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Leonard D. Schaeffer Center
for Health Policy & Economics

The Value of Research and Development Targeting Disorders of the Central Nervous System

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Research disclosures

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Overview

- About the Schaeffer Center
- Understanding barriers to private R&D funding targeting disorders of the central nervous system
- A framework for valuing R&D spending
  - Map clinical endpoints to non-clinical outcomes
  - Evaluate lifetime impacts
- Implications

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Who we are

- **Researchers at the University of Southern California (n>40)**
  - **Faculty from various schools, including: policy, pharmacy, medicine, engineering, gerontology, economics**

- **External collaborators**
  - **International: OECD, University of Tokyo, University of Rome, National University of Singapore, University of Quebec in Montreal, University of Colima, Korea Institute for Health and Social Affairs, Trinity College Dublin, University of Leeds**
  - **United States: Harvard University, University of Chicago, Stanford University, University of Pittsburgh, University of Texas, University of South Carolina, RAND**
  - **California: Los Angeles County Department of Public Health, Steinberg Institute, California Institute for Regenerative Medicine**

What we do

The **Schaeffer Center** measurably **improves value in health** through **evidence-based** policy solutions, **research** excellence, and private and public sector **engagement**.

We seek to improve value in health care delivery:

Health costs should be seen as **investments** instead of expenses, with value judged by relating the dollars involved to **improved outcomes.**

USC Schaeffer Center researchers are finding **cost-effective solutions** to reach as many people as possible with the finest medical care available — for **healthier communities and happier lives.**

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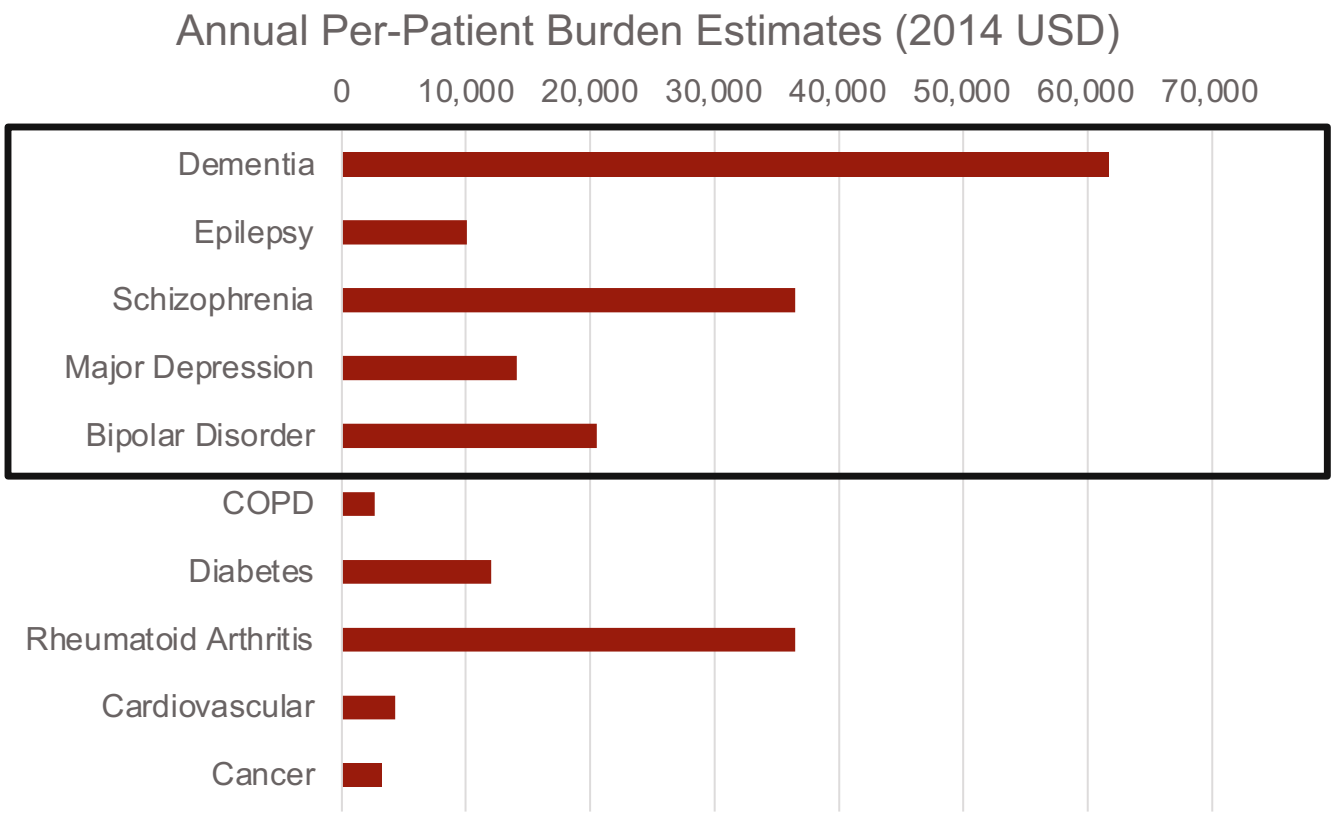
Neurological and psychiatric disorders generate significant societal burden



