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The Preventable Burden of Untreated Eye Disorders

FINAL REPORT

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1. Executive Summary

Vision loss and eye disorders are among the costliest health conditions facing the nation – not only due to the costs of medical treatment, but due to the substantial indirect costs of disability caused by visual impairment and blindness. Despite its impact, vision loss and eye disorder often remain undiagnosed, even after the presentation of visual symptoms. Four major eye disorders, along with uncorrected refractive error (URE) cause the large majority of low vision in the United States. However, the epidemiology, treatment and outcomes of each of these conditions are so different that it complicates our understanding of the potential benefits of detecting and treating eye disorders. For example, uncorrected refractive error can be easily addressed through the provision of eyeglasses, while other conditions, such as age related macular degeneration can lead to extremely costly treatment with mixed results.

Goals of this Analysis

This analysis seeks to estimate the potential preventable burden attributable to undiagnosed or untreated prevalence of five eye disorders, including age related macular degeneration (AMD) reported based on the subtypes choroidal neovascularization (CNV) and geographic atrophy (GA), diabetic retinopathy (DR), cataract and glaucoma, as well as uncorrected refractive error (URE). Essentially, we attempt to quantify the outcomes of a purely hypothetical intervention in which all current undiagnosed or untreated patients with an eye disease are immediately identified and treated using currently available medical technology, and that all future incident cases are similarly identified and treated.

We do this by first estimating the currently unknown epidemiology of undiagnosed or untreated eye disorders. We then estimate a hypothetical counterfactual of 100% identification and treatment, based on current treatment efficacy. This analysis does not seek to analyze or evaluate any actual or potential intervention to diagnose or treat patients as no such intervention nor policy could achieve 100% identification, and we do not include any costs of any such intervention. This analysis is meant to frame the maximum potential gains of any policies or interventions that may be considered to improve the diagnosis of disease or access to care. In this respect, policy makers could consider the costs of potential interventions or policies against the estimated potential benefits estimated in this analysis.

Limitations

While this analysis attempts to provide a comprehensive, and comparable measure of visual outcomes and costs of treatment of the different major eye disorders at the national level, caution should be used when considering these results. We relied on best-available data to complete this analysis. Nonetheless, we identified numerous data gaps and limitations that require major assumptions. In many cases, this required the combination of parameters estimated from several different data sources. While such practice is considered routine in the field of disease modeling, it nonetheless may introduce bias or error due to differences in data source design and thus the results of this analysis should be considered to be predictions whose accuracy is dependent on the quality of data and the strength of underlying assumptions. Where assumptions were required, we attempt to always err towards the conservative – minimizing the potential benefits, or maximizing potential costs of treatment.

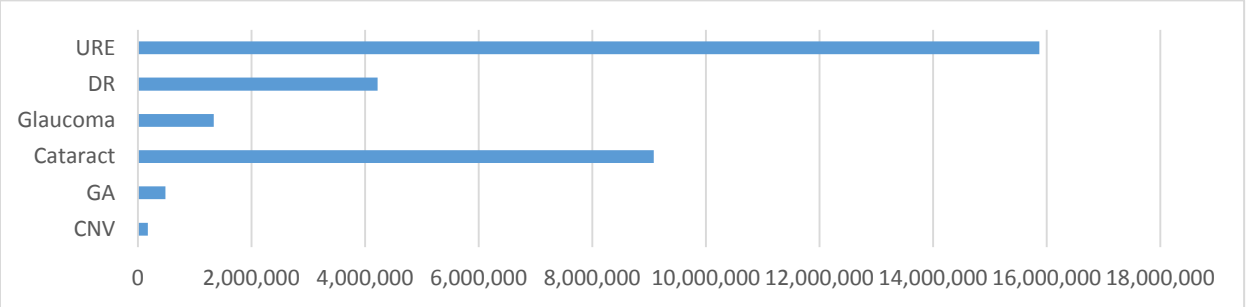
Despite these limitations, we believe this report provides important insight to frame the prevalent burden of eye disorders and their resulting vision loss, and estimate the potential maximum gains of diagnosis and treatment of currently undiagnosed or untreated individuals now and in future years.

Highlighted Results

Prevalence of Undiagnosed Conditions

We found high levels of undiagnosed or untreated eye conditions among the five disorders included in the analysis, totaling 31.2 million cases, although some people may have more than one condition. This prevalence is dominated by URE and cataract, which constitute 51% and 29% of total undiagnosed/untreated prevalence, respectively. While undiagnosed prevalence of the other four eye conditions is lower at 6.2 million cases, vision lost due to these conditions is generally unrecoverable, increasing the importance of identification and treatment of these patients.

Figure EX1. Current Estimated Undiagnosed or Untreated Prevalence



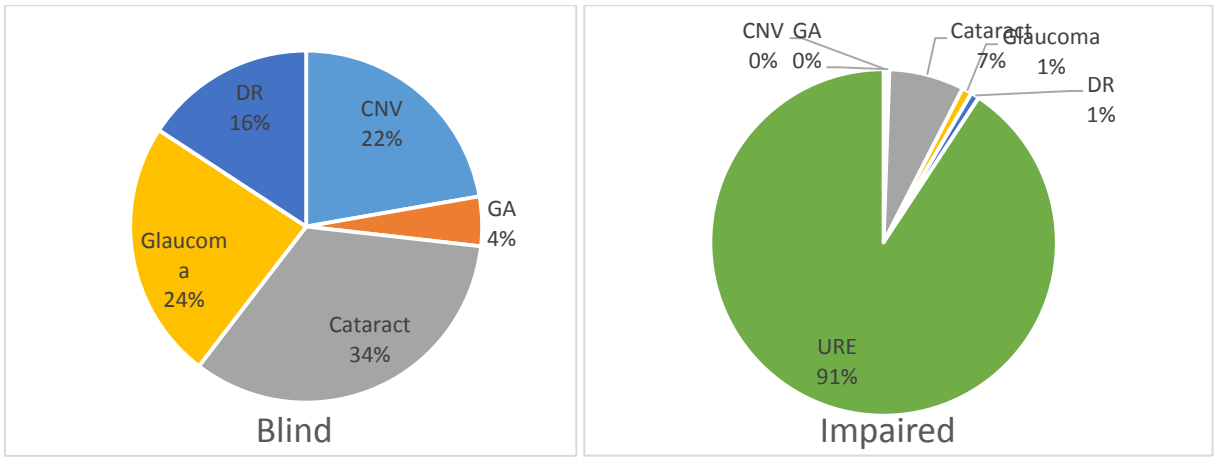
Prevalence of Vision Loss

We estimate that up to 18 million Americans suffer vision loss, including impairment or blindness due to an undiagnosed or untreated condition. Of this, 15.9 million or 88% is due to URE, and a further 8% is due to cataract. Nearly all of this vision loss could be restored through treatment. As many as 700,000 patients may have some vision loss due to undiagnosed or untreated AMD, glaucoma or DR, and for most patients, this vision cannot be recovered.

We find that as many as 468,000 Americans may be blind (acuity in the better-seeing eye ≥20/200) due to undiagnosed or untreated eye disorders. Of this vision loss, 34% is due to cataract and is likely recoverable, while 24% may be attributable to glaucoma and is likely unrecoverable.

By definition, all patients with URE are either untreated or undiagnosed, and with a prevalence of 15.9 million, URE leads to extremely high numbers of Americans with visual impairment, including mild visual impairment (acuity in the better-seeing eye 20/40- <20/80) and moderate visual impairment (acuity in the better-seeing eye 20/80 - > 20/200). We estimate as many as 17.5 million Americans are visually impaired, the vast majority (91%) due to URE, and a further 7% due to cataract. Thus, of the 17.5 million persons visually impaired due to undiagnosed/untreated conditions, 98%, or 17.1 million are impaired due to URE or cataract and are therefore treatable. We estimate that only 2% of prevalent visual impairment is due to AMD, glaucoma, and DR for which limited vision may be restored from treatment. It is important to note that the majority of patients with AMD, glaucoma and DR do not have bilateral visual loss, but these patients are at risk for developing permanent vision loss in the future.

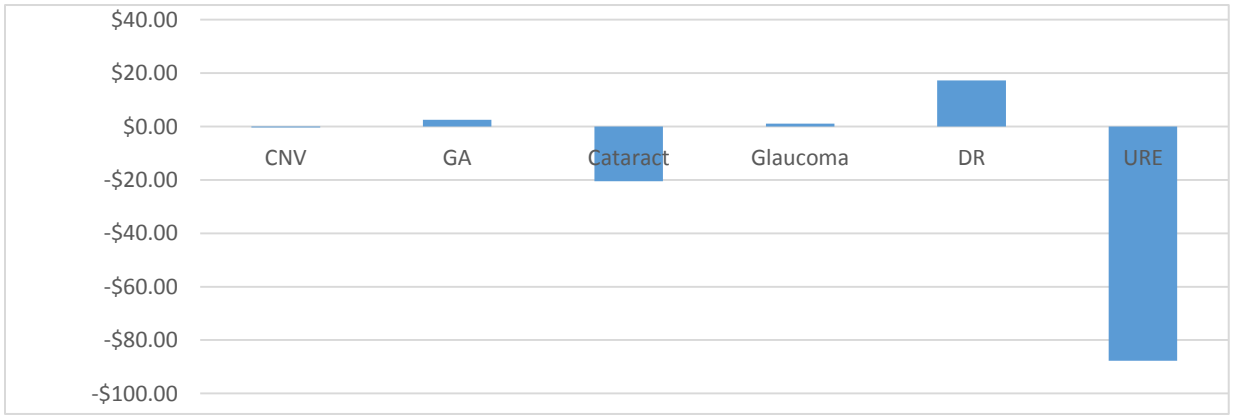
Figure EX2. Current Estimated Vision Loss Prevalence among Undiagnosed/Untreated persons



Economic Impact

We find that overall, the immediate treatment of the conditions included in this analysis would achieve significant economic savings over 10 years of implementation. This again is due almost entirely to URE and cataract, which are estimated to achieve $87.7 and $20.5bn in savings per year over that timeframe, respectively. Treatment of the other conditions would incur a net cost of $20.3bn. We find near parity in costs for CNV treatment, with savings of $340 million over 10 years, but this is due to our assumption of a decline in anti-VEGF treatment after 3 years. Without this assumption CNV treatment would also incur net costs. It must be remembered that this analysis does not include any costs related to any intervention or policy to increase case finding, diagnosis or access to care, and is intended only to demonstrate the maximum avoidable burden. Any real-world intervention or policy to increase diagnosis or treatment would lead to higher costs.

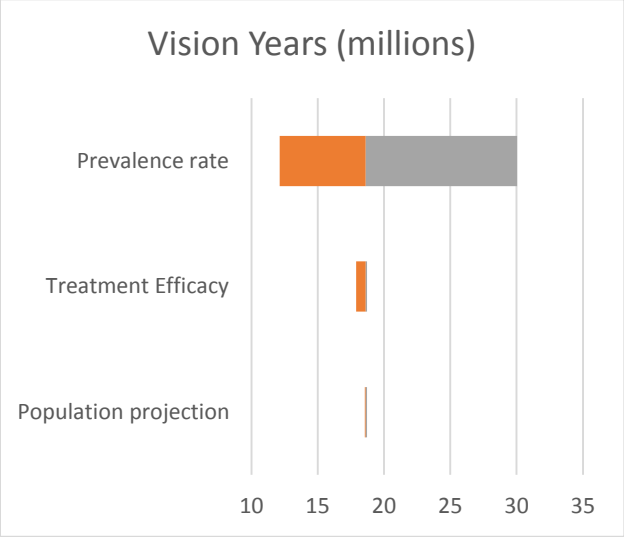
Figure EX3. Net Costs of Treatment over 10 Years, $bns

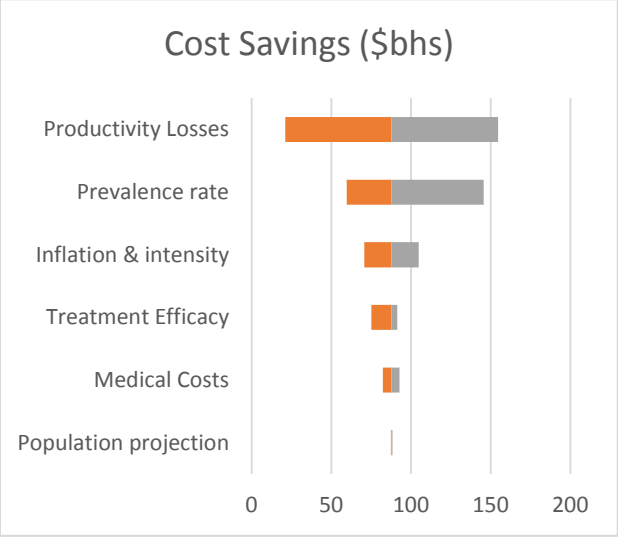


Uncertainty and Sensitivity Analysis

Many underlying parameters in this analysis are subject to uncertainty. Health outcome projections are most sensitive to the prevalence rate and treatment efficacy values. However, treatment efficacy is highly

influential on health outcomes for CNV, DR and glaucoma, where these parameters are more uncertain. Productivity losses have the greatest impact on the economic outcome projections, with the minimum productivity estimate associated with a 75% reduction in the projected net cost savings of treatment. The prevalence rate also had significant impact on cost projections, followed by changes in assumed inflation, medical costs and healthcare intensity, treatment efficacy, and medical costs. Population projections had little impact on outcomes because most treatment is assumed to occur in the base year, before low and high population projection estimates diverge from baseline values. However, if treatment were to be more evenly spread over time, the relative importance of population projections would increase.





2. Methods

Overview of Approach

While the specific methodology was adapted for each condition included in the analysis, in general we estimated the undiagnosed or untreated prevalence of eye conditions, calculated the prevalent burden of vision loss and low-vision associated costs due to each condition, estimated the potential impact of treatment, including the costs of treatment, the potential amount of vision loss that could be averted, and the associated costs of this averted vision. We based our analysis on four primary data sources. True prevalence of conditions is based on the Vision Problems in the U.S. database (VPUS).[1] We obtain diagnosis rates from the National Health and Nutrition Examination Survey (NHANES).[2] Costs of treatment and costs of low vision are based on the Cost of Vision Problems report, while we updated productivity estimates based on new analysis of NHANES.[3] Current and future population estimates are based on Census projections.[4]

The general approach of the analysis can be considered in the following six steps:

1. Estimate undiagnosed prevalence rates of each disease
2. Calculate the prevalence of vision loss among those with each eye disease
3. Multiply these prevalence rates by population estimates to derive total prevalence
4. Estimate the economic burden of this vision loss

5. Estimate the reduction in vision loss under a scenario where all undiagnosed/untreated persons are immediately treated
6. Calculate the medical costs of treatment, and the economic savings of any averted vision loss

Below we review the data sources used in this analysis, and then describe the calculation process in more detail for vision disorders and URE.

Data Sources

The four primary data sources used in this analysis are the National Health and Nutrition Examination Survey (NHANES), the Vision Problems in the U.S. database (VPUS) the Cost of Vision Problems report, and US Census Bureau population projections. We summarize VPUS, NHANES and Cost of Vision below.

Vision Problems in the U.S. (VPUS) - www.visionproblemsus.org

VPUS is a dataset developed by Dr. David Friedman under the support of Prevent Blindness. The dataset results are available online at http://www.visionproblemsus.org/. The underlying data of VPUS is a series of 12 population-based epidemiological studies, five of which were based outside of the United States. These studies each attempted to provide comprehensive eye examinations to all persons living within defined geographic areas. Major eye diseases are diagnosed, and reported on the basis of prevalence rates by age, race and gender. VPUS, and the Eye Disease Prevalence Research Group (EDPRG) study papers that came before it consisted of meta-analyses that combined the samples of the underlying population-based studies to produce more robust estimates of prevalence by all combinations of age group, race and sex.[5-11] VPUS then applied these prevalence rates to 2010 US Census population estimates, nationally and by state. VPUS reports prevalence and prevalence rates for impairment and blindness, refractive error, AMD, DR, cataract, and glaucoma.

The strengths of VPUS are that the underlying data is based on gold-standard examinations and is the only source for reported national prevalence of multiple eye diseases by combinations of age, race and sex. The prevalence reported in VPUS represents the true prevalence of conditions, and are not based on existing diagnosis or self-reporting. However, VPUS does have certain limitations that preclude it from serving as the only source of data for this analysis. VPUS does not report diagnosis information. Therefore, it cannot by itself produce estimates of the undiagnosed prevalence of vision loss, refractive error or eye disease. Another limitation is that VPUS does not separately report prevalence of disease by stage, which can be important for conditions such as AMD where wet-form is treatable, while dry-form generally is not. In addition, VPUS does not report confidence intervals or any level of uncertainty in the data. Finally, while VPUS is the latest and best source of prevalence data available, the fact that 5 of 12 studies included are international, some of the underlying data is up to 30 years old, and that all underlying studies are based on small geographic areas means that VPUS is not truly nationally representative.

National Health and Nutrition Examination Survey (NHANES)

NHANES is a series of biannual national examination surveys and served as the only nationally representative vision and eye examination survey in the United States. Before 2009, NHANES included additional vision and eye disease supplements. These included self-reported questions on eye care utilization and diagnosis history for DR, AMD, and glaucoma, as well as history of cataract surgery. NHANES also included vision testing, including presenting acuity and corrected acuity using

autorefractors. From 2005-2008 NHANES included two ophthalmology supplemental examinations; a retinal image and a visual field assessment. Based on the retinal image, NHANES includes variables for AMD and DR by stage, and optic nerve damage associated with glaucoma diagnosis. The visual field test can be used to assess for signs of field loss, often associated with glaucoma.

The strengths of NHANES is that it includes self-reported diagnosis history along with estimates of true prevalence from limited eye examinations in the same survey. Thus, NHANES could potentially identify both true prevalence and undiagnosed prevalence. In addition, unlike VPUS, NHANES includes disease stage information. However, the major weakness of NHANES is limited sample sizes and limitations of the eye examinations. In particular, a large proportion of many of the examination variable responses indicate that the tests were ungradable or insufficient to identify a stage of disease. Also, the small scale and limited duration of NHANES eye examination modules limit the epidemiological estimates that can be derived from it. Thus, while NHANES can identify patients with disease, and with specific stages of disease, it is likely that the limitations of testing and sample size preclude NHANES as a source for national prevalence of specific stages of eye disease.

Cost of Vision Problems - costofvision.preventblindness.org

The Cost of Vision report was developed under the support of CDC and Prevent Blindness in 2013, and primary results are available online at http://costofvision.preventblindness.org/, with the full report available for download. It is the only comprehensive estimate of the economic costs of low vision and eye disorders to include all age groups. Much of the report builds on prior cost estimates by Rein et al and Frick et al published under contract with CDC in 2006 and 2007, both of which focused on different components of the economic burden for persons aged 40 and older. [12, 13] In 2013, Wittenborn et al published a CDC funded estimate of the economic burden of the population younger than age 40.[14] This analysis updated estimates from the earlier papers while greatly expanding the scope of the analysis to include all eye and vision disorders as well as to include a more comprehensive assessment of all related direct and indirect costs as summarized in a consensus document.[15]

The Cost of Vision report builds directly on the 2013 estimate by expanding the analysis to include persons age 40 and older in 2013. For this analysis, we have converted all included costs into a per-person basis by dividing national costs by age group by the estimated prevalent population with vision loss.

We include two primary categories of costs; costs of medical disorder costs, and costs of low vision.

Medical Disorder Costs

Cost of medical treatment were estimated econometrically in 2003-2008 Medical Expenditure Panel Survey (MEPS) by vision disorder category, as shown in **Table M1**. Full details of the calculation are available in the Cost of Vision report. Costs of blindness are those associated with diagnosed blindness or low vision, which we assign only to those legally blind. MEPS reports diagnoses at the 3rd ICD-9 code digit, precluding differentiation of different types of retinal disorders, including AMD and DR. We approximated AMD and DR costs by differentiating retinal disorders among those with and without diabetes, which we assume is analogous to DR and AMD, respectively. Other costs included in this analysis include cataracts, glaucoma and refractive error. In this analysis, we use these costs as the baseline annual costs of medical care for diagnosed disorders. In some cases, these costs are supplemented to include costs associated with treatment initiation. In addition, these costs generally do not include anti-VEGF costs, which we calculate and include separately for AMD and DR.

Table M1. Annual Medical Costs of Diagnosed Eye Disorders

Vision Disorder	Age 0-17	Age 18-39	Age 40-64	Age 65+	All ages
Blindness and low vision	$1,490	$2,820	$5,870	$10,020	$6,680
Retinal disorder, no diabetes	$830	$1,690	$2,730	$4,210	$3,740
Retinal disorder, with diabetes	$770	$1,610	$2,930	$3,950	$3,640
Cataracts	$810	$1,410	$2,640	$3,730	$3,480
Strabismus	$1,750	$3,090	$4,120	$9,500	$2,370
Glaucoma and optic nerve	$350	$910	$1,490	$2,580	$2,170
Other	$630	$1,290	$1,850	$3,130	$2,020
Disorders of the globe	$500	$960	$1,610	$2,780	$1,440
Conjunctivitis, lacrimal/eye lid	$500	$1,000	$1,540	$2,750	$1,290
Injuries and burns	$410	$830	$990	$1,910	$950
Undiagnosed low vision	$189	$505	$825	$703	$734
Refractive error	$36	$61	$103	$83	$81

Costs of Low Vision

In addition to treatment costs, we assign annual costs attributable to blindness and moderate impairment. To ensure conservative results, the Cost of Vision report did not assign costs to mild impairment, and thus costs are only assigned to patients with moderate visual impairment (≥20/80-<20/200) or blindness (≥20/200). Moderate impairment costs include medical costs of undiagnosed low vision and indirect costs of nursing home placement, skilled nursing facility placement, productivity losses and informal care costs. Costs of blindness include direct costs including the medical costs of diagnosed blindness, vision rehabilitation, assistive devices, assistance programs, and special education. Indirect costs of blindness include those of moderate impairment, plus the deadweight loss from economic inefficiency from transfer payments (SSI, SSDI, tax deductions, food stamps etc), which are not themselves considered costs. Assistive devices include low vision devices, home adaptations and guide dogs, estimated based on reported utilization rates and costs in the literature. Assistance programs include federal programs providing products or services including the American Printing House for the Blind and Books for the Blind programs. Special education is based on the national average annual cost of special education, and by assumption is applied to all blind persons aged 6-21. Most vision rehabilitation costs were not included in the Cost of Vision report. We have updated these costs to account for total program expenditures of VisionServe Alliance organizations.

Nursing home placement is based on the differential prevalence of visual impairment and blindness in nursing homes reported by the Baltimore Eye Study and the National Nursing Home Survey, multiplied the annual cost of nursing home placement as reported in the Genworth Cost of Care Survey.[16, 17] Skilled Nursing Facility costs are based on the findings by Javitt et al.[18]

In the Cost of Vision report, productivity losses are calculated using data from the Survey of Income and Program Participation, and represent the reduction in annual income by age associated with those who report “difficulty seeing”, which we consider analogous to moderate impairment, and those who report

"inability to see", which we consider analogous to blindness.[19] However, for this analysis, we have re-estimated the productivity impacts of low vision using NHANES data. NHANES has the advantage of including actual visual function assessment, and therefore we estimated productivity associated with blindness, visual impairment, and URE. Productivity is based on self-reported household income, which respondents report based on ranges. We assign the minimum bound of the range as household income. We estimated productivity impacts using a 2-part GLM model with log-link, controlling for household size, education, race, sex, and age. To ensure results are not biased by age, we calculated costs separately by age group and used age and age squared variables. NHANES is generally not considered an economic survey, but since our NHANES estimates are based on actual, rather than self-reported visual function, and the NHANES-based costs are lower than were found in SIPP, we conservatively elected to use these measures in this analysis. However, while we make every effort to calculate these costs with a conservative bias, productivity estimates are still highly uncertain and there is potential for upward bias since there are limited indicators to include as controls.

Informal care for children is based on the increased daily hours of care needed for children with disability, by age 0-5 and 6-17 as reported in the American Time Use Survey.[20] Informal care for adults aged 40 and older is based on the annual days of care estimated by Frick et al 2007.[12] In both cases, we value the time of informal care based on a $5.15 minimum wage.

Table M2. Annual Costs of Moderate Visual Impairment

Cost of Moderate Impairment per Person	0-17	18-39	40-64	65+	Average
Direct Costs					
Medical Costs of Low Vision	$189	$505	$825	$703	$734
Indirect Costs					
Nursing Home				$3,634	$2,894
SNF				$835	$665
Productivity		$7,799	$7,390	$6,572	$7,416
Informal Care	$1,785		$49	$49	$55
Total Indirect Costs	**$1,785**	**$7,799**	**$7,439**	**$11,090**	**$11,029**
Total Moderate Impairment Costs	**$1,975**	**$8,305**	**$8,264**	**$11,793**	**$11,763**

Table M3. Annual Costs of Blindness

Cost of Blindness per Person	0-17	18-39	40-64	65+	Average
Direct Costs					
Medical Costs of Diagnosed blindness	$1,490	$2,820	$5,870	$10,020	$6,680*
Vision Rehabilitation**	$1,518	$1,518	$1,518	$1,518	$1,518
Assistive Devices	$5,968	$831	$518	$555	$598
Assistance Programs	$3,949	$145	$145	$145	$165
Special Education***	$8,889	$1,872			$65
Total Direct Costs	**$21,815**	**$7,187**	**$8,052**	**$12,238**	**$9,026**
Indirect Costs					
Nursing Home				$7,582	$6,037
SNF				$3,437	$2,737
Productivity		$11,457	$10,654	$9,423	$10,754
Informal Care	$4,106		$214	$214	$218
Deadweight Loss	$28	$1,059	$3,442	$810	$1,153
Total Indirect Costs	**$4,134**	**$12,516**	**$14,311**	**$21,466**	**$20,900**
Total Blindness Costs	**$25,949**	**$19,703**	**$22,362**	**$33,704**	**$29,925**

*Weighted average medical costs are calculated based on the distribution of diagnosed blindness in MEPS. For all other costs, weighted average is calculated from the blindness population estimates calculated in NHANES.
**Vision rehabilitation was not included in the Cost of Vision report. Vision rehabilitation costs are estimated based on the total budgets for vision rehabilitation providers who are members of VisionServe Alliance, $1.8bn, based on 2015 revenues. We assume vision rehabilitation is equally allocated by age.
**We assume special education services will be provided to all blind persons from ages 6-21.

Table M4. Annual Costs of URE

Cost of URE per Person	0-17	18-39	40-64	65+	Average
Medical Costs of Undiagnosed Low Vision	$189	$505	$825	$703	$734
Productivity		$4,939	$4,518	$3,984	$4,588
Informal Care	$1,785		$49	$49	$55
Total Costs	**$1,975**	**$5,444**	**$5,393**	**$4,736**	**$5,377**

Quality Adjusted Life Years (QALYs)

The Cost of Vision report included estimates of quality of life losses due to visual impairment and blindness. QALYs are calculated by indexing life years by a utility value. A total of 12 different sets of published estimates of the QALY impact of vision loss were reviewed, but ultimately these estimates were based solely on Brown et al 2003, which reported utility values for a range of better-seeing eye acuity values. We applied these utility values to the patients with visual acuity values in NHANES data to capture the distribution of QALY losses among the existing population. We calculated the average utility values to be 0.88 for normal, 0.72 for impairment, and 0.61 for legal blindness, indicating utility decrements of 0.16 for impairment and 0.27 for blindness.

Approach for Calculating Uncorrected Refractive Error

Overview of Approach

Our process for calculating the prevalent burden of URE and the potential costs and benefits of treating URE can be summarized in the following steps.

1. Identify the prevalence rate of URE
    a. Any URE
    b. Severe URE indicative of moderate impairment without correction
2. Calculate prevalent population with URE in current and future years
3. Estimate cost and impact of treatment
    a. Apply costs of treatment to all URE cases,
    b. Apply benefits of averted moderate impairment to the subset with presenting acuity of 20/80 or worse.

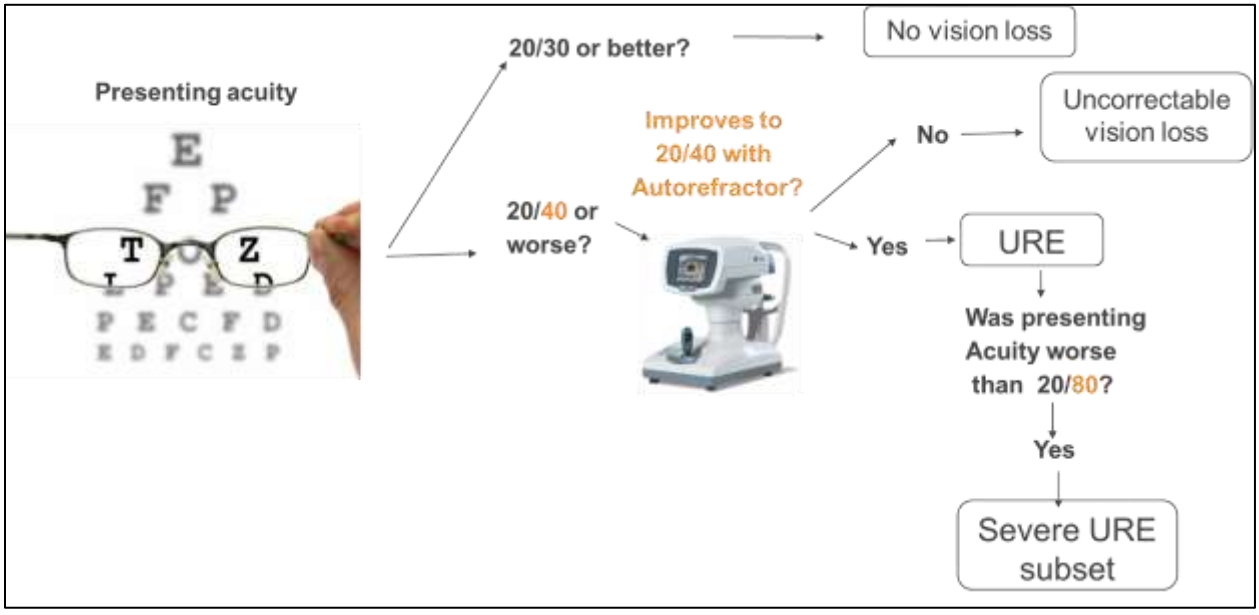
Step 1. Identify the prevalence rate of URE

We identify the prevalence of URE entirely in NHANES data using the visual acuity tests following the process first reported by Vitale et al using older NHANES III data.[21] First, we identified patients with low vision based on if their presenting acuity in the better-seeing eye was 20/40 or worse. All patients

who achieved presenting acuity of 20/30 or worse in NHANES 1999-2008 were further tested using an autorefractor. Those whose acuity improved to 20/30 or better with the autorefractor were assumed to have URE. Using the NHANES sample weights, we calculated the prevalence rate of URE by age groups, race and gender combinations.

We delineated the prevalent population with URE into two categories; all URE cases and a subset with severe URE, defined as patients who presented with acuity of 20/80 or worse, equivalent to moderate impairment, and improved to 20/30 or better on the autorefractor. We found a significant prevalence rate of severe URE of 0.85% of the total population, but the sample size was insufficient to estimate severe URE prevalence by each of the 64 age group, race and gender combinations included in the model. We instead calculated the proportion of all URE patients who meet the severe URE definition, finding that 16.13% of all URE patients met the severe URE criteria. We then assumed this proportion was equally allocated by age, race and gender. The process for calculating URE prevalence rates is summarized in **Figure U1**.

Figure U1. Process for Identification of URE



Step 2. Calculate Prevalent Population with URE

The second step is to calculate population level prevalence of URE and severe URE in the current and future years. In this step, we multiply the URE prevalence rates by the corresponding US Census population projections for the corresponding age, race, and gender for 2016-2045. In subsequent calculations, we use the differences in prevalence from year to year to estimate incidence. When calculating prevalence rates by age group, in some cases prevalence drops or increases substantially at the thresholds of the age groups which results in substantial swings in apparent incidence. We controlled for this by using OLS regression to fit a spline function between the means of each 10-year age group and generated a continuous prevalence rate function. This provides a prevalence estimate at each single year of age, while holding the integral, or the actual predicted prevalence by age group, as a constraint. Therefore, this process does not change the number of patients predicted to have URE, but does distribute these patients among the single years of age within the 10-year age groups such that the overall prevalence function is linear. The resulting prevalence rate curves are shown in **Figure URE1** later in this report.

Step 3. Estimate cost and impact of treatment

After calculating the prevalent population of URE, we then estimate the impact of hypothetical treatment of URE, including treatment costs and averted costs of low vision. Costs of treatment are assigned to all URE patients, while costs of low vision, and thus any economic gains from treatment are assumed to only accrue among individuals with severe URE, with presenting acuity equivalent to moderate visual impairment or worse. We make this assumption because the Cost of Vision report, by assumption, also did not assign costs to mild impairment. Many costs of low vision, such as productivity losses, are derived from survey data with self-reported visual function. To ensure conservative results, costs among those with self-reported difficulty seeing were only applied to the population with moderate impairment.

Thus, in this analysis, while the costs of correcting URE are assigned to all patients with URE, benefits are only accrued among the 16.82% of URE patients who meet the severe URE criteria.

Approach for Calculating Eye Diseases

Overview of Approach

VPUS and NHANES include information on the four major eye disorders, AMD, glaucoma, DR and cataract. Together, these cause nearly three quarters of all prevalent blindness among the population aged 40 and older.[9] Our overall approach for calculating the undiagnosed prevalence of eye diseases, attributing vision loss to the eye diseases, estimating the potential impact of treatment, and calculating cost and QALY impacts is summarized in the following 5 steps:

1. Estimate undiagnosed prevalence rates for each disease
2. Allocate prevalent visual impairment and blindness to each disease,
3. Estimate current and predicted future undiagnosed prevalence of each disease, including the resulting number impaired and blind
4. Apply a treatment efficacy rate to estimate the potential benefits of identification and treatment
5. Apply costs of treatment, and cost offsets of avoided impairment and blindness

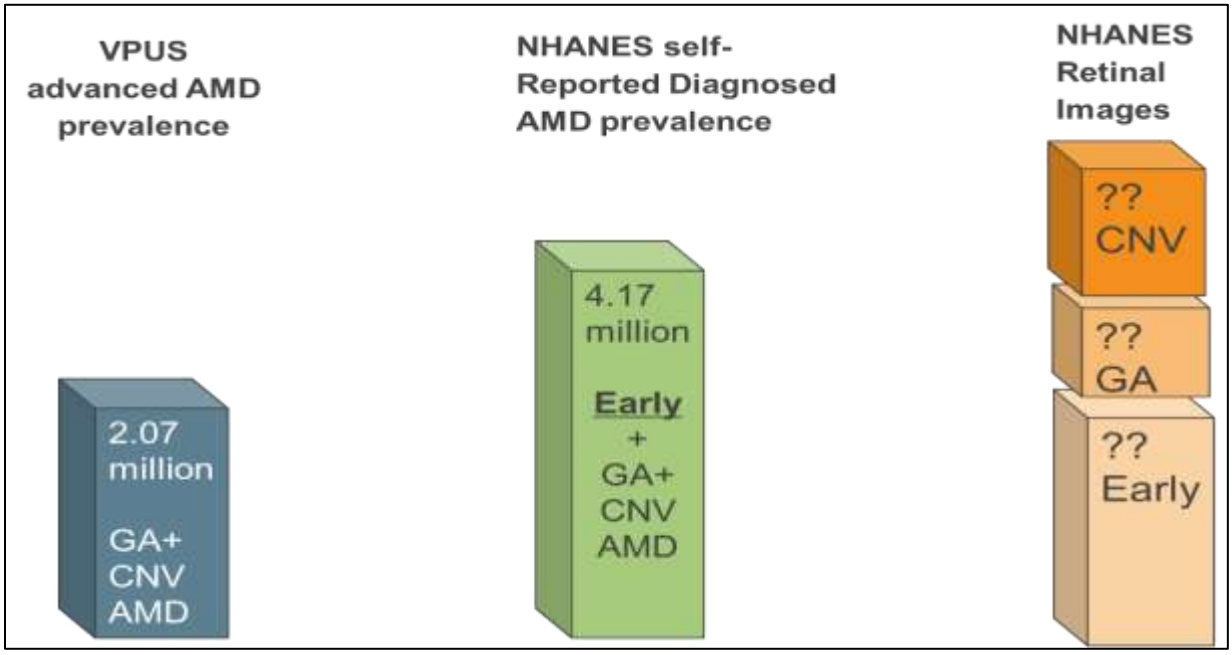
Below, we explain the procedure for completing each step, using the example of AMD. The overall process is similar for all conditions; where different approaches are used we highlight these differences and their rationale in the corresponding disease results sections.

Step 1. Estimate undiagnosed prevalence rates for each disease

Our approach for calculating the undiagnosed prevalence of eye disease differs from that of URE because we rely on VPUS to estimate true prevalence, and then use information from NHANES to allocated prevalence by stage and estimate the proportion of cases that are undiagnosed. We use this approach because of limitations in each dataset. NHANES alone is generally insufficient to estimate true prevalence of eye diseases by age, race and gender due to limited sample size and, potentially, limitations of the retinal image tests. VPUS includes true prevalence by age, race and gender derived from gold-standard ophthalmologic examinations, but does not report diagnosis rates nor does it differentiate major eye disease stages.

Using the example of AMD, as depicted in **Figure E1**, NHANES shows much higher diagnosed prevalence than is reported by VPUS, but presumably most of this prevalence is due to early AMD. Using retinal image results, we identified NHANES patients by stage of AMD, but found the sample sizes too small to calculate full prevalence tables by age, race and gender. However, we were able to calculate the allocation of AMD by stage, finding that 39% of late AMD (equivalent to VPUS' definition) were in CNV, while 61% were in GA, and none had both. We used this 39/61% breakdown from NHANES to allocate the advanced AMD prevalence rated reported by VPUS into the component stages of CNV and GA. This constitutes a major assumption in this analysis, as we are applying rates from one data source to another, which may potentially introduce bias that we note in the data limitations section.

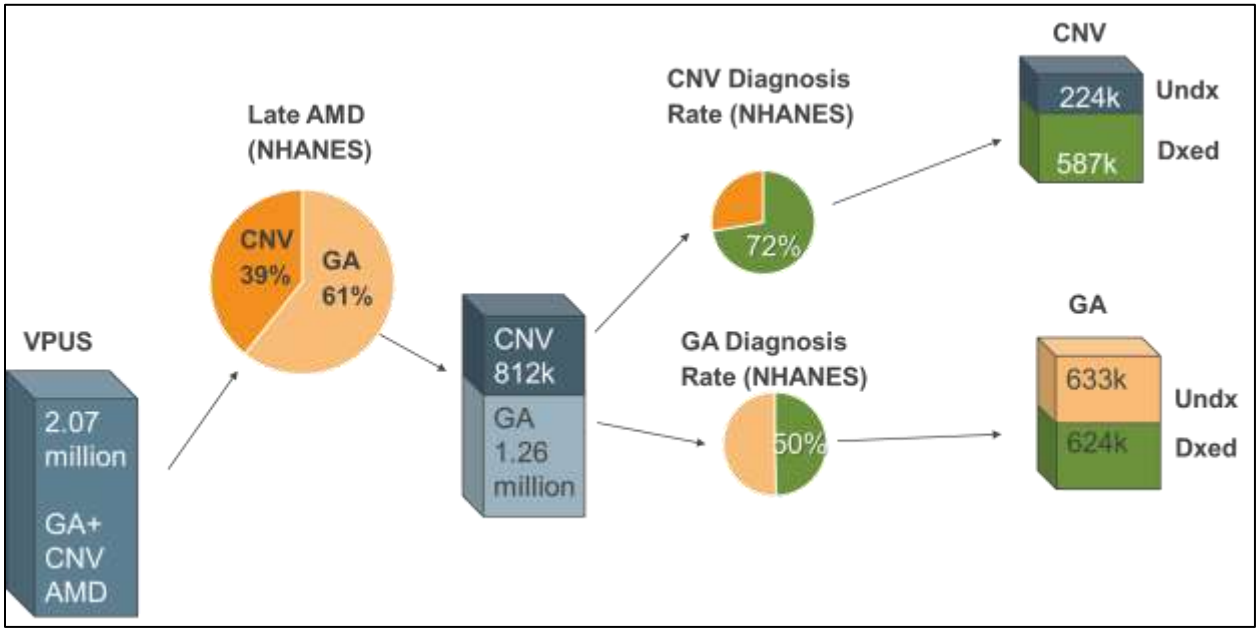
Figure E1. AMD Prevalence in VPUS and NHANES



We then calculated the diagnosis rate of AMD by stage in NHANES, defined as the proportion of patients identified in CNV or GA in the retinal image who had earlier self-reported a history of diagnosis of AMD. We found that diagnosis rates increased with severity of disease; 72% of CNV patients had been diagnosed with AMD, as were 50% of GA patients, and 12% of early AMD patients. Again, we recognize this process as a major assumption of the analysis.

Figure E2 depicts this process for allocating VPUS prevalence by stage, and then applying the diagnosis rates. This figure is a simplification; actual calculations are conducted on the rates, not prevalence estimates, and are then calculated for all 488 age, race and gender combinations.

Figure E2. Calculating Allocation of Advanced AMD



Step 2. Allocating blindness and visual impairment by condition

Limited information exists on the causes of prevalent vision loss. In 2004, the EDPRG reported the allocations of apparent causes of uncorrectable visual impairment and blindness among the 4 major eye diseases, and a separate "other" category. They found that the major 4 diseases caused approximately 74% of blindness and 85% of impairment, and released the disease allocations by race. We use these allocation rates to apportion the prevalent burden of blindness and impairment, as reported by the VPUS, to specific disease causes.

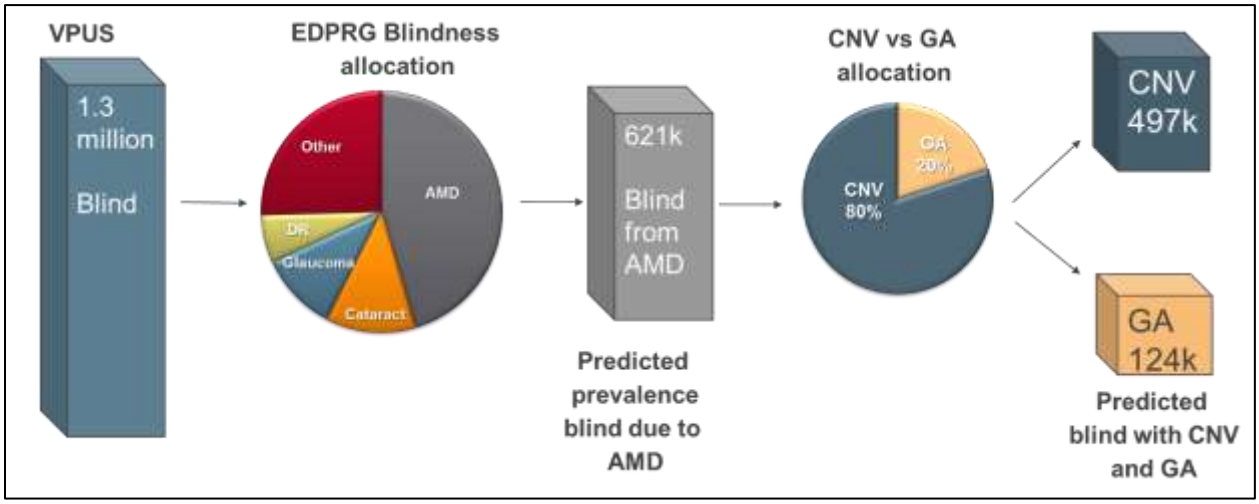
In the example of AMD, we require the prevalence of impairment and burden by disease not for AMD in total, but for CNV and GA, because these stages have drastically different visual outcomes, treatments, and costs. We were unable to locate any data showing the allocation of prevalent vision loss among AMD patients to GA and CNV. Due to this limitation, we instead used the Multiple Eye Disease Simulation (MEDS) model to predict the allocation of vision loss between GA and CNV. Full details of the MEDS model's AMD module are available in the MEDS model technical report.[22] In brief, the model simulates the progression of AMD patients through stages, including GA and CNV, and potentially both, and among patients with CNV, among those with subfoveal, extrafoveal or juxtafoveal CNV.

The model then used data from early clinical trial control groups to predict the amount of vision lost, based on the annual risk of losing vision, and the corresponding distribution of vision lost per stage if it were to occur, as measured in logMar units of acuity or contrast sensitivity.[23-26] Based on these parameters, we estimate that 80% of prevalent vision loss due to AMD occurs in patients with CNV, and the remaining 20% occurs in patients with GA. This may represent the single most uncertain parameter in our analysis, and warrants future investigation. However, an important consideration is that these data all pre-date the emergence of recent, highly effective therapy for CNV. This is necessary because the

purpose of this calculation is to predict the burden of vision loss from disease that would arise in the undiagnosed population, should they remain untreated.

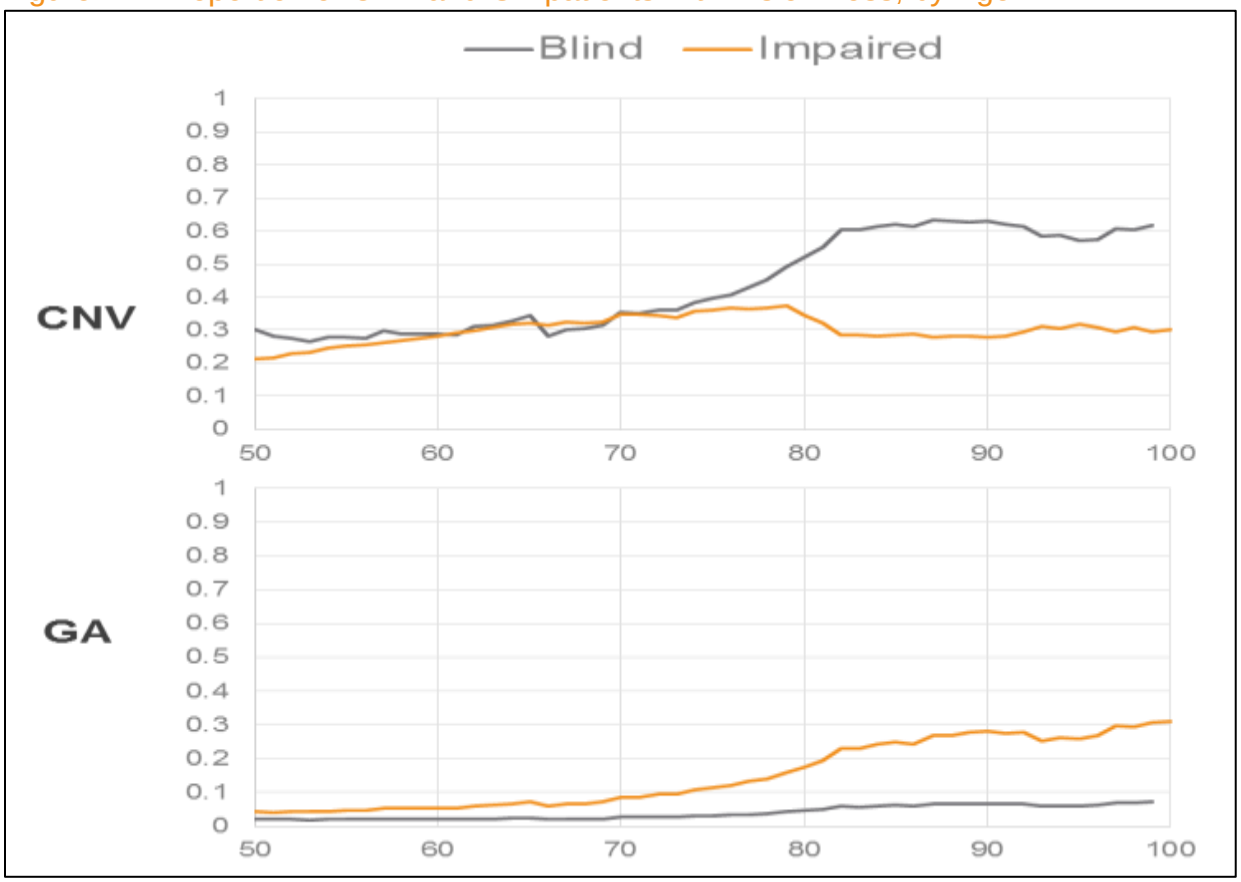
As therapies such as anti-VEGF have since become standard of care, it is not possible to directly observe the impact of non-treatment in an ethical study. Nonetheless, assuming this allocation between GA and CNV, we calculate the prevalence of impairment and blindness among patients with CNV and GA. This process is depicted in **Figure E3**. Again, this depiction is a simplification; in practice all calculations are performed on the prevalence rates, not prevalence numbers, and is conducted separately for all 488 age, race and gender combinations.

