Supplementary Online Content

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

eTable 1. Input Parameters

Parameter	Parameter Value	Range Explored in Sensitivity Analysis	Distribution for Probabilistic Sensitivity Analysis	Source
Unit Costs (per procedure)				
Aqueous tap	$123.12	(111-135)	Uniform (111,135)	Medicare[1] CPT 65800
Cataract extraction with intraocular lens placement	$3,279.37	(2788-3408)	Uniform (2951,3607)	Medicare CPT 66984
Cataract extraction without intraocular lens placement	$2,566.63	(2155-2634)	Uniform (2310,2823)	Medicare CPT 66984
Diode laser (open angle glaucoma)	$2,214.91	(1620-1980)	Uniform (1993,2436)	Medicare CPT 66710
Endolaser	$5,909.70	(5177-6327)	Uniform (5319,6501)	Medicare CPT 67108
Extended ophthalmoscopy	$27.72	(24-30)	Uniform (25,30)	Medicare CPT 92225
Fluorescein angiography	$87.84	(100-122)	Uniform (79,97)	Medicare CPT 92235
Focal/grid laser	$531.71	(472-577)	Uniform (479,585)	Medicare CPT 67210
Fundus photography	$58.32	(72-87)	Uniform (52,64)	Medicare CPT 92250
Intravitreous injection procedure	$104.40	(93-114)	Uniform (94,115)	Medicare CPT 67028
Bevacizumab drug (repackaged 1.25mg/0.05 mL)	$63.72	(57-70)	Uniform (57,70)	HHS Report[2]
Ranibizumab drug (0.05-mg)	$1,866.82	(1755-2145)	Uniform (1680,2054)	Medicare pricing files of ASP +6%

Laser Retinopexy	$542.15	(480-587)	Uniform (488,596)	Medicare CPT 6585
Laser Trabeculoplasty	$252.00	(227-277)	Uniform (227,277)	Medicare CPT 67145
Optical coherence tomography	$42.48	(41-50)	Uniform (38,47)	Medicare CPT 92134
Oculomotor Surgery	$713.87	(642-785)	Uniform (642,785)	Medicare CPTs 67311, 67312, 67314, and 67316
Paracentesis	$123.12	(109-133)	Uniform (111,135)	Medicare CPT 65800
Panretinal photocoagulation	$351.00	(311-380)	Uniform (316,386)	Medicare CPT 67228
Retinal cryopexy	$336.96	(714-873)	Uniform (303,371)	Medicare CPT 67101
Retinal detachment repair-injection of air/gas	$2,745.19	(2207-2697)	Uniform (2471,3020)	Medicare CPT 67110
Silicone oil injection	$3,629.26	(3099-3787)	Uniform (3266,3992)	Medicare CPT 67025
Subtenons triamcinolone acetonide injection for uveitis	$99.36	(88-108)	Uniform (89,109)	Medicare CPT 67515
Total air-fluid exchange	$3,629.26	(3099-3787)	Uniform (3266,3992)	Medicare CPT 67025
Ocular ultrasound	$76.68	(84-103)	Uniform (69,84)	Medicare CPT 76512
Vitrectomy	$5,602.62	(3344-4087)	Uniform (5042,6163)	Medicare CPT 67036
vitrectomy with endolaser	$5,668.14	(4874-5957)	Uniform (5101,6235)	Medicare CPT 67039

Vitrectomy with epiretinal membrane peel	$5,860.38	(3574-4368)	Uniform (5274,6446)	Medicare CPT 67041
YAG capsulotomy	$338.40	(305-372)	Uniform (305,372)	Medicare CPT 66821
Annual Costs (first year)				
Myocardial infarction	$0	(0-53,764)	Not in probabilistic sensitivity analysis	Bonafede[3]
Cerebrovascular accident	$0	(0-59,147)	Not in probabilistic sensitivity analysis	Bonafede
Annual Costs (year 2)				
Myocardial infarction	$0	(0-19,615)	Not in probabilistic sensitivity analysis	Bonafede
Cerebrovascular accident	$0	(0-37,007)	Not in probabilistic sensitivity analysis	Bonafede
Other				
Discount rate	3%	(0-5)		
Vision change per year (lines) with ranibizumab	0	(-1 1)	Uniform (-1,1)	Assumption
Vision change per year (lines) with panretinal photocoagulation	0	(-1 1)	Uniform (-1,1)	Assumption
Annual injections after year 5 with ranibizumab	3	(1.5-4.5)	Uniform (1.5,4.5)	Assumption
Utility associated with visual acuity in the better-seeing eye				
20/20	0.92	(0.87-0.97)	Normal (0.92,0.025)*	Brown[4]
20/25	0.87	(0.82-0.92)	Normal (0.87,0.025)*	Brown
20/30	0.84	(0.79-0.89)	Normal (0.84,0.025)*	Brown
20/40	0.8	(0.74-0.86)	Normal (0.8,0.03)*	Brown
20/50	0.77	(0.7-0.84)	Normal (0.77,0.035)*	Brown
20/70	0.74	(0.67-0.81)	Normal (0.74,0.035)*	Brown
20/100	0.67	(0.57-0.77)	Normal (0.67,0.05)*	Brown
20/200	0.66	(0.55-0.77)	Normal (0.66,0.055)*	Brown

20/300	0.63	(0.54-0.72)	Normal (0.63,0.045)*	Brown
20/400	0.54	(0.43-0.65)	Normal (0.54,0.055)*	Brown

CPT, current procedural terminology

* All utilities were correlated with a correlation coefficient of 0.75 to preserve the relative ranking of the vision states.

Note on Mortality

The mean age of this population when they started the study was 52. The mortality rate of diabetics is about twice that of the general population and with annual mortality ranges between ages 52 and 62 of approximately 0.5% to 1% per year, we would expect about 6% of the population would die within 5 years and 13% of the population would die over that whole 10-year period. We observed that approximately 9% of participants did die within 5 years. We accounted for actual observed mortality within the first 5 years based on the trial mortality data but, we simulate mortality in years 5-10. It is difficult to speculate on what long-term differential mortality might be between the ranibizumab and panretinal photocoagulation groups between years 5 and 10. Therefore we assumed both groups have the same mortality, which is based on standard US mortality and a relative risk from having diabetes.