Source: MacEwan JP, Seabury SA, Aigbogun MS, Kamat S, van Eijndhoven E, Francois C, Henderson C, Citrome L. "Pharmaceutical Innovation in the Treatment of Schizophrenia and Mental Disorders Compared with Other Diseases." *Innovations in Clinical Neuroscience*. 13(7-8): 17-25. 2016.

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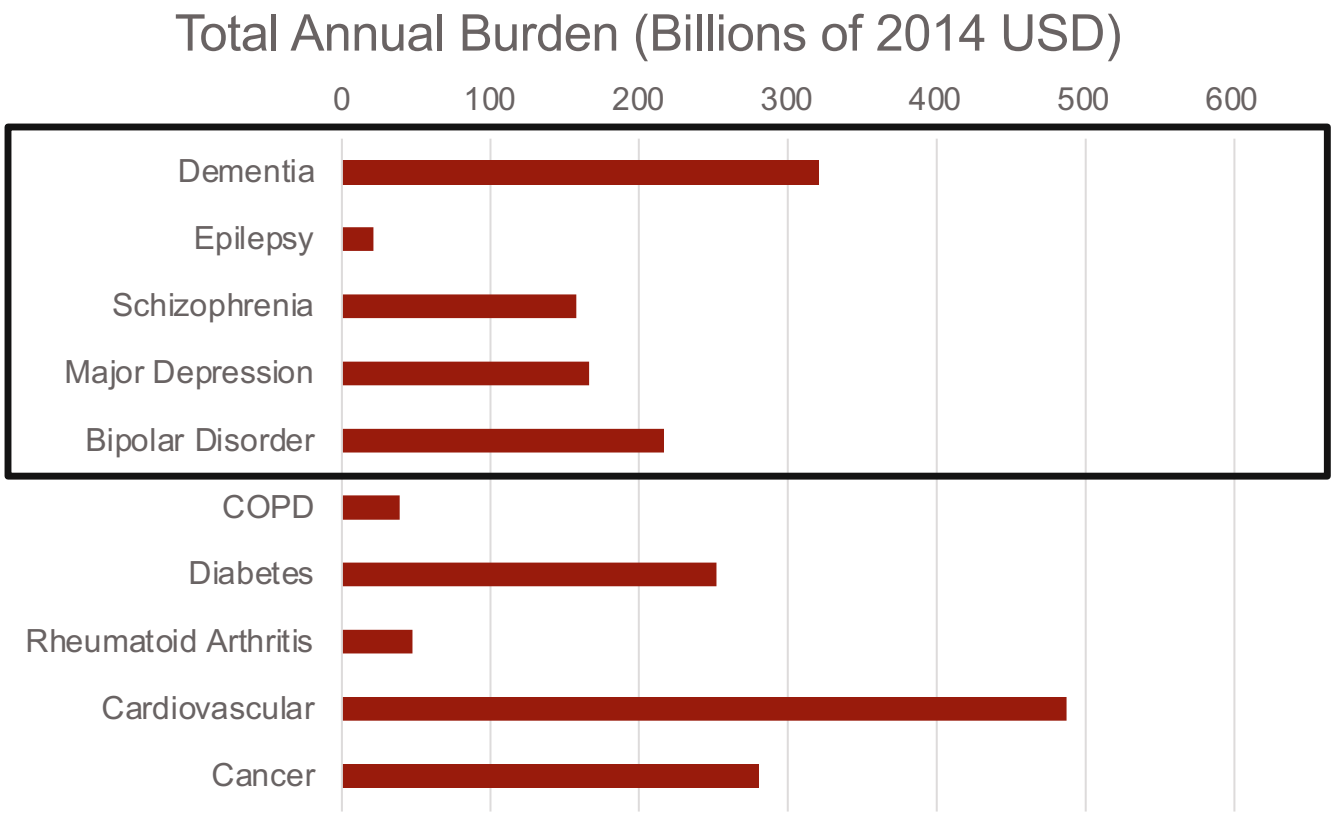

