Voretigene Neparvovec for Biallelic *RPE65*-Mediated Retinal Disease: Effectiveness and Value

Public Meeting – January 25, 2018

ICER

INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Welcome and Introduction

Why are we here today?

- Visual impairment and blindness can profoundly affect patients and families

"We hear from families whose children cannot make eye contact with their own parents and the devastating impact it has on the child and the entire family. We hear from kids who face social and academic challenges that range from bullying and exclusion to being perceived as less intelligent — when the only difference they struggle with is that they cannot see as well as their sighted peers. Even in the best of circumstances they are growing up with a tremendous pressure that most of us never had to — that they will someday live in a world of complete darkness. The emotional, social and educational toll of this vision loss at a young age is tremendous."

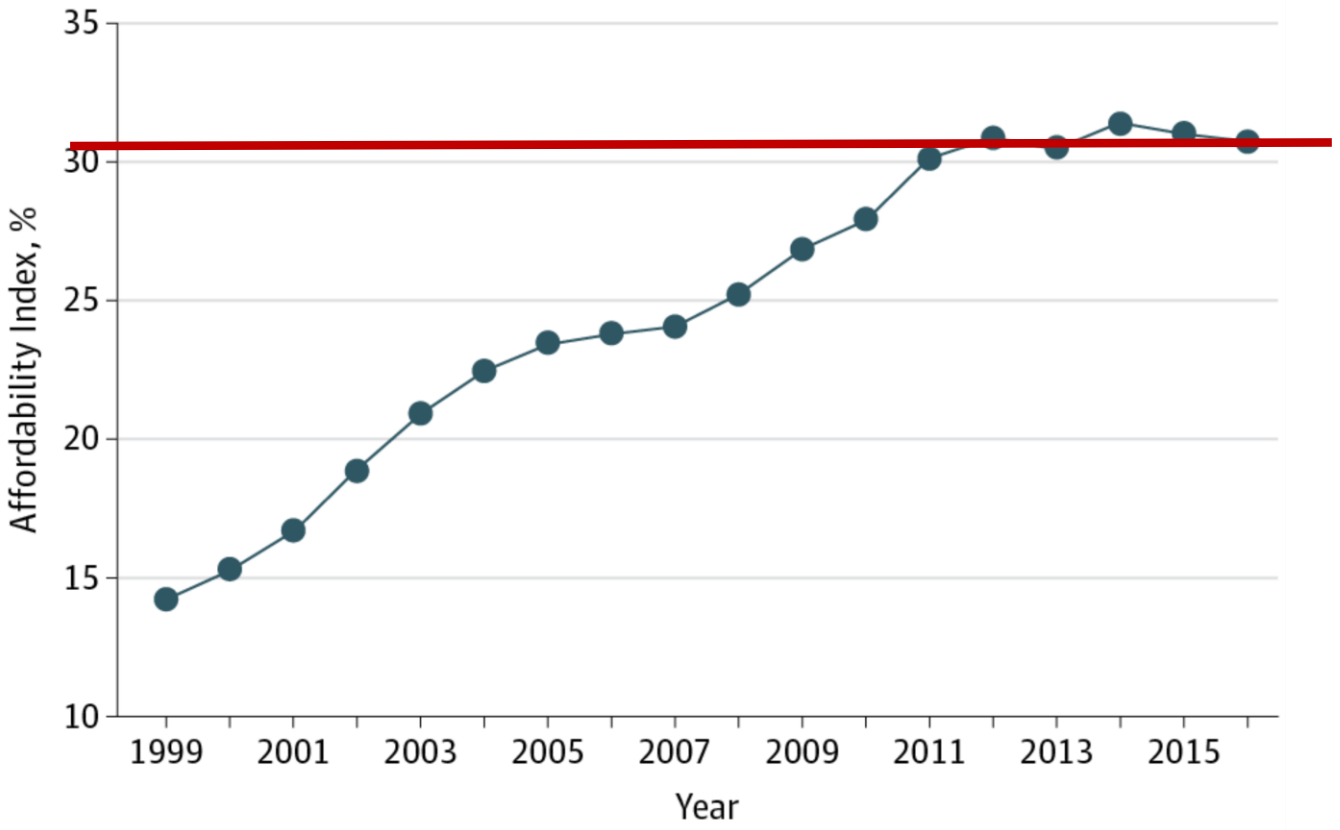
-Laura Manfre, Sofia Sees Hope, FDA Advisory Committee Testimony

Welcome and Introduction

Why are we here today?

- Voretigene represents a true scientific milestone
- As with other paradigm-shifting treatments, important questions about appropriate use, pricing, and coverage
- Treatments for small patient populations often raise particular issues about the types of studies that can be done and the relationship of pricing to the size of the population
- Gene therapies will heighten concerns about the affordability of emerging treatments under existing paradigms of pricing and payment.
  - Even if gene therapies are developed to treat only one in ten patients with a genetic condition – approximately 1% of the total population -- the cumulative budget impact at that price could rise to $3 trillion, as much as is currently spent in a year on all healthcare in the US.

An Affordability Index



Emanuel EJ, Glickman A, Johnson D. Measuring the Burden of Health Care Costs on US Families: The Affordability Index. JAMA. Published online November 02, 2017. doi:10.1001/jama.2017.15686

Welcome and Introduction

Why are we here today?

- We need to get this right, for patients today, and patients of the future
- Benefit of independent evaluation and public discussion of the evidence on effectiveness and value
- Exploration of innovative ways to adapt pricing and payment mechanisms to reflect the special context of gene therapies and other single or short-term treatments

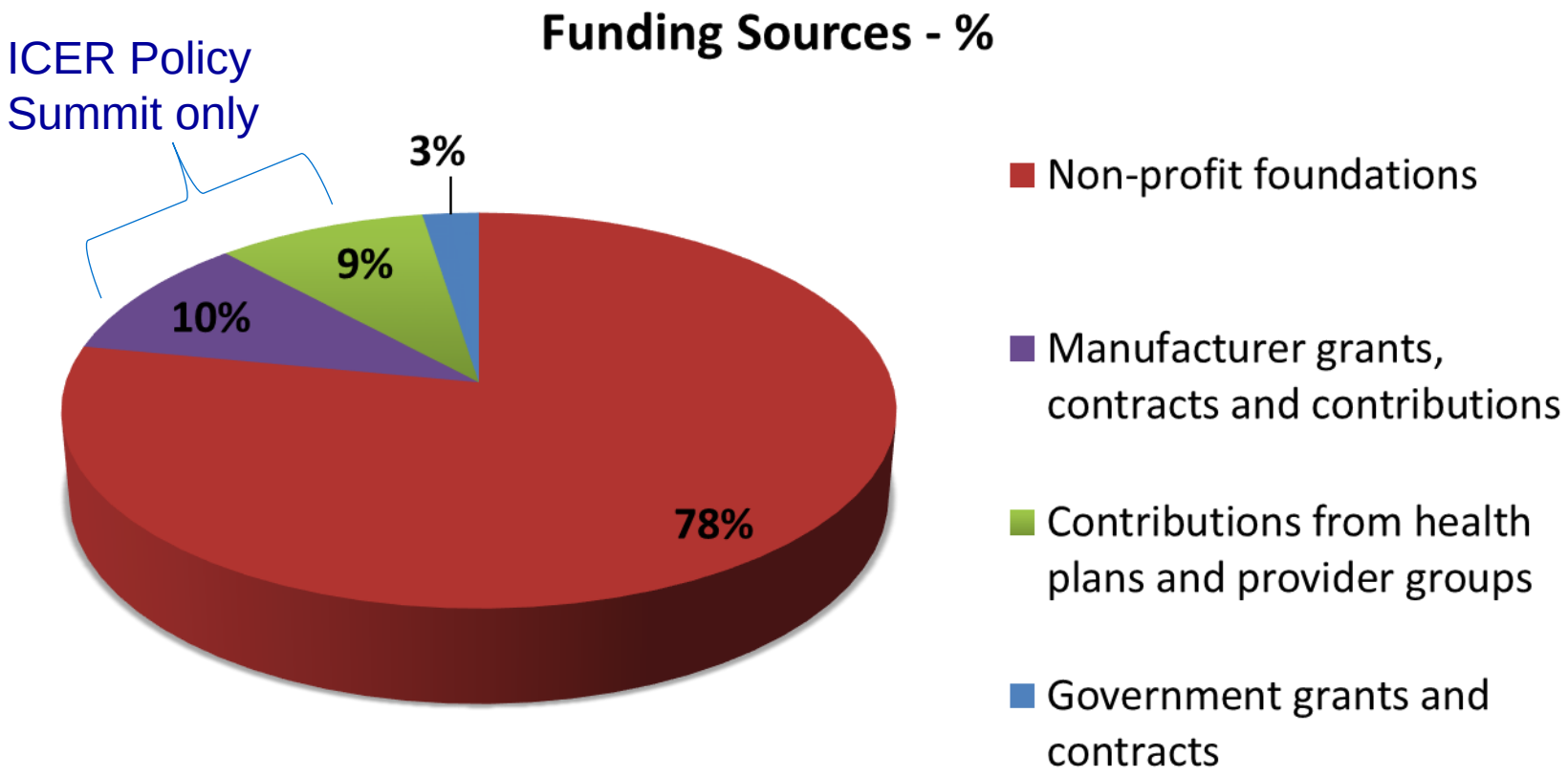
Welcome and Introduction

- The Midwest Comparative Effectiveness Public Advisory Council (CEPAC)

- The Institute for Clinical and Economic Review (ICER)

Sources of Funding, 2018

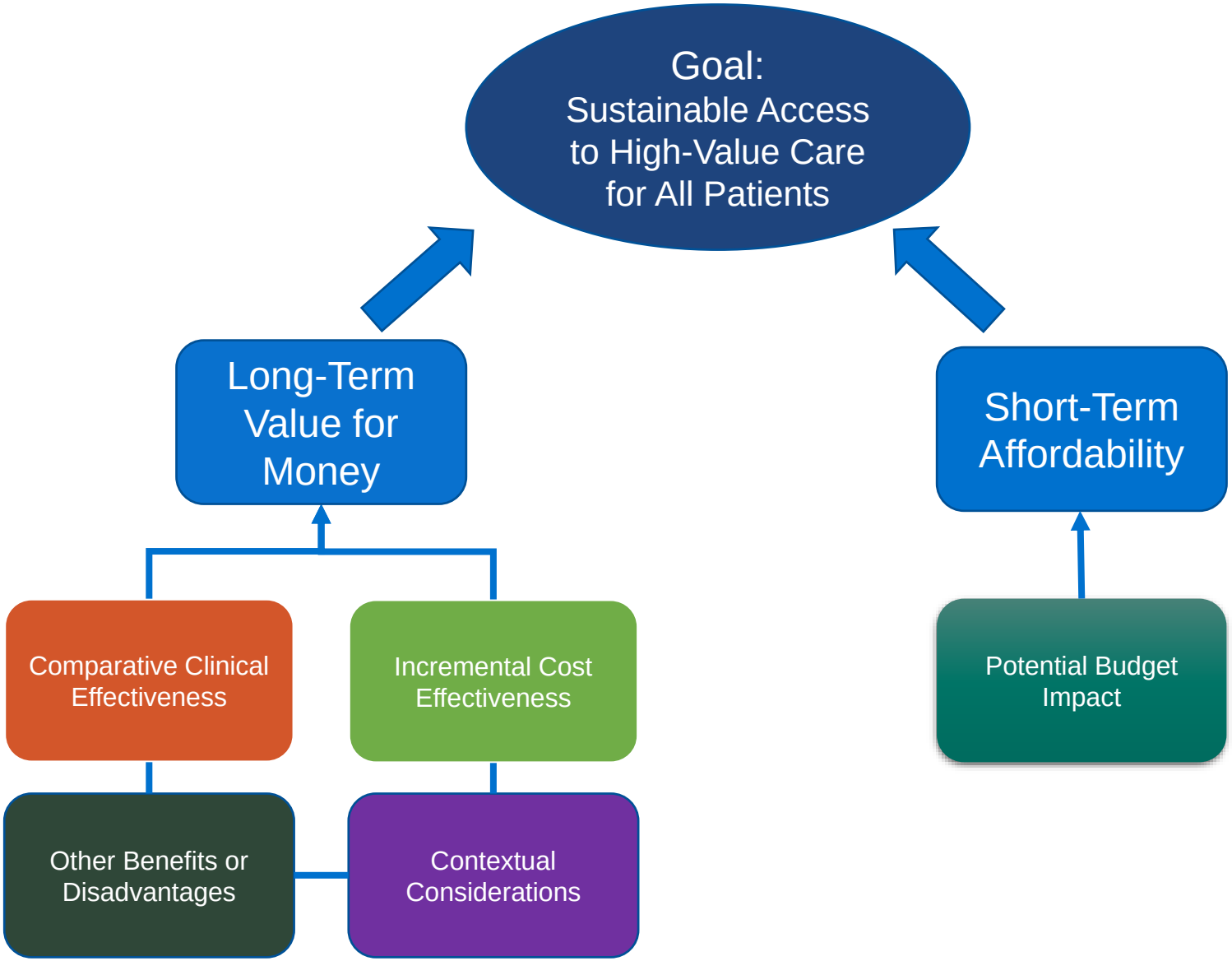
ICER Policy Summit only



Welcome and Introduction

How was the ICER report on treatments for Voretigene developed?

