Supplemental Table 1: Procedure Costs Based on 2019 National Average Medicare Reimbursement Fee Schedule

Parameter	CPT or HCPCS Code	Cost per eye per visit
Aflibercept	J0178	$1,850.00
Bevacizumab	J9035	$63.72
Cataract extraction with IOL placement	66984	$ 3,242.20*
Ciliary body destruction by transscleral cyclophotocoagulation	66710	$2,215.24
Established patient, intermediate examination	92012	$89.74
Intravitreous injection procedure	67028	$104.15
Laser retinopexy	67145	$541.31
Macular laser photocoagulation	67210	$530.50
Optical coherence tomography (OCT) of macula	92134	$41.81
Panretinal (scatter) photocoagulation	67228	$350.66
Paracentesis of anterior chamber	65800	$123.25
Repair of retinal detachment with scleral buckle	67107	$5,869.46
Repair of retinal detachment with vitrectomy	67108	$5,938.30
Retinal detachment repair with gas injection (e.g. pneumatic retinopexy)	67110	$2,750.38
Vitrectomy	67036	$5,632.33
Vitrectomy with focal endolaser photocoagulation	67039	$5,697.92
Vitrectomy with removal of preretinal cellular membrane	67041	$5,889.64
YAG capsulotomy	66821	$339.49

CPT, Current Procedural Terminology Codes; HCPCS, Healthcare Common Procedure Coding System; IOL, intraocular lens

*Including proposed cut to physician reimbursement in 2020 to Work RVU of 7.35

Supplemental Table 2: Additional Assumptions for Population Long-term Modeling

Epidemiology		
	Assumptions	**Notes**
Starting Diagnosed Diabetes Prevalence		CDC national diabetes statisics report estimates 26.7 million adults with diagnosed diabetes in 2018. Incidence (see next row) for two years is added to estimate 2020 prevelance.[8] This total is consistent with he ADA reporting 23 million diagnosed in 2015[13] but Boyle et al 2010[14] projected about 35 million in 2020
White, Non-Hispanic	15.4 million	CDC national diabetes statisics report estimates
Black, Non-Hispanic	4.2 million	CDC national diabetes statisics report estimates
Asian, Non-Hispanic	1.6 million	CDC national diabetes statisics report estimates
Hispanic	4.9 million	CDC national diabetes statisics report estimates
Annual Incidence of Diagnosed Diabetes		CDC national diabetes statisics report estimates
White, Non-Hispanic	786 thousand	CDC national diabetes statisics report estimates
Black, Non-Hispanic	213 thousand	CDC national diabetes statisics report estimates
Asian, Non-Hispanic	97 thousand	CDC national diabetes statisics report estimates
Hispanic	334 thousand	CDC national diabetes statisics report estimates
Existing Prevalence of DME in diagnosed diabetes		Varma, 2014 [9]
White, Non-Hispanic	2.6	Varma, 2014
Black, Non-Hispanic	8.4	Varma, 2014
Asian, Non-Hispanic	2.6	Assumed to be same as White. Varma, 2014
Hispanic	5.1	Varma, 2014
Proportion of DME that is center-involved	0.704	ETDRS
Proportion of CI DME with 20/32 or worse	0.602	ETDRS
Annual incidence of DME		

White, Non-Hispanic[15]	1.19%	Converted from 4-year incidence, Klein, 1989[15]
Black, Non-Hispanic	1.14%	Converted from 4-year incidence, Leske 2003[16]
Asian, Non-Hispanic	1.19%	Assumed to be same as White.
Hispanic	1.61%	Converted from 4-year incidence, Varma, 2010[17]
Proportion of incident CI DME with 20/32 or worse	0.602	ETDRS, VARMA 2010[17]
Model initialization of treatment		
Of those treated at time 0, fraction starting in year 1	0.33	
Of those treated at time 0 and not in year 1, those in year 2 (vs. 3+)	0.50	
US Mortality	0.008447	From 2017 Life Tables (Arias, 2017[18]) at age 59 (mean age at enrollment from Protocol V[1])
Diabetes vs. Nondiabetes Relative Mortality	2.31	Gregg, 2007[19]

Mean Number of injections by treatment group

	Years			
Treatment Group	**1**	**2**	**≥3**	
Aflibercept	5.81	2.23	0.5	From Protocol V analysis
Laser	0.70	1.21	0.5	From Protocol V Analysis
Observation	1.32	1.50	0.5	From Protocol V Analysis
Cost per unit			$1954	Medicare

Mean Number of laser treatments by treatment groups

	Years		
Treatment Group	**1**	**2**	
Aflibercept	0.04	0.04	From Protocol V Analysis
Laser	1.30	0.19	From Protocol V Analysis
Observation	0.01	0.03	From Protocol V Analysis
Cost per unit		$ 530	See Supplmental Table 1