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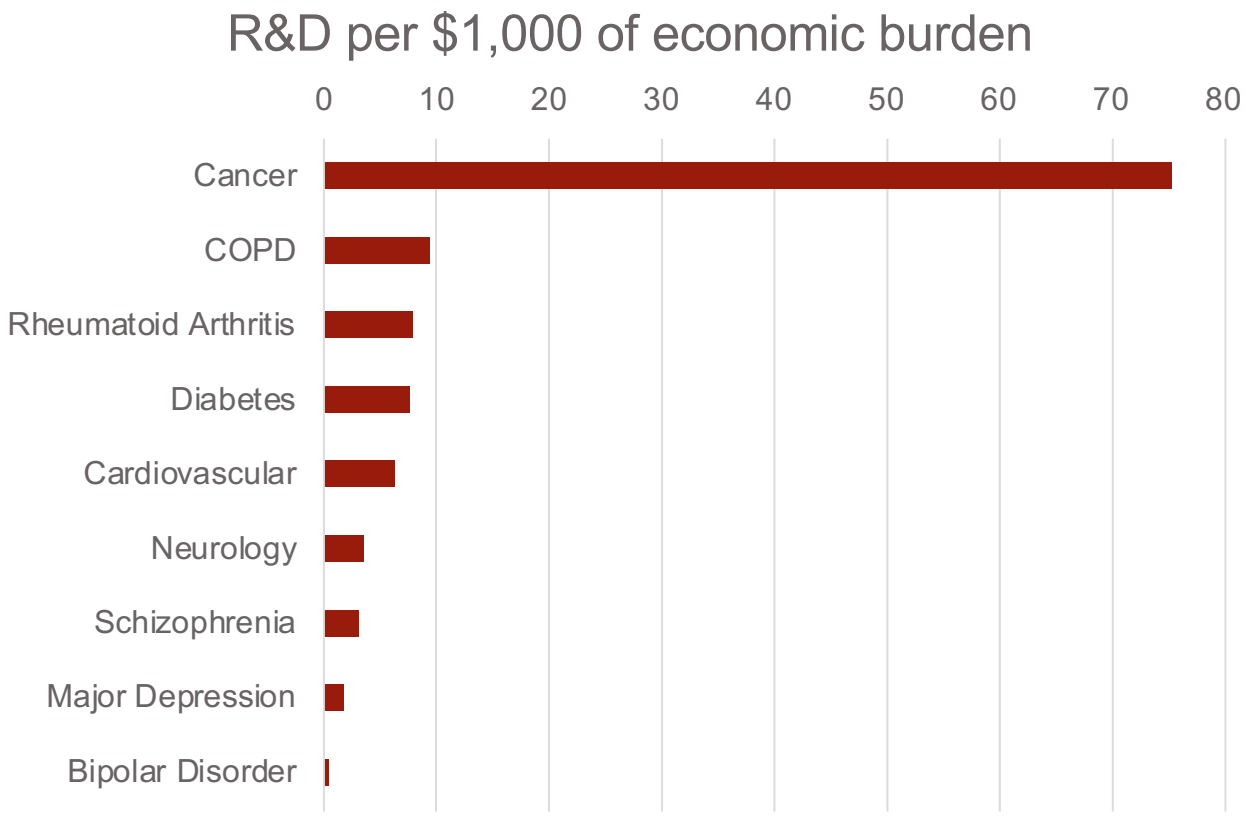
Private R&D expenditures for neurological conditions are low relative to disease burden



