

**FUTURE HEALTH DIVIDENDS
FOR CALIFORNIA:
VALUING MEDICAL INNOVATIONS TO FIGHT
CANCER, DIABETES, STROKE, AND DRY
AGE-RELATED MACULAR DEGENERATION**

Bryan Tysinger, PhD(c)

Karen Mulligan, PhD

Henu Zhao, PhD

Alwyn Cassil

Dana Goldman, PhD

USC Schaeffer

Leonard D. Schaeffer Center
for Health Policy & Economics

AUTHOR AFFILIATIONS

Bryan Tysinger, PhD(c), is the director of health policy microsimulation at the USC Schaeffer Center. He is also a research assistant professor at the USC Price School of Public Policy.

Karen Mulligan, PhD, is a research assistant professor at the USC Price School of Public Policy.

Henu Zhao, PhD, is a senior quantitative analyst at the USC Schaeffer Center.

Alwyn Cassil is a principal at Policy Translation, LLC.

Dana Goldman, PhD, holds the Leonard D. Schaeffer Director's Chair at the USC Schaeffer Center. He is a distinguished professor of public policy, pharmacy & economics at the USC School of Pharmacy and the USC Price School of Public Policy.

FEBRUARY 2019

The report was funded by a contract from the California Institute for Regenerative Medicine (CIRM) to the Leonard D. Schaeffer Center for Health Policy & Economics.

TABLE OF CONTENTS

Executive Summary 1
Valuing Medical Innovations to Fight Cancer, Diabetes, and Stroke 3
 Appendix A 7
The Value of a Cure for Dry Age-Related Macular Degeneration in California 9
 Appendix B 13

INNOVATIVE TREATMENTS AND CURES FOR SELECT DISEASES WORTH BILLIONS IN VALUE FOR CALIFORNIANS

Within biomedical innovation, slow but steady advances in basic science often serve as the springboard to breakthrough treatments. Fifteen years ago, Californians supported a unique public policy experiment: Proposition 71 (The California Stem Cell Research and Cures Initiative) authorized \$3 billion over 10 years to create the California Institute for Regenerative Medicine (CIRM) and finance stem cell research aimed at jumpstarting treatments for diseases that are currently incurable and affect millions of state residents: cancer, diabetes, blindness, and more than 70 other diseases and injuries.

To help policymakers and the public understand the potential return on investment of stem cell research, CIRM commissioned researchers at the USC Leonard D. Schaeffer Center for Health Policy & Economics to estimate the value of hypothetical future interventions to reduce or cure specific diseases. The two analyses summarized below leverage a unique microsimulation model adapted to California demographics.

The Future Elderly Model (FEM) is a validated microsimulation model of health and economic outcomes for Americans aged 50 and older. It has been leveraged to analyze and predict consequences of disease prevention, policy changes, biomedical innovations, and demographic trends. Development of FEM has been supported by the National Institutes of Health, the Centers for Medicare and Medicaid Services, the Social Security Administration, the MacArthur Foundation, the Robert Wood Johnson Foundation, and others. To date, researchers have published over sixty-five publications utilizing the model. The results of these studies have been cited – or commissioned – by government agencies, the White House, the National Academies of Science, and private organizations.

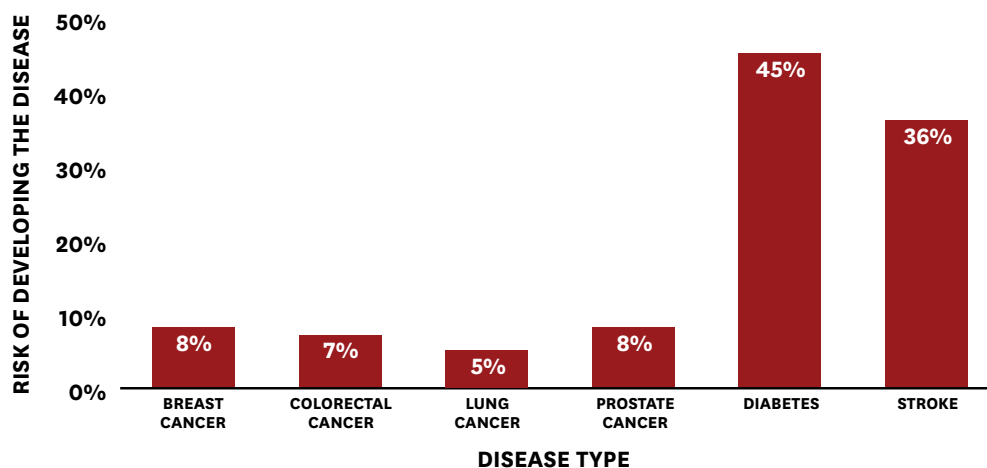
At its core, FEM is a data-driven model that projects individuals’ trajectories for health risk factors, chronic disease incidence, functional limitations, mortality and economic outcomes using the nationally-representative Health and Retirement Study. For the analyses presented here, FEM is adapted to reflect California’s population using data from the California Department of Finance. The social value of innovation is calculated using gains in quality-adjusted life years, a measure of disease burden that incorporates both quality and quantity of life.

THE VALUE OF REDUCING THE INCIDENCE OF SELECTED DISEASES IN CALIFORNIA

In 2018, nearly half of Californians aged 50 and older will develop diabetes during their lifetime. Furthermore, more than one-third will experience a stroke, and between 5 and 8 percent will develop either breast, colorectal, lung, or prostate cancer.

Taking into account the high prevalence and the social and economic burden of these diseases, the researchers predict an intervention that reduces the incidence of these selected cancers, diabetes, and stroke by 50 percent would generate almost \$900 billion in social value between 2018 and 2050. A more modest 10 percent decline in incidence translates to \$175 billion in social value during the same period.

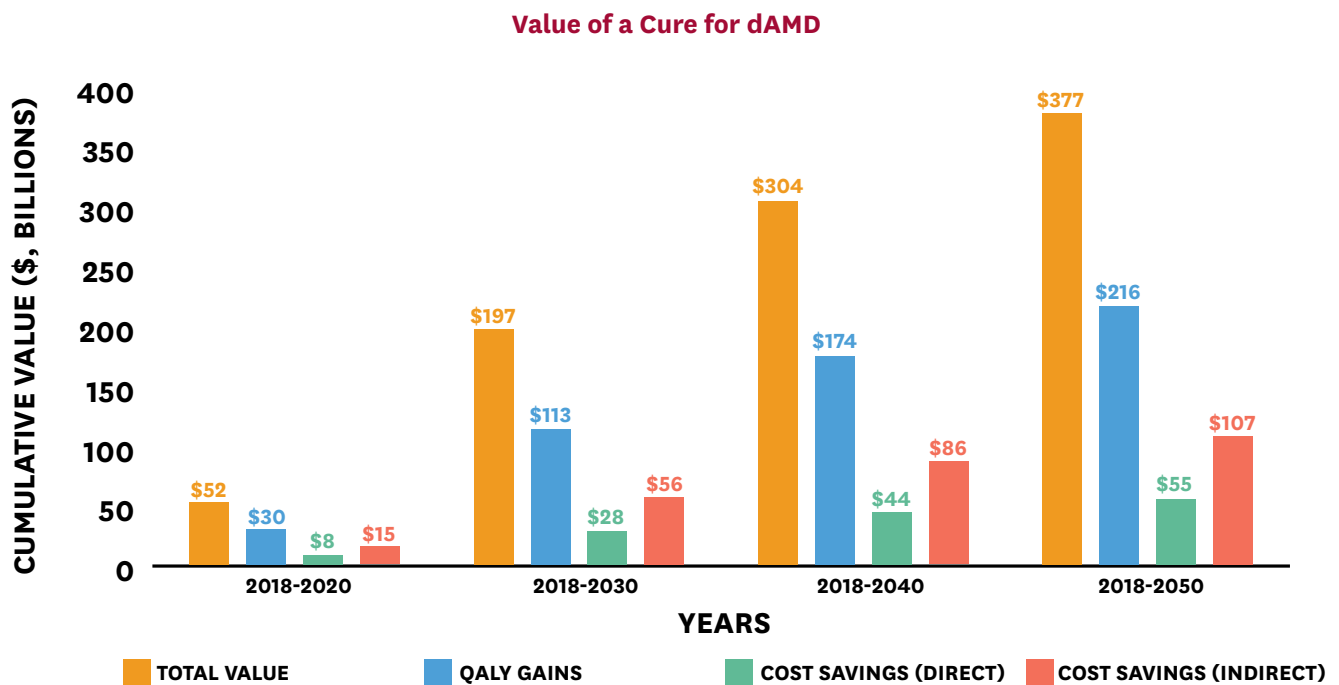
Risk of Developing Specified Diseases after Age 50 for Current 51- and 52-Year-Old Californians



THE VALUE OF A CURE FOR DRY AGE-RELATED MACULAR DEGENERATION IN CALIFORNIA

Age-related macular degeneration (AMD) is the leading cause of vision loss in the United States, and dry AMD (dAMD) accounts for the majority of AMD cases. Between 2018 and 2050, an estimated 400,000 Californians will develop dAMD and face vision losses that could keep them from reading, working, driving, and living independently. Patients who develop dAMD experience quality of life declines related to poor visual acuity. The disease also generates societal costs—both direct costs, such as medical care and visual aids and devices, and indirect costs, such as unemployment and productivity losses, caregiver burden, and nursing home care. The researchers took all of this into account and estimate that a cure for dAMD would generate \$377 billion in value for California between 2018 and 2050.