Figure E3. Estimating the Number Blind from AMD by CNV and GA



Once we have estimated the prevalence of visual impairment and blindness due to each disease, we then divide this rate by the overall disease prevalence rate to calculate the proportion of patients with disease who suffer vision loss. This is calculated for all age, race and gender groups. The resulting proportions by age alone are shown in **Figure E4** for CNV and GA. Our results indicate that with no treatment, by age 80, 50% of prevalent CNV patients and 5% of GA patients would be blind.

Figure E4. Proportion of CNV and GA patients with Vision Loss, by Age



Step 3. Estimate current and predicted future undiagnosed prevalence of each disease, including the resulting number impaired and blind

In the third step of our analysis, we calculate population-level prevalence of disease, undiagnosed disease and vision loss for each condition using the rates calculated in Steps 1 and 2, multiplied by US Census population projection tables for 2016 and future years. Total prevalence is based on the VPUS prevalence alone. This figure is then multiplied by the undiagnosed rate calculated in NHANES. For AMD, we also allocate the prevalent population by stage of disease, also calculated in NHANES data. For vision loss among the undiagnosed population, we multiply the rates calculated by age, race and gender, as shown in **Figure E4**, by the undiagnosed disease prevalence projections. This represents our estimate of the current and future visual burden of undiagnosed disease.

Step 4. Apply a treatment efficacy estimate to estimate the potential benefits of identification and treatment

The next step of the analysis is to calculate a counterfactual where we assume all undiagnosed patients are immediately identified and treated. This is of course an implausible scenario. The purpose of this is not to simulate a potential outcome of policy interventions, but to estimate the total existing burden due to undiagnosed or untreated eye disorders. Any benefits from treatment in this scenario could be weighed

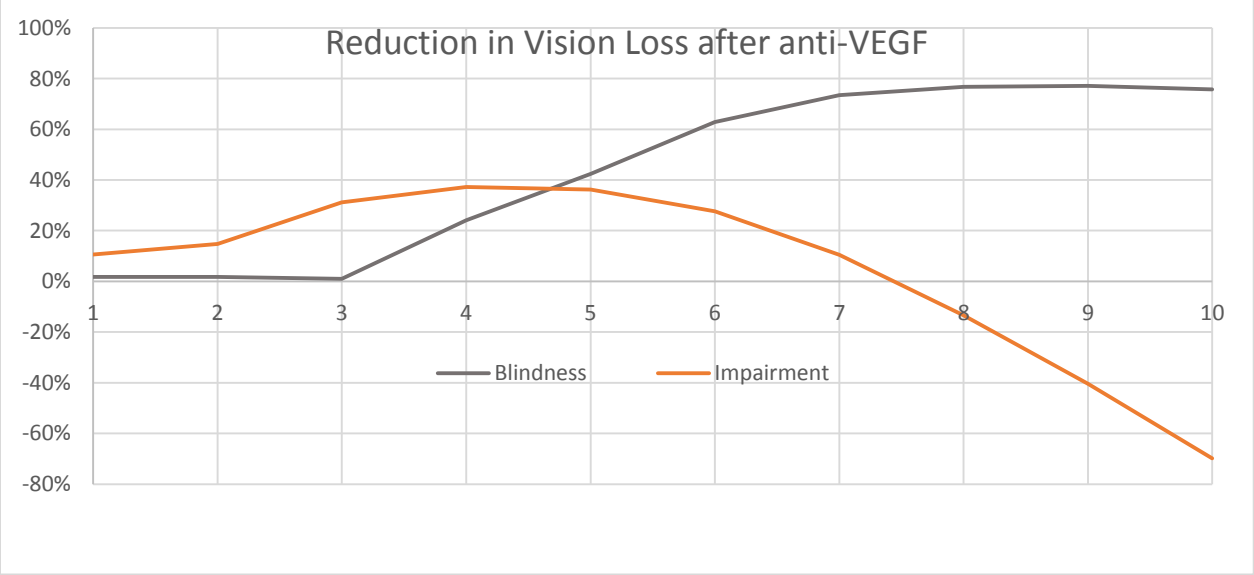
against the potential costs and reach of actual potential case identification and treatment policies and interventions to provide policymakers on net benefits and cost-effectiveness.

In addition, the forecast untreated prevalence and outcomes are not anticipated to correctly predict real-world outcomes, as by assumption we allow no treatment. In reality, some of the undiagnosed population will be diagnosed before or after vision loss. However, as noted in the literature, many patients today are not diagnosed with major eye disease until after reaching impairment or blindness.[27-32]

In the treatment scenario, while we do not attempt to represent real-world identification, we do attempt to accurately represent the efficacy and costs of current standard of treatment by disease, either through calculations or assumptions. In the example of AMD, we use a separate model to calculate the population-level treatment efficacy for CNV, while assuming GA is untreatable. In future analyses, we can alter these parameters to assess different potential levels of treatment efficacy.

In the example of CNV, we use the MEDS model to estimate treatment efficacy. In brief, we assume anti-VEGF injections in a population with incident CNV. The distribution of visual function, treatment efficacy, and injection frequency and type are all based on Wills Eye Hospital Treat & Extend (T&E) study data.[33] The T&E study data includes 3 years of follow-up. We predict longer-term efficacy of treatment based on the 7-year follow-up of the 7-Up study. This shows gradually declining efficacy after the third year, along with declining injection frequency. By assumption, we limit treatment to 7 years. The effect of treatment is to slow progression of acuity loss among CNV patients. This is immediately apparent in the reduction in impairment, but does not impact blindness for 3 years, which is the minimum amount of time that a patient can reach bilateral blindness from incident CNV in the model. After 3 years treatment reduces blindness but by year 5 treatment actually increases impairment – this is because treatment is slowing progression such that patients stay in impairment rather than progress to blindness, as shown **in Figure E5**.

Figure E5. Treatment Efficacy Rates for CNV



Step 5. Apply costs of treatment, and cost offsets of avoided impairment and blindness

The final step is to apply cost and utility outcomes, including costs and QALY losses from low vision and treatment costs. The process for applying low vision costs and QALYs is identical across all diseases. Per person costs of moderate visual impairment and blindness, as shown in **Tables M2** and **M3** above, are applied to the prevalent undiagnosed population with impairment or blindness, respectively. These costs are also applied to the predicted prevalent impaired and blind population assuming treatment of the currently undiagnosed, untreated population. The difference between these costs is expressed as the vision loss cost offsets, or the costs that would potentially be avoided with immediate treatment. Treatment costs are based primarily on the annual medical costs attributable to diagnosis and treatment of each condition, as shown in Table 1. However, these costs were calculated from cross-sectional MEPS data for patients who were currently undergoing treatment for the respective costs. This requires assumptions about how and when to apply these costs, depending on the expected course of treatment for the condition. For example, the annual cataract costs was calculated as $3,480. This closely approximates the $3,432 average single eye cataract surgery fee reported by AllAboutVision.com.[34] Given the immediate nature of cataract surgery and the relatively low rates of follow-up care, we assume that the cost of cataract surgery is applied only for the single year of treatment. However, other chronic eye conditions such as AMD and DR may require constant ongoing monitoring, management and treatment, and thus we apply these costs to all prevalent, diagnosed cases. In the case of CNV AMD, we supplement treatment costs derived from MEPS data with additional costs of anti-VEGF therapy as described in the AMD CNV section.

Adjusting Costs for Inflation and Cost Growth

Multiplying the per-capita costs by the projected population in each year yields projections in terms of real costs in constant 2016 dollars. However, this will ignore the likely impacts of general inflation, excess medical cost growth, and wage growth in future years. Controlling for these price increases yields nominal costs, which are the basis of the expenditure projections reported in this analysis.

Real and Nominal Costs

This analysis provides forecast costs in nominal terms, in which costs are adjusted to account for price changes due to general inflation, wage growth, and excess medical cost inflation and healthcare technology change. Essentially, the nominal expenditures in future years represents our predictions of the number of dollars spent in that year, reflecting the change in value of dollars.

Nominal cost inflators

For nominal expenditures, general inflation and wage inflation projections are based on the 2013 Annual Report of the Board of Trustees of the Federal Old-Age and Survivors Insurance and Federal Disability Insurance Trust Funds.[35] This report includes annual projections of general inflation and wage growth. Medical cost inflation is complex, and includes the combined effects of general inflation, excess cost inflation observed in the healthcare sector, increased per-person healthcare utilization rates (driven largely by insurance coverage), and increases in intensity and/or complexity of services (driven largely by increasing standards of care and technology). For years 2016-2022, we use annual projections of per-capita health care expenditures reported by the CMS Office of the Actuary, which accounts for projected cost changes as well as anticipated impacts of implementation of the Affordable Care Act.[36] However, these projections are only reported through year 2022. Beginning in year 2023, we use the medical cost inflation estimate from the 2012 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, which assumes a constant annual increase in medical costs of 5.1% based on historical trends.[37]

Real medical cost inflators

Real costs are not adjusted to account for price and wage changes, but do account for changes in medical care utilization and intensity. The Medicare Board of Trustees report calculates a constant 5.1% of per-person medical cost changes, which includes 3.2% total medical cost inflation and 1.9% annual cost increases due to increased medical care utilization and intensity.[37] We calculate annual changes in medical care utilization and intensity by subtracting the 3.2% price change component from our medical inflation estimates, which are based on CMS Office of the Actuary annual estimates through 2022, and the Medicare Trustees' assumed 5.1% rate in years 2023-2050.[36]

	General Inflation	Average annual wage in covered employment	Medical inflation (GDP+1 assumption Medicare trustees)	National Health Expenditures per capita (CMS health affairs)	Healthcare utilization growth CMS trustees	REAL MEDICAL UTILIZATION/ INTENSITY GROWTH
2016	2.54	5.58	4.9	4.9	1.9	1.7
2017	2.7	5.36	4.9	4.9	1.9	1.7
2018	2.8	4.98	5	5	1.9	1.8
2019	2.8	4.36	5	5	1.9	1.8
2020-2025	2.8	3.92	5	5	1.9	1.8
2021	2.8	3.92	5	5	1.9	1.8
2022	2.8	3.92	5.6	5.6	1.9	2.4
2023	2.8	3.92	5.1		1.9	1.9
2024	2.8	3.92	5.1		1.9	1.9
2025-2087	2.8	3.93	5.1		1.9	1.9
2026+	2.8	3.93	5.1		1.9	1.9

Discounting

This analysis does not discount future costs or outcomes. Discounting future costs or outcomes to reflect the time value of money is standard practice for economic evaluations such as cost-effectiveness or cost-benefit analysis. This is necessary for decision analyses where choices affect future, downstream outcomes. However, this analysis does not involve decision analysis and is analogous to a budgetary forecast. Based on standard practice for budgetary forecasts, we report costs in nominal expenditures in each year, not the current value of future costs.

Results

Uncorrected Refractive Error

Prevalence

The prevalence rates of URE by age, race and gender as estimated in NHANES data is shown in **Table URE1**. Age groups included ages 12-17, 18-29, 30-39, 40-49, 50-59, 60-69, 70-79, and 80+. Race/ethnicity groups include white (W), black (B), Mexican American or Hispanic (H), and other (O). Sex is represented by F or M.

Table URE1. URE Prevalence Rates by Age Bin

	WM	WF	HM	HF	BM	BF	OM	OF
12-17	0.067954	0.069474	0.144827	0.147207	0.116683	0.149438	0.088559	0.161513
18-29	0.043087	0.045532	0.120973	0.102475	0.090598	0.098244	0.095227	0.082635
30-39	0.042109	0.037299	0.040101	0.112214	0.119197	0.103474	0.111359	0.031934
40-49	0.035989	0.043257	0.083102	0.052925	0.10231	0.082621	0.067521	0.060197
50-59	0.029241	0.008565	0.035904	0.075851	0.016416	0.050101	0.051759	0.015885
60-69	0.030016	0.037802	0.038814	0.070295	0.03252	0.034851	0.103499	0.061364
70-79	0.04816	0.046627	0.114395	0.108434	0.075296	0.0742	0.04143	0.067183
80+	0.063983	0.081298	0.127958	0.131093	0.160197	0.059608	0.055357	0.071284

Linearized prevalence rates of URE by age, race and sex are shown in **Figure URE1**. These prevalence rate functions represent the same age-bin prevalence values shown in **Table URE1**.

Figure URE1. Prevalence Rate of URE by single Years of Age

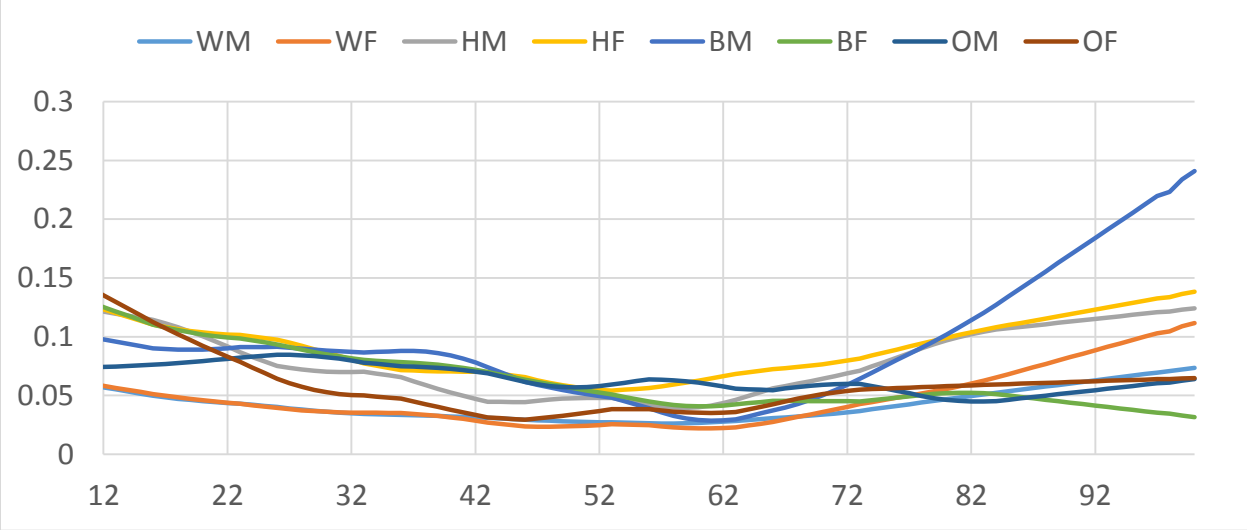
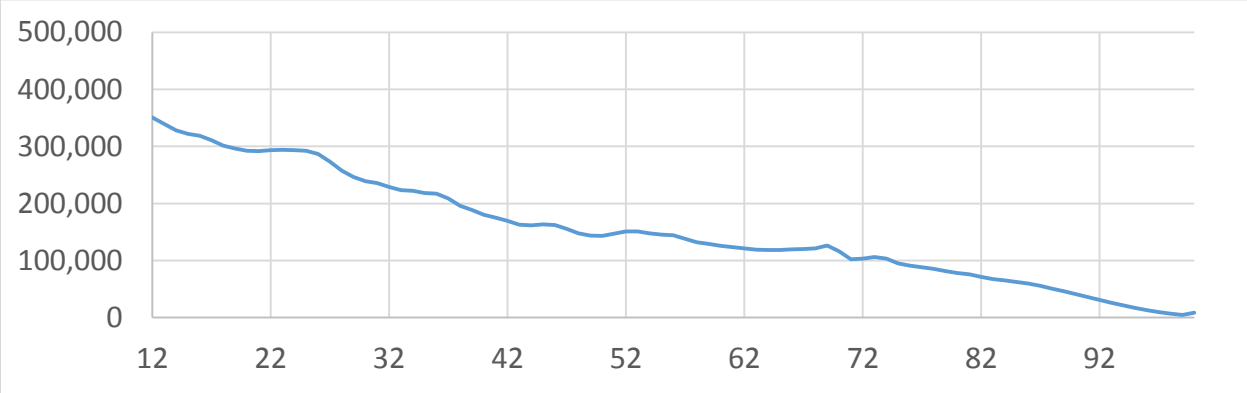


Figure URE 2 shows the estimated national prevalence of URE by age based on the prevalence rates in **figure URE 1** multiplied by the US Census population projection. Total prevalence is estimated to be 15.87 million in 2016.

Figure URE2. National Prevalence Estimate of URE in 2016



Prevalence of URE by year is shown in **Figure URE3**, indicating that prevalence is forecast to increase roughly linearly over time. The leading edge of **Figure URE3** is the same line shown in **Figure URE2**.

Figure URE3. Prevalence of URE over Time

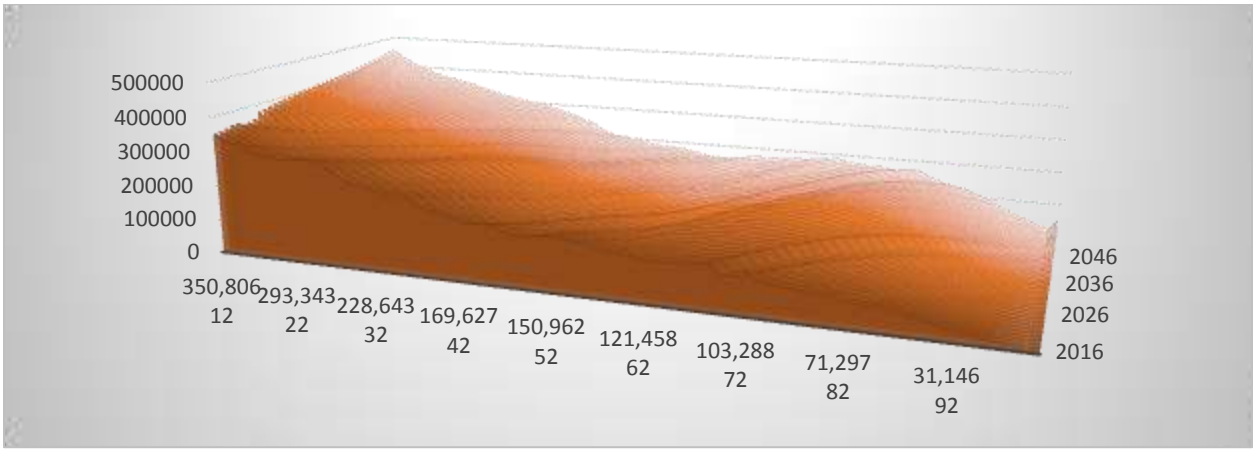


Table URE2. Prevalence of URE by Age Group and Year

Total Pop	Age 0-17	Age 18-39	Age 40-64	Age 65+	Total
2016	4,270,022	5,570,339	3,649,615	2,384,020	15,873,996
2017	4,283,680	5,617,280	3,662,939	2,460,552	16,024,450
2018	4,310,825	5,669,588	3,675,092	2,541,406	16,196,912
2019	4,344,786	5,714,910	3,687,996	2,626,867	16,374,560
2020	4,387,883	5,741,678	3,709,524	2,717,882	16,556,967
2021	4,431,432	5,775,921	3,726,575	2,809,809	16,743,737
2022	4,473,979	5,811,591	3,742,930	2,906,063	16,934,564
2023	4,517,105	5,849,167	3,759,189	3,003,567	17,129,027
2024	4,559,432	5,892,475	3,772,776	3,101,953	17,326,637
2025	4,599,165	5,933,598	3,788,518	3,205,387	17,526,669
2026	4,640,580	5,975,451	3,805,965	3,306,488	17,728,483
2027	4,692,137	6,007,981	3,825,749	3,405,585	17,931,452
2028	4,742,345	6,037,903	3,850,232	3,504,416	18,134,896
2029	4,790,004	6,064,685	3,881,284	3,602,409	18,338,382
2030	4,823,444	6,096,187	3,924,895	3,696,874	18,541,400
2031	4,854,807	6,127,441	3,977,831	3,781,793	18,741,872
2032	4,884,377	6,162,077	4,031,353	3,861,644	18,939,452
2033	4,912,388	6,202,217	4,080,219	3,939,056	19,133,879
2034	4,939,040	6,245,798	4,124,234	4,015,760	19,324,832
2035	4,964,622	6,294,210	4,156,680	4,096,678	19,512,190
2036	4,989,548	6,347,397	4,186,378	4,172,846	19,696,168
2037	5,014,285	6,401,534	4,221,798	4,239,303	19,876,920
2038	5,039,279	6,455,546	4,262,688	4,297,351	20,054,864
2039	5,064,929	6,509,084	4,306,221	4,349,968	20,230,201
2040	5,091,556	6,558,166	4,350,493	4,402,895	20,403,109
2041	5,119,371	6,609,549	4,396,537	4,448,444	20,573,901
2042	5,148,506	6,664,949	4,435,323	4,493,932	20,742,709
2043	5,179,047	6,718,946	4,474,480	4,537,207	20,909,680
2044	5,211,052	6,770,645	4,513,560	4,579,915	21,075,172
2045	5,244,584	6,821,296	4,544,080	4,629,331	21,239,291

Impact on Costs

Treatment costs are assigned based on two values. The national average full cost of refraction correction for a new patient, including optometric examination, lenses and frames is $397, based on a report by the vision insurer VSP Inc. We apply this cost to all URE patients in the first year. In subsequent years, this cost is assigned to incident cases of URE, calculated based on the differential between prevalence P(age $_{t+1}$)– P(age $_{t}$). The second value is the average annual refraction correction costs as calculated in MEPS data, reported in the Cost of Vision report, shown in Table 1. This cost reflects the real-world utilization of optometric services, glasses and contact lenses and is assigned to all URE patients in years in follow-up years, or those in which they are not assigned the $397 cost.

Figure URE4. Net Costs of URE Treatment

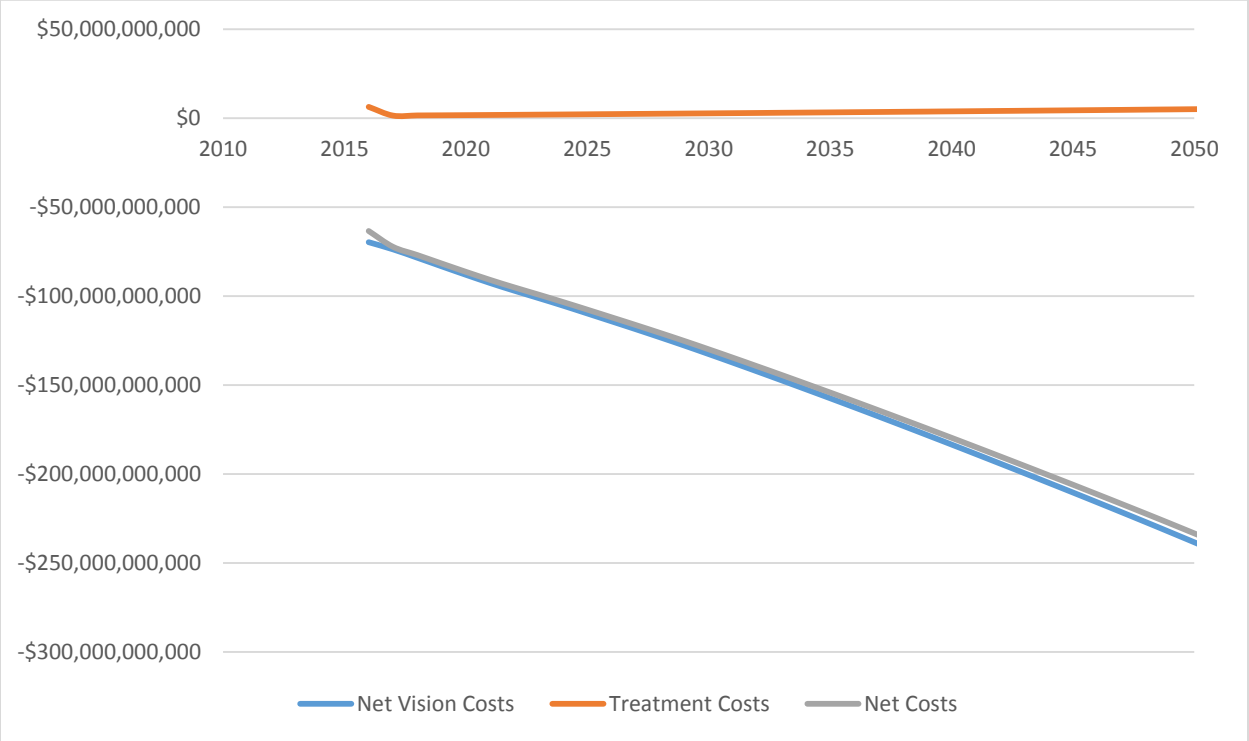


Table URE3. URE Low Vision and Treatment Costs

	No Treatment	Treatment	Net Vision Costs	Treatment Costs	Net Costs
2016	$69,730,545,581	$0	-$69,730,545,581	$6,301,976,347	-$63,428,569,234
2017	$73,738,376,088	$0	-$73,738,376,088	$1,415,491,419	-$72,322,884,668
2018	$78,441,446,580	$0	-$78,441,446,580	$1,504,458,745	-$76,936,987,835
2019	$83,269,700,659	$0	-$83,269,700,659	$1,589,847,545	-$81,679,853,113
2020	$88,031,164,547	$0	-$88,031,164,547	$1,677,107,259	-$86,354,057,289
2021	$92,665,177,541	$0	-$92,665,177,541	$1,767,662,380	-$90,897,515,162
2022	$97,002,225,560	$0	-$97,002,225,560	$1,860,169,043	-$95,142,056,517
2023	$101,143,703,317	$0	-$101,143,703,317	$1,954,568,514	-$99,189,134,803
2024	$105,380,172,005	$0	-$105,380,172,005	$2,050,796,986	-$103,329,375,019
2025	$109,768,241,724	$0	-$109,768,241,724	$2,157,576,288	-$107,610,665,435
2026	$114,190,051,621	$0	-$114,190,051,621	$2,258,669,562	-$111,931,382,060
2027	$118,642,208,226	$0	-$118,642,208,226	$2,361,323,661	-$116,280,884,565
2028	$123,182,301,048	$0	-$123,182,301,048	$2,465,409,686	-$120,716,891,362
2029	$127,807,778,102	$0	-$127,807,778,102	$2,570,970,033	-$125,236,808,070
2030	$132,583,884,960	$0	-$132,583,884,960	$2,677,872,000	-$129,906,012,960
2031	$137,434,656,540	$0	-$137,434,656,540	$2,784,917,151	-$134,649,739,390
2032	$142,350,329,532	$0	-$142,350,329,532	$2,892,913,706	-$139,457,415,826
2033	$147,323,343,869	$0	-$147,323,343,869	$3,001,821,012	-$144,321,522,857
2034	$152,345,919,292	$0	-$152,345,919,292	$3,111,498,553	-$149,234,420,739
2035	$157,407,472,000	$0	-$157,407,472,000	$3,221,995,643	-$154,185,476,357
2036	$162,516,300,962	$0	-$162,516,300,962	$3,333,509,952	-$159,182,791,010
2037	$167,675,424,127	$0	-$167,675,424,127	$3,445,994,965	-$164,229,429,161
2038	$172,883,275,246	$0	-$172,883,275,246	$3,559,668,078	-$169,323,607,167
2039	$178,134,058,422	$0	-$178,134,058,422	$3,674,400,818	-$174,459,657,603
2040	$183,418,040,628	$0	-$183,418,040,628	$3,790,185,689	-$179,627,854,939
2041	$188,745,975,867	$0	-$188,745,975,867	$3,907,155,799	-$184,838,820,067
2042	$194,106,924,818	$0	-$194,106,924,818	$4,025,193,324	-$190,081,731,494
2043	$199,502,963,330	$0	-$199,502,963,330	$4,144,318,586	-$195,358,644,744
2044	$204,933,859,625	$0	-$204,933,859,625	$4,264,748,061	-$200,669,111,564
2045	$210,388,109,992	$0	-$210,388,109,992	$4,386,304,018	-$206,001,805,974

Impact on QALYs

The impact of medical care on QALYs is shown in **Table URE4**.

Table URE4. QALY Impacts of URE Treatment

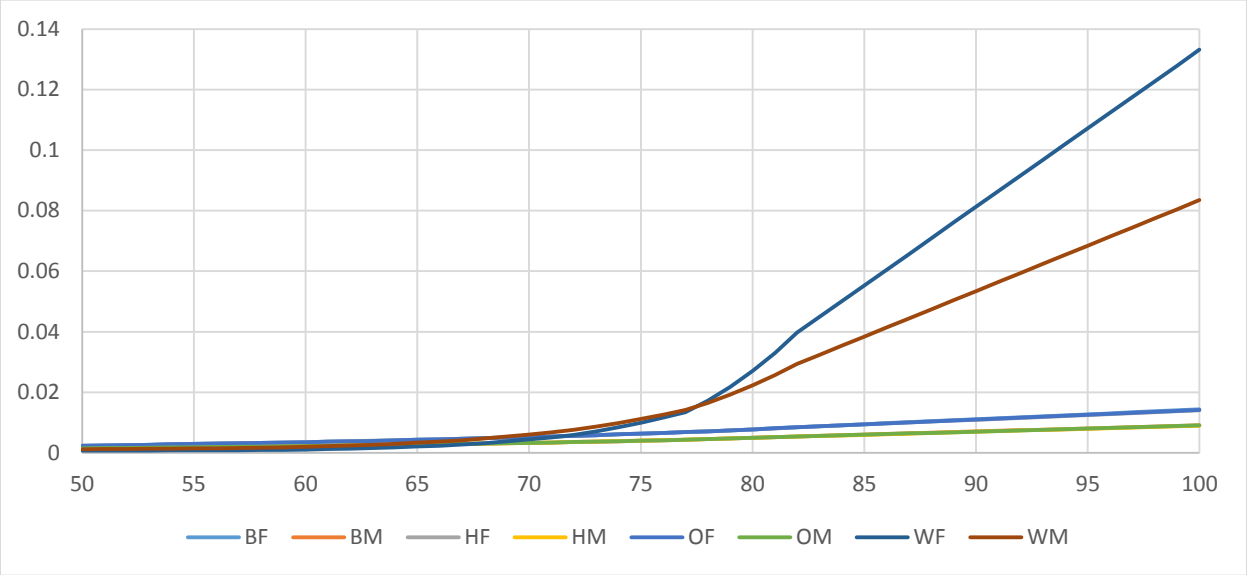
	No Treatment	Treatment	Net QALY Gain
2016	401,949	0	401,949
2017	405,758	0	405,758
2018	410,125	0	410,125
2019	414,624	0	414,624
2020	419,242	0	419,242
2021	423,972	0	423,972
2022	428,804	0	428,804
2023	433,728	0	433,728
2024	438,731	0	438,731
2025	443,796	0	443,796
2026	448,907	0	448,907
2027	454,046	0	454,046
2028	459,197	0	459,197
2029	464,350	0	464,350
2030	469,491	0	469,491
2031	474,567	0	474,567
2032	479,570	0	479,570
2033	484,493	0	484,493
2034	489,328	0	489,328
2035	494,072	0	494,072
2036	498,731	0	498,731
2037	503,308	0	503,308
2038	507,813	0	507,813
2039	512,253	0	512,253
2040	516,631	0	516,631
2041	520,956	0	520,956
2042	525,230	0	525,230
2043	529,458	0	529,458
2044	533,649	0	533,649
2045	537,804	0	537,804

Age-related Macular Degeneration – Choroidal Neovascularization

Prevalence

VPUS reports prevalence rates for ages 50 and older. Based on the NHANES retinal image results, 60.74% of patients with advanced AMD had GA, while the balance (39.26%) had CNV. We apply this breakdown to the prevalence rates of AMD by all age groups. Linearized prevalence rates by age, race and gender are shown in Figure 1, which shows that whites, and white females have disproportionately high incidence of CNV at older ages.

Figure CNV1. CNV AMD Prevalence Rates by Age



Multiplying the prevalence rates by the population projections by age, race, and gender results in the population prevalence forecasts shown in **Figure CNV2**. The leading edge of this figure depicts the prevalence of CNV by age in 2016. Subsequent lines represent the prevalence distribution in future years. **Table CNV1** includes the prevalence predictions by age group.

Figure CNV2. Current and future prevalence of CNV

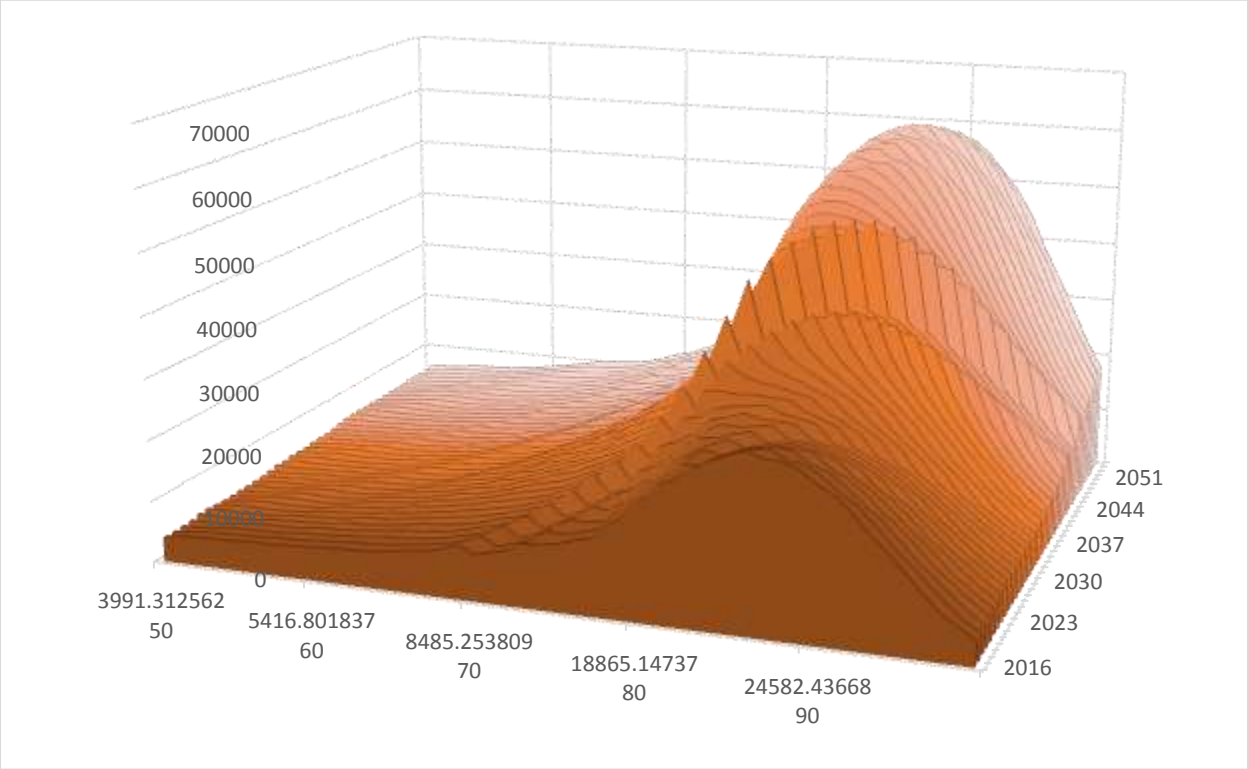


Table CNV1. Prevalence Predictions by Age Group

	age50-64	age 65-89	age 90+	Total Age 50+
2016	75,317	396,575	148,053	**619,945**
2017	76,581	402,660	151,495	**630,736**
2018	77,719	410,000	154,391	**642,110**
2019	78,727	419,185	156,345	**654,257**
2020	79,723	429,303	158,641	**667,667**
2021	80,690	441,526	160,096	**682,312**
2022	81,365	455,739	161,033	**698,138**
2023	81,901	471,710	161,598	**715,208**
2024	82,327	489,469	161,727	**733,523**
2025	82,555	507,613	163,531	**753,698**
2026	82,809	527,071	165,354	**775,234**
2027	83,181	547,640	167,511	**798,332**
2028	83,475	568,393	171,009	**822,877**
2029	83,802	590,292	174,763	**848,857**
2030	84,484	611,939	179,358	**875,781**
2031	85,436	632,845	184,890	**903,170**
2032	86,624	652,039	192,378	**931,041**
2033	87,772	667,647	203,747	**959,166**
2034	88,760	685,828	212,646	**987,234**
2035	89,453	704,916	220,850	**1,015,218**
2036	90,186	724,335	228,217	**1,042,739**
2037	91,216	730,369	247,994	**1,069,579**
2038	92,615	739,784	263,240	**1,095,640**
2039	94,330	749,473	276,974	**1,120,777**
2040	96,141	758,777	289,889	**1,144,808**
2041	98,297	766,659	302,418	**1,167,374**
2042	100,332	773,037	314,891	**1,188,259**
2043	102,309	777,339	327,558	**1,207,207**
2044	104,176	779,545	340,406	**1,224,127**
2045	105,485	779,993	353,470	**1,238,948**

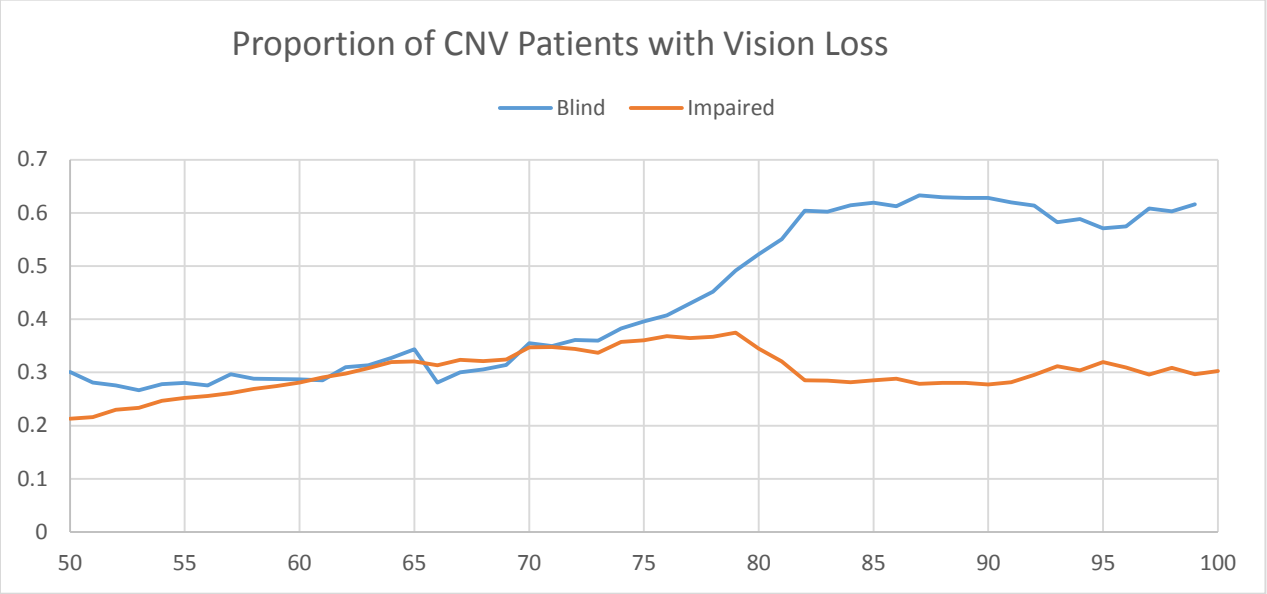
Diagnosis Rate

In 2005-2008 NHANES data, 72.31% of all patients identified with CNV in the retinal image had self-reported a history of AMD diagnosis, indicating the diagnosis rate. We apply the inverse of this diagnosis rate to the prevalence predictions to estimate the undiagnosed population with CNV.

We predicted the total number of patients impaired or blind based on the EDPRG disease allocations of vision loss by disorder type, which is based on data pre-dating most effective treatments such as anti-VEGF, and the prevalence of visual impairment and blindness reported by VPUS. However, neither source differentiated CNV vs GA. Using a separate model, we estimated the allocation of vision loss due to AMD between CNV and GA, which is a function of both the relative incidence of each condition, as well as the amount of vision loss accrued per year, as measured in the probability of vision loss times the acuity loss as measured in logMar. Based on this approach, we estimated that on average, GA yields 0.04331 logMar of acuity loss per year, while untreated CNV causes 0.2557 logMar of acuity loss per year. Based on the relative proportions of GA to CNV identified in NHANES, we estimate that 80% of prevalent AMD impairment and blindness is due to CNV, and 20% is due to GA.

Based on this level of vision loss, we estimated the proportion of CNV patients with impairment or blindness per year, as shown in **Figure CNV3**. Total vision loss equates to the sum of these lines, and thus we predict that the majority of untreated CNV patients would suffer impairment or blindness.

Figure CNV3. Proportion of CNV Patients with Impairment or Blindness



Treatment

The annual costs of medical management of AMD is $3,740 based on 2003-2008 MEPS data. These costs pre-date the emergence of anti-VEGF therapy. We also include costs of anti-VEGF for 3 full years after diagnosis or incidence of CNV, then taper this costs for a further 4 years for a total of 7 years of anti-VEGF therapy. We estimated the population-level efficacy of anti-VEGF therapy on reducing progression of vision loss. The net result of treatment is a reduction in blindness, but over time an increase in impairment. This is because treatment prevents some patients from progressing from impairment to blindness.

Figure CNV4. Treatment Efficacy of anti-VEGF, by year of treatment

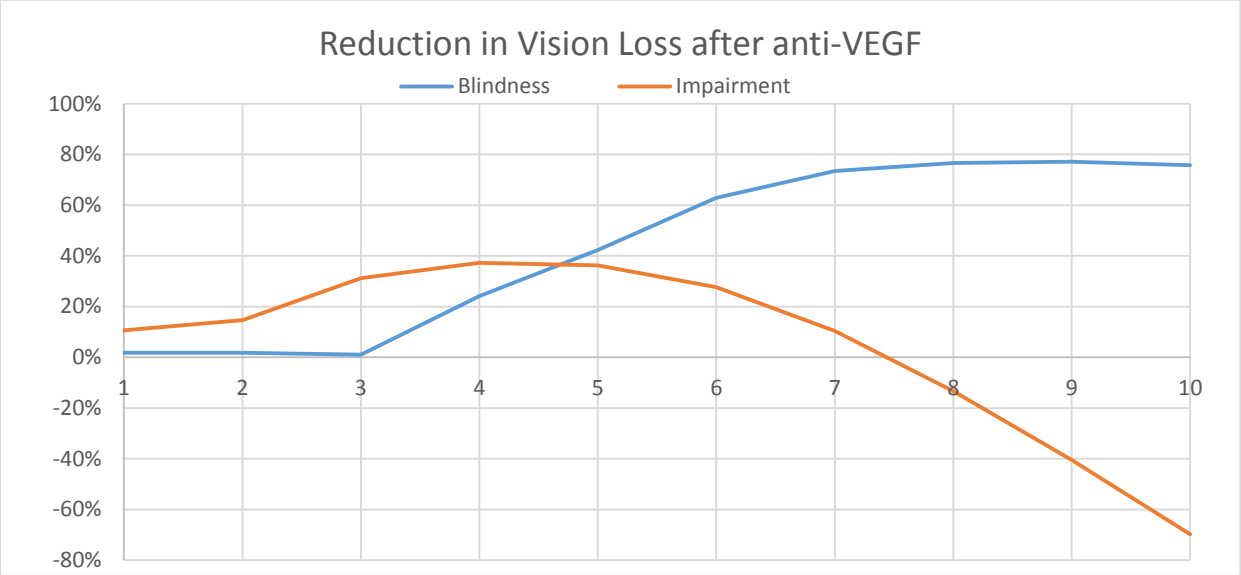


Table CNV2. Prevalence of Vision Loss

	No Treatment			Treatment			Net		
	Impaired	Blind	Total	Impaired	Blind	Total	Impaired	Blind	Total
2016	51,965	104,138	156,103	46,461	102,311	148,772	-5,504	-1,827	-7,331
2017	53,244	105,385	158,630	45,417	103,537	148,954	-7,827	-1,849	-9,676
2018	54,551	106,674	161,225	37,540	105,544	143,083	-17,011	-1,130	-18,142
2019	55,900	108,106	164,006	35,070	82,040	117,110	-20,830	-26,066	-46,896
2020	57,285	109,761	167,046	36,538	63,283	99,822	-20,747	-46,478	-67,225
2021	58,823	111,700	170,523	42,539	41,498	84,037	-16,284	-70,202	-86,486
2022	60,395	113,978	174,373	54,103	30,271	84,374	-6,292	-83,707	-89,999
2023	61,974	116,545	178,520	70,243	27,177	97,420	8,269	-89,369	-81,100
2024	63,569	119,435	183,004	89,287	27,339	116,625	25,718	-92,096	-66,379
2025	65,197	122,817	188,014	110,689	29,824	140,513	45,492	-92,993	-47,502
2026	67,065	126,527	193,591	113,860	30,725	144,585	46,795	-95,802	-49,007
2027	68,854	130,664	199,518	116,898	31,729	148,628	48,044	-98,935	-50,891
2028	70,664	135,153	205,817	119,971	32,819	152,790	49,307	-102,333	-53,027
2029	72,283	140,211	212,494	122,720	34,048	156,767	50,436	-106,163	-55,727
2030	74,086	145,323	219,409	125,781	35,289	161,070	51,695	-110,034	-58,339
2031	75,915	150,586	226,501	128,886	36,567	165,453	52,971	-114,019	-61,048
2032	77,787	155,977	233,764	132,063	37,876	169,940	54,277	-118,101	-63,824
2033	79,745	161,395	241,140	135,388	39,192	174,580	55,643	-122,203	-66,560
2034	81,534	167,016	248,549	138,425	40,557	178,982	56,891	-126,459	-69,568
2035	83,388	172,531	255,919	141,573	41,896	183,469	58,185	-130,635	-72,450
2036	85,239	177,929	263,168	144,716	43,207	187,923	59,477	-134,722	-75,245
2037	86,878	183,368	270,246	147,498	44,528	192,025	60,620	-138,840	-78,220
2038	88,575	188,559	277,134	150,380	45,788	196,168	61,805	-142,771	-80,966
2039	90,208	193,601	283,809	153,152	47,012	200,165	62,944	-146,588	-83,644
2040	91,827	198,332	290,159	155,900	48,161	204,062	64,073	-150,170	-86,097
2041	93,277	202,796	296,073	158,362	49,245	207,607	65,085	-153,550	-88,465
2042	94,637	206,873	301,510	160,671	50,235	210,906	66,034	-156,638	-90,604
2043	95,845	210,561	306,406	162,722	51,131	213,853	66,877	-159,430	-92,553
2044	96,855	213,878	310,733	164,437	51,936	216,373	67,582	-161,942	-94,360
2045	97,847	216,620	314,466	166,120	52,602	218,722	68,274	-164,017	-95,744

Impact on Costs

Figure CNV5 and **Table CNV3** show the incremental treatment costs, incremental vision costs, and the net costs as the difference between treatment and vision costs.