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Challenges to private R&D funding for disorders of the central nervous system

- **Scientific uncertainty**
  - **Market approval rate of drugs entering clinical trials treating central nervous system (CNS) disorders is 6.2%**
    - **Compared to 13.2% for non-CNS drugs***
- **Market challenges**
  - **Patients with psychiatric disorders are disproportionately more likely to be uninsured or covered by Medicaid**
    - **Less profitable**
  - **Some conditions are rare diseases with uncertain markets**

* DiMasi J. CNS drugs take longer to develop, have lower success rates, than other drugs. Tufts Center for the Study of Drug Development website. http://csdd.tufts.edu/news/complete_story/pr_ir_nov_dec_ir. November 4, 2014. Accessed June 5, 2015.

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Understanding the value of R&D as an investment

- The potential benefits of improving outcomes for individuals with neurological and psychological disorders are large
  - Could alleviate tens or hundreds of billions in economic burden
- But the benefits are diffuse
  - Spread across different healthcare payers
  - Indirect benefits accrue outside the healthcare system
  - Recognized over long time horizon

- Individual agents (or agencies) may fail to recognize the benefits of treatment innovations
  - Focus on costs

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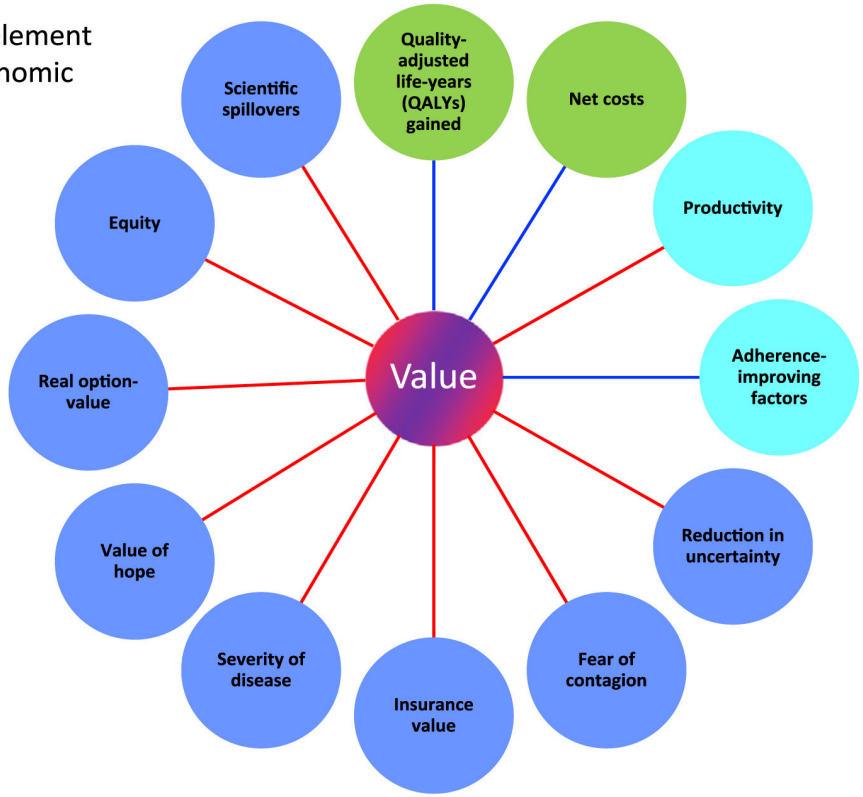
There are many dimensions to the value of innovation