Given that someone is alive at the end of year 5, the following are the probabilities of survival at the end of each year:

End of Year	6	7	8	9	10
Probability of Survival	0.985	0.970	0.953	0.936	0.918

eTable 2. Details on Procedure Costing

Parameter	Source CPT/ HCPCS†	Physician Non Facility Fee	Physician Facility Fee	OPPS Payment	Anesthesia Fees	Facility*	Total Cost
Aqueous tap	65800	$123.12	$93.96	$1,910.36	N/A	0	$123.12
Cataract extraction with intraocular lense placement	66984 + Anesthesia	$656.27	$656.27	$1,910.36	712.736	1	$3,279.37
Cataract extraction without intraocular lens placement	66984	$656.27	$656.27	$1,910.36	N/A	1	$2,566.63
Diode laser (open angle glaucoma)	66710	$453.59	$403.56	$1,811.35	N/A	1	$2,214.91
Endolaser	67108 + Anesthesia	$1,231.91	$1,231.91	$3,608.69	1069.10	1	$5,909.70
Extended ophthalmoscopy	92225	$27.72	$21.96	$55.96	N/A	0	$27.72
Fluorescein angiography	92235	$87.84	$87.84	$248.83	N/A	0	$87.84
Focal/grid laser (non-center involved diabetic macular edema)	67210	$531.71	$514.07	$487.98	N/A	0	$531.71
Fundus photography	92250	$58.32	$58.32	$105.04	N/A	0	$58.32

Intravitreous injection procedure	67028	$104.40	$102.96	$297.57	N/A	0	$104.40
Bevacizumab drug (repackaged 1.25mg/0.05 mL)							$63.72
Ranibizumab drug (0.05-mg)							$1,866.82
Laser retinopexy	67145	$542.15	$511.55	$487.98	N/A	0	$542.15
Laser trabeculoplasty		$252.00	$213.48	$487.98	N/A	0	$252.00
Ocular coherence tomography	92134	$42.48	$42.48	$55.96	N/A	0	$42.48
Oculomotor surgery	Average of 67311, 67312, 67314, and 67316	$713.87	$713.87	$2,096.37	N/A	No	$713.87
Paracentesis	65800	$123.12	$93.96	$1,910.36	N/A	0	$123.12
Panretinal photocoagulation	67228	$351.00	$315.00	$487.98	N/A	0	$351.00
Retinal cryopexy	67101	$336.96	$292.68	$1,910.36	N/A	0	$336.96
Retinal detachment repair-injection of air/gas	67110	$899.63	$834.83	$1,910.36	N/A	1	$2,745.19

Silicone oil injection	67025 + Anesthesia	$746.27	$649.79	$1,910.36	1069.104	1	$3,629.26
Subtenons kenalog injection for uveitis	67515	$99.36	$91.44	$267.66	N/A	0	$99.36
Total air-fluid exchange	67025 + Anesthesia	$746.27	$649.79	$1,910.36	1069.104	1	$3,629.26
Ultrasound	76512	$76.68	$76.68	$114.46	N/A	0	$76.68
Vitrectomy	67036+ Anesthesia	$924.83	$924.83	$3,608.69	1069.104	1	$5,602.62
Vitrectomy with endolaser	67039 + Anesthesia	$990.35	$990.35	$3,608.69	1069.104	1	$5,668.14
Vitrectomy with epiretinal membrane peel	67041 + Anesthesia	$1,182.59	$1,182.59	$3,608.69	1069.104	1	$5,860.38
YAG capsulotomy	66821	$338.40	$319.32	$487.98	N/A	0	$338.40

CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System; OPPS, Outpatient Prospective Payment System
*One if performed in a facility, 0 otherwise.
†All anesthesia was assumed to use CPT 00145 and billed for 2 hours.

eTable 3. Baseline Characteristics of the Study Population

	With Vision-Impairing CI-DME at Baseline		Without Vision-Impairing CI-DME at Baseline	
	Ranibizumab	**PRP**	**Ranibizumab**	**PRP**
Participant characteristics				
Participants with 1 study eye (included in this analysis), No.	21	25	80	87
Female, No. (%)	6 (29)	13 (52)	36 (45)	37 (43)
Age, Median (IQR), y	56 (52-61)	56 (49-62)	54 (45-60)	52 (45-60)
Race/ethnicity, No. (%)				
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)
Diabetes type, No. (%)				
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)
Duration of diabetes, median (IQR), y	15 (11-21)	11 (7-27)	20 (13-27)	16 (11-23)
Hemoglobin A1c, median (IQR), %	7.8 (7-9.3)	7.8 (7.1-9.6)	8.3 (7-9.8)	8.9 (7.3-10.3)
Ocular characteristics				
Baseline visual acuity letter score, 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)

No. (%) with visual acuity letter score				
≥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)
OCT central subfield thickness (Stratus equivalent), μm				
Mean	417.4	327.2	213.7	219.6
Median (IQR)	365 (333-504)	296 (270-319)	210 (193-235)	222 (200-237)
Diabetic retinopathy severity (ETDRS level), No. (%), as determined by photograph reading center				
NPDR or better (level 53 or better)	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)
Prior treatment for DME, No. (%)	5 (24)	7 (28)	21 (26)	16 (18)
Prior anti-VEGF treatment for DME, No. (%)	4 (19)	2 (8)	9 (11)	6 (7)

CI-DME, center-involved 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; DME, diabetic macular edema; VEGF, vascular endothelial growth factor

eTable 4. Change in QALYs*

	With vision-impairing center-involved DME at baseline			Without vision-impairing center-involved DME at baseline		
	PRP (N = 25)	**Ranibizumab (N = 21)**	**Difference**	**PRP (N = 87)**	**Ranibizumab (N = 80)**	**Difference**
Results over 5 Years						
Change in QALYS (95% CI)	-0.016 (-0.042,0.01)	0.142 (0.116, 0.168)	0.159 (-0.017, 0.335)	-0.028 (-0.062, 0.006)	0.016 (-0.015, 0.047)	0.044 (-0.002, 0.09)
Results over 10 Years						
Change in QALYS (95% CI)	-0.062 (-0.114,-0.01)	0.219 (0.163, 0.274)	0.281 (-0.083, 0.644)	-0.038 (-0.104, 0.027)	0.052 (0.003, 0.102)	0.091 (0.009, 0.173)

QALY, quality-adjusted life-years; DME, diabetic macular edema; PRP, panretinal photocoagulation; CI, confidence interval
*Utilities converted from visual acuity in the treated eye.

