

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

## **Details of Utility Assessment Methods**

To capture changes in health-related quality-of-life associated with receipt of the two interventions over the course of the trial, four methods were used. In method one, visual acuities from the better-seeing eye over the two years of the trial were converted into quality-adjusted life-years (QALYs) using commonly-used mappings of Snellen vision categories to utilities by Brown et al.<sup>1</sup> Those utilities are measured on a scale from death to perfect vision. Best-corrected visual acuities in the better-seeing eye at the 16, 32, 52, 68, 84, and 104-week visit were converted to the closest Snellen categories, then converted to utilities. These were then converted into gains/losses compared with the baseline utility associated with the patient's best-corrected visual acuity in the better-seeing eye at randomization (see details in Table S1).

Method two was similar to method one, but instead of using the better-seeing eye, best-corrected visual acuities from the treated eye were used from a study that used the EuroQoL (EQ-5D) questionnaire to assess utility in DME patients.<sup>2</sup>

Method three was similar to methods one and two, but used a formula estimating the relationship between LogMAR visual acuity of the best-seeing eye to utilities, where utilities are measured on a scale from death to perfect health.<sup>3</sup>

Method four used utilities collected directly from participant responses at the randomization, 52- and 104-week visits. Iterative time-trade-off questions compared life with current vision to perfect health. Because this was not a primary or secondary outcome from the main trial, power calculations had not been performed a priori to evaluate if the study size was large enough to detect differences in time tradeoff utility between the groups.

**Table 1: Input Parameters**

<b>Parameter</b>	<b>Parameter Value*†</b>	<b>Range Explored in Cost-Effectiveness Acceptability Curves ‡</b>	<b>Source</b>
<b>Unit Costs (per procedure)</b>			
Cataract extraction with IOL placement	\$3,098	(2788-3408)	Medicare 4 CPT 66984
Cataract extraction without IOL placement	\$2,394	(2155-2634)	Medicare CPT 66984
Diode laser (open angle glaucoma)	\$1,800	(1620-1980)	Medicare CPT 66710
Endolaser	\$5,752	(5177-6327)	Medicare CPT 67108
Extended ophthalmoscopy	\$27	(24-30)	Medicare CPT 92225
Fluorescein angiography	\$111	(100-122)	Medicare CPT 92235
Focal/grid laser	\$525	(472-577)	Medicare CPT 67210
Fundus photography	\$79	(72-87)	Medicare CPT 92250
Intravitreal injection procedure	\$103	(93-114)	Medicare CPT 67028
0.5-mg ranibizumab drug	\$1,916.14	(1755-2145)	Medicare pricing files of ASP +6%
Laser retinopathy	\$534	(480-587)	Medicare CPT 67145
OCT	\$45	(41-50)	Medicare CPT

			92134
Paracentesis	\$121	(109-133)	Medicare CPT 65800
Panretinal photocoagulation	\$345	(311-380)	Medicare CPT 67228
Retinal cryopexy	\$793	(714-873)	Medicare CPT 67101
Retinal detachment repair-injection of air/gas	\$2,452	(2207-2697)	Medicare CPT 67110
Silicone oil injection	\$3,443		
Total air-fluid exchange	\$3,443	(3099-3787)	Medicare CPT 67108
Ocular ultrasound	\$94	(84-103)	Medicare CPT 76512
Vitrectomy	\$3,716	(3344-4087)	Medicare CPT 67036
vitrectomy with endolaser	\$5,416	(4874-5957)	Medicare CPT 67108
Vitrectomy with epiretinal membrane peel	\$3,971	(3574-4368)	Medicare CPT 67041
<b>Annual Costs (first year)</b>			
MI	\$53,764	(40323-67205)	Bonafede <sub>5</sub>
CVA	\$59,147	(44360-73934)	Bonafede
<b>Annual Costs (year 2)</b>			
MI	\$19,615	(14711-24519)	Bonafede
CVA	\$37,007	(27755-46259)	Bonafede
<b>Utility associated with Visual Acuity in the Better-Seeing Eye</b>			
20/20	0.92	(0.87-0.97)	Brown <sup>1</sup>
20/25	0.87	(0.82-0.92)	Brown
20/30	0.84	(0.79-0.89)	Brown
20/40	0.8	(0.74-0.86)	Brown