Elements of Value

Challenge: Map each element into an underlying economic framework for value assessment.



Source: Lakdawalla, Darius N., Jalpa A. Doshi, Louis P. Garrison Jr, Charles E. Phelps, Anirban Basu, and Patricia M. Danzon. "Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3]." *Value in Health* 21, no. 2 (2018): 131-139.

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Microsimulation is useful to study the lifetime returns to health and social investment

Since 2004, we have answered **salient policy questions** about social investments using two microsimulations:

- **Future Elderly Model** (FEM)
- **Future Adult Model** (FAM)

Supported by the National Institute on Aging, our research studies the determinants of health and health spending and translates these findings for policymakers. These models have been used to study:

- Aging
- Early childhood education
- Adverse childhood events
- Serious mental illness
- Obesity
- Tobacco
- Alzheimer's disease
- Medical innovation
- Cardiovascular risk factors
- Pharmaceutical price controls
- Medicare reform
- Progressivity of government programs

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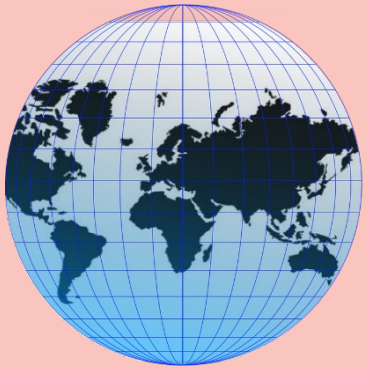
Forecasts long-term population health in:

- Los Angeles County
- California
- United States
- 19 other countries



Contributions featured by:

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World Economic Forum
Economic Report of the President
LA County Department of Public Health
California Institute for Regenerative Medicine

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Why use microsimulation?

- The US faces important questions regarding the future of health
  - Disease burden
  - Disparities
  - Health care costs
  - Implications for government programs
- Answers are difficult due to the complexity of health processes and powerful trends in demography, health behavior, and medical technology
- Our microsimulations, FEM and FAM, enable us to project future risk factors, morbidity, mortality, disability, and economic outcomes using a data-driven approach

What is microsimulation?