Figure CNV5. Net Costs from CNV Treatment

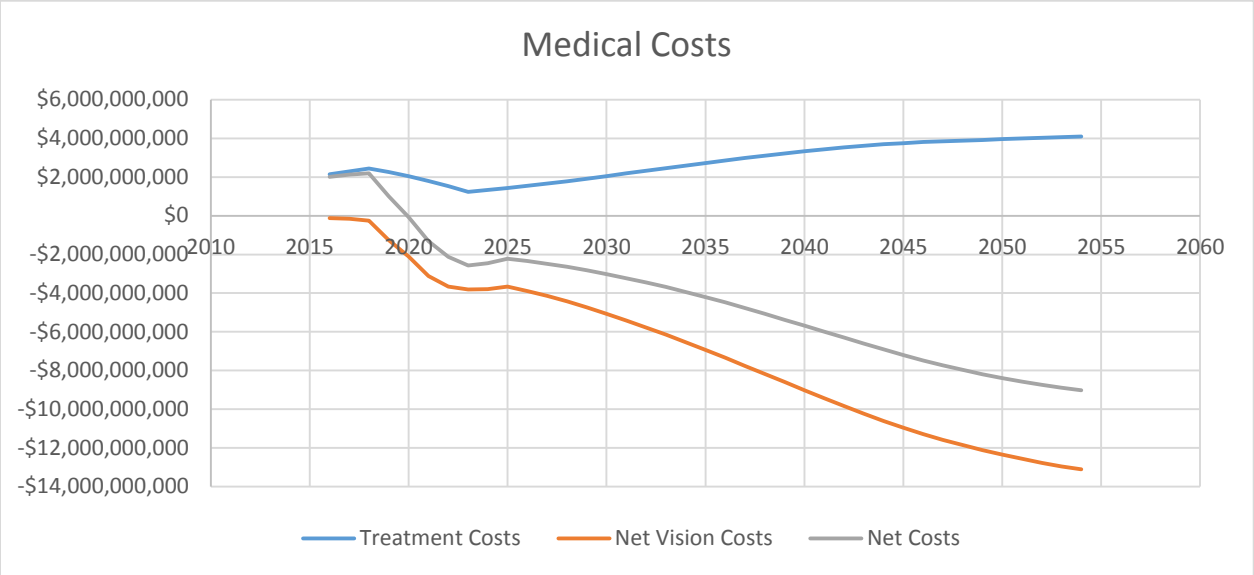


Table CNV3. Net Costs

	Treatment Costs	Net Vision Costs	Net Costs
2016	$2,141,202,510	-$121,854,277	$2,019,348,234
2017	$2,291,314,574	-$155,672,627	$2,135,641,947
2018	$2,440,803,362	-$250,316,070	$2,190,487,292
2019	$2,254,049,957	-$1,254,960,072	$999,089,885
2020	$2,041,140,048	-$2,112,767,352	-$71,627,305
2021	$1,802,928,433	-$3,109,067,891	-$1,306,139,459
2022	$1,536,557,868	-$3,654,711,806	-$2,118,153,938
2023	$1,241,250,449	-$3,813,192,477	-$2,571,942,028
2024	$1,333,231,757	-$3,795,568,950	-$2,462,337,193
2025	$1,440,170,080	-$3,655,400,821	-$2,215,230,741
2026	$1,549,014,799	-$3,889,703,737	-$2,340,688,938
2027	$1,665,549,470	-$4,148,662,651	-$2,483,113,181
2028	$1,789,049,315	-$4,429,850,229	-$2,640,800,914
2029	$1,919,612,654	-$4,745,944,171	-$2,826,331,517
2030	$2,054,309,322	-$5,072,043,145	-$3,017,733,823
2031	$2,190,056,885	-$5,414,706,773	-$3,224,649,888
2032	$2,326,491,734	-$5,773,105,231	-$3,446,613,497
2033	$2,462,669,441	-$6,142,612,032	-$3,679,942,592
2034	$2,597,019,877	-$6,535,530,584	-$3,938,510,707
2035	$2,729,910,011	-$6,934,231,819	-$4,204,321,808
2036	$2,859,489,181	-$7,338,628,595	-$4,479,139,414
2037	$2,985,185,177	-$7,759,511,800	-$4,774,326,623
2038	$3,106,809,586	-$8,177,775,628	-$5,070,966,042
2039	$3,223,765,522	-$8,599,803,882	-$5,376,038,360
2040	$3,335,413,065	-$9,015,781,668	-$5,680,368,603
2041	$3,439,577,225	-$9,429,671,393	-$5,990,094,168
2042	$3,534,894,740	-$9,832,958,961	-$6,298,064,221
2043	$3,619,768,696	-$10,225,292,346	-$6,605,523,650
2044	$3,693,888,612	-$10,607,425,917	-$6,913,537,305
2045	$3,757,131,321	-$10,962,865,745	-$7,205,734,424

Impact on QALYs

Figure CNV6 and **Table CNV4** show the impact of CNV on QALYS with and without treatment, and the incremental QALY gains of treatment.

Figure CNV6. Net QALYs

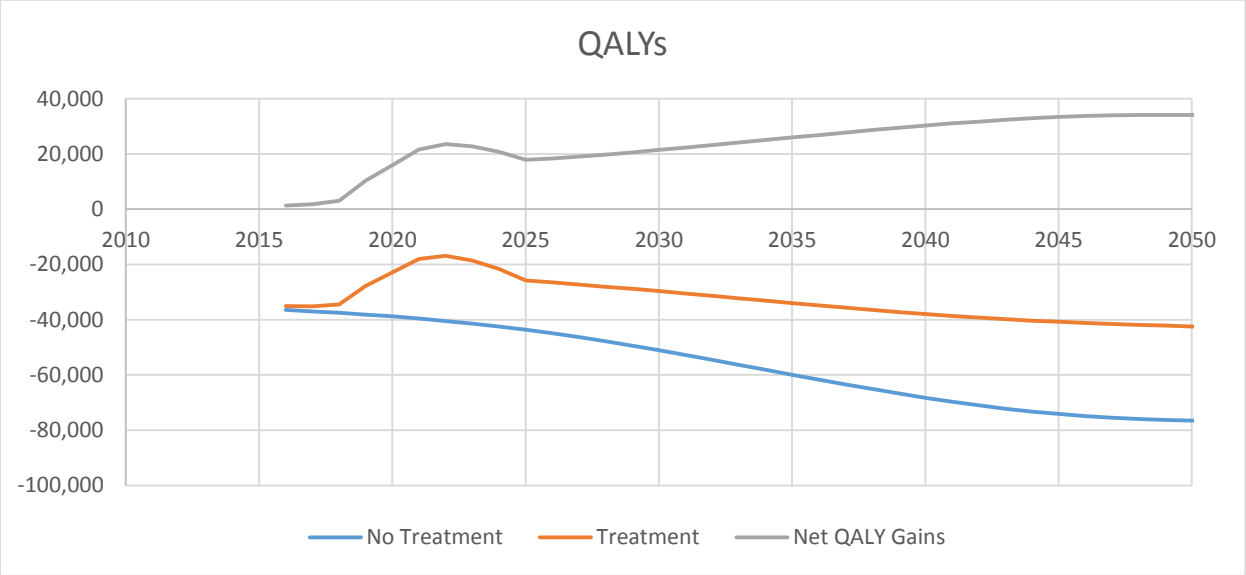


Table CNV4. Net QALYs

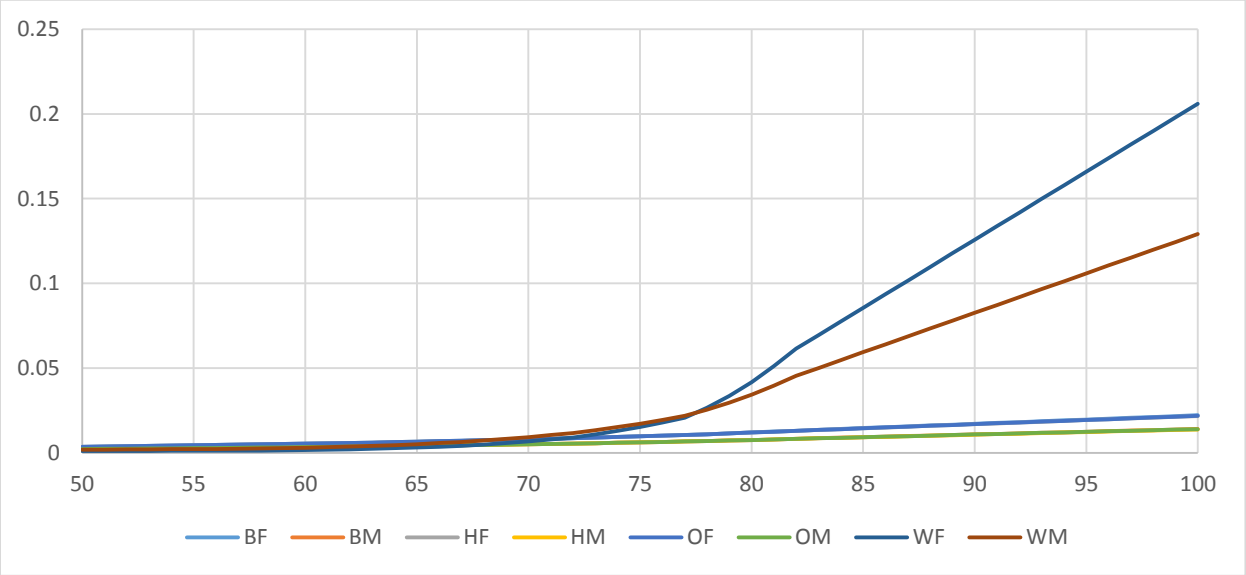
	No Treatment	Treatment	Net QALY Gains
2016	-36,432	-35,058	1,374
2017	-36,973	-35,222	1,752
2018	-37,530	-34,503	3,027
2019	-38,133	-27,762	10,371
2020	-38,801	-22,933	15,869
2021	-39,571	-18,011	21,560
2022	-40,437	-16,830	23,608
2023	-41,383	-18,577	22,807
2024	-42,419	-21,667	20,751
2025	-43,592	-25,763	17,830
2026	-44,893	-26,513	18,379
2027	-46,296	-27,271	19,025
2028	-47,798	-28,057	19,741
2029	-49,422	-28,828	20,594
2030	-51,091	-29,653	21,438
2031	-52,805	-30,495	22,310
2032	-54,560	-31,357	23,203
2033	-56,336	-32,244	24,092
2034	-58,140	-33,098	25,041
2035	-59,926	-33,964	25,962
2036	-61,679	-34,820	26,859
2037	-63,410	-35,622	27,788
2038	-65,083	-36,424	28,659
2039	-66,705	-37,198	29,508
2040	-68,242	-37,948	30,294
2041	-69,679	-38,634	31,045
2042	-70,998	-39,271	31,727
2043	-72,187	-39,841	32,346
2044	-73,244	-40,333	32,911
2045	-74,143	-40,782	33,361

AMD – Geographic Atrophy

Prevalence

VPUS reports prevalence rates for ages 50 and older. Based on the NHANES retinal image results, 60.74% of patients with advanced AMD had GA, while the balance (39.26%) had CNV. We apply this breakdown to the prevalence rates of AMD by all age groups. Linearized prevalence rates by age, race and gender are shown in **Figure GA1**, which shows that whites, and white females have disproportionately high incidence of GA at older ages.

Figure GA1. CNV AMD Prevalence Rates by Age



Multiplying the prevalence rates by the population projections by age, race, and gender results in the population prevalence forecasts shown in **Figure 2**. The leading edge of this figure depicts the prevalence of GA by age in 2016. Subsequent lines represent the prevalence distribution in future years. **Table 1** includes the prevalence predictions by age group.

Figure GA2. Current and future prevalence of GA

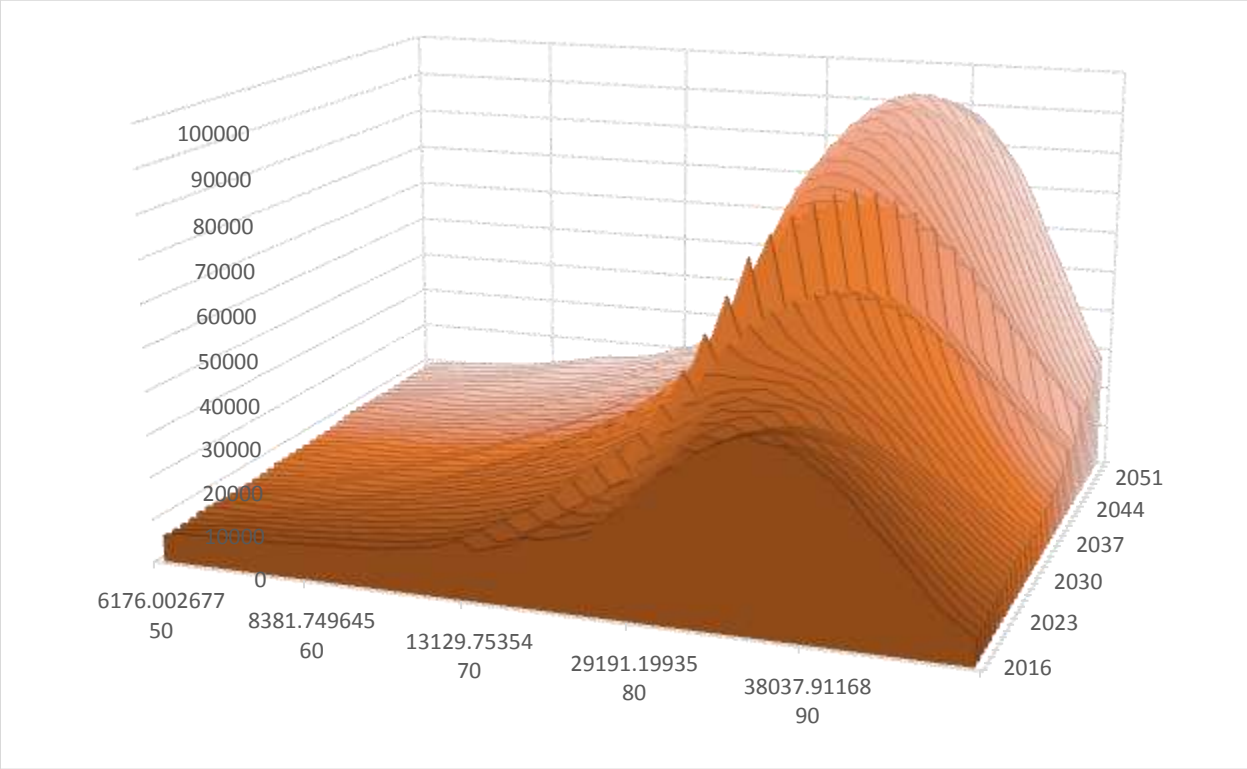


Table GA1. Prevalence Predictions by Age Group

	age50-64	age 65-89	age 90+	Total Age 50+
2016	116,542	613,645	229,091	959,278
2017	118,498	623,061	234,418	975,977
2018	120,259	634,418	238,899	993,576
2019	121,818	648,631	241,922	1,012,372
2020	123,360	664,287	245,475	1,033,122
2021	124,857	683,200	247,726	1,055,784
2022	125,901	705,194	249,177	1,080,272
2023	126,730	729,906	250,050	1,106,686
2024	127,390	757,385	250,251	1,135,026
2025	127,742	785,460	253,042	1,166,244
2026	128,136	815,569	255,863	1,199,567
2027	128,710	847,398	259,201	1,235,309
2028	129,166	879,509	264,613	1,273,289
2029	129,672	913,395	270,422	1,313,489
2030	130,727	946,891	277,532	1,355,150
2031	132,200	979,240	286,091	1,397,531
2032	134,039	1,008,939	297,679	1,440,657
2033	135,815	1,033,091	315,270	1,484,176
2034	137,344	1,061,224	329,040	1,527,608
2035	138,415	1,090,759	341,734	1,570,909
2036	139,550	1,120,808	353,135	1,613,493
2037	141,145	1,130,145	383,736	1,655,025
2038	143,310	1,144,714	407,327	1,695,351
2039	145,962	1,159,705	428,579	1,734,246
2040	148,765	1,174,103	448,563	1,771,431
2041	152,101	1,186,298	467,950	1,806,349
2042	155,250	1,196,167	487,250	1,838,666
2043	158,310	1,202,825	506,851	1,867,985
2044	161,199	1,206,238	526,731	1,894,167
2045	163,223	1,206,931	546,947	1,917,101

Diagnosis Rate

In 2005-2008 NHANES data, 49.66% of all patients identified with GA in the retinal image had self-reported a history of AMD diagnosis, indicating the diagnosis rate. We apply the inverse of this diagnosis rate to the prevalence predictions to estimate the undiagnosed population with GA.

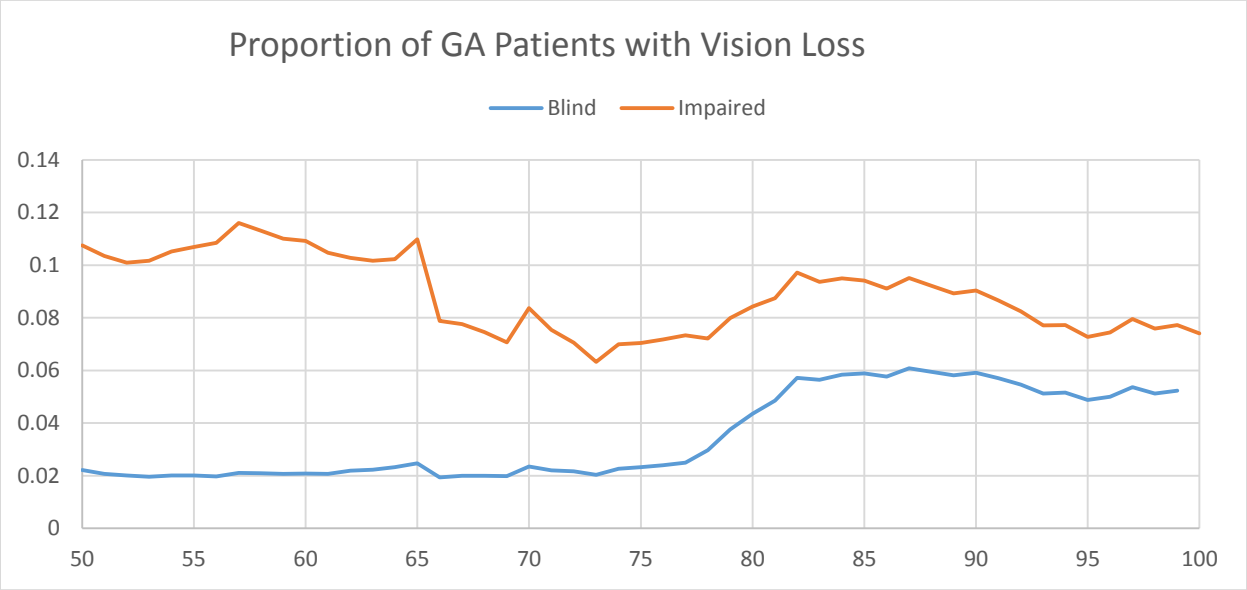
Proportion of GA Patients with Vision Loss

We predicted the total number of patients impaired or blind based on the EDPRG disease allocations of vision loss by disorder type, which is based on data pre-dating most effective treatments such as anti-VEGF, and the prevalence of visual impairment and blindness reported by VPUS. However, neither source differentiated CNV vs GA. Using a separate model, we estimated the allocation of vision loss due to AMD between CNV and GA, which is a function of both the relative incidence of each condition, as well as the amount of vision loss accrued per year, as measured in the probability of vision loss times the acuity loss as measured in logMar. Based on this approach, we estimated that on average, GA yields 0.04331 logMar of acuity loss per year, while untreated CNV causes 0.2557 logMar of acuity loss per

year. Based on the relative proportions of GA to CNV identified in NHANES, we estimate that 80% of prevalent AMD impairment and blindness is due to CNV, and 20% is due to GA.

Based on this level of vision loss, we estimated the proportion of GA patients with impairment or blindness per year, as shown in **Figure GA3**. Total vision loss equates to the sum of these lines, and thus we predict that approximately 5% of GA patients currently have visual impairment or blindness.

Figure GA3. Proportion of GA Patients with Impairment or Blindness



Treatment

We assume zero effective treatments for GA. Potentially, high anti-oxidant vitamins may slow the progression of early AMD, leading to decreased future incidence of GA. The AREDS study indicated that progression may be reduced by 25%. For this analysis, we did not include the impact of vitamin therapy, both because of continued controversy over its effectiveness, and because the VPUS does not include the prevalence of early AMD.

Table GA2. Prevalence of Vision Loss

	No Treatment			Treatment			Net		
	Impaired	Blind	Total	Impaired	Blind	Total	Impaired	Blind	Total
2016	42,084	21,254	63,338	42,084	21,254	63,338	0	0	0
2017	42,771	21,516	64,287	42,771	21,516	64,287	0	0	0
2018	43,474	21,786	65,260	43,474	21,786	65,260	0	0	0
2019	44,227	22,086	66,314	44,227	22,086	66,314	0	0	0
2020	45,062	22,433	67,495	45,062	22,433	67,495	0	0	0
2021	45,986	22,837	68,822	45,986	22,837	68,822	0	0	0
2022	47,014	23,311	70,324	47,014	23,311	70,324	0	0	0
2023	48,126	23,843	71,970	48,126	23,843	71,970	0	0	0
2024	49,341	24,443	73,784	49,341	24,443	73,784	0	0	0
2025	50,694	25,142	75,836	50,694	25,142	75,836	0	0	0
2026	52,130	25,909	78,039	52,130	25,909	78,039	0	0	0
2027	53,696	26,765	80,461	53,696	26,765	80,461	0	0	0
2028	55,355	27,692	83,047	55,355	27,692	83,047	0	0	0
2029	57,183	28,737	85,920	57,183	28,737	85,920	0	0	0
2030	59,032	29,792	88,824	59,032	29,792	88,824	0	0	0
2031	60,902	30,880	91,781	60,902	30,880	91,781	0	0	0
2032	62,805	31,994	94,800	62,805	31,994	94,800	0	0	0
2033	64,705	33,113	97,818	64,705	33,113	97,818	0	0	0
2034	66,657	34,276	100,932	66,657	34,276	100,932	0	0	0
2035	68,567	35,417	103,984	68,567	35,417	103,984	0	0	0
2036	70,411	36,534	106,945	70,411	36,534	106,945	0	0	0
2037	72,257	37,661	109,918	72,257	37,661	109,918	0	0	0
2038	74,021	38,736	112,757	74,021	38,736	112,757	0	0	0
2039	75,740	39,782	115,523	75,740	39,782	115,523	0	0	0
2040	77,373	40,765	118,137	77,373	40,765	118,137	0	0	0
2041	78,904	41,693	120,596	78,904	41,693	120,596	0	0	0
2042	80,308	42,544	122,852	80,308	42,544	122,852	0	0	0
2043	81,576	43,314	124,890	81,576	43,314	124,890	0	0	0
2044	82,736	44,011	126,747	82,736	44,011	126,747	0	0	0
2045	83,725	44,591	128,316	83,725	44,591	128,316	0	0	0

Impact on Costs

The annual costs of medical management of AMD is $3,740 based on 2003-2008 MEPS data. This cost is likely an overestimate because we cannot differentiate costs for different types of retinal disorders in the MEPS data, and thus much of this costs may reflect treatment for CNV, although it is unlikely to be biased by anti-VEGF therapy as the costs are based on 2003-2008 data.

Costs of GA are shown in **Figure GA5** and **Table GA3**. Because we assume no treatment, there are no impacts on vision loss costs shown.

Figure GA5. Net Costs

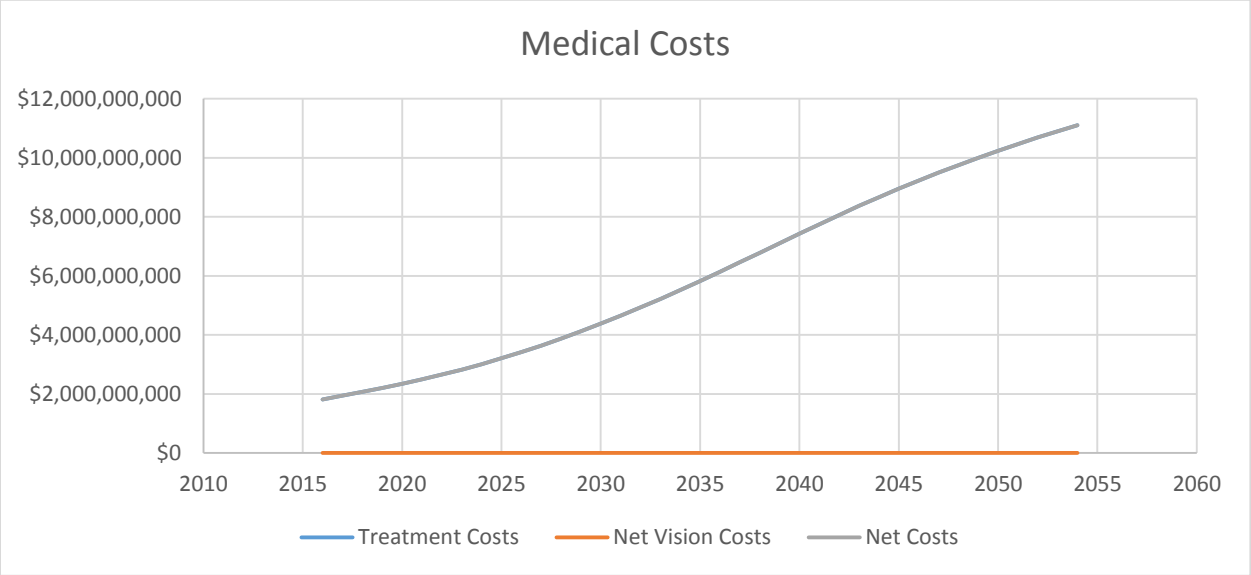


Table GA3. Net Costs

	Treatment Costs	Net Vision Costs	Net Costs
2016	$1,813,685,438	$0	$1,813,685,438
2017	$1,845,129,630	$0	$1,845,129,630
2018	$1,878,270,357	$0	$1,878,270,357
2019	$1,913,662,905	$0	$1,913,662,905
2020	$1,952,736,501	$0	$1,952,736,501
2021	$1,995,407,526	$0	$1,995,407,526
2022	$2,041,518,184	$0	$2,041,518,184
2023	$2,091,255,193	$0	$2,091,255,193
2024	$2,144,617,918	$0	$2,144,617,918
2025	$2,203,400,013	$0	$2,203,400,013
2026	$2,266,146,804	$0	$2,266,146,804
2027	$2,333,445,662	$0	$2,333,445,662
2028	$2,404,959,233	$0	$2,404,959,233
2029	$2,480,653,811	$0	$2,480,653,811
2030	$2,559,098,211	$0	$2,559,098,211
2031	$2,638,898,182	$0	$2,638,898,182
2032	$2,720,101,572	$0	$2,720,101,572
2033	$2,802,044,083	$0	$2,802,044,083
2034	$2,883,822,006	$0	$2,883,822,006
2035	$2,965,353,835	$0	$2,965,353,835
2036	$3,045,537,601	$0	$3,045,537,601
2037	$3,123,738,922	$0	$3,123,738,922
2038	$3,199,668,897	$0	$3,199,668,897
2039	$3,272,906,541	$0	$3,272,906,541
2040	$3,342,923,343	$0	$3,342,923,343
2041	$3,408,671,334	$0	$3,408,671,334
2042	$3,469,523,359	$0	$3,469,523,359
2043	$3,524,729,591	$0	$3,524,729,591
2044	$3,574,028,862	$0	$3,574,028,862
2045	$3,617,213,582	$0	$3,617,213,582

Impact on QALYs

QALY outcomes of GA are shown in **Figure GA6** and **Table GA4**. Because we assume no treatment, there are no impacts on QALYs from treatment shown.

Figure GA6. QALY Losses from Undiagnosed GA

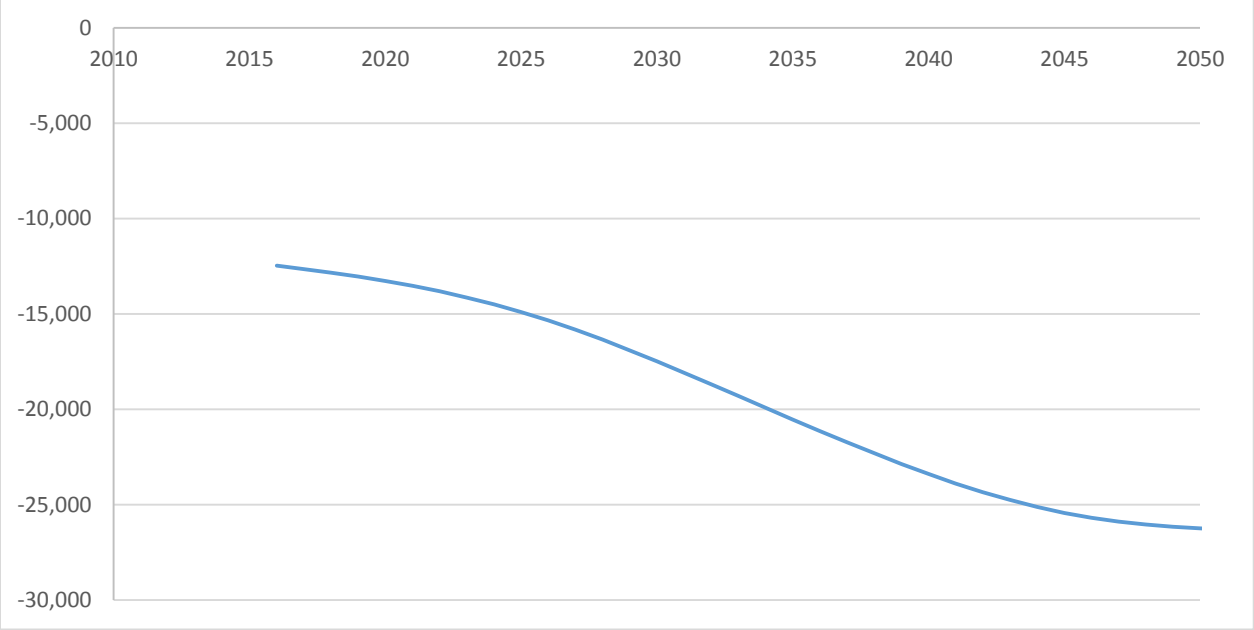


Table GA4. Net QALYs

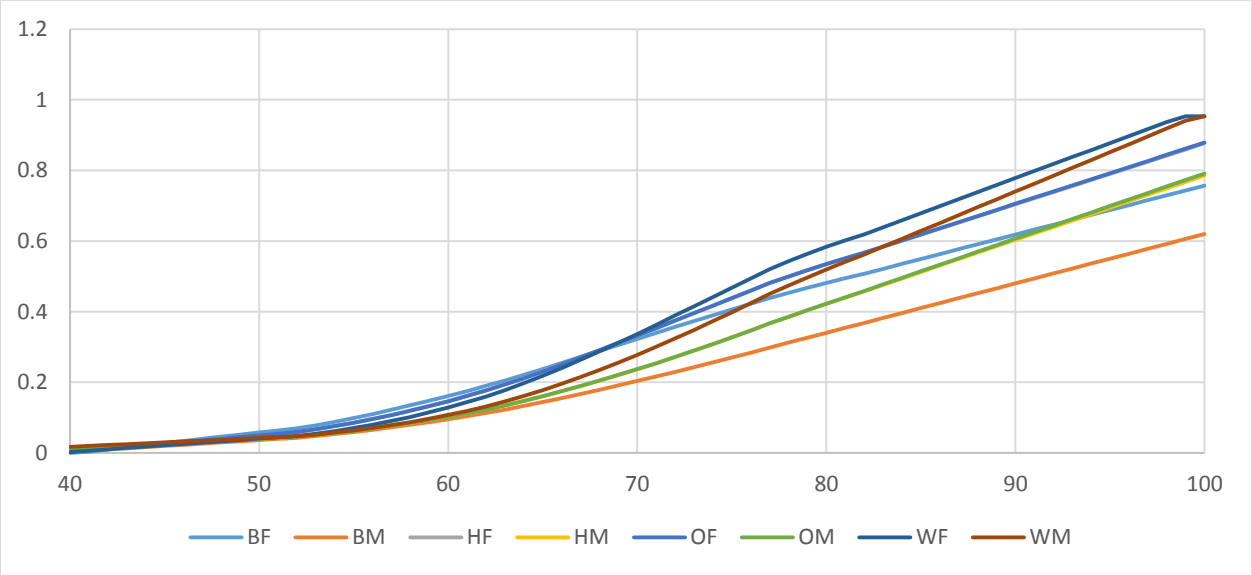
	No Treatment	Treatment	Net QALY Gains
2016	-12,472	-12,472	0
2017	-12,653	-12,653	0
2018	-12,838	-12,838	0
2019	-13,040	-13,040	0
2020	-13,267	-13,267	0
2021	-13,524	-13,524	0
2022	-13,816	-13,816	0
2023	-14,138	-14,138	0
2024	-14,494	-14,494	0
2025	-14,899	-14,899	0
2026	-15,336	-15,336	0
2027	-15,818	-15,818	0
2028	-16,334	-16,334	0
2029	-16,908	-16,908	0
2030	-17,489	-17,489	0
2031	-18,082	-18,082	0
2032	-18,687	-18,687	0
2033	-19,293	-19,293	0
2034	-19,920	-19,920	0
2035	-20,533	-20,533	0
2036	-21,130	-21,130	0
2037	-21,730	-21,730	0
2038	-22,302	-22,302	0
2039	-22,860	-22,860	0
2040	-23,386	-23,386	0
2041	-23,882	-23,882	0
2042	-24,336	-24,336	0
2043	-24,747	-24,747	0
2044	-25,121	-25,121	0
2045	-25,436	-25,436	0

Cataract

Prevalence

VPUS reports prevalence rates of cataract for ages 40 and older. Linearized prevalence rates by age, race and gender are shown in **Figure CAT1**, which shows that cataract prevalence, defined as lifetime incidence of ever having cataract, increases linearly with age and may exceed 80% among the oldest age groups.

Figure CAT1. Cataract Prevalence Rates by Age



Multiplying the prevalence rates by the population projections by age, race, and gender results in the population prevalence forecasts shown in **Figure CAT2**. Cataract prevalence includes cataract or psuedophakia, and thus represents the cumulative total of cataract and prior cataract surgery. The leading edge of this figure depicts the prevalence of cataract by age in 2016. Subsequent lines represent the prevalence distribution in future years. **Table 1** includes the prevalence predictions by age group.

Figure CAT2. Current and future prevalence of cataract

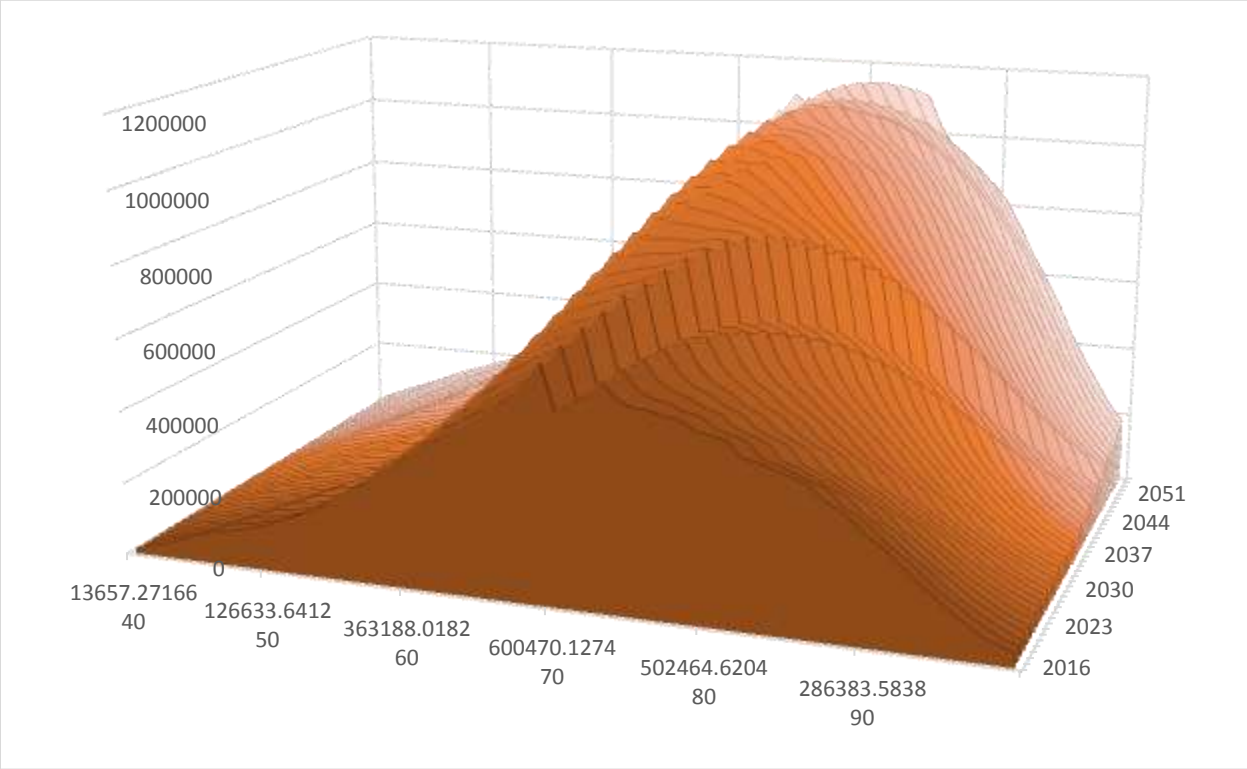


Table CAT1. Prevalence Predictions by Age Group

	Age 40-64	Age 65-89	Age 90+	Total Age 40+
2016	4,915,660	12,432,339	1,533,820	18,881,819
2017	4,984,142	12,808,475	1,575,190	19,367,807
2018	5,040,513	13,217,785	1,611,641	19,869,939
2019	5,083,427	13,665,473	1,639,023	20,387,923
2020	5,109,758	14,138,582	1,672,649	20,920,989
2021	5,135,275	14,636,489	1,695,421	21,467,185
2022	5,146,499	15,166,265	1,713,340	22,026,104
2023	5,154,659	15,713,450	1,728,535	22,596,644
2024	5,160,720	16,276,761	1,739,495	23,176,976
2025	5,146,899	16,846,500	1,770,490	23,763,889
2026	5,139,812	17,414,426	1,800,970	24,355,209
2027	5,137,553	17,976,475	1,833,933	24,947,961
2028	5,131,288	18,527,049	1,881,329	25,539,665
2029	5,123,871	19,073,047	1,930,683	26,127,601
2030	5,125,726	19,593,453	1,991,246	26,710,425
2031	5,159,271	20,066,765	2,058,712	27,284,747
2032	5,206,602	20,495,232	2,145,976	27,847,810
2033	5,256,193	20,867,331	2,273,705	28,397,229
2034	5,299,177	21,256,378	2,375,404	28,930,960
2035	5,314,424	21,659,594	2,472,768	29,446,786
2036	5,335,893	22,047,706	2,560,846	29,944,444
2037	5,384,015	22,253,338	2,785,336	30,422,689
2038	5,454,993	22,462,154	2,963,605	30,880,752
2039	5,539,341	22,652,512	3,126,692	31,318,545
2040	5,614,655	22,835,545	3,286,641	31,736,841
2041	5,710,691	22,987,399	3,438,213	32,136,304
2042	5,799,412	23,130,328	3,587,813	32,517,553
2043	5,890,251	23,248,548	3,743,661	32,882,461
2044	5,976,976	23,351,230	3,905,886	33,234,092
2045	6,032,787	23,464,834	4,077,032	33,574,654

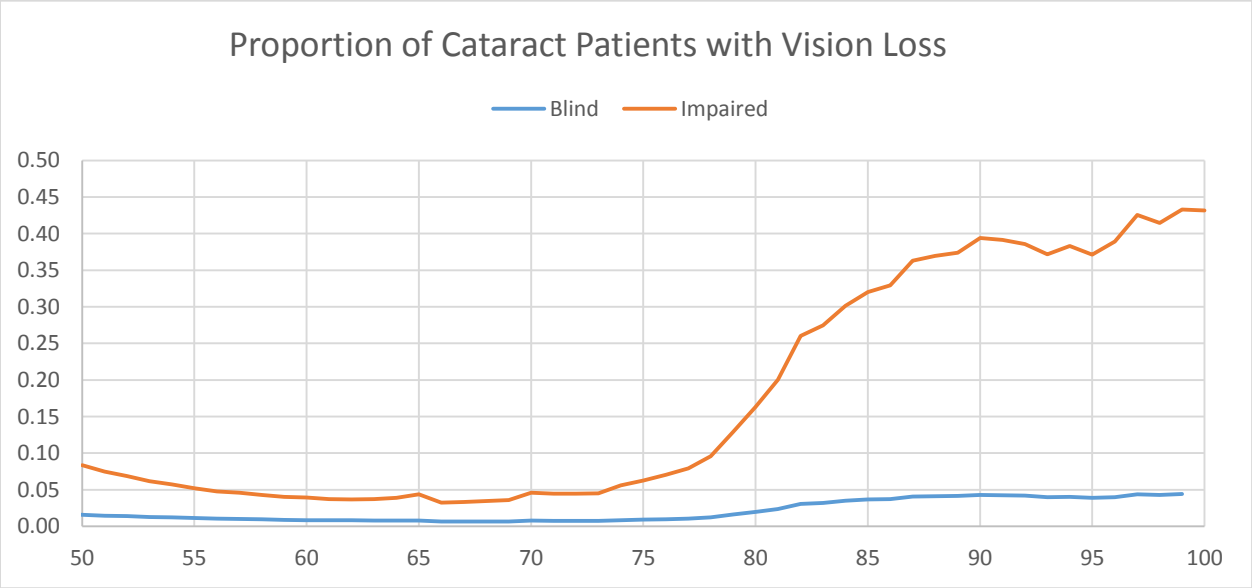
Diagnosis Rate

In 2005-2008 NHANES data, patients were asked if they had a history of cataract surgery. The total prevalence of cataract surgery was the equivalent of 12.67million persons, or 51.92% of the estimated true prevalence of cataract from VPUS. The VPUS estimate represents patients with current cataract, as well as previously treated cataract, while NHANES would only represent previously treated cataract. Thus, we assume that overall, 51.92% of prevalent cataract patients reported by VPUS are treated, and the remaining 48.08% are untreated. We apply this untreated rate to the VPUS prevalence predictions to estimate the untreated population with cataract.

Vision Loss Attributable to Cataract

We predicted the total number of patients impaired or blind based on the EDPRG disease allocations of vision loss by disorder type, and the prevalence of visual impairment and blindness reported by VPUS. Based on this level of vision loss, we estimated the proportion of cataract patients with impairment or blindness per year, as shown in **Figure CAT3**. Total vision loss equates to the sum of these lines, and thus we predict that 13.4% of currently untreated cataract patients have visual impairment and less than 1.7% are blind.

Figure CAT3. Proportion of Cataract Patients with Impairment or Blindness



Treatment

Treatment for cataract is considered to include one-time surgery. We assume that cataract surgery will have a 95% success rate for eliminating blindness and visual impairment.
Table CAT2 shows our projected prevalent burden of cataract-attributable visual impairment with and without treatment, and net difference from treatment.

Table CAT2. Prevalence of Vision Loss

	No Treatment			Treatment			Net		
	Impaired	Blind	Total	Impaired	Blind	Total	Impaired	Blind	Total
2016	1,225,654	157,469	1,383,123	61,283	7,873	69,156	-1,164,371	-149,596	-1,313,967
2017	1,248,583	161,456	1,410,039	62,429	8,073	70,502	-1,186,154	-153,383	-1,339,537
2018	1,272,148	165,587	1,437,735	63,607	8,279	71,887	-1,208,541	-157,307	-1,365,848
2019	1,297,386	169,994	1,467,380	64,869	8,500	73,369	-1,232,517	-161,494	-1,394,011
2020	1,325,070	174,721	1,499,791	66,254	8,736	74,990	-1,258,817	-165,985	-1,424,801
2021	1,355,483	179,780	1,535,263	67,774	8,989	76,763	-1,287,709	-170,791	-1,458,500
2022	1,389,773	185,307	1,575,080	69,489	9,265	78,754	-1,320,284	-176,041	-1,496,326
2023	1,427,099	191,170	1,618,269	71,355	9,558	80,913	-1,355,744	-181,611	-1,537,356
2024	1,467,927	197,491	1,665,418	73,396	9,875	83,271	-1,394,531	-187,616	-1,582,147
2025	1,513,217	204,356	1,717,573	75,661	10,218	85,879	-1,437,556	-194,138	-1,631,695
2026	1,562,005	211,644	1,773,649	78,100	10,582	88,682	-1,483,905	-201,062	-1,684,967
2027	1,615,217	219,522	1,834,739	80,761	10,976	91,737	-1,534,456	-208,546	-1,743,002
2028	1,672,123	227,816	1,899,939	83,606	11,391	94,997	-1,588,517	-216,425	-1,804,942
2029	1,734,987	236,812	1,971,799	86,749	11,841	98,590	-1,648,238	-224,971	-1,873,209
2030	1,799,022	246,011	2,045,033	89,951	12,301	102,252	-1,709,071	-233,710	-1,942,781
2031	1,864,928	255,483	2,120,410	93,246	12,774	106,021	-1,771,681	-242,709	-2,014,390
2032	1,932,536	265,276	2,197,812	96,627	13,264	109,891	-1,835,909	-252,013	-2,087,922
2033	2,000,548	275,071	2,275,619	100,027	13,754	113,781	-1,900,520	-261,317	-2,161,838
2034	2,071,113	285,191	2,356,304	103,556	14,260	117,815	-1,967,557	-270,931	-2,238,488
2035	2,141,031	295,269	2,436,301	107,052	14,763	121,815	-2,033,980	-280,506	-2,314,485
2036	2,210,123	305,231	2,515,353	110,506	15,262	125,768	-2,099,617	-289,969	-2,389,586
2037	2,280,183	315,345	2,595,528	114,009	15,767	129,776	-2,166,174	-299,578	-2,465,751
2038	2,348,254	325,185	2,673,439	117,413	16,259	133,672	-2,230,841	-308,926	-2,539,767
2039	2,415,291	334,913	2,750,205	120,765	16,746	137,510	-2,294,527	-318,167	-2,612,694
2040	2,479,768	344,310	2,824,078	123,988	17,215	141,204	-2,355,780	-327,094	-2,682,874
2041	2,541,670	353,385	2,895,055	127,084	17,669	144,753	-2,414,587	-335,715	-2,750,302
2042	2,600,287	362,191	2,962,478	130,014	18,110	148,124	-2,470,273	-344,082	-2,814,354
2043	2,655,298	370,488	3,025,785	132,765	18,524	151,289	-2,522,533	-351,963	-2,874,496
2044	2,707,636	378,511	3,086,147	135,382	18,926	154,307	-2,572,254	-359,586	-2,931,840
2045	2,755,219	386,013	3,141,232	137,761	19,301	157,062	-2,617,458	-366,712	-2,984,170

Impact on Costs

The annual costs of medical management of cataract is $2,640 for ages 40-64 and $3,740, based on 2003-2008 MEPS data. We apply this cost of treatment for one year per patient. In 2016, this cost is applied to all prevalent cases, in future years this cost is applied to incident cases of cataract. It is plausible that this cost is an underestimate, as it closely approximates reported surgery fees per eye. However, it may also be possible that MEPS may capture cataract costs for associated for patients receiving follow-up care, when the actual surgery occurred prior to the survey period. By not assigning follow-up costs in later years, we may also be underestimating these costs.

