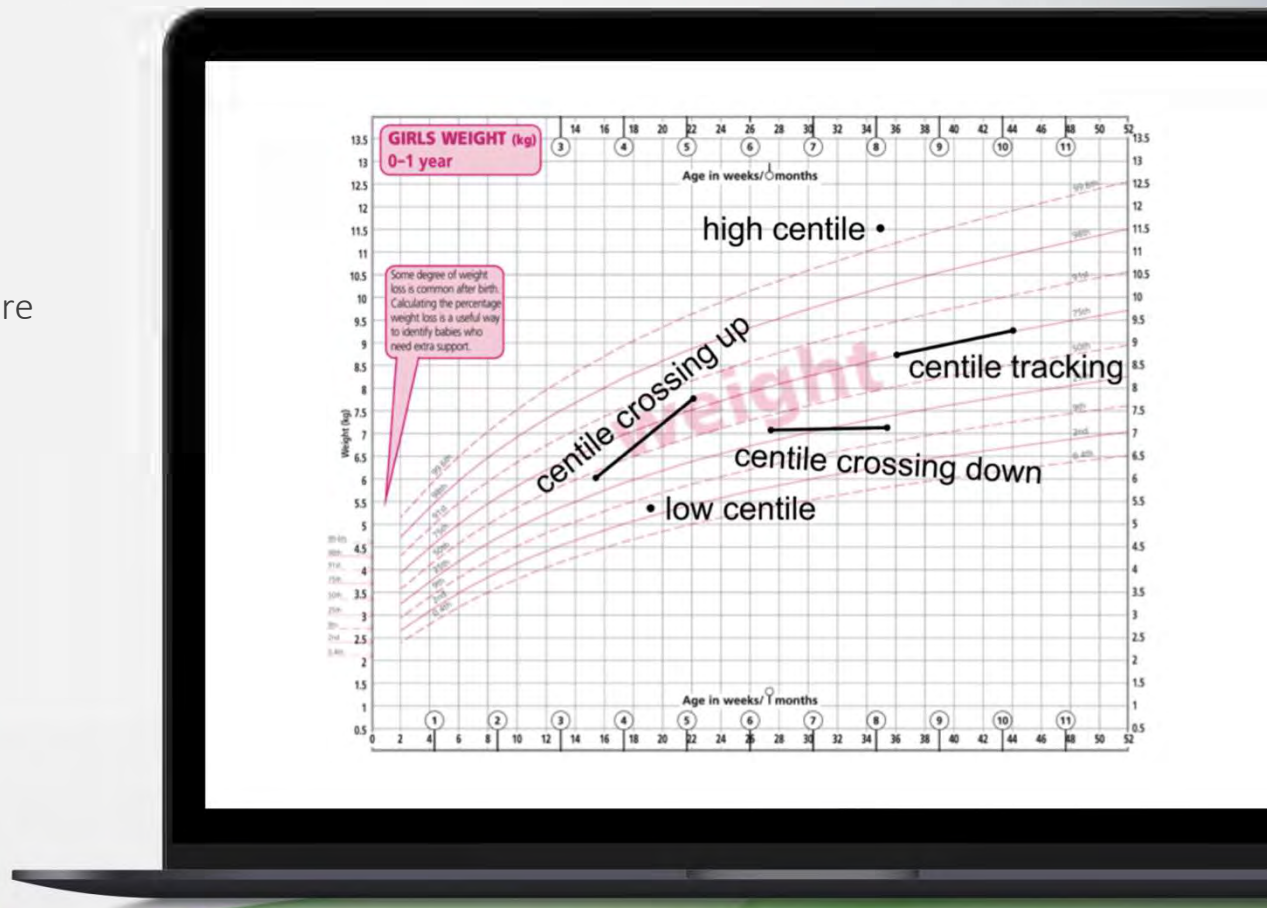
Centiles - a well established concept in paediatrics

- Gives immediate snapshot of where a child is in terms of growth and allows monitoring over time
- Great advantage is that most parents have been trained in the concept before you ever meet them



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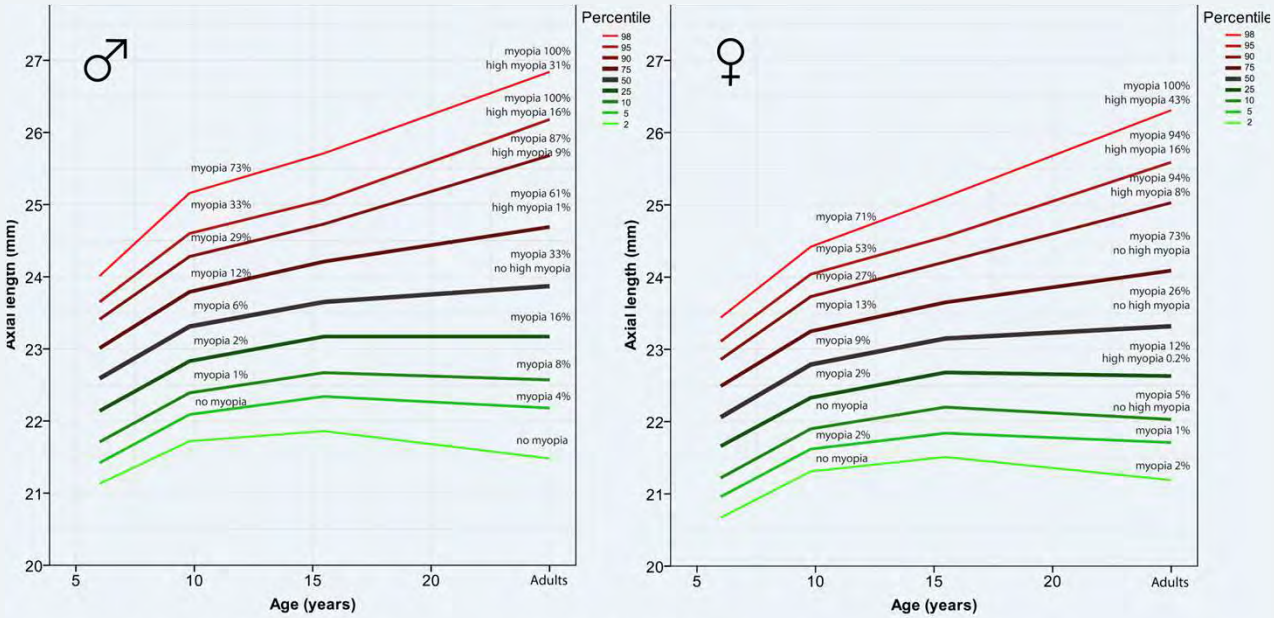
“Relatively” new in eye care

Originally introduced by *Monroe J. Hirsch* in 1952. Recently emerged as a clinical priority.