Currently, CIRM funds over 50 clinical trials testing stem-cell treatments in more than 35 disease areas, and has additional candidate treatments in the pipeline, including a clinical trial underway focused on dAMD. Though advances in scientific research defy easy predictions, investing in biomedical research is important if we want to reduce the burden of common and costly diseases for individuals, their families, and society. These findings show the value and impact breakthrough treatments could have for California.



FUTURE HEALTH DIVIDENDS FOR CALIFORNIA: VALUING MEDICAL INNOVATIONS TO FIGHT CANCER, DIABETES, AND STROKE

While the course of scientific innovation is difficult to predict, slow but steady advances in basic science often serve as the springboard to treatment breakthroughs. California is now 15 years into a unique public policy experiment—a voter-approved \$3-billion investment in stem-cell research—aimed at jumpstarting treatments for diseases affecting millions of state residents. A new analysis by researchers at the University of Southern California (USC) Leonard D. Schaeffer Center for Health Policy & Economics quantifies the potential return on investment of reducing the disease burden in California through new discoveries. We estimate that interventions that reduce the incidence of breast, colon, lung, and prostate cancer; diabetes; and stroke by 50 percent would generate almost \$900 billion in social value to the State between 2018 and 2050. Even more modest reductions would result in significant gains to California—a 10-percent decline in the incidence of selected cancers, diabetes, and stroke translates to \$175 billion in social benefit during the same period.

A SCIENTIFIC LEAP OF FAITH

Fifteen years ago, California voters took a leap of faith to speed treatment advances for scores of devastating diseases and injuries by passing [Proposition 71: the California Stem Cell Research and Cures Initiative](#). Approved by 59 percent of voters in 2004, Prop 71 created the California Institute for Regenerative Medicine (CIRM) and authorized \$3 billion in bond funding over 10 years to finance stem cell research aimed at accelerating treatments to patients with unmet medical needs. Diseases or injuries targeted by Prop 71 include cancer, diabetes, heart disease, Alzheimer’s, Parkinson’s, spinal cord injuries, blindness, Lou Gehrig’s disease, HIV/AIDS, mental health disorders, multiple sclerosis, Huntington’s disease, and more than 70 other diseases and injuries [1].

“About half of California’s families have a child or adult who has suffered or will suffer from a serious, often critical or terminal, medical condition that could potentially be treated or cured with stem cell therapies. In these cases of chronic illness or when patients face a medical crisis, the health care system may simply not be able to meet the needs of patients or control spiraling costs, unless therapy focus switches away from maintenance and toward prevention and cures,” the law states [1].

In the intervening years, California has leveraged that initial \$3 billion investment into a stem-cell research endeavor that leads the nation. Most CIRM funding goes directly to research. In the early years, because stem cell research was such a new field, funding focused on creating the infrastructure to conduct research and conducting basic science research to help develop a deeper understanding of stem cells and how they work. More recently, CIRM has begun to move the most promising ideas from earlier funding into clinical trials where they can be tested in people. Just this year, CIRM funded its 50th clinical trial [2]. CIRM also established the [Alpha Stem Cell Clinics Network](#), which conducts high-quality stem cell trials for a wide variety of diseases at leading medical centers in California.

MOVING SCIENCE FROM THE BENCH TO THE BEDSIDE

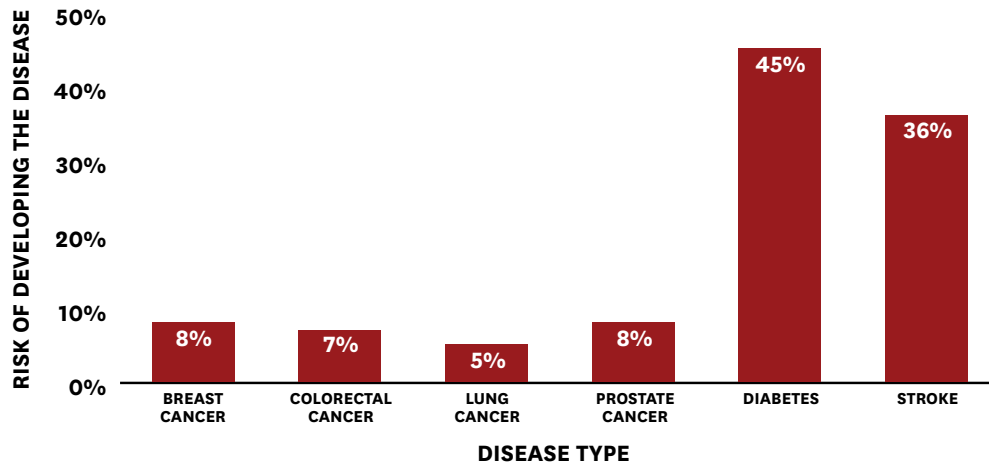
While the costs of CIRM are easy to see, the potential benefits are not as easy to compute. Some of it surely can show up in medical spending, but the real gains come from forestalling disease—something that is not as easily measured. The potential value of reducing the incidence of common diseases—for example, breast, colorectal, lung, and prostate cancer and diabetes and stroke—in California is large. A relatively small research investment can potentially return great value at the individual and societal levels by reducing disease burden.

To help policymakers and the public understand the potential return on investment of stem cell research, CIRM commissioned Schaeffer Center researchers to estimate the value of interventions to reduce the incidence of selected cancers, diabetes, and stroke. Adapting the Future Elderly Model (FEM)—a microsimulation model of health and economic outcomes for older Americans—to California demographics, researchers generated a snapshot of what scientific advances in treating certain diseases would mean at both the individual and societal level in California (see [Appendix A](#) for more about the FEM and analytic methods).

DISEASE INCIDENCE IN CALIFORNIA

With nearly 40 million people, California is the nation’s most populous state and home to about an eighth of the U.S. population [3]. As such, California bears a large burden from common diseases. The projected lifetime risk after age 50 of selected cancers, diabetes and stroke in California is large. For example, of the estimated 1 million 51- and 52-year-olds in California today, nearly 1 in 2 (45%) will develop diabetes during their remaining lifetime, more than a third (36%) will have a stroke, and between 1 in nearly 10 to 1 in 20 will experience one of the following cancers—breast, colorectal, lung or prostate cancer (see **Exhibit A1**).

EXHIBIT A1: Lifetime Risk of Developing Disease for Californians Aged 51 and 52 in 2018

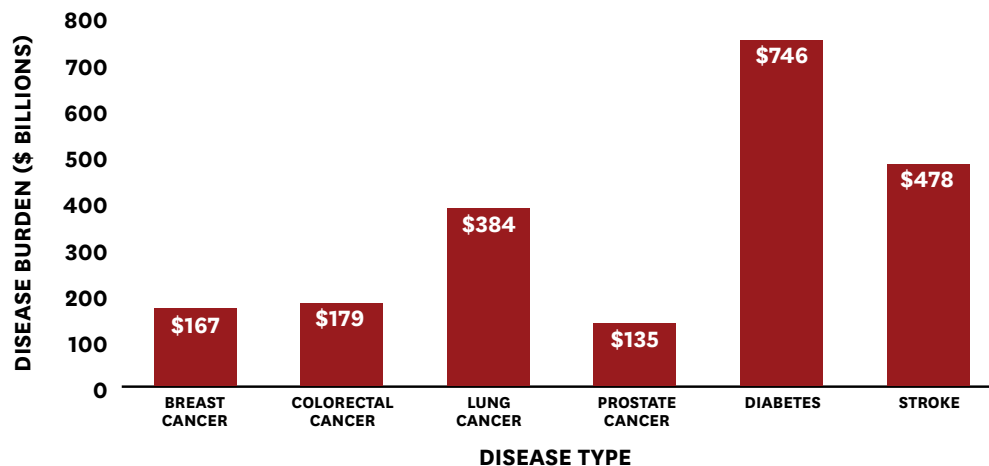


Source: Authors’ calculations using the California Future Elderly Model

BURDEN OF SELECTED DISEASES IS \$2.1 TRILLION BY 2050 IN CALIFORNIA

The burden of disease is often a hidden cost to a society. Using a measure known as a quality-adjusted life-year (QALY), researchers can estimate the societal burden of specific diseases over time. A QALY is a proxy of the value of a year in perfect health for an individual. In this analysis, a QALY is valued at \$150,000, and disease burden is measured by decreased QALYs. For example, among Californians 51 and older, diabetes would generate nearly \$750 billion in societal disease burden as measured by QALYs (\$150,000) between 2018 and 2050. Similarly, the estimated disease burden for stroke would reach \$500 billion and more than \$850 billion combined for lung, breast, colorectal, and prostate cancer. Collectively, burden from the six diseases for Californians aged 51 and older is more than \$2 trillion from 2018 to 2050 (see **Exhibit A2**).