Figure CAT5. Net Costs

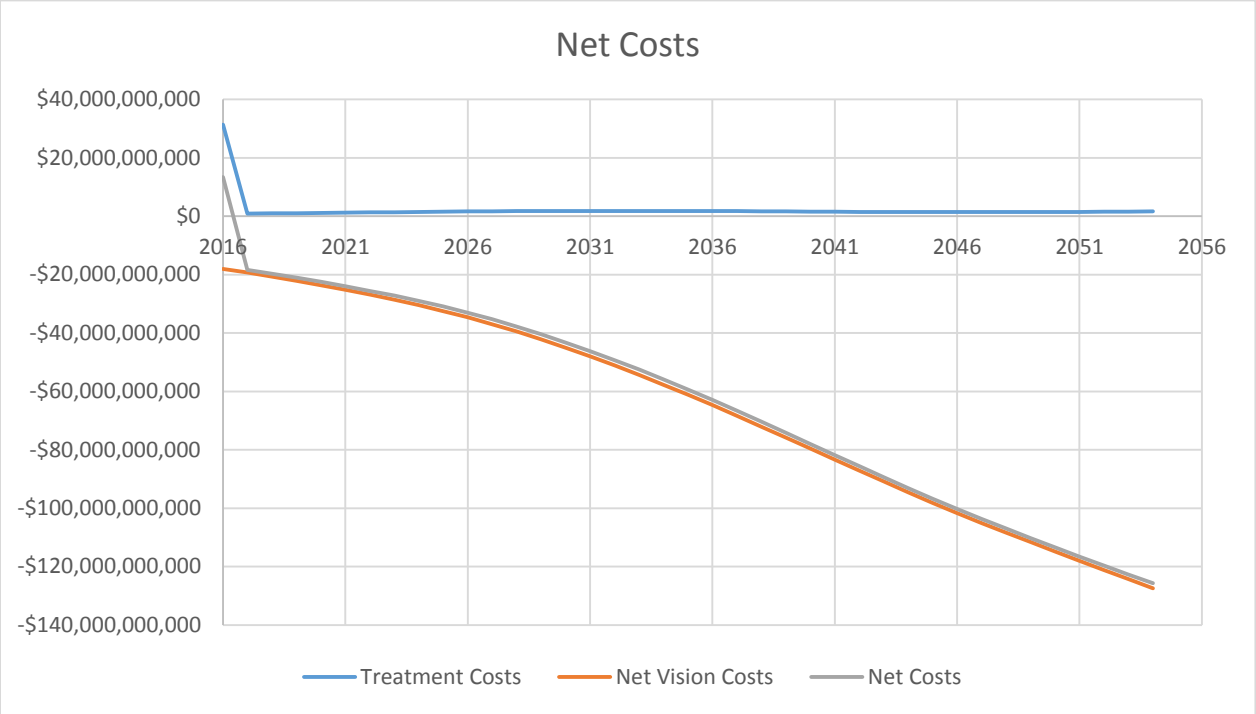


Table CAT3. Net Costs

	Treatment Costs	Net Vision Costs	Net Costs
2016	$31,355,553,152	-$18,018,863,719	$13,336,689,434
2017	$881,301,824	-$19,279,081,186	-$18,397,779,363
2018	$961,369,358	-$20,653,698,762	-$19,692,329,405
2019	$1,045,122,544	-$22,107,807,984	-$21,062,685,439
2020	$1,132,690,448	-$23,629,693,192	-$22,497,002,744
2021	$1,209,954,984	-$25,221,043,747	-$24,011,088,763
2022	$1,297,931,913	-$26,872,822,373	-$25,574,890,461
2023	$1,378,269,095	-$28,589,033,064	-$27,210,763,970
2024	$1,455,540,956	-$30,433,952,508	-$28,978,411,553
2025	$1,571,853,649	-$32,498,591,333	-$30,926,737,684
2026	$1,620,644,778	-$34,653,433,466	-$33,032,788,688
2027	$1,666,021,037	-$36,980,527,000	-$35,314,505,963
2028	$1,729,147,628	-$39,470,124,939	-$37,740,977,312
2029	$1,776,179,344	-$42,183,427,763	-$40,407,248,418
2030	$1,790,580,669	-$45,014,928,112	-$43,224,347,443
2031	$1,787,540,468	-$47,980,862,201	-$46,193,321,733
2032	$1,789,408,960	-$51,087,057,791	-$49,297,648,831
2033	$1,791,833,861	-$54,296,979,151	-$52,505,145,290
2034	$1,793,577,084	-$57,674,586,512	-$55,881,009,428
2035	$1,806,927,851	-$61,142,209,193	-$59,335,281,341
2036	$1,781,323,330	-$64,682,703,238	-$62,901,379,908
2037	$1,725,085,581	-$68,345,457,892	-$66,620,372,312
2038	$1,665,173,063	-$72,038,825,984	-$70,373,652,921
2039	$1,610,870,190	-$75,792,536,856	-$74,181,666,667
2040	$1,581,516,484	-$79,558,845,688	-$77,977,329,204
2041	$1,516,043,572	-$83,326,874,143	-$81,810,830,571
2042	$1,483,019,728	-$87,085,444,938	-$85,602,425,210
2043	$1,443,196,846	-$90,798,806,488	-$89,355,609,641
2044	$1,421,613,448	-$94,502,966,760	-$93,081,353,311
2045	$1,442,726,245	-$98,127,299,634	-$96,684,573,390

Impact on QALYs

Figure CAT6. QALY Losses from Cataract, Gains from Treatment

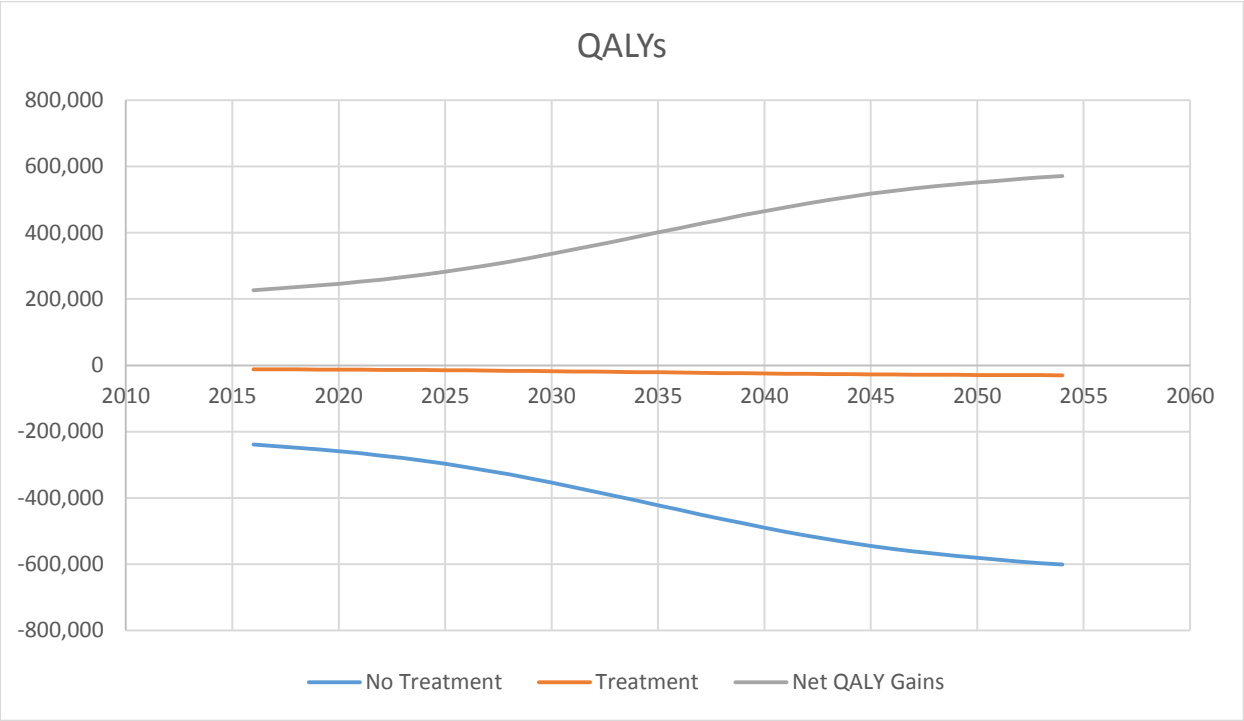


Table CAT4. Net QALYs

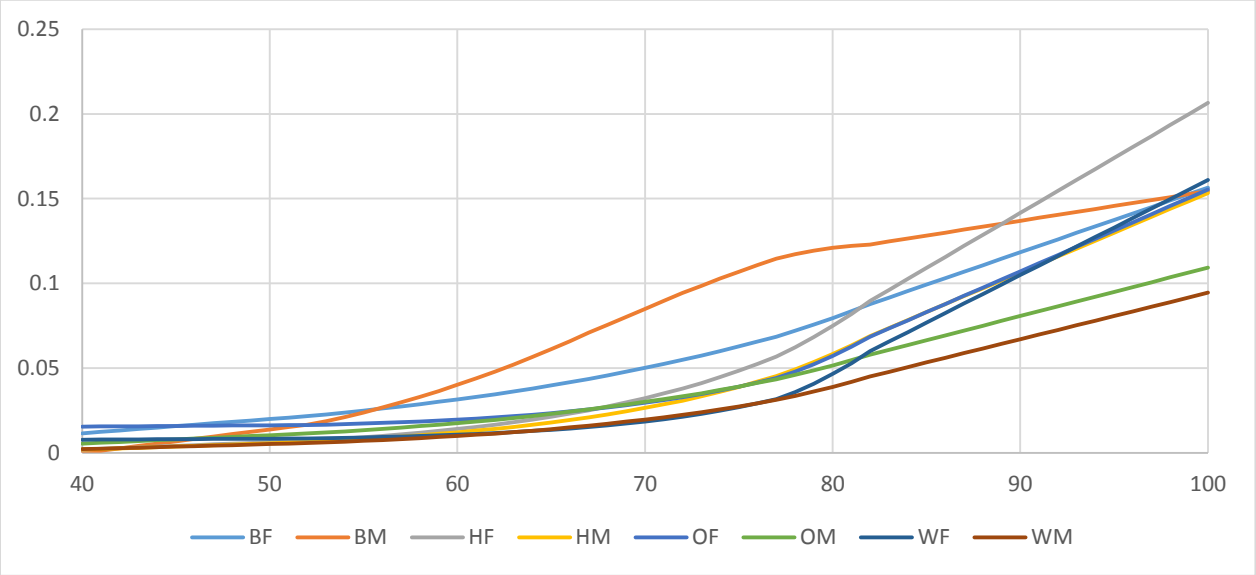
	No Treatment	Treatment	Net QALY Gains
2016	-238,621	-11,931	226,690
2017	-243,366	-12,168	231,198
2018	-248,252	-12,413	235,840
2019	-253,480	-12,674	240,806
2020	-259,186	-12,959	246,227
2021	-265,418	-13,271	252,147
2022	-272,396	-13,620	258,777
2023	-279,952	-13,998	265,954
2024	-288,191	-14,410	273,781
2025	-297,291	-14,865	282,426
2026	-307,065	-15,353	291,712
2027	-317,706	-15,885	301,820
2028	-329,050	-16,453	312,598
2029	-341,537	-17,077	324,460
2030	-354,266	-17,713	336,553
2031	-367,369	-18,368	349,000
2032	-380,830	-19,042	361,789
2033	-394,357	-19,718	374,639
2034	-408,380	-20,419	387,961
2035	-422,288	-21,114	401,173
2036	-436,032	-21,802	414,230
2037	-449,972	-22,499	427,474
2038	-463,521	-23,176	440,345
2039	-476,873	-23,844	453,030
2040	-489,727	-24,486	465,240
2041	-502,081	-25,104	476,977
2042	-513,838	-25,692	488,146
2043	-524,879	-26,244	498,635
2044	-535,420	-26,771	508,649
2045	-545,058	-27,253	517,806

Glaucoma

Prevalence

VPUS reports prevalence rates of glaucoma for ages 40 and older. Glaucoma is defined as primary open angle glaucoma with signs of optic nerve damage, visual field loss or both. The prevalence estimates do not include patients with only elevated intraocular pressure (IOC), or suspect glaucoma. Linearized prevalence rates by age, race and gender are shown in **Figure G1**.

Figure G1. Glaucoma Prevalence Rates by Age



Multiplying the prevalence rates by the population projections by age, race, and gender results in the population prevalence forecasts shown in **Figure G2**. The leading edge of this figure depicts the prevalence of glaucoma by age in 2016. Subsequent lines represent the prevalence distribution in future years. Currently, the prevalence of glaucoma is relatively flat from the late 50's through the 80's. However, this figure shows that glaucoma prevalence will increase dramatically in the coming years, driven by the aging baby-boomers and increasing minority populations, which generally have higher prevalence of glaucoma than whites. **Table G1** includes the prevalence predictions by age group.

Figure G2. Current and future prevalence of glaucoma

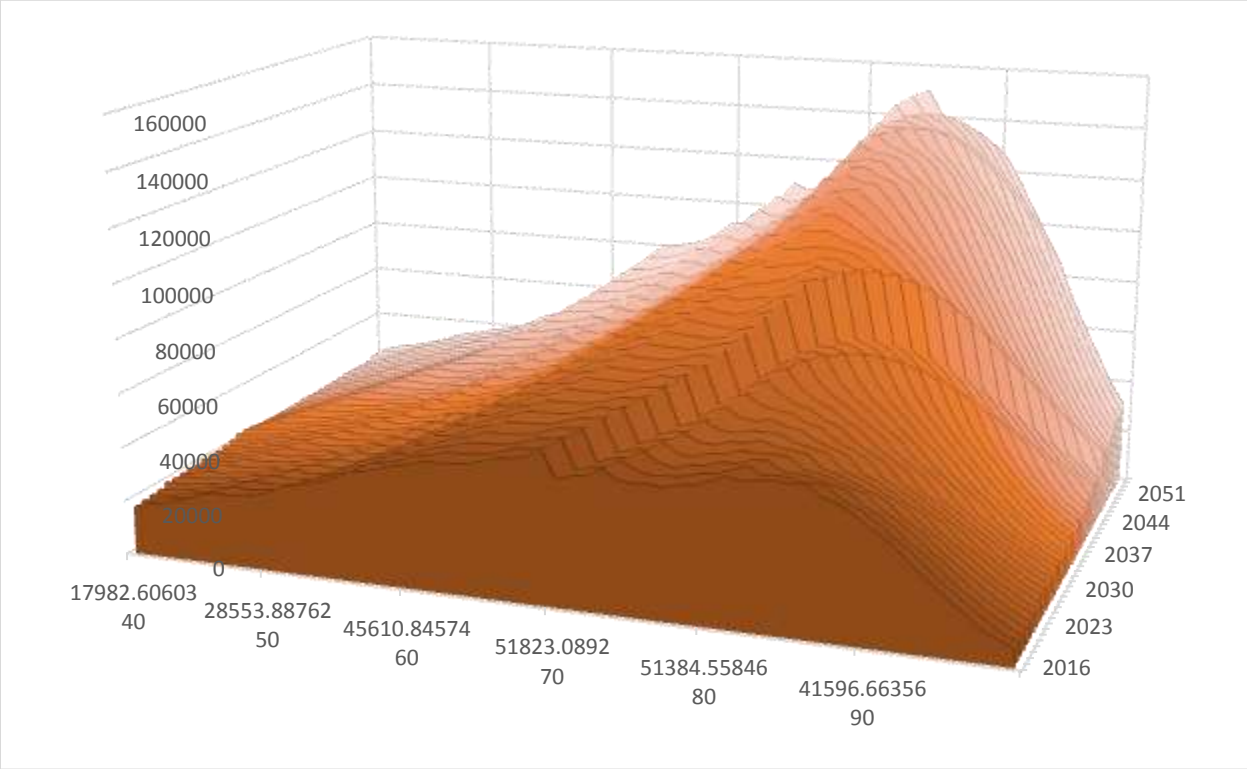


Table G1. Glaucoma Prevalence Predictions by Age Group

	Age 40-64	Age 65-89	Age 90+	Total Age 40+
2016	831,899	1,251,071	236,703	2,319,674
2017	839,653	1,288,798	243,743	2,372,193
2018	846,224	1,330,044	250,055	2,426,323
2019	851,626	1,375,842	255,050	2,482,518
2020	856,131	1,424,711	260,940	2,541,783
2021	860,241	1,477,490	265,138	2,602,869
2022	863,280	1,534,531	268,598	2,666,409
2023	866,244	1,594,304	271,637	2,732,185
2024	868,636	1,657,162	274,023	2,799,820
2025	869,469	1,721,790	279,255	2,870,514
2026	871,619	1,787,169	284,390	2,943,179
2027	874,420	1,853,628	289,813	3,017,861
2028	877,318	1,920,242	297,315	3,094,875
2029	880,804	1,988,246	305,168	3,174,218
2030	885,866	2,054,634	314,796	3,255,297
2031	894,430	2,117,346	325,362	3,337,138
2032	904,530	2,175,668	338,785	3,418,984
2033	914,358	2,228,037	358,139	3,500,535
2034	923,860	2,283,701	374,147	3,581,708
2035	929,929	2,342,236	389,845	3,662,010
2036	936,553	2,400,469	404,267	3,741,288
2037	945,849	2,435,469	438,113	3,819,430
2038	957,470	2,472,502	466,210	3,896,182
2039	970,683	2,508,144	492,489	3,971,316
2040	983,138	2,543,041	518,734	4,044,914
2041	997,639	2,574,812	543,819	4,116,270
2042	1,010,810	2,605,779	568,479	4,185,068
2043	1,024,249	2,633,270	594,189	4,251,708
2044	1,037,092	2,658,049	621,035	4,316,176
2045	1,046,273	2,682,592	649,494	4,378,358

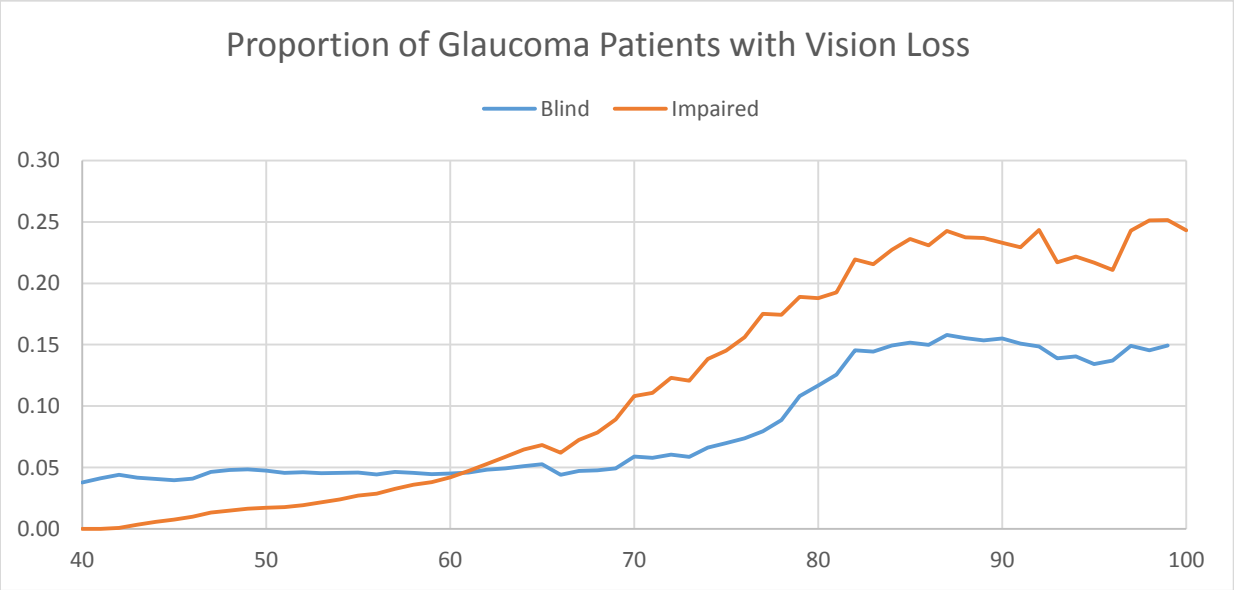
Diagnosis Rate

We calculated the diagnosis rate of glaucoma in NHANES data. From 2005-2008, respondents were asked if they had ever been diagnosed with glaucoma, and were administered a retinal image and visual field test. In 2012, selected NHANES retinal images were regraded to assess for signs of glaucoma. Due to the relatively small sample of glaucoma cases identified, and uncertainty over the method for selecting images for regrading, we did not attempt to calculate the prevalence of glaucoma using NHANES data. However, we were able to estimate that 42.57% of respondents identified with glaucoma who previously reported a glaucoma diagnosis. We apply the inverse of this rate, 57.43% as the undiagnosed rate to the VPUS prevalence predictions to estimate the undiagnosed population with glaucoma.

Vision Loss Attributable to Glaucoma

We predicted the total number of patients impaired or blind based on the EDPRG disease allocations of vision loss by disorder type, and the prevalence of visual impairment and blindness reported by VPUS. Based on this level of vision loss, we estimated the proportion of glaucoma patients with impairment or blindness per year, as shown in **Figure G3**. Total vision loss equates to the sum of these lines. Overall, we estimate that 8.3% of glaucoma patients are blind and 12.1% are impaired. Among glaucoma patients in their 80's and 90's, approximately 15% are blind and nearly 25% are impaired.

Figure G3. Proportion of Cataract Patients with Impairment or Blindness



Treatment

We calculated the efficacy of glaucoma treatment using the MEDS model. The MEDS model simulates the progression of glaucoma as measured in visual field. The baseline probability of losing visual field per year is a function of treatment efficacy, age, intraocular pressure, and prior history of glaucoma assessed across both eyes. [38] Treatment of glaucoma is assumed to follow a pattern in which a succession of up to four medications are used to control IOP, including beta blockers, prostaglandin analogues, alpha-2 agonists and topical carbonic inhibitors. Each medication is associated with a risk of treatment failure, indicating a failure to control IOP. [39] Failure of a medication immediately triggers the next medication in the sequence, but treatment benefit in that year is considered lost even if a patient experiences immediate failure and begins taking another medication. The model also simulates the prevalence of contraindications and allergy rates for each therapy.
Surgical interventions are initiated once a patient experiences three failures of medication treatment. Surgical interventions consist of two procedures, trabeculoplasty (A) and trabeculectomy (T) in a sequence of up to three; A-T-T. As with medication, subsequent surgeries are triggered by a treatment failure which can occur immediately or annually thereafter. [40]

Figure G4 shows the predicted efficacy of glaucoma treatment by year of administration as predicted using the MEDS model. The predicted prevalence of glaucoma-vision loss with and without treatment is shown in **Table G2**.

Figure G4. Efficacy of Glaucoma Treatment

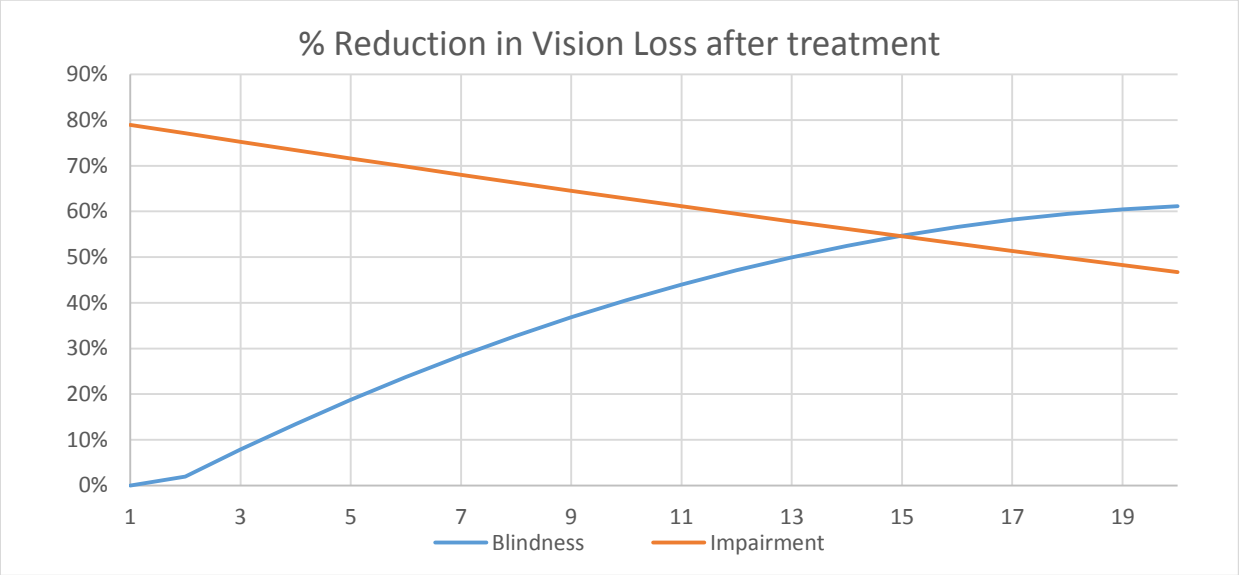


Table G2. Prevalence of Vision Loss

	No Treatment			Treatment			Net		
	Impaired	Blind	Total	Impaired	Blind	Total	Impaired	Blind	Total
2016	161,486	111,392	272,879	33,960	111,392	145,352	-127,526	0	-127,526
2017	165,709	114,191	279,900	37,945	111,945	149,891	-127,764	-2,246	-130,009
2018	170,039	117,065	287,104	42,083	107,852	149,934	-127,956	-9,213	-137,170
2019	174,706	120,111	294,817	46,437	103,936	150,373	-128,270	-16,174	-144,444
2020	179,611	123,348	302,959	50,995	100,215	151,209	-128,617	-23,133	-151,750
2021	184,857	126,799	311,655	55,798	96,704	152,502	-129,059	-30,095	-159,154
2022	190,542	130,557	321,098	60,894	93,470	154,363	-129,648	-37,087	-166,735
2023	196,527	134,533	331,060	66,255	90,445	156,700	-130,272	-44,088	-174,360
2024	203,054	138,806	341,860	71,980	87,687	159,667	-131,074	-51,119	-182,193
2025	209,977	143,445	353,423	78,039	85,240	163,279	-131,938	-58,205	-190,144
2026	217,258	148,372	365,631	84,433	83,062	167,495	-132,825	-65,310	-198,135
2027	224,948	153,652	378,600	91,197	81,204	172,402	-133,751	-72,448	-206,198
2028	232,873	159,173	392,046	98,275	79,626	177,900	-134,598	-79,548	-214,146
2029	241,386	165,111	406,497	105,827	78,440	184,266	-135,559	-86,671	-222,230
2030	249,988	171,126	421,114	113,652	77,516	191,168	-136,337	-93,610	-229,946
2031	258,795	177,288	436,084	121,802	76,937	198,739	-136,993	-100,352	-237,345
2032	267,887	183,642	451,529	130,322	76,767	207,090	-137,564	-106,874	-244,439
2033	276,853	190,019	466,872	139,015	76,990	216,005	-137,838	-113,029	-250,867
2034	286,035	196,559	482,594	148,045	77,718	225,763	-137,990	-118,841	-256,831
2035	295,067	203,034	498,101	157,223	78,918	236,141	-137,844	-124,116	-261,961
2036	303,904	209,419	513,323	166,512	80,641	247,153	-137,393	-128,778	-266,171
2037	312,701	215,859	528,560	175,984	83,004	258,988	-136,717	-132,855	-269,572
2038	321,244	222,134	543,378	185,511	85,980	271,491	-135,733	-136,154	-271,887
2039	329,853	228,354	558,206	195,265	89,670	284,935	-134,588	-138,684	-273,272
2040	337,966	234,343	572,309	204,903	94,059	298,962	-133,062	-140,284	-273,346
2041	345,808	240,150	585,959	214,540	99,217	313,757	-131,268	-140,933	-272,201
2042	353,355	245,774	599,129	224,143	105,191	329,334	-129,212	-140,583	-269,795
2043	360,313	251,057	611,371	233,507	111,953	345,460	-126,807	-139,104	-265,911
2044	367,133	256,115	623,248	242,900	119,589	362,489	-124,234	-136,525	-260,759
2045	373,564	260,804	634,367	252,143	128,061	380,204	-121,420	-132,743	-254,163

Impact on Costs

The annual costs of medical management of glaucoma is $1,490 for ages 40-64 and $2,170, based on 2003-2008 MEPS data. This costs represents all medical costs attributable to glaucoma diagnosis, and thus includes office visits and management, prescription medications and surgical costs. We apply this cost annually to all patients diagnosed with glaucoma.

Figure G5. Net Medical Costs of Diagnosis and Treatment

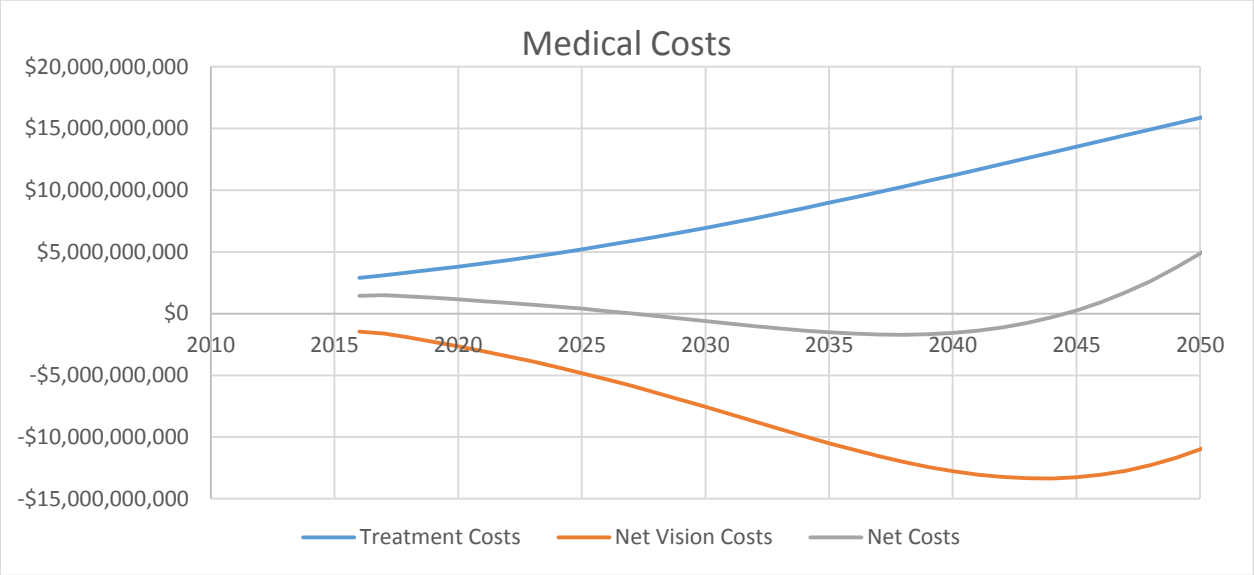


Table G3. Net Medical Costs of Diagnosis and Treatment

	Treatment Costs	Net Vision Costs	Net Costs
2016	$2,895,303,535	-$1,465,054,955	$1,430,248,580
2017	$3,114,718,549	-$1,613,275,019	$1,501,443,531
2018	$3,334,071,302	-$1,937,286,239	$1,396,785,063
2019	$3,562,996,215	-$2,285,480,089	$1,277,516,125
2020	$3,803,371,216	-$2,654,451,015	$1,148,920,200
2021	$4,057,066,834	-$3,044,218,031	$1,012,848,803
2022	$4,322,346,452	-$3,452,523,232	$869,823,220
2023	$4,599,304,940	-$3,877,994,217	$721,310,723
2024	$4,887,703,915	-$4,329,421,776	$558,282,139
2025	$5,211,545,523	-$4,817,484,518	$394,061,005
2026	$5,530,604,277	-$5,321,026,618	$209,577,659
2027	$5,862,814,910	-$5,849,520,361	$13,294,549
2028	$6,209,194,448	-$6,398,061,319	-$188,866,872
2029	$6,570,177,100	-$6,973,099,373	-$402,922,273
2030	$6,944,946,068	-$7,557,368,394	-$612,422,326
2031	$7,331,694,908	-$8,149,079,865	-$817,384,957
2032	$7,728,859,001	-$8,746,965,724	-$1,018,106,723
2033	$8,135,740,768	-$9,337,938,293	-$1,202,197,526
2034	$8,552,090,726	-$9,925,265,339	-$1,373,174,613
2035	$8,976,623,758	-$10,493,331,711	-$1,516,707,953
2036	$9,408,795,302	-$11,032,004,107	-$1,623,208,805
2037	$9,848,116,271	-$11,540,615,454	-$1,692,499,183
2038	$10,293,702,690	-$12,001,523,175	-$1,707,820,485
2039	$10,744,669,643	-$12,415,236,406	-$1,670,566,763
2040	$11,200,940,325	-$12,763,003,989	-$1,562,063,663
2041	$11,660,223,111	-$13,039,553,026	-$1,379,329,915
2042	$12,121,170,349	-$13,238,929,938	-$1,117,759,590
2043	$12,584,485,561	-$13,343,635,457	-$759,149,896
2044	$13,049,709,290	-$13,355,918,168	-$306,208,878
2045	$13,516,075,526	-$13,262,502,396	$253,573,130

Impact on QALYs

Figure G6. QALY Losses from Cataract, Gains from Treatment

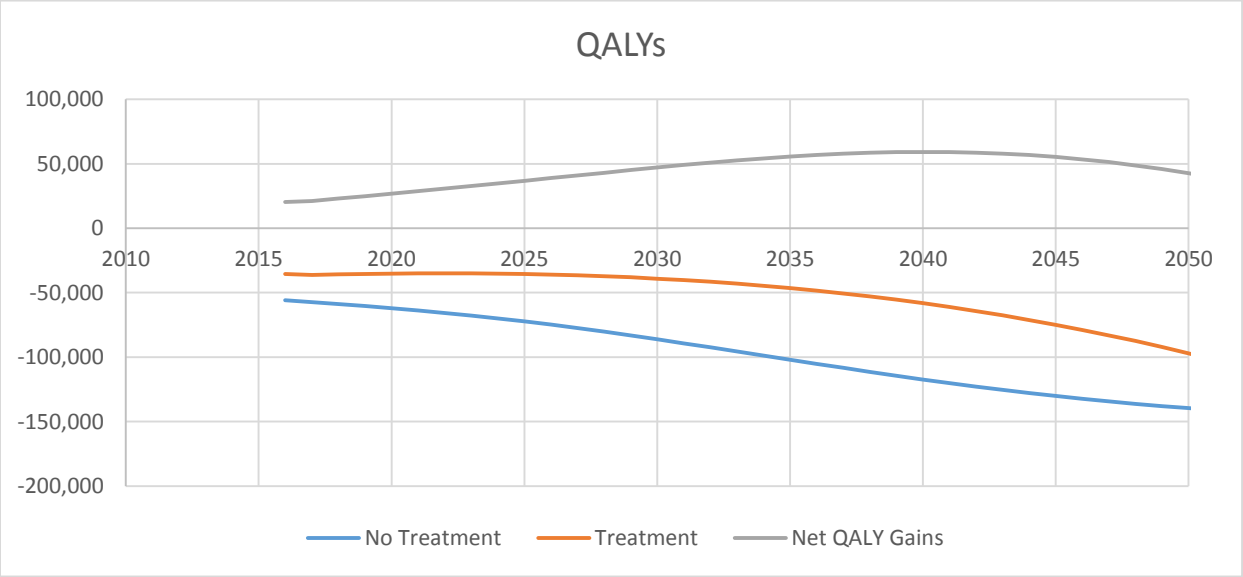


Table G4. Net QALYs

	No Treatment	Treatment	Net QALY Gains
2016	-55,914	-35,510	20,404
2017	-57,345	-36,297	21,049
2018	-58,814	-35,853	22,961
2019	-60,383	-35,493	24,890
2020	-62,042	-35,217	26,825
2021	-63,813	-35,038	28,775
2022	-65,737	-34,980	30,757
2023	-67,768	-35,021	32,747
2024	-69,966	-35,192	34,774
2025	-72,327	-35,501	36,826
2026	-74,822	-35,936	38,886
2027	-77,478	-36,517	40,961
2028	-80,236	-37,223	43,014
2029	-83,202	-38,111	45,091
2030	-86,202	-39,114	47,088
2031	-89,275	-40,261	49,014
2032	-92,445	-41,579	50,866
2033	-95,602	-43,030	52,572
2034	-98,837	-44,671	54,166
2035	-102,030	-46,463	55,567
2036	-105,168	-48,415	56,753
2037	-108,314	-50,569	57,745
2038	-111,375	-52,896	58,479
2039	-114,432	-55,453	58,979
2040	-117,347	-58,180	59,167
2041	-120,170	-61,115	59,055
2042	-122,896	-64,264	58,631
2043	-125,436	-67,588	57,847
2044	-127,892	-71,153	56,739
2045	-130,187	-74,919	55,268

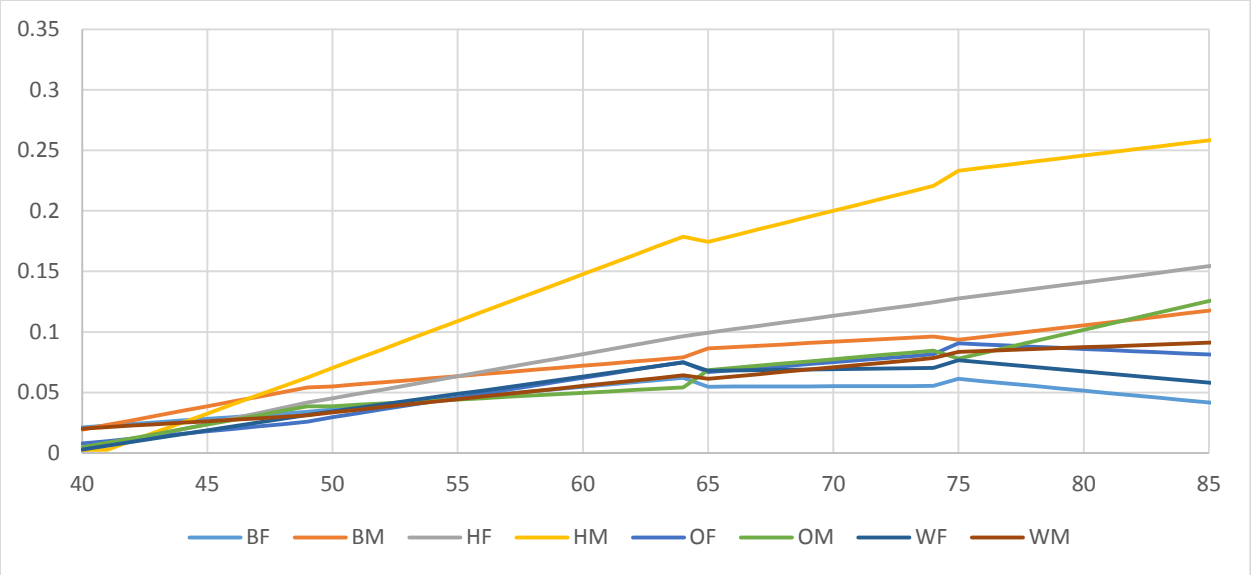
Diabetic Retinopathy

Prevalence

VPUS reports prevalence rates of DR for ages 40 and older. Linearized prevalence rates by age, race and gender are shown in **Figure DR1**. In some cases prevalence rates appear to decline with age. This is likely driven due to the fact that the denominator of these prevalence rates is the overall US population, while DR is limited to the diabetic population. The diabetic population declines relative to the overall population at older ages. This may be an artifact of recent increases in diabetes prevalence at younger

ages, as well as the higher mortality rates of persons with diabetes. The prevalence figures for Hispanic males is extremely high, and may warrant further investigation.

Figure DR1. Diabetic Retinopathy Prevalence Rates by Age



Multiplying the prevalence rates by the population projections by age, race, and gender results in the population prevalence forecasts shown in **Figure DR2**. The leading edge of this figure depicts the prevalence of DR by age in 2016. Subsequent lines represent the prevalence distribution in future years. The prevalence of DR is skewed towards younger ages relative to the other eye diseases. We forecast this population to grow substantially due to in the coming years, driven by the aging baby-boomers and increasing minority populations, which generally have higher prevalence of diabetic retinopathy than whites. We also assume that our forecast is an underestimate because growth projections are based on national population growth projections, it is plausible that the diabetes population will grow at a faster rate. **Table DR1** includes the prevalence predictions by age group.

Figure DR2. Current and future prevalence of DR

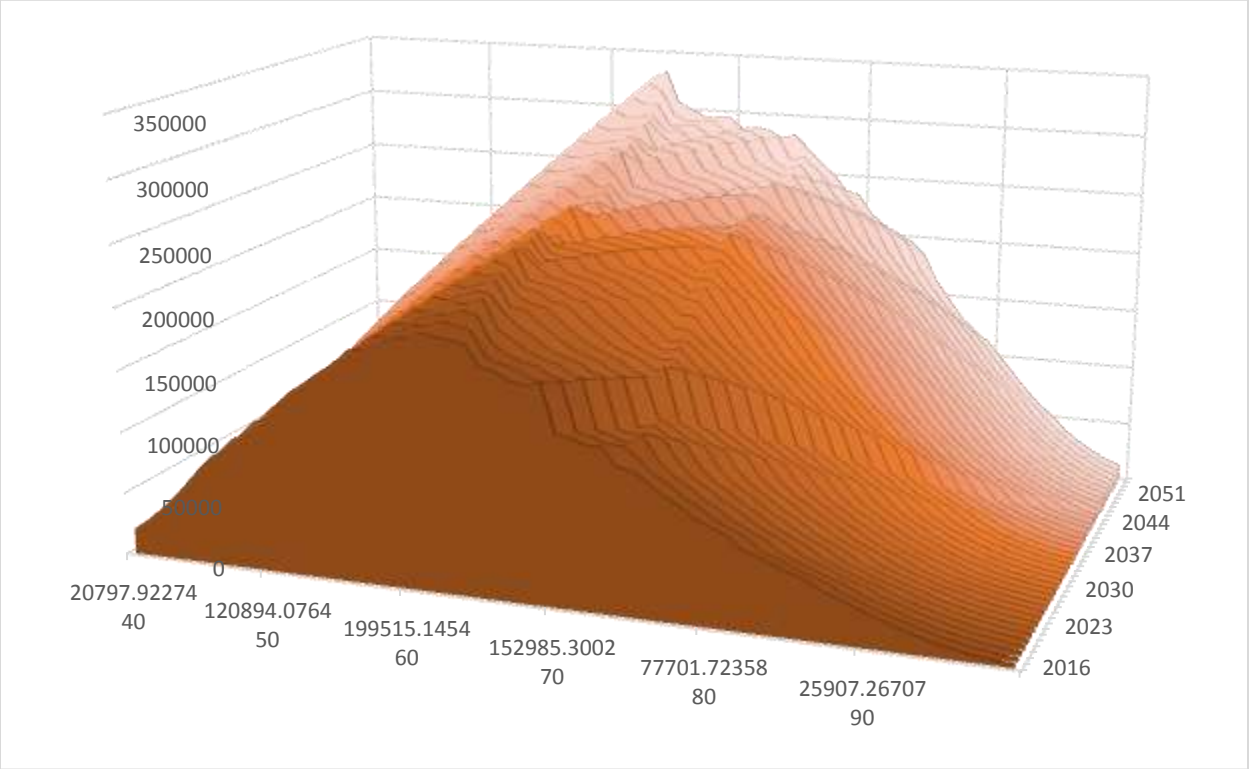


Table DR1. DR Prevalence Predictions by Age Group

	Age 40-64	Age 65-89	Age 90+	Total Age 40+
2016	3,310,463	2,520,587	116,567	5,947,617
2017	3,353,186	2,614,822	120,820	6,088,828
2018	3,389,845	2,715,982	124,844	6,230,671
2019	3,420,752	2,823,065	128,285	6,372,102
2020	3,444,909	2,936,795	132,566	6,514,271
2021	3,468,611	3,051,490	135,690	6,655,791
2022	3,487,579	3,173,671	138,376	6,799,626
2023	3,506,051	3,295,155	140,833	6,942,039
2024	3,523,602	3,416,756	143,084	7,083,442
2025	3,533,247	3,543,764	147,246	7,224,258
2026	3,548,171	3,665,031	151,205	7,364,408
2027	3,566,078	3,782,903	155,237	7,504,217
2028	3,584,229	3,899,390	160,419	7,644,038
2029	3,603,771	4,014,703	165,707	7,784,182
2030	3,628,561	4,124,628	172,070	7,925,259
2031	3,668,307	4,220,138	178,462	8,066,908
2032	3,714,929	4,307,243	186,285	8,208,457
2033	3,762,085	4,389,776	197,252	8,349,113
2034	3,807,320	4,474,705	206,359	8,488,384
2035	3,840,497	4,569,256	215,652	8,625,405
2036	3,878,038	4,658,667	224,319	8,761,024
2037	3,926,936	4,725,548	244,009	8,896,493
2038	3,985,085	4,786,560	260,432	9,032,077
2039	4,047,940	4,843,881	275,671	9,167,492
2040	4,105,968	4,905,065	291,505	9,302,538
2041	4,172,287	4,958,803	306,103	9,437,192
2042	4,234,551	5,016,124	320,430	9,571,106
2043	4,296,649	5,072,640	336,039	9,705,329
2044	4,356,856	5,130,671	352,812	9,840,338
2045	4,400,795	5,203,266	371,529	9,975,590

Diagnosis Rate

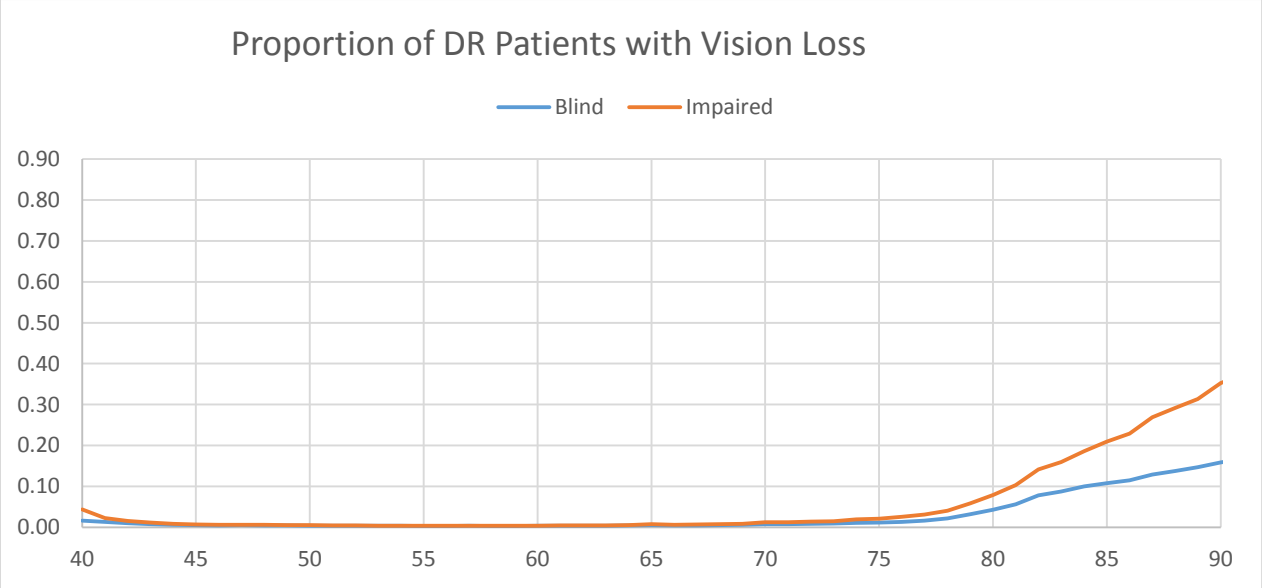
We calculated the diagnosis rate of DR in NHANES data. From 1999-2012 NHANES respondents received a glycohemoglobin test. Respondents were also asked if a doctor ever told them that they had diabetes. We defined persons with diabetes as having either self-reported a diabetes diagnosis, or having a glycohemoglobin result of greater or equal to 6.5%. We define this population as "HasDM". Respondents who reported a diabetes diagnosis were asked follow-up questions including if a doctor ever told them "that diabetes has affected your eyes or that you had retinopathy", which we define as "ToldDR". From 2005-2008, the NHANES retinal images included an assessment of retinopathy level. Those who received a non-questionable retinopathy grade were defined as "Has DR".
We then calculated the diagnosis rates as the proportion of respondents who were identified with both diabetes and a non-questionable retinopathy grade who reported they were told that they had DR or

retinopathy. Thus, diagnosis rate equals the proportion of respondents with ToldDR=true given HasDR=true and HasDM=true, which equals 29%.

Proportion of DR Patients with Vision Loss

We predicted the total number of patients impaired or blind based on the EDPRG disease allocations of vision loss by disorder type, and the prevalence of visual impairment and blindness reported by VPUS. Based on this process and assumption, we estimated the proportion of DR patients with impairment or blindness per year, as shown in **Figure DR3**. Total vision loss equates to the sum of these lines.