20/50	0.77	(0.7-0.84)	Brown
20/70	0.74	(0.67-0.81)	Brown
20/100	0.67	(0.57-0.77)	Brown
20/200	0.66	(0.55-0.77)	Brown
20/300	0.63	(0.54-0.72)	Brown
20/400	0.54	(0.43-0.65)	Brown

IOL = intraocular lens; CPT = current procedural terminology; ASP = average sales price; OCT = optical coherence tomography; MI = myocardial infarction; CVA = cerebrovascular accident.

\* The cost values are calculated from the various Medicare fees. Table 2 provides details of how the parameter values were determined.

† All costs in 2016 United States Dollars (inflated using gross domestic product deflator if necessary).

‡ Normal distributions were used where the ranges in this table represent 95% confidence intervals. All distributions were assumed to be independent with the exception of the utilities, where a correlation of .75 was used between adjacent vision levels.

**Table 2: Detailed Procedure Costs**

<b>Parameter</b>	<b>Source CPT/HCPCS*</b>	<b>Physician Non-Facility Fee</b>	<b>Physician Facility Fee</b>	<b>OPPS Payment</b>	<b>Anesthesia Fees</b>	<b>Facility</b>	<b>Total Cost</b>
Cataract extraction with IOL placement	66984 + Anesthesia <sup>†</sup>	\$648.42	\$648.42	\$1,745.70	703.792	Yes	\$3,097.91
Cataract extraction without IOL placement	66984	\$648.42	\$648.42	\$1,745.70	N/A	Yes	\$2,394.12
Diode laser (open angle glaucoma)	66710	\$445.41	\$398.50	\$1,401.16	N/A	Yes	\$1,799.66
Endolaser	67108 + Anesthesia <sup>†</sup>	\$1,315.81	\$1,315.81	\$3,380.77	1055.69	Yes	\$4,696.58
Extended ophthalmoscopy	92225	\$27.21	\$21.48	\$55.94	N/A	No	\$27.21
Fluorescein angiography	92235	\$110.64	\$110.64	\$220.35	N/A	No	\$110.64
Focal/grid laser (non-center involved DME)	67210	\$524.89	\$507.35	\$440.38	N/A	No	\$524.89
Fundus photography	92250	\$79.49	\$79.49	\$91.18	N/A	No	\$79.49
Intravitreal injection procedure	67028	\$103.47	\$101.68	\$280.27	N/A	No	\$103.47
Bevacizumab drug (repackaged 1.25mg/0.05 mL)		\$59.65					\$59.65
0.05-mg ranibizumab drug		\$2,027.79					\$2,027.79
Laser retinopexy	67145	\$533.84	\$505.20	\$440.38	N/A	No	\$533.84
OCT	92134	\$45.47	\$45.47	\$55.94	N/A	No	\$45.47

Paracentesis	65800	\$120.66	\$93.09	\$1,745.70	N/A	No	\$120.66
Panretinal photocoagulation	67228	\$345.15	\$311.86	\$440.38	N/A	No	\$345.15
Retinal cryopexy	67101	\$793.42	\$683.50	\$1,745.70	N/A	No	\$793.42
Retinal detachment repair-injection of air/gas	67110	\$770.15	\$706.42	\$1,745.70	N/A	Yes	\$2,452.12
Silicone oil injection	67025 + Anesthesia <sup>†</sup>	\$735.06	\$641.61	\$1,745.70	N/A	No	\$3,443.00
Subtenons triamcinolone acetate injection for uveitis	67515	\$98.10	\$90.58	\$261.03	N/A	No	\$98.10
Total air-fluid exchange	67025 + Anesthesia <sup>†</sup>	\$735.06	\$641.61	\$1,745.70	1055.688	Yes	\$3,443.00
Ultrasound	76512	\$93.81	\$93.81	\$92.07	N/A	No	\$93.81
Vitrectomy	67036	\$914.44	\$914.44	\$1,745.70	1055.69	Yes	\$3,715.83
	Anesthesia <sup>†</sup> CPT – 00145						
	Procedure hours - 2						
Vitrectomy with endolaser	67039 + Anesthesia <sup>†</sup>	\$979.25	\$979.25	\$3,380.77	1055.688	Yes	\$5,415.71
Vitrectomy with epiretinal membrane peel	67041 + Anesthesia <sup>†</sup>	\$1,169.37	\$1,169.37	\$1,745.70	1055.69	Yes	\$3,970.76