EXHIBIT A2: California Disease Burden, by Selected Disease, 2018-2050



Source: Authors’ calculations using the California Future Elderly Model

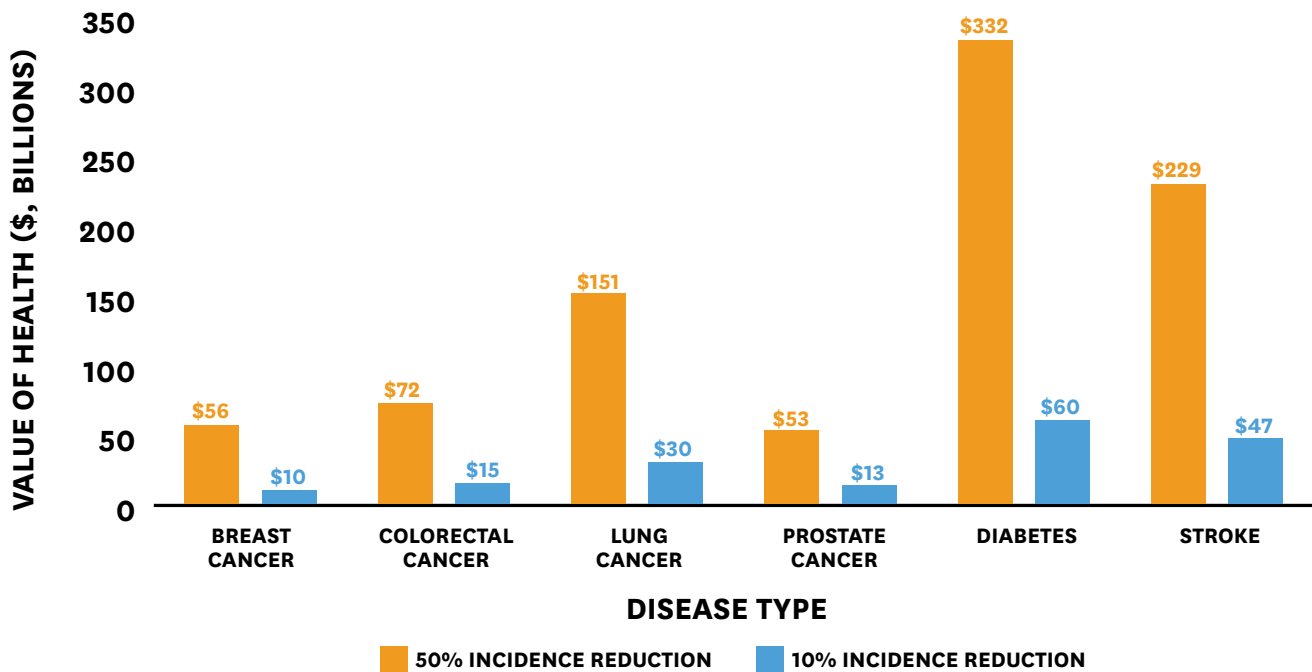
Note: Values are in 2018 dollars with a 3 percent annual discount rate applied.

ESTIMATED VALUE OF REDUCED DISEASE INCIDENCE IN CALIFORNIA

Potential gains from research advances that decrease disease incidence are significant. For example, a scientific advance that decreases diabetes incidence in Californians 51 and older by 50 percent translates to a \$332 billion gain between 2018 and 2050 in social value based on QALYs valued at \$150,000 (see **Exhibit A3**). Even a more modest decline in diabetes incidence—10 percent—results in a gain of social value of \$60 billion over the same period. Similarly, a 10-percent reduction in strokes would generate \$47 billion in social value, while a 50-percent reduction would generate an estimated \$229 billion in social value between 2018 and 2050.

For cancer, the potential gains from a 50-percent reduction in the incidence of breast cancer would be \$56 billion between 2018 and 2050 in California, \$72 billion for colorectal cancer; \$151 billion for lung cancer, and \$53 billion for prostate cancer. A 10-percent reduction in incidence of breast cancer would generate \$10 billion in social value, \$15 billion for colorectal cancer, \$30 billion for lung cancer, and \$13 billion for prostate cancer.

EXHIBIT A3: Gains in Social Value if Disease Incidence in California Reduced by 50 Percent and 10 Percent, by Disease, 2018-2050



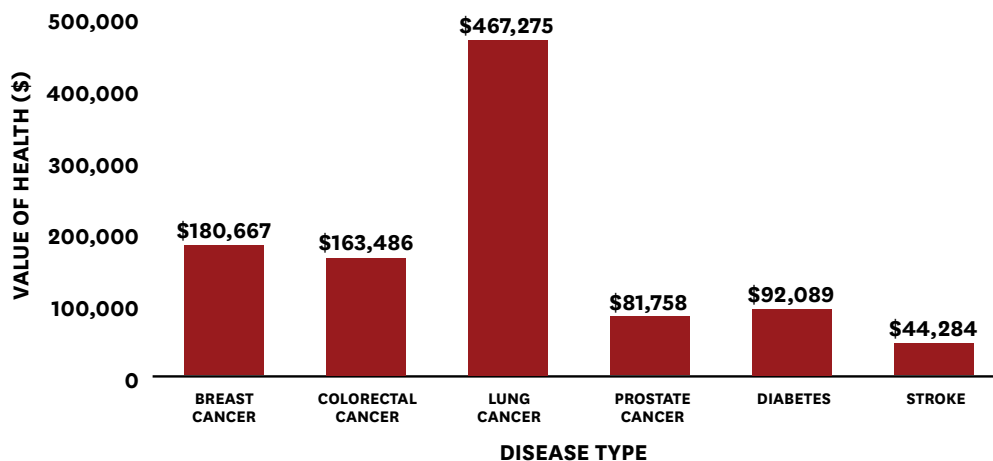
Source: Authors' calculations using the California Future Elderly Model

Note: Social value is measured by the increase in quality-adjusted life-years (QALYs). Values are expressed in 2018 dollars using \$150,000 per QALY with a 3 percent annual discount rate applied.

THE VALUE OF A CURE TO CALIFORNIANS

For those who benefit from new innovation, the lifetime social gains are equally striking. For example, a cure for lung cancer would result in per-capita lifetime social value gained for a single 51- or 52-year-old Californian patient of almost a half-million dollars (\$467,275) (see **Exhibit A4**). Similarly, for Californians cured of breast or colorectal cancer, the lifetime social value gained would be \$180,667 and \$163,486, respectively, per capita. The much higher value of a cure for lung cancer reflects the higher prevalence of the disease at a younger age and the resulting larger gain in life expectancy. While smaller, the lifetime per-capita social gains for diabetes, prostate cancer, and stroke are still significant.

EXHIBIT A4: Per-Capita Lifetime Social Value Gained for Curing Selected Diseases



Source: Authors' calculations using the California Future Elderly Model

Note: Values are in 2018 dollars with a 3 percent annual discount rate applied.

IMPLICATIONS

Much is made about the cost of health care treatment, without understanding the full benefits [4, 5]. Improvements in life expectancy due to medical research added approximately \$5 trillion per year to U.S. wealth, according to the best estimates [6, 7]. The experience with cancer is instructive. Today, cancer patients live longer, healthier, and happier lives than those in prior decades. Survival increased almost 4 years from 1988–2000 [8], creating 23 million additional life-years, and generating almost \$2 trillion in additional value to society, once the health gains are appropriately tallied [9], and the gains continue to accrue [9, 10]. When compared with total R&D spending — both private and public — we have clearly gotten a substantial return on our investment to fight the disease. So, while cancer still remains a pernicious disease, there is hope that in many instances it can be managed as a chronic illness, with modest side effects [11].

More generally, it can be shown that we dramatically underinvest in medical innovation [12, 13]. In 2004, California voters, concerned by inadequate federal investments in stem cell research, made finding cures a priority for the state. In the ensuing 15 years, CIRM has funded 50 clinical trials, with targeted enrollment of more than 3,500 patients. Researchers supported by CIRM are using stem cells to help unravel the complexities of diseases ranging from diabetes to cancer to stroke.

We find that nearly half of Californians aged 50 and older will develop diabetes during their lifetime. Furthermore, more than one-third will experience a stroke, and between 5 and 8 percent will develop either breast, colorectal, lung, or prostate cancer. Taking into account the high prevalence and the social and economic burden of these diseases, an intervention that reduces the incidence of these selected cancers, diabetes, and stroke by 50 percent would generate almost \$900 billion in social value between 2018 and 2050. A more modest 10 percent decline in incidence translates to \$175 billion in social value during the same period. Put in this context, the CIRM investment would be worthwhile if it increased our chances of success even modestly. Against the billions of dollars in disease burden facing California, the relatively small initial investment is already paying dividends as researchers work to bring new therapies to patients.