Visits without treatment (injections or lasers)

	Years			
Treatment Group	**1**	**2**	**≥3**	
Aflibercept	4.21	4.70	3	From Protocol V Analysis
Laser	3.80	4.52	3	From Protocol V Analysis

Observation	5.06	4.63	3	From Protocol V Analysis
Cost per unit			$ 132	See Supplemental Table 1
Other annual costs				
	Years			
Treatment Group	**1**	**2**		
Aflibercept	$ 110	$ 97		From Protocol V Analysis
Laser	$ 147	$ 76		From Protocol V Analysis
Observation	$ 27	$ 77		From Protocol V Analysis

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Supplemental Table 3a: U.S. Population Costs assuming lower diabetes prevalence and incidence

	Total Annual Costs (billions)			Differences (billions)		
	Aflibercept	**Laser**	**Observation**	**A-L**	**O-L**	**A-O**
2020	$1.76 billion	$0.69 billion	$0.79 billion	$1.07 billion	$0.10 billion	$0.97 billion
2021	$1.82 billion	$0.79 billion	$0.89 billion	$1.02 billion	$0.09 billion	$0.93 billion
2022	$1.94 billion	$0.91 billion	$1.00 billion	$1.03 billion	$0.09 billion	$0.94 billion
2023	$2.09 billion	$1.03 billion	$1.13 billion	$1.06 billion	$0.10 billion	$0.96 billion
2024	$2.23 billion	$1.15 billion	$1.25 billion	$1.08 billion	$0.10 billion	$0.98 billion
2025	$2.38 billion	$1.28 billion	$1.38 billion	$1.10 billion	$0.10 billion	$1.00 billion
2026	$2.53 billion	$1.40 billion	$1.50 billion	$1.12 billion	$0.10 billion	$1.02 billion
2027	$2.67 billion	$1.53 billion	$1.63 billion	$1.15 billion	$0.10 billion	$1.04 billion
2028	$2.82 billion	$1.65 billion	$1.76 billion	$1.17 billion	$0.11 billion	$1.06 billion
2029	$2.96 billion	$1.78 billion	$1.88 billion	$1.19 billion	$0.11 billion	$1.08 billion
Cumulative Undiscounted*	$23.20 billion	$12.21 billion	$13.21 billion	$10.99 billion	$0.99 billion	$10.00 billion
Cumulative Discounted**	$20.09 billion	$10.47 billion	$11.34 billion	$9.62 billion	$0.87 billion	$8.75 billion

A: Aflibercept; L: Laser; O: Observation

These estimates are based on the same assumptions underlying the main results (Table 2 of the main text) except they are based on the lower end of the 95% confidence intervals on diabetes incidence (Table 2 of the 2020 CDC National Diabetes Statistics Report) and diabetes prevalence (Table 1b of the 2020 CDC National Diabetes Statistics Report).

*Sum of the costs from 2020 through2029.
**Discounts cost from 2021 through 2029 by 3% for each year in the future and then sums them together.

Supplemental Table 3b: U.S. Population Costs assuming higher diabetes prevalence and incidence