CPT= current procedural terminology; OPSS = outpatient prospective payment system; IOL = intraocular lens; DME = diabetic macular edema; OCT = optical coherence tomography.

<sup>†</sup> All anesthesia was assumed to use CPT 00145 and billed for 2 hours.

**Table 3: Study Population Baseline Characteristics\***

	With Vision-Impairing DME at Baseline <sup>†</sup>		Without Vision-Impairing DME at Baseline	
	Ranibizumab N = 21	PRP N = 25	Ranibizu mab N = 80	PRP N = 87
<b>Participant Characteristics</b>				
<b>Female, No. (%)</b>	6 (29)	13 (52)	36 (45)	37 (43)
<b>Age, Median (IQR), y</b>	56 (52-61)	56 (49-62)	54 (45-60)	52 (45-60)
<b>Race/ethnicity, No. (%)</b>				
White	11 (52)	16 (64)	47 (59)	43 (49)
Hispanic or Latino	7 (33)	6 (24)	20 (25)	23 (26)
Black/African American	3 (14)	2 (8)	12 (15)	18 (21)
Other	0 (0)	1 (4)	1 (1)	3 (3)
<b>Diabetes type, No. (%)</b>				
Type 1	3 (14)	5 (20)	17 (21)	14 (16)
Type 2	17 (81)	18 (72)	59 (74)	71 (82)
Uncertain	1 (5)	2 (8)	4 (5)	2 (2)
<b>Duration of diabetes, median (IQR), y</b>	15 (11-21)	11 (7-27)	20 (13-27)	16 (11-23)
<b>Hemoglobin A1c, median (IQR), %</b>	7.8 (7-9.3)	7.8 (7.1-9.6)	8.3 (7-9.8)	8.9 (7.3-10.3)
<b>Ocular characteristics</b>				
<b>Baseline visual acuity letter score</b>				
Mean	62.1	63.9	77.3	78.4
Median (IQR)	64 (57-76)	71 (57-74)	80 (74-85)	81 (74-85)
Approximate Snellen equivalent, median (IQR)	20/50 (20/80–20/32)	20/40 (20/80–20/32)	20/25 (20/32–20/20)	20/25 (20/32–20/20)
≥84 (≥20/20)	0 (0)	0 (0)	31 (39)	35 (40)
83-79 (20/25)	0 (0)	0 (0)	17 (21)	18 (21)
78-69 (20/32-20/40)	10 (48)	14 (56)	19 (24)	21 (24)
68-49 (20/50-20/100)	6 (29)	7 (28)	10 (13)	12 (14)
48-24 (20/125-20/320)	5 (24)	4 (16)	3 (4)	1 (1)
<b>OCT central subfield thickness (Stratus equivalent), micron</b>				
Mean	417.4	327.2	213.7	219.6