APPENDIX A

This analysis is based on the Future Elderly Model (FEM), which is a microsimulation model projecting future health and economic outcomes by individual trajectories. The FEM can be used to simulate different scenarios and calculate the burden of diseases and value of interventions and cures. For detailed information, technical documentation is available at (https://roybalhealthpolicy.usc.edu/files/2015/05/FEM_techdoc.pdf).

The FEM consists of three modules: the initial cohort module, the transition module, and the outcome module. The initial cohort module uses data from the Health and Retirement Study (HRS) and trends calculated from other sources to predict the economic and health outcomes of new cohorts of 51- and 52-year-olds. Then, the transition module estimates a two-year transition between chronic diseases, functional status, and economic outcomes. The transition models are also based on HRS data. As a complement, the Medical Expenditure Panel Survey (MEPS) is used to calculate quality-adjusted life-years, or QALYs. The outcome module is then used to summarize the QALY estimation.

Datasets used in FEM include HRS, MEPS, and the Medicare Current Beneficiary Survey. HRS is a nationally representative longitudinal survey for individuals 51 and older that provides rich information on respondents' health status, functional limitations, and economic status. The HRS also allows tracking of older individuals over time and provides a good understanding of how their health and economic situation change. The other two datasets are used to better estimate health spending and quality of life.

The initial cohort in FEM is a nationally representative sample of people aged 51 years and older. To estimate California outcomes, the initial cohort is reweighted using state and county population projections data from the California Department of Finance to make the initial cohort representative of California residents 51 and older [14].

The analysis also incorporates the restricted cancer site data from the HRS to break down the general cancer variable to several major cancer sites. The cancer sites in the analysis include female breast, colon, lung, and prostate. Specifically, HRS asks respondents who reported cancer about where their cancer started, both in the main interview and the exit interview. Since cancer kills some individuals quickly, a portion of respondents did not have a chance to report their cancer in the main interview. Therefore, the exit interview information was used to assign cancer incidence to the survey wave prior to death for those who died with cancer prior to reporting the diagnosis.

Scenarios

To estimate the social value of curing the six diseases, multiple scenarios were simulated for Californians aged 51 and older. The base scenario simulates the status quo health and economic outcomes for Californians from 2018 to 2050. In the second set of scenarios, each disease is removed and the corresponding outcomes are simulated. This presents a hypothetical scenario in which the specific disease does not exist. A comparison of the outcomes with the base scenario enables calculation of the burden of each disease. The third scenario estimates the social value of potential innovations in treating each disease. In this scenario, two-year disease incidence is reduced by 50 percent and 10 percent, respectively. The outcomes then are compared with the base scenario to estimate the social value gained by a reduction of disease incidence by certain level—relatively small (10%) and relatively large (50%). Lastly, a cohort simulation is conducted to follow the 51- and 52 year-olds over their entire lives. From this scenario, the per-capita social value of curing each disease can be estimated, along with the risk of developing each disease after age 50. In all of scenarios, only the social value of potential treatments is estimated, not the cost of potential treatments.

QALY Estimation

The main outcome used to measure social values is QALYs. The FEM uses the EQ-5D, a commonly used quality-of-life index to predict QALYs. EQ-5D is estimated using an OLS regression based on MEPS data. The factors contributing to QALYs include mobility, daily activities, self-care, chronic diseases, smoking status, obesity, and marital status. The chronic diseases include the six diseases of interest, allowing them to have their impact individually on quality of life. We then predict a QALY value for each individual using HRS data based on the OLS regression model. Each QALY unit is finally translated to dollar values as \$150,000. Dollar values are reported in 2018 dollars, with future dollars discounted using a 3 percent rate.

Limitations

A limitation of this analysis is the focus on the older Californian population. This population captures the majority of individuals in California with these chronic diseases, but not all. The incidence models for chronic diseases are estimated using self-reported data in the Health and Retirement Study. While this survey is designed to be nationally representative of the 51 and older population, biases in reporting diseases potentially exist. Additionally, this analysis applies the nationally estimated disease incidence models to the subset of Californians. While the models control for key demographics and risk factors, it is possible that the incidence rates produced with this method are too high or too low. When estimating incidence of the cancers we supplement the self-report measure for the living with information from the exit interviews for decedents, assigning the cancer incidence to the last survey year in which the individual was living. This relies on accurate reporting of cancer at the time of death in the exit interview. The interventions presented are hypothetical, chosen to demonstrate the burden of disease and potential value of incremental innovation, but there is no guarantee that these interventions reflect what will happen.

REFERENCES

1. *Proposition 71, Text of Proposed Law*. [cited 2018 December 13]; Available from: https://www.cirm.ca.gov/sites/default/files/files/about_cirm/prop71.pdf.
2. McCormak, K., *Stem cell agency board approves 50th clinical trial*. The Stem Cellar Blog. 2018; Available from: <https://blog.cirm.ca.gov/2018/12/13/stem-cell-agency-board-approves-50th-clinical-trial/>.
3. California Department of Finance, *New Demographic Report Shows California Population Nearing 40 Million Mark With Growth of 309,000 in 2017*. Available from: http://www.dof.ca.gov/Forecasting/Demographics/Estimates/e-1/documents/E-1_2018PressRelease.pdf.
4. Experts in Chronic Myeloid Leukemia, *The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts*. *Blood*, 2013. 121(22): p. 4439-42.
5. Bach, P.B., L.B. Saltz, and R.E. Wittes, *In cancer care, cost matters*, in *New York Times*. 2012: New York. p. A25.
6. Murphy, K.M. and R.H. Topel, *The economic value of medical research, in Measuring the gains from medical research: An economic approach*, K.M. Murphy and R.H. Topel, Editors. 2003, University of Chicago Press: Chicago. p. 41-73.
7. Murphy, K.M. and R.H. Topel, *The value of health and longevity*. *Journal of Political Economy*, 2006. 114(5): p. 871-904.
8. Sun, E., et al., *The contributions of improved therapy and earlier detection to cancer survival gains, 1988-2000*. *Forum for Health Economics and Policy*, 2010. 13(2): p. 1-20.
9. Lakdawalla, D.N., et al., *An economic evaluation of the war on cancer*. *Journal of Health Economics*, 2010. 29(3): p. 333-46.
10. Surveillance Epidemiology and End Results Program, *Cancer statistics*, N.C. Institute, Editor. 1973-2011.
11. Goldman, D.P. and T. Philipson, *Five myths about cancer care in America*. *Health Affairs*, 2014. 33(10): p. 1801-4.
12. Goldman, D.P., et al., *Substantial health and economic returns from delayed aging may warrant a new focus for medical research*. *Health Affairs*, 2013. 32(10): p. 1698-705.
13. Dzau, V.J., et al., *Aligning incentives to fulfil the promise of personalised medicine*. *Lancet*, 2015. 385(9982): p. 2118-9.
14. *P-3 State and County Projections Dataset*, D.o.F. State of California, Editor. 2018: Sacramento, California.

THE VALUE OF A CURE FOR DRY AGE-RELATED MACULAR DEGENERATION IN CALIFORNIA

In 2004, California voters approved \$3-billion investment in stem cell research to speed development of treatments and cures for diseases affecting millions of Californians, including age-related macular degeneration. A new analysis by researchers at the University of Southern California Leonard D. Schaeffer Center for Health Policy & Economics quantifies the potential return on investment of a cure for the most common form of the disease—dry age-related macular degeneration, or dAMD. Between 2018 and 2050, a cure for dAMD would generate an estimated \$377 billion in value for California.

CALIFORNIA'S UNIQUE COMMITMENT TO SCIENTIFIC RESEARCH

Approved by 59 percent of voters in 2004, Proposition 71: the California Stem Cell Research and Cures Initiative created the California Institute for Regenerative Medicine (CIRM). The measure also authorized \$3 billion in bond funding over 10 years to finance stem cell research aimed at accelerating treatments to patients with unmet medical needs [1]. Most CIRM funding goes directly to research—both investments in basic science to develop a deeper understanding of stem cells and how they work and clinical trials to test interventions in people. In 2018, CIRM funded its 50th clinical trial [2]. CIRM also established the Alpha Stem Cell Clinics Network, which conducts high-quality stem cell trials for a wide variety of diseases, including dAMD, at leading medical centers in California [3].

To help policymakers and the public understand the potential return on investment of stem cell research, CIRM commissioned Schaeffer Center researchers to estimate the value of a hypothetical cure for dAMD. Adapting the Future Elderly Model (FEM)¹—a microsimulation model of health and economic outcomes for older Americans—to California demographics, as well as drawing model parameters related to dAMD from the published literature, researchers generated an estimate of the value of a cure for dAMD at both the individual and societal levels in California (see [Appendix B](#) for more about the FEM and analytic methods).