- Scoping with guidance from patients, patient groups, clinical experts, and manufacturers
- ICER evidence analysis and cost-effectiveness modeling
- Public comment and revision
- Clinical expert report reviewers
  - **Stephen Russell, MD,** Carver College of Medicine, University of Iowa
  - **Byron Lam, MD,** Bascom Palmer Eye Institute
- How is the evidence report structured to support CEPAC voting and policy discussion?


Goal:
Sustainable Access to High-Value Care for All Patients
Long-Term Value for Money
Short-Term Affordability
Comparative Clinical Effectiveness
Incremental Cost Effectiveness
Potential Budget Impact
Other Benefits or Disadvantages
Contextual Considerations

Modifications of the ICER value framework for treatments of ultra-rare disorders

- Provide context around potential evidence limitations common to these treatments
- Present a broader range of cost-effectiveness results
- Present cost-effectiveness results incorporating broader societal costs alongside traditional analyses of health system costs
- Note in all reports that decision-makers often give special weight to additional benefits and contextual considerations when determining coverage of more expensive treatments for ultra-rare disorders

Agenda

10:00 am: Welcome and Opening Remarks

10:15 am: Presentation of the Evidence

Evidence Review: Reiner Banken, MD, MSc

Cost Effectiveness: Marita Zimmerman, MPH, PhD

11:15 am: Manufacturer Comments and Discussion

11:30 am: Lunch

12:45 pm: CEPAC Deliberation and Votes

2:00 pm: Policy Roundtable

3:30 pm: Reflections and Wrap Up

4:00 pm: Meeting Adjourned

Evidence Review

Reiner Banken, MD, MSc
Senior Fellow
Institute for Clinical and Economic Review

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Disclosures:
Consulting work in a Canadian context for Patient Organisations (Canadian Cancer Survival Network, Save Your Skin, Colorectal Cancer Canada), for Industry (Roche, Lundbeck) and Government (Génome Québec, Ministère de l'Économie, de la Science et de l'Innovation du Québec)

Key review team members:
Geri Cramer, BSN, MBA
Patricia Synnott, MALD, MS
David Rind, MD, MSc

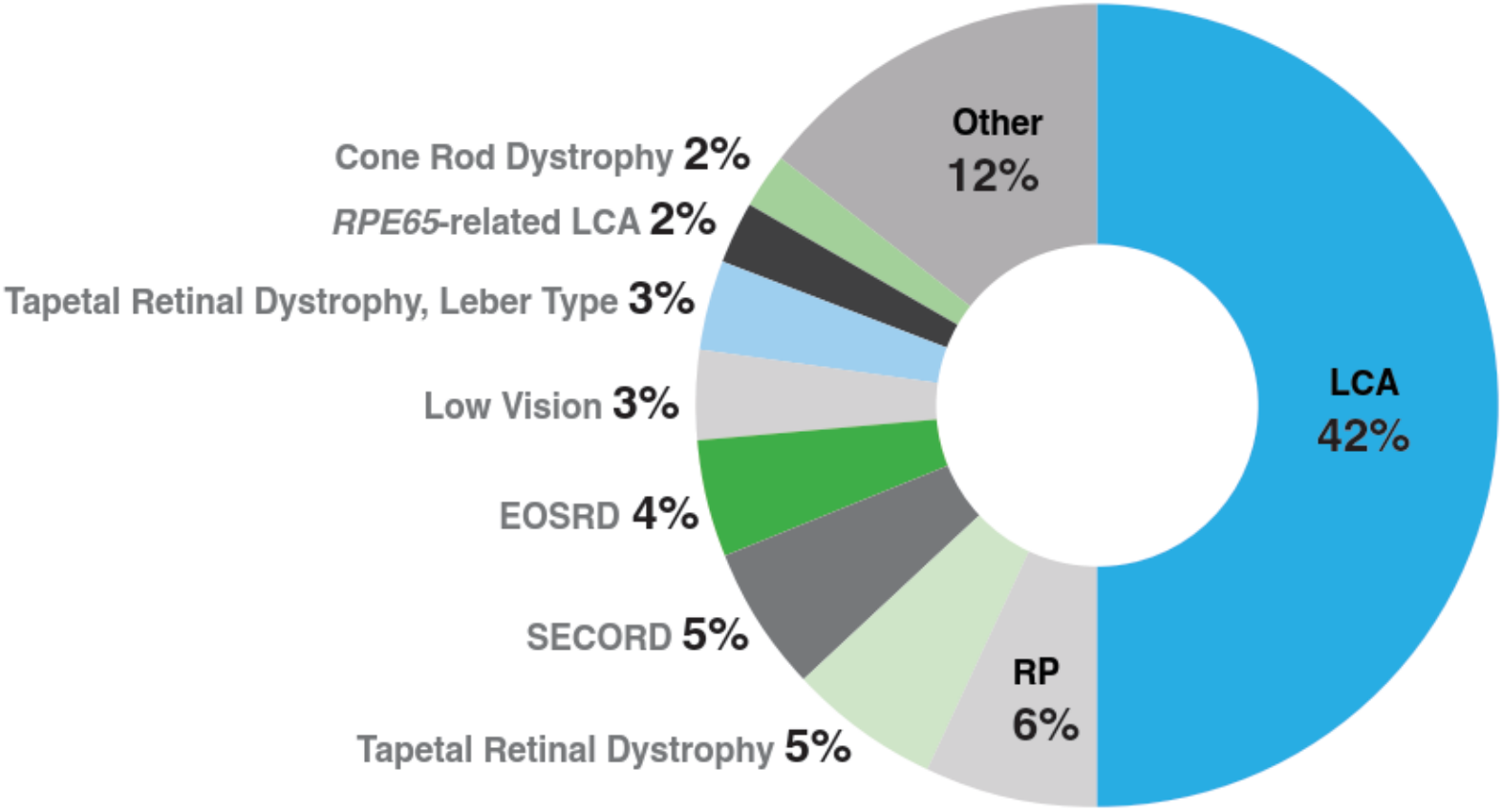
Inherited Retinal Diseases

- Important cause of childhood blindness
- Affecting approximately 1 in 2,300 people
- Group of genetic diseases, usually caused by recessive mutations
- Over the last 20 years, an increasing number of causal genes have been identified

RPE65-associated Retinal Dystrophy

- Biallelic mutations in the *RPE65* gene produce a defective enzyme needed for regeneration of light-reacting proteins in the retina
- Different IRDs caused by *RPE65*
- Genetic testing needed to identify patients with *RPE65*-mediated IRDs
- Estimation of 1,000 and 3,000 persons in the US with *RPE65*-mediated IRDs
- Progressive vision loss with severe visually impairment during childhood, adolescence, or early adulthood.
- No therapies that alter the natural history

Initial Clinical Diagnosis in 70 Individuals with Biallelic Mutations in RPE65



Disease Process of *RPE65*-associated Retinal Dystrophy

- Congenital absence of normal retinoid isomerohydrolase needed for regeneration of light-reacting proteins in the retina (biochemical blockade)
- Rod photoceptors affected first (night vision and peripheral vision), cone photoceptors later (visual acuity and color vision)
- Initially preserved retinal structure degenerating over time. Distinct processes of biochemical blockade and degeneration.

Impacts on patients and families

- Challenges of growing up with constantly deteriorating vision for affected children and their parents/families
- Inability to navigate independently in dimly-lit settings one of the most limiting handicaps
- Important socio-economic disadvantage in education and employment

Voretigene Neparvovec

- As of December 19, 2017, first gene therapy entering the market in the US that targets a disease caused by mutations in a specific gene
- AAV2 virus transfects cells in the RPE with a functioning copy of *RPE65,* adding a normal copy of the gene into the cell working in parallel to the mutated gene
- Vitrectomy and subretinal injection for delivery close to the RPE
- Bilateral treatment with second eye being treated at least six days after the first eye
- Administration in a very limited number of centers with prior intensive hands-on training of eye surgeons

Comparative Clinical Effectiveness

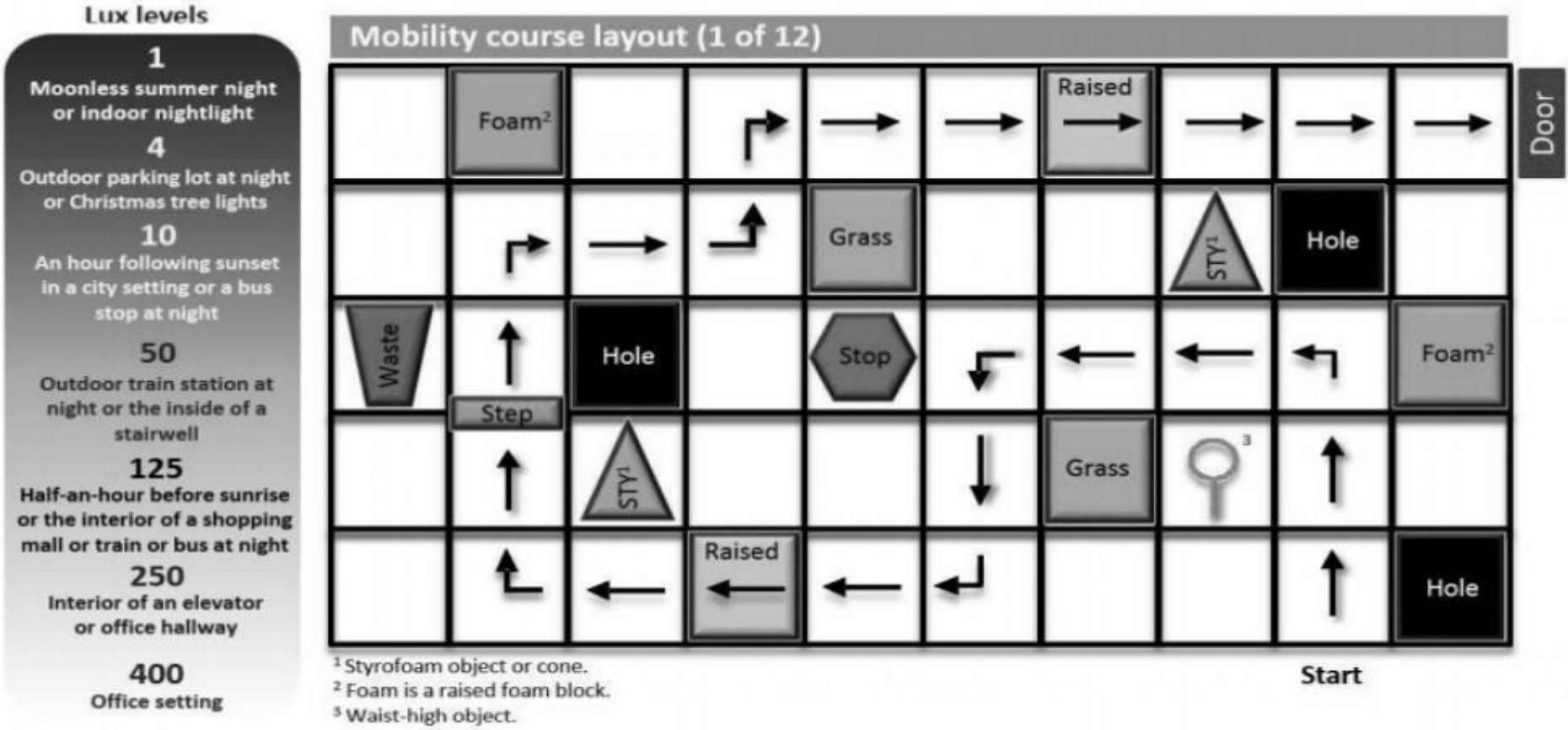
- Results for 41 patients in phase I and III trials with 34 unique mutations in the *RPE65* gene
- Phase III trial with 31 patients
- Average age 15.1 years (SD 10.9) with ages ranging from four to 44 years
- Three year follow-up available as of today