Median (IQR)	365 (333-504)	296 (270-319)	210 (193-235)	222 (200-237)
<b>Diabetic retinopathy severity<sup>§</sup> on fundus photographs, No. (%)</b>				
NPDR or better (level 53 or lower)	0 (0)	2 (8)	7 (9)	12 (14)
Mild PDR (level 61)	2 (10)	3 (12)	12 (15)	13 (15)
Moderate PDR (level 65)	7 (33)	11 (44)	28 (35)	34 (39)
High-risk PDR (level 71 and 75)	12 (57)	9 (36)	30 (38)	26 (30)
Advanced PDR, macula center attached (level 81)	0 (0)	0 (0)	2 (3)	0 (0)
Advanced PDR, macula center detached (level 85)	0 (0)	0 (0)	0 (0)	1 (1)
<b>Prior treatment for DME, No. (%)</b>	5 (24)	7 (28)	21 (26)	16 (18)
<b>Prior anti-VEGF treatment for DME, No. (%)</b>	4 (19)	2 (8)	9 (11)	6 (7)

DME = diabetic macular edema; PRP = panretinal photocoagulation; IQR = interquartile range; OCT = optical coherence tomography; ETDRS = Early Treatment Diabetic Retinopathy Study; NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; anti-VEGF = anti-vascular endothelial growth factor

\*Participants included in this analyses had one study eye

†Visual acuity letter score 69 or less (approximate Snellen equivalent 20/32 or worse) at baseline

§Early Treatment Diabetic Retinopathy Study severity level determined by the Fundus Photograph Reading Center

**Table 4: Patient-reported Vision-related Outcomes**

		<b>PRP</b>	<b>PRP</b>	<b>Ranibizumab</b>	<b>Ranibizumab</b>
		<b>Count</b>	<b>Average</b>	<b>Count</b>	<b>Average</b>
<b>LLQ<sup>6</sup></b>	<b>Driving Subscale Score</b>	83	0.57	80	-5.05
	<b>General Dim Lighting Subscale Score</b>	90	-0.65	80	-0.63
	<b>Peripheral Vision Subscale Score</b>	90	-1.39	80	-3.13
	<b>Color Vision Score</b>	83	0.57	80	-5.05
<b>VFQ-25<sup>7</sup></b>	<b>Driving Subscale</b>	79	1.69	72	0.81
	<b>Peripheral Vision</b>	94	-0.80	82	-2.74
	<b>Color Vision</b>	95	-0.26	83	-1.51
	<b>Gave up Driving</b>	92	0.08	82	0.40
	<b>Stopped Driving at Night</b>	92	0.06	82	0.06
<b>WPAI<sup>8</sup></b>	<b>Work time missed due to vision, %</b>	47	-4.03	36	0.10
	<b>Impaired, %</b>	45	6.67	34	-9.41
	<b>Overall Work Impairment, %</b>	45	4.96	34	-10.75
	<b>Activity Impairment</b>	94	-6.60	83	-1.08

PRP = panretinal photocoagulation; LLQ = low luminance questionnaire; VFQ-25 = National Eye Institutes Visual Function Questionnaire; WPAI = Work Productivity and Activity Impairment Questionnaire

When visual acuities in the treated eye were transferred to quality adjusted life years, participants randomized to ranibizumab had slightly better utility changes versus PRP; all *P*-values for the difference between the groups were greater than 0.05.

**Table 5: Change in Quality Adjusted Life Years over Two-Years**

	With vision-impairing DME at baseline*			Without vision-impairing DME at baseline		
	PRP (N = 25)	Ranibizum ab (N = 21)	Difference	PRP (N = 87)	Ranibizum ab (N = 80)	Difference
<b>Utilities Converted from Visual Acuity in The Treated Eye</b>						
<b>Change in QALYS* (95% CI)</b>	-0.061	-0.034	0.026 (-0.129,0.182)	-0.047	-0.018	0.029 (-0.026,0.084)
<b>Utilities Measured on a Scale from Death to Perfect Health</b>						
<b>Change in QALYS (95% CI)</b>	-0.038	0.067	0.105 (-0.067,0.277)	-0.015	0.019	0.034 (-0.019,0.087)
<b>Directly-Elicited Utilities</b>						
<b>Change in QALYS (95% CI)</b>	0.26	0.046	-0.214 (-0.571,0.143)	0.097	0.116	0.018 (-0.211,0.248)