eTable 5. Cost-Effectiveness Results*

	With vision-impairing center-involved DME at baseline			Without vision-impairing center-involved DME at baseline		
	PRP (N = 25)	**Ranibizumab (N = 21)**	**Difference**	**PRP (N = 87)**	**Ranibizumab (N = 80)**	**Difference**
Results over 5 Years						
Costs	$22,355	$40,825	$18,470 (6,320; 30,619)	$8,887	$32,300	$23,413 (18,567; 28,258)
QALYs	-0.016	0.142	0.159 (-0.017,0.335)	-0.028	0.016	0.044 (-0.002,0.09)
ICER			$116,352/QALY			$534,352/QALY
Results over 10 Years						
Costs	$28,889	$60,979	$32,090 (20486;43693)	$9,509	$53,183	$43,675 (38849;48500)
QALYs	-0.062	0.219	0.281 (-0.083,0.644)	-0.038	0.052	0.091 (0.009,0.173)
ICER			$114,281/QALY			$482,109/QALY

DME, diabetic macular edema; PRP, panretinal photocoagulation; QALY, quality-adjusted life-years; ICER, Incremental cost-effectiveness ratios

*Utilities converted from visual acuity in treated eye.

eTable 6. Scenario Analysis: Including Costs of Systemic Adverse Events

	With vision-impairing CI-DME* at baseline		Without vision-impairing CI-DME at baseline	
	PRP for PDR, Ranibizumab for CI-DME (N = 25)	**Ranibizumab for PDR and CI-DME (N = 21)**	**PRP (N = 87)**	**Ranibizumab (N = 80)**
Five years of follow-up				
Clinic visits/diagnostic procedures	1282	1954	1051	1971
Panretinal Photocoagulation	351	16	351	21
Anti-VEGF Injection Procedure	947	1916	255	1542
0.5-mg ranibizumab	16925	34264	4562	27572
Vitrectomies	1096	1336	1404	387
Other Intraocular Therapies‡	1755	1338	1264	807
Systemic Adverse Events†	13266	24734	11606	13831
TOTAL	35622 (15910,55334)	65559 (36897,94221)	20493 (12249,28738)	46131 (36454,55808)
QALYs	0.017	0.299	0.015	0.055
ICER		106,289/QALY		637,613/QALY
Simulated 10 years				
Additional costs of Ranibizumab Injection Procedures and Drug	6534	20154	621	20883
Additional long-term costs of Systemic Adverse Events†	12425	19156	11872	12911

TOTAL	54003 (18812,89195)	100241 (58641,141841)	31533 (16474,46591)	79325 (62107,96543)
QALYs	0.039	0.541	0.040	0.098
ICER		92,114/QALY		812,185/QALY

CI-DME, center involved diabetic macular edema; PRP, panretinal photocoagulation; Anti-VEGF, anti-vascular endothelial growth factor; CI, confidence interval; QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratios; PDR, proliferative diabetic retinopathy
* With visual acuity letter score less than 78 (approximate Snellen equivalent 20/32 or worse) at baseline
‡ Includes treatment for ocular adverse events like endophthalmitis
†systemic adverse events include myocardial infarction and cerebrovascular accident.
Participants in all group received 0.5-mg ranibizumab if they developed DME over the 2 years of the trial.
Note: Individuals who died had a utility of 0 after the date of death. In converting from best-corrected visual acuity, letter scores were converted to Snellen visual acuities and then to utility levels using the mapping from Brown et al.[4]

eTable 7a. Incremental Cost-Effectiveness Ratio Values as Each Parameter Assumption is Changed From Low to High, One-at-a-Time

	With center-involved DME and vision loss		Without center-involved DME and vision loss	
Parameter\Parameter Value	**Low**	**High**	**Low**	**High**
Unit Costs (per procedure)				
Aqueous tap	$ 63,930	$ 63,930	$ 742,199	$ 742,204
Cataract extraction with intraocular lens placement	$ 63,965	$ 63,895	$ 742,522	$ 741,881
Cataract extraction without intraocular lens placement	$ 63,950	$ 63,910	$ 742,202	$ 742,202
Diode laser (open angle glaucoma)	$ 63,947	$ 63,913	$ 742,202	$ 742,202
Endolaser	$ 63,822	$ 64,037	$ 741,972	$ 742,431
Extended ophthalmoscopy	$ 63,900	$ 63,959	$ 741,603	$ 742,800
Fluorescein angiography	$ 63,928	$ 63,931	$ 742,161	$ 742,243
Focal/grid laser (non-center involved diabetic macular edema)	$ 63,934	$ 63,926	$ 742,211	$ 742,192
Fundus photography	$ 63,900	$ 63,959	$ 742,107	$ 742,296
Injection Procedure	$ 63,592	$ 64,268	$ 738,202	$ 746,201
Bevacizumab drug (repackaged 1.25mg/0.05 mL)	$ 63,929	$ 63,930	$ 742,211	$ 742,192
Ranibizumab drug (0.5-mg)	$ 57,920	$ 69,939	$ 670,375	$ 814,028
Laser retinopexy	$ 63,930	$ 63,930	$ 742,190	$ 742,213
Laser trabeculoplasty	$ 63,930	$ 63,930	$ 742,196	$ 742,207
Optical coherence tomography	$ 63,856	$ 64,004	$ 741,363	$ 743,040
Oculomotor surgery	$ 63,930	$ 63,930	$ 742,188	$ 742,215
Paracentesis	$ 63,931	$ 63,929	$ 742,194	$ 742,209
Panretinal photocoagulation	$ 64,048	$ 63,812	$ 743,366	$ 741,037
Retinal cryopexy	$ 63,930	$ 63,930	$ 742,208	$ 742,195

Retinal detachment repair-injection of air/gas	$ 63,904	$ 63,956	$ 742,202	$ 742,202
Silicone oil injection	$ 63,958	$ 63,902	$ 742,202	$ 742,202
Subtenons kenalog injection for uveitis	$ 63,930	$ 63,930	$ 742,203	$ 742,200
Total air-fluid exchange	$ 63,930	$ 63,930	$ 742,270	$ 742,133
Ultrasound	$ 63,931	$ 63,929	$ 742,212	$ 742,191
Vitrectomy	$ 64,016	$ 63,843	$ 742,619	$ 741,784
Vitrectomy with endolaser	$ 63,851	$ 64,009	$ 742,949	$ 741,454
Vitrectomy with epiretinal membrane peel	$ 63,874	$ 63,985	$ 742,764	$ 741,639
YAG capsulotomy	$ 63,926	$ 63,933	$ 742,207	$ 742,196
Other				
Discount rate	$ 64,075	$ 63,982	$ 766,002	$ 728,975
Vision change per year (lines) with Ranibizumab	$ 74,548	$ 57,583	$ 5,314,927	$ 373,541
Vision change per year (lines) with PRP	$ 57,043	$ 74,236	$ 375,100	$ 1,405,575
Annual injections after year 5 with Ranibizumab	$ 43,854	$ 84,005	$ 564,756	$ 919,647
Utility associated with visual acuity in the better-seeing eye				
20/20	$ 80,680	$ 52,939	$ 701,596	$ 787,796
20/25	$ 73,210	$ 56,738	$ 875,954	$ 643,885
20/30	$ 54,807	$ 76,696	$ 909,088	$ 627,084
20/40	$ 76,146	$ 55,091	$ 754,455	$ 730,339
20/50	$ 58,555	$ 70,391	$ 590,650	$ 998,368
20/70	$ 53,142	$ 80,212	$ 806,226	$ 687,597
20/100	$ 57,637	$ 71,765	$ 521,110	$ 1,289,149
20/200	$ 58,677	$ 70,215	$ 740,624	$ 743,786
20/300	$ 64,558	$ 63,314	$ 738,324	$ 746,120
20/400	$ 63,930	$ 63,930	$ 742,202	$ 742,202