Outcome measures

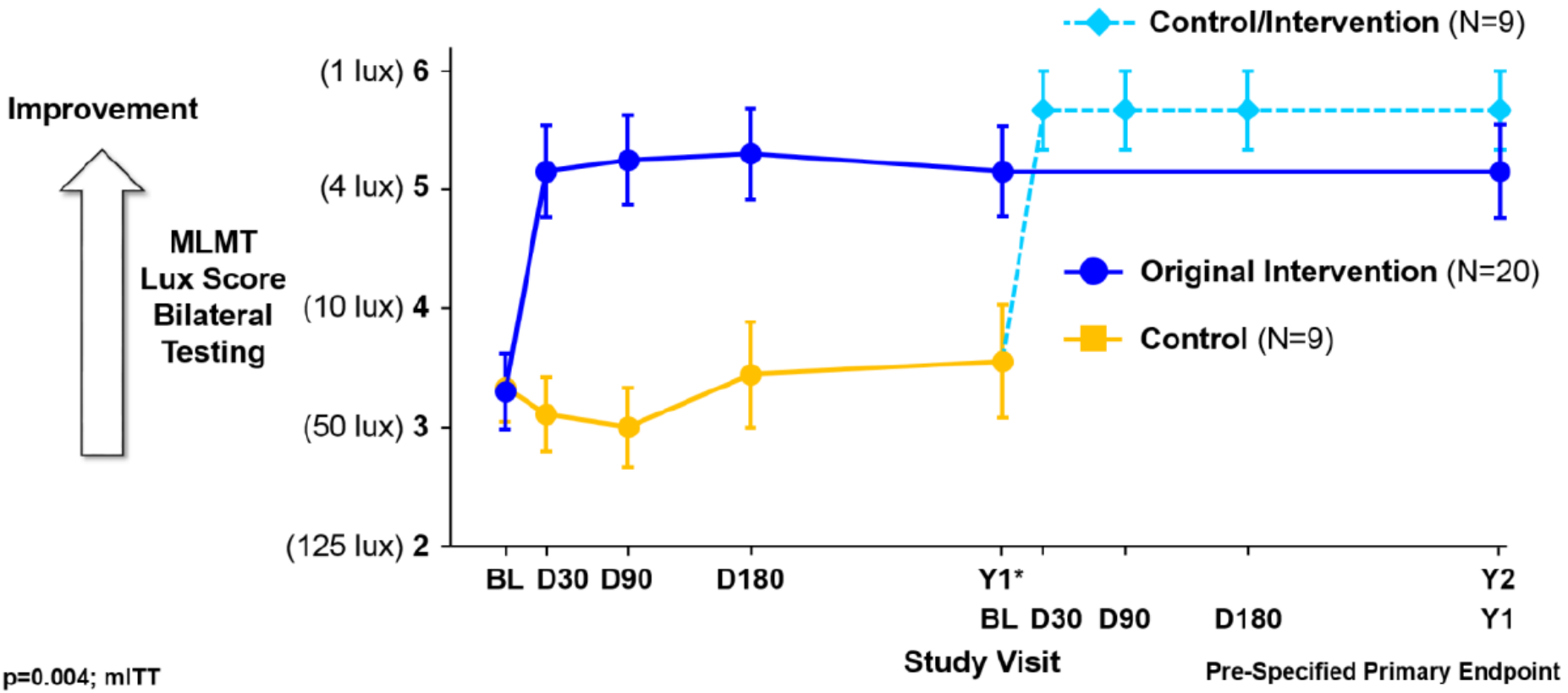
- Primary endpoint: Multi-luminance Mobility Test (MLMT) score at 1 year for bilateral vision
- Secondary endpoints:
  - Full-field Light Sensitivity Threshold (FST) testing, averaged over both eyes
  - MLMT change score, assigned first eye
  - Best-corrected Visual Acuity (BCVA), averaged over both eyes
- Exploratory endpoints: Visual field tests

- *Note: US legal blindness = Snellen 20/200 = LogMar 1 = Decimal 0.10*

Multi-luminance Mobility Test (MLMT) Example and Light Levels



Mean Bilateral MLMT Lux Score in Modified Intent-to-Treat Participants



Other Outcomes measures

- Full-field light sensitivity improved and stable out to three-years. Strong correlation with MLMT (-0.74; $p<0.001$)
- Visual acuity not statistically different when averaged over both eyes, but visual acuity of the better seeing eye did show improvement
- Visual field improvements, however slight declines in original results at three years

Harms

- Absence of causes of death in past gene therapy trials :
  - No cytotoxic immune response (retina-blood barrier, administration protocol, oral prednisone)
  - Insertional mutagenesis highly unlikely (no insertion of transfected gene into the genome, RPE cells do not divide after birth)
- Risks essentially related to the surgical aspects of the procedure : cataracts, infections, retinal tears, transient elevated intraocular pressure
- Two patients sustained permanent vision loss

Controversies and Uncertainties

- Variability in therapeutic effect
- MLMT as a novel endpoint not correlated to outcomes measured in real-world settings
- No published data on therapeutic effect beyond 3 years. Uncertainty of long term effect
- Long term safety data

Conclusion

- High certainty of at least a small to substantial improvement over standard care in a population perspective
- Thus, we consider the evidence on VN in biallelic RPE65-associated retinal dystrophy to be “incremental or better” (B+)
- Some of the benefits for patients and families not captured in effectiveness study

RPE-65 Mediated Retinal Disease Cost-effectiveness

Marita Zimmerman, PhD, MPH, Pharmaceutical Outcomes Research and Policy Program, University of Washington

Josh Carlson, PhD, MPH, Pharmaceutical Outcomes Research and Policy Program, University of Washington

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Disclosures

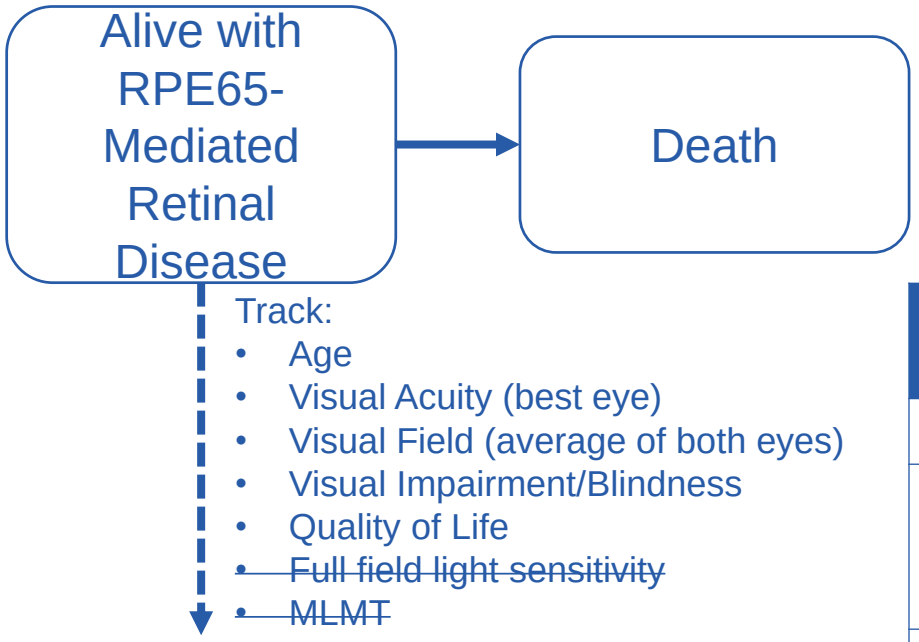
- Marita Zimmermann has no disclosures to report.
- Josh Carlson has no disclosures to report.

Objective

The primary aim of this analysis was to estimate the cost-effectiveness of voretigene neparvovec for vision loss associated with biallelic RPE65-mediated inherited retinal disease compared to the standard of care over a lifetime horizon.

Methods in Brief

Overall Approach



Target population: individuals in the United States with biallelic RPE65-mediated inherited retinal disease:

	Older population	Younger population
Mean age at treatment	15	3
Mean baseline visual acuity (decimals, best eye)	0.096	0.249
Mean baseline visual field (degrees)	363	655

Overall Approach

	US Health Care System Perspective	Modified Societal Perspective
Direct medical costs		
Physicians/providers	X	X
Medical treatment	X	X
Ophthalmic-related depression care	X	X
Ophthalmic-related trauma care	X	X
Direct non-medical costs		
Caregivers		X
Transportation		X
Nursing home care		X
Indirect costs		
Education		X
Productivity loss		X

Key Model Assumptions

- Biallelic *RPE65*-mediated inherited retinal disease and VN treatment do not affect mortality.
- Treatment effect is maintained for 10 years, followed by a 10-year waning of effect, after which the rate of decline in vision is the same as with SoC.
- Impacted individuals are considered visually impaired when VA<0.63 decimals or VF<1200 degrees, and blind when VA<0.015 decimals or VF<48 degrees.