DME = diabetic macular edema; PRP = panretinal photocoagulation; QALYs = quality adjusted life years; CI = confidence intervals

\*Visual acuity letter score 69 or less (approximate Snellen equivalent 20/32 or worse) at baseline

**Table 6: Cost-Effectiveness Results with Alternative Utility Measurements**

Utilities converted from visual acuity in the treated eye						
	With vision-impairing DME at baseline*			Without vision-impairing DME at baseline		
	PRP (N = 25)	Ranibizumab (N = 21)	Difference	PRP (N = 87)	Ranibizumab (N = 80)	Difference
<b>Costs (95% CI)</b>	\$24,520	\$29,574	\$5,053 (-7,695 to 17,801)	\$7,445	\$22,576	\$15,131 (11,480 to 18,782)
<b>QALYs (95% CI)</b>	-0.061	-0.034	0.026 (-0.129 to 0.182)	-0.047	-0.018	0.029 (-0.026 to 0.084)
<b>ICER</b>			\$191,653/QALY			\$521,771/QALY
Utilities Measured on a Scale from Death to Perfect Health						
	With vision-impairing DME at baseline*			Without vision-impairing DME at baseline		
	PRP (N = 25)	Ranibizumab (N = 21)	Difference	PRP (N = 87)	Ranibizumab (N = 80)	Difference
<b>Costs (95% CI)</b>	\$24,520	\$29,574	\$5,053 (-7,695, 17,801)	\$7,445	\$22,576	\$15,131 (11,480, 18,782)
<b>QALYs (95% CI)</b>	-0.038	0.067	0.105 (-0.067, 0.277)	-0.015	0.019	0.034 (-0.019, 0.087)
<b>ICER</b>			\$48,020/QALY			\$446,774/QALY

DME = diabetic macular edema; PRP = panretinal photocoagulation; CI = confidence interval; QALY = quality adjusted life years; ICER = incremental cost-effectiveness ratios

\*Visual acuity letter score 69 or less (approximate Snellen equivalent 20/32 or worse) at baseline

**Table 7: Incremental Cost-Effectiveness Ratios Values\* as Each Parameter Assumption is Changed from Low to High, One-at-a-time**

Parameter\Parameter Value	With vision-impairing DME at baseline		Without vision-impairing DME at baseline	
	Low	High	Low	High
<b>Unit Costs (per procedure)</b>				
Cataract extraction with IOL placement	\$ 55,542	\$ 55,593	\$ 663,914	\$ 662,042
Cataract extraction without IOL placement	\$ 55,673	\$ 55,462	\$ 662,978	\$ 662,978
Diode laser (open angle glaucoma)	\$ 55,647	\$ 55,488	\$ 662,978	\$ 662,978
Endolaser	\$ 55,266	\$ 55,869	\$ 662,978	\$ 662,978
Extended ophthalmoscopy	\$ 55,511	\$ 55,624	\$ 662,032	\$ 663,923
Fluorescein angiography	\$ 55,580	\$ 55,555	\$ 662,933	\$ 663,022
Focal/grid laser (non-center involved DME)	\$ 55,591	\$ 55,544	\$ 662,978	\$ 662,978
Fundus photography	\$ 55,467	\$ 55,669	\$ 662,772	\$ 663,183
Intravitreal injection procedure	\$ 55,002	\$ 56,133	\$ 659,327	\$ 666,629
0.5-mg ranibizumab drug	\$ 45,032	\$ 66,103	\$ 594,867	\$ 731,088
Laser retinopexy	\$ 55,568	\$ 55,568	\$ 662,949	\$ 663,007
OCT	\$ 55,612	\$ 55,524	\$ 662,978	\$ 662,978