DME, diabetic macular edema; PRP, panretinal photocoagulation

eTable 7b. Incremental Cost-Effectiveness Ratio Values as Each Parameter Assumption is Changed From Low to High, One-at-a-Time*

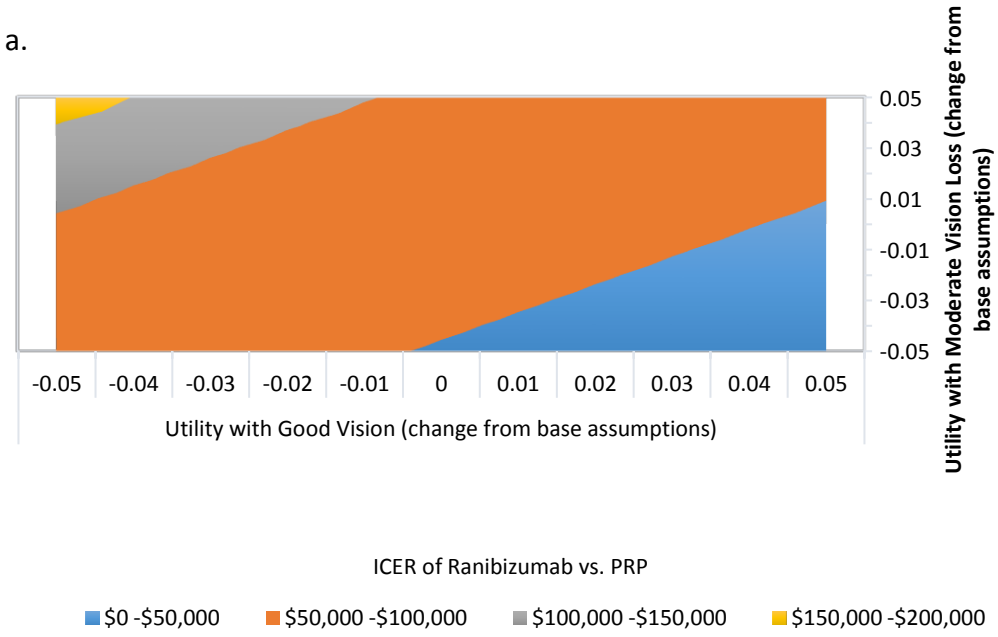
	With Center-involved DME and vision Loss		Without Center-involved DME and Vision Loss	
Parameter\Parameter Value	**Low**	**High**	**Low**	**High**
Unit Costs (per procedure)				
Aqueous tap	$ 114,281	$ 114,281	$ 482,108	$ 482,111
Cataract extraction with intraocular lens placement	$ 114,344	$ 114,219	$ 482,318	$ 481,901
Cataract extraction without intraocular lens placement	$ 114,317	$ 114,246	$ 482,109	$ 482,109
Diode laser (open angle glaucoma)	$ 114,312	$ 114,251	$ 482,109	$ 482,109
Endolaser	$ 114,089	$ 114,473	$ 481,960	$ 482,258
Extended ophthalmoscopy	$ 114,228	$ 114,334	$ 481,720	$ 482,498
Fluorescein angiography	$ 114,278	$ 114,284	$ 482,083	$ 482,136
Focal/grid laser (non-center involved diabetic macular edema)	$ 114,289	$ 114,274	$ 482,116	$ 482,103
Fundus photography	$ 114,229	$ 114,334	$ 482,048	$ 482,171
Injection procedure	$ 113,677	$ 114,886	$ 479,511	$ 484,707
Bevacizumab drug (repackaged 1.25mg/0.05 mL)	$ 114,280	$ 114,282	$ 482,115	$ 482,103
Ranibizumab drug (0.5-mg)	$ 103,538	$ 125,024	$ 435,453	$ 528,766
Laser retinopexsy	$ 114,281	$ 114,281	$ 482,102	$ 482,117
Laser trabeculoplasty	$ 114,281	$ 114,281	$ 482,106	$ 482,113
Optical coherence tomography	$ 114,149	$ 114,413	$ 481,565	$ 482,654