THE TOLL OF VISION LOSS

Age-related macular degeneration is the leading cause of vision loss in the United States, with as many as 11 million Americans affected by the disease, 2.1 million of which are advanced cases [4, 5]. There are two types of AMD—dry and wet. Dry is the most common form of the disease, accounting for 85 percent to 90 percent of all diagnoses [6]. AMD damages the macula, which is the central part of the retina. As the disease progresses, the center part of a person's vision becomes blurred or wavy, and a blind spot may develop. The resulting vision loss can make reading, sewing, cooking, and driving difficult. AMD rarely causes total blindness because it usually does not affect side, or peripheral, vision [6]. Although dAMD progresses slowly compared with wet AMD, there is currently no approved treatment or cure for dAMD other than dietary supplements, which show some promise in slow progression of some stages of dAMD.

QUANTIFYING THE VALUE AND COST SAVINGS OF A dAMD CURE

Using a measure known as a quality-adjusted life-year (QALY), researchers can estimate the value of a cure for a disease over time at the individual and societal level. A QALY is a proxy of the value of a year adjusted for health for an individual. In this analysis, a QALY is valued at \$150,000 (assumed based on the range of values

¹ *The Future Elderly Model (FEM) is an economic-demographic microsimulation developed over the last decade by researchers with funding from the Centers for Medicare and Medicaid Services, the National Institute on Aging, the Department of Labor and the MacArthur Foundation. Its development is led by the USC Roybal Center for Health Policy Simulation, with collaborators from Harvard University, Stanford University, RAND Corporation, the University of Michigan and the University of Pennsylvania. Center researchers have used the FEM to explore a variety of policy questions, ranging from the fiscal future of the U.S., to the role biomedical innovation can play in future health outcomes. The Center has produced over sixty-five peer-reviewed manuscripts, including two special issues of Health Affairs devoted to FEM findings. FEM findings have been featured by several government agencies (in both the White House and Congress) and private organizations interested in aging policy. FEM research has resulted in approximately \$15 million in additional funding beyond its core grant, prizes from both Research!America and the MetLife Foundation for impact, and is a frequent reference in national media outlets.*

cited in the literature), and value is measured by increased QALYs [7, 8]. Visual acuity outcomes were simulated for a cohort of dAMD patients over a lifetime horizon, and these outcomes were translated into QALYs using parameters from the published literature [9]. The parameters that translate visual acuity to QALYs are specific to the population with AMD, and have been used in other economic models for AMD [10,11].

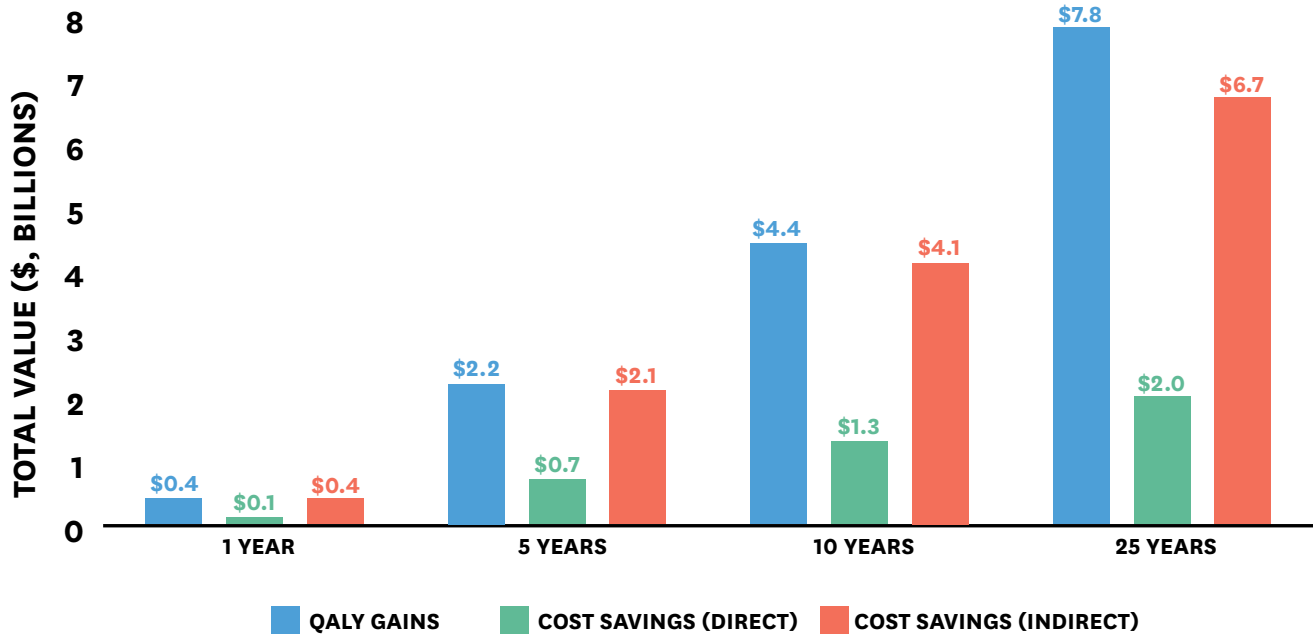
In estimating the value of a dAMD cure, researchers examined three factors associated with the disease; (1) quality of life declines related to poor visual acuity; (2) direct costs associated with dAMD, such as medical costs and visual aids and devices; and (3) indirect costs, such as unemployment and productivity losses, caregiver burden—both the direct cost of caregiving and caregiver wage and productivity losses—and nursing home care. When feasible, the model cost parameters were stratified by dAMD disease severity, which results in higher costs for patients with more advanced dAMD.

Researchers first looked at a single group of 12,488 Californians aged 51 and 52—a single incident cohort—and simulated what would happen over their lifetimes if they had dAMD. The analysis found that a hypothetical cure for dAMD would generate \$0.4 billion in QALY gains after a single year, increasing to \$4.4 billion over 10 years and \$7.8 billion over 25 years (see **Exhibit B1**).

Direct cost savings would total \$0.1 billion after one year, increasing to \$2.0 billion after 25 years, while indirect cost savings would be \$0.4 billion after one year and \$6.7 billion after 25 years. Direct cost savings are driven by reduced medical spending for dAMD, and indirect cost savings are driven by a reduction in caregiver burden (see **Exhibit B2** and **Exhibit B3**).

EXHIBIT B1: Potential Lifetime Value of a dAMD Cure for Californians Aged 51 and 52

**VALUE OF QUALITY-ADJUSTED LIFE YEAR (QALY) GAINS AND COSTS
SAVINGS FROM dAMD CURE
(SINGLE INCIDENT COHORT)**

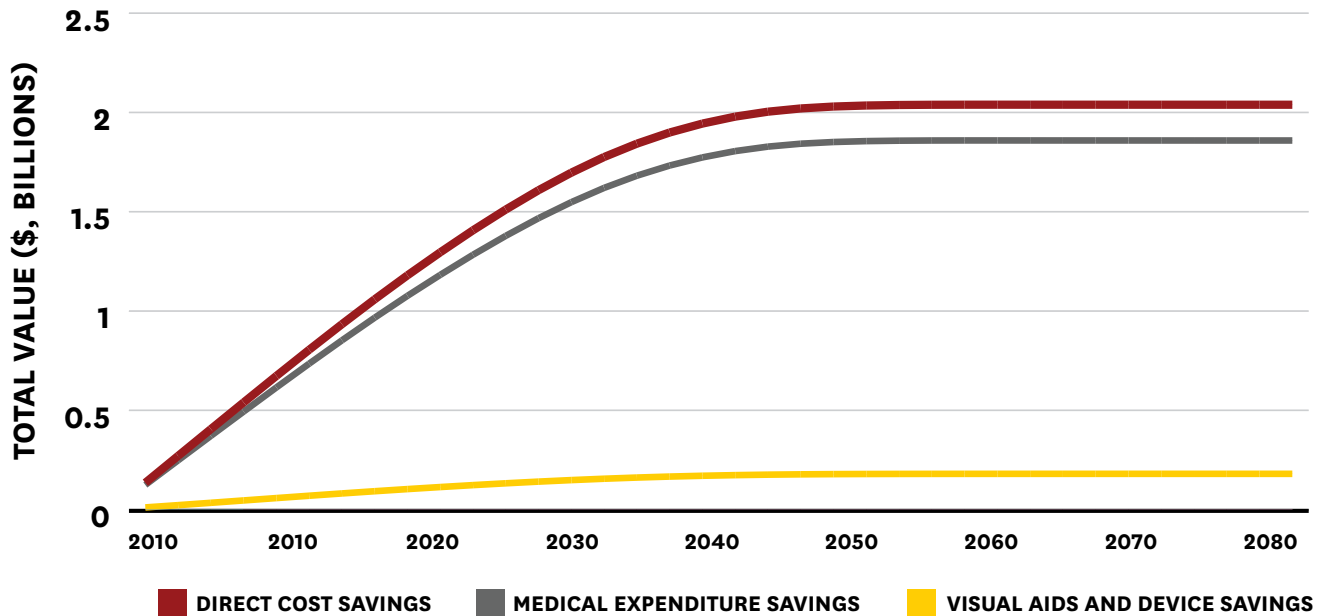


Source: Authors' calculations. See appendix for model parameter values and sources.