Paracentesis	\$ 55,573	\$ 55,562	\$ 662,971	\$ 662,985
Panretinal photocoagulation	\$ 56,325	\$ 54,810	\$ 666,376	\$ 659,580
Retinal cryopexy	\$ 55,568	\$ 55,568	\$ 663,018	\$ 662,938
Retinal detachment repair-injection of air/gas	\$ 55,439	\$ 55,696	\$ 662,978	\$ 662,978
Silicone oil Injection	\$ 55,719	\$ 55,416	\$ 662,978	\$ 662,978
Subtenons triamcinolone acetonide injection for uveitis	\$ 55,568	\$ 55,568	\$ 662,983	\$ 662,973
Total air-fluid exchange	\$ 55,568	\$ 55,568	\$ 663,151	\$ 662,805
Ultrasound	\$ 55,580	\$ 55,555	\$ 663,015	\$ 662,941
Vitrectomy	\$ 55,894	\$ 55,241	\$ 663,539	\$ 662,416
Vitrectomy with endolaser	\$ 55,715	\$ 55,420	\$ 665,160	\$ 660,796
Vitrectomy with epiretinal membrane peel	\$ 55,360	\$ 55,775	\$ 664,178	\$ 661,778
<b>Annual Costs (year 1)</b>				
MI	\$ 48,529	\$ 62,606	\$ 662,386	\$ 663,570
CVA	\$ 75,080	\$ 36,055	\$ 662,326	\$ 663,630
<b>Annual Costs (year 2)</b>				
MI	\$ 55,568	\$ 55,568	\$ 662,978	\$ 662,978
CVA	\$ 55,568	\$ 55,568	\$ 662,978	\$ 662,978

			78	978
<b>Utility associated with visual acuity in the better-seeing eye</b>				
20/20	\$ 81,226	\$ 42,228	\$ 1,128,206	\$ 469,411
20/25	\$ 61,132	\$ 50,931	\$ 561,725	\$ 808,760
20/30	\$ 46,816	\$ 68,343	\$ 695,005	\$ 633,772
20/40	\$ 61,427	\$ 50,729	\$ 588,536	\$ 758,978
20/50	\$ 51,545	\$ 60,271	\$ 591,632	\$ 753,891
20/70	\$ 45,627	\$ 71,045	\$ 638,852	\$ 688,998
20/100	\$ 47,268	\$ 67,402	\$ 623,638	\$ 707,616
20/200	\$ 49,931	\$ 62,639	\$ 678,383	\$ 648,257
20/300	\$ 59,971	\$ 51,767	\$ 654,039	\$ 672,165
20/400	\$ 55,568	\$ 55,568	\$ 662,978	\$ 662,978

DME = diabetic macular edema; IOL = intraocular lens; OCT = optical coherence tomography; MI = myocardial infarction; CVA = cerebrovascular accident.

\*All costs in 2016 United States Dollars (inflated using gross domestic product deflator, if necessary).

**Table 8: Incremental Cost-Effectiveness Ratio Values as Costs of Panretinal Photocoagulation and Anti-Vascular Endothelial Growth Factor Therapy Change\* for Eyes with Vision-Impairing Diabetic Macular Edema at Baseline**

		Cost of PRP								
		200	300	400	500	600	700	800	900	1000
<b>Cost of Anti-VEGF</b>	<b>1000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>2000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>3000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>4000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>5000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>6000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>7000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>8000</b>	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>9000</b>	\$2,884	\$689	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>10000</b>	\$8,383	\$6,187	\$3,992	\$1,797	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>11000</b>	\$13,881	\$11,686	\$9,491	\$7,295	\$5,100	\$2,905	\$710	Cost-Saving	Cost-Saving
	<b>12000</b>	\$19,379	\$17,184	\$14,989	\$12,794	\$10,599	\$8,403	\$6,208	\$4,013	\$1,818
	<b>13000</b>	\$24,877	\$22,682	\$20,487	\$18,292	\$16,097	\$13,902	\$11,707	\$9,512	\$7,316
	<b>14000</b>	\$30,375	\$28,180	\$25,985	\$23,790	\$21,595	\$19,400	\$17,205	\$15,010	\$12,815
	<b>15000</b>	\$35,874	\$33,679	\$31,484	\$29,288	\$27,093	\$24,898	\$22,703	\$20,508	\$18,313
	<b>16000</b>	\$41,372	\$39,177	\$36,982	\$34,787	\$32,592	\$30,396	\$28,201	\$26,006	\$23,811
	<b>17000</b>	\$46,870	\$44,675	\$42,480	\$40,285	\$38,090	\$35,895	\$33,700	\$31,504	\$29,309
	<b>18000</b>	\$52,368	\$50,173	\$47,978	\$45,783	\$43,588	\$41,393	\$39,198	\$37,003	\$34,808
	<b>19000</b>	\$57,867	\$55,672	\$53,476	\$51,281	\$49,086	\$46,891	\$44,696	\$42,501	\$40,306
	<b>20000</b>	\$63,365	\$61,170	\$58,975	\$56,780	\$54,584	\$52,389	\$50,194	\$47,999	\$45,804



