POTENTIAL ECONOMIC IMPACT OF NOVEL STEM CELL TREATMENT IN THE STATE OF CALIFORNIA

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EXECUTIVE SUMMARY

Analysis Group, Inc. has been retained to examine the potential economic benefit to the state of California of emerging stem cell treatments, in terms of direct health care costs as well as quality of life gains. The development of these novel treatments has been funded by grants from the California Institute for Regenerative Medicine (CIRM).

Our report examines the potential cost savings to the state of California through the modeling the effects of emerging stem cell therapies in eight disease areas: type 1 diabetes, diffuse large B-cell lymphoma, spinal cord injury, acute myeloid leukemia, chronic lymphocytic leukemia, myelodysplastic syndrome, sickle cell disease, and amyotrophic lateral sclerosis. These disease areas were selected as case studies illustrating diseases with high prevalence, high financial burden, or high levels of morbidity or mortality, for which there are promising stem cell treatments in development. They are illustrative of the substantial benefits associated with stem cell treatments, though do not purport to capture the total impact of stem cell therapies across other therapeutic areas and additional economic dimensions.

Model inputs were derived from published literature and informed by in-depth interviews with leading clinical expert. The cost savings resulting from the introduction of novel treatments were modeled for each of the disease areas separately, to account for the specific characteristics of each disease and treatment. The economic model tracked cost savings compared to the current standard of care for patients in California from 2020-2050. We incorporate assumptions regarding likelihood and timing of FDA approval, as well as expansion of indications and broader adoption over time. To account for the uncertainty involved with modeling emerging therapies, scenario analyses were used to project cost savings under base case, conservative, and optimistic assumptions.

Under the base case scenario, our model projected $47 billion in total direct healthcare cost savings during the 30-year time horizon across the eight disease areas, with about half of these cost saving ($23 billion) accruing to the state of California and its residents. The conservative and optimistic scenarios estimated $17 billion and $107 billion in total direct healthcare cost savings, respectively. When incorporating the value gained from improved quality of life and extended survival, base case cost savings increase to $95 billion. This analysis suggests that emerging CIRM-funded stem cell initiatives are expected to generate substantial economic benefits to the state of California.

INTRODUCTION

The passing of Proposition 71 in 2004 established the California Institute for Regenerative Medicine (CIRM) with the mandate to fund stem cell research in the state of California. Since 2004, the institute has funded over 60 clinical trials of stem cell-based treatments in close to 40 disease areas.[1] Over the last 15 years, CIRM funding has provided critical support for developing stem cell therapies by funding clinical trials, improving manufacturing processes, conducting research in new disease areas, and facilitating synergies across the stem cell research community. As a result, multiple stem cell treatment programs have reached advanced stages of testing and demonstrated efficacy in treating conditions with high unmet needs. In some cases, such as the recent acquisition of Forty Seven Inc. by Gilead, partnerships have been initiated with established pharmaceutical manufacturers to advance clinical development programs.[2]

As new stem cell therapies become available to improve patient treatment, lifetime benefits from reduced burden of illness and healthcare costs are expected to accrue over time. To help policymakers assess the potential impact of advancements in the stem cell treatment landscape, we developed an economic model to estimate the potential for direct healthcare cost savings to the state of California from novel stem cell treatments across eight selected disease areas. We also examined the value of potential gains in life years and improved quality of life due to novel treatment.

METHODS

Economic model

The economic model was developed to estimate the potential health economic value from stem cell therapy to the state of California across eight therapeutic areas. The model focused on a 30-year time horizon (2020 to 2050) and estimated total direct healthcare costs for California patients with select conditions. The model compared total direct healthcare costs in each therapeutic area across two separate perspectives:

- *Perspective 1* modeled under the assumption that only current standard of care (SOC) therapy is available
- *Perspective 2* modeled under the assumption that stem cell therapy becomes available to treat patients

The model also evaluated the potential for stem cell therapy to improve quality of life and extend survival for patients in each disease area.