Notes: Results calculated as the difference between a single incident cohort (N=12,488) of dry age-related macular degeneration (dAMD) patients in California aged 51-52 at the start of the model simulation and a same-size cohort of patients without dAMD. QALY=quality-adjusted life-year. Direct costs include medical expenditures and visual aids and devices. Indirect costs include lost productivity and unemployment, caregiver burden, and nursing home costs. The value of a QALY is assumed to be \$150K. All future dollar values are discounted at a rate of 3%.

EXHIBIT B2: Direct Cost Savings from dAMD Cure

**TOTAL DIRECT COST SAVINGS FROM dAMD CURE
(SINGLE INCIDENT COHORT)**

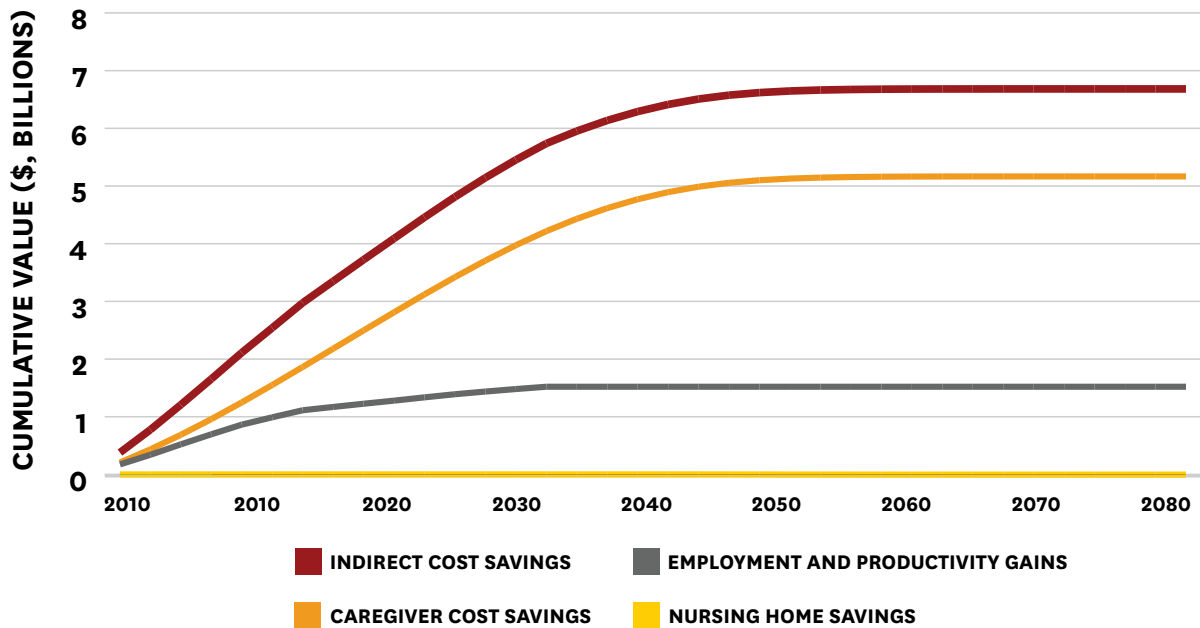


Source: Authors' calculations. See appendix for model parameter values and sources.

Notes: Results calculated as the difference between a single incident cohort (N=12,488) of dry age-related macular degeneration (dAMD) patients in California aged 51-52 at the start of the model simulation and a same-size cohort of patients without dAMD. All future dollar values are discounted at a rate of 3%.

EXHIBIT B3: Indirect Cost Savings from dAMD Cure

**INDIRECT COST SAVINGS CATEGORIES
(SINGLE INCIDENT COHORT)**

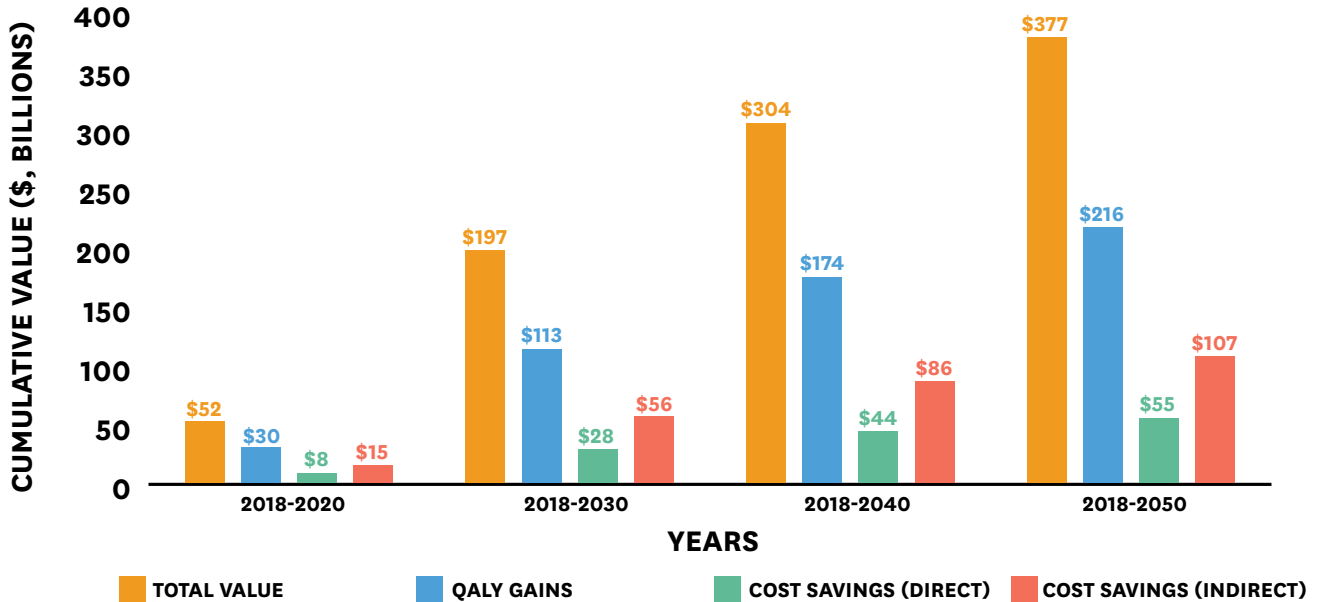


Source: Authors' calculations. See appendix for model parameter values and sources.

Notes: Results calculated as the difference between a single incident cohort (N=12,488) of dry age-related macular degeneration (dAMD) patients in California aged 51-52 at the start of the model simulation and a same-size cohort of patients without dAMD. All future dollar values are discounted at a rate of 3%.

Researchers also estimated the value of a potential cure for the full population of dAMD patients in California for different time horizons between 2018 and 2050. First, they included Californians aged 51 and older with dAMD in 2018 and then added new cases aged 51-52 in subsequent years. A hypothetical cure for dAMD would generate \$377 billion in total value—QALY gains plus cost savings—between 2018 and 2050 (see **Exhibit B4**).

EXHIBIT B4: Potential Value of a dAMD Cure in California, 2018-2050



Source: Authors' calculations. See appendix for model parameter values and sources.

Notes: Total value is equal to QALY gains net of direct and indirect costs. Results calculated as the difference between the full population with dAMD (incident plus prevalent cohorts aged 51+ in 2018, with new incident cohorts aged 51-52 each year from 2019-2050) and a same-size population without dAMD. The value of a QALY is assumed to be \$150K. All future dollar values are discounted at a rate of 3%.

IMPLICATIONS

Much is made about the cost of health care treatment, without understanding the full benefits of that spending [12, 13]. Improvements in life expectancy due to medical research added approximately \$5 trillion per year to U.S. wealth, according to the best estimates [14, 15]. The experience with cancer is instructive. Today, cancer patients live longer, healthier, and happier lives than those in prior decades. Survival increased almost 4 years from 1988–2000 [16], creating 23 million additional life-years, and generating almost \$2 trillion in additional value to society, once the health gains are appropriately tallied [17], and the gains continue to accrue [17, 18]. When compared with total R&D spending — both private and public — we have clearly gotten a substantial return on our investment to fight the disease. So, while cancer still remains a pernicious disease, there is hope that in many instances it can be managed as a chronic illness, with modest side effects [19].

A similar story holds for eye disease [20, 21]. Between 2018 and 2050, an estimated 400,000 Californians will develop dAMD and face vision losses that could keep them from reading, working, driving, and living independently in some cases. Along with the direct gain in quality of life associated with better visual acuity for individuals valued at \$216 billion between 2018 and 2050, a cure for dAMD would save an estimated \$162 billion by reducing medical spending, caregiver burden, and other direct and indirect costs.

Currently, CIRM funds over 50 clinical trials testing stem-cell treatments in more than 35 disease areas, and has additional candidate treatments in the pipeline. Within this portfolio, they are working to advance treatment for dAMD through implants. It is still early, but of the four patients who received an implant during a Phase I trial, none showed progression of vision loss in the implanted eye, one eye improved by 17 letters, and two eyes demonstrated improved fixation [22]. In the next stage of the trial, patients with less severe vision loss from dAMD will receive the implant [23]. While the course of scientific innovation twists and turns and defies easy predictions, the foresight of Californians to make stem cell research a public policy priority has positioned the state as a leader in finding new treatments for dAMD and other diseases affecting millions of people in California and beyond.