Clinical Inputs – Natural History

Figure 2. Visual Acuity (Holladay) by Age Group—Right Eye and Left Eye

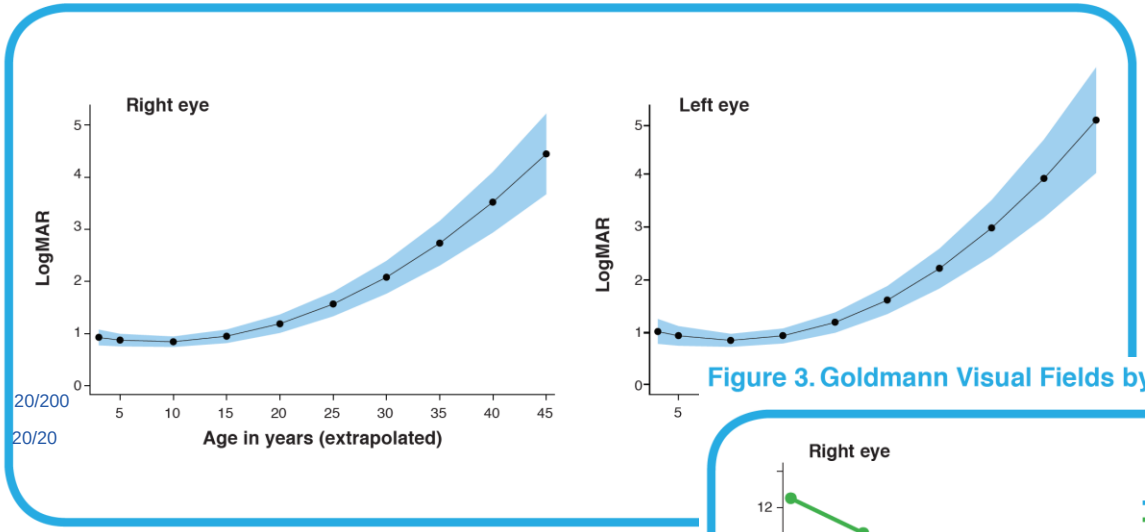
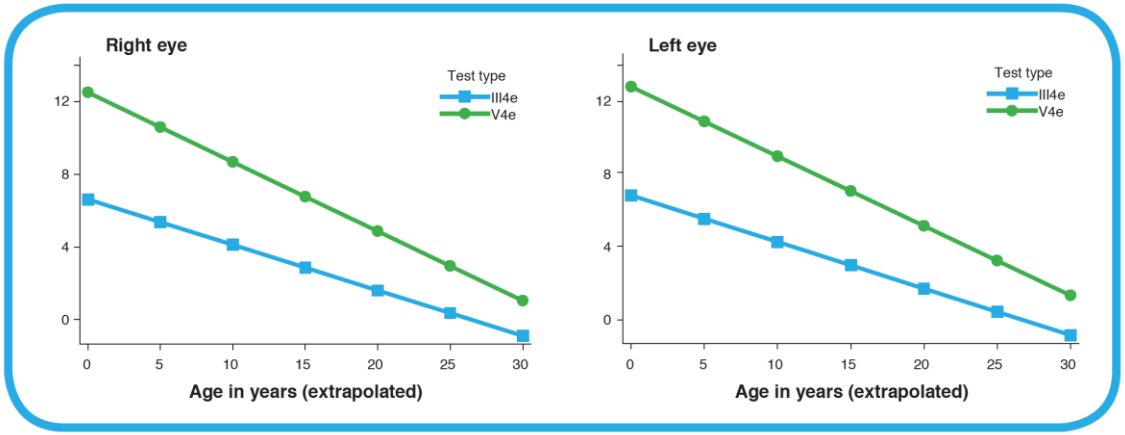


Figure 3. Goldmann Visual Fields by Age and Test Type (Right and Left Eyes)



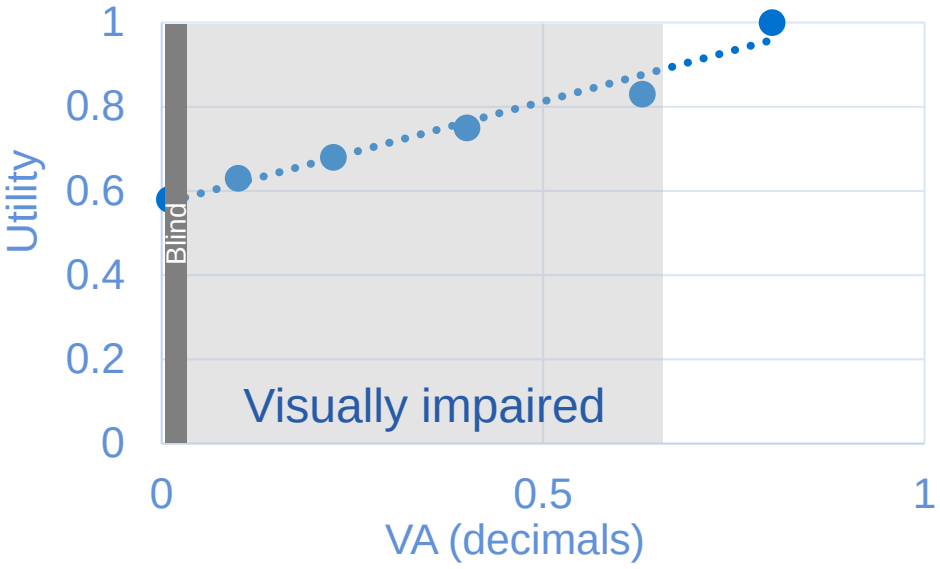
Source: poster, Reape et al. Presented at The Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting,May 7–11, 2017, Baltimore, MD, USA

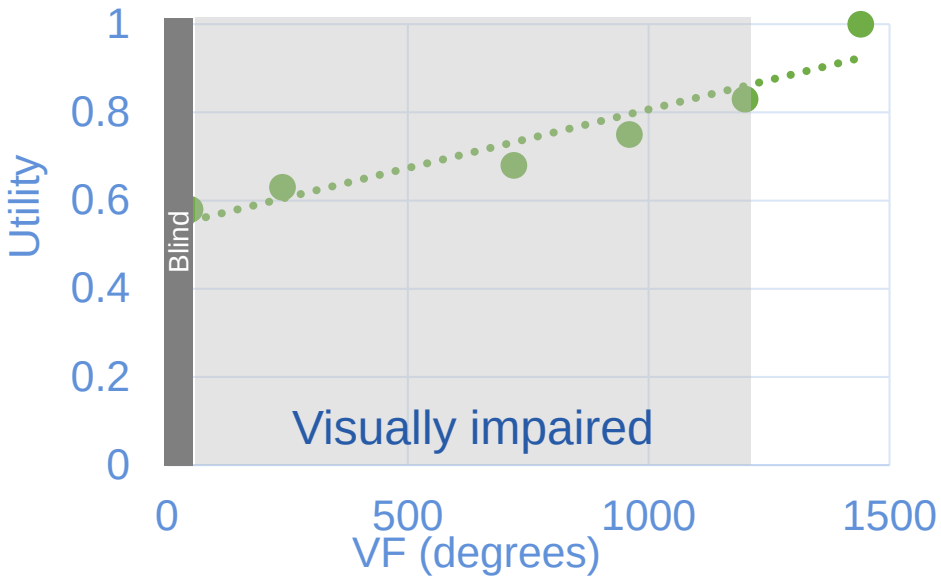
Clinical Inputs – Change with Voretigene

	Value
Best Eye VA Change (logMAR)	-0.05
VF Change (degrees)	282
Duration of Treatment Effect	10 years
Duration of Waning Period	10 years

Clinical Inputs – Utilities

Based on VA or VF, whichever is lower





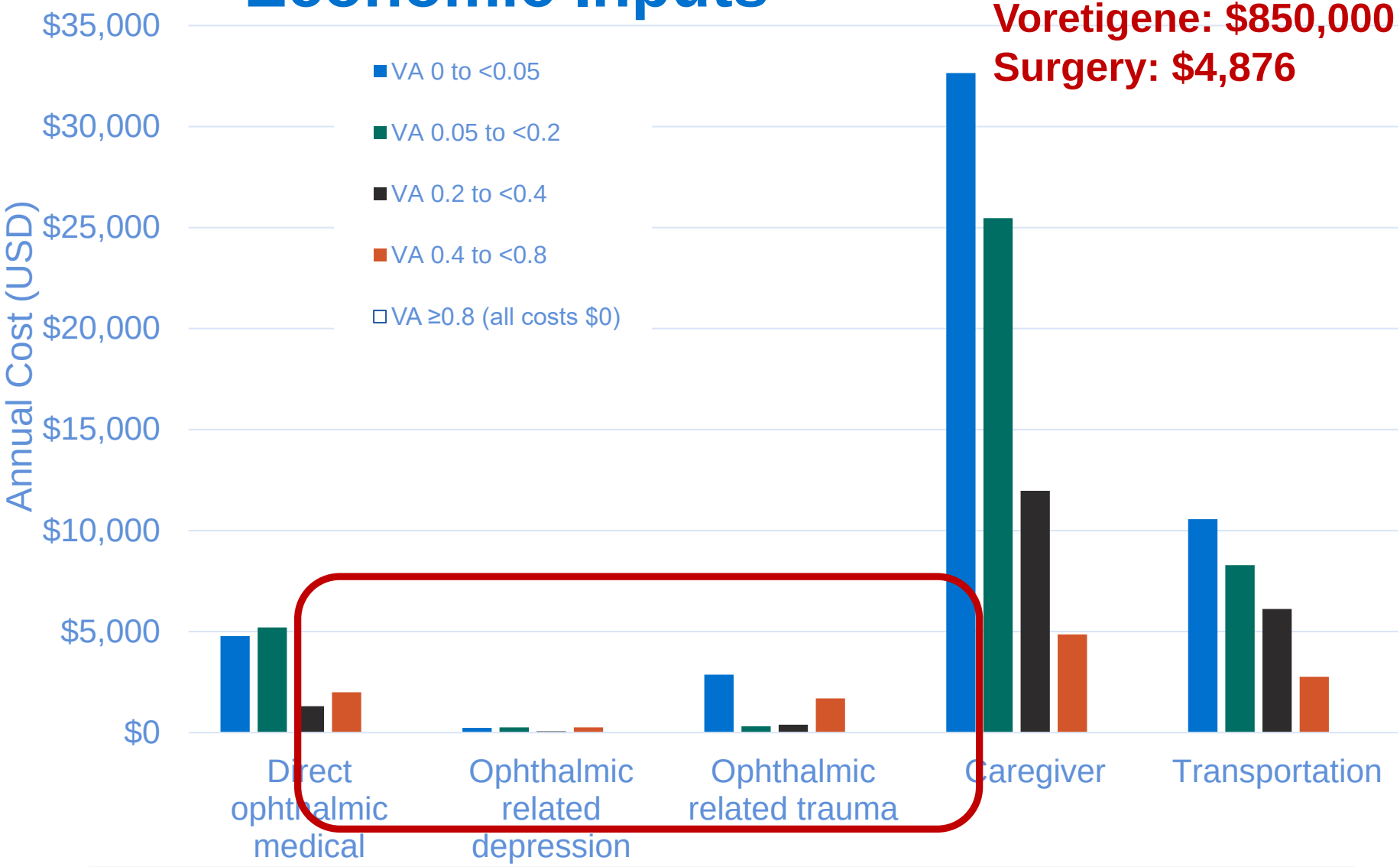
Source: Lloyd et al., 2008

Clinical Inputs – Adverse Events

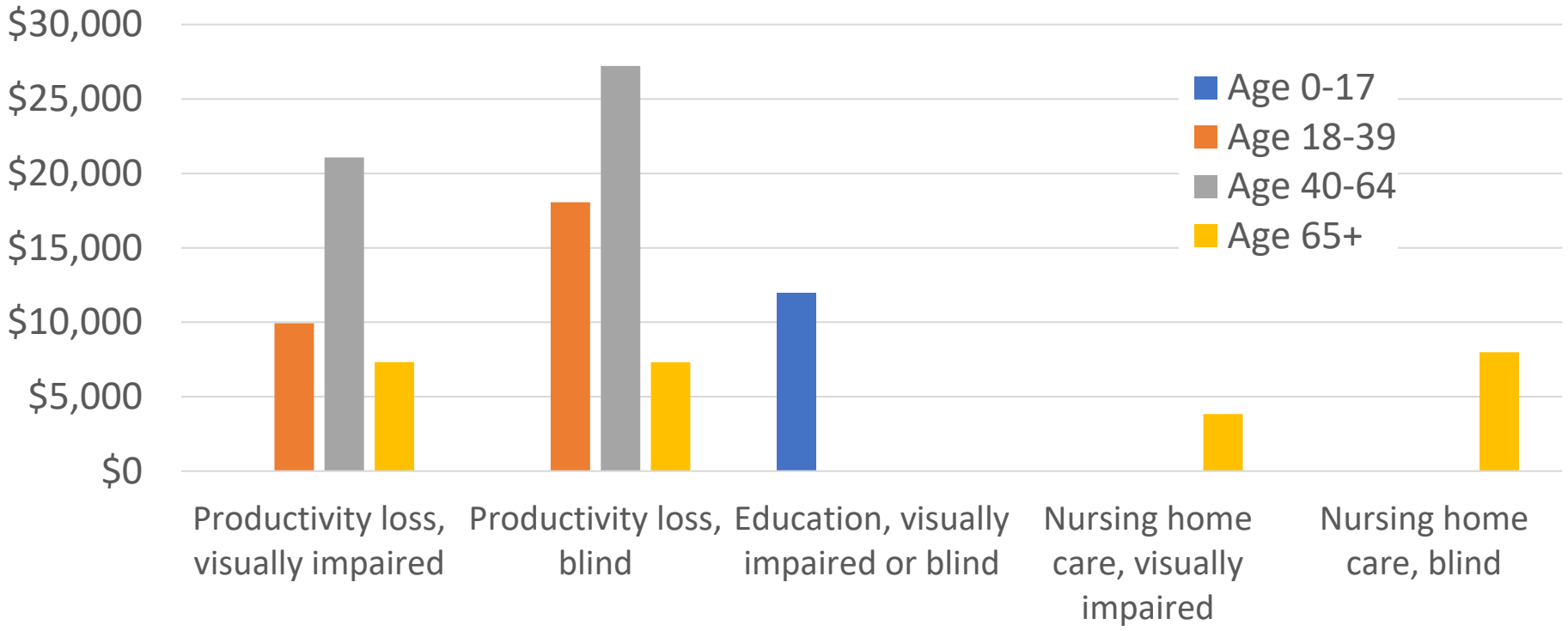
Adverse Event	Rate	Cost	Disutility
Eye Irritation	5%	$80 Source: CPT 99214	0 Assumed
Eye Pruritus, Ongoing	5%	$80 Source: CPT 99214	0 Assumed
Macular Hole/ Degeneration	5%	$4,447 Source: DRG 124	0.0533 for 6 months*