AXIAL LENGTH CENTILE CHARTS INTEGRATED INTO BIOMETRY DEVICES



Growth curves with axial length (mm) versus age for European population; boys (left) and girls (right)

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2016

RESEARCH ARTICLE

Identifying Children at Risk of High Myopia Using Population Centile Curves of Refraction

Yanxian Chen[1], Jian Zhang[1], Ian G. Morgan[2], Mingguang He[1,3]*

2018

Axial length growth and the risk of developing myopia in European children

Jan Willem Lodewijk Tideman,[1,2] Jan Roelof Polling,[1,3] Johannes R. Vingerling,[1] Vincent W. V. Jaddoe,[2] Cathy Williams,[4] Jeremy A. Guggenheim[5] and Caroline C. W. Klaver[1,2]

2019

Growth curves of myopia-related parameters to clinically monitor the refractive development in Chinese schoolchildren

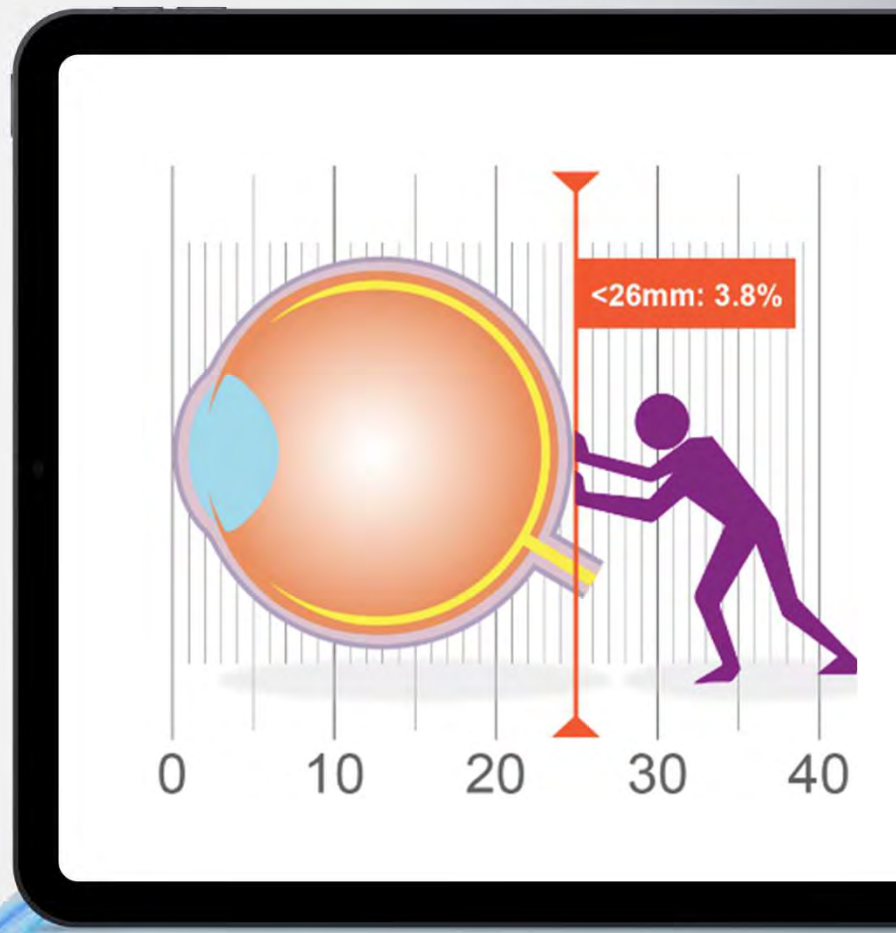
Pablo Sanz Diez[1,5] · Li-Hua Yang[2] · Mei-Xia Lu[3,4] · Siegfried Wahl[1,5] · Arne Ohlendorf[1,5]

Why refraction centiles

- Axial length centiles already available
- Axial length is a key metric for myopia management

BUT…

- Very few practitioners have access to biometry right now
- Population-Based Refractive centiles:
  - Are a precise indicator of likely future progression
  - Allow clinicians to explain what a child's prescription means in terms of risk in a way that is intuitive to parents (more difficult with axial length)
  - Support evidence-based personalised clinical decision making



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CENTILE METHODOLOGY

Data Sources – published epidemiological data from Asia, USA, Europe

- 35,645 refraction measurements
- 8 large population-based studies
- 12,965 European/North American eyes
- 22,680 Asian eyes

WESTERN		
NHANES	USA	8,915 [a]
NICER	Northern Ireland	2,424 [b]
IES	Republic of Ireland	1,626 [b]

ASIAN		
KNHANES	South Korea	11,569 [a]
GTES	China	1,563 [b]
RESC	China	3,940 [b]
HSS	China	3,676 [b]
JDES	China	1.932 [a]

Table 1: Data summary of studies included in the meta-analysis
Abbreviations: KNHANES, Korean National Health and Nutrition Examination Survey; GTES, Guangzhou Twin Eye Study; RESC, Refractive Error Study in Children; HSS, Haidian School Survey; JDES, Jinshan District Eye Study; NHANES, National Health and Nutrition Examination Survey; NICER, Northern Ireland Childhood Errors of Refraction study; IES, Ireland Eye Study; N, number
[a] Non-cycloplegic refraction [b] Cycloplegic refraction