For each perspective and disease area, the model incorporated disease prevalence, expected clinical benefits, likelihood of FDA approval, expected market entry year, total healthcare cost implications, and proportion of patients receiving treatment. Inputs for the economic model were derived from targeted literature review (including public information and press releases) and informed by in-depth discussions with leading clinical experts.

Other indirect costs, such as effects on work-loss, productivity, human capital accumulation and caregiver burden were not included in the model. Due to uncertainty as to commercial conditions at launch, potential treatment costs for stem cell therapies were not included in the model.

To mitigate uncertainty in modeling assumptions, scenario analyses and one-way sensitivities were conducted to provide a range of estimated cost-savings given more conservative or optimistic assumptions. Additional details on model structure, inputs, and sensitivity analyses are included in the report's *Technical Appendix*.

Disease areas included in economic model

Based on review of the clinical, epidemiological, and economic literature, and informed by discussions with clinical experts, eight disease areas were selected as central case studies for estimating the economic impact of stem cell therapy. The eight disease areas included: type 1 diabetes (T1D), diffuse large B-cell lymphoma (DLBCL), spinal cord injury (SCI), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), myelodysplastic syndrome (MDS), sickle cell disease (SCD), and amyotrophic lateral sclerosis (ALS).

These disease areas reflected some combination of high prevalence, substantial cost of care, or high levels of morbidity or mortality with significant unmet need. They also reflect important heterogeneity in patient populations (***Table 1***). All have promising stem cell treatments in development.

Table 1: Summary of CA prevalence, burden, and unmet needs for selected disease areas

Disease	Approximate prevalence in California (2020)	Estimated annual economic burden in California (2020)	Current unmet need
T1D	450,000	$9.4B	o Lifelong insulin therapy o Continuous monitoring of glucose levels o Potential for serious micro- and macro-vascular complications
DLBCL	26,000	$4.1B	o Inpatient and ER visits common after diagnosis o One-third of patients are relapsed/refractory to SOC and have few alternative treatment options
SCI	36,000	$3.4B	o Extensive rehabilitation o Physical immobility requiring attendant care and equipment o Respiratory and circulatory complications
AML	8,000	$2.4B	o Frequent transfusions and prolonged hospitalizations o Rapid progression and low survival rates o Limited options for elderly patients not eligible for intensive treatments
CLL	22,000	$2.3B	o Intensive, recurring treatments o Complications such as weakened immune system and infections o Increased risk of other cancers and shortened life expectancy
MDS	14,500	$1.5B	o Anemia, increased risk of infection, extended fatigue o Treatment failure with standard chemotherapy is common o One-third of patients progress to AML
SCD	12,000	$0.5B	o Frequent inpatient stays and reduced quality of life due to pain crises o Complications such as organ damage and hypertension o Costly medications
ALS	2,000	$0.1B	o Loss of muscle control requires supportive care o Difficulty with day-to-day tasks such as eating and dressing o Rapidly progressive disease with high mortality burden

Disease areas are ordered by annual economic burden in California (2020).

ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

RESULTS

For each disease area, expected clinical impact and implications for modeling economic impacts were determined using in-depth interviews with clinical experts and targeted literature review. ***Table 2*** presents a summary, and additional details can be found in the *Technical Appendix*.