*Source: Ternent L, Vale L, Boachie C, Burr JM, Lois N. Cost-effectiveness of internal limiting membrane peeling versus no peeling for patients with an idiopathic full-thickness macular hole: results from a randomised controlled trial. Br J Ophthalmol. 2012;96(3):438-443.

Economic Inputs

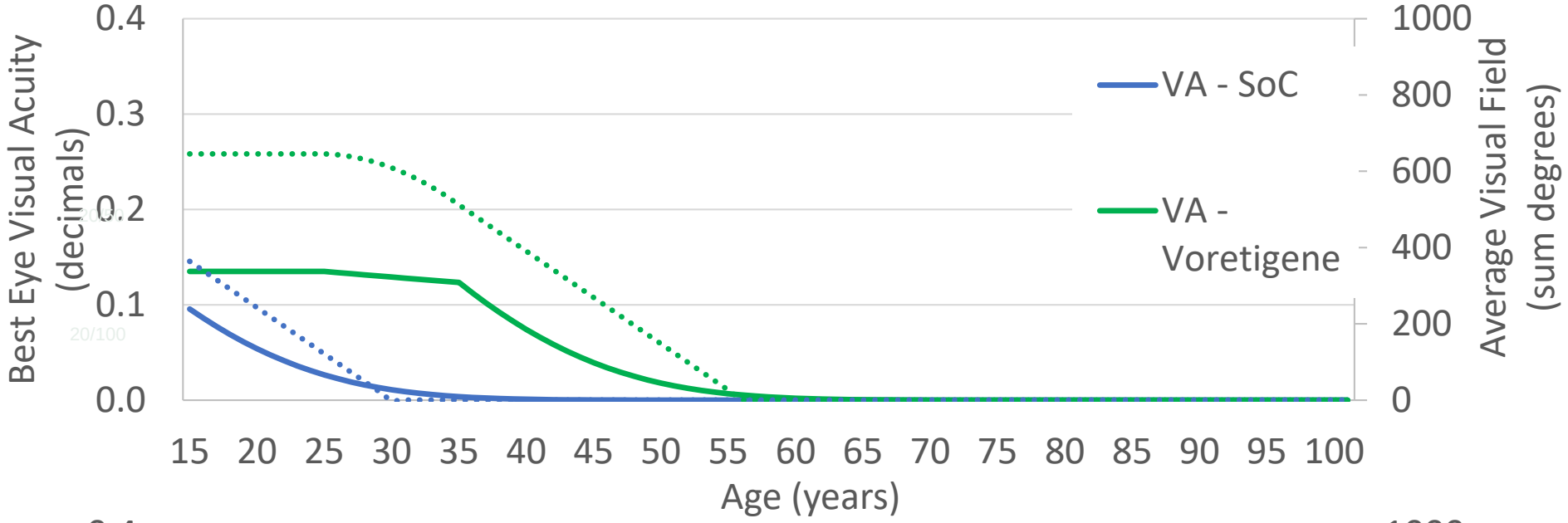


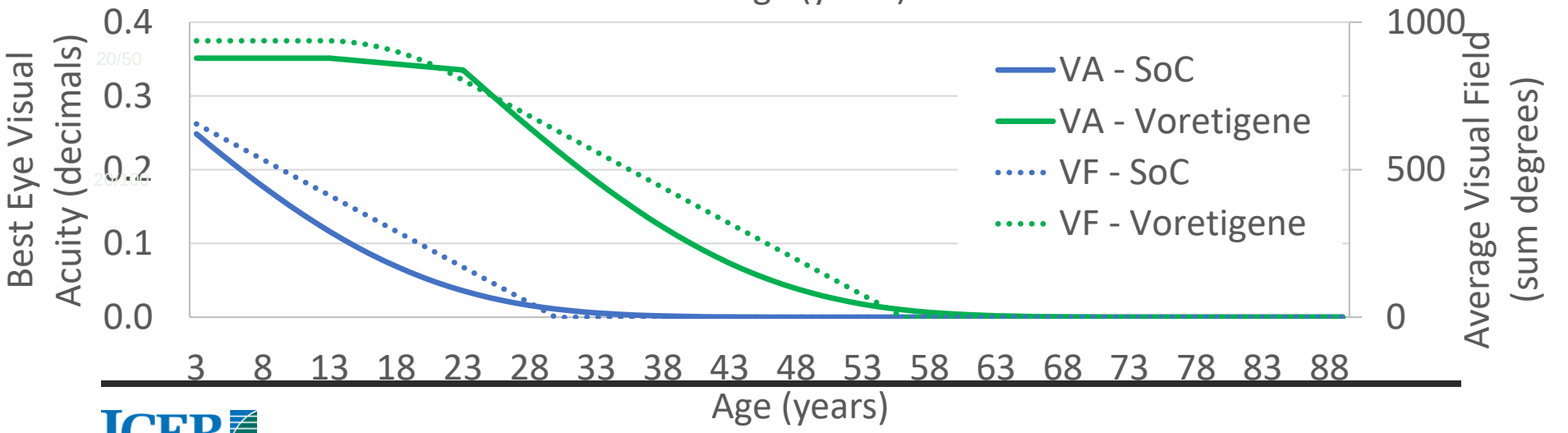
Economic Inputs



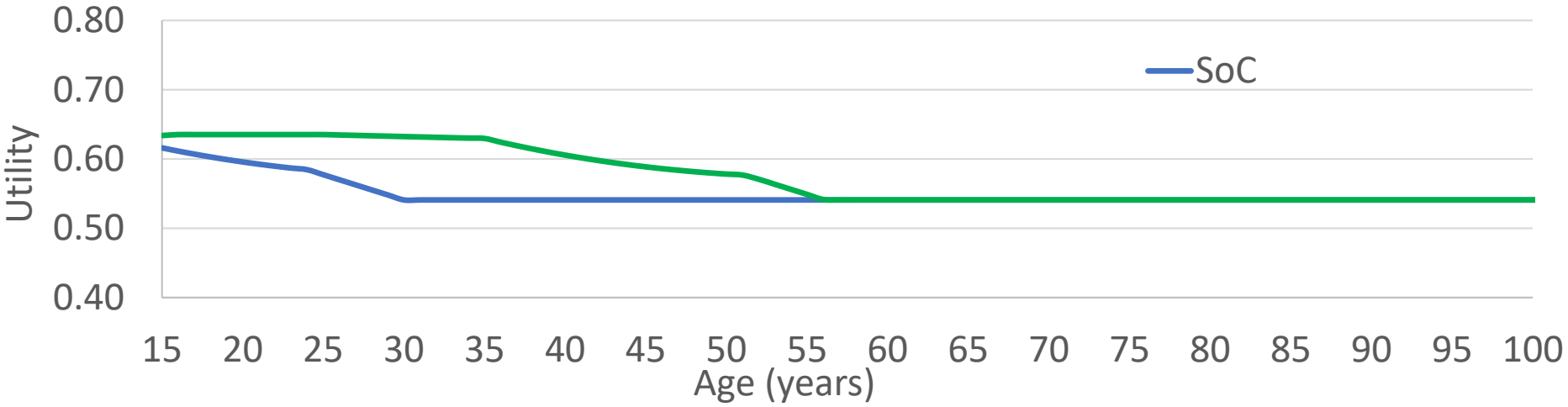
Results

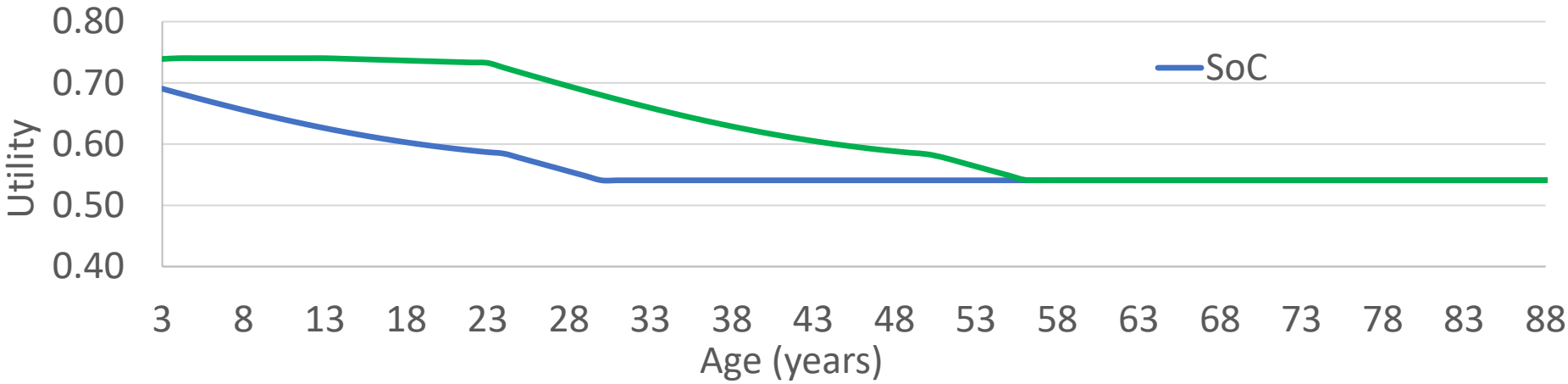
Results – VA and VF





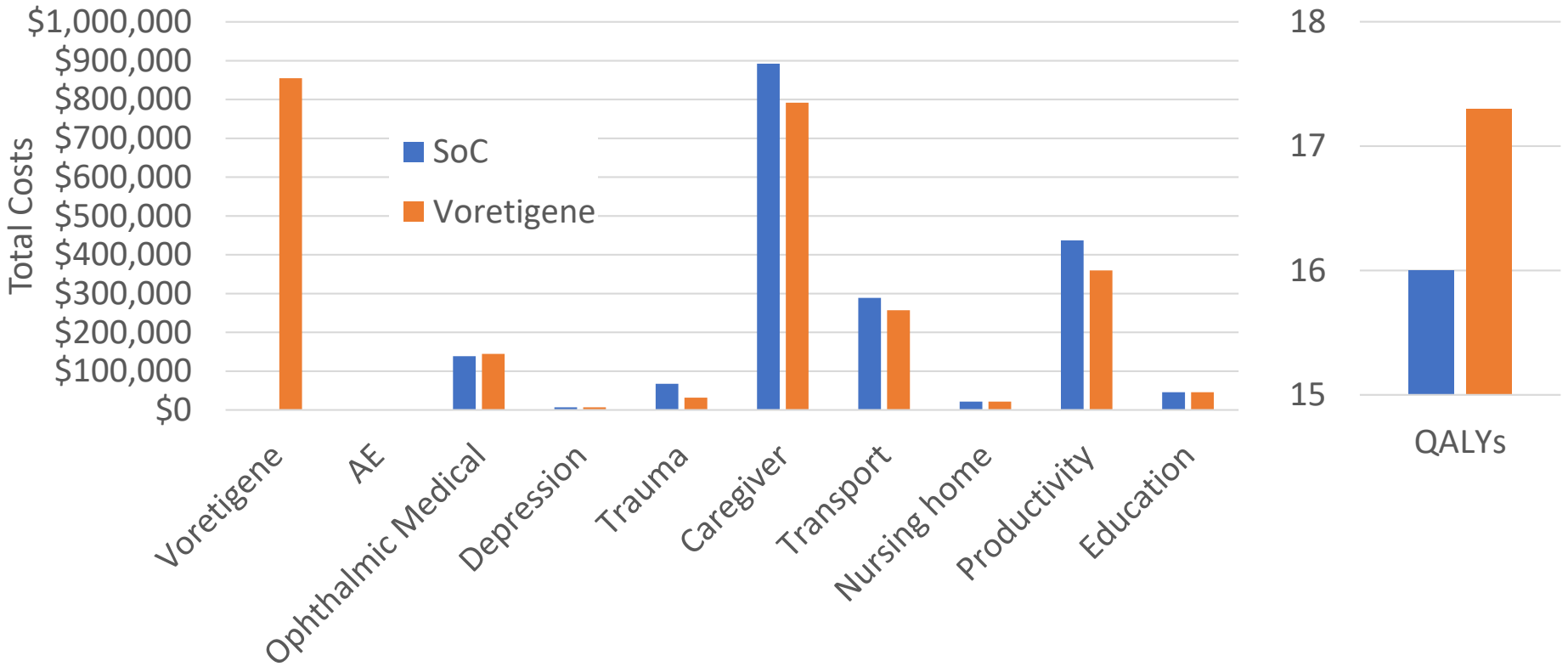
Results – Utility





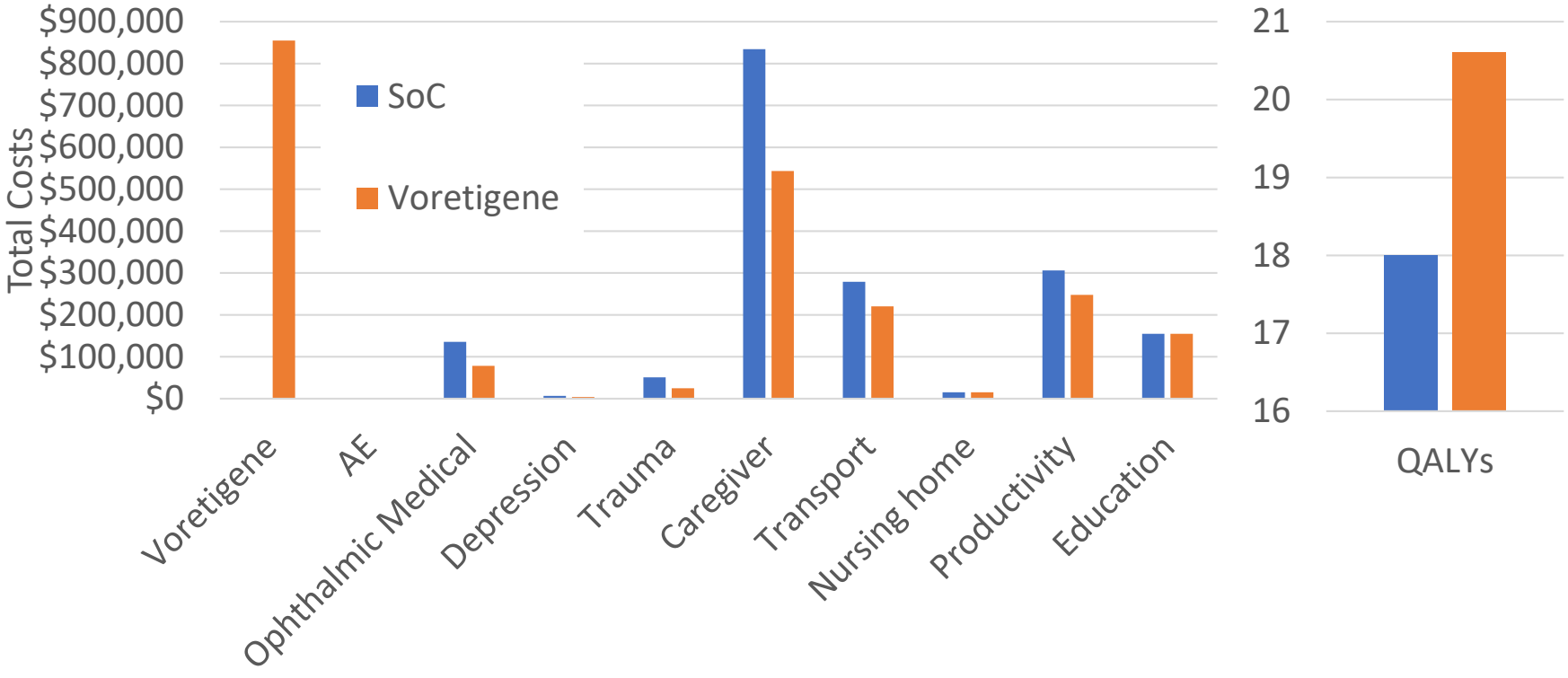
Results – Older Population
(Age 15)

Perspective	ICER
US Health Care System	$643,813/QALY
Modified Societal	$480,130/QALY