APPENDIX B. METHODS

We modeled a cohort of patients in California who are newly diagnosed with non-neovascular (also referred to as “dry”) age-related macular degeneration (dAMD) over a lifetime horizon. Our model translates visual acuity (VA) outcomes into quality of life weights, which are used to calculate the economic value of a cure. Our model also incorporates direct and indirect costs associated with dAMD from the published literature.

Model Parameters

Table B1 presents the model parameters and sources related to dAMD. Some model parameters were not available for the dAMD population in the literature. (This is a common limitation for literature-based economic models, and highlights the need for additional studies related to dAMD.) Therefore, we used the following hierarchy when selecting model parameters: 1) parameters specific to dAMD; 2) parameters specific to AMD (but not necessarily dAMD); 3) parameters specific to the visually impaired population (but not necessarily AMD specific). Approximately 80% of the model parameters were either specific to AMD or dAMD; **Figure B1** provides a visual representation of the underlying population for the model parameters.

Our incident cohort size (N=12,488) was derived by applying the dAMD incidence rate to the California population aged 51-52 in 2018. The California population size was derived from a California-specific adaptation of the Future Elderly Model (FEM). Mortality risk was adjusted to account for increased mortality associated with poor VA outcomes [24]. Disease severity was modeled using four states (mild, medium 1, medium 2, and advanced) derived from the AREDS study [25]. **Figure B1** provides a diagram of the state-transition model. The direct costs associated with dAMD included medical expenditures and the cost of visual aids and devices. Indirect costs associated with dAMD included unemployment and productivity losses, nursing home costs, and caregiver burden. All cost parameters were derived from the literature for the dAMD population when feasible. If dAMD-specific estimates were not available, we relied on estimates for the wAMD population or population with vision loss. All cost parameters and sources are provided in **Table B2**.

To estimate the value of a cure for dAMD, we ran two model scenarios: one with a cohort of dAMD patients, and one with a (same-size) cohort of healthy patients. The difference in outcomes between these two cohorts reflects the value of a hypothetical cure.

Model Outcomes

We estimated several outcomes: total population in each dAMD state, patient benefit, total direct costs, and total indirect costs. Patient benefit is calculated as the total quality-adjusted life years (QALY) multiplied by \$150,000. All future values are discounted at a rate of 3% per year. We also present social value estimates, which are calculated as the difference between patient benefit and total costs. All outcomes are estimated for a single incident cohort as well as the population level. The population level results assume a starting cohort of all dAMD patients in California aged 51 and older in 2018, with new incident cohorts (aged 51-52) entering the model each year between 2019 and 2050.

Limitations

As in any model-based approach, ours has several limitations due to simplifying assumptions. First, since we relied on a single-age cohort model, we used one value for dAMD incidence and inferred the prevalent population from that value. Therefore, our model did not incorporate the fact that dAMD incidence increases with age and as a consequence we likely underestimate the total prevalent cases of dAMD and slightly overestimate the incident cases. Second, our patient benefits only reflect the QALY gain from improved VA. The true impact of vision loss for dAMD patients may be better captured through other measures such as frequency that patients bump into objects or are able to cook or do other household tasks. Unfortunately, we do not have data on these outcomes, and to our knowledge no publications have explored them. This shortcoming highlights the need for more data and research linking patient outcomes beyond VA to quality of life.

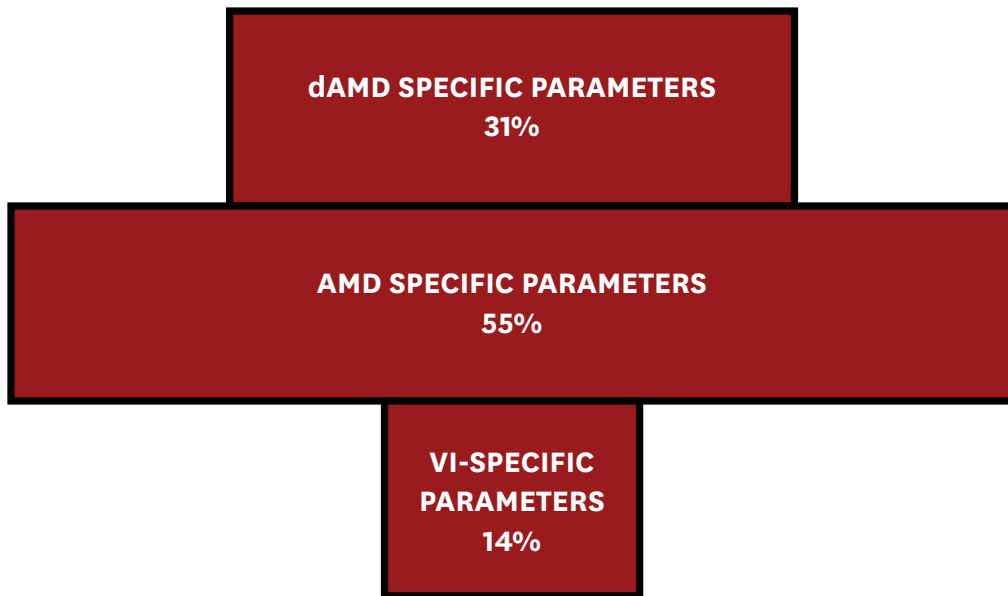
APPENDIX B. METHODS

TABLE B1: Population and Clinical Model Parameters

	Value	Source
<i>Population parameters</i>		
California population aged 51-52	1.03 million	FEM
dAMD incidence	0.0121	Klein (2002) [26]
Mortality rate	Varies by age	FEM
Mortality risk adjustment factor for dAMD patients	1.17	Thiagarajan (2005) [24]
<i>Baseline model state proportions</i>		
Mild dAMD	0.458	AREDS [25]
Medium 1 dAMD	0.372	
Medium 2 dAMD	0.000	
Advanced dAMD	0.170	
<i>dAMD state transition probabilities</i>		
Mild to Medium 1	0.132	AREDS [25]
Mild to Advanced	0.005	
Medium 1 to Medium 2	0.046	
Medium 1 to Advanced	0.088	
Medium 2 to Advanced	0.244	
<i>Quality of life weights</i>		
Healthy (no dAMD)	0.97	Brown (2005) [27]
Mild dAMD	0.84	
Medium 1 dAMD	0.74	
Medium 2 dAMD	0.66	
Advanced dAMD	0.52	
<i>Economic parameters</i>		
Value of a QALY	\$150,000	Assumption
Discount rate	3%	Assumption

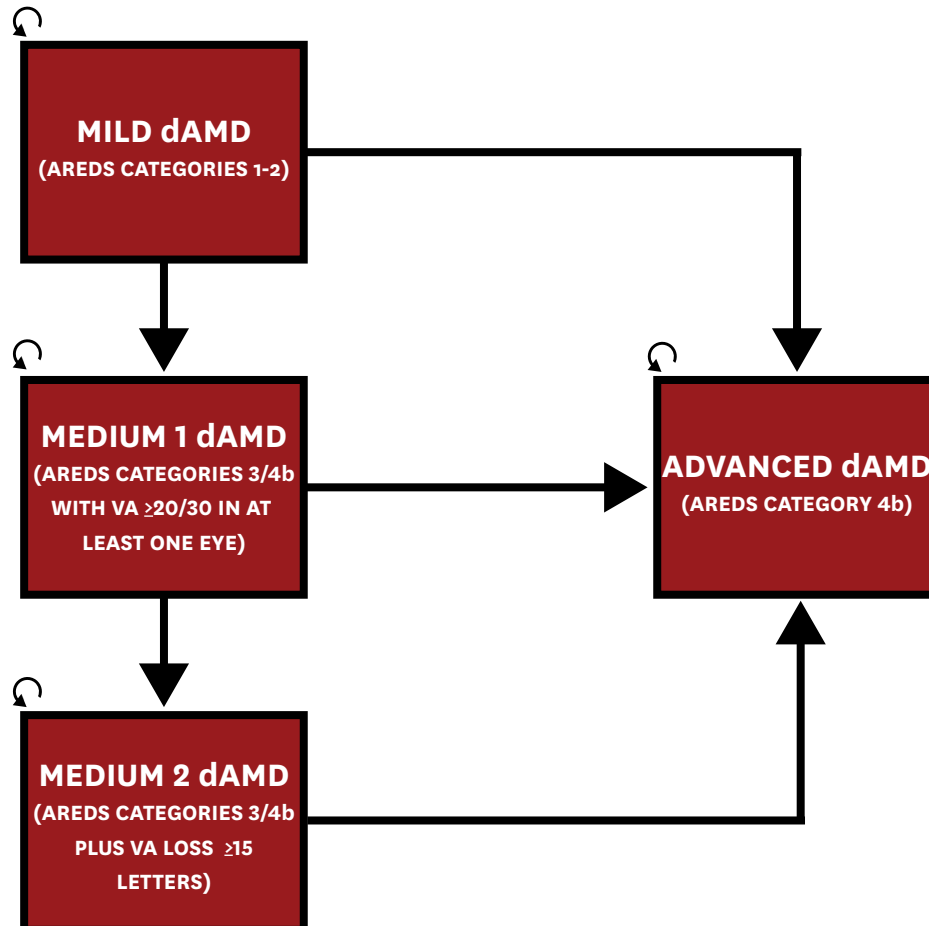
Notes: Transition probabilities are for a 2 year model cycle.