Table 2: Expected clinical impact of stem cell treatment in select disease areas

Disease	Expected clinical impact of treatment	Modeled effect	Initial population eligible for treatment
T1D	○ Implanted stem cells capable of producing insulin ○ Eliminates need for daily doses of insulin and continuous glucose monitoring ○ Lower risk of complications and hypoglycemic events	Curative	Highest-risk patients with immunosuppression
DLBCL	○ Stem-cell directed treatment enables macrophages to identify and destroy cancer cells more easily ○ Eliminates cancer in B-cells, resulting in greater ability to fight infections and the formation of enlarged masses	Disease-modifying	Relapsed/refractory patients
SCI	○ Engraftment of stem cells supports generation and growth of neurons along with formulation of new blood cells ○ Increases limb function and mobility	Disease-modifying	Patients with tetraplegia
AML	○ Stem-cell directed treatment enables macrophages to identify and destroy cancer cells more easily ○ Disrupts and eliminates immature white blood cell buildup	Disease-modifying	Patients not eligible for high dose chemotherapy or allogeneic hematopoietic cell transplantation
CLL	○ Implanted antibody/protein blocks the formation and proliferation of white blood cells	Disease-modifying	Patients with relapsed or refractory disease
MDS	○ Stem-cell directed treatment enables macrophages to identify and destroy cancer cells more easily ○ Can halt disease progression to AML ○ Reduces risk of anemia and additional infections	Disease-modifying	Highest risk patients
SCD	○ Stem cell transplant and gene therapy introduces healthy blood cells and eliminates sickling ○ Eliminates pain episodes which may lead to hospitalization	Curative	Patients eligible for stem cell transplant
ALS	○ Growth factor injection into the spinal cord prevents motor neurons from dying ○ Potential for mobility and survival improvement	Disease-modifying	Patients with early-stage ALS

ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

Cost impact per-patient from stem cell treatment

For each of the eight disease areas, average total annual direct healthcare costs per patient were estimated for *Perspective 1* (only SOC treatment available between 2020 and 2050) and for *Perspective 2* (stem cell treatment becomes available). Healthcare cost reductions from stem cell treatment were estimated based on the expected impact of clinical improvements on healthcare resource use and treatment reductions. For conditions where stem cell treatment was modeled as having a curative effect (i.e., T1D, SCD), cost reductions were derived from available literature estimates for disease-specific healthcare costs. For the remaining conditions where stem cell treatment was modeled as having a disease-modifying effect, cost reductions were derived from available literature estimates comparing patients with different levels of disease severity, disease control, and disease stage (see *Technical Appendix* for additional details). Average estimated reductions in total healthcare costs for stem cell-treated patients ranged from $7K per year in T1D to $90K per year in AML (see ***Figure 1***).

Population-level impact from stem cell treatment

Population-level assumptions were incorporated in the economic model to account for market factors such as estimated launch year and market size. Applying these population-level assumptions, availability of stem cell treatment was estimated to reduce total direct healthcare costs in the state of California by 4% (~$47B) across the eight selected disease areas from 2020 through 2050 (see ***Table 3***). Total stem-cell related healthcare cost savings were estimated to increase over time as a higher proportion of patients become eligible for treatment, with an annual direct cost savings of ~$3.3B per year estimated by 2050 (see ***Figure 2***).

Scenario analyses were also conducted to estimate population-level cost savings for the eight disease areas across base-case, conservative, and optimistic scenarios (***Figure 3***). Scenario analyses varied key parameters from the base-case, including estimated cost savings from stem cell therapy, likelihood of FDA approval, anticipated launch year, and estimated size of the eligible patient population throughout the modeling timeframe. Relative to the base-case cost reduction estimate of $47B (4%) from 2020 through 2050, cost reduction from stem cell treatment ranged from $17B (1%) to $107B (9%) across the eight disease areas using more conservative and optimistic assumptions. One-way sensitivities were also conducted to evaluate the impact of individual assumptions on annual cost reduction (see *Technical Appendix*).

Figure 1. Annual healthcare cost reductions for patients receiving stem cell treatment