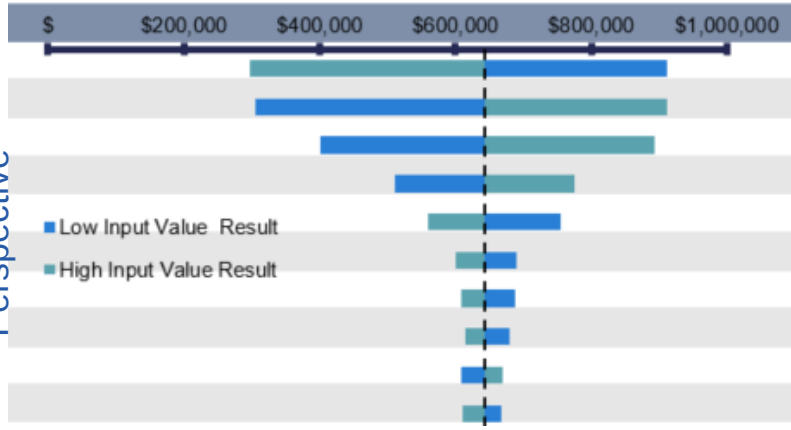
Results – Younger Population
(Age 3)

Perspective	ICER
US Health Care System	$287,915/QALY
Modified Societal	$135,331/QALY



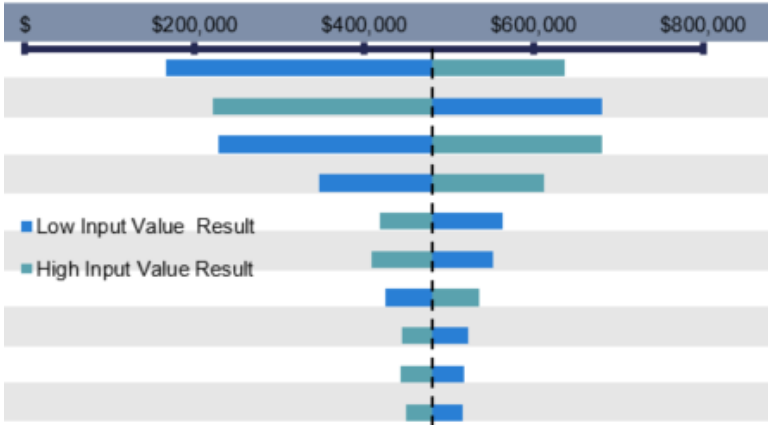
Sensitivity Analysis – Older Population

US Health System Perspective



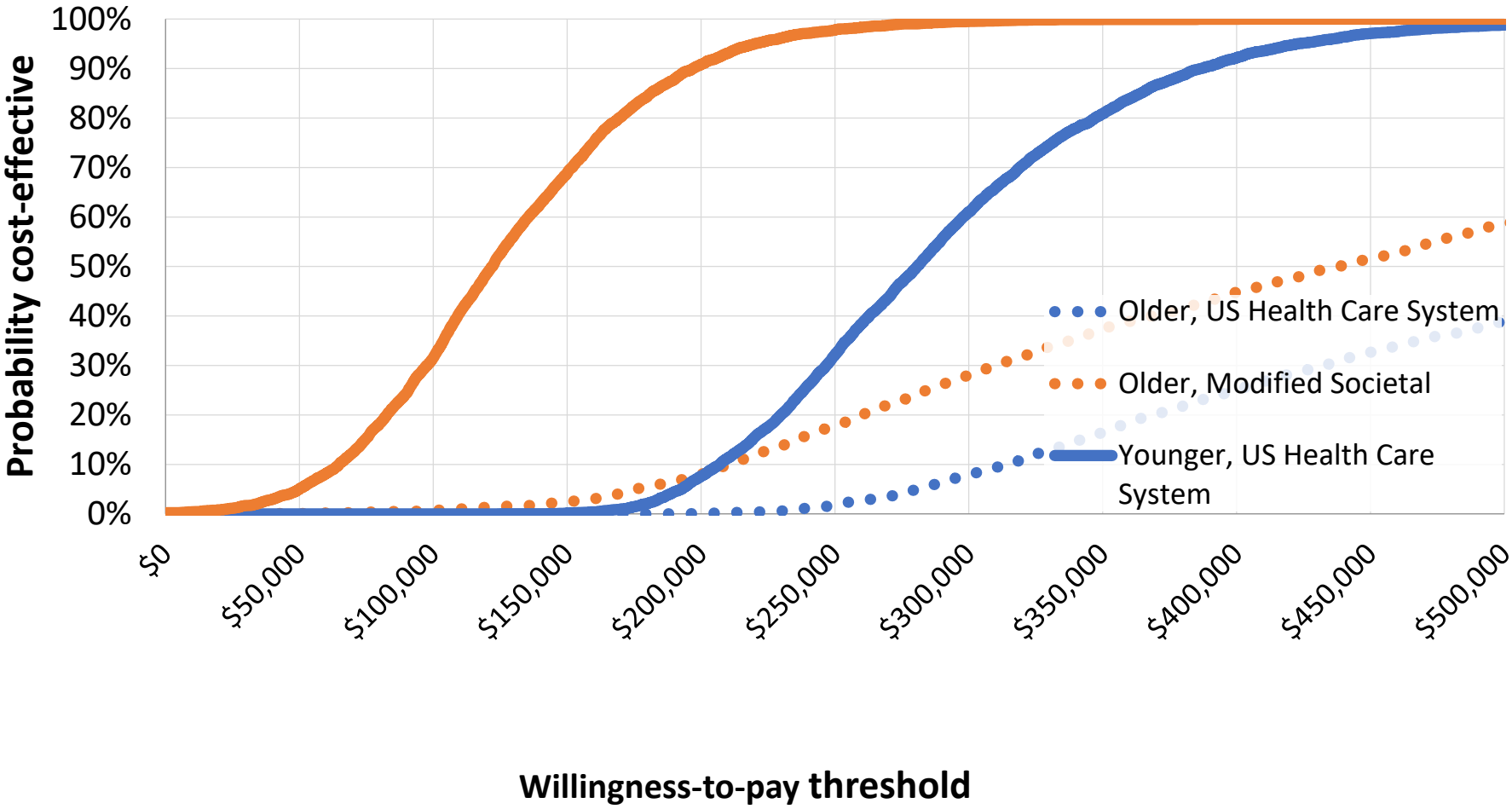
Parameter	Low Input Value	High Input Value
Utility (VF function intercept)	-0.59	-0.88
Utility (VA function intercept)	-0.58	-0.87
Baseline best eye VA (logMAR)	0.82	1.22
Cost of voretigene	680000.00	1020000.00
Utility (VA function slope)	4.44	6.66
Best VA effectiveness	-0.12	-0.18
Duration of treatment effect	8.00	12.00
Duration of waning effect	8.00	12.00
Baseline visual field, average	291.05	436.57
Age at intervention	12.00	18.00