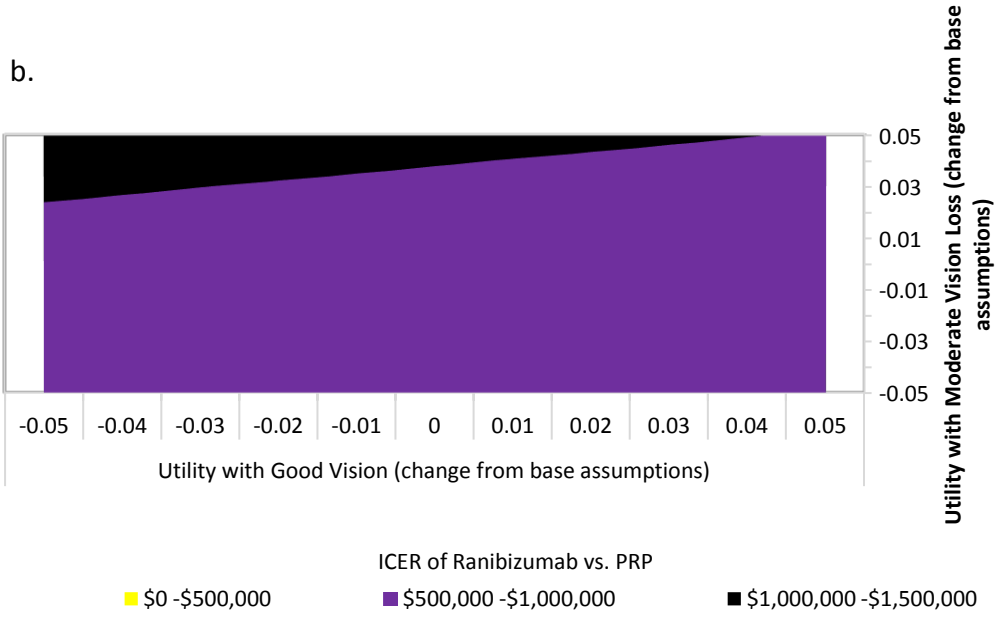
Oculomotor surgery	$ 114,281	$ 114,281	$ 482,101	$ 482,118
Paracentesis	$ 114,283	$ 114,279	$ 482,105	$ 482,114
Panretinal photocoagulation	$ 114,492	$ 114,070	$ 482,866	$ 481,353
Retinal cryopexy	$ 114,281	$ 114,281	$ 482,113	$ 482,105
Retinal detachment repair-injection of air/gas	$ 114,235	$ 114,328	$ 482,109	$ 482,109
Silicone oil injection	$ 114,331	$ 114,231	$ 482,109	$ 482,109
Subtenons kenalog injection for uveitis	$ 114,281	$ 114,281	$ 482,111	$ 482,108
Total air-fluid exchange	$ 114,281	$ 114,281	$ 482,154	$ 482,065
Ultrasound	$ 114,283	$ 114,279	$ 482,116	$ 482,103
Vitrectomy	$ 114,436	$ 114,126	$ 482,380	$ 481,838
Vitrectomy with endolaser	$ 114,140	$ 114,422	$ 482,595	$ 481,624
Vitrectomy with epiretinal membrane peel	$ 114,182	$ 114,381	$ 482,475	$ 481,744
YAG capsulotomy	$ 114,275	$ 114,287	$ 482,113	$ 482,106
Other				
Discount rate	$ 114,335	$ 114,533	$ 484,279	$ 481,474
Vision change per year (lines) with ranibizumab	$ 126,200	$ 108,158	$ 603,383	$ 441,926
Vision change per year (lines) with panretinal photocoaculation	$ 102,366	$ 127,818	$ 414,085	$ 591,603
Annual Injections after year 5 with Ranibizumab	$ 78,394	$ 150,168	$ 366,847	$ 597,372

DME, diabetic macular edema

*Utilities converted from visual acuity in treated eye.

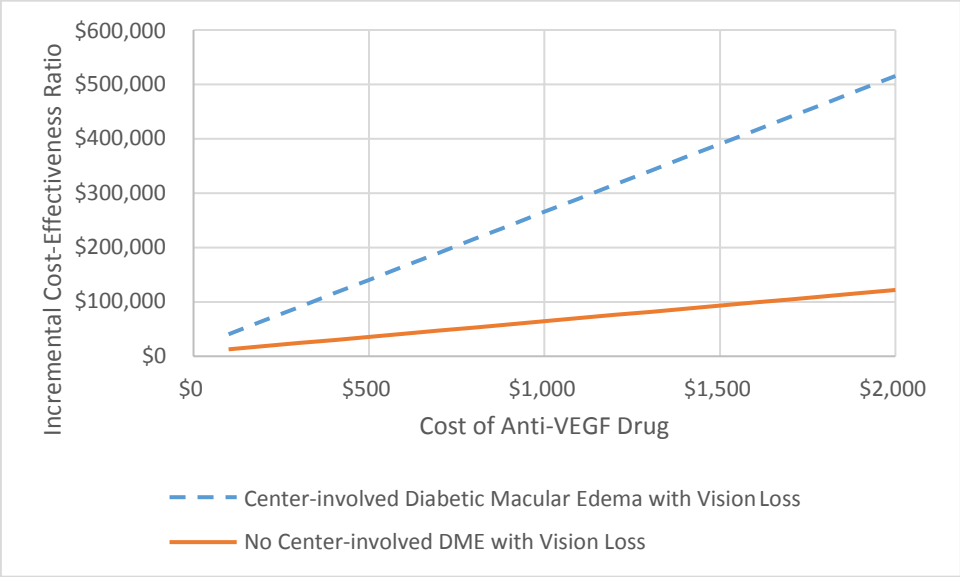
eFigure 1. Two-Way Sensitivity Analysis on Utility With Good Vision (20/20 – 20/25) Versus Moderate Vision Loss (20/50-20/200)* With (a) and Without (b) Baseline Center-Involved Diabetic Macular Edema and Vision Loss