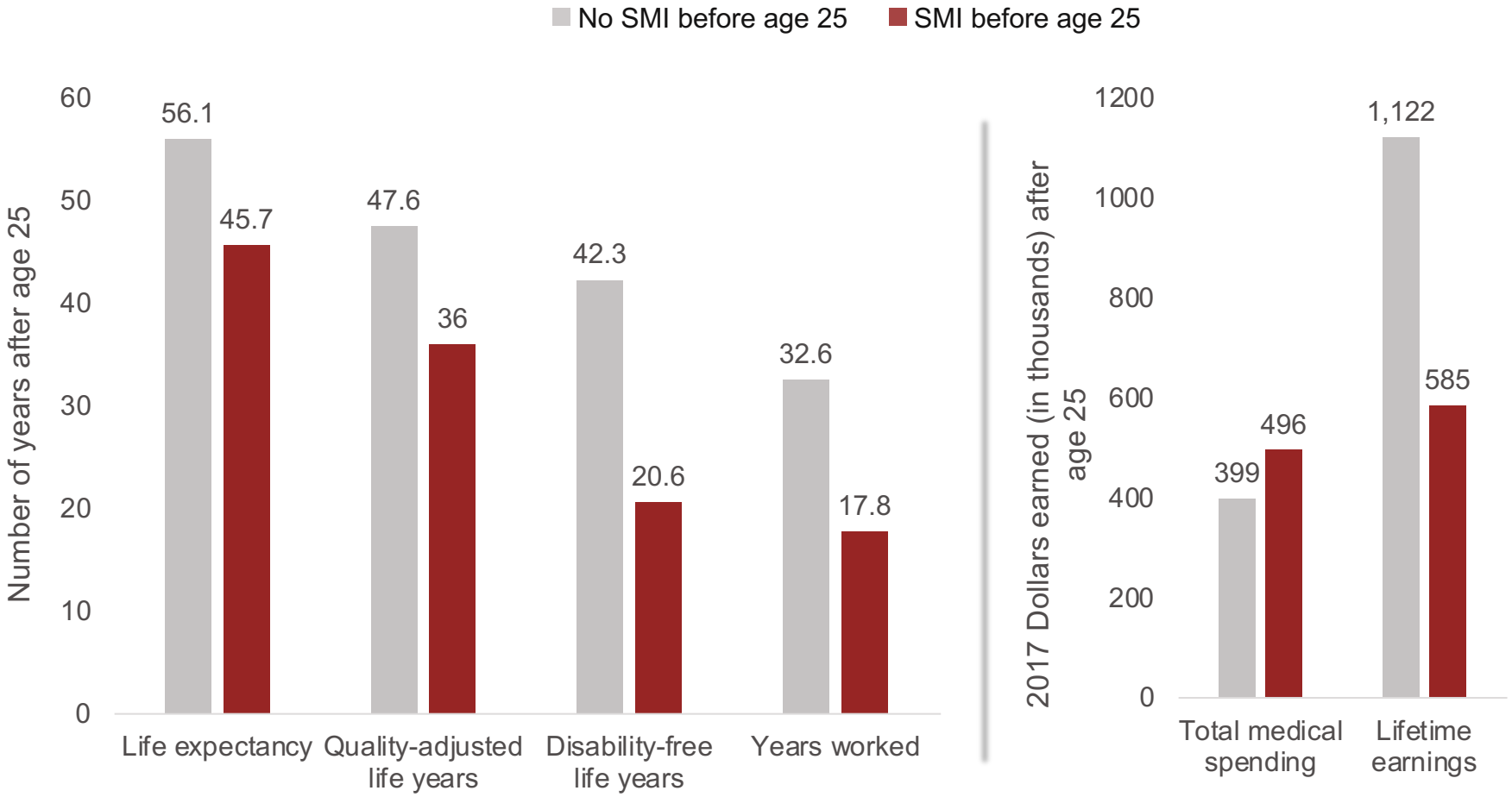
- **Microsimulation: models tha programs and policies to cre demographic, behavioral, an and societal outcomes**

- **Two central microsimulation**
  - **Future Elderly Model (FE**
    - **Ages 51+, centered a**
    - **10+ year model devel**
    - **International, US, Cal**
  - **Future Adult Model (FAM)**
    - **Ages 25+, centered around Panel Study of Income Dynamics**
    - **Extends the FEM to the entire adult population**
    - **US, California, and LA County**

We used the FAM to estimate the lifetime burden of patients reporting being diagnosed with serious mental illness (SMI) by age 25

- **Estimate the life trajectory of health and economic outcomes for a randomly selected 25 year old**
- **Compare to the trajectories of a 25-year old with SMI**
  - **The difference represents the impact of the disease**

Example: Expected lifetime health and economic outcomes for people with and without serious mental illness (SMI)



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Lost years of life make up the biggest component of disease burden

Total Incremental Lifetime Cost of SMI from Age 25, 2017 US Dollars (1,000s)	
Incremental medical spending	96.5
Incremental SSDI costs	38.8
Incremental SSI costs	20.3
Lost Earnings	537.1
Value of Quality-Adjusted Life Years Lost[a]	1,160.0
Total Lifetime Cost	1,852.8

Approximately 63% of the total lifetime patient burden comes from the decline in quality-adjusted life years.

a. Assumes a value of $100,000 per QALY.