Figure DR3. Proportion of Cataract Patients with Impairment or Blindness



Treatment for DR

We estimated the efficacy of medical treatment for DR using the MEDS model. Full details of the MEDS model's diabetic retinopathy module are provided in the MEDS model technical report. Briefly, we assign initial prevalence of diabetes based on NHANES data. For diabetes patients, DR stage is based on the Arlie House states representing retonopathy level by each eye, from 10 (no retinopathy) to 43. {Stratton IM, Kohner EM, et al. 2001 #2560} Each eye faces annual risk of incidence of advanced DR, including high risk (HR) and non-HR proliferative DR (PDR), clinically significant macular edema (CSME), and any combination thereof based on a function of DR stage, duration of diabetes, and the trailing 14-year average HbA1c level as derived from UKPDS data. {Stevens RJ, Stratton IM, et al. 2002 #2550}

The MEDS model simulates vision loss in the absence of treatment by calculating the annual risk of vision loss, and the resulting amount of vision loss measured in acuity logMar based on the outcomes of the Diabetic Retinopathy Study (1987) and the Early Treatment Diabetic Retinopathy Study (1985). [41] [42] Any patient diagnosed with DR is assumed to undergo recommended levels of treatment. Treatment efficacy is expressed in terms of a relative rate reduction in the annual probability of vision loss faced by

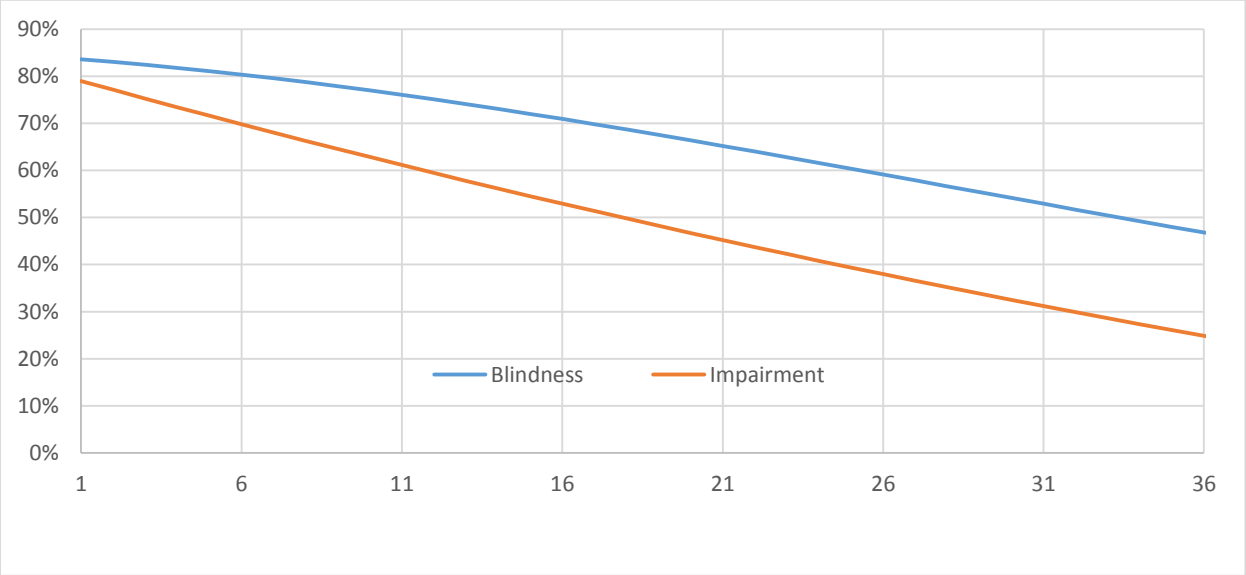
eyes in advanced DR states.).[41, 42] While the model costs treatment based on a specific sequence of ophthalmologic procedures, the treatment effect is captures only through a net relative risk of vision loss per year in an advanced state. The model includes the possibility of incorporating glycemic control treatment to reduce progression to advanced states, but we do not employ this treatment option in this analysis.

Treatment is assumed to follow the following algorithms by stage:

- **NonHR-PDR and HR-PDR:** Scatter photocoagulation upon diagnosis in state. 0.143 probability of adverse event which reduces acuity by 0.18 logMar. In subsequent years, if eye's acuity loss is less than 1.6 logMar, then 0.024 * scatter photocoagulation.
- **CSME:** 1 year of anti-VEGF therapy, resulting in a one-time gain of 0.2 logMar. 3.5 * flourescein angiography and 3.5 * focal photocoagulation every year diagnosed in state. Subsequent years in state with diagnosis and eye acuity losses of less than 1.6 logMar receive an additional .3968* focal photocoagulation.
- **NonHR-PDR + CSME and HR-PDR + CSME:** Upon diagnosis in state, 1 year of anti-VEGF therapy, resulting in a one-time gain of 0.2 logMar, and scatter photocoagulation and 3.5 * flourescein angiography and one focal photocoagulation. Scatter photocoagulation is associated with 0.143 probability of adverse event which reduces acuity by 0.18 logMar. In subsequent years, 3.5 flourescein angiography every year, and if acuity losses < 1.6, then 0.024 * scatter photocoagulation and 0.4 * scatter photocoagulation.

We separately simulate the percent reduction in blindness and visual impairment using the MEDS model on a representative DR population using the above progression and treatment parameters. We find substantial, immediate reductions in vision loss due to treatment, as shown in **Figure DR4**.

Figure DR4. Population Vision Loss Reduction from DR Treatment



Prevalence of Vision Loss with and Without Treatment.

Applying the vision loss proportions to the undiagnosed population yields the projected DR-attributable vision loss prevalence estimates with "No Treatment" as shown in **Table DR2**. With treatment, prevalence projects are as depicted in the "Treatment" columns, while the difference is shown as "Net Vision Loss"

Table DR2. Prevalence of Vision Loss

	No Treatment			Treatment			Net Vision Loss		
	Impaired	Blind	Total	Impaired	Blind	Total	Impaired	Blind	Total
2016	138,112	73,814	211,926	29,045	12,119	41,163	-109,067	-85,933	-253,089
2017	141,877	75,558	217,434	32,488	12,822	45,310	-109,389	-88,380	-262,744
2018	145,717	77,378	223,094	36,063	13,596	49,660	-109,654	-90,974	-272,754
2019	149,760	79,331	229,091	39,806	14,455	54,261	-109,954	-93,786	-283,352
2020	154,072	81,449	235,521	43,743	15,408	59,151	-110,328	-96,857	-294,672
2021	158,641	83,740	242,381	47,885	16,461	64,346	-110,756	-100,200	-306,726
2022	163,624	86,267	249,891	52,291	17,633	69,924	-111,332	-103,900	-319,815
2023	168,936	88,965	257,901	56,954	18,916	75,870	-111,983	-107,881	-333,771
2024	174,667	91,886	266,553	61,917	20,329	82,247	-112,750	-112,215	-348,800
2025	180,932	95,092	276,024	67,244	21,893	89,137	-113,688	-116,985	-365,161
2026	187,635	98,529	286,165	72,921	23,604	96,525	-114,715	-122,133	-382,689
2027	194,915	102,267	297,182	79,021	25,488	104,509	-115,894	-127,755	-401,692
2028	202,684	106,252	308,935	85,534	27,541	113,076	-117,149	-133,793	-422,011
2029	211,219	110,606	321,825	92,601	29,806	122,407	-118,618	-140,412	-444,233
2030	220,055	115,048	335,103	100,043	32,216	132,259	-120,012	-147,264	-467,362
2031	229,226	119,619	348,845	107,885	34,788	142,674	-121,341	-154,407	-491,519
2032	238,763	124,287	363,050	116,154	37,518	153,672	-122,609	-161,805	-516,722
2033	248,510	128,950	377,459	124,783	40,377	165,160	-123,727	-169,327	-542,619
2034	258,721	133,734	392,455	133,908	43,408	177,315	-124,813	-177,141	-569,770
2035	269,074	138,475	407,549	143,372	46,558	189,931	-125,701	-185,034	-597,480
2036	279,596	143,192	422,788	153,193	49,834	203,027	-126,403	-193,026	-625,815
2037	290,510	147,972	438,482	163,495	53,266	216,761	-127,015	-201,237	-655,243
2038	301,455	152,633	454,088	174,084	56,786	230,870	-127,372	-209,419	-684,958
2039	312,547	157,231	469,777	185,020	60,411	245,431	-127,527	-217,642	-715,209
2040	323,628	161,659	485,287	196,211	64,096	260,306	-127,418	-225,754	-745,593
2041	334,673	165,941	500,614	207,632	67,841	275,472	-127,041	-233,782	-776,086
2042	345,641	170,078	515,719	219,250	71,639	290,889	-126,391	-241,717	-806,607
2043	356,405	173,983	530,388	230,974	75,444	306,418	-125,431	-249,427	-836,806
2044	367,142	177,733	544,875	242,906	79,280	322,186	-124,237	-257,013	-867,061
2045	377,559	181,199	558,759	254,840	83,078	337,918	-122,719	-264,277	-896,677

Impact on Costs

The annual costs of medical management of DR, using the definition of retinal disorders with diabetes, controlling for diabetes costs in 2003-2008 MEPS data is $2,930 for ages 40-64 and $3,950 for ages 65+. This costs represents all medical costs attributable to DR diagnosis, and thus includes office visits and management, prescription medications and surgical costs. We apply this cost annually to all patients diagnosed with DR. However, these costs do not include anti-VEGF administration, which was not standard of care when these costs were observed. We therefore add addition treatment costs of anti-VEGF therapy for the first year of diagnosis (in the base year) or incidence in future years. We use the same anti-VEGF costs as assigned to CNV treatments ($8,589 per year), as observed in the Treat & Extend study. We apply this cost to 7.6% of all newly diagnosed DR patients, as this is the proportion of DR patients identified in 2005-2006 NHANES who had CSME. By assumption, we apply this cost for 1 year. In future analyses, actual costs estimates for treating DR patients should be employed.

Net medical costs are shown in **Figure DR5**. We estimate the cost to treat the entire undiagnosed DR population in 2016 diagnosis/treatment year to exceed $18.1bn.

Figure DR5. Net Medical Costs of Diagnosis and Treatment

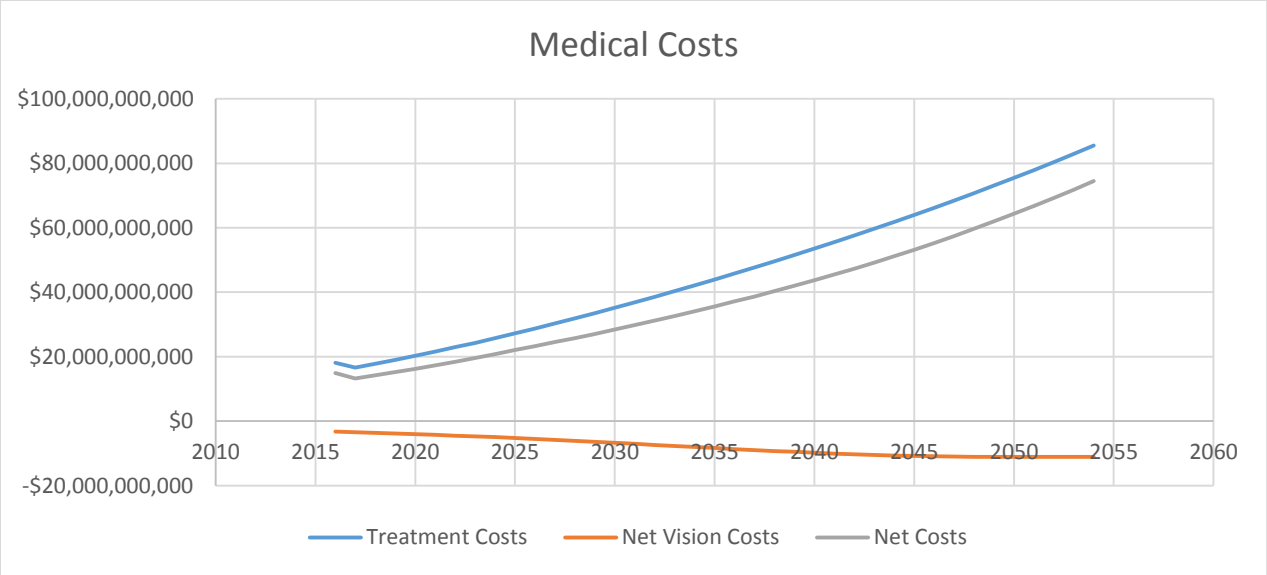


Table DR3. Net Medical Costs of Diagnosis and Treatment

	Treatment Costs	Net Vision Costs	Net Costs
2016	$18,133,999,256	-$3,229,297,871	$14,904,701,385
2017	$16,628,839,997	-$3,423,103,330	$13,205,736,667
2018	$17,807,261,014	-$3,628,088,019	$14,179,172,994
2019	$19,019,848,635	-$3,840,531,490	$15,179,317,145
2020	$20,271,159,043	-$4,058,386,559	$16,212,772,484
2021	$21,572,887,994	-$4,281,313,929	$17,291,574,066
2022	$22,920,707,573	-$4,507,601,543	$18,413,106,029
2023	$24,298,512,960	-$4,736,436,016	$19,562,076,943
2024	$25,709,667,981	-$4,976,773,671	$20,732,894,309
2025	$27,267,845,312	-$5,244,110,169	$22,023,735,144
2026	$28,768,581,087	-$5,513,437,086	$23,255,144,001
2027	$30,305,090,372	-$5,798,413,578	$24,506,676,794
2028	$31,878,743,550	-$6,096,266,332	$25,782,477,218
2029	$33,490,876,547	-$6,414,098,111	$27,076,778,436
2030	$35,144,572,655	-$6,735,113,422	$28,409,459,234
2031	$36,837,802,701	-$7,060,067,957	$29,777,734,745
2032	$38,567,367,332	-$7,387,517,565	$31,179,849,767
2033	$40,329,248,191	-$7,711,431,467	$32,617,816,724
2034	$42,120,877,439	-$8,038,723,049	$34,082,154,390
2035	$43,936,934,936	-$8,359,133,729	$35,577,801,208
2036	$45,782,492,828	-$8,671,563,793	$37,110,929,035
2037	$47,664,130,227	-$8,980,510,209	$38,683,620,017
2038	$49,582,357,795	-$9,273,801,067	$40,308,556,728
2039	$51,535,095,429	-$9,554,236,530	$41,980,858,899
2040	$53,521,192,483	-$9,815,543,539	$43,705,648,944
2041	$55,540,542,687	-$10,057,017,860	$45,483,524,827
2042	$57,590,549,370	-$10,278,529,309	$47,312,020,062
2043	$59,678,870,212	-$10,474,282,468	$49,204,587,745
2044	$61,808,048,975	-$10,649,110,732	$51,158,938,244
2045	$63,973,772,123	-$10,795,603,320	$53,178,168,803

Impact on QALYs

The impact of treatment on QALYs is shown in Figure DR6 and Table DR4. Treatment is associated with immediate gains in QALYs, and these gains are generally static in future years.

Figure DR6. QALY Losses from Cataract, Gains from Treatment

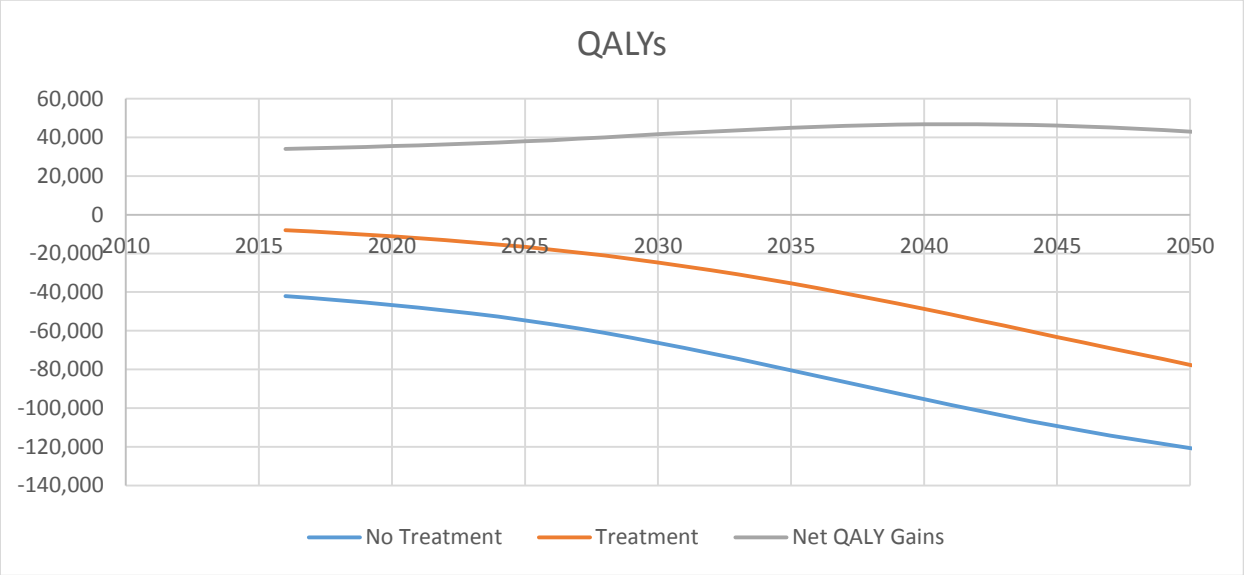


Table DR4. Net QALYs

	No Treatment	Treatment	Net QALY Gains
2016	-42,028	-8,038	33,990
2017	-43,101	-8,626	34,475
2018	-44,207	-9,280	34,926
2019	-45,381	-10,014	35,367
2020	-46,643	-10,838	35,804
2021	-47,992	-11,759	36,233
2022	-49,472	-12,796	36,676
2023	-51,050	-13,951	37,099
2024	-52,756	-15,242	37,514
2025	-54,624	-16,691	37,933
2026	-56,625	-18,302	38,322
2027	-58,799	-20,105	38,693
2028	-61,117	-22,106	39,011
2029	-63,659	-24,352	39,307
2030	-66,272	-26,806	39,465
2031	-68,973	-29,490	39,483
2032	-71,760	-32,420	39,339
2033	-74,578	-35,590	38,988
2034	-77,503	-39,051	38,453
2035	-80,440	-42,773	37,667
2036	-83,397	-46,776	36,622
2037	-86,434	-51,110	35,324
2038	-89,444	-55,732	33,712
2039	-92,460	-60,675	31,785
2040	-95,428	-65,919	29,509
2041	-98,352	-71,475	26,876
2042	-101,224	-77,347	23,877
2043	-104,000	-83,511	20,489
2044	-106,731	-90,015	16,716
2045	-109,333	-96,796	12,537

Summary of Diseases

Prevalence

The prevalence of each condition is shown in Figure SUM1 and Table SUM1 below. Cataract is the most prevalent condition, followed by URE and DR.

Figure SUM1. Prevalence of Eye Disorders

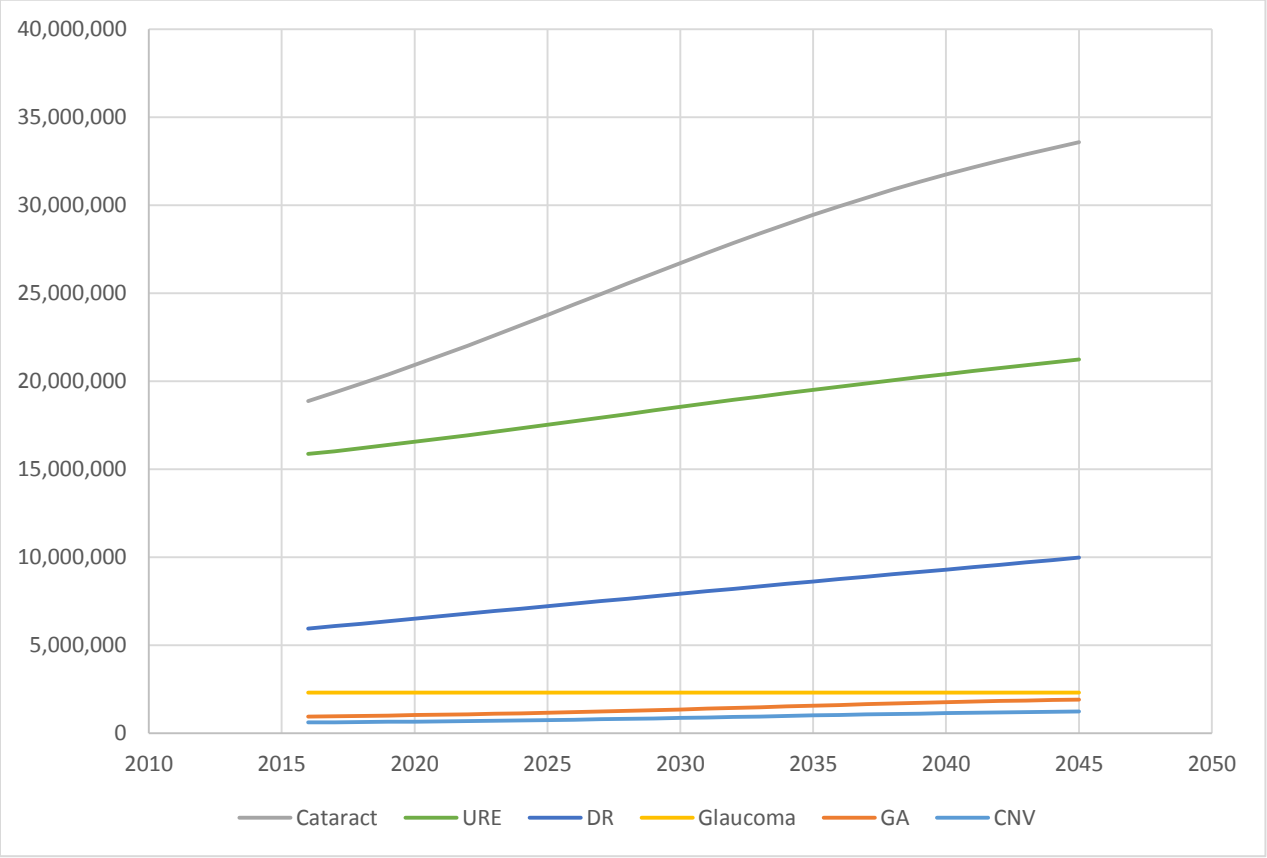


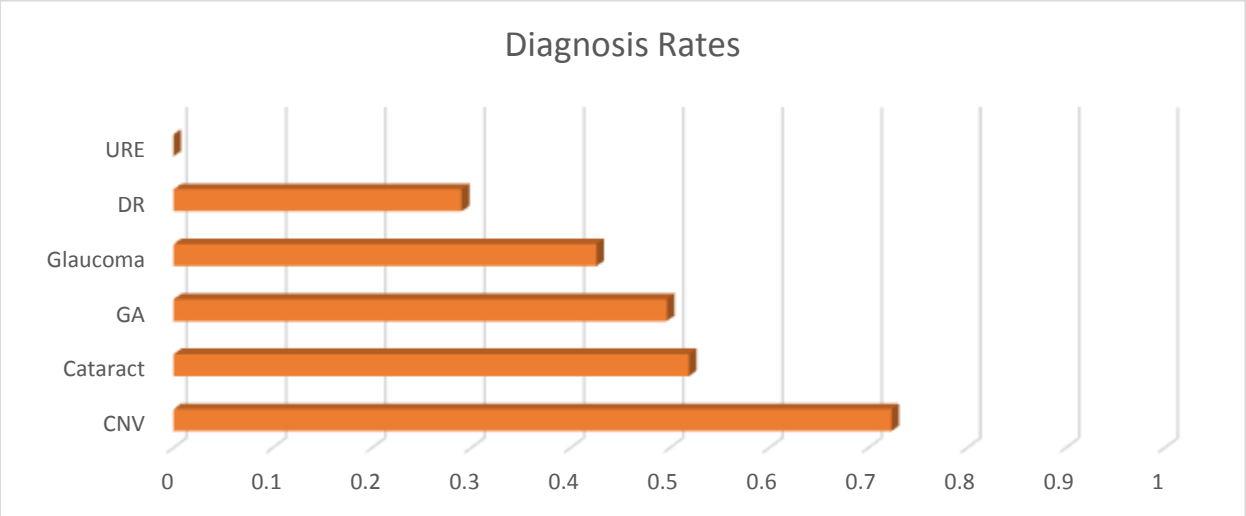
Table SUM1. Prevalence of Eye Disorders

	CNV	GA	Cataract	Glaucoma	DR	URE
2016	619,945	959,278	18,881,819	2,319,674	5,947,617	15,873,996
2017	630,736	975,977	19,367,807	2,319,674	6,088,828	16,024,450
2018	642,110	993,576	19,869,939	2,319,674	6,230,671	16,196,912
2019	654,257	1,012,372	20,387,923	2,319,674	6,372,102	16,374,560
2020	667,667	1,033,122	20,920,989	2,319,674	6,514,271	16,556,967
2021	682,312	1,055,784	21,467,185	2,319,674	6,655,791	16,743,737
2022	698,138	1,080,272	22,026,104	2,319,674	6,799,626	16,934,564
2023	715,208	1,106,686	22,596,644	2,319,674	6,942,039	17,129,027
2024	733,523	1,135,026	23,176,976	2,319,674	7,083,442	17,326,637
2025	753,698	1,166,244	23,763,889	2,319,674	7,224,258	17,526,669
2026	775,234	1,199,567	24,355,209	2,319,674	7,364,408	17,728,483
2027	798,332	1,235,309	24,947,961	2,319,674	7,504,217	17,931,452
2028	822,877	1,273,289	25,539,665	2,319,674	7,644,038	18,134,896
2029	848,857	1,313,489	26,127,601	2,319,674	7,784,182	18,338,382
2030	875,781	1,355,150	26,710,425	2,319,674	7,925,259	18,541,400
2031	903,170	1,397,531	27,284,747	2,319,674	8,066,908	18,741,872
2032	931,041	1,440,657	27,847,810	2,319,674	8,208,457	18,939,452
2033	959,166	1,484,176	28,397,229	2,319,674	8,349,113	19,133,879
2034	987,234	1,527,608	28,930,960	2,319,674	8,488,384	19,324,832
2035	1,015,218	1,570,909	29,446,786	2,319,674	8,625,405	19,512,190
2036	1,042,739	1,613,493	29,944,444	2,319,674	8,761,024	19,696,168
2037	1,069,579	1,655,025	30,422,689	2,319,674	8,896,493	19,876,920
2038	1,095,640	1,695,351	30,880,752	2,319,674	9,032,077	20,054,864
2039	1,120,777	1,734,246	31,318,545	2,319,674	9,167,492	20,230,201
2040	1,144,808	1,771,431	31,736,841	2,319,674	9,302,538	20,403,109
2041	1,167,374	1,806,349	32,136,304	2,319,674	9,437,192	20,573,901
2042	1,188,259	1,838,666	32,517,553	2,319,674	9,571,106	20,742,709
2043	1,207,207	1,867,985	32,882,461	2,319,674	9,705,329	20,909,680
2044	1,224,127	1,894,167	33,234,092	2,319,674	9,840,338	21,075,172
2045	1,238,948	1,917,101	33,574,654	2,319,674	9,975,590	21,239,291

Diagnosis Rates

The Diagnosis rates for each disorder are shown in Figure SUM2. CNV has the highest diagnosis rate. Cataract represents treatment rate, not diagnosis rate as NHANES includes only treatment history for cataract, no diagnosis history. Of the eye diseases, DR shows the lowest diagnosis rates based on NHANES data. It should be noted that the DR diagnosis history question was included in a separate module of NHANES, is worded differently from the other diagnosis history questions, and is only asked among respondents who previously stated they had diabetes. Our definition of URE is uncorrected, correctable vision loss and by assumption none is diagnosed/treated.

Figure SUM2. Diagnosis and/or Treatment Rate by Disorder



Undiagnosed/Untreated Prevalence

Undiagnosed/untreated prevalence of each condition is shown in Table SUM2 and figure SUM2. By definition, all URE is untreated. Cataract is also defined as untreated based on the self-reported cataract surgery rate in NHANES, while CNV, GA, glaucoma and DR are defined as undiagnosed based on the self-reported diagnosis rate in NHANES.

Figure SUM3. Prevalence of Undiagnosed or Untreated Eye Disorders

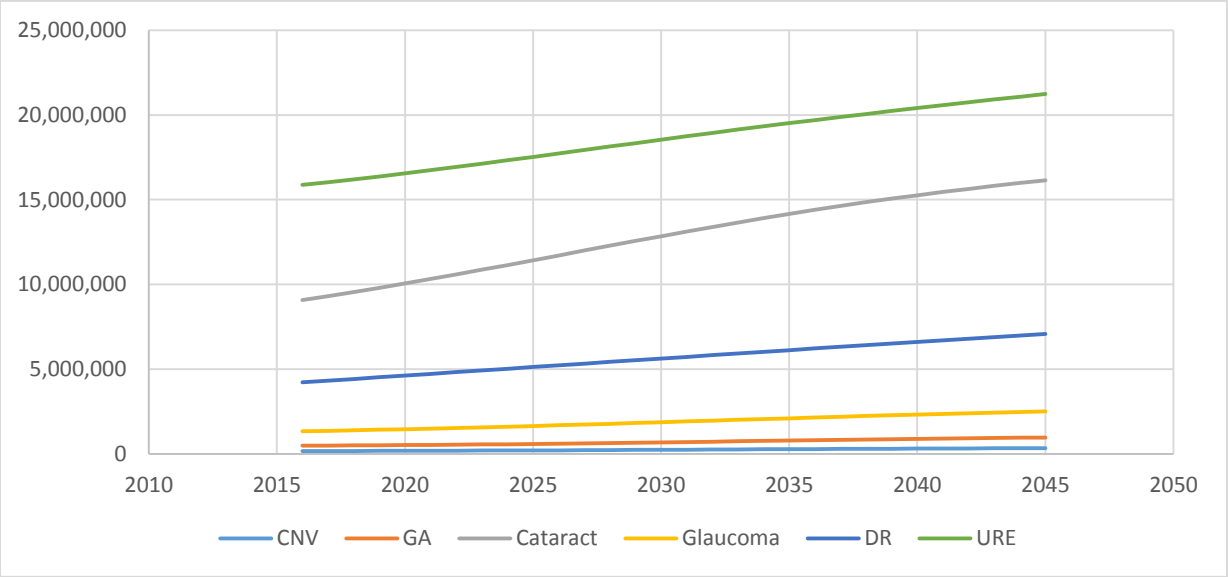


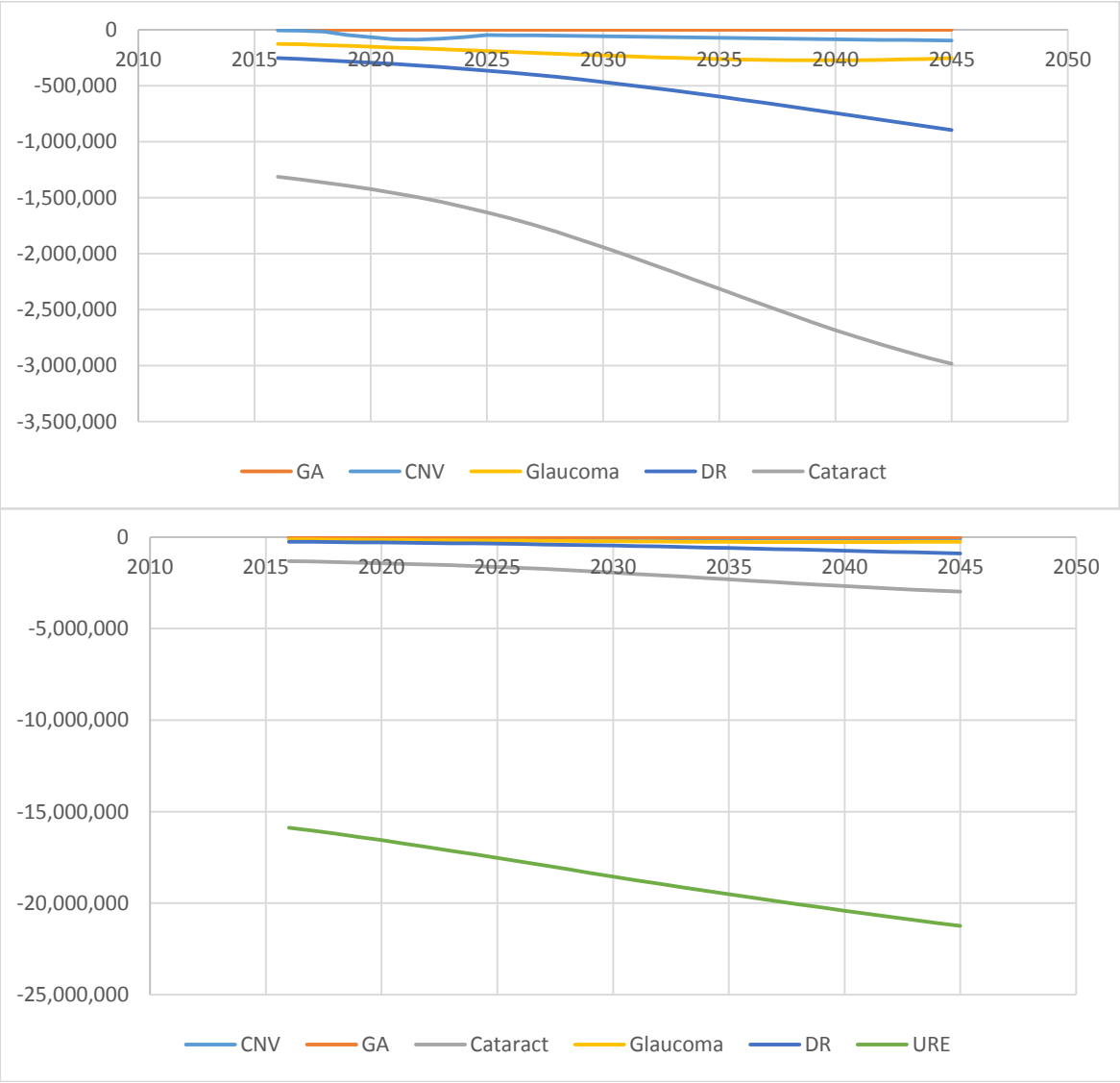
Table SUM2. Prevalence of Undiagnosed/Untreated Eye Disorders

	CNV	GA	Cataract	Glaucoma	DR	URE
2016	173,673	484,943	9,081,031	1,334,241	4,224,323	15,873,996
2017	176,662	493,350	9,314,711	1,364,405	4,324,572	16,024,450
2018	179,813	502,211	9,556,154	1,395,494	4,425,270	16,196,912
2019	183,177	511,675	9,805,220	1,427,768	4,525,675	16,374,560
2020	186,891	522,122	10,061,537	1,461,806	4,626,604	16,556,967
2021	190,947	533,531	10,324,168	1,496,890	4,727,073	16,743,737
2022	195,331	545,860	10,592,916	1,533,383	4,829,185	16,934,564
2023	200,058	559,159	10,867,252	1,571,160	4,930,287	17,129,027
2024	205,131	573,427	11,146,296	1,610,006	5,030,672	17,326,637
2025	210,718	589,144	11,428,505	1,650,607	5,130,641	17,526,669
2026	216,682	605,922	11,712,832	1,692,341	5,230,136	17,728,483
2027	223,079	623,916	11,997,849	1,735,233	5,329,390	17,931,452
2028	229,877	643,037	12,282,361	1,779,465	5,428,653	18,134,896
2029	237,071	663,276	12,565,062	1,825,034	5,528,144	18,338,382
2030	244,528	684,251	12,845,304	1,871,600	5,628,298	18,541,400
2031	252,113	705,588	13,121,459	1,918,604	5,728,858	18,741,872
2032	259,831	727,300	13,392,200	1,965,610	5,829,347	18,939,452
2033	267,620	749,210	13,656,380	2,012,447	5,929,202	19,133,879
2034	275,393	771,075	13,913,017	2,059,068	6,028,074	19,324,832
2035	283,142	792,875	14,161,044	2,105,187	6,125,348	19,512,190
2036	290,764	814,315	14,400,336	2,150,719	6,221,627	19,696,168
2037	298,197	835,224	14,630,294	2,195,599	6,317,800	19,876,920
2038	305,414	855,526	14,850,547	2,239,680	6,414,055	20,054,864
2039	312,375	875,109	15,061,054	2,282,831	6,510,189	20,230,201
2040	319,030	893,830	15,262,185	2,325,101	6,606,061	20,403,109
2041	325,280	911,409	15,454,262	2,366,083	6,701,655	20,573,901
2042	331,064	927,680	15,637,580	2,405,596	6,796,724	20,742,709
2043	336,311	942,441	15,813,041	2,443,869	6,892,012	20,909,680
2044	340,998	955,623	15,982,118	2,480,896	6,987,859	21,075,172
2045	345,103	967,169	16,145,873	2,516,609	7,083,877	21,239,291

Vision Loss from Treatment

The net impact of treatment of vision loss attributable to each condition is shown in **Figure SUM3a and b**. SUM 3a shows results without URE, showing that cataract surgery has a much larger impact on vision loss prevalence than treatment of the other eye diseases combined. However, SUM3b shows that URE treatment dwarfs the vision impact of treatment even of cataract. URE treatment has by far the largest impact on total prevalence of vision loss, although this is by assumption all impairment, and not blindness.

Figure SUM3a and b. Impact of Treatment on Vision Loss Prevalence Projections



Impact on Costs

Cost impacts from treatment are shown in **Figure SUM4**, which shows the net costs from increased treatment costs and potential averted low vision costs. Treatment cost is highest in year 1, particularly for single-procedure treatments such as URE and cataract, as in our hypothetical detection and treatment scenario, all prevalent undiagnosed or untreated cases are treated in the first year. Treatment cost for CNV and DR decline based on our assumptions of the duration of anti-VEGF therapy. URE is always substantially cost-saving, while cataract achieves savings in the second year, and net cost-savings over the first four years. CNV achieves costs savings beginning in year 5, and is cumulatively cost saving over the first 9 years.

Overall, we estimate $29.9bn in cost savings in the first year. This savings is driven entirely by URE, excluding URE, first year costs would be $33.5bn. Averaged over the initial five years, cost savings are even larger ($70.2bn in savings), and again is driven by URE as net costs for the other eye disorders would average $6bn in costs. The costliest condition overall is predicted to by DR, which would cost $17.2bn per year over the initial 10 years to treat, which is driven by the high, continued costs associated with treatment. GA is the second costliest condition, expected to incur net costs of management of $2.5bn per year over the initial 10 years, and achieves no cost offsets from treatment. Glaucoma is the third costliest condition at $1bn per year, while CNV is estimated to achieve cost savings of $340million per year over the initial 10 years, which is a result of both the higher estimated prevalence of vision loss among CNV than other conditions, but also our assumption that anti-VEGF injection frequency would decline beginning in the third year of treatment, and end after 7 years of treatment. Cataract is substantially cost-saving as treatment costs are confined to a single year, and treatment achieves large cost offsets from avoided vision loss thereafter.

URE however completely dwarfs the savings of any eye disorder, achieving a predicted $87.7bn per year in savings over 10 years. Of these savings, 88%, or $76.9bn per year, is driven by the estimated productivity losses of URE estimated in NHANES data, based on the attributable impact on household income associated with measured URE while controlling for age, race, sex, insurance type, and household size. These productivity losses estimates are actually lower than productivity losses calculated in SIPP data, which was based on self-reported difficulty seeing. Nonetheless, the scale of these results, and the fact that NHANES was not primarily designed to measure productivity losses indicate that estimating the productivity impact of URE in more detail in existing and new data sources should be considered a high research priority. Until such time as this research is available, these results should be considered in the context of remaining uncertainty over the productivity impact of URE. Nonetheless, these results do show that the economic costs of URE are likely to be extremely high, particularly compared to the low costs of treatment.

Figure SUM4. Impact of Treatment on Costs

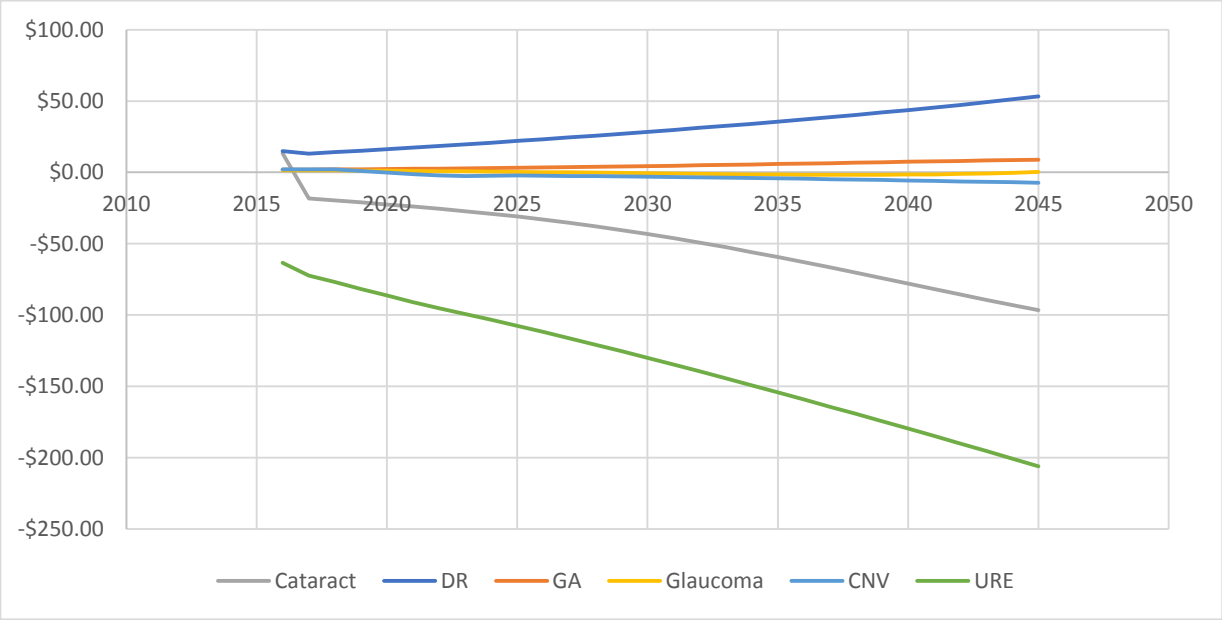


Figure SUM5. 10-year Average Impact of Treatment on Net Costs

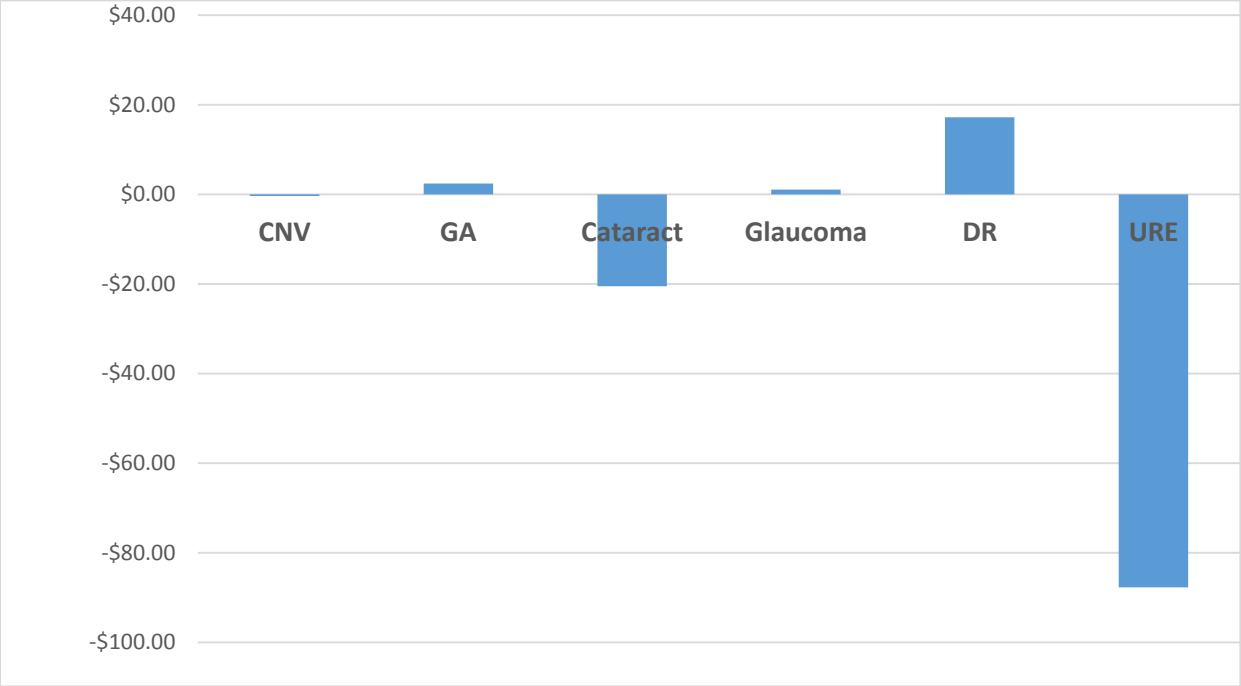


Table SUM2. Cost Impacts of Treatment by Disorder, $bns

	CNV	GA	Cataract	Glaucoma	DR	URE	Total
2016	$2.02	$1.81	$13.34	$1.43	$14.90	-$63.43	-$29.92
2017	$2.14	$1.94	-$18.40	$1.50	$13.21	-$72.32	-$71.94
2018	$2.19	$2.07	-$19.69	$1.40	$14.18	-$76.94	-$76.79
2019	$1.00	$2.20	-$21.06	$1.28	$15.18	-$81.68	-$83.09
2020	-$0.07	$2.34	-$22.50	$1.15	$16.21	-$86.35	-$89.22
2021	-$1.31	$2.49	-$24.01	$1.01	$17.29	-$90.90	-$95.42
2022	-$2.12	$2.65	-$25.57	$0.87	$18.41	-$95.14	-$100.90
2023	-$2.57	$2.82	-$27.21	$0.72	$19.56	-$99.19	-$105.87
2024	-$2.46	$3.00	-$28.98	$0.56	$20.73	-$103.33	-$110.48
2025	-$2.22	$3.21	-$30.93	$0.39	$22.02	-$107.61	-$115.13
2026	-$2.34	$3.41	-$33.03	$0.21	$23.26	-$111.93	-$120.43
2027	-$2.48	$3.63	-$35.31	$0.01	$24.51	-$116.28	-$125.93
2028	-$2.64	$3.87	-$37.74	-$0.19	$25.78	-$120.72	-$131.64
2029	-$2.83	$4.12	-$40.41	-$0.40	$27.08	-$125.24	-$137.68
2030	-$3.02	$4.38	-$43.22	-$0.61	$28.41	-$129.91	-$143.97
2031	-$3.22	$4.65	-$46.19	-$0.82	$29.78	-$134.65	-$150.46
2032	-$3.45	$4.93	-$49.30	-$1.02	$31.18	-$139.46	-$157.11
2033	-$3.68	$5.22	-$52.51	-$1.20	$32.62	-$144.32	-$163.87
2034	-$3.94	$5.52	-$55.88	-$1.37	$34.08	-$149.23	-$170.83
2035	-$4.20	$5.83	-$59.34	-$1.52	$35.58	-$154.19	-$177.84
2036	-$4.48	$6.14	-$62.90	-$1.62	$37.11	-$159.18	-$184.94
2037	-$4.77	$6.46	-$66.62	-$1.69	$38.68	-$164.23	-$192.18
2038	-$5.07	$6.78	-$70.37	-$1.71	$40.31	-$169.32	-$199.39
2039	-$5.38	$7.10	-$74.18	-$1.67	$41.98	-$174.46	-$206.61
2040	-$5.68	$7.42	-$77.98	-$1.56	$43.71	-$179.63	-$213.72
2041	-$5.99	$7.74	-$81.81	-$1.38	$45.48	-$184.84	-$220.79
2042	-$6.30	$8.06	-$85.60	-$1.12	$47.31	-$190.08	-$227.73
2043	-$6.61	$8.36	-$89.36	-$0.76	$49.20	-$195.36	-$234.51
2044	-$6.91	$8.66	-$93.08	-$0.31	$51.16	-$200.67	-$241.15
2045	-$7.21	$8.95	-$96.68	$0.25	$53.18	-$206.00	-$247.51

Impact on QALYs

All treatments increase net QALYs. URE has the largest impact, followed by cataract surgery. We find no QALY gains from GA because we assume no efficacy of treatment.