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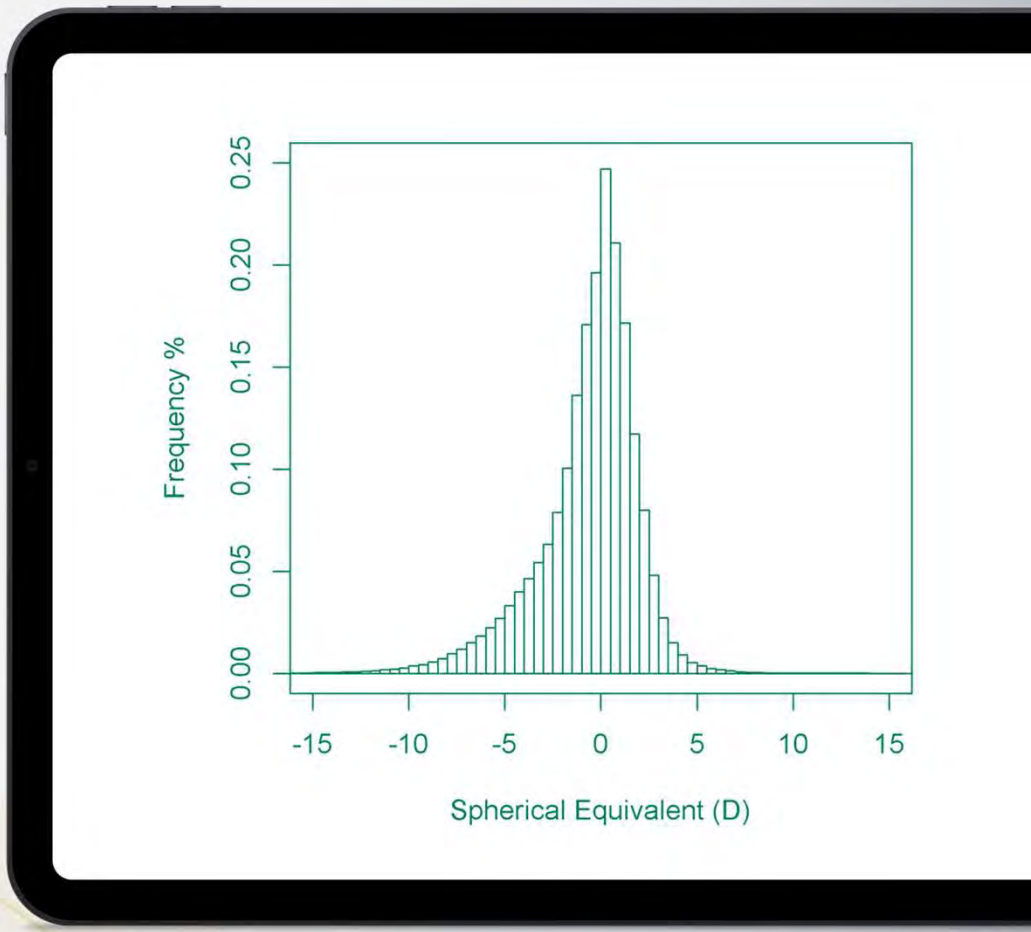
Centile Methodology

- Secondary data meta-analysis of refraction data
- Multi-Gaussian
- Better fit than Box Cox Power Exponential
  - Empirical quantiles were generated by age, group and gender
  - Cumulative Distribution Function model created
  - Specific centile curves generated by weighted cubic spline interpolation according to the number of participants in each age group in each study

Refractive error data non-normal



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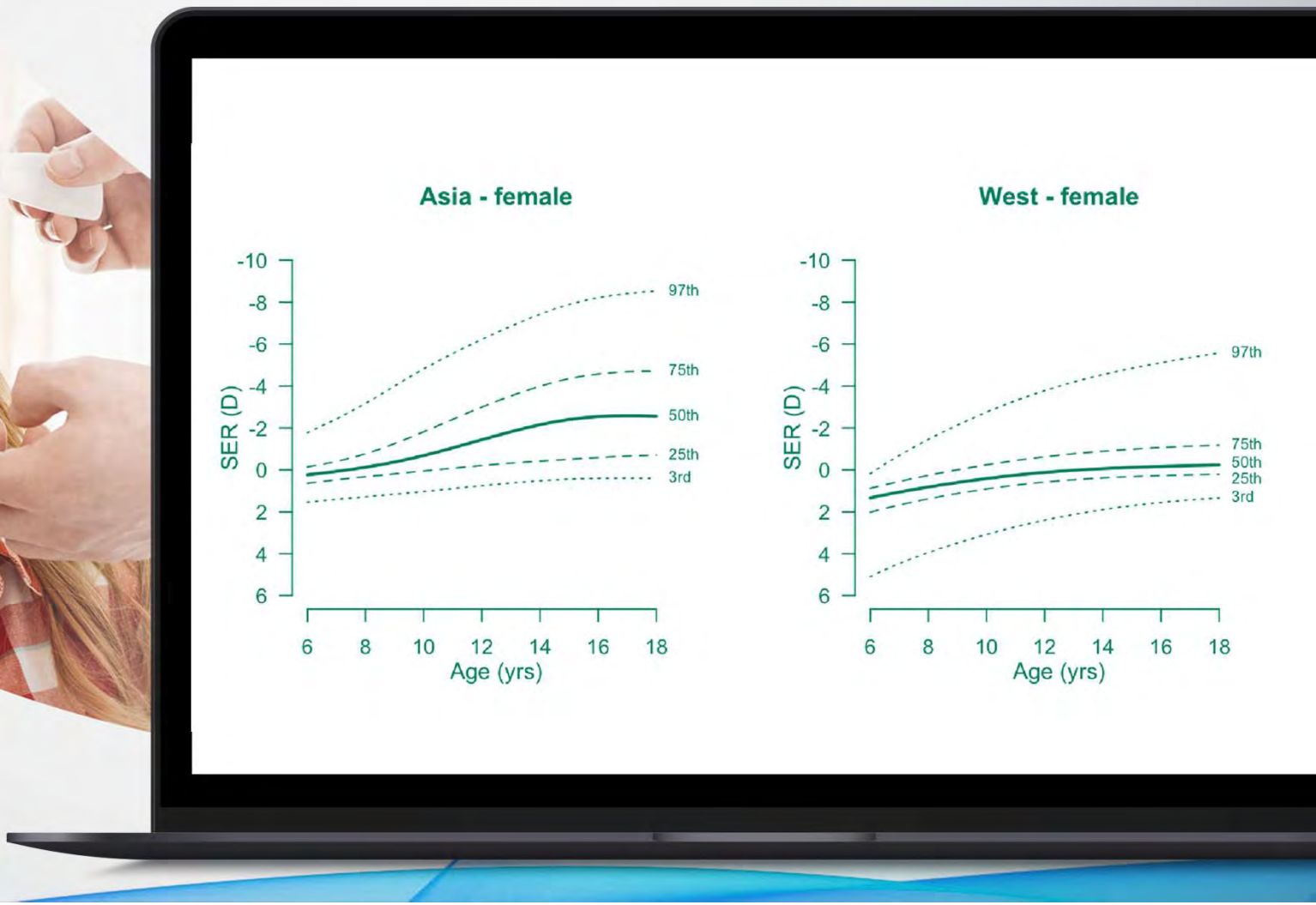
Centile Charts: Regional Comparison - Girls