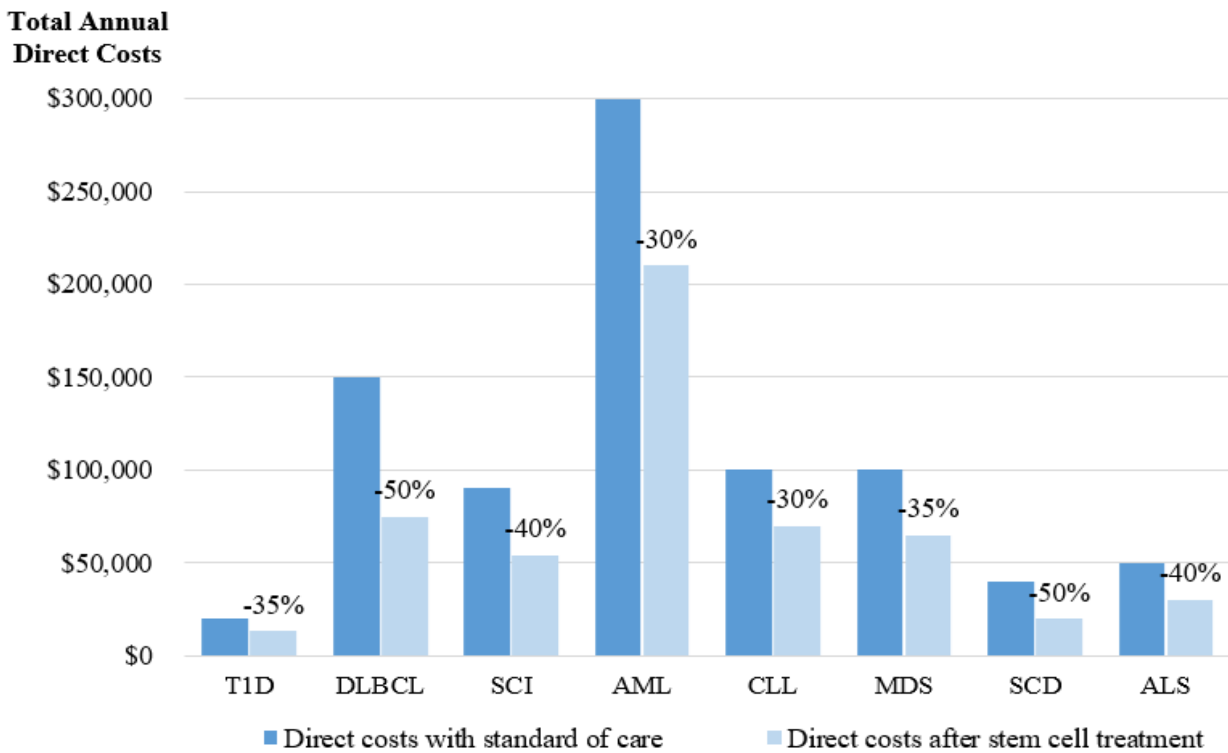


Table 3. Total direct healthcare cost savings for California patients across the eight selected disease areas, 2020-2050

Disease Area	Annual Direct Cost Savings per Patient	Estimated Number of California Patients Receiving Stem Cell Treatment		Estimated Total Direct Cost Savings for California (2020 - 2050)
		2030	2050	
T1D	$7,000	61,000	142,000	$16.8B
DLBCL	$75,000	1,000	3,000	$6.2B
SCI	$36,000	< 1,000	10,000	$5.7B
AML	$90,000	1,000	2,000	$5.9B
CLL	$30,000	4,000	7,000	$4.9B
MDS	$35,000	2,000	4,000	$4.3B
SCD	$20,000	4,000	9,000	$2.9B
ALS	$20,000	< 1,000	< 1,000	$0.4B
Total	**--**	**74,000**	**178,000**	**$47.1B**

ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

Figure 2. Total direct healthcare cost savings for California patients (across the eight selected disease areas), 2020-2050 (billions)