Figure SUM6. QALY Gains from Treatment

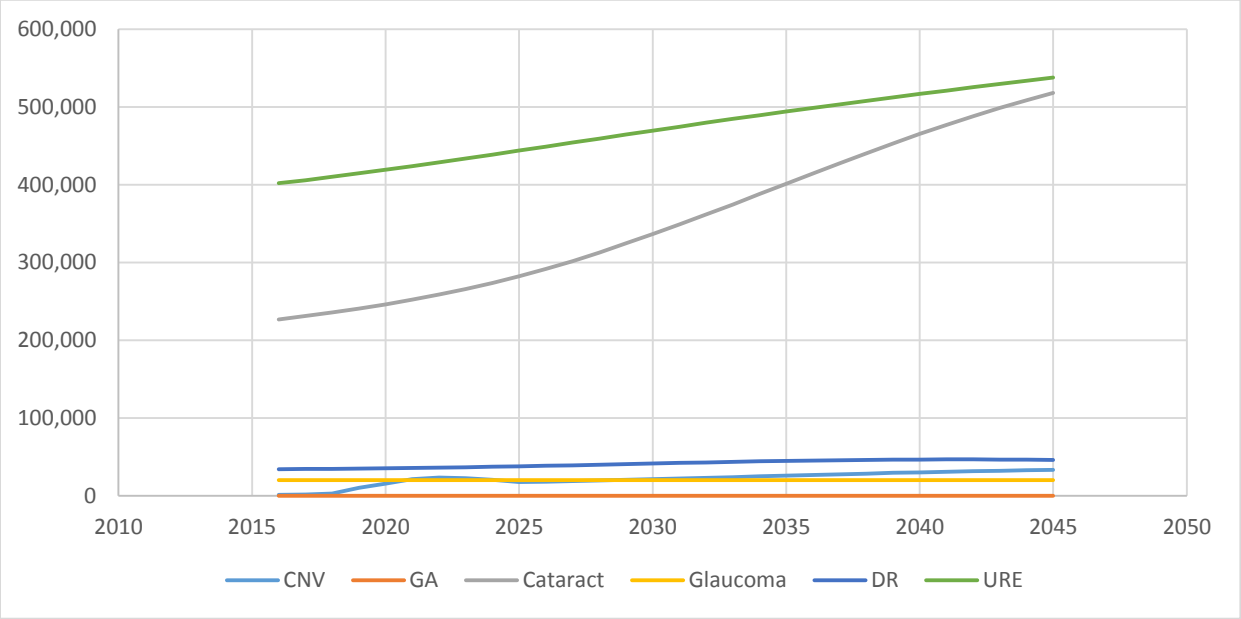


Table SUM3. QALY Gains from Treatment

	CNV	GA	Cataract	Glaucoma	DR	URE	Total
2016	1,374	0	226,690	20,404	34,109	401,949	684,526
2017	1,752	0	231,198	20,404	34,441	405,758	693,553
2018	3,027	0	235,840	20,404	34,766	410,125	704,162
2019	10,371	0	240,806	20,404	35,109	414,624	721,314
2020	15,869	0	246,227	20,404	35,484	419,242	737,225
2021	21,560	0	252,147	20,404	35,886	423,972	753,969
2022	23,608	0	258,777	20,404	36,345	428,804	767,937
2023	22,807	0	265,954	20,404	36,830	433,728	779,723
2024	20,751	0	273,781	20,404	37,360	438,731	791,028
2025	17,830	0	282,426	20,404	37,954	443,796	802,410
2026	18,379	0	291,712	20,404	38,584	448,907	817,986
2027	19,025	0	301,820	20,404	39,273	454,046	834,569
2028	19,741	0	312,598	20,404	39,996	459,197	851,936
2029	20,594	0	324,460	20,404	40,795	464,350	870,603
2030	21,438	0	336,553	20,404	41,566	469,491	889,452
2031	22,310	0	349,000	20,404	42,319	474,567	908,600
2032	23,203	0	361,789	20,404	43,045	479,570	928,011
2033	24,092	0	374,639	20,404	43,711	484,493	947,339
2034	25,041	0	387,961	20,404	44,358	489,328	967,092
2035	25,962	0	401,173	20,404	44,930	494,072	986,541
2036	26,859	0	414,230	20,404	45,431	498,731	1,005,655
2037	27,788	0	427,474	20,404	45,893	503,308	1,024,866
2038	28,659	0	440,345	20,404	46,258	507,813	1,043,480
2039	29,508	0	453,030	20,404	46,545	512,253	1,061,740
2040	30,294	0	465,240	20,404	46,729	516,631	1,079,299
2041	31,045	0	476,977	20,404	46,814	520,956	1,096,196
2042	31,727	0	488,146	20,404	46,801	525,230	1,112,308
2043	32,346	0	498,635	20,404	46,674	529,458	1,127,518
2044	32,911	0	508,649	20,404	46,460	533,649	1,142,073
2045	33,361	0	517,806	20,404	46,128	537,804	1,155,503

Per-person Results

The prior results represent the hypothetical national outcomes from universal identification and treatment of all undiagnosed persons. Below, we present major results on a per-person basis. These results are presented as either overall per person, or per-person based on a specifically defined population. The basis of per-person results is indicated for each table, but fall in the following two categories defined by their denominator population:

- Per American: Denominator represents the entire US resident population
- Per Undiagnosed: Denominator represents the estimated undiagnosed population with each respective eye condition

Prevalence of Eye Disorders Per-person

Table P1 reports the prevalence rates of eye disease per US resident. Table P2 reports the prevalence rates of undiagnosed eye disease per US resident. We do not report the prevalence of diagnosed eye disease, but this would be represented by the difference in rates between Tables P1 and P2.

Table P1. Prevalence Rates of Eye Disorders per US Resident Population

Per American	CNV	GA	Cataract	Glaucoma	DR	URE
2016	0.001914	0.002962	0.0583045	0.007163	0.0183654	0.0490167
2017	0.001933	0.002991	0.0593471	0.007108	0.0186575	0.0491024
2018	0.001953	0.003021	0.0604211	0.007054	0.0189464	0.0492521
2019	0.001974	0.003055	0.0615253	0.007	0.0192293	0.049414
2020	0.002	0.003094	0.0626573	0.006947	0.0195099	0.0495873
2021	0.002028	0.003138	0.0638115	0.006895	0.0197844	0.049771
2022	0.00206	0.003187	0.0649871	0.006844	0.020062	0.0499647
2023	0.002095	0.003241	0.0661812	0.006794	0.0203319	0.0501676
2024	0.002133	0.0033	0.0673887	0.006745	0.0205956	0.0503785
2025	0.002176	0.003367	0.068601	0.006696	0.0208548	0.0505956
2026	0.002222	0.003438	0.0698124	0.006649	0.0211095	0.0508174
2027	0.002272	0.003516	0.0710153	0.006603	0.021361	0.0510425
2028	0.002326	0.0036	0.0722035	0.006558	0.0216105	0.0512694
2029	0.002384	0.003688	0.0733701	0.006514	0.0218591	0.0514969
2030	0.002443	0.00378	0.0745121	0.006471	0.0221085	0.0517236
2031	0.002503	0.003874	0.0756246	0.006429	0.0223589	0.0519465
2032	0.002564	0.003968	0.0767009	0.006389	0.0226085	0.0521647
2033	0.002626	0.004063	0.0777353	0.00635	0.0228551	0.0523776
2034	0.002686	0.004157	0.078723	0.006312	0.0230974	0.0525841
2035	0.002746	0.00425	0.0796587	0.006275	0.0233332	0.0527839
2036	0.002805	0.00434	0.0805418	0.006239	0.0235646	0.0529769
2037	0.002861	0.004427	0.0813696	0.006204	0.0237949	0.0531635
2038	0.002914	0.00451	0.0821405	0.00617	0.0240247	0.0533445
2039	0.002965	0.004588	0.0828547	0.006137	0.024253	0.05352
2040	0.003013	0.004661	0.0835146	0.006104	0.0244794	0.0536902
2041	0.003056	0.004728	0.0841219	0.006072	0.0247034	0.0538555
2042	0.003094	0.004788	0.0846786	0.006041	0.024924	0.0540158
2043	0.003128	0.004839	0.0851896	0.00601	0.0251439	0.0541713
2044	0.003155	0.004882	0.0856626	0.005979	0.025364	0.0543224
2045	0.003177	0.004916	0.0861034	0.005949	0.0255828	0.0544689

Table P1. Prevalence Rates of Undiagnosed Eye Disorders per US Resident Population

Per American	CNV	GA	Cataract	Glaucoma	DR	URE
2016	0.000536	0.001497	0.02804097	0.00412	0.013044	0.0490167
2017	0.000541	0.001512	0.028542282	0.004181	0.013251	0.0491024
2018	0.000547	0.001527	0.029058654	0.004243	0.013457	0.0492521
2019	0.000553	0.001544	0.029589531	0.004309	0.013657	0.049414
2020	0.00056	0.001564	0.030133785	0.004378	0.013856	0.0495873
2021	0.000568	0.001586	0.030688729	0.00445	0.014051	0.049771
2022	0.000576	0.001611	0.031253959	0.004524	0.014248	0.0499647
2023	0.000586	0.001638	0.031828068	0.004602	0.01444	0.0501676
2024	0.000596	0.001667	0.032408669	0.004681	0.014627	0.0503785
2025	0.000608	0.001701	0.032991531	0.004765	0.014811	0.0505956
2026	0.000621	0.001737	0.033573964	0.004851	0.014992	0.0508174
2027	0.000635	0.001776	0.034152299	0.004939	0.01517	0.0510425
2028	0.00065	0.001818	0.034723609	0.005031	0.015347	0.0512694
2029	0.000666	0.001863	0.03528454	0.005125	0.015524	0.0514969
2030	0.000682	0.001909	0.03583358	0.005221	0.015701	0.0517236
2031	0.000699	0.001956	0.036368487	0.005318	0.015879	0.0519465
2032	0.000716	0.002003	0.036885993	0.005414	0.016056	0.0521647
2033	0.000733	0.002051	0.037383334	0.005509	0.016231	0.0523776
2034	0.000749	0.002098	0.037858195	0.005603	0.016403	0.0525841
2035	0.000766	0.002145	0.038308086	0.005695	0.01657	0.0527839
2036	0.000782	0.00219	0.038732688	0.005785	0.016734	0.0529769
2037	0.000798	0.002234	0.039130701	0.005872	0.016898	0.0531635
2038	0.000812	0.002276	0.039501368	0.005957	0.017061	0.0533445
2039	0.000826	0.002315	0.03984475	0.006039	0.017223	0.05352
2040	0.00084	0.002352	0.040161988	0.006118	0.017384	0.0536902
2041	0.000851	0.002386	0.040453997	0.006194	0.017543	0.0538555
2042	0.000862	0.002416	0.040721634	0.006264	0.017699	0.0540158
2043	0.000871	0.002442	0.04096732	0.006331	0.017855	0.0541713
2044	0.000879	0.002463	0.041194756	0.006395	0.018012	0.0543224
2045	0.000885	0.00248	0.041406664	0.006454	0.018167	0.0544689

Prevalence of Vision Loss Per-person

In Table P3, we report the predicted prevalence rate of blindness among the prevalent undiagnosed or untreated population with each condition. We estimate that nearly 60% of undiagnosed or untreated CNV patients are blind, vastly higher than for any of the other conditions. This result is driven by several parameters, including the prevalence of blindness due to AMD as reported by the EDPRG study and the allocation of blindness from AMD between CNV and GA as simulated in the MEDS model, and the prevalence of CNV. While each of these parameters, and thus the overall result is subject to uncertainty, it is likely that CNV left untreated would result in high rates of blindness among those affected. Table P4 presents the same information for visual impairment prevalence.

Table P3. Prevalence of Blindness among Undiagnosed or Untreated

Per undiagnosed	CNV	GA	Cataract	Glaucoma	DR	URE
2016	0.600	0.044	0.017	0.083	0.017	0.000
2017	0.597	0.044	0.017	0.084	0.017	0.000
2018	0.593	0.043	0.017	0.084	0.017	0.000
2019	0.590	0.043	0.017	0.084	0.018	0.000
2020	0.587	0.043	0.017	0.084	0.018	0.000
2021	0.585	0.043	0.017	0.085	0.018	0.000
2022	0.584	0.043	0.017	0.085	0.018	0.000
2023	0.583	0.043	0.018	0.086	0.018	0.000
2024	0.582	0.043	0.018	0.086	0.018	0.000
2025	0.583	0.043	0.018	0.087	0.019	0.000
2026	0.584	0.043	0.018	0.088	0.019	0.000
2027	0.586	0.043	0.018	0.089	0.019	0.000
2028	0.588	0.043	0.019	0.089	0.020	0.000
2029	0.591	0.043	0.019	0.090	0.020	0.000
2030	0.594	0.044	0.019	0.091	0.020	0.000
2031	0.597	0.044	0.019	0.092	0.021	0.000
2032	0.600	0.044	0.020	0.093	0.021	0.000
2033	0.603	0.044	0.020	0.094	0.022	0.000
2034	0.606	0.044	0.020	0.095	0.022	0.000
2035	0.609	0.045	0.021	0.096	0.023	0.000
2036	0.612	0.045	0.021	0.097	0.023	0.000
2037	0.615	0.045	0.022	0.098	0.023	0.000
2038	0.617	0.045	0.022	0.099	0.024	0.000
2039	0.620	0.045	0.022	0.100	0.024	0.000
2040	0.622	0.046	0.023	0.101	0.024	0.000
2041	0.623	0.046	0.023	0.101	0.025	0.000
2042	0.625	0.046	0.023	0.102	0.025	0.000
2043	0.626	0.046	0.023	0.103	0.025	0.000
2044	0.627	0.046	0.024	0.103	0.025	0.000
2045	0.628	0.046	0.024	0.104	0.026	0.000

Table P4. Prevalence of Visual Impairment among Undiagnosed or Untreated

Per undiagnosed	CNV	GA	Cataract	Glaucoma	DR	URE
2016	0.299	0.087	0.135	0.121	0.033	1.000
2017	0.301	0.087	0.134	0.121	0.033	1.000
2018	0.303	0.087	0.133	0.122	0.033	1.000
2019	0.305	0.086	0.132	0.122	0.033	1.000
2020	0.307	0.086	0.132	0.123	0.033	1.000
2021	0.308	0.086	0.131	0.123	0.034	1.000
2022	0.309	0.086	0.131	0.124	0.034	1.000
2023	0.310	0.086	0.131	0.125	0.034	1.000
2024	0.310	0.086	0.132	0.126	0.035	1.000
2025	0.309	0.086	0.132	0.127	0.035	1.000
2026	0.310	0.086	0.133	0.128	0.036	1.000
2027	0.309	0.086	0.135	0.130	0.037	1.000
2028	0.307	0.086	0.136	0.131	0.037	1.000
2029	0.305	0.086	0.138	0.132	0.038	1.000
2030	0.303	0.086	0.140	0.134	0.039	1.000
2031	0.301	0.086	0.142	0.135	0.040	1.000
2032	0.299	0.086	0.144	0.136	0.041	1.000
2033	0.298	0.086	0.146	0.138	0.042	1.000
2034	0.296	0.086	0.149	0.139	0.043	1.000
2035	0.295	0.086	0.151	0.140	0.044	1.000
2036	0.293	0.086	0.153	0.141	0.045	1.000
2037	0.291	0.087	0.156	0.142	0.046	1.000
2038	0.290	0.087	0.158	0.143	0.047	1.000
2039	0.289	0.087	0.160	0.144	0.048	1.000
2040	0.288	0.087	0.162	0.145	0.049	1.000
2041	0.287	0.087	0.164	0.146	0.050	1.000
2042	0.286	0.087	0.166	0.147	0.051	1.000
2043	0.285	0.087	0.168	0.147	0.052	1.000
2044	0.284	0.087	0.169	0.148	0.053	1.000
2045	0.284	0.087	0.171	0.148	0.053	1.000

Impact of Treatment on Vision Loss Prevalence

Table P5 contains predicted impact of treatment on vision loss prevalence rates (based on the sum of the rates of blindness in Table P3 and visual impairment in Table P4).

Table P5. Impact of Treatment on Vision Loss Prevalence among Undiagnosed/Untreated

Per undiagnosed	CNV	GA	Cataract	Glaucoma	DR	URE
2016	-4%	0%	-14%	-10%	-6%	-100%
2017	-5%	0%	-14%	-10%	-6%	-100%
2018	-10%	0%	-14%	-10%	-6%	-100%
2019	-26%	0%	-14%	-10%	-6%	-100%
2020	-36%	0%	-14%	-10%	-6%	-100%
2021	-45%	0%	-14%	-11%	-6%	-100%
2022	-46%	0%	-14%	-11%	-7%	-100%
2023	-41%	0%	-14%	-11%	-7%	-100%
2024	-32%	0%	-14%	-11%	-7%	-100%
2025	-23%	0%	-14%	-12%	-7%	-100%
2026	-23%	0%	-14%	-12%	-7%	-100%
2027	-23%	0%	-15%	-12%	-8%	-100%
2028	-23%	0%	-15%	-12%	-8%	-100%
2029	-24%	0%	-15%	-12%	-8%	-100%
2030	-24%	0%	-15%	-12%	-8%	-100%
2031	-24%	0%	-15%	-12%	-9%	-100%
2032	-25%	0%	-16%	-12%	-9%	-100%
2033	-25%	0%	-16%	-12%	-9%	-100%
2034	-25%	0%	-16%	-12%	-9%	-100%
2035	-26%	0%	-16%	-12%	-10%	-100%
2036	-26%	0%	-17%	-12%	-10%	-100%
2037	-26%	0%	-17%	-12%	-10%	-100%
2038	-27%	0%	-17%	-12%	-11%	-100%
2039	-27%	0%	-17%	-12%	-11%	-100%
2040	-27%	0%	-18%	-12%	-11%	-100%
2041	-27%	0%	-18%	-12%	-12%	-100%
2042	-27%	0%	-18%	-11%	-12%	-100%
2043	-28%	0%	-18%	-11%	-12%	-100%
2044	-28%	0%	-18%	-11%	-12%	-100%
2045	-28%	0%	-18%	-10%	-13%	-100%

Per-person Net Costs and QALY Impacts from Treatment

Table P6 represents the net impact on costs from immediate treatment of an undiagnosed person. Positive values represent costs, negative values represent savings. Initial costs are highest for CNV, but reduce substantially after 3 years when we assume the frequency of anti-VEGF therapy will decline, and substantial cost-offsets from avoided vision loss begin to accrue. GA and DR incur generally static costs which increase annually due primarily to inflation and projected medical intensity. Relatively lower treatment efficacy for these conditions prevent increases in cost-offsets over time, while glaucoma costs gradually decrease as savings from averted vision loss increasingly offset medical treatment costs. Cataract achieves cost savings after the first year of treatment. URE treatment is cost saving in every year due to the very low costs of treatment, our assumption of 100% treatment efficacy, and the savings from averted productivity losses from URE. Predicted QALY gains from treatment, per undiagnosed person, are presented in Table P7.

Table P6. Per Person Net Costs

Per undiagnosed	CNV	GA	Cataract	Glaucoma	DR	URE
2016	$11,627	$3,740	$1,469	$1,072	$3,528	-$3,996
2017	$12,089	$3,934	-$1,975	$1,100	$3,054	-$4,513
2018	$12,182	$4,118	-$2,061	$1,001	$3,204	-$4,750
2019	$5,454	$4,301	-$2,148	$895	$3,354	-$4,988
2020	-$383	$4,484	-$2,236	$786	$3,504	-$5,216
2021	-$6,840	$4,671	-$2,326	$677	$3,658	-$5,429
2022	-$10,844	$4,858	-$2,414	$567	$3,813	-$5,618
2023	-$12,856	$5,045	-$2,504	$459	$3,968	-$5,791
2024	-$12,004	$5,232	-$2,600	$347	$4,121	-$5,964
2025	-$10,513	$5,442	-$2,706	$239	$4,293	-$6,140
2026	-$10,802	$5,632	-$2,820	$124	$4,446	-$6,314
2027	-$11,131	$5,823	-$2,943	$8	$4,598	-$6,485
2028	-$11,488	$6,014	-$3,073	-$106	$4,749	-$6,657
2029	-$11,922	$6,205	-$3,216	-$221	$4,898	-$6,829
2030	-$12,341	$6,395	-$3,365	-$327	$5,048	-$7,006
2031	-$12,791	$6,586	-$3,520	-$426	$5,198	-$7,184
2032	-$13,265	$6,777	-$3,681	-$518	$5,349	-$7,363
2033	-$13,751	$6,968	-$3,845	-$597	$5,501	-$7,543
2034	-$14,301	$7,158	-$4,016	-$667	$5,654	-$7,722
2035	-$14,849	$7,349	-$4,190	-$720	$5,808	-$7,902
2036	-$15,405	$7,540	-$4,368	-$755	$5,965	-$8,082
2037	-$16,011	$7,731	-$4,554	-$771	$6,123	-$8,262
2038	-$16,604	$7,921	-$4,739	-$763	$6,284	-$8,443
2039	-$17,210	$8,112	-$4,925	-$732	$6,448	-$8,624
2040	-$17,805	$8,303	-$5,109	-$672	$6,616	-$8,804
2041	-$18,415	$8,494	-$5,294	-$583	$6,787	-$8,984
2042	-$19,024	$8,684	-$5,474	-$465	$6,961	-$9,164
2043	-$19,641	$8,875	-$5,651	-$311	$7,139	-$9,343
2044	-$20,274	$9,066	-$5,824	-$123	$7,321	-$9,522
2045	-$20,880	$9,257	-$5,988	$101	$7,507	-$9,699

Table P7. Per Person Net Costs and Net QALYs

Per undiagnosed	CNV	GA	Cataract	Glaucoma	DR	URE
2016	0.008	0.000	0.025	0.015	0.008	0.025
2017	0.010	0.000	0.025	0.015	0.008	0.025
2018	0.017	0.000	0.025	0.015	0.008	0.025
2019	0.057	0.000	0.025	0.014	0.008	0.025
2020	0.085	0.000	0.024	0.014	0.008	0.025
2021	0.113	0.000	0.024	0.014	0.008	0.025
2022	0.121	0.000	0.024	0.013	0.008	0.025
2023	0.114	0.000	0.024	0.013	0.007	0.025
2024	0.101	0.000	0.025	0.013	0.007	0.025
2025	0.085	0.000	0.025	0.012	0.007	0.025
2026	0.085	0.000	0.025	0.012	0.007	0.025
2027	0.085	0.000	0.025	0.012	0.007	0.025
2028	0.086	0.000	0.025	0.011	0.007	0.025
2029	0.087	0.000	0.026	0.011	0.007	0.025
2030	0.088	0.000	0.026	0.011	0.007	0.025
2031	0.088	0.000	0.027	0.011	0.007	0.025
2032	0.089	0.000	0.027	0.010	0.007	0.025
2033	0.090	0.000	0.027	0.010	0.007	0.025
2034	0.091	0.000	0.028	0.010	0.007	0.025
2035	0.092	0.000	0.028	0.010	0.007	0.025
2036	0.092	0.000	0.029	0.009	0.007	0.025
2037	0.093	0.000	0.029	0.009	0.007	0.025
2038	0.094	0.000	0.030	0.009	0.007	0.025
2039	0.094	0.000	0.030	0.009	0.007	0.025
2040	0.095	0.000	0.030	0.009	0.007	0.025
2041	0.095	0.000	0.031	0.009	0.007	0.025
2042	0.096	0.000	0.031	0.008	0.007	0.025
2043	0.096	0.000	0.032	0.008	0.007	0.025
2044	0.097	0.000	0.032	0.008	0.007	0.025
2045	0.097	0.000	0.032	0.008	0.007	0.025

Sensitivity Analysis

Many underlying parameters in this analysis are subject to uncertainty. We conducted a univariate sensitivity analysis of six major parameter categories to better understand the potential impact of each on the results. The parameter categories included in the sensitivity analysis included the following:

- Treatment efficacy (75%-125% of mean values)
- Population projections (Low and high series)
- Disease and vision loss prevalence rates (95% C.I.)
- Inflation, medical costs growth and healthcare intensity (none – double)
- Productivity losses (95% C.I.)
- Medical Costs (95% C.I.)

Below, we describe each parameter group, including the range of variation, showing line graphs depicting the relative impact of each parameter group on each condition for three primary outcomes; vision loss prevalence, net costs and net QALYs due to the impact of the hypothetical treatment scenario. In the second part of this section, we present summary tables and tornado diagrams showing the actual and relative impact of each parameter group on the projected 10-year average outcomes of the treatment scenario.

Description of Parameter Group Variation

Treatment Efficacy

Treatment efficacy was predicted by the MEDS model for DR, CNV, and glaucoma, while we assumed 0% efficacy for GA, 95% efficacy for cataract surgery, 100% efficacy for URE treatment. For DR, CNV and glaucoma we calculated the 95% credible interval of treatment efficacy in the MEDS model, but found very small variation at the population level. However, this variation would not reflect any uncertainty in the assumptions of treatment, simply the parameter values. Therefore, for the model-based treatment efficacy values, we varied treatment efficacy based on a range of 75% to 125% the baseline efficacy to show the potential impact of larger levels of uncertainty. For cataract, we assumed a range of 90%-100%, and for URE we assessed the impact with a 90% efficacy.

We found that treatment efficacy had relatively large impacts on CNV and glaucoma outcomes, since both conditions are associated with rapid vision loss without treatment, and high efficacy of treatment. GA exhibits no impact on vision loss or QALYs because we assume to effective treatment exists. URE and cataract exhibit generally low variation because we assumed a narrow range of efficacy values.

Figure SENS1. Impact of Treatment Efficacy on Vision Loss Impact of Treatment

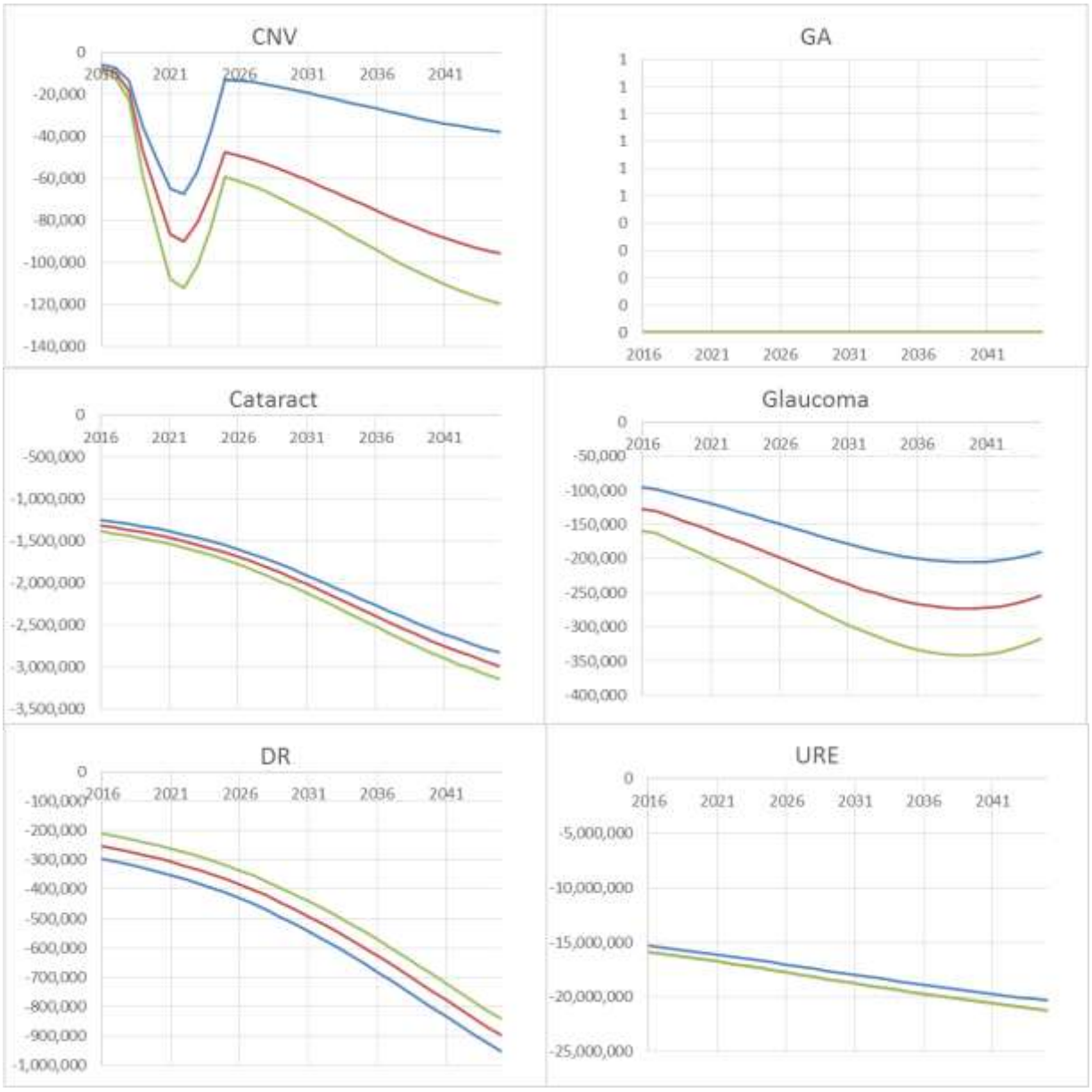


Figure SENS2. Impact of Treatment Efficacy on Net Costs from Treatment

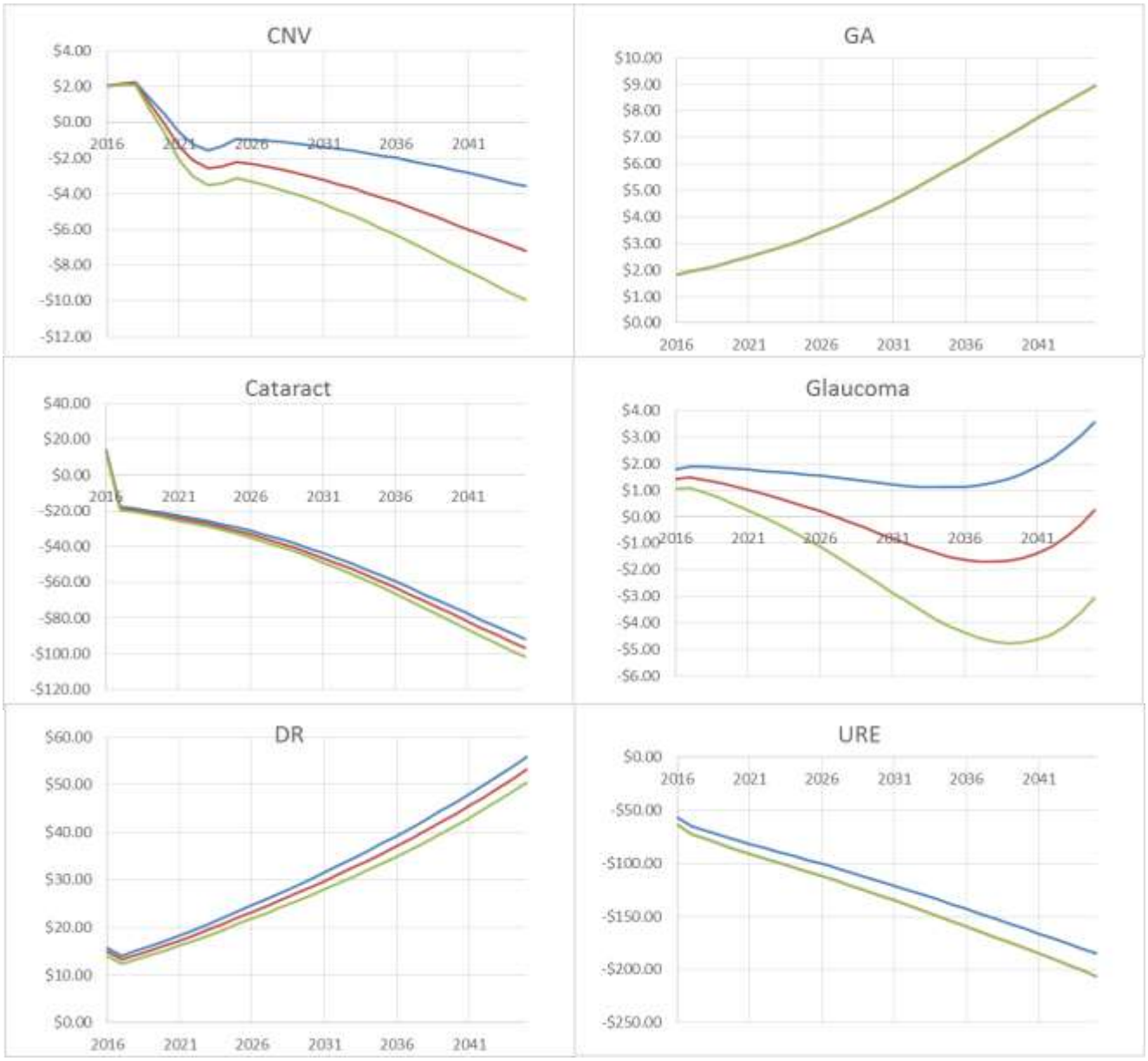
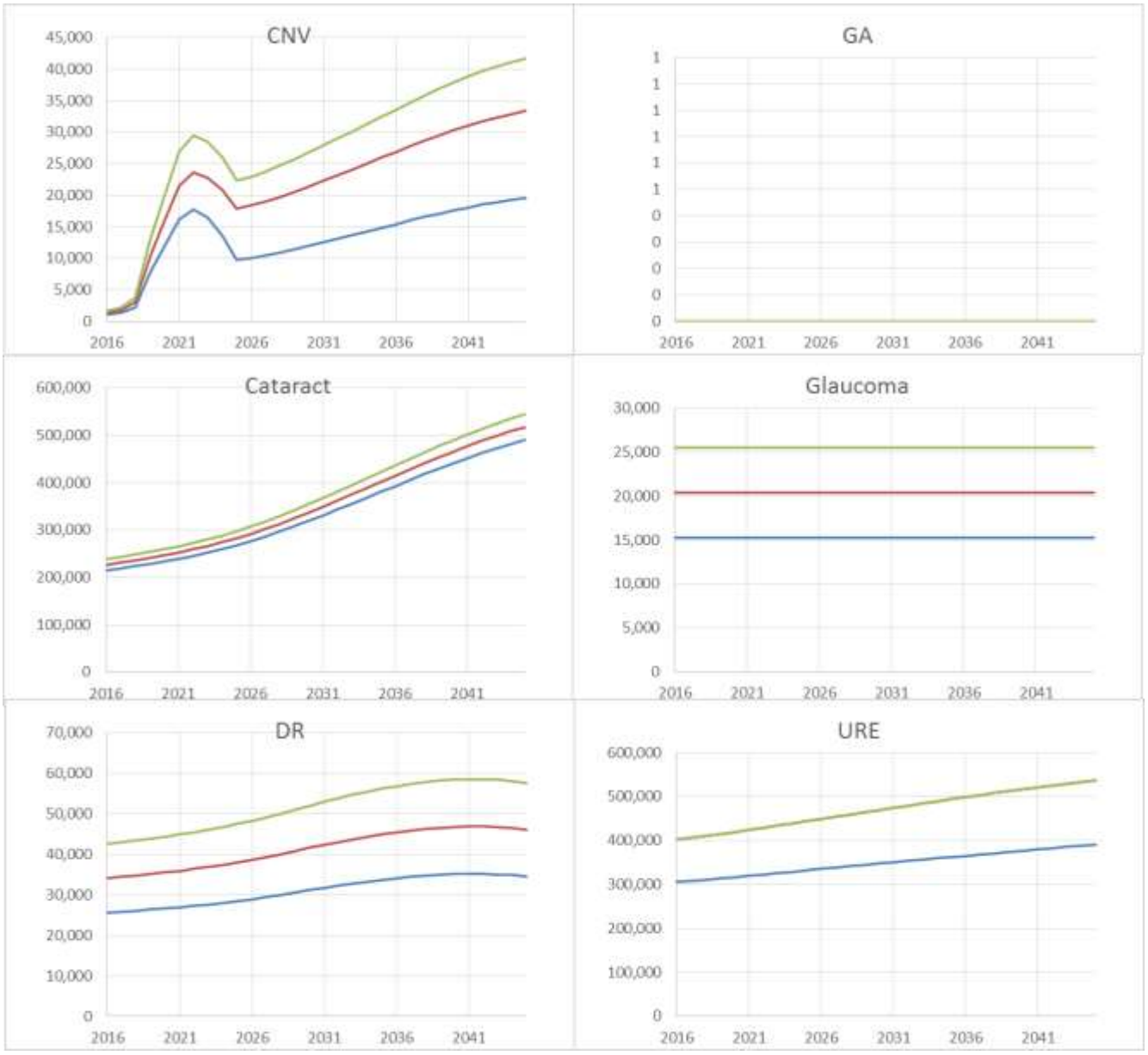


Figure SENS3. Impact of Treatment Efficacy on QALY Gains from Treatment



Population Projections

Since this analysis uses a prevalence-based approach and does not track individuals, we were unable to assess the impact of different levels of life expectancy or longevity. However, the Census projections used to create future population estimates are reported in a low, middle and high series. Our baseline projections use the middle series. For the sensitivity analysis, we varied the projections based on the low and high series. The differences in these projections reflect different assumptions for both longevity and other population factors such as birth rates and net migration. However, birth rates only factor into the

URE prevalence estimates, since the other disorders are only estimated for ages 40 and older, and our results are reported for the next 30 years, no new births would be captured in our results. Thus, the population projections may be considered to reflect uncertainty in life expectancy and migration.

In general, population projections had very little impact on the net impact of treatment. This is due to two factors. First, the low, middle and high series demonstrate relatively little variation. Secondly, since the large majority of treatment occurs in the first year of the analysis (assuming 100% treatment of the prevalent undiagnosed or untreated population), the impact of future population projections is only applied to a relatively smaller number undergoing treatment.

Figure SENS4. Impact of Population Projections on Vision Loss Impact of Treatment

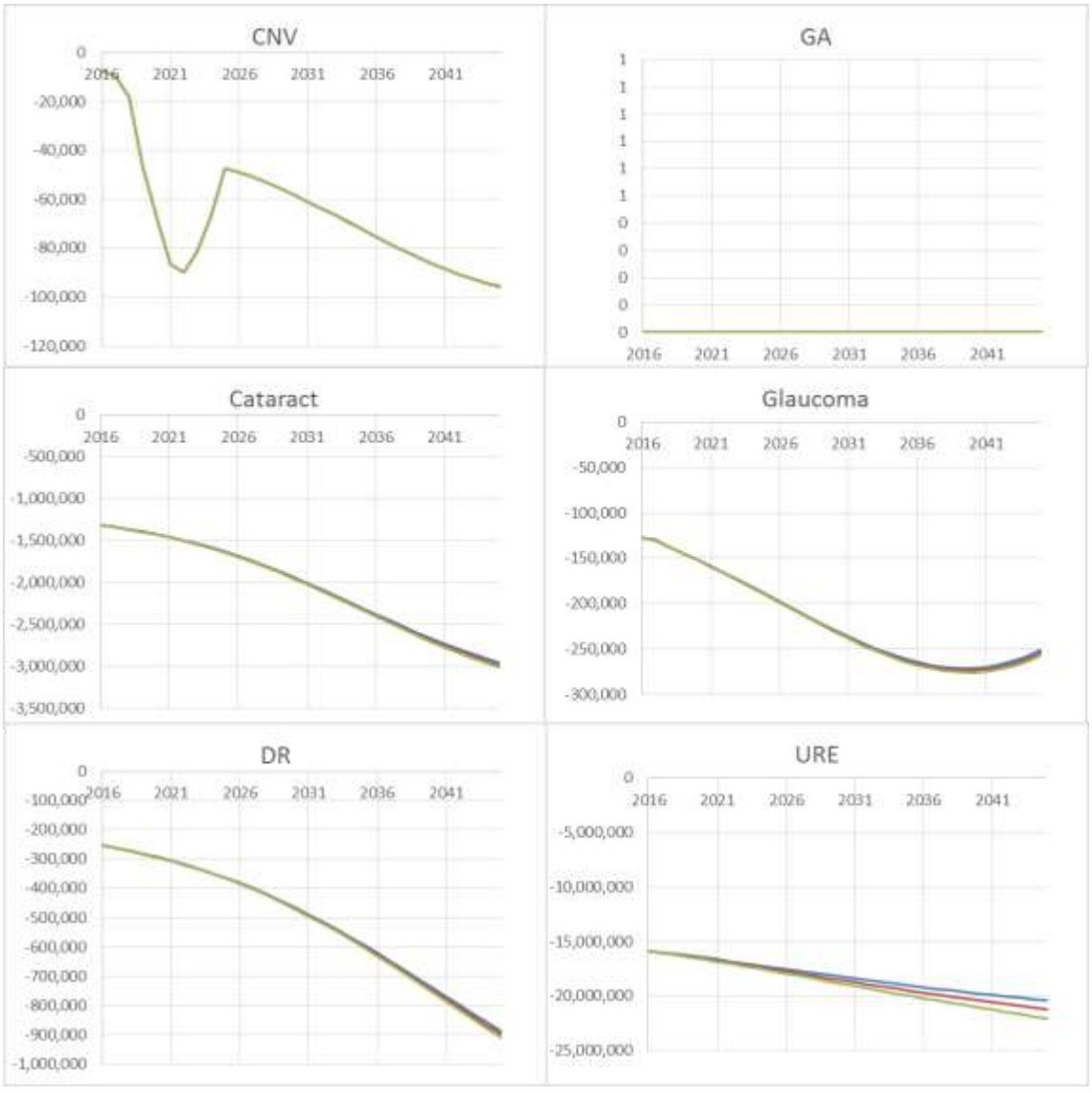


Figure SENS5. Impact of Population Projections on Net Costs from Treatment

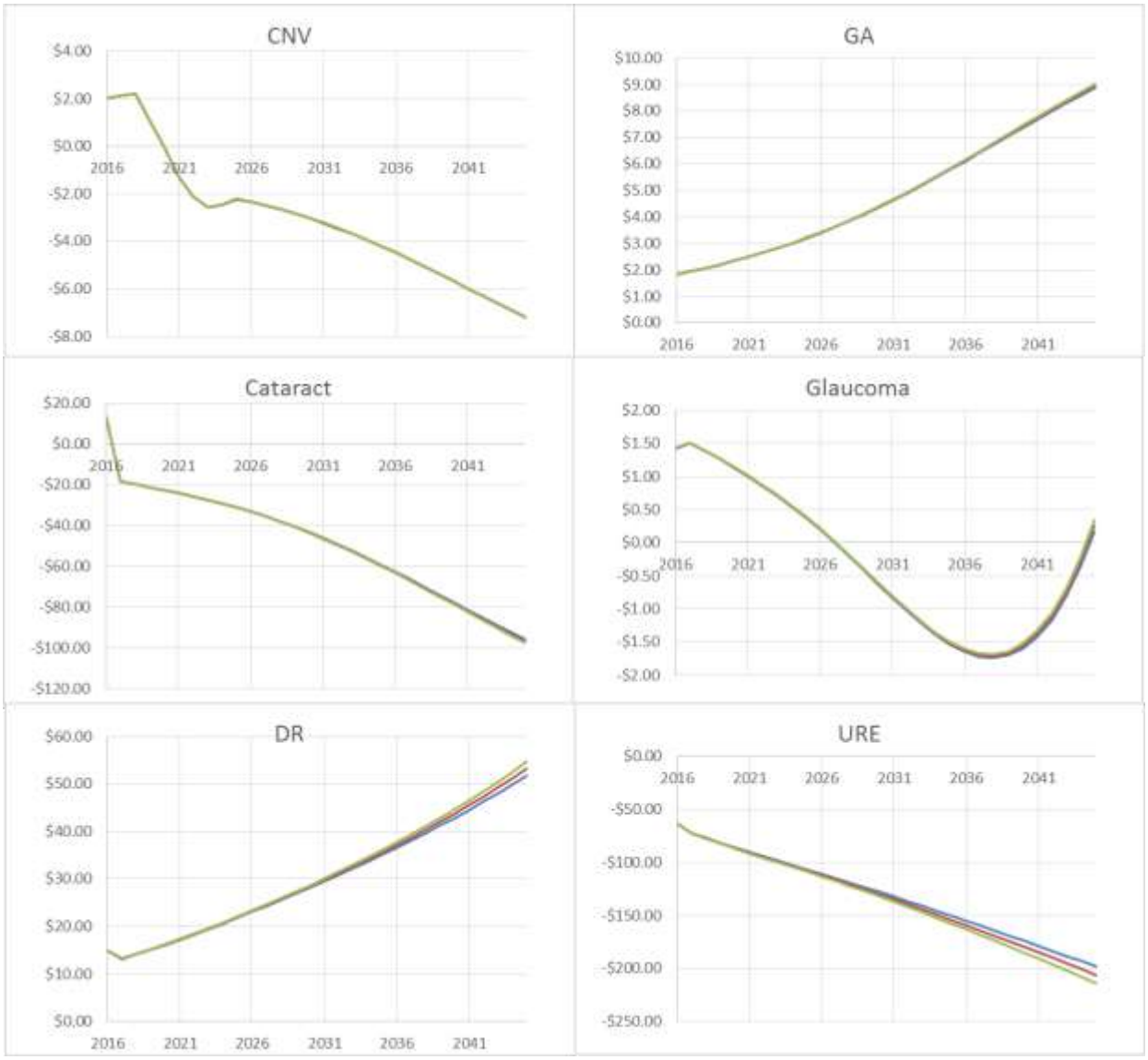
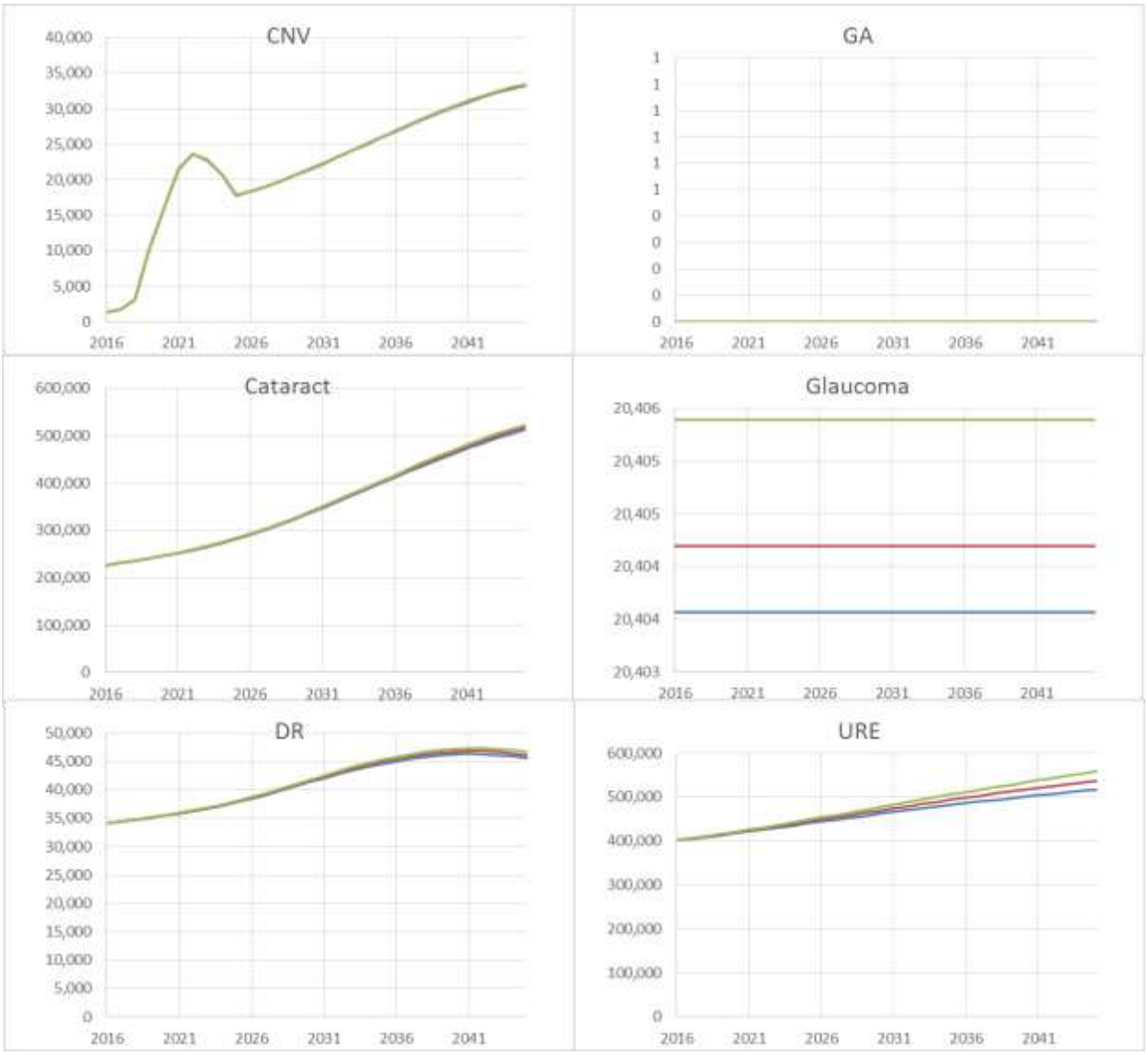


Figure SENS6. Impact of Treatment Efficacy on QALY Gains from Treatment



Prevalence Rates

We varied the prevalence rates of eye disorders and visual impairment and blindness. The prevalence of URE was calculated in NHANES data. Applying a logistic regression, we calculated the 95% confidence intervals of the prevalence rates of URE by age, race and sex directly from the NHANES data. However, prevalence of the other eye conditions and vision loss are based on the VPUS, which does not report confidence intervals nor other measures of uncertainty. However, since VPUS is an expansion on the 2004 EDPRG prevalence studies, we therefor assume that the level of uncertainty in EDPRG, which did report confidence intervals, is likely to approximate the uncertainty of the estimates in VPUS. While this is an assumption, this could plausibly be considered a conservative assumption (conservative in the sense of over-estimating the level of uncertainty) since VPUS is based on larger overall samples, including a subset representing the EDPRG data. Thus, it is plausible that VPUS would therefore exhibit lower statistical uncertainty than EDPRG, which is a component of VPUS. To apply EDPRG-levels of uncertainty to VPUS, we calculated the percent change from the mean values to the lower and upper bounds of the reported 95% confidence interval in EDPRG, and then multiplied the VPUS prevalence estimates by these multipliers.