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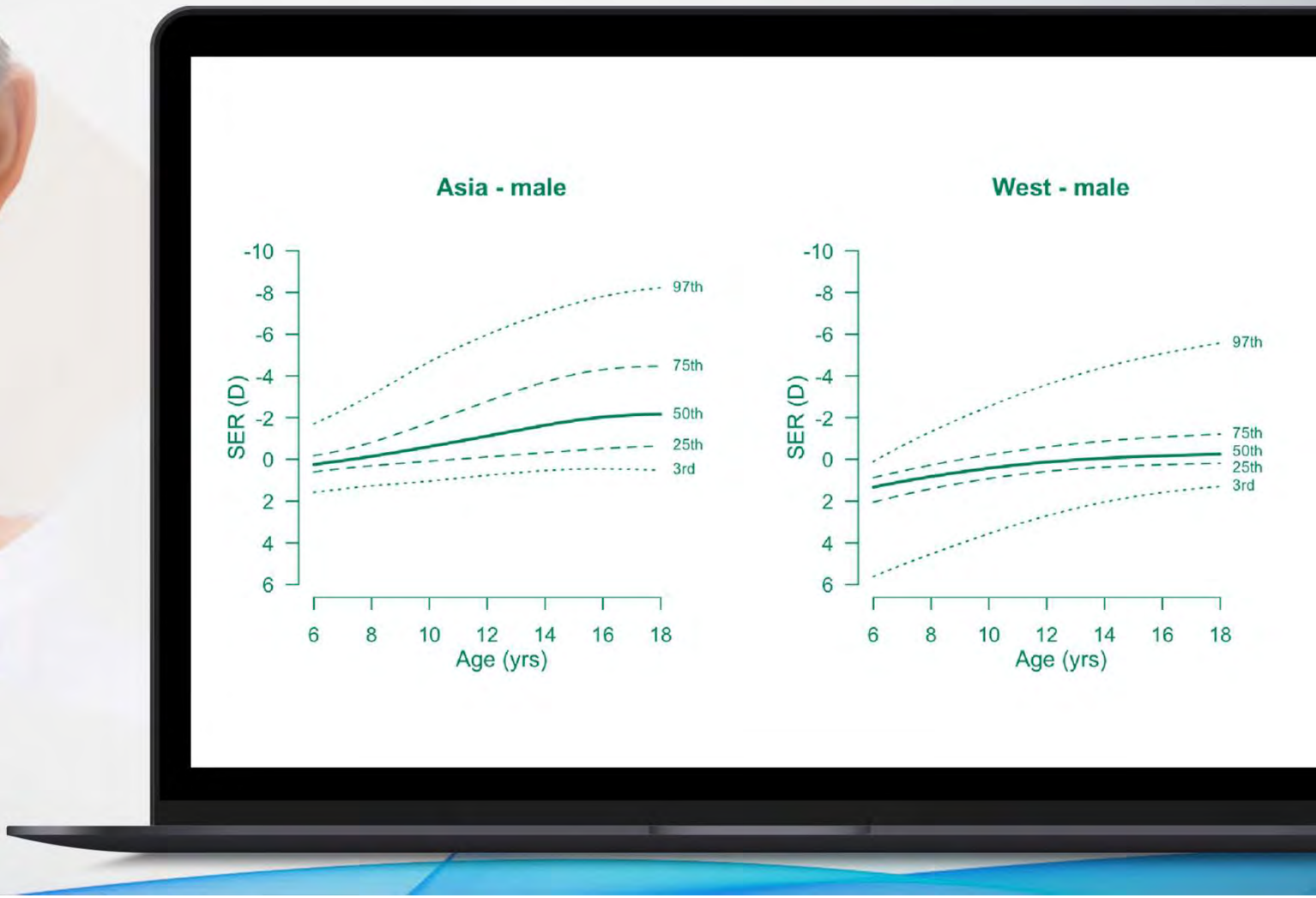
Centile Charts: Regional Comparison - Boys