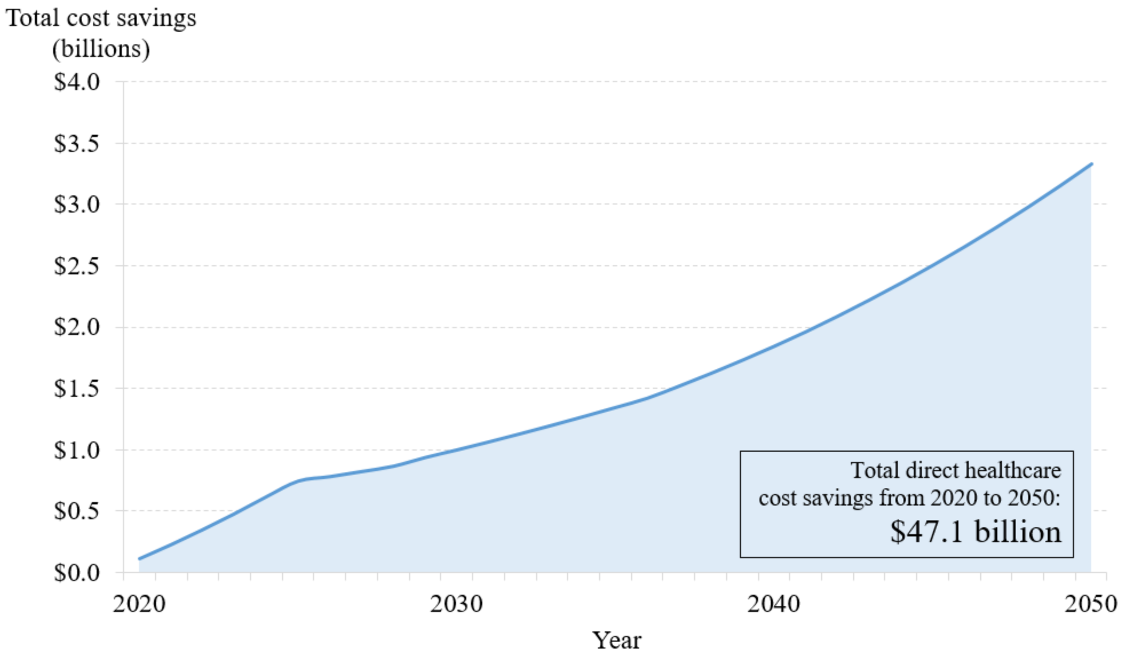
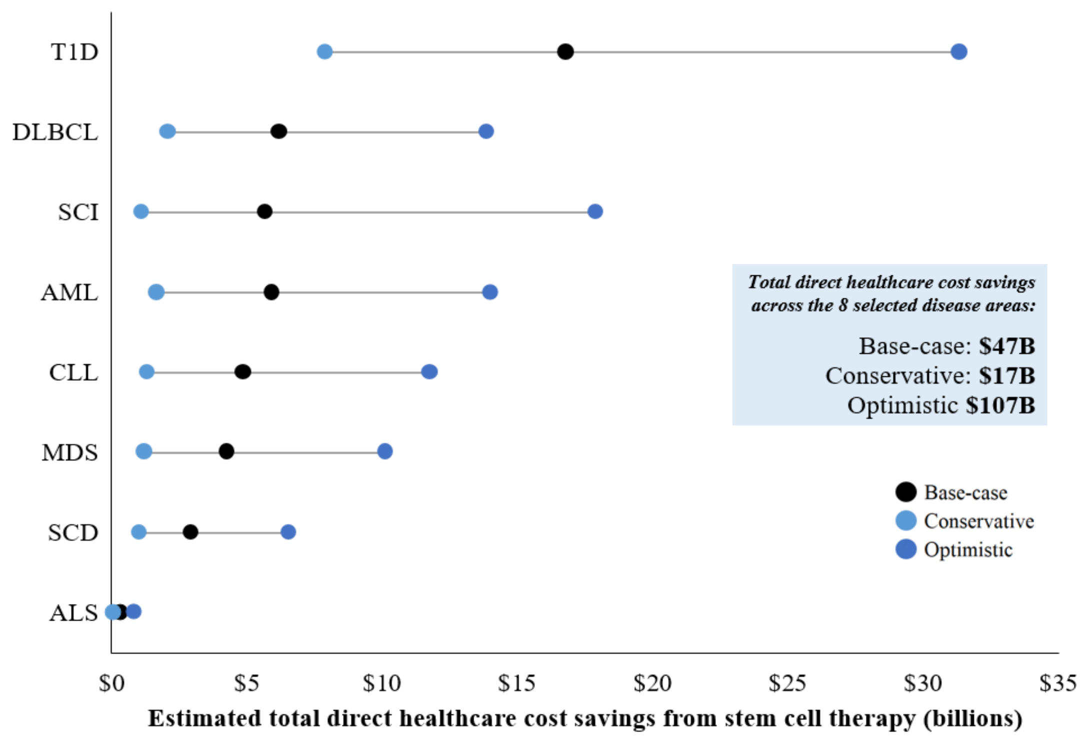