Figure SENS7. Impact of Prevalence Rates on Vision Loss Impact of Treatment

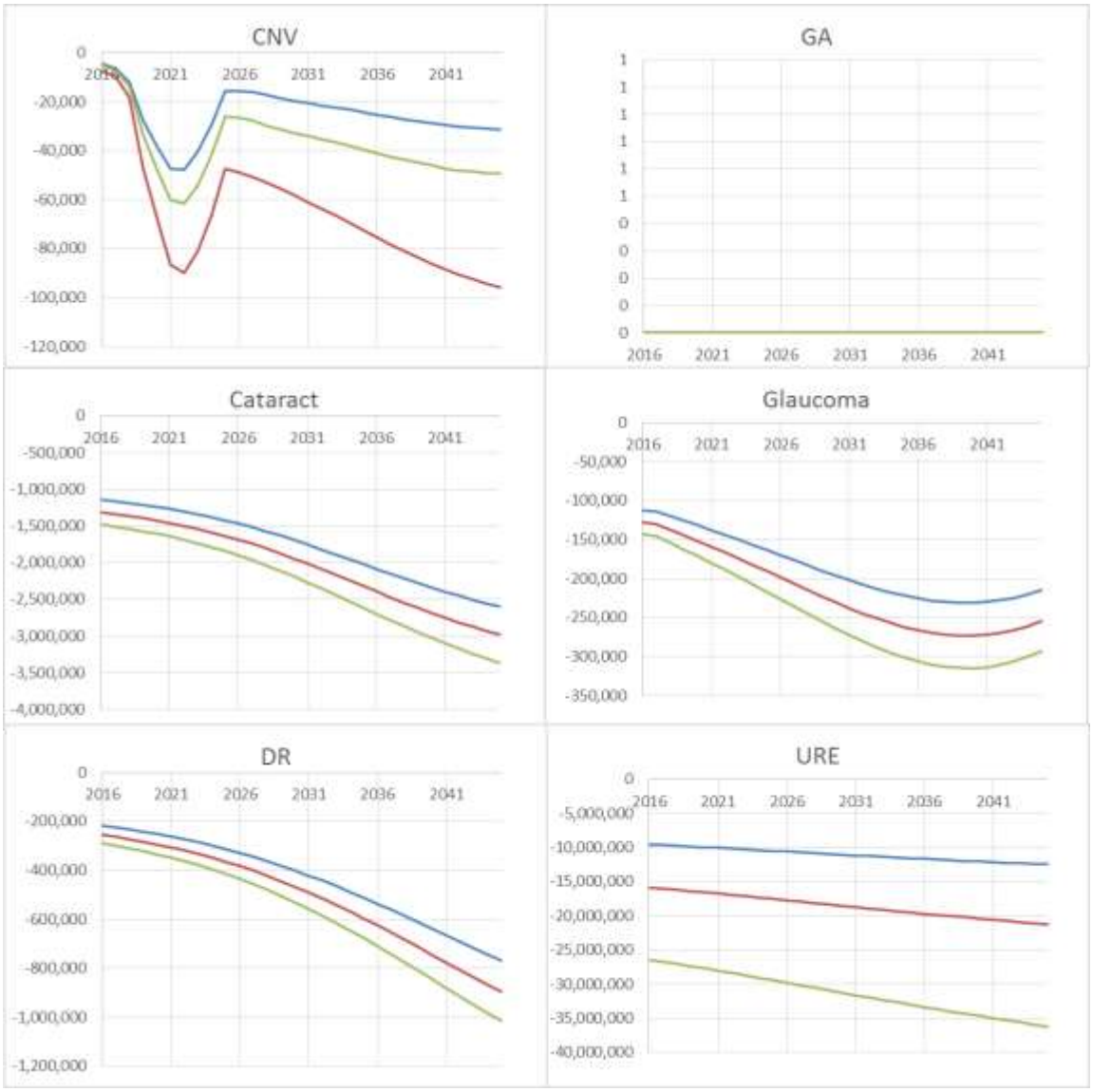


Figure SENS8. Impact of Prevalence Rates on Net Costs from Treatment

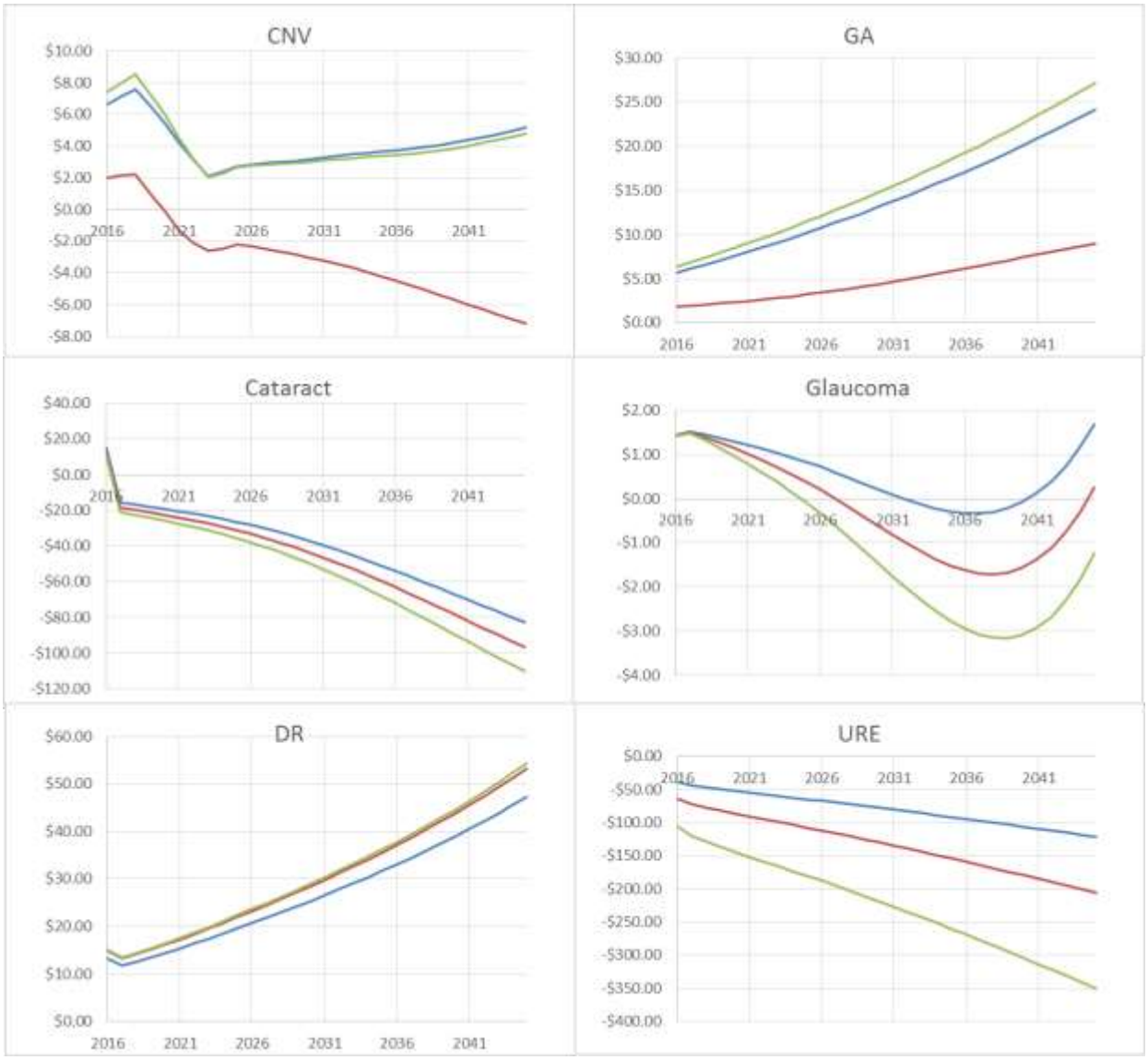
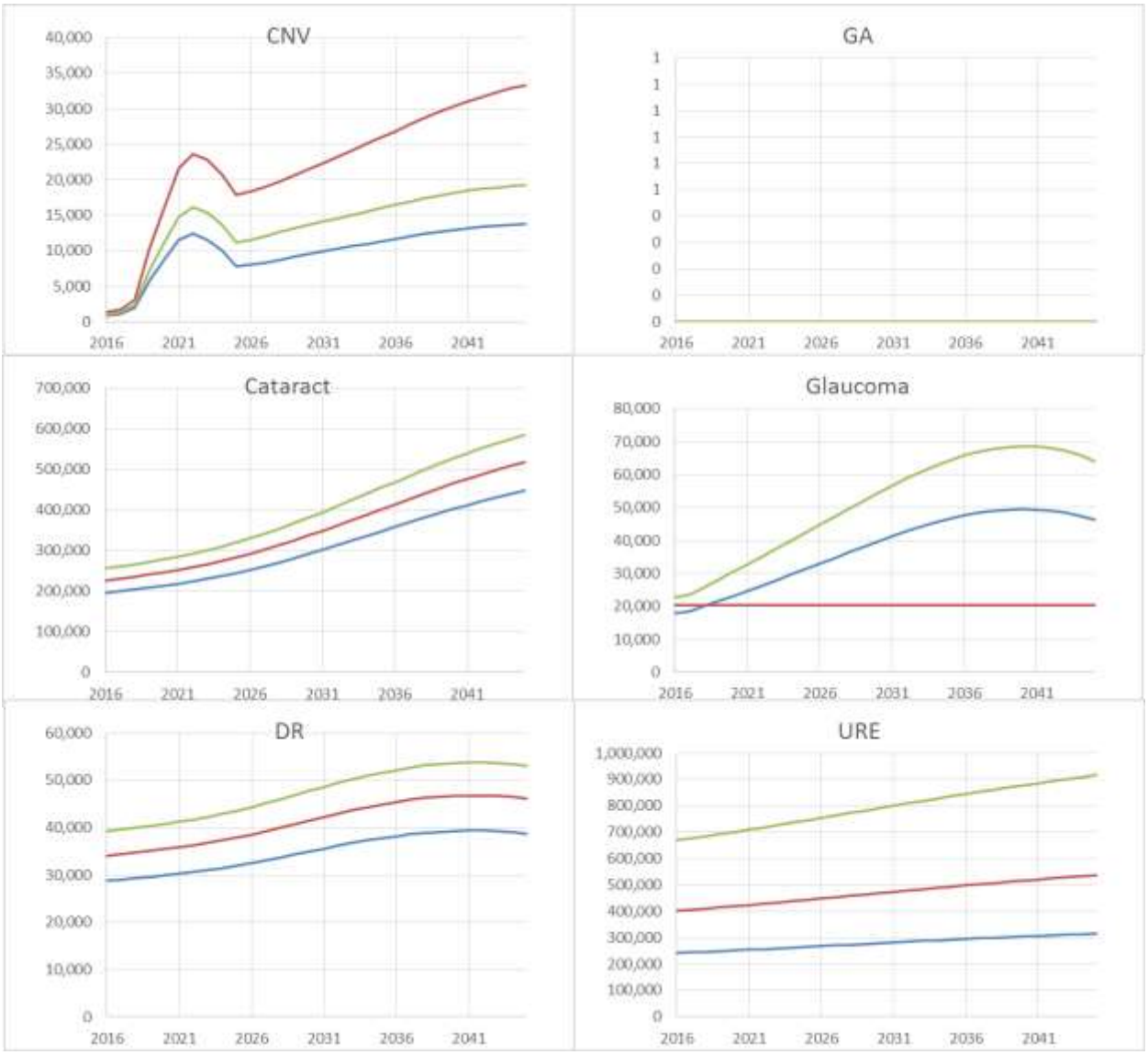


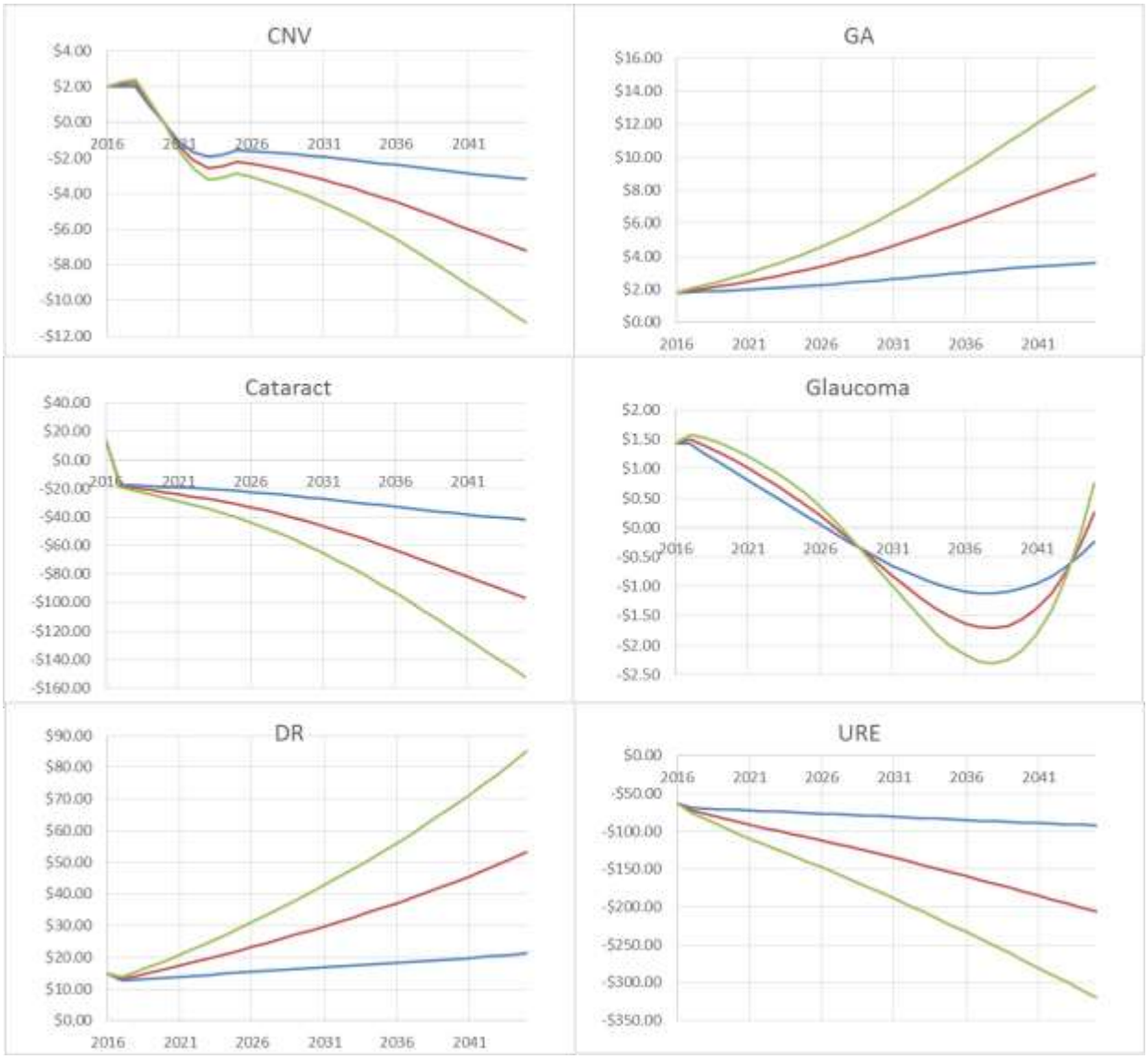
Figure SENS9. Impact of Prevalence Rates on QALY Gains from Treatment



Inflation, Medical Cost Growth, and Healthcare Intensity

Our baseline results include three cost growth multipliers, which together inflate costs to represent nominal predictions. General economic costs, including productivity and non-medical care services are inflated based on projections of general inflation. Medical costs are increased at a faster rate of inflation. In addition, we include an inflator for predicted increases in healthcare intensity, which represents assumed increases in the relative share of resources devoted to healthcare, including higher access to care, higher utilizations, and increased technology. For the sensitivity analysis, we range these inflators from none (assuming no changes in underlying costs) to double their normal amount. Since these inflators only affect costs, we show only the impact on medical costs below.

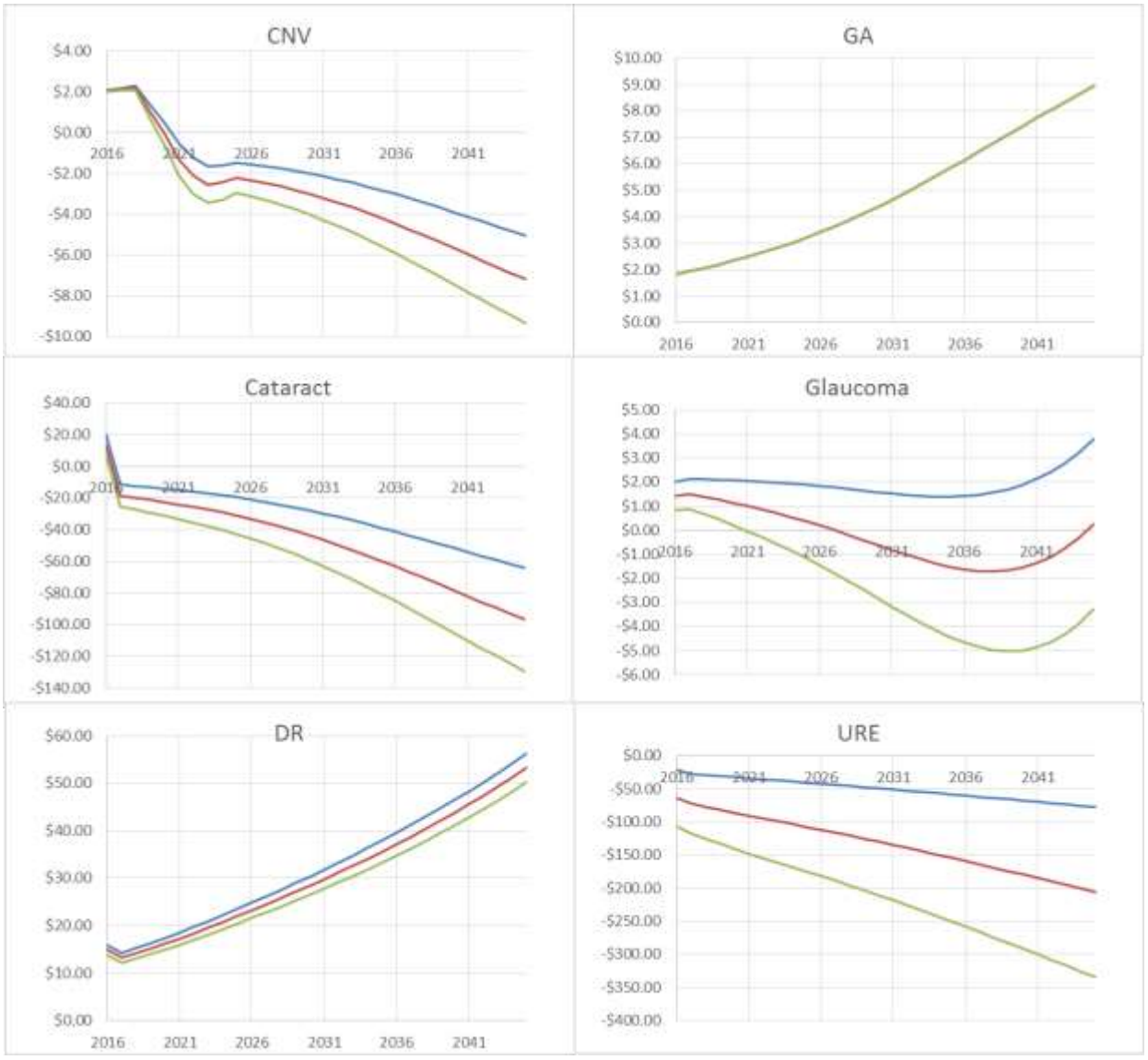
Figure SENS10. Impact of Inflation and Intensity on Net Costs from Treatment



Productivity Losses

We used NHANES to estimate the impact of vision loss, including blindness, visual impairment and URE on net household income. Previously, we estimated costs using the Survey of Income and Program Participation (SIPP), which used self-reported visual function. The productivity losses are high and subject to statistical uncertainty, which leads to large impacts in projected cost impacts of treatment. We ranged the productivity loss estimates based on their 95% confidence interval. As with inflation, only costs are affected and thus only costs are shown below.

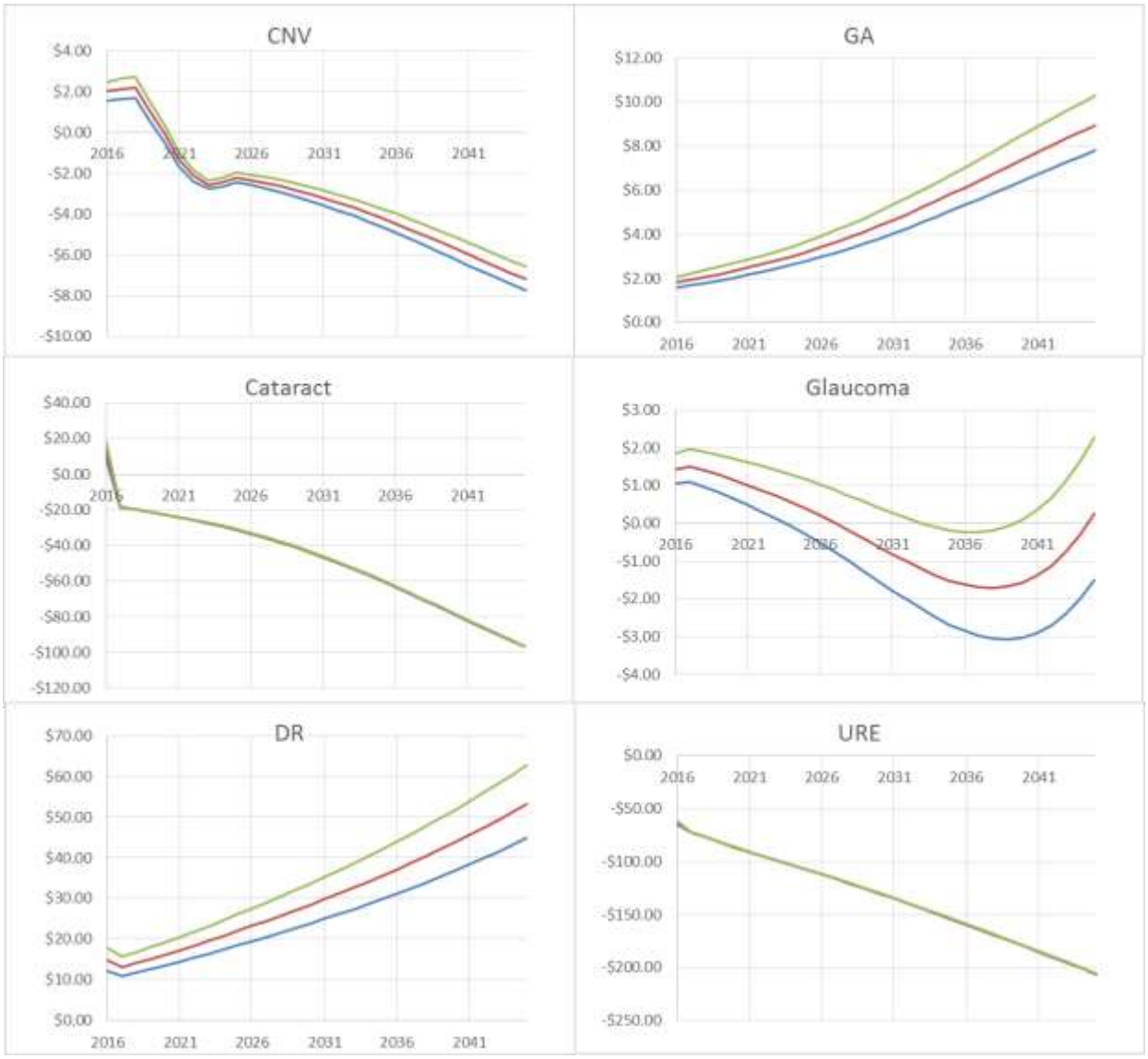
Figure SENS11. Impact of Productivity Losses on Net Costs from Treatment



Medical Costs

Most medical costs were calculated in 2003-2008 MEPS data. In the sensitivity analysis, we varied these costs based on their 95% confidence interval. The MEPS data used to calculate costs is generally too early to include substantial anti-VEGF treatment costs, which have dramatically changed the course of treatment for CNV and DR associated CSME. We separately calculated anti-VEGF costs based on injection frequencies and list prices. We vary this cost from 75% to 125% of the baseline estimate. We also varied URE treatment costs for current or incident cases based on 75% to 125%. Changing medical costs had a relatively large impact on glaucoma and DR, followed by GA and CNV. URE was highly insensitive to changes in treatment costs due to the extremely low cost of URE treatment.

Figure SENS12. Impact of Medical Costs on Net Costs from Treatment



Summary Results of Sensitivity Analysis

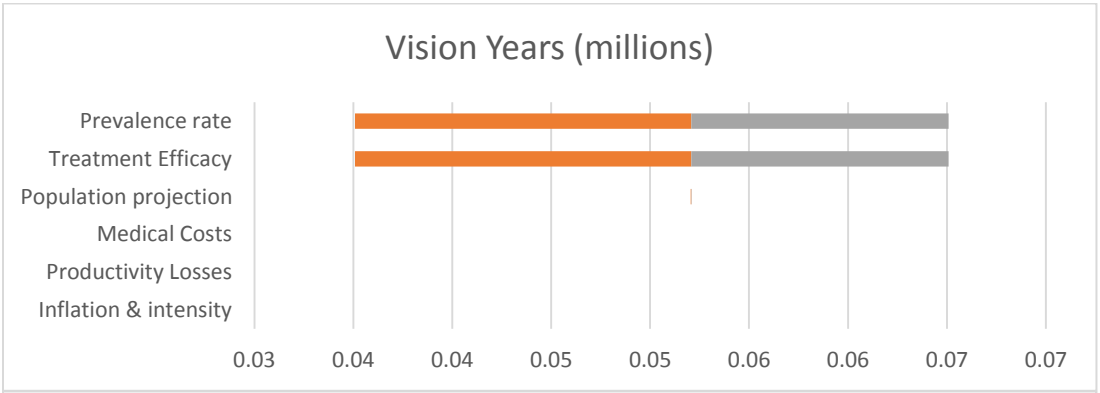
The tables and figures below present sensitivity analysis results grouped by condition, showing the relative impact of each of the six parameter groups on results. For each condition, we report the net impact of treatment represented by the 10-year average vision loss prevalence, net costs and QALY gains in table form and in tornado diagrams.

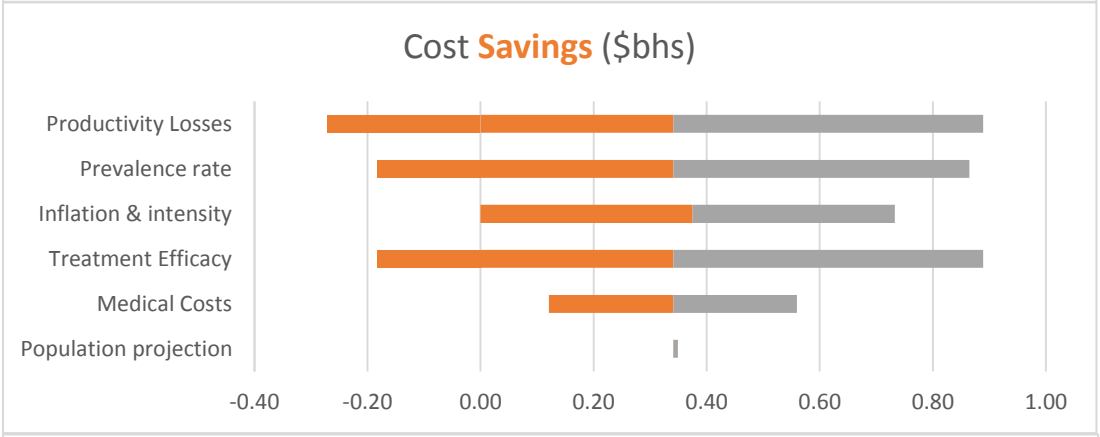
Inflation, productivity losses and medical costs have no impact on the health outcomes of vision loss prevalence or QALYs. In general, the prevalence rate has a large influence on health outcomes. Treatment efficacy has a large impact on CNV, glaucoma and DR health outcomes. Productivity losses have the greatest impact on net costs for all conditions except for DR, which is due to the high ongoing costs of DR treatment and the fact that the DR population declines rapidly with age, limiting the potential years of productivity loss.

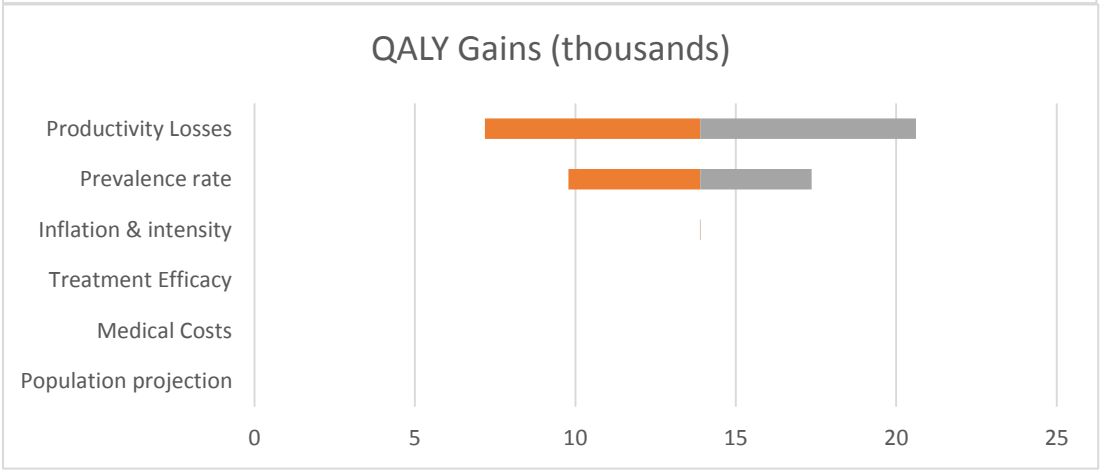
Care must be taken when considering the Net Cost of Net Cost Savings graphs. Since tornado diagrams are typically shown in a positive axis, for cost saving interventions such as URE, the x-axis represents costs. For net positive cost interventions such as DR treatment, the x-axis represents costs. The title of each graph indicated whether it is reporting net costs or net savings.

CNV Treatment Sensitivity

CNV	Vision Loss				Net Costs ($bns)				QALY Gains (thousands)		
	Low	Medium	High		Low	Medium	High		Low	Medium	High
Treatment Efficacy	0.035	0.052	0.065		-0.27	0.34	0.89		9,785	13,895	17,368
Population projection	0.052	0.052	0.052		0.34	0.34	0.34		13,886	13,895	13,903
Prevalence rate	0.027	0.052	0.035		-4.80	0.34	-5.19		7,178	13,895	20,611
Inflation & intensity	0.052	0.052	0.052		0.12	0.34	0.56		13,895	13,895	13,895
Productivity Losses	0.052	0.052	0.052		-0.18	0.34	0.86		13,895	13,895	13,895
Medical Costs	0.052	0.052	0.052		0.70	0.34	-0.03		13,895	13,895	13,895

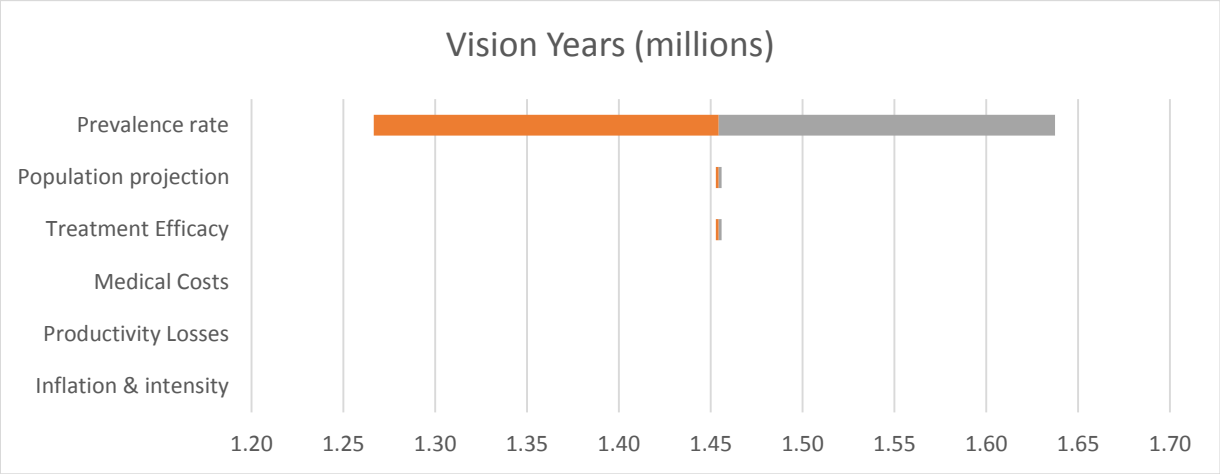


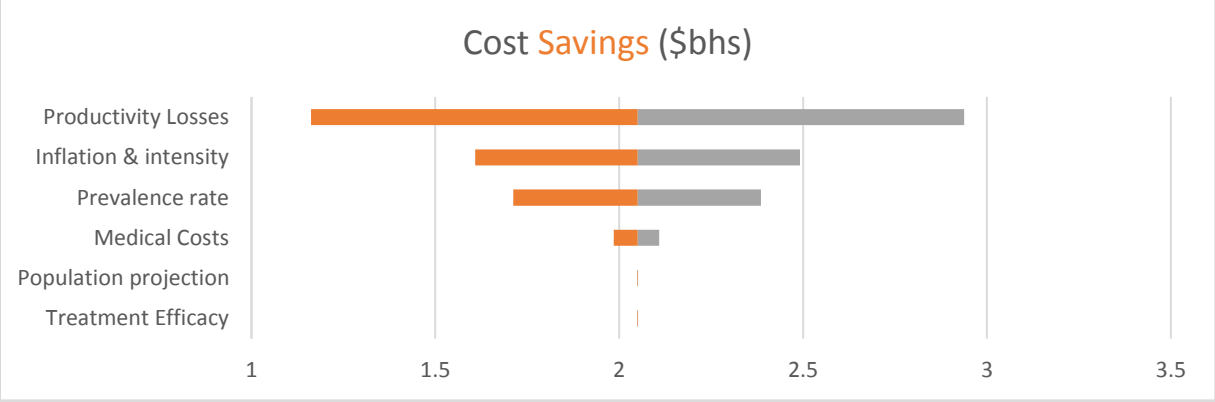


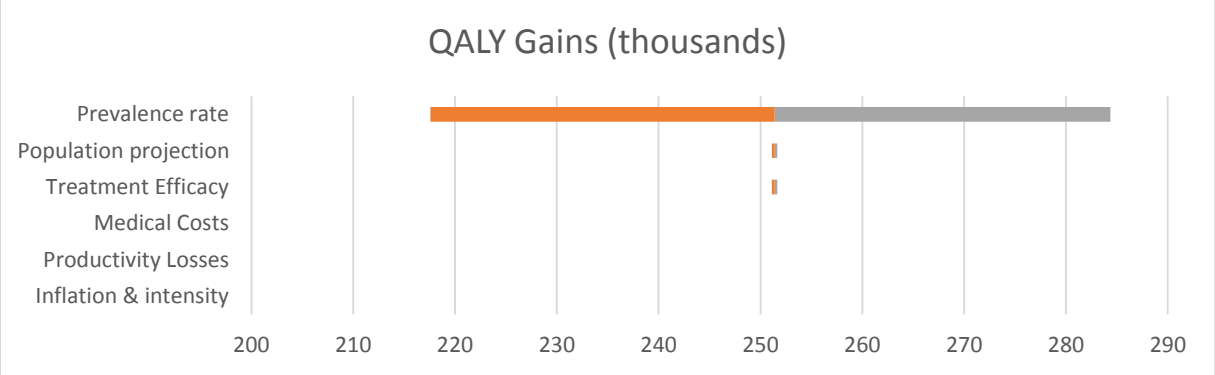


Cataract Treatment Sensitivity

Cataract	Vision Loss				Net Costs ($bns)				QALY Gains (thousands)		
	Low	Medium	High		Low	Medium	High		Low	Medium	High
Treatment Efficacy	1.45	1.45	1.46		2.04869	2.05015	2.05158		251.11	251.38	251.65
Population projection	1.45	1.45	1.46		2.04869	2.05015	2.05158		251.11	251.38	251.65
Prevalence rate	1.27	1.45	1.64		1.71187	2.05015	2.38554		217.58	251.38	284.38
Inflation & intensity	1.45	1.45	1.45		1.60886	2.05015	2.49144		251.38	251.38	251.38
Productivity Losses	1.45	1.45	1.45		1.16202	2.05015	2.93828		251.38	251.38	251.38
Medical Costs	1.45	1.45	1.45		1.98491	2.05015	2.10863		13,895	13,895	13,895

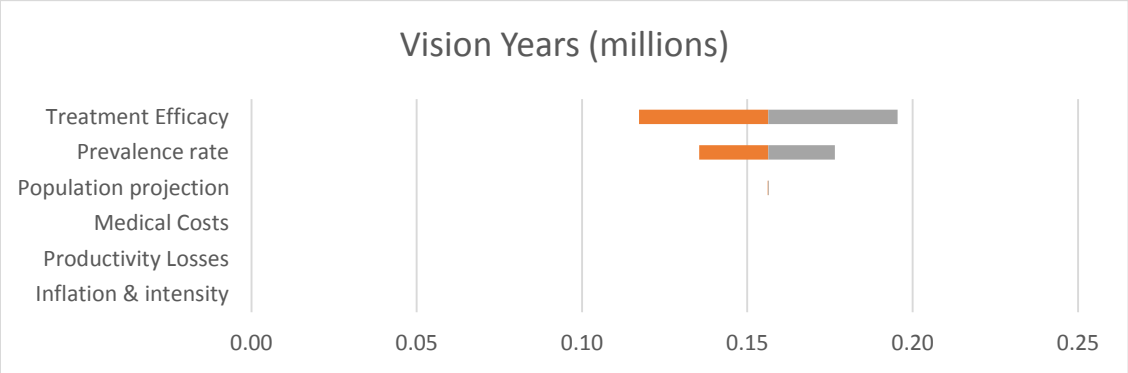


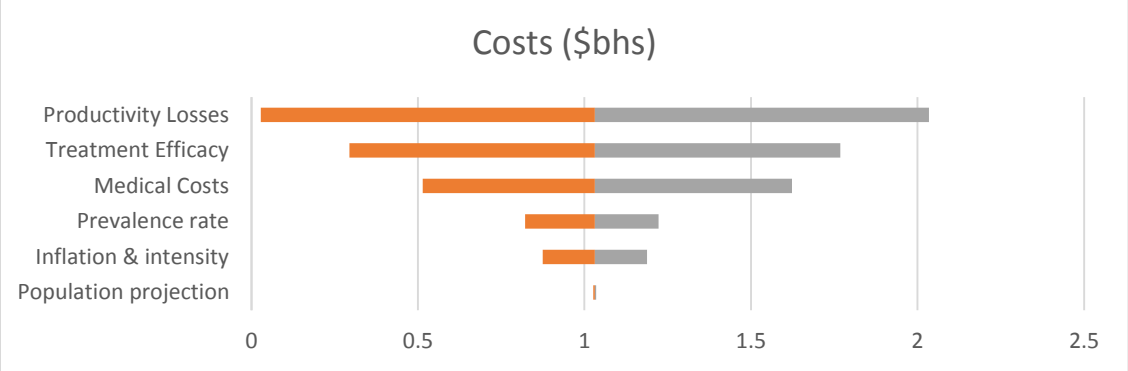


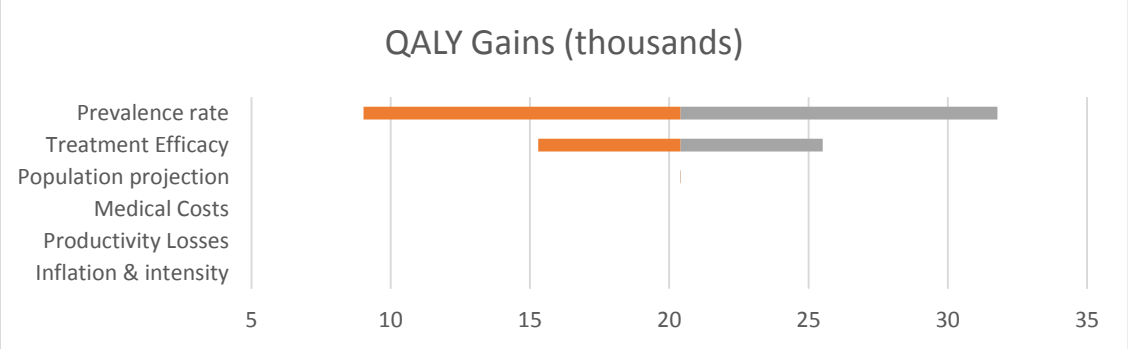


Glaucoma Treatment Sensitivity

Glaucoma	Vision Loss				Net Costs ($bns)				QALY Gains (thousands)		
	Low	Medium	High		Low	Medium	High		Low	Medium	High
Treatment Efficacy	0.12	0.16	0.20		0.2942	1.0311	1.7681		15.3	20.4	25.5
Population projection	0.16	0.16	0.16		1.0269	1.0311	1.0352		20.4	20.4	20.4
Prevalence rate	0.14	0.16	0.18		0.8221	1.0311	1.2226		9.0	20.4	31.8
Inflation & intensity	0.16	0.16	0.16		0.8742	1.0311	1.1880		28.0	28.0	28.0
Productivity Losses	0.16	0.16	0.16		0.0277	1.0311	2.0345		28.0	28.0	28.0
Medical Costs	0.16	0.16	0.16		0.5141	1.0311	1.6231		28.0	28.0	28.0

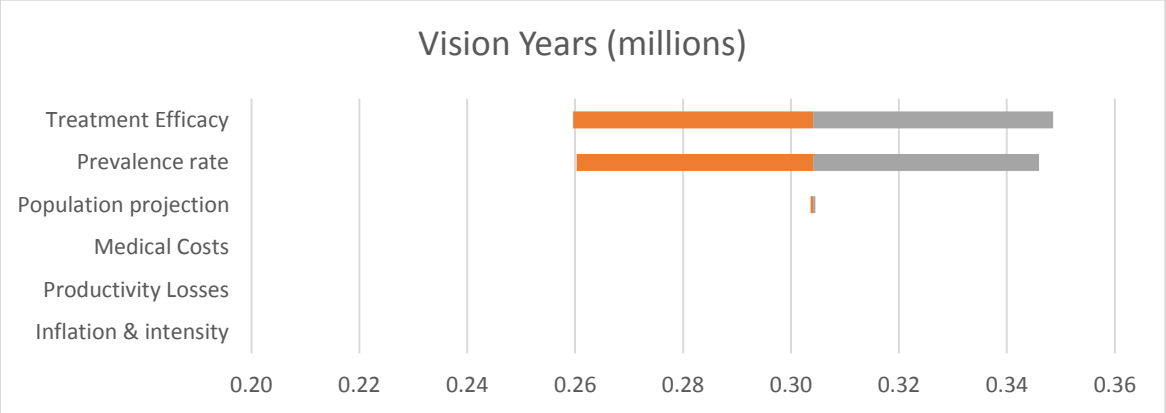


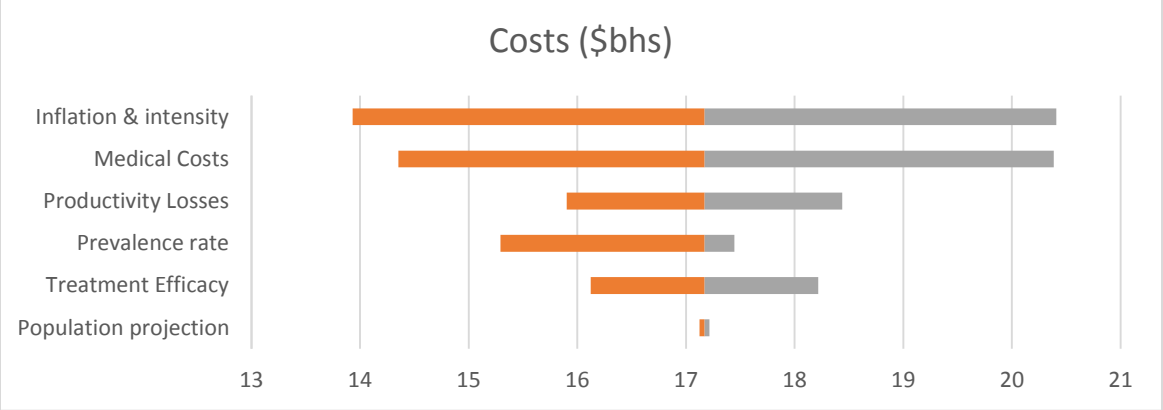


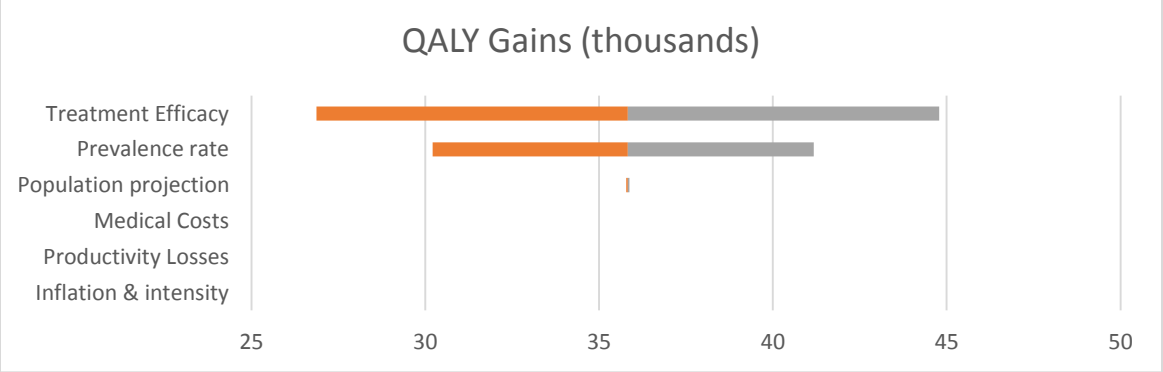


DR Treatment Sensitivity

DR	Vision Loss				Net Costs ($bns)				QALY Gains (thousands)		
	Low	Medium	High		Low	Medium	High		Low	Medium	High
Treatment Efficacy	0.26	0.30	0.35		16.12	17.17	18.22		26.87	35.83	44.79
Population projection	0.30	0.30	0.30		17.12	17.17	17.22		35.78	35.83	35.88
Prevalence rate	0.26	0.30	0.35		15.29	17.17	17.45		30.21	35.83	41.18
Inflation & intensity	0.30	0.30	0.30		13.93	17.17	20.41		35.83	35.83	35.83
Productivity Losses	0.30	0.30	0.30		15.90	17.17	18.44		35.83	35.83	35.83
Medical Costs	0.30	0.30	0.30		14.35	17.17	20.38		35.83	35.83	35.83

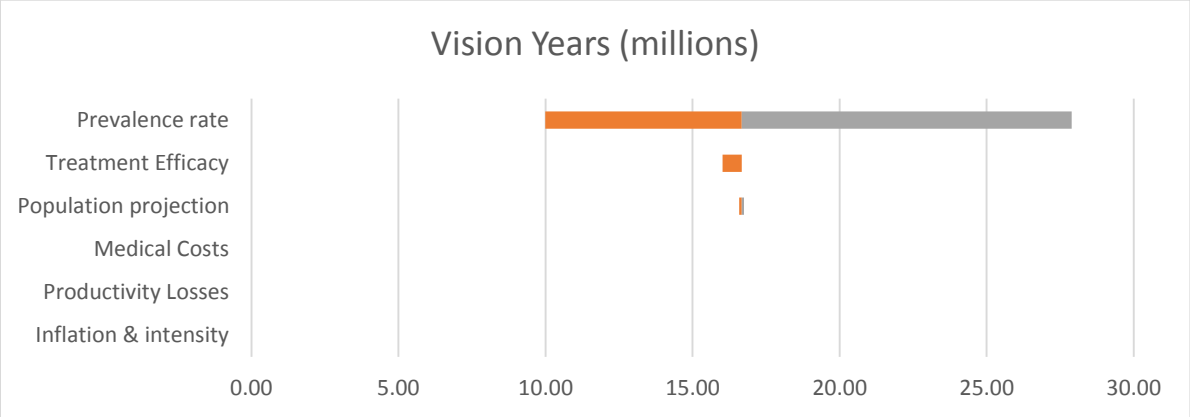


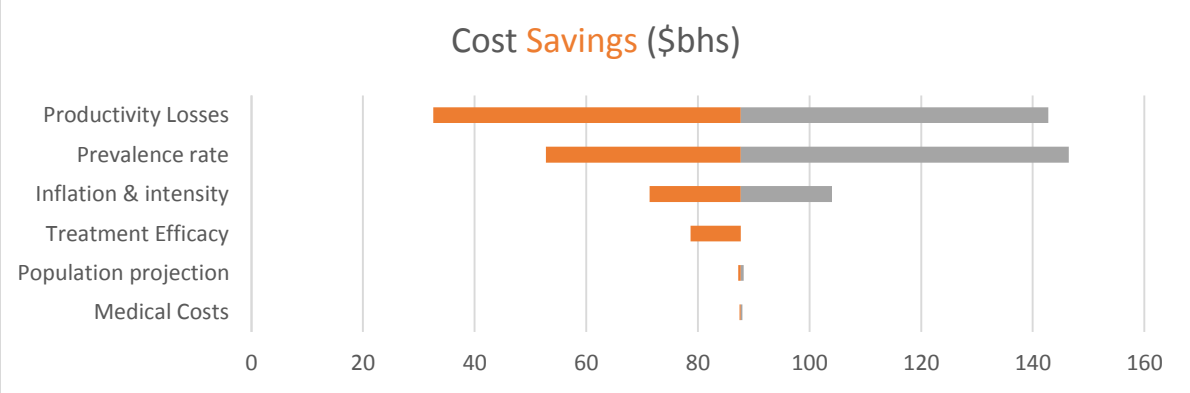


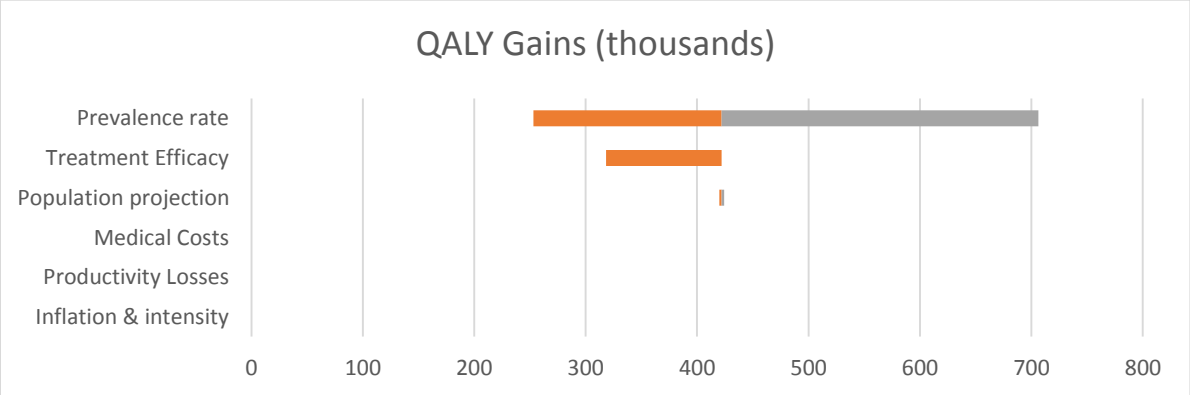


URE Treatment Sensitivity

URE	Vision Loss				Net Costs ($bns)				QALY Gains (thousands)		
	Low	Medium	High		Low	Medium	High		Low	Medium	High
Treatment Efficacy	16.02	16.67	16.67		78.70	87.69	87.69		318.18	422.07	422.07
Population projection	16.59	16.67	16.75		87.20	87.69	88.18		419.97	422.07	424.17
Prevalence rate	9.99	16.67	27.89		52.77	87.69	146.42		253.01	422.07	706.33
Inflation & intensity	16.67	16.67	16.67		71.36	87.69	104.02		422.07	422.07	422.07
Productivity Losses	16.67	16.67	16.67		32.60	87.69	142.78		422.07	422.07	422.07
Medical Costs	16.67	16.67	16.67		87.43	87.69	87.95		422.07	422.07	422.07







Limitations and Major Assumptions

The results presented in this report should be considered in the context of the limitations of this analysis and the underlying data, as well as with an understanding of how these results should be interpreted. The goal of this analysis was not to produce a definitive number to quantify the benefits of any intervention or policy, but to produce a general estimate of the potential maximum possible benefits that could possibly be accrued due to policies and interventions designed to increase diagnoses and expand access to care. Essentially, we attempt to frame the scale of the current problem of undiagnosed vision loss, and provide a target against which different policy and intervention approaches may be measured.