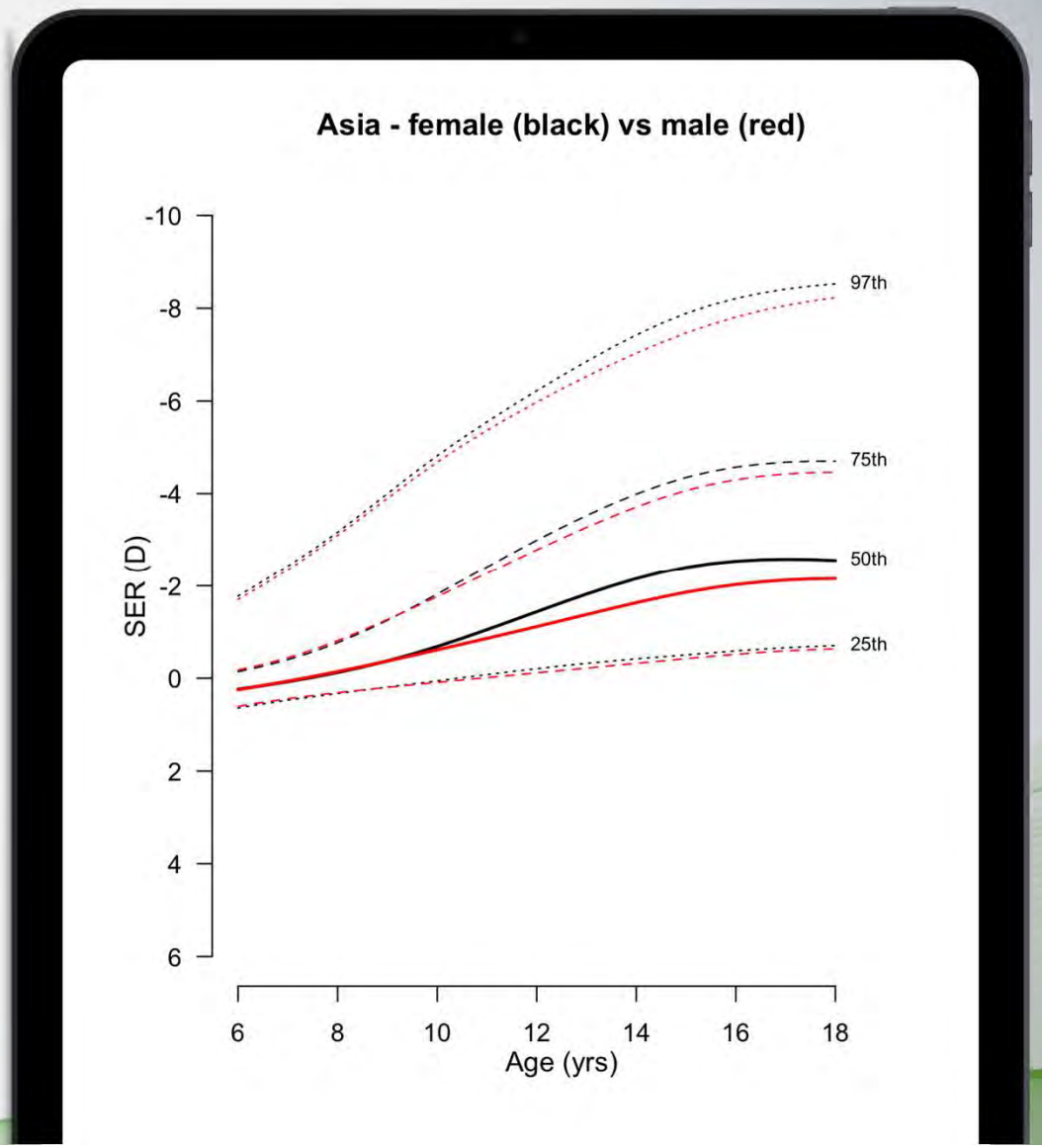
Centile Charts: Gender Comparison

ASIA

Median refraction (age 6) **+0.25D Boys +0.24D Girls**

Median refraction myopic by age 10 (boys), 9.5(girls)

Gender differences minimal until age 11, increased with age and were greatest in myopes



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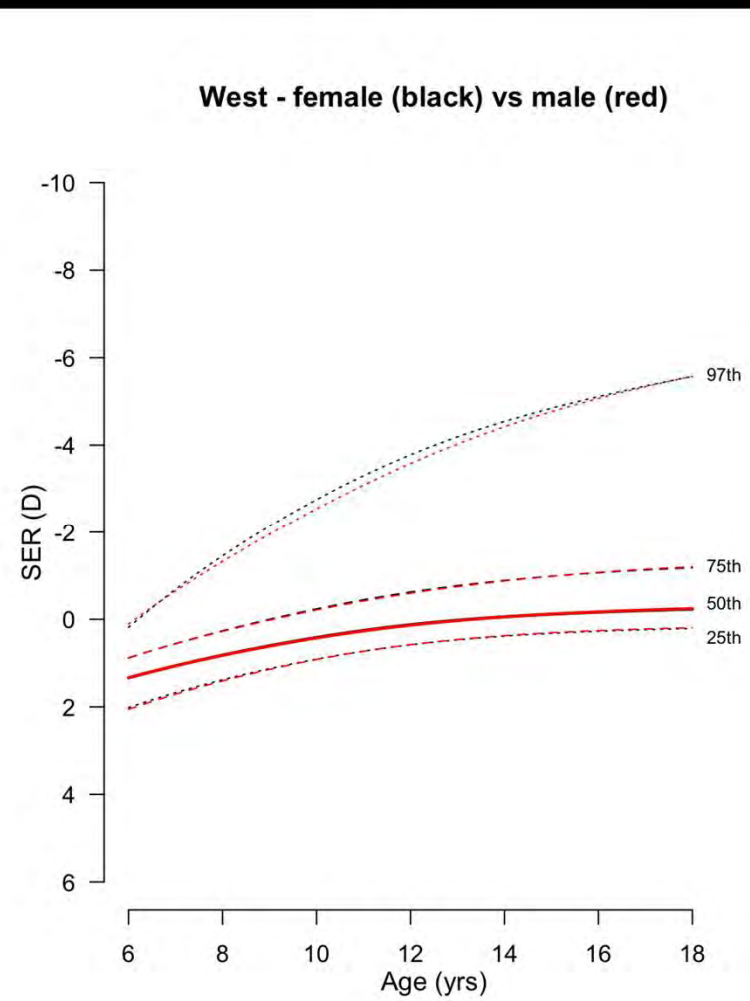
Centile Charts: Gender Comparison

WEST

Median refraction (age 6) **+1.33D Boys +1.34D Girls**

Median refraction did not reach myopia by age 18

Gender differences most marked in hyperopes



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Some Practical Applications

ADULT EQUIVALENT REFRACTION

ASIA

For incipient myopia (-0.5D) at different ages

GENDER	AGE	CENTILE	AT 16 YRS
male	6	centile = 85.53%	-9
	7	centile = 76.91%	-7.38
	8	centile = 66.63%	-6.3
	9	centile = 55.62%	-5.42
	10	centile = 46.64%	-4.88
female	6	centile = 85.7%	-9.97
	7	centile = 78.3%	-7.73
	8	centile = 67.36%	-6.29
	9	centile = 55.34%	-5.56
	10	centile = 44.88%	-5.06