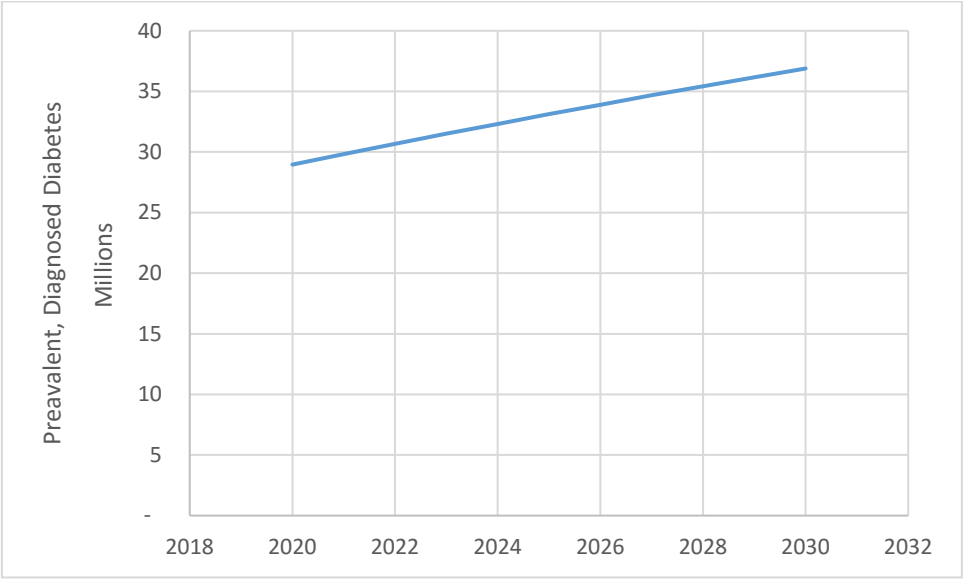
	Total Annual Costs (billions)			Differences (billions)		
	Aflibercept	**Laser**	**Observation**	**A-L**	**O-L**	**A-O**
2020	$2.32 billion	$0.91 billion	$1.04 billion	$1.41 billion	$0.13 billion	$1.28 billion
2021	$2.39 billion	$1.05 billion	$1.17 billion	$1.35 billion	$0.12 billion	$1.22 billion
2022	$2.57 billion	$1.20 billion	$1.32 billion	$1.37 billion	$0.12 billion	$1.25 billion
2023	$2.79 billion	$1.37 billion	$1.50 billion	$1.42 billion	$0.13 billion	$1.29 billion
2024	$3.01 billion	$1.54 billion	$1.67 billion	$1.47 billion	$0.13 billion	$1.34 billion
2025	$3.23 billion	$1.72 billion	$1.85 billion	$1.51 billion	$0.14 billion	$1.38 billion
2026	$3.45 billion	$1.89 billion	$2.03 billion	$1.56 billion	$0.14 billion	$1.42 billion
2027	$3.67 billion	$2.07 billion	$2.22 billion	$1.60 billion	$0.14 billion	$1.46 billion
2028	$3.90 billion	$2.25 billion	$2.40 billion	$1.64 billion	$0.15 billion	$1.50 billion
2029	$4.12 billion	$2.44 billion	$2.59 billion	$1.69 billion	$0.15 billion	$1.53 billion
Cumulative Undiscounted*	$31.45 billion	$16.44 billion	$17.79 billion	$15.02 billion	$1.36 billion	$13.66 billion
Cumulative Discounted**	$27.19 billion	$14.07 billion	$15.26 billion	$13.11 billion	$1.18 billion	$11.93 billion

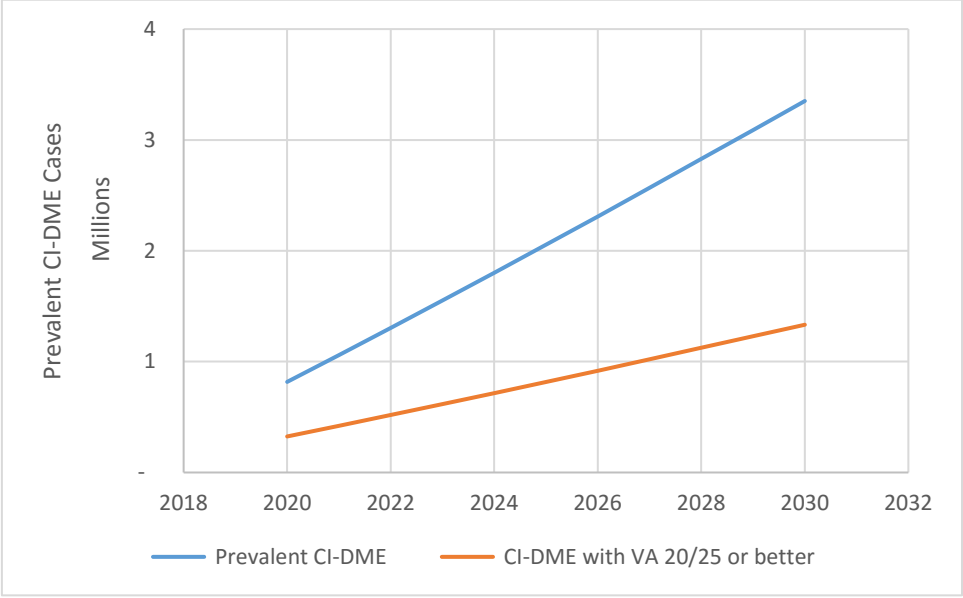
A: Aflibercept; L: Laser; O: Observation

These estimates are based on the same assumptions underlying the main results (Table 2 of the main text) except they are based on the upper end of the 95% confidence intervals on diabetes incidence (Table 2 of the 2020 CDC National Diabetes Statistics Report) and diabetes prevalence (Table 1b of the 2020 CDC National Diabetes Statistics Report).

*Sum of the costs from 2020 through2029.
**Discounts cost from 2021 through 2029 by 3% for each year in the future and then sums them together.