Figure 3. Scenario analyses of direct healthcare cost savings, 2020-2050 (billions)



ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

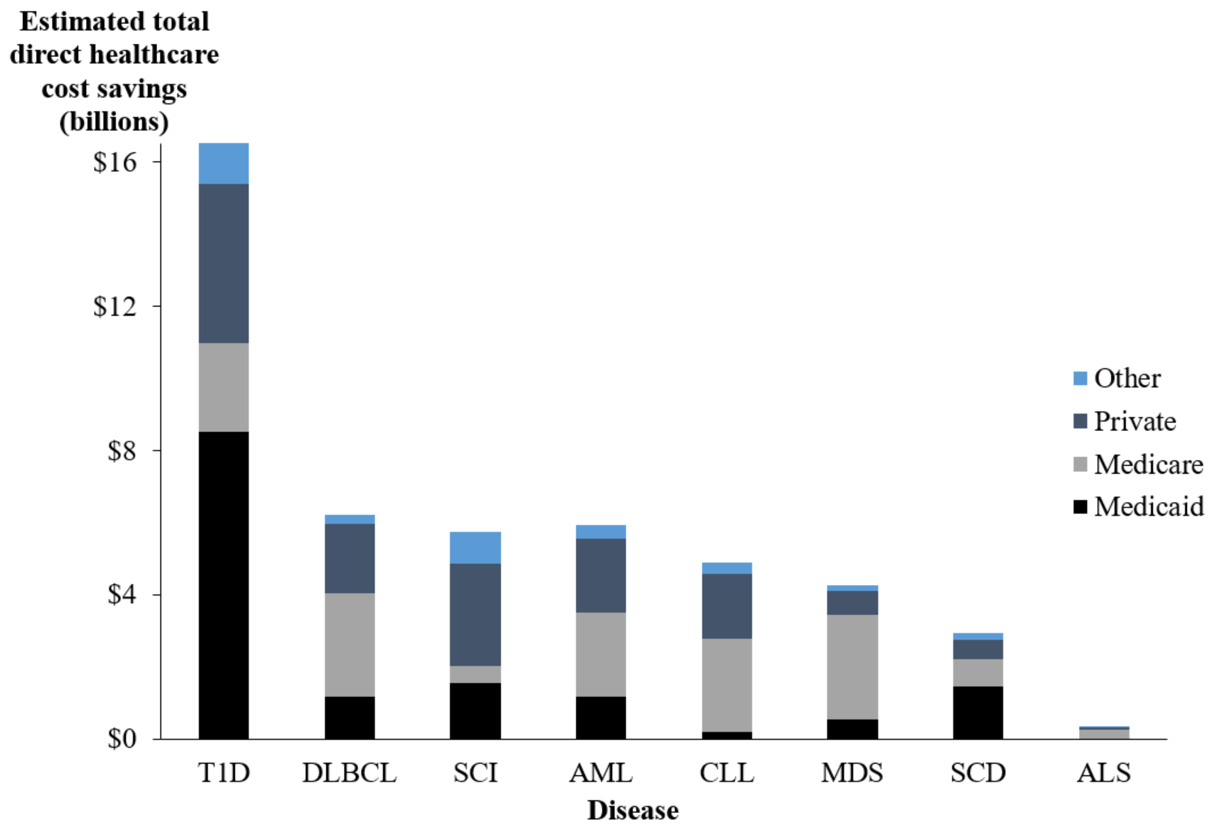
Estimated breakdown of the cost savings from stem cell treatment by payer