WEST

For incipient myopia (-0.5D) at different ages

GENDER	AGE	CENTILE	AT 16 YRS
male	6	centile = 99.37%	-7
	7	centile = 96.63%	-4.9
	8	centile = 91.93%	-3.36
	9	centile = 85.71%	-2.11
	10	centile = 80.87%	-1.55
female	6	centile = 99.56%	-6.82
	7	centile = 96.26%	-4.44
	8	centile = 90.83%	-3.11
	9	centile = 85.47%	-2.28
	10	centile = 80.62%	-1.66

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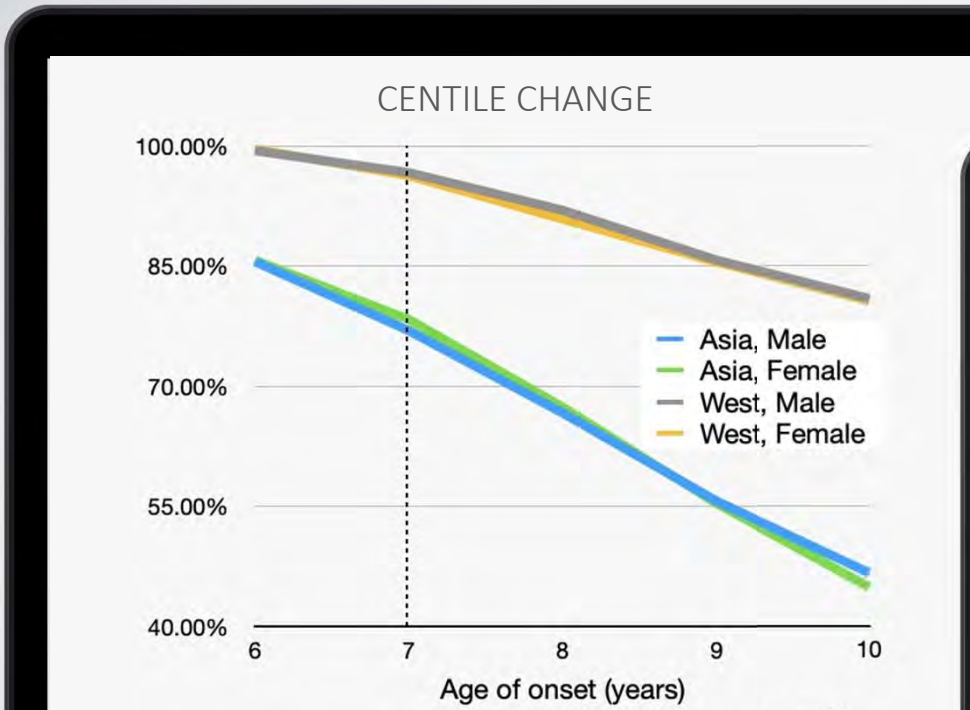
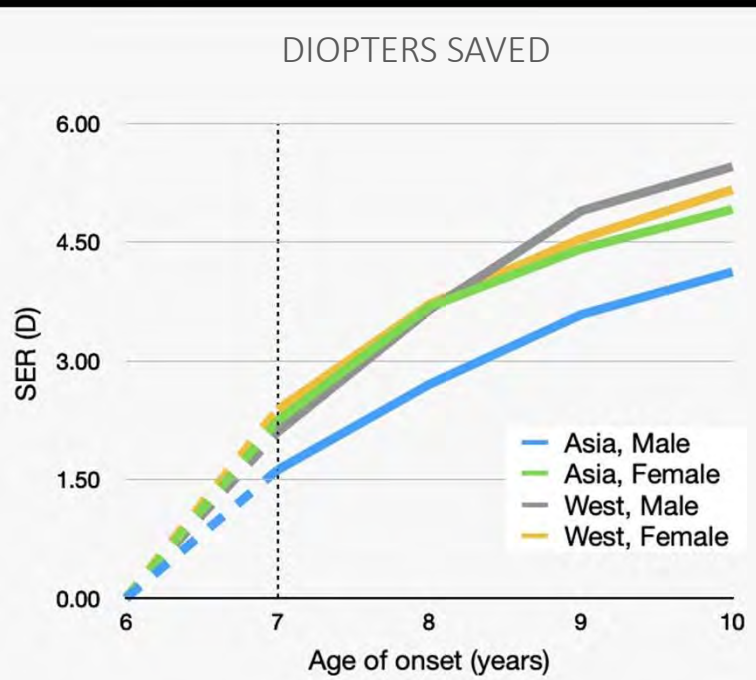


Delaying onset equates to a lower centile position at time of onset



Which equates to a lower

ADULT EQUIVALENT REFRACTION

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Some Practical Applications

ANNUAL PROGRESSION

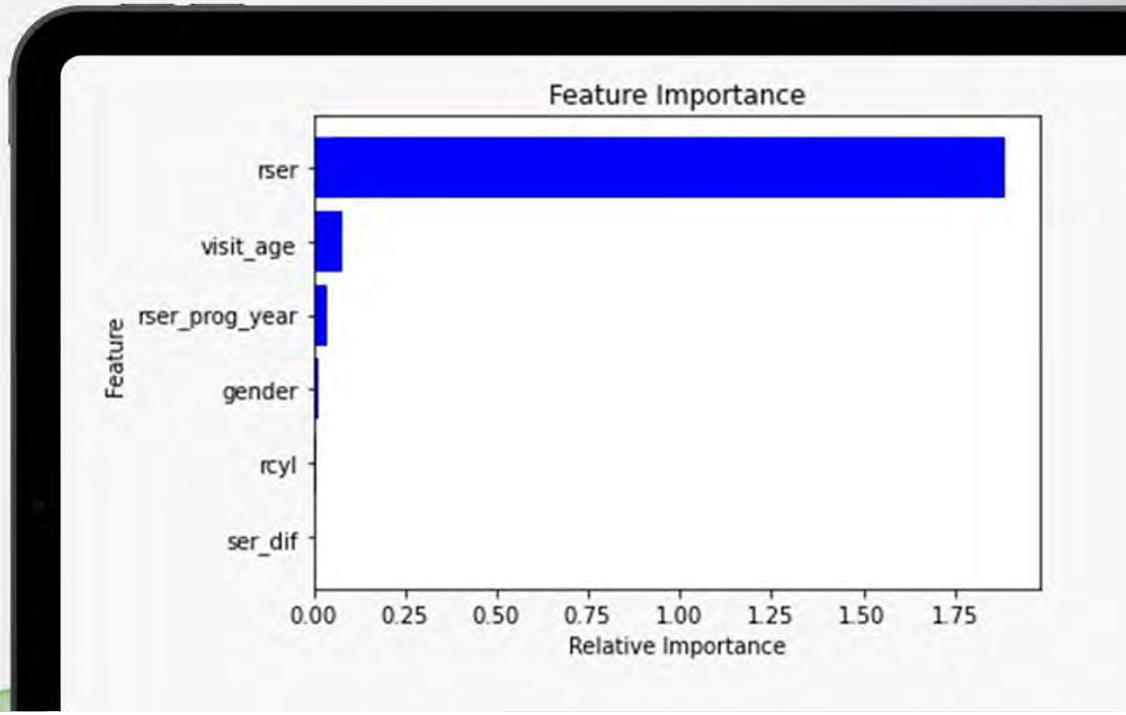
Evaluation of centile predicted progression