PRP = panretinal photocoagulation, Anti-VEGF = anti-vascular endothelial growth factor  
\*Colors represent levels of value of ranibizumab as compared to panretinal photocoagulation. Dark green color indicates that ranibizumab saves costs and improves vision compared to panretinal photocoagulation. Light green color indicates that ranibizumab has a net cost increase and improves vision compared to panretinal photocoagulation, and the rate at which quality adjusted life years (QALY) are gained is between \$0 and \$50,000 per QALY gained. Yellow color indicates that ranibizumab has a net cost increase and improves vision compared to panretinal photocoagulation, and the rate at which QALYS are gained is between \$50,000 and \$100,000 per QALY gained.

**Table 9: Incremental Cost-Effectiveness Ratio values as costs of Panretinal Photocoagulation and Anti-Vascular Endothelial Growth Factor Therapy Change for Eyes Without Vision-Impairing Diabetic Macular Edema at Baseline\***

		Cost of PRP								
		200	300	400	500	600	700	800	900	1000
<b>Cost of Anti-VEGF</b>	<b>100</b>	\$ 31,713	\$ 21,868	\$ 12,023	\$ 2,178	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving	Cost-Saving
	<b>200</b>	\$ 67,259	\$ 57,414	\$ 47,569	\$ 37,724	\$ 27,879	\$ 18,034	\$ 8,189	Cost-Saving	Cost-Saving
	<b>300</b>	\$102,804	\$ 92,959	\$ 83,114	\$ 73,270	\$ 63,425	\$ 53,580	\$ 43,735	\$ 33,890	\$ 24,045
	<b>400</b>	\$138,350	\$128,505	\$118,660	\$108,815	\$ 98,970	\$ 89,125	\$ 79,280	\$ 69,436	\$ 59,591
	<b>500</b>	\$173,895	\$164,050	\$154,205	\$144,361	\$134,516	\$124,671	\$114,826	\$104,981	\$ 95,136
	<b>600</b>	\$209,441	\$199,596	\$189,751	\$179,906	\$170,061	\$160,216	\$150,372	\$140,527	\$130,682
	<b>700</b>	\$244,986	\$235,141	\$225,297	\$215,452	\$205,607	\$195,762	\$185,917	\$176,072	\$166,227
	<b>800</b>	\$280,532	\$270,687	\$260,842	\$250,997	\$241,152	\$231,307	\$221,463	\$211,618	\$201,773
	<b>900</b>	\$316,077	\$306,233	\$296,388	\$286,543	\$276,698	\$266,853	\$257,008	\$247,163	\$237,318
	<b>1000</b>	\$351,623	\$341,778	\$331,933	\$322,088	\$312,243	\$302,399	\$292,554	\$282,709	\$272,864
	<b>1100</b>	\$387,168	\$377,324	\$367,479	\$357,634	\$347,789	\$337,944	\$328,099	\$318,254	\$308,409
	<b>1200</b>	\$422,714	\$412,869	\$403,024	\$393,179	\$383,335	\$373,490	\$363,645	\$353,800	\$343,955
	<b>1300</b>	\$458,260	\$448,415	\$438,570	\$428,725	\$418,880	\$409,035	\$399,190	\$389,345	\$379,501
	<b>1400</b>	\$493,	\$483,	\$474,	\$464,	\$454,4	\$444,5	\$434,7	\$424,8	\$415,0