In the state of California, several entities are expected to capture direct healthcare cost savings from stem cell treatment, including the California Medicaid program (Medi-Cal), private insurance companies, and uninsured patients. ***Figure 4*** shows the proportion of anticipated cost savings in each disease area projected to be accrued by all major payer types, including Medicare, Medicaid, and private insurers. Medi-Cal currently incurs a large proportion of direct healthcare costs related to the eight selected disease areas, and is expected to save as much as $14.5B from 2020 through 2050 due to stem cell treatment (of which the state-sponsored share is $5.6 billion). Of the total amount of cost savings, 49% ($23.1 billion) will directly benefit taxpayers in California (see ***Table 4***). Californian public sector employees (and their dependents) are estimated to save $3.3 billion, with close to $1.7 billion in savings attributed to California public education employees (i.e., 'Elementary and Secondary', 'Higher Education', 'Other') based on full-time employment data from the 2019 Annual Survey of Public Employment & Payroll from the U.S. Census Bureau.[3]

Total estimated value inclusive of quality of life and survival benefits

The economic model also estimated value gained from improved quality of life and extended survival across the eight selected disease areas (see ***Table 5***). Accounting for the additional health economic impacts from improved quality of life and extended patient survival yields an estimated value of $95B from 2020 through 2050 for stem cell treatment across the eight selected disease areas.

Figure 4. Total direct healthcare cost savings by payer type, 2020-2050 (billions)



ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

Notes:

[1] "Other" category includes Military/VA insurance, unreported/no insurance, worker's compensation, or no pay.

[2] Payer composition information was obtained from HCUPnet[4] (inpatient stays; T1D, DLBCL, AML, and MDS), the 2018 National Spinal Cord Injury Statistical Center Annual Report[5] (SCI), Mato et al. 2018[6] (CLL), Fingar et al. 2019[7] (SCD), and Lewin Group, Inc.[8] (ALS).

Table 4. Federal and State shares of total direct healthcare cost savings for California patients across the eight selected disease areas, 2020-2050 (billions)

Disease	**Federal Cost Savings (Medicare, Medicaid, Military/VA)**	**California Cost Savings**		
		Medicaid	**Public Employee Plans**	**Private Insurance/Other**
T1D	$7.9B	$3.3B	$1.1B	$4.6B
DLBCL	$3.6B	$0.5B	$0.4B	$1.7B
SCI	$1.5B	$0.6B	$0.7B	$3.0B
AML	$3.1B	$0.4B	$0.5B	$1.9B
CLL	$2.7B	$0.1B	$0.4B	$1.7B
MDS	$3.2B	$0.2B	$0.2B	$0.7B
SCD	$1.7B	$0.6B	$0.1B	$0.6B
ALS	$0.2B	$0.0B	$0.0B	$0.1B
Total (% total savings)	**$24.0B (50.9%)**	**$5.6B (11.9%)**	**$3.3B (7.1%)**	**$14.2B (30.1%)**

ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

Notes:

[1] "Other" category includes unreported/no insurance, worker's compensation, or no pay.

[2] Medicaid estimates apportioned according to the Federal and State Share of Medicaid Spending for CA.[9]

Table 5. Value of quality adjusted life year gains from stem cell treatment for California patients across the eight selected disease areas, 2020-2050 (billions)

Disease	Value of Healthcare Cost Reductions	Value of Quality of Life / Survival Gains	Cost Difference Plus Quality of Life / Survival Gains
T1D	$16.8B	$39.9B	$56.7B
DLBCL	$6.2B	$0.5B	$6.7B
SCI	$5.7B	$1.1B	$6.8B
AML	$5.9B	$0.2B	$6.1B
CLL	$4.9B	$1.9B	$6.7B
MDS	$4.3B	$0.7B	$5.0B
SCD	$2.9B	$3.5B	$6.4B
ALS	$0.4B	$0.1B	$0.5B
Total	**$47.1B**	**$47.8B**	**$94.9B**