Modified Societal Perspective



Parameter	Low Input Value	High Input Value
Baseline best eye VA (logMAR)	0.82	1.22
Utility (VF function intercept)	-0.37	-0.55
Utility (VA function intercept)	-0.34	-0.52
Cost of voretigene	680000.00	1020000.00
Utility (VA function slope)	0.39	0.58
Direct non-medical costs, caregiver, VA 0-0.05	26121.92	39182.88
Direct non-medical costs, caregiver, VA 0.05-0.2	20374.22	30561.33
Duration of treatment effect	8.00	12.00
Best VA effectiveness	-0.12	-0.18
Duration of waning effect	8.00	12.00

Probabilistic Sensitivity Analysis



Scenario Analysis – Lifetime Treatment Effect

Incremental Results	Base Case Age 15	Base Case Age 3	Effect Duration Scenario Age 15	Effect Duration Scenario Age 3
Voretigene costs	$854,875	$854,875	$854,875	$854,875
Direct Medical Costs	-$29,478	-$86,107	-$48,404	-$139,946
Direct Non-Medical Costs	-$132,442	-$349,224	-$228,817	-$574,031
Indirect Costs	-$77,464	-$58,312	-$99,888	-$69,943
QALYs	1.3	2.7	2.1	4.4
Blindness-Free Years	10.6	8.1	17.0	11.9
ICER, US Health Care System Perspective	$643,813/QALY	$287,915/QALY	$384,624/QALY	$161,187/QALY
ICER, Modified Societal Perspective	$480,130/QALY	$135,331/QALY	$227,901/QALY	$16,043/QALY
$/Additional Blindness Free Year, US Health Care System Perspective	$77,937/Year	$95,175/Year	$47,541/Year	$60,191/Year
$/Additional Blindness Free Year, Modified Societal Perspective	$58,123/Year	$44,736/Year	$28,170/Year	$5,991/Year

Comments Received

- Utility values and methods for utility calculation not appropriate for population.
  - Response: We changed base case source for utility values and performed a scenario analysis. We also removed underlying population utilities.
- Costs were not high or inclusive enough for population.
  - Response: We used additional cost sources with more inclusive severity-based cost categories.
- Treatment effect duration is longer than modeled.
  - Response: We expanded the treatment effect duration to 10 years, added a waning period, and performed a lifetime duration scenario analysis.

Limitations

- Natural history of *RPE65*-mediated inherited retinal disease has not been thoroughly studied.
- Limited in measures of effectiveness for VN to those measures that were captured in the clinical trials as outcomes, as well as in what measures could be linked to quality of life.
- Costs and quality of life measures have not, to our knowledge, been published for this specific patient population.

Summary

- Voretigene improves patient health outcomes compared to standard of care.
- High cost makes this unlikely to be a cost-effective intervention in the types of patients studied, at commonly used cost-effectiveness thresholds.
- If, in the future, it becomes possible to select patients early with preserved vision, and also if you use a societal perspective rather than the usual health system perspective, Voretigene may then be cost effective at typical thresholds.

Appendix

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Results – Older Population

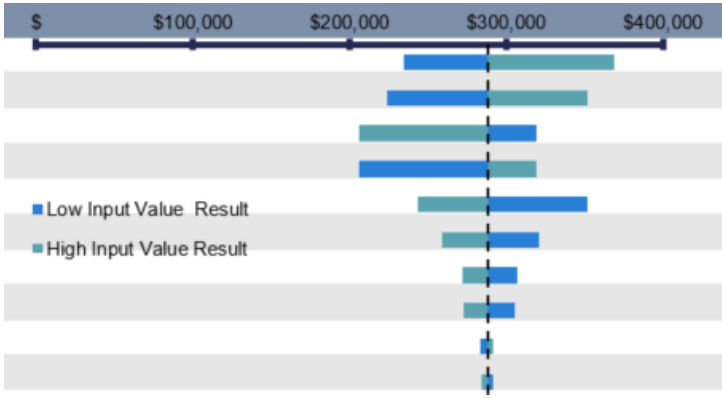
	SoC	Voretigene	Incremental
Total Costs, US Health Care System Perspective	$213,399	$1,039,019	$825,621
Total Costs, Modified Societal Perspective	$1,899,605	$2,515,320	$615,715
Voretigene Costs	$0	$854,876	$854,876
AE Costs	$0	$222	$222
Direct Ophthalmic Medical Costs	$138,833	$144,793	$5,960
Direct Medical Costs, Depression	$6,834	$7,171	$336
Direct Medical Costs, Trauma	$67,731	$31,957	-$35,774
Direct Non-Medical Costs, Caregiver	$892,528	$791,951	-$100,577
Direct Non-Medical Costs, Transport	$288,997	$257,132	-$31,865
Direct Non-Medical Costs, Nursing home	$21,783	$21,783	$0
Indirect Costs, Productivity	$437,043	$359,579	-$77,464
Indirect Costs, Education	$45,856	$45,856	$0
Total QALYs	16.0	17.3	1.3
Blindness-Free Years	11.6	22.2	10.6
ICER, US Health Care System Perspective	--	--	$643,813/QALY
ICER, Modified Societal Perspective	--	--	$480,130/QALY
$/Additional Blindness Free Year, US Health Care System Perspective	--	--	$77,937/Year
$/Additional Blindness Free Year, Modified Societal Perspective	--	--	$58,123/Year

Results – Younger Population

	SoC	Voretigene	Incremental
Total Costs, US Health Care System Perspective	$193,249	$962,240	$768,991
Total Costs, Modified Societal Perspective	$1,782,630	$2,144,086	$361,456
Voretigene Costs	$0	$854,876	$854,876
AE Costs	$0	$222	$222
Direct Ophthalmic Medical Costs	$135,618	$78,329	-$57,290
Direct Medical Costs, Depression	$6,682	$3,814	-$2,868
Direct Medical Costs, Trauma	$50,948	$24,999	-$25,950
Direct Non-Medical Costs, Caregiver	$834,242	$543,647	-$290,595
Direct Non-Medical Costs, Transport	$278,964	$220,336	-$58,628
Direct Non-Medical Costs, Nursing home	$15,252	$15,252	$0
Indirect Costs, Productivity	$306,021	$247,710	-$58,312
Indirect Costs, Education	$154,901	$154,901	$0
Total QALYs	18.0	20.6	2.7
Blindness-Free Years	18.4	26.4	8.1
ICER, US Health Care System Perspective	--	--	$287,915/QALY
ICER, Modified Societal Perspective	--	--	$135,331/QALY
$/Additional Blindness Free Year, US Health Care System Perspective	--	--	$95,175/Year
$/Additional Blindness Free Year, Modified Societal Perspective	--	--	$44,736/Year

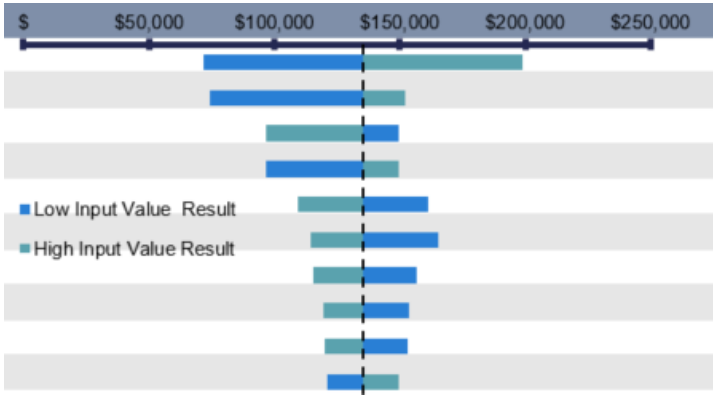
Sensitivity Analysis – Younger Population

US Health System Perspective



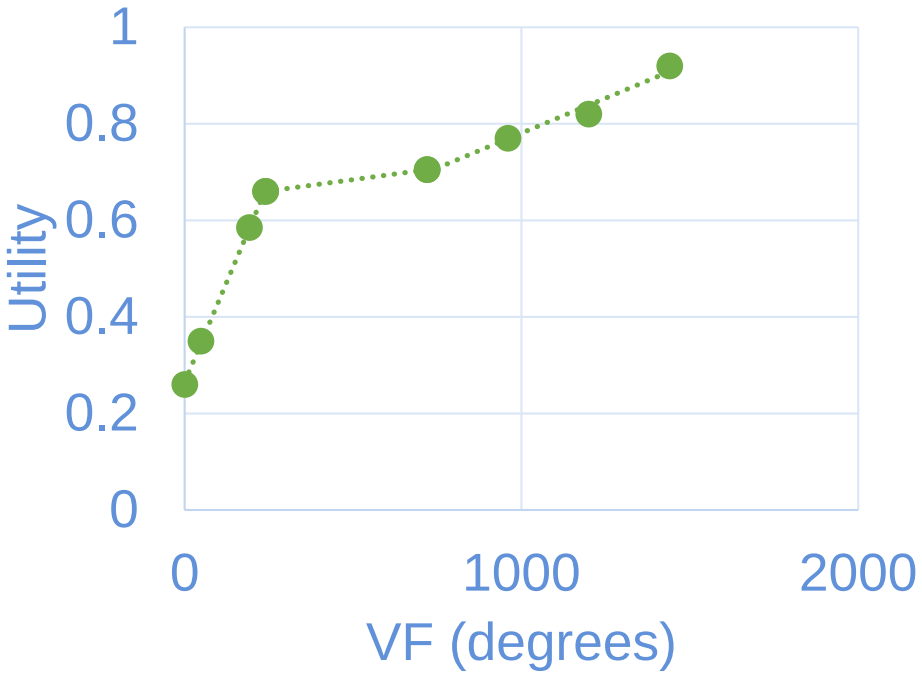
Parameter	Low Input Value	High Input Value
Baseline best eye VA (logMAR)	0.48	0.73
Cost of voretigene	680000.00	1020000.00
Utility (VF function intercept)	-0.37	-0.55
Utility (VA function intercept)	-0.34	-0.52
Utility (VA function slope)	0.39	0.58
Best VA effectiveness	-0.12	-0.18
Duration of treatment effect	8.00	12.00
Duration of waning effect	8.00	12.00
Baseline visual field, average	291.05	436.57
Direct medical costs, VA 0-0.05	3822.34	5733.51