FIGURE B1: Visual Distribution of Parameter Sources



Acronyms: dAMD=dry age-related macular degeneration; AMD=age-related macular degeneration; VI=visually impaired

FIGURE B2: State-Transition Model



Notes: All states have transition to death.

TABLE B2: Direct and Indirect Cost Parameters

	Value	Source
<i>Direct cost parameters</i>		
Medical costs, no dAMD	\$20,006	Schmier (2012) [28]
Medical costs, dAMD	\$28,045 (mild/medium) \$39,281 (advanced)	
Vision services and device cost, no dAMD	\$336	Schmier (2006) [29]
Vision services and device cost, dAMD	\$571 (mild) \$1,696 (medium) \$1,899 (advanced)	
<i>Indirect cost parameters</i>		
Probability of employed	Varies by age	FEM, NHIS calculations [30]
Probability of employed adjustment factor for dAMD	0.6353	NHIS calculations [30]
Earnings, no dAMD	Varies by age	
Earnings, dAMD	Varies by age	
Caregiving cost, no dAMD	\$1,199	Rainville (2016) [31]
Caregiving cost, dAMD	\$1,468 (mild) \$15,359 (medium) \$66,271 (advanced)	Schmier (2006) [32]
Probability of nursing home use	Varies by age	FEM
Probability of nursing home use adjustment factor for dAMD	1.08	Evans (2008) [33]
Cost of nursing home	\$7,271	DHHS (2016) [34]

Notes: All cost parameters inflated to 2018 USD using the Consumer Price Index (CPI-U). The probability of visual services and device use, medical costs, and caregiving are incorporated into the annual cost parameters.

REFERENCES

1. *Proposition 71, Text of Proposed Law*. [cited 2018 December 13]; Available from: https://www.cirm.ca.gov/sites/default/files/files/about_cirm/prop71.pdf.
2. McCormak, K., *Stem cell agency board approves 50th clinical trial*. The Stem Cellar Blog. 2018; Available from: <https://blog.cirm.ca.gov/2018/12/13/stem-cell-agency-board-approves-50th-clinical-trial/>.
3. California Institute for Regenerative Medicine, *Blindness fact sheet*. Available from: <https://www.cirm.ca.gov/our-progress/disease-information/blindness-fact-sheet>.
4. Bright Focus Foundation, *Age-related macular degeneration: Facts and figures*. 2016; Available from: <https://www.brightfocus.org/macular/article/age-related-macular-facts-figures>.
5. Prevent Blindness, *Living with AMD*. Available from: <https://www.preventblindness.org/living-amd>
6. Prevent Blindness, *Dry-age-related macular degeneration fact sheet*. Available from: <https://www.preventblindness.org/dry-amd>.
7. Hirth, R.A., et al., *Willingness to pay for a quality-adjusted life year: in search of a standard*. Medical decision making : an international journal of the Society for Medical Decision Making, 2000. 20(3): p. 332-42.
8. Neumann, P.J., J.T. Cohen, and M.C. Weinstein, *Updating Cost-Effectiveness — The Curious Resilience of the \$50,000-per-QALY Threshold*. The New England Journal of Medicine, 2014. 371(9): p. 796-797.
9. Brown, G.C., et al., *The burden of age-related macular degeneration: a value-based medicine analysis*. Trans Am Ophthalmol Soc, 2005. 103: p. 173-84; discussion 184-6.
10. Lee, A., et al., *Cost-effectiveness of age-related macular degeneration study supplements in the UK: combined trial and real-world outcomes data*. British Journal of Ophthalmology, 2018. 102 (4) p. 465-472.
11. Rein, D.B., et al., *Cost-effectiveness of Vitamin Therapy for Age-Related Macular Degeneration*. Ophthalmology, 2007. 114(7): p. 1319-1326.
12. Experts in Chronic Myeloid Leukemia, *The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts*. Blood, 2013. 121(22): p. 4439-4442.
13. Bach, P.B., L.B. Saltz, and R.E. Wittes, *In cancer care, cost matters*, in New York Times. 2012: New York. p. A25.
14. Murphy, K.M. and R.H. Topel, *The economic value of medical research, in Measuring the gains from medical research: An economic approach*, K.M. Murphy and R.H. Topel, Editors. 2003, University of Chicago Press: Chicago. p. 41-73.
15. Murphy, K.M. and R.H. Topel, *The value of health and longevity*. Journal of Political Economy, 2006. 114(5): p. 871-904.
16. Sun, E., et al., *The contributions of improved therapy and earlier detection to cancer survival gains, 1988-2000*. Forum for Health Economics and Policy, 2010. 13(2): p. 1-20.
17. Lakdawalla, D.N., et al., *An economic evaluation of the war on cancer*. Journal of Health Economics, 2010. 29(3): p. 333-46.
18. Surveillance Epidemiology and End Results Program. *Cancer statistics*, N.C. Institute, Editor. 1973-2011.
19. Goldman, D.P. and T. Philipson, *Five myths about cancer care in America*. Health Affairs, 2014. 33(10): p. 1801-4.
20. Goldman, D.P., et al., *Substantial health and economic returns from delayed aging may warrant a new focus for medical research*. Health Affairs, 2013. 32(10): p. 1698-705.
21. Dzau, V.J., et al., *Aligning incentives to fulfil the promise of personalised medicine*. Lancet, 2015. 385(9982): p. 2118-9.
22. Kashani, A.H., et al., *A bioengineered retinal pigment epithelial monolayer for advanced, dry age-related macular degeneration*. Science Translational Medicine, 2018. 10(435): p. eaao4097.
23. Regenerative Patch Technologies, LLC. *Study of subretinal implantation of human embryonic stem cell-derived RPE cells in advanced dry AMD*. NLM Identifier: NCT02590692; Available from: <https://clinicaltrials.gov/ct2/show/NCT02590692>.
24. Thiagarajan, M., et al., *Cause-specific visual impairment and mortality: results from a population-based study of older people in the United Kingdom*. Archives of Ophthalmology, 2005. 123(10): p. 1397-403.

25. Age-Related Eye Disease Study Research Group. *A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8*. Archives of Ophthalmology, 2001. 119(10): p. 1417-36.
26. Klein, R., et al., *Ten-year incidence and progression of age-related maculopathy: The Beaver Dam eye study*. Ophthalmology, 2002. 109(10): p. 1767-79.
27. Brown, G.C., et al., *The burden of age-related macular degeneration: a value-based medicine analysis*. Transactions of the American Ophthalmological Society, 2005. 103: p. 173-186.
28. Schmier, J.K., D.W. Covert, and E.C. Lau, *Patterns and costs associated with progression of age-related macular degeneration*. Am J Ophthalmol, 2012. 154(4): p. 675-681.e1.
29. Schmier, J.K., et al., *Impact of visual impairment on service and device use by individuals with age-related macular degeneration (AMD)*. Disability and Rehabilitation, 2006. 28(21): p. 1331-7.
30. Centers for Disease Control and Prevention. *National health interview survey*. 2013-2017.
31. Rainville, C., L. Skufca, and L. Mehegan, *Family caregiving and out-of-pocket costs: 2016 report*. AARP Research, 2016 November; Available from: <https://www.aarp.org/research/topics/care/info-2016/family-caregivers-cost-survey.html>.
32. Schmier, J.K., et al., *Impact of visual impairment on use of caregiving by individuals with age-related macular degeneration*. Retina, 2006. 26(9): p. 1056-62.
33. Evans, J.R., L. Smeeth, and A.E. Fletcher, *Risk of admission to a nursing home among older people with visual impairment in Great Britain*. Archives of Ophthalmology, 2008. 126(10): p. 1428-1433.
34. U.S. Department of Health and Human Services. *Long term costs of care*. 2017; Available from: <https://longtermcare.acl.gov/costs-how-to-pay/costs-of-care.html>.

The mission of the Leonard D. Schaeffer Center for Health Policy & Economics is to measurably improve value in health through evidence-based policy solutions, research and educational excellence, and private and public sector engagement. A unique collaboration between the Sol Price School of Public Policy at the University of Southern California (USC) and the USC School of Pharmacy, the Center brings together health policy experts, pharmacoeconomics researchers and affiliated scholars from across USC and other institutions. The Center's work aims to improve the performance of health care markets, increase value in health care delivery, improve health and reduce disparities, and foster better pharmaceutical policy and regulation.

USC Schaeffer

Leonard D. Schaeffer Center
for Health Policy & Economics

Kukla Vera

Director of External Affairs
Schaeffer Center for Health Policy & Economics
University of Southern California
kuklaver@usc.edu
213.821.7978