ALS: amyotrophic lateral sclerosis; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; MDS: myelodysplastic syndrome; SCD: sickle cell disease; SCI: spinal cord injury; T1D: type I diabetes

***Note**: Value of quality of life and survival gains estimated at $150,000 per additional quality-adjusted life year (QALY) gained*

DISCUSSION

This study modeled the potential economic impact to the state of California for novel stem cell treatments currently being investigated in clinical trials across eight disease areas, and provides an update to analyses conducted in 2004 prior to the approval of California Proposition 71.[10] The present analysis provides a significant update to the 2004 model due to advancements in stem cell treatments and expanded availability of health economic literature across selected disease areas. Interviews with clinical experts suggest that novel stem cell treatments have the potential to provide substantial patient benefits by improving clinical outcomes, reducing healthcare resource utilization and costs, and increasing quality of life and survival.

This economic model incorporated inputs from clinical expert interviews and review of the available literature to calculate the potential for $47B in direct healthcare cost savings for residents of the state of California over a 30-year time horizon across the eight disease areas. Accounting for additional quality of life and survival benefits, these novel stem cell therapies are expected to provide a higher economic value of $95B from 2020 through 2050. Findings from the current model also highlight key sources of value likely to be derived from stem cell treatment. While per-patient healthcare cost savings from stem cell treatment are expected to be high for diseases with low prevalence but high unmet need (e.g., DLBCL, SCI, AML, MDS), other diseases may see more modest cost reductions across a broader patient population (e.g., T1D). Findings are also in-line with previously-conducted economic analyses assessing the potential impact of novel stem cell treatments for different disease areas. Similarly, the current economic analysis estimated substantial treatment cost reductions, improved quality of life, and extended survival for patients from stem cell therapies.[10,11]

Results from this study underscore the high potential for stem cell treatments to radically change the treatment landscape and potentially provide disease-modifying or curative therapies for patients with currently limited treatment alternatives. Across these eight case studies alone, the direct healthcare cost savings are several times greater than the Proposition 71 investment of $3B in stem cell research. These results can be used to inform long-term planning decisions related to budgeting of healthcare spending and further investment in stem cell research in the state of California.

Limitations

The present economic analysis is subject to several limitations, including inherent uncertainty in estimating benefits from therapies which have not yet reached the market. To mitigate the risk of modeling uncertainty over a long time horizon, scenario analyses and one-way sensitivities were generated to evaluate the impact of key parameters in the model. While the current economic model evaluated health economic impacts from stem cell treatment across eight disease areas, CIRM has funded over 60 clinical trials for stem cell treatments across several additional disease areas[1] (e.g., kidney disease, solid tumors, HIV/AIDS, COVID-19, heart disease). Given the targeted scope of the current analysis, results certainly under-represent the full potential impact of stem cell treatment across all relevant disease areas.

In addition, several important sources of value were not considered in the model. For example, indirect savings related to work-loss and work productivity were not included in the current analysis and may represent a substantial source of value generated from stem cell treatment. Future research is warranted to evaluate indirect cost savings and other sources of potential value from stem cell therapy across these disease areas.

Importantly, the economic analysis modeled cost savings relative to current standard of care treatment options, and did not attempt to predict other clinical and therapeutic developments. Finally, the model did not attempt to estimate future prices of emerging stem cell therapies, which could be substantial. Given the nature of the economic analyses conducted, the findings can be interpreted as a lower-bound estimate of California residents' willingness to pay for the emerging treatments.

CONCLUSIONS

Recent advances in stem cell research have demonstrated the potential to radically change the treatment paradigm for multiple high-burden diseases with limited treatment options. The current economic analysis estimated that improved disease control from stem cell treatment will have a substantial health economic impact for California residents through lower healthcare resource use, improved quality of life, and extended survival across eight selected disease areas.

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