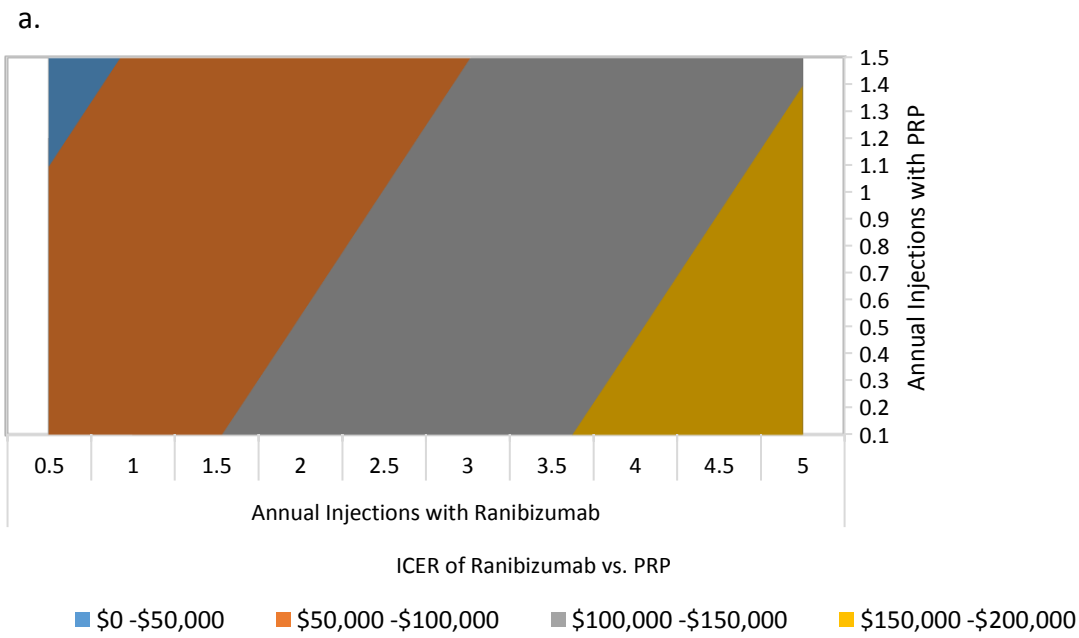


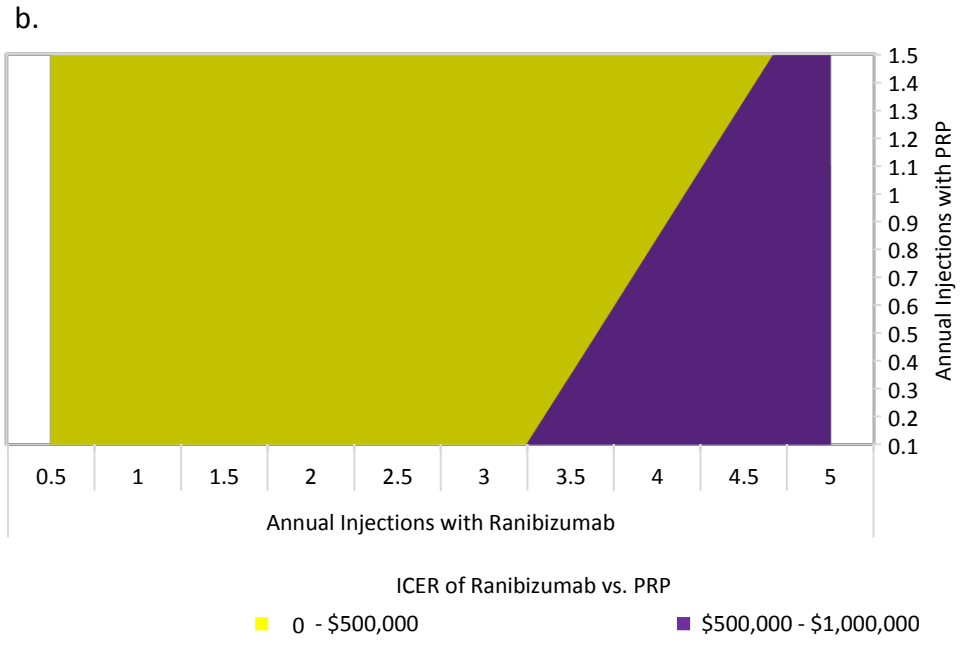
Good Vision = (20/20-20/25); Moderate Vision Loss = (20/50-20/200)
*Utilities converted from visual acuity in better-seeing eye.

eFigure 2. One-Way Sensitivity Analysis Varying Cost of Anti–Vascular Endothelial Growth Factor With Utilities Converted From Visual Acuity in Treated Eye Assuming Effectiveness of 0.5-mg Ranibizumab



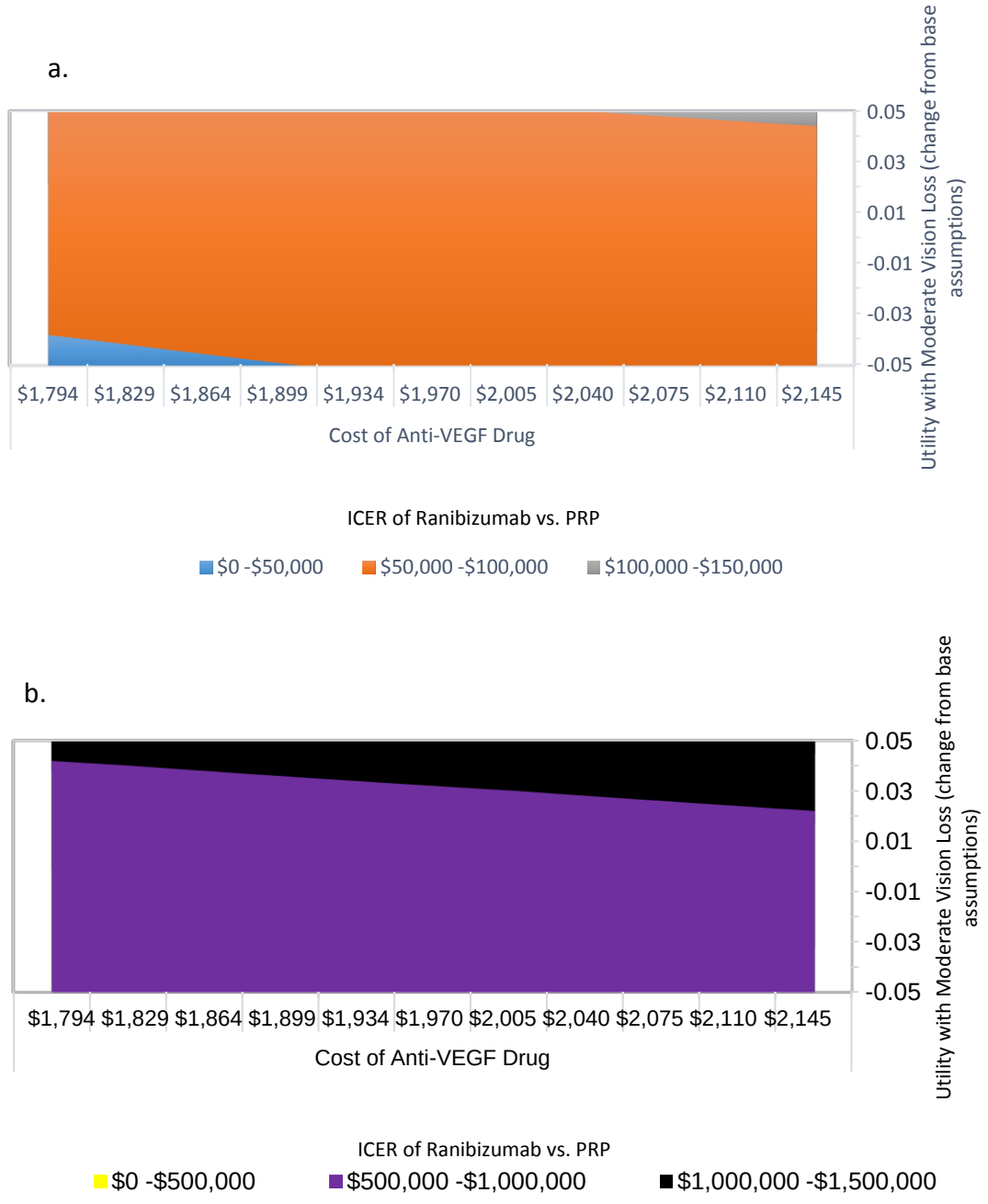
eFigure 3. Two-Way Sensitivity Analysis on Number of Annual Injections With (a) and Without (b) Baseline Center-Involved Diabetic Macular Edema and Vision Loss*





PRP, panretinal photocoagulation; ICER, Incremental Cost-Effectiveness Ratio
*Utilities converted from visual acuity in better-seeing eye.