Data limitations

In this analysis we relied on both the VPUS and NHANES datasets to provide the underlying epidemiological estimates, the Cost of Vision report to provide most treatment costs and the economic impact of low vision, and the Multiple Eye Disease Simulation (MEDS) model to estimate the efficacy of treatment for CNV, DR and glaucoma. Each includes inherent limitations that should be considered when evaluating the results of this analysis, and these limitations affected the results generated by the analysis.

Limitations of the VPUS Report: The VPUS is arguably the best available and only source for true prevalence of the major eye disorders in the United States. The prevalence estimates are derived from meta-analyses of high quality, gold-standard ophthalmologic examinations. However, the underlying studies do not use a probabilistic sampling frame, and are generally defined by geographic areas which are not representative of the nation. In fact, five of the twelve included studies were based outside of the United States in Africa, Australia, Europe and the Caribbean. Also, much of the underlying data could be considered dated, possibly up to 30 years old. Finally, while VPUS is the only source to provide detailed prevalence at the age, race, and gender combinations, it nonetheless is still limited in that it did not include confidence intervals, nor did it differentiate prevalence across important disease stages. This is a particularly important limitation for the diseases of AMD and diabetic retinopathy.

Limitations of the NHANES Data: NHANES is the nation's only nationally representative examination survey, and in prior years included substantial vision and ophthalmologic data. From 1999-2008, NHANES included presenting and autorefractor corrected visual acuity, and self-reported visual function and DR and cataract surgery history. For the 2005/2006 and 2007/2008 waves, NHANES included supplemental retinal imaging and visual field assessments, as well as additional eye health questions including AMD and glaucoma diagnosis history. NHANES provides important information on diagnosed prevalence of eye disorders, actual visual function and eye health. NHANES is probabilistically sampled from a selection of states, and thus should be considered more representative of the overall US population than VPUS. However, NHANES does not include institutionalized populations such as persons residing in nursing homes, which may result in undercounting of persons with low vision, particularly at older ages. In addition, NHANES has a relatively low sample size per year, and the ophthalmological examination data was only included in two waves from the 2005-2008 and therefore the outcomes of these exams suffer from particularly low sample size, preventing the assessment of age, race, gender specific prevalence rates.

Limitations of the Cost of Vision Report: Medical and low vision costs are based largely on the results of the Cost of Vision Problems report. This report provides the most comprehensive assessment of the economic burden of eye disorders and vision loss, and was based closely on prior published studies that considered specific cost categories. However, these cost estimates are also limited by the underlying data. Medical costs are based on MEPS data, which can provide a more comprehensive assessment of total

costs than is possible using other sources such as claims data, but the diagnosis information in MEPS is subject to uncertainty. In particular, MEPS's publicly releases only the first 3-digits of diagnosis codes, limiting the identification of specific diseases and preventing the identification of diseases stages. In addition, much of the economic burden is due to indirect costs such as productivity losses which are based on self-reported visual function and wages.

Cost of Vision problems did not include URE. Due to the relative importance of URE in this analysis, we estimated an economic cost of URE. However, we deemed the productivity losses calculated from SIPP data, and based on self-reported difficulty seeing, as unsuitable to apply to URE. We therefore calculated new productivity estimates for vision loss and URE in NHANES data for this analysis. We made every effort to ensure conservative (low) estimates of the productivity losses from lost vision in this analysis, including controlling for age, race, sex, household size, and education level in the regressions. NHANES reports income in ranges, and we used the minimum of each range as the income estimate, including income of zero for some patients. The resulting productivity losses are lower than previously published estimates from SIPP data. However, there remains a risk of bias. While we make every effort to conservatively estimate the impact of low vision on income, we cannot state that this income discrepancy would disappear if vision was restored. Thus, these costs may be technically correct in terms of framing the current burden of undiagnosed or untreated vision loss, but may nonetheless overstate the *correctable* burden if vision loss was treated. Readers should bear this in mind when considering potential policies or interventions that may reduce vision loss but would not necessarily restore previously lost earning potential.

Limitations of Estimates of the Impact of Treatment: The estimated efficacy of medical treatment is based on assumptions for URE, cataract and geographic atrophy, and estimated using the separate MEDS model for CNV, DR and glaucoma. The MEDS model simulates incidence, natural history, vision loss, medical utilization and treatment and outcomes of six major eye disorders. Time and resource constraints prevented us from using the MEDS model to conduct the entire analysis, but we used the progression and medical treatment modules to calculate a population-level treatment efficacy estimate assuming immediate population treatment. The MEDS model is based on underlying parameters from many clinical trials and other sources, and thus reflect the cumulative uncertainty and bias across the underlying sources. However, in some cases treatment parameters in the MEDS model may not be fully updated – treatment for CNV is based on results of the Wills Eye Hospital Treat & Extend study from 2015, but most parameters for glaucoma and DR treatment are up to 10 years old. We did incorporate an estimated impact of anti-VEGF therapy for CSME in DR, but may not fully account for the impact of new treatments available.

Methodological limitations and major assumptions

This study is also limited by the assumptions required to combine parameters derived from disparate data sources into a single framework used to estimate preventable burden. We used a prevalence-based approach to estimate the current and future prevalent burden of eye disorders and vision loss. This approach is simpler than an incidence-based forecast analysis and does not require simulation of disease incidence and progression over time. However, a prevalence approach cannot account for any secular trends in disease epidemiology that would change the prevalence rates by age, race and gender over time.

In addition, due to limited scope of this analysis as well as the fact that VPUS prevalence rates do not include confidence interval information, we did not conduct sensitivity analyses. All parameters in the analysis model are static.

Our analysis required several explicit assumptions or calculations which potentially could introduce bias, which we summarize below. We have tried to specifically highlight instances in which major assumptions of the analysis may have led to a less conservative result. The most important assumptions are:

- *Applying diagnosis rates in NHANES to VPUS prevalence rates. VPUS does not include diagnosis information.* Applying diagnosis rates from NHANES to VPUS is potentially invalid as diagnosed disease rates are drawn from the probabilistic NHANES sample which is limited by its exclusion of institutionalized populations, including persons in nursing homes. VPUS prevalence of disease numbers represent those estimated from a meta-analysis of population based studies, some of which included institutionalized populations and some of which did not. In addition, the diagnosis history is based on self-report which is subject to recall bias. Consequently, the combined effect of these limitations may lead to an estimate of a greater number of undiagnosed cases than actually exists. Although every attempt was made in the our analyses to error on the side of more conservative estimations, in this instance these unavoidable limitations may have led to an less conservative estimate of the number of undiagnosed individuals.

- *Applying AMD stage allocations from NHANES to VPUS prevalence rates.* VPUS does not report prevalence by stage, which is a major limitation for AMD where CNV and GA have widely disparate diagnosis rates, visual outcomes, treatment efficacy and costs. Applying stage allocation rates from NHANES to VPUS could potentially introduce bias due to the structural differences between the data sources, but it is unclear whether and how any such bias would impact results.

- *Applying vision loss allocations by disease from EDPRG to the VPUS prevalence rates.* VPUS reports the prevalence of visual impairment and blindness, but does not allocate this to conditions. This is necessary in order to quantify the potential visual loss burden that could be prevented through treatment. These vision losses by disease allocations represent some of the weakest data in the entire analysis. Their use was unavoidable, but any analyses based on them are subject to their inherent weakness and uncertainty. The impact of this limitation would lead to an estimate of greater preventable burden if vision loss attributable to a disorder that is not currently treatable were mistakenly allocated to a disease state that is treatable, and to a more conservative estimate if the opposite were true. Because of the complete inability to verify this information using other data sources, the impact of this limitation on our estimates cannot be known.

- *Assuming treatment efficacy rates for URE (100%), cataract (95%), and geographic atrophy (0%).* For simplification, we assumed treatment efficacy for these conditions, which may not reflect actual potential gains.

- *Assuming prevalent vision loss is equally allocated among the diagnosed and undiagnosed populations.* This is a major assumption as it is likely that persons with worse vision are more likely to be diagnosed. We considered assumptions to shift prevalent vision loss more heavily towards the diagnosed population, but did not find any evidence to support this. In fact, surprisingly some evidence suggests that vision loss is not a significant predictor of eye disease diagnosis.[43] This assumption does not impact the results of URE or cataract, as these are defined based on untreated rather than undiagnosed, and since these conditions cause 88% of vision loss identified in this study, the effect of this assumption is limited to the remaining 12% due to AMD, glaucoma and DR. Nonetheless, this is a major assumption that if incorrect, could potentially bias the results towards an estimate of greater preventable burden.

- *Current prevalence rates will remain static by age, race and gender.* A major assumption of prevalence-based forecasts is that prevalence rates will remain static. Epidemiological shifts predicted in this analysis are due entirely to demographic shifts, and do not include any potential changes in disease prevalence due to secular changes in epidemiology, for example, we do not incorporate the full impact of rising diabetes prevalence in future years. We also do not account for possibly declining prevalence rates of AMD. In addition, future vision loss prevalence rates do not account for impacts of changes in treatment efficacy that may reduce vision loss prevalence rates.

- *Prevalent vision loss rates are equally allocated by age and gender.* The EDPRG vision loss allocations do not differentiate gender or age, only race. This likely causes bias as current and future age distributions of prevalent disease may not match that of the underlying EDPRG population. For example, the DR population is skewed towards younger ages relative to the other conditions, which may not be accounted for in the vision loss allocations.

- *Lack of data for the population aged 80 and older.* For visual health, no age group has a larger impact of the future increases in prevalence of eye disease and vision loss than the population age 80 or 85 and older, which is the highest prevalence group as well as, by far, the fastest growing segment of the population, with some studies predicting a 5-fold increase in the population aged 90 and older over the next 40 years. However, very limited data exists at these age groups. NHANES "top codes" age at 85, while VPUS only reports prevalence for ages 80+ or 75+ for DR. For this analysis, it was necessary to fit prevalence curves to single years of age. For younger age groups, we could simply fit a polynomial spline curve between the mid-points of each age bin, while holding the integral constant. For the oldest age groups, we assumed this slope would continue with age. While we ensure that this function does not change the current predicted prevalence by age group, the slope of this line may bias the impact of future aging of the population within this age group. If the slope of the line is too steep, then we will overestimate growth of prevalence in future years when the population of the 80+ age groups are more heavily skewed towards age 100. However, while nationally representative prevalence data at these ages is not available in the US, a UK-based study of vision loss among the elderly by Evans et al supports this trend, and in fact shows much faster increases in prevalence from ages 80-84 to 90+ than we predict, lending credence that our prevalence functions are biased towards the conservative.[44]

We made a number of assumptions that may potentially impact the results of this analysis. Where possible, we attempted to err on the conservative, minimizing potential benefits and maximizing costs. However, this was not always possible as in the instances above, as the available data provided only one possible solution to estimate burden.

Limits of the knowledge claim

The goal of this analysis was to produce estimates of the maximum potential benefits of diagnosis and treatment of the currently undiagnosed populations with eye disorders. The outcomes show the impact of immediate diagnosis and treatment of the entire estimated prevalent population with undiagnosed major eye disease, with zero costs for case finding. This analysis is not meant to represent actual, real-world outcomes of any intervention or policy. Interventions or policies that increase diagnosis or access to care would of course incur costs while achieving limited success. This report *is* meant to provide the IOM committee with a set of general estimates of the maximum potential gains available, including the prevalent population in the current and future years, current estimates of the diagnosis rate, predictions of

the general impact of treatment on visual outcomes, and the net cost and QALY impact of treatment. In discussing potential policies or recommendations, the committee may consider the extent to which any specific policies or recommendations may address current gaps in diagnosis or access to care and to what extent they may mitigate the burden of undiagnosed eye disorders.

Addressing Data Limitations and the Need for Vision and Eye Health Surveillance

Introduction

This analysis attempts to create an estimate with a very broad scope; quantifying the burden attributable to undiagnosed eye disorders now and in the future, and estimating how much of this burden could possibly be averted. In doing so, we calculate the existing prevalent burden of eye disorders, estimate the costs of low vision, identify current diagnosis rates, and show the potential costs and benefits of treatment. However, we also demonstrate many of the limitations of existing vision and eye health data sources. No one single data source could provide all, or even most of the parameters needed to address this question and these and other limitations forced assumptions and introduced potential bias. Conducting this analysis reaffirmed our view that to fully understand the scope of vision and eye health problems, additional, new epidemiological estimates are needed.

Limits of Current Evidence

The consideration of almost all vision and eye health medical and public policy will be driven by our understanding of the current burden of eye and visual disorders. Unfortunately, our current understanding is limited by a number of factors, including limits in the scope of existing data, discordance in existing measures and definitions of disease, high variation among different potential sources and a general lack of consensus estimates to capture the full scope of the problem. Today, even answering a simple question such as "how many people are blind" can only be answered with complex answers, wide ranges of numbers, and just as many caveats. The impact of this lack of clarity may prove to have wide ranging impacts, as policy and investment in visual health suffer due to a lack of consensus on the needs for progress and policy, confusion and disagreement among stakeholders and the public at large, and the simple fact that vision may prove too complex to fit in the overall conversation of chronic disease.

The end goal of health and medical policy in visual health is to preserve vision, but the foundation of all policy is a solid understanding and consensus of the scope of the current problem, and this understanding is built from our existing resources meant to measure this scope, from the existing methods and tools for surveillance. However, as evidenced in this report, currently available data is subject to many limitations, with many due to the unique nature and challenges associated with measuring visual health.

Defining and measuring vision

Perhaps the greatest limitation in our current knowledge – the limitation to answer "how many people are blind", is our inability to reach consensus on how blindness and other vision loss should be defined and measured. Many of our national surveillance resources such as BRFSS and ACS include self-reported vision loss. However, there is evidence that individuals are surprisingly bad at assessing their own vision, not to mention that of others in the case of household surveys. NHANES however did field a visual function assessment and eye examinations, but this was only included for two rounds and yielded small samples with some implausible patterns – such as higher prevalence at certain younger age groups. EDPRG and VPUS relied on superior ophthalmologic examinations, yet their underlying basis as non-probabilistically sampled localized population studies, many outside the United States, limits their applicability to national estimates.

Which conditions are measured

Another major limitation is the current limitation in the number of conditions included in surveys and major prevalence studies. While the "big 4" of AMD, DR, cataract and glaucoma likely cause the majority of permanent vision loss in the United States, these may not necessarily always be the most common, most costly, or even most disabling conditions. However, almost no data is currently available on the prevalence of other eye disorders. Even URE is generally excluded from most data sets, often due to difficulty in measurement. But as shown in this report, URE may well be by far the costliest vision condition facing the nation. The narrow focus of existing evidence on the burden of eye disorders directly limits the scope of the policy debate to the same few conditions.

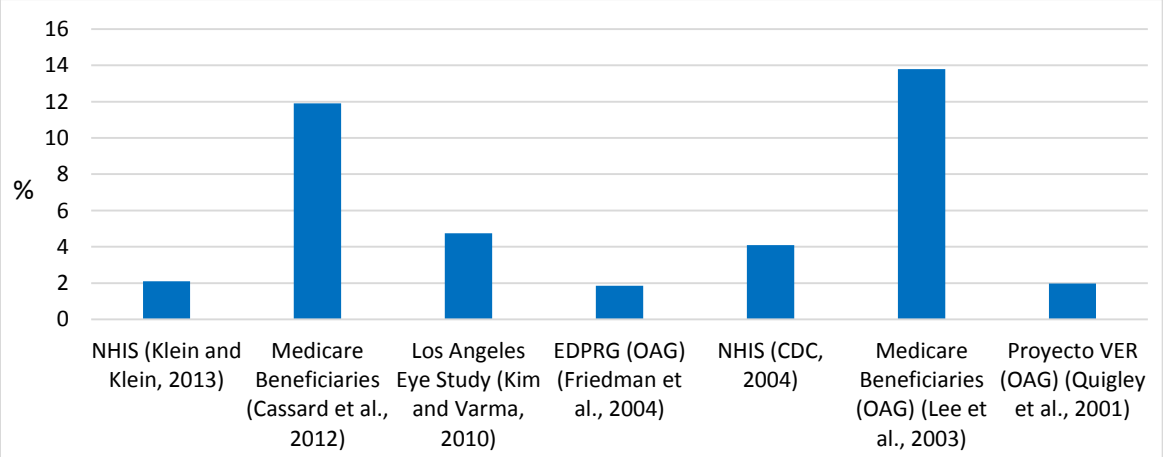
Extending measurement to utilization and access to care

Aside from the limited scope of current knowledge to a handful of conditions, existing data is also primarily limited to prevalence and incidence. Very little information is available related to national utilization and access to care, particularly in regards to disparities. As much of the debate on health policy is essentially a debate on ways to influence optometric and ophthalmologic eye care systems, there is very limited understanding of the scope and limits of these eye care systems for reaching the people in need.

Public dissemination and access to information

Finally, a major limitation of existing knowledge on eye and vision health is simply that it is often difficult to find, and it is impossible to reconcile what can be found. The published literature of vision and eye health contains many different estimates of prevalence of major eye conditions, but navigating this literature is difficult, requires significant substantive-area knowledge, and as evidenced in Figure X1 below, which demonstrates the wide variation in published prevalence rates for glaucoma, the published literature simply cannot provide a single definitive answer.

Figure X1. Wide Disparity in Published Glaucoma Prevalence Rates



Epidemiologic information is only of use if it is accessible, and today most of our knowledge is not. Prevent Blindness has made substantial progress in communicating the current and future scope and costs

of vision problems in the VPUS, Cost of Vision and Future of Vision report. Recently, CDC's Vision Health Initiative have begun adding limited self-report data from BRFSS to their website. However, the continuing limitation is the lack of ability for end-users to compare different types of measures, and the continued lack of harmonization among sources makes it virtually impossible to select a single source or measure to answer the "simple" questions.

Requirements for a national vision and eye health surveillance system

The WHO defines public health surveillance as the "continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice", with specific requirements to "document the impact of an intervention, or track progress towards specified goals; and monitor and clarify the epidemiology of health problems, to allow priorities to be set and to inform public health policy and strategies."

While a number of studies and data sources focusing on vision and eye health currently exist, arguably none meet the criteria to be considered a surveillance system. Our most detailed epidemiological information such as VPUS are derived from older population-based studies, and do not meet the definition of a continuous or sustained system. Likewise, important examination data was collected in NHANES from 2005-2008, but the limited duration and small sample size limits it efficacy as well. Other national surveys collect data on a continuous basis, but vision and eye health information in these surveys is extremely limited and derived from self-reported vision function.

Recognizing the limitations of eye and vision health data, in 2012 the CDC convened a panel of 14 national and international experts to "identify action steps and priorities to strengthen national and state surveillance systems to help assess and monitor disparities in eye health, vision loss, and access to eye care over time and respond to national, state, and local needs". This panel determined that there is a need for national vision surveillance, and identified 6 goals of such a program:

1. Link data collection and analyses with ongoing public health interventions to improve eye health disparities.
2. Effectively assess vision loss.
3. Effectively assess eye care use.
4. Include defined populations to assess the disparities in vision loss and in using eye care services.
5. Include and sustain ophthalmic and vision measurement and question components within national surveys.
6. Be forged among federal agencies and other stakeholders to monitor the nation's eye health and eye care use for trends in disparity.

However, to achieve these goals, a surveillance system must first address the existing shortcomings of our visual health and eye disease epidemiologic knowledge, take steps to address these limitations, and forge the establishment of consensus processes and steps to create a definitive surveillance measure.

Unique Challenges posed by Vision and Eye Health

A vision and eye health surveillance system must account for and overcome a number of challenges that are perhaps unique among health conditions. Below we describe four facets of vision and eye health that may pose significant challenges for the successful development of a surveillance system.

Complex and Difficult to Measure Outcomes

First, vision is a complex outcome caused by a number of factors. Vision may be measured through acuity, contrast sensitivity, visual field, color perception, night vision, or any number of different, and differently measured functional measures. This is in stark contrast to many conditions captured in existing surveillance systems. For example, the HIV/AIDS surveillance system is considered the nations' premiere surveillance system. However, this system relies on case counting – cases are reported based on diagnosis through positive lab tests and a patient either has HIV/AIDS or does not. This is inherently unlike vision, where defining whether someone suffers from vision loss is difficult to define, and even more difficult to measure.

Broad Range of Included Conditions

Secondly, there are a wide variety of eye disorders with a broad range of manifestations and outcomes. Even among the small sample of the five conditions included in this report, some can be successfully treated (URE and cataract), while there is almost no effective treatment for GA, and treatment for CNV, DR and glaucoma is complex and met with mixed success. There are conditions that affect acuity and contrast sensitivity, while glaucoma primarily affects visual field. Beyond the conditions included in this analysis, others such as dry-eyes may cause pain or discomfort, and eye cancer can be fatal. The scope of eye health is even inclusive of related issues affecting the ocular adnexa, such as disorders of the globe, orbit and lacrimal system, and even injuries and burns represent a substantial portion of overall eye care. This complexity in the range of disorders and the varied link to outcomes poses an additional challenge. Compared to surveillance systems such as those in the National Notifiable Diseases Surveillance System where a case identified *is* the end-point for surveillance, among eye disorders, identification is only the beginning of surveillance.

High Undiagnosed Prevalence

A third complication is that vision loss and eye disease are often undiagnosed, and may remain so even while incurring measurable impacts on medical costs and productivity. The SEER cancer surveillance system identifies cancer through diagnosis at hospitals and cancer centers in sentinel sites located in 12 states. While one may presume that nearly all cases of cancer will be eventually identified, this is certainly not the case for vision and eye disorders, where this report finds low diagnosis even among the conditions with the greatest impact on vision. Other evidence consistently points to low diagnosis rates of eye disease and even low self-referral for vision loss. Thus, we cannot count on medical encounters nor self-reporting to eventually identify all or perhaps even most prevalent cases.

Separation of Eye Care among Multiple Health and Payment Systems

Fourth, a complication that may prove to have substantial implications for data collection is that vision and eye health are treated through essentially three largely separate medical systems; optometry, ophthalmology and general practice. Optometry is almost entirely covered by a separate vision insurance system or paid out of pocket, and not included in private medical or Medicare claims. Ophthalmology may be captured by ophthalmology EHR or registry systems, but a possibly substantial volume of eye care may be provided by general practitioners or through emergency departments or hospitals that are not covered by these data systems. The fractured nature of eye care is very different than most other conditions treated through primary care or hospitals. For example, the United States Renal Data System is based primarily on Medicare claims analysis, especially for end-stage renal disease (ESRD) covered under the ESRD Medicare benefit, which extends Medicare benefits to all advanced kidney disease

patients regardless of age. This is very different from vision and eye health, where medical care, claims and payment are distributed among many different types of providers and payers, and much is paid out of pocket.

The unique and multi-faceted challenges associated with vision and eye health surveillance means that no single traditional surveillance methodology would be sufficient. For this reason, it is essential that a vision and eye health surveillance system incorporates an integrated approach – many different and disparate data sources must be brought to bear to form a complete landscape of vision, eye health and care.

Building a Comprehensive Vision and Eye Health Surveillance System

The unique challenges posed by vision and eye health will necessitate a broad-based, integrated approach in order to build a surveillance system capable of addressing current knowledge gaps regarding the scale of current vision loss and eye disorder epidemiology. The system will need to include a broad range of outcome measures, including visual function, vision-threatening disorders, and other eye disorders impacting public health and costs. To do so, it is apparent that no single data source is likely to be sufficient; the system will need to capture, collect and integrate a wide range of data sources. Finally, an effective surveillance system must also employ effective communications throughout its development.

Selecting Conditions and Measures

The system should consider options to expand the scope of existing knowledge by including additional conditions. Assessment of conditions for which there is currently strong or numerous estimates may be a priority, as this will provide an opportunity for validation of the system, while also forging consensus measures among the existing estimates. The system then should consider options for applying established processes to identify prevalence of conditions currently unmeasured, or with limited measurement.

However, identifying additional conditions for inclusion may be a complex process, particularly for areas with little existing evidence. The solicitation of advice and guidance from stakeholders and recognized experts may be vital for defining and prioritizing conditions. Conditions must also be defined and selected in the context of their inclusion and definition in data sources. For example, administrative claims and health registry data may define conditions based on ICD-9 or ICD-10 diagnosis codes. Identifying these codes, grouping like codes into meaningful eye disease categories, and defining a crosswalk between the approximately 1,022 eye and vision related ICD-9 codes and their corresponding conditions among an estimated 2,900 eye and vision ICD-10 codes will not only be a challenging process, but one whose decisions and outcomes may have far-reaching impacts on how and which vision and eye disorders are included in the surveillance system.

Identifying and selecting data sources

Concurrent to the definition and selection of conditions and outcome measures, a surveillance system must carefully consider the inclusion of data sources. Sources currently in the public domain such as NHANES and VPUS currently provide our best measures of vision and eye health prevalence. However, the surveillance system must expand beyond these sources to provide a more comprehensive assessment of vision and eye disorder epidemiology. A number of different categories of data are available, and in most cases, there are numerous sources within each category. In some cases, these provide different

perspectives or different measures of the same conditions or outcomes. In other cases, multiple data are required to complete a full composite picture of the outcome or condition. Below, we describe four categories of data, including data not previously included in public vision surveillance, and discuss options for future data collection.

National surveys

The national federally-sponsored health surveys are perhaps the most obvious source of data that may be included in an integrated surveillance system. We have identified 15 different national surveys containing eye or visual health information, eye care or both.

Table S1 provides an overview of each survey and the types of vision-related data collected between 1999 and 2015. There is no standardized set of vision health self-report questions for use by surveys in the U.S. As a result, while many surveys ask about similar questions about similar domains (i.e., visual functioning, eye disease, healthcare utilization, etc.), there is variation in question wording between surveys as well as between years within the same survey. Additionally, some surveys are deployed intermittently, or may field visual content only in some locations or years, while others have permanently discontinued all vision content.

TABLE S1. OVERVIEW OF NATIONAL SURVEYS COLLECTING VISION-RELATED DATA

		ACS	BRFSS	HRS	LSoA	MCBS	MEPS	NAMCS	NHIS	NHANES	NNHS	NSHAP	NSCAW	NSCH	NSC-SHCN	SIPP
Sample	*Nationally Representative*	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
	Sample Size- (most recent year)	3 million	506,000	9,600	9,500	40,000	35,100	76,300	87,500	9,800	8,200	3,400	5,900	95,700	40,200	34,900
	State	•	•					•	•					•	•	
	Age	All	18+	50+	70+	65+	All	All	All	All*	18+	50+	0-14	<18	<18	All
Eye Health	*Visual function*	•	•	•	•	•	•		•	•	•	•	•	•	•	•
	Cataract		•	•	•	•			•	•						
	Glaucoma		•	•		•			•	•						
	AMD		•			•			•	•						
	DR					•	•		•							
	URE									•						
	Examination			•						•		•				
Med.	*Utilization*		•	•	•	•	•	•	•	•				•		
	Costs					•	•									

American Community Survey (ACS); Behavioral Risk Factors Surveillance System (BRFSS); Health and Retirement Study (HRS); Longitudinal Supplement on Aging (LSoA); Medicare Current Beneficiary Survey (MCBS); Medical Expenditure Panel Survey (MEPS); National Ambulatory Medical Care Survey (NAMCS) National Health Interview Survey (NHIS); National Health and Nutrition Examination Survey (NHANES); National Nursing Home Survey (NNHS); National Social Life, Health, and Aging Project (NSHAP); National Survey of Child and Adolescent Well-Being (NSCAW); National Survey of Children's Health (NSCH); National Survey of Children with Special Health Care Needs (NSC-SHCN); Survey on Income and Program Participation (SIPP)

The benefits of including national surveys is that they provide a broad range of measures and outcomes captured in probabilistically sampled populations, and in all cases yield nationally representative results. The complication of utilizing surveys include the fact that all but a few surveys rely on self-report data, and many collect self-report data using a wide range of non-harmonized questions and measures. However, some surveys can provide important information such as state prevalence, examination utilization, self-reported diagnosis rates, and treated prevalence.

Population-based studies

The backbone of eye disease epidemiological knowledge has long been the array of population-based studies deployed in research sites around the United States and other countries. For the purpose of this report, we rely on the EDPRG and VPUS projects which conducted meta-analyses of these disparate studies. The strength of these studies is that the underlying data is based on gold-standard examinations and report prevalence considered to be representative of the racial/ethnic and sex-specific groups within their defined populations. The prevalence reported in these studies represents the true prevalence of conditions, and are not based on existing diagnosis or self-reporting. However, these studies do have certain limitations that preclude them from serving as the only source of data in a surveillance system.

In considering VPUS, which is the most recent meta-analyses of population-based studies, this data has several specific limitations. First, VPUS and most of its underlying studies are limited to four eye disorders and vision loss. Furthermore, it does not report diagnosis information. Therefore, it cannot by itself produce estimates of the undiagnosed prevalence of vision loss, refractive error or eye disease. Another limitation is that VPUS does not separately report prevalence of disease by stage, which can be important for conditions such as AMD where wet-form is treatable, while dry-form generally is not. VPUS also does not include certain disease stages such as early AMD. In addition, VPUS does not report confidence intervals or any level of uncertainty in the data. Finally, while VPUS may be considered the latest and best source of prevalence data available, the fact that 5 of 12 studies included are international, some of the underlying data is up to 30 years old, and that all underlying studies are based on small geographic areas, and the respondents were not probabilistically sampled means that VPUS and its underlying population-based study data alone cannot be considered truly nationally representative.

Administrative claims data

Administrative claims data are an important source of information on access to care, cost, and utilization of medical services related to eye health and vision disorders. Claims also have long time horizons, which permit longitudinal analyses, contain useful information on demographic (age, sex, sometimes race), geographic (location of patient and provider) and clinical (comorbidities) characteristics of individuals, offer large sample sizes, and uniquely allow investigation of risk factors such as diabetes or smoking and outcomes such as falls and depression. However, claims data systems only capture medical utilization, and are not appropriate for assessing the full scope of vision and eye health due to the likely low rates of diagnosis, nor can claims data alone identify most measures of access to care or disparities in care. Also, claims are limited in the amount of medical and demographic information they capture. Medical outcomes are defined through diagnosis codes, and in some cases codes selected for billing may not accurately or fully reflect the nuances of underlying health. In addition, claims data generally do not include any information on acuity. Two partial exceptions may include limited commercial claims data where it can be linked to electronic medical records containing acuity, and Medicare claims which can be linked the MCBS survey, which includes self-reported vision, self-reported utilization, and self-reported history of diagnosis for AMD, cataract, DR and glaucoma.

Perhaps the greatest challenge posed by vision and eye health related to administrative claims is the fragmentation of the payer market for eye care. Medicaid is an important payer for eye services, especially among children, but Medicaid benefits and data exhibit wide variations among states, especially after the uneven implementation of Medicaid expansion under the ACA. Medicare typically is considered to capture older Americans, but may also include younger Americans with disabilities such as blindness. However, Medicare does not cover routine eye examinations. Private medical insurance can be measured through private insurance claims databases, but these insurers, and thus their claims data, generally exclude optometry care. Optometry care may be captured through private vision insurance databases, but no such vision insurance database has yet been publicly disseminated.

However, for a comprehensive surveillance system that seeks to not only identify diagnosed prevalence but also service utilization and access to care, administrative claims may prove to be a vital component. However, the fractured nature of eye care financing means that a comprehensive surveillance system may need to capture Medicare, Medicaid, private medical and also private vision insurance claims databases.

EHR and health registry data

Recent years have seen much promise and speculation pertaining to the promise and potential of EHR databases and EHR-based registries for capturing highly detailed medical information. However, persistent data quality issues and complexity mean that systematically incorporating EHR data into a surveillance system will pose a challenge. Unlike administrative claims which essentially only contain information pertinent to payment (diagnoses and charges) and minimal demographic data, EHR contains the full spectrum of medical information collected from patients through intake forms, examinations, lab results, test results, and in some cases even chart notes. This additional detail then is strengthened even more by some of the same strengths denoted in claims data, such as large sample sizes and longitudinal observation. Another area where EHR data may be superior to claims data is that EHR is generally independent of payer, and thus one database can capture the full market of different payers including out of pocket. Finally, EHR may contain information on visual function such as acuity. However, experience has shown than EHR data is often difficult to use, with many existing available databases built from multiple underlying medical systems or medical record formats, leading to issues related to data validity, quality and ease of use. EHR is also often limited through loss of follow-up as patients are lost as they move or switch to different, or multiple providers.

However, while EHR data and registries continue to pose a challenge for integration into public health data collection, their potential for providing substantially more, and more detailed medical and health information than is captured through any other source make inclusion of this type of data highly enticing. Integration of EHR or EHR-based registry data would provide a vision and eye health surveillance system with the capacity to introduce a level of comprehensive detail beyond that not only of existing vision and eye health epidemiological data, but perhaps beyond any other existing health surveillance system. This would open new horizons for potential analysis, ranging from not only framing the epidemiology, but large-scale studies of longitudinal progression, outcomes and treatment efficacy. However, no EHR system or registry will be nationally representative on its own, as these cannot capture the full market, and of course will not capture undiagnosed eye disease.

Options for new data collection or revision

As shown above, a broad-based vision and eye health surveillance system can be built by leveraging multiple existing data sources, such as national surveys and population based studies, as well as harnessing potentially new data such as broad-based claims and EHR registries. However, each of these

sources continues to be limited by numerous factors, whether that is non-harmonized measures and questions, non-representative populations, or limited scope in condition and outcome measures. A vision and eye health surveillance system may also serve as a platform to assess and evaluate the potential for new data collection efforts. Some such efforts may include expansion or improvement in vision measure collection in existing surveys. It may include providing guidance for a resumption in visual data collection in examination surveys such as NHANES. The system may also serve as a platform to support renewed analysis of existing population based surveys to create an expanded, and updated meta-analysis of these resources. Or, the system may identify a yet unknown need and help policymakers define the scope and requirements of future primary data collection efforts. One plausible need may be the establishment of stronger nationally-representative datasets that can be used to anchor new measures identifiable in more detailed, but systematically biased data sources such as EHR registries.

Developing National Surveillance Estimates

Through the steps outlined above, a vision and eye health surveillance system will determine important conditions for inclusion and consideration, define meaningful outcomes for measurement, and select a broad range of data capable of capturing the different important sectors of vision, eye health and eye care. However, the system then must effectively translate these various measures from different data sources into a standardized and consistent set of outcome estimates.

Single source prevalence and utilization

Perhaps the first step in this process is to simply account for the various data and measures that can be collected. Many of the myriad of data sources described above have already been analyzed and reported in the published literature. However, the cumulative literature often shows that these estimates vary widely between data sources and between studies. Analyzing each of these data using a consistent process, consistent measures, and consistent reporting format is necessary before any data may be integrated. This process will also more definitively show the true variation and potential bias of different data sources.

Harmonization and Integration of Data

An important goal of a vision and eye health surveillance system is to harmonize data to the extent possible. Data harmonization refers to the identification of similar data elements collected by different data sources that were intended to capture similar underlying concepts, but that use different wording or sampling in their collection elements. True harmonization is a process through the articulation of the underlying data concept of true interest, creation of common data collection standards to capture that concept, and the subsequent propagation of those standards across various data collection efforts to lead to the adoption of uniform and directly comparable measurement across different data sources. However, due to the limitations of existing data collection and a desire to maintain historical consistency, true harmonization of vision and eye health data collection is likely an impossible goal. However, the process of harmonization will allow the surveillance system to meaningfully link and compare different sources of data in the support of data integration, which refers to the short term combination and analysis of conceptually similar items across different data sources.

Statistical surveillance

Even without true data harmonization, integrated data can be combined and analyzed through statistical surveillance techniques such as small area estimation. These techniques allow the consideration of multiple data sources within the context of a single model. For example, variation measured in one data source may be used to more accurately propagate national prevalence estimated in another dataset than could be achieved by simply allocating the prevalence by population. For example, the state variation in self-reported vision loss by state in BRFSS, while controlling for demographic characteristics and risk factors, could potentially be applied to national estimates of URE prevalence calculated in NHANES to produce state-specific URE estimates with known confidence. Similarly, nationally representative survey data may be used to anchor more detailed, but structurally biased data. For example, this may allow for the inference of national prevalence estimates for stages of AMD based on EHR-derived stage allocations and national estimates from surveys for AMD overall.

Through these state of the science biostatics techniques, a surveillance system with strong underlying but disparate data sources may produce statistically robust estimates for outcomes that cannot be fully quantified or observed by any single data source. This can allow the system to report a much broader range of outcomes than otherwise possible, and perhaps most importantly, facilitate the identification of important factors and causes of health and care disparities.

Stakeholder Involvement, Scientific Oversight and Public Dissemination

The final, but still vital requirement for building a comprehensive vision and eye health surveillance system is to ensure open and wide-ranging communications throughout the development process. Initially, this will include making every effort to achieve buy-in and acceptance in its design through an open development process, inviting the participation of scientific expert advisors and fostering two-way communications with stakeholders. All decision made in the development of the system, including the selection of conditions, the definition of measures and outcomes, the integration of data, and the analysis of these data should be conducted in a transparent manner, allowing and accepting comment and feedback during the process. Doing this will help establish understanding and buy-in of the program, which are vital to ensure acceptance and recognition of the surveillance system results. Finally, the results of the system should be disseminated through a comprehensive approach.

Strategies that may be employed for fostering openness and buy-in may include conducting program presentations and briefings for the duration of its development, and engagement of stakeholders and end-users of the system through open dialogues and discussion sessions. The scientific integrity of the system would be ensured through the establishment of an independent expert advisory panel during its development, and through the publication of major outcomes in the peer-reviewed literature. Public and policy-maker utilization of the project may be maximized through the establishment of a comprehensive surveillance system website to house and present major and detailed findings of the system.

Conclusion

The Institute of Medicine Committee on Public Health Approaches to Reduce Vision Impairment and Promote Eye Health commissioned this report to attempt to answer a deceptively simple question: what is the potentially preventable burden of vision loss and eye disorders. Understanding the answer to this question is key for guiding policy makers and informing public debate towards the optimal decisions to try to mitigate this burden. However, in vision and eye health, the simplest questions often have the most complex answers. While there exists a substantial literature of specific knowledge, continued limitations borne from information gaps and non-harmonized and non-comparable information across different manifestations of vision and eye health make it nearly impossible to draw overarching conclusions based on solid evidence. However, despite these challenges, we feel it is nonetheless important to tackle such questions not only to begin to understand the answers, but in doing so, to find and highlight knowledge gaps that must be filled in order to continue to refine our understanding of the public health burden of vision loss and eye disorders.

In attempting to answer this question, we conduct an analysis drawing on a wide range of currently available data and epidemiological knowledge. Our solution pieces together the information we do know by leveraging multiple sources of publicly available epidemiological information, harnessing sophisticated treatment and outcome models, and filling in additional gaps with novel research. From VPUS, we find high prevalence of major eye disorders and vision loss. From the earlier EDPRG study, we find the allocation of causes of this vision loss. From NHANES, we find the diagnosis or treatment rates of eye disorders, as well as the prevalence and severity of URE. From the Cost of Vision report we find the direct and indirect costs of low vision and medical treatment, and from the MEDS model we calculate treatment efficacy on a population level. From Census projections and the Future of Vision report we forecast the future changes and shifts in epidemiology and costs.

Our results indicate that there is likely to be high prevalence of untreated or undiagnosed low vision, with as many as 468,000 blind and 17.5 million impaired. The vast majority - 96% is attributable to URE and cataract, both of which can be treated with extremely high efficacy at relatively low cost. The remaining prevalent vision loss is due to chronic conditions including AMD, glaucoma and diabetic retinopathy; conditions that lead to high, ongoing medical management costs and may lead to unrecoverable vision loss.

The economic costs of prevalent and future untreated and undiagnosed vision loss is staggering; potentially preventable vision loss will cost an average $88 billion per year over the next 10 years. But as with the prevalence of vision loss, this figure is dominated by URE, and to a lesser extent, cataract. Immediately treating all prevalent and incident URE alone would save $88 billion per year over 10 years, while treating cataract would save $20 billion per year over this period. Treating the other chronic conditions leads to positive costs $20 billion, almost exactly offsetting cataract, thus the total savings for treating all conditions is essentially the same as the savings of treating URE alone. The immediate treatment of URE and cataract together would lead to savings of $108 billion per year over 10 years. Of course, this cost does not include the costs of any intervention to actually identify and provide access to treatment. No policy or intervention could ever achieve the complete elimination of the preventable burden, and all would incur substantial costs and resources that would greatly reduce the projected savings.

This analysis is limited in a number of ways, which we have described in detail throughout the report. Limitations in data have necessitated leveraging multiple data sources and models, and many parts of the analysis are dependent on a number of key assumptions. However, despite the limitations inherent in such a "broad scope" analysis, we believe the high level findings are clear and robust;

- There is a large pool of potentially preventable vision loss
- This vision loss leads to a high economic and quality of life burden
- The large majority of this vision loss is due to easily treatable conditions of URE and cataract
- Case finding costs notwithstanding, treatment of URE and cataract would likely achieve large economic savings

The results are so stark that no underlying data uncertainty, nor even reverses of major assumptions are likely change these conclusions. However, these conclusions do not answers the important follow-on questions of how public health should attempt to mitigate this burden. Answering these questions is likely to be much more challenging, and in this respect, the underlying limitations of the existing epidemiology and economic knowledge of vision and eye health will continue to impose a substantial impediment towards achieving the goal of reducing vision impairment and promoting eye health. This is why we believe that it is vital to improve the foundation of our knowledge of vision and eye health epidemiology and impacts through a robust, and integrated surveillance system.

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