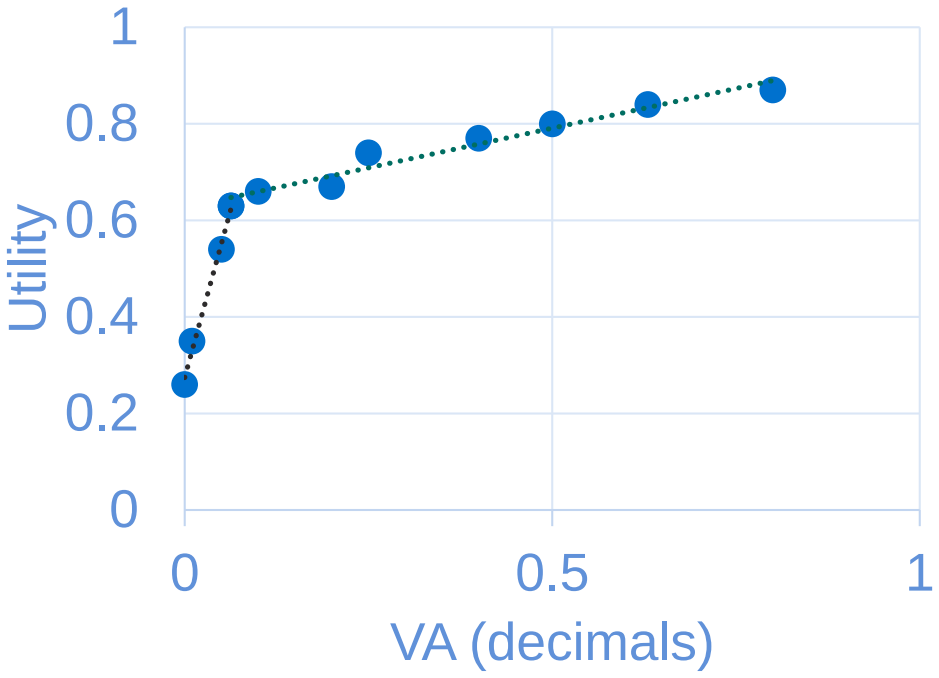
Modified Societal Perspective



Parameter	Low Input Value	High Input Value
Cost of voretigene	680000.00	1020000.00
Baseline best eye VA (logMAR)	0.48	0.73
Utility (VF function intercept)	-0.37	-0.55
Utility (VA function intercept)	-0.34	-0.52
Direct non-medical costs, caregiver, VA 0-0.05	26121.92	39182.88
Utility (VA function slope)	0.39	0.58
Best VA effectiveness	-0.12	-0.18
Duration of treatment effect	8.00	12.00
Duration of waning effect	8.00	12.00
Direct non-medical costs, caregiver, VA 0.2-0.4	9577.37	14366.05

Scenario Analysis – Utility Function



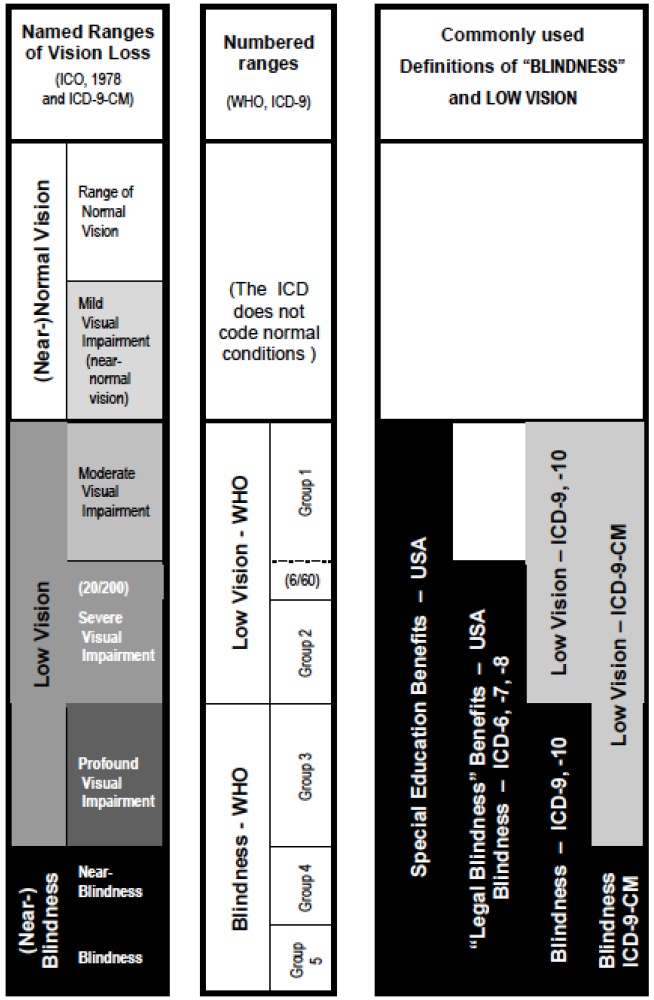


Source: Brown et al., 2001

Scenario Analysis – Utility Function

Incremental Results	Base Case Age 15	Base Case Age 3	Utility scenario Age 15	Utility scenario Age 3
Voretigene costs	$854,875	$854,875	$854,875	$854,875
Direct Medical Costs	-$29,478	-$86,107	-$29,478	-$86,107
Direct Non-Medical Costs	-$132,442	-$349,224	-$132,442	-$349,224
Indirect Costs	-$77,464	-$58,312	-$77,464	-$58,312
QALYs	1.3	2.7	5.2	4.8
Blindness-Free Years	10.6	8.1	10.6	8.1
ICER, US Health Care System Perspective	$643,813/QALY	$287,915/QALY	$157,844/QALY	$160,593/QALY
ICER, Modified Societal Perspective	$480,130/QALY	$135,331/QALY	$117,713/QALY	$75,485/QALY
$/Additional Blindness Free Year, US Health Care System Perspective	$77,937/Year	$95,175/Year	$77,937/Year	$95,175/Year
$/Additional Blindness Free Year, Modified Societal Perspective	$58,123/Year	$44,736/Year	$58,123/Year	$44,736/Year

TABLE 3 – **RANGES of VISUAL ACUITY LOSS** in ICD-9, ICD-10 and in ICD-9-CM



Visual Acuity			Linear scales	
Decimal notation	U.S. notation	6 m notation	Letter count	Log MAR
1.6	20/12	6/4	110	-0.2
1.25	20/16	6/5	105	-0.1
1.0	**20/20**	**6/6**	100	0
0.8	20/25	6/7.5	95	0.1
0.63	20/32	6/10	90	0.2
0.5	20/40	6/12	85	0.3
0.4	20/50	6/15	80	0.4
0.32	20/63	6/18	75	0.5
0.25	20/80	6/24	70	0.6
0.2	20/100	6/30	65	0.7
0.16	20/125	6/36	60	0.8
0.125	20/160	6/48	55	0.9
0.1	**20/200**	**6/60**	**50**	**1.0**
0.08	20/250		45	1.1
0.063	20/300		40	1.2
0.05	20/400	3/60	35	1.3
0.04	20/500		30	1.4
0.032	20/600	2/60	25	1.5
0.025	20/800		20	1.6
0.02	20/1000		15	1.7
less	less	1/60 or less	10	1.8
			5	1.9
0.0	NLP	NLP	0	2.0

TABLE 7 – **RANGES of FIELD LOSS and O&M ABILITY**

Ranges of Vision Loss	Visual Field (how the eye functions)		Statistical estimates of O&M Ability (how the person functions)		
	Average field radius (diam.)	Grid score	Ability Ranges	Visual O&M Ability	Comments
Range of Normal Vision	60° (120°)	110 100	Has reserves (100 ± 10)	Normal visual orientation Normal Mobility skills	
Mild Visual Impairment	50° (100°) 40° (80°)	90 80	Lost reserves (80 ± 10)	Normal O&M performance Needs more scanning	*Occasionally surprised by events on the side*
Moderate Visual Impairment	30° (60°) 20° (40°) loss upper field hemianopia	70 60	Normal with aids (60 ± 10)	Near-normal performance	*Requires scanning for obstacles*
Severe Visual Impairment	10° (20°) 8° (16°) loss lower field	50 40	Restricted with aids (40 ± 10)	Visual mobility is slower than normal	*Needs continuous scanning* *May use cane as an adjunct*
Profound Visual Impairment	6° (12°) 4° (8°)	30 20	Marginal with aids (20 ± 10)	Limited visual mobility	*Needs cane to detect obstacles* *May use vision as adjunct for identification*
Near-Blindness Blindness	2° (4°) 0°	10 0	(Near-) impossible (0 – 10)	Visual orientation unreliable or impossible	*Must rely on long cane, hearing, guide dog, other blind mobility skills*

Public Comment: Manufacturer Representatives

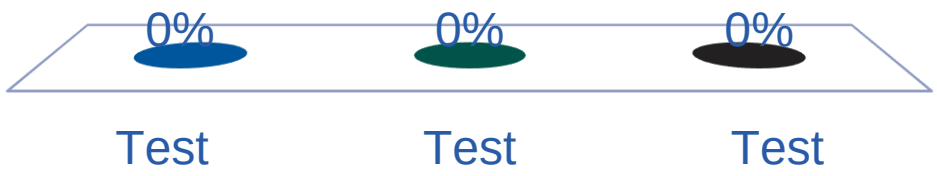
Break for Lunch

Meeting will resume at 12:45 pm

Voting Questions

0. Test Question

A. Test
B. Test
C. Test



1. For patients with RPE-65 mediated inherited retinal disease, is the evidence adequate to demonstrate that the net health benefit of treatment with voretigene neparvovec is greater than that of supportive care?

A. Yes

B. No

2. When compared to best supportive care, does voretigene neparvovec offer one or more of the following “other benefits” for patients with RPE-65 mediated inherited retinal disease? Please select all that apply.

A. Significant direct patient health benefits not adequately captured by the QALY

B. Reduced complexity that will significantly improve outcomes

C. Reduce important health disparities

D. Significantly reduce caregiver/family burden

E. Novel mechanism of action or approach….

F. Significant impact on improving return to work/overall productivity

G. Significant positive impact outside the family

H. Significant impact on the entire “infrastructure” of care

3. Are any of the following contextual considerations important in assessing voretigene neparvovec's long-term value for money in patients with RPE-65 mediated inherited retinal disease? Please select all that apply.

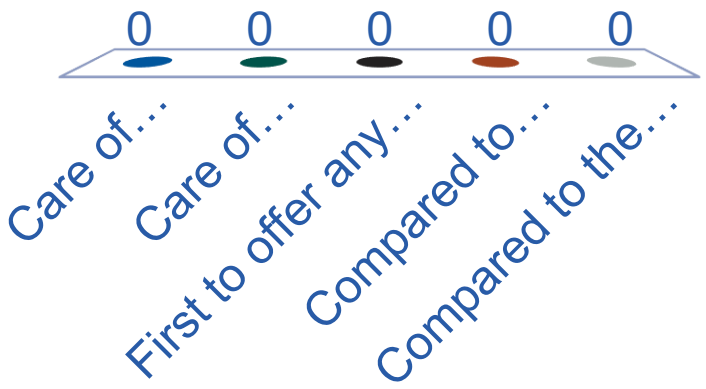
A. Care of individuals with condition of high severity

B. Care of individuals with condition with high lifetime burden of illness

C. First to offer any improvement

D. Compared to comparator, there is significant uncertainty about long-term risk of serious side effects

E. Compared to the comparator, significant uncertainty about magnitude or durability of the long term benefits of this intervention

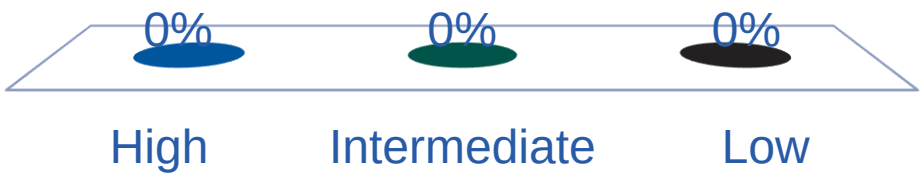


4. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of voretigene neparvovec compared with supportive care for patients with RPE-65 mediated inherited retinal disease?

A. High

B. Intermediate

C. Low



Policy Roundtable

Policy Roundtable Participants

Policy Roundtable	
Katelyn Corey VN Trial Participant	**Janet LaBreck** Former Commissioner, Rehabilitation Services Administration
Patrick Gleason Prime Therapeutics	**Bill Martin** Express Scripts, Inc
Christine Kay, MD Vitreo Retinal Associates	

CEPAC Panel Reflections

Next Steps

- Final Report and accompanying materials expected on or before February 15, 2018

- Meeting materials and outputs: https://icer-review.org/meeting/voretigene-neparvovec/

For more information please visit:

https://icer-review.org/programs/midwest-cepac/

Adjourn