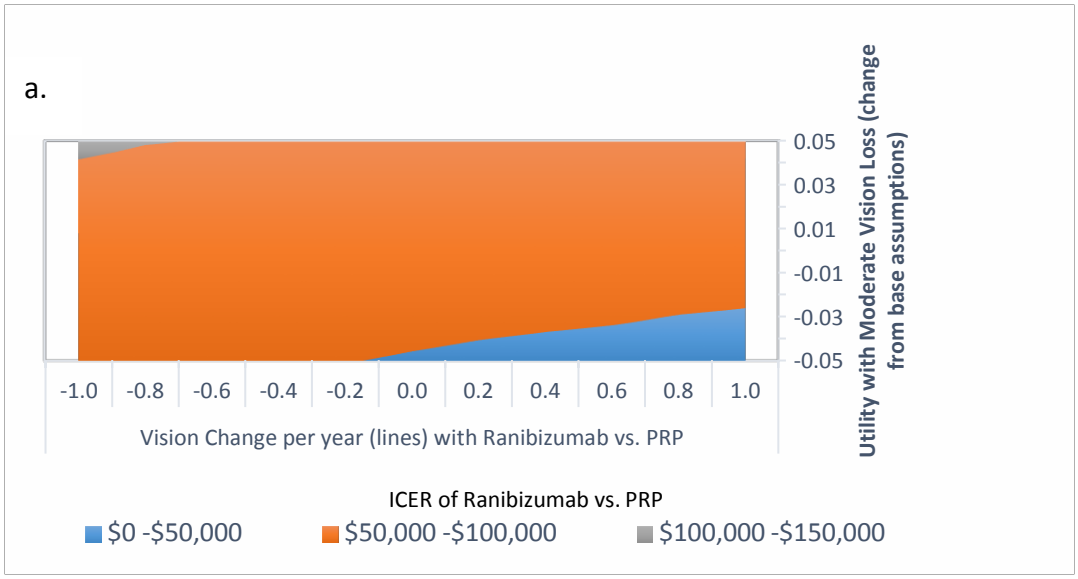
eFigure 4. Two-Way Sensitivity Analysis on Utility With Moderate Vision Loss (20/50-20/200) Versus Cost of Anti-VEGF Drug Injections With (a) and Without (b) Baseline Center-Involved Diabetic Macular Edema and Vision Loss*



Anti-VEGF, anti-vascualr endothelial growth factor; ICER, incremental cost-effectiveness ratio; PRP, panretinal photocoagulation

*Utilities converted from visual acuity in better-seeing eye.

eFigure 5. Two-Way Sensitivity Analysis on Utility With Moderate Vision Loss (20/50-20/200) Versus Effectiveness in Terms of Long-term Improvements in Vision With (a) and Without (b) Baseline Center-Involved Diabetic Macular Edema and Vision Loss*



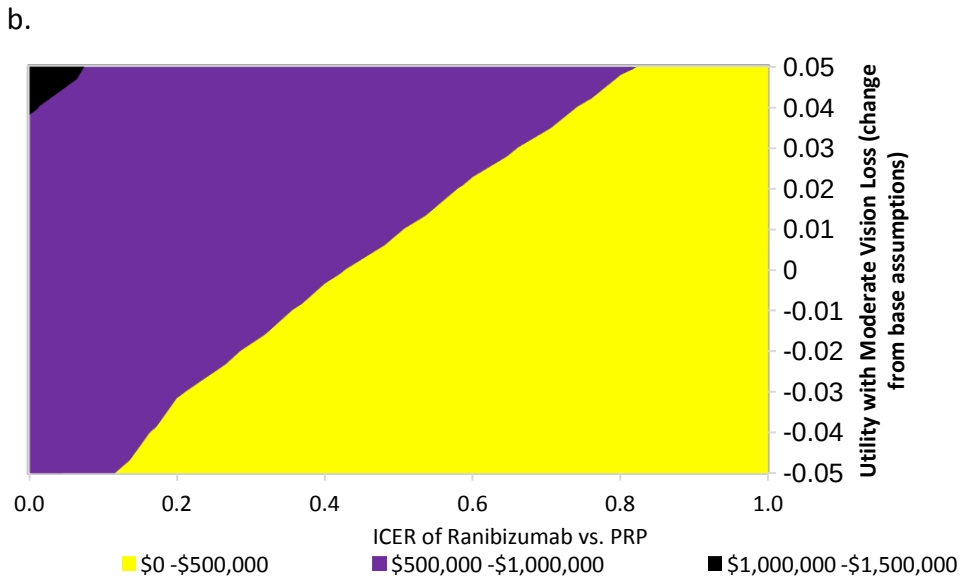
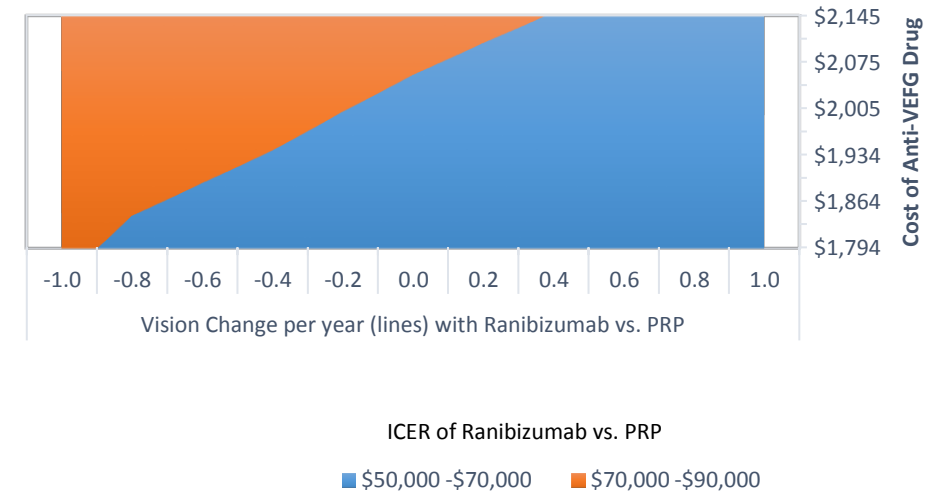


Figure 5b has an X-axis with a different scale than Figure 5a. It only includes improving long-term vision of ranibizumab vs. PRP. If ranibizumab patients have worsening vision compared to PRP, the ICER or ranibizumab vs. PRP can increase to tens of millions of dollars per QALY.