10,774 myopes < 20 years with longitudinal EHR data (at least three visits)

Correlation between centile predicted progression and measured progression

Using SER centile position: $R^2 = 0.93$. MAE: 0.24D
Using Progression centiles: $R^2 = 0.85$. MAE: 0.32D

Using Enhanced Machine Learning Model:
$R^2 = 0.95$. MAE: 0.21D



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Clinical Value

- Centile charts utilised by agencies such as the CDC & WHO as clinically important means of monitoring child growth

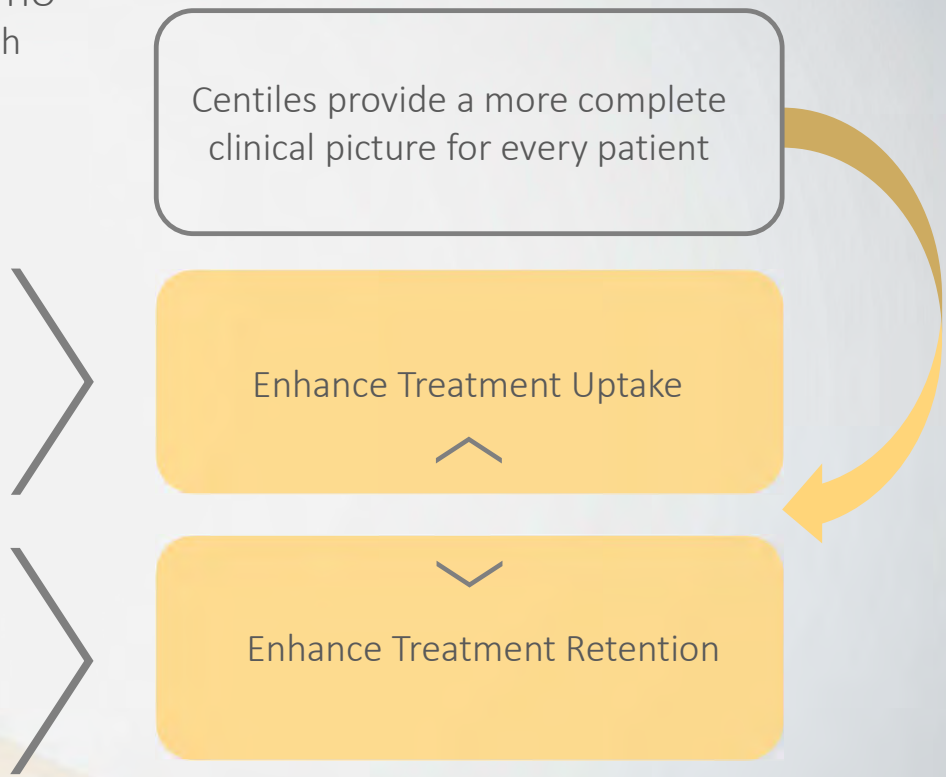
For Refractive Error

Risk Profiling

- Identification of Pre-myopes
- Adult predictions of future refraction and axial length
- Ocular disease and vision impairment risk estimation

Myopia control treatment monitoring

- Treatment efficacy analysis
- Personalised clinical decision making



Better Health Outcomes

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Clinical Trial Value

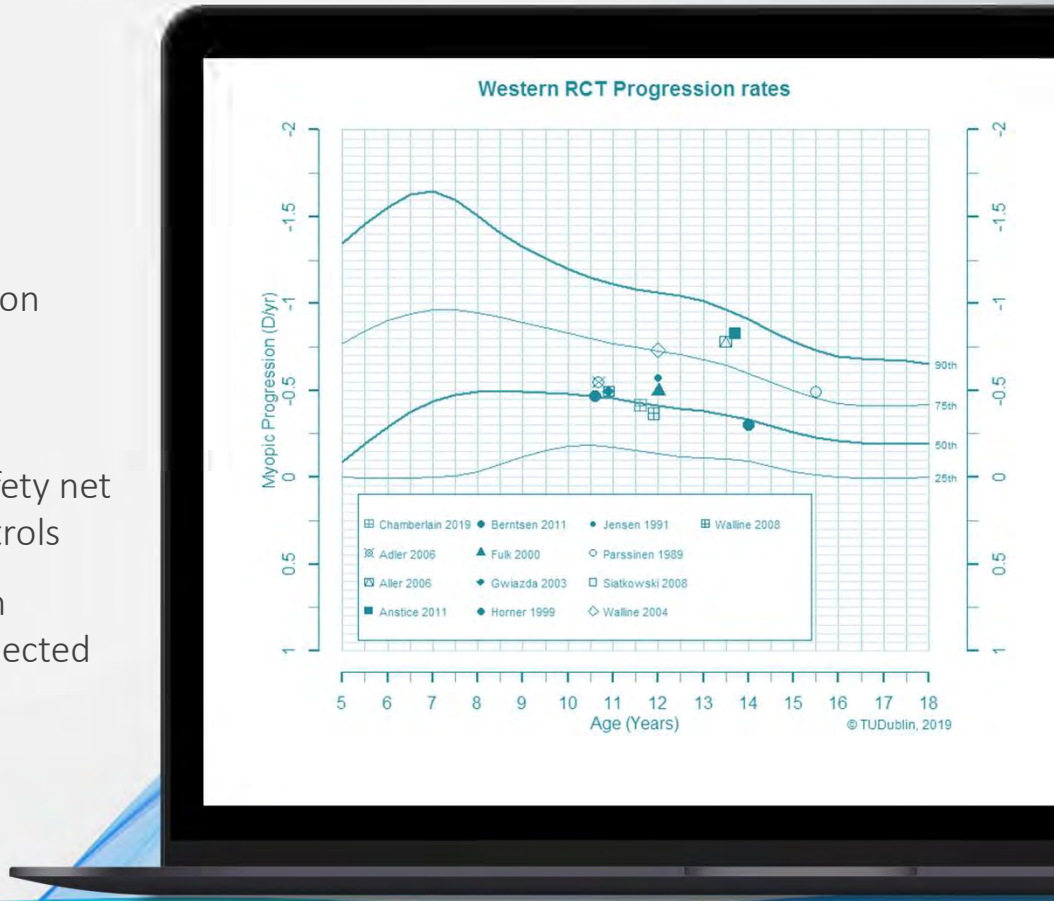
- Ethical Concerns
- Recruitment & Retention Concerns