Supplemental Figure 1: Forecast of cases of prevalent and diagnosed diabetes from 2020-2030 (A); cases of with CI-DME and CI-DME with VA of 20/25 or better (B)

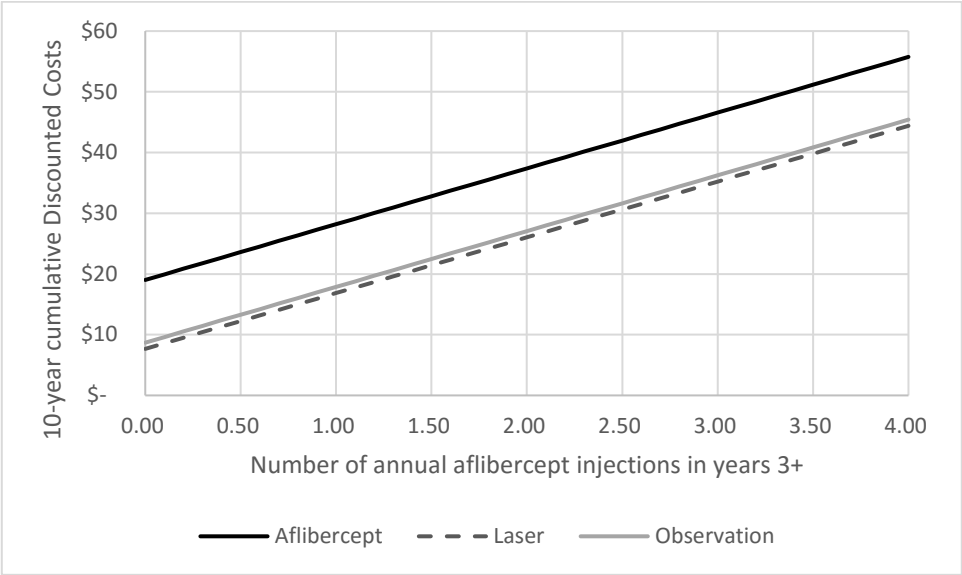




CI-DME, Center-involved diabetic macular edema; VA, visual acuity
Panel A: A relatively simple model of diabetes prevalence in the United States was used to simulate prevalent, diagnosed diabetes; starting with a diagnosed diabetes prevalence of 28.96 million adults in 2020. The prevalence increases with annual incidence of 1.43 million cases, but drops with mortality based on annual US mortality of 0.84% (mortality at age 59,[18] which was the average age from protocol V) [20] multiplied by a relative risk of mortality in diabetics of 2.31 for an overall annual mortality of 1.94%.

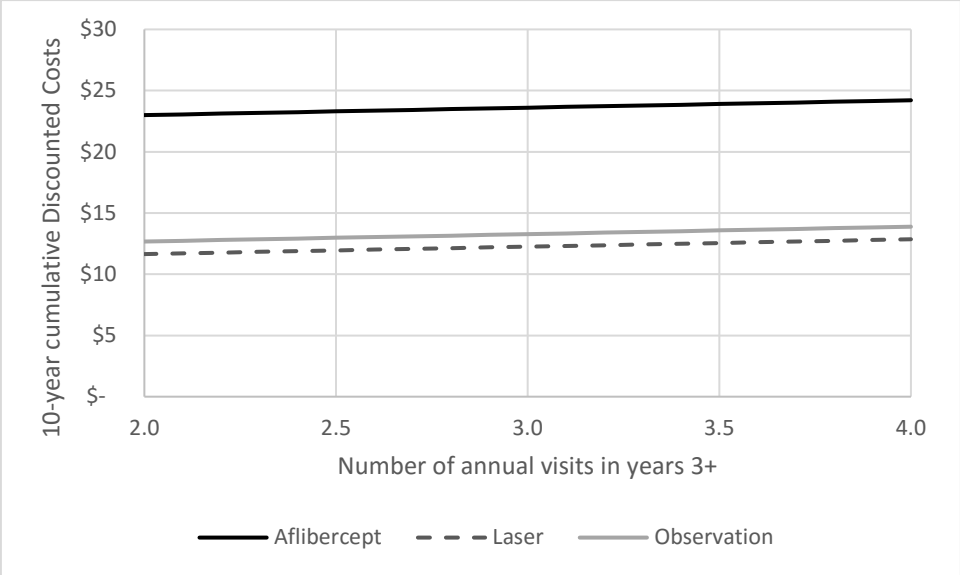
Panel B uses the prevalence of diabetes and adds incidence of CI-DME, a proportion of which has VA 20/25 or better.

Supplemental Figure 2: Sensitivity on numbers of annual aflibercept injections in years 3+



The base case assumption was 0.5 injections per year in each group.

Supplemental Figure 3: Sensitivity on numbers of annual visits in years 3+



The base case assumption was 3 visits per year in each group.