	805	960	115	270	26	81	36	91	46
<b>15 00</b>	\$529, 351	\$519, 506	\$509, 661	\$499, 816	\$489,9 71	\$480,1 26	\$470,2 81	\$460,4 37	\$450,5 92
<b>16 00</b>	\$564, 896	\$555, 051	\$545, 206	\$535, 362	\$525,5 17	\$515,6 72	\$505,8 27	\$495,9 82	\$486,1 37
<b>17 00</b>	\$600, 442	\$590, 597	\$580, 752	\$570, 907	\$561,0 62	\$551,2 17	\$541,3 72	\$531,5 28	\$521,6 83
<b>18 00</b>	\$635, 987	\$626, 142	\$616, 298	\$606, 453	\$596,6 08	\$586,7 63	\$576,9 18	\$567,0 73	\$557,2 28
<b>19 00</b>	\$671, 533	\$661, 688	\$651, 843	\$641, 998	\$632,1 53	\$622,3 08	\$612,4 64	\$602,6 19	\$592,7 74
<b>20 00</b>	\$707, 078	\$697, 233	\$687, 389	\$677, 544	\$667,6 99	\$657,8 54	\$648,0 09	\$638,1 64	\$628,3 19

PRP = panretinal photocoagulation, Anti-VEGF = anti-vascular endothelial growth factor

\*Colors represent levels of value of ranibizumab as compared with panretinal photocoagulation. Dark green color indicates that ranibizumab saves costs and improves vision compared to panretinal photocoagulation. Light green color indicates that ranibizumab has a net cost increase and improves vision compared to panretinal photocoagulation, and the rate at which quality-adjusted life years (QALYs) are gained is between \$0 and \$50,000 per QALY gained. Yellow color indicates that ranibizumab has a net cost increase and improves vision compared to panretinal photocoagulation, and the rate at which QALYs are gained is between \$50,000 and \$100,000 per QALY gained. Orange color indicates that ranibizumab has a net cost increase and improves vision compared to panretinal photocoagulation, and the rate at which QALYs are gained is between \$100,000 and \$150,000 per QALY gained. Red color indicates that ranibizumab has a net cost increase and improves vision compared to panretinal photocoagulation, and the rate at which QALYs are gained is above \$150,000 per QALY gained.

Table 10: Letter Changes in Eyes

<b>Study Group</b>	<b>Letter-Years Gained (study eye)</b>	<b>Letter-Years Gained (study eye)</b>
<i>With Diabetic Macular Edema</i>		
<b>PRP</b>	1.8	1.2
<b>Ranibizumab</b>	7.9	6.8
<i>Without Diabetic Macular Edema</i>		
<b>PRP</b>	-1.8	0.2
<b>Ranibizumab</b>	2.5	2.0

**Table 11: Percentage Changes in Quality-of-Life**

<b>Study Group</b>	<b>Starting utility</b>	<b>Anticipated QALYs over 2 years *</b>	<b>QALYs lost over 2 years (excluding deaths)</b>	<b>QALYs lost over 2 years (including deaths)</b>	<b>% QALYs lost over 2 years (excluding deaths)</b>	<b>% QALYs lost over 2 years (including deaths)</b>
<i>With Diabetic Macular Edema</i>						
PRP	0.82	1.64	0.000	-0.070	0.0%	-4.3%
Ranibizumab	0.80	1.60	0.118	0.028	7.4%	1.7%
<i>Without Diabetic Macular Edema</i>						
PRP	0.88	1.75	-0.010	-0.032	-0.6%	-1.9%
Ranibizumab	0.87	1.75	0.020	-0.008	1.2%	-0.5%

\* Assuming no vision changes, no deaths

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