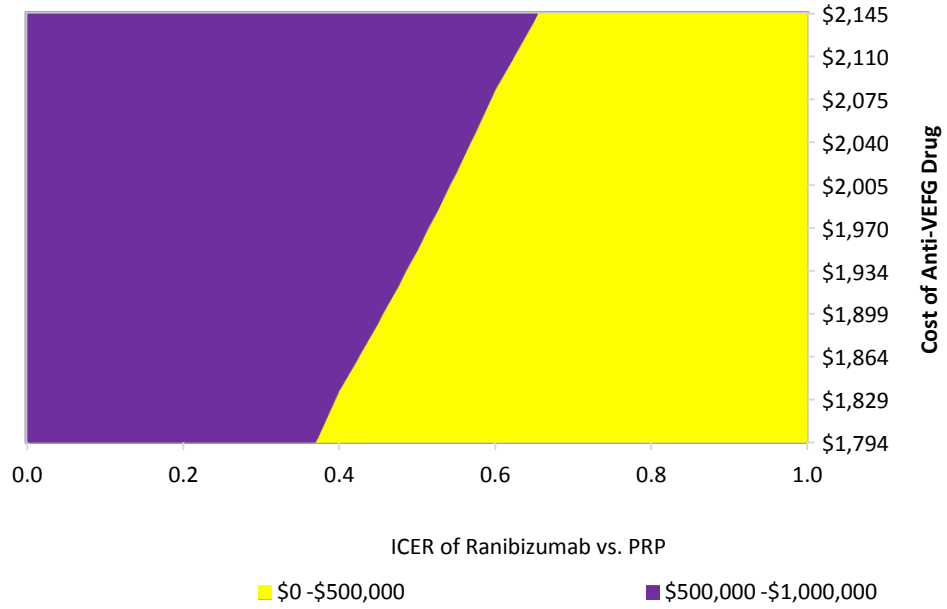
*Utilities converted from visual acuity in better-seeing eye.

eFigure 6. Two-Way Sensitivity Analysis on Cost of Anti-VEGF Drug Versus Effectiveness in Terms of Long-term Improvements in Vision With (a) and Without (b) Baseline Center-Involved Diabetic Macular Edema and Vision Loss*

a.



b.

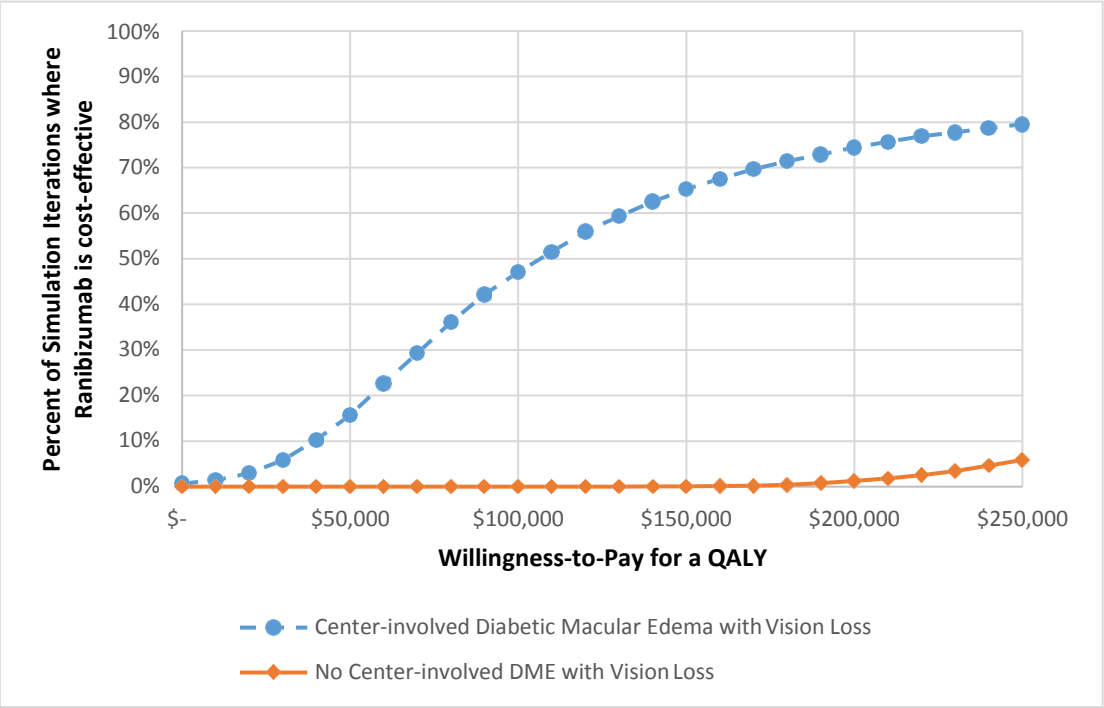


eFigure 6a: the Scale for the colors is more constrained than in Figures 4a and 5a. These variables make a smaller impact on the ICER. The colors range from $50,000 to $70,000 to $90,000.

eFigure 6b: has a X-axis with a different scale than Figure 5a. It only includes improving long-term vision of ranibizumab vs. PRP. If ranibizumab patients have worsening vision compared to PRP, the ICER or ranibizumab vs. PRP can increase to many millions of dollars per QALY.

*Utilities Converted from Visual Acuity in Better-Seeing Eye.

eFigure 7: Cost-effectiveness Acceptability Curves With Utilities Converted From Visual Acuity in Treated Eye



eReferences

1. Centers for Medicare and Medicaid Services. Medicare fee for service payment: Physician fee schedule. 2018; https://www.cms.gov/Medicare/Medicare-Fee-For-Service-Payment/PhysicianFeeSched/Index.html. Accessed November 1, 2018.
2. Office of Inspector General. *Medicare payments for drugs used to treat wet age related macular degeneration.* Washington (DC): Department of Health and Human Services; April 20, 2012 2012.
3. Bonafede MM, Johnson BH, Richhariya A, Gandra SR. Medical costs associated with cardiovascular events among high-risk patients with hyperlipidemia. *ClinicoEconomics and outcomes research: CEOR.* 2015;7:337.
4. Brown MM, Brown GC, Sharma S, Landy J. Health care economic analyses and value-based medicine. *Survey of ophthalmology.* 2003;48(2):204-223.