Applications

- Patient selection – trial participants often not representative of clinical populations
- Evaluating trial representativeness
- Trial risk management – safety, efficacy and protection against dropout

Virtual Control Group

- Avoid the need for placebo control group and/or safety net against preferential dropout of fast progressing controls
- Individual patient-level efficacy analytics – how each participants progression compares to real world expected progression



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Conclusion

Refraction centile charts

- Support evidence based clinical decision making
- Are more relevant to clinicians than axial centiles right now
- Can promote better uptake and retention for myopia control treatments
- Bring added value in the clinical trial space

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Thanks to my co-authors and wider team at CERI

Prof. Kathryn J. Saunders

Dr. Siofra Harrington

Prof. Daniel I. Flitcroft

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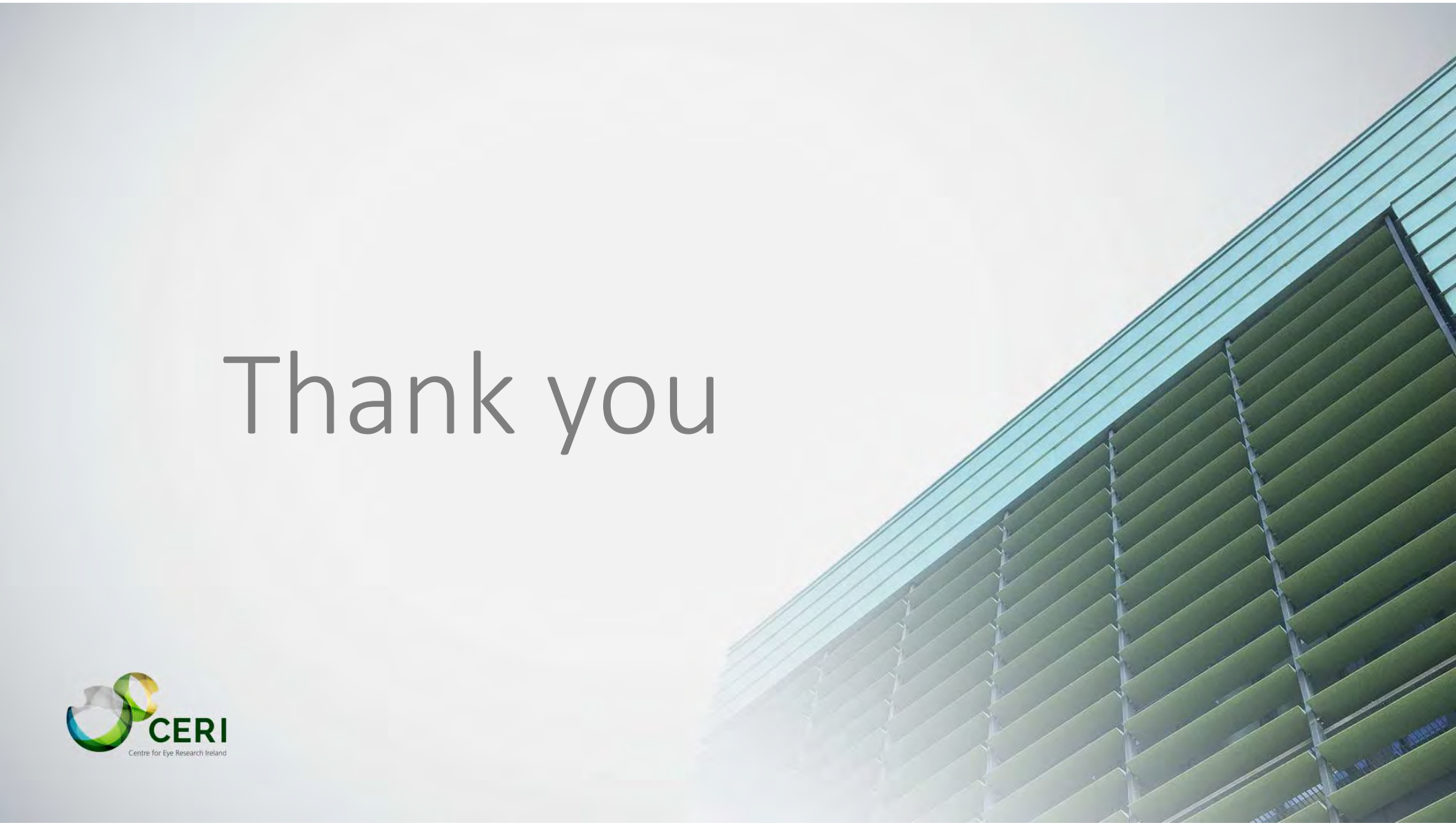
Thank you



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