Source: Seabury, SA, S Axeen, G Pauley, B Tysinger, D Schlosser, J Hernandez, H Heun-Johnson, H Zhao, DP Goldman. "Measuring the Lifetime Costs Of Serious Mental Illness And The Mitigating Effects Of Educational Attainment." *Health Affairs*. 38(4): 652-659. 2019.

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Types of simulated experiments

- **Alter initial characteristics of population**
  - Decrease risk factors or disease prevalence
- **Simulate change in policy characteristics**
  - Increase Medicare eligibility age, federal benefit levels, or Social Security claiming rules
- **Intervene on the prevalence or severity of diseases**
  - Decrease likelihood of developing a disease, delay onset of a disease
    - ***Each of these provides the opportunity to quantify the potential value of a new health innovation***

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Example: What if everyone with SMI received a supported education program?

- Modeled lifetime benefits based on the program used in the RAISE-ETP clinical trial (NIMH)

Significant lifetime benefits:

- About one year of increased educational attainment
- Reduced the economic burden to individuals with SMI by $73,600 (4%)
- Results in a 2-to-1 return on investment
  - Likely underestimates return because it assumes full program costs and ignores other program benefits, such as from improved medical treatment
  - The key is that we were able to estimate the impact of the program because educational attainment was included in the trial data and in our model

Source: Seabury, SA, S Axeen, G Pauley, B Tysinger, D Schlosser, J Hernandez, H Heun-Johnson, H Zhao, DP Goldman. "Measuring the Lifetime Costs Of Serious Mental Illness And The Mitigating Effects Of Educational Attainment." *Health Affairs*. 38(4): 652-659. 2019.

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Example: What would this mean for California?

16,603

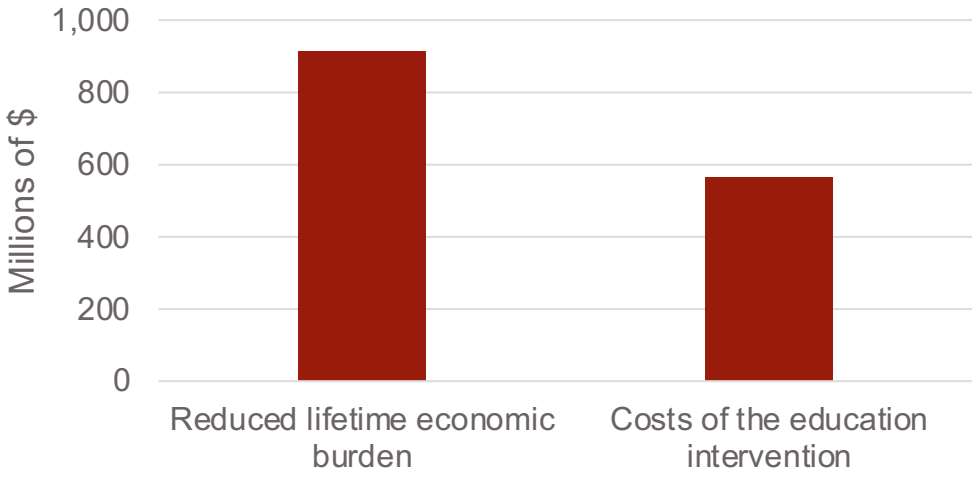
Individuals age 25 with new SMI diagnoses each year

This results in

$30.6 Billion

In economic burden over the course of their lives

Even with a conservative estimate, an education intervention would generate significant benefits:



Value could be improved with greater targeting to at-risk students and measuring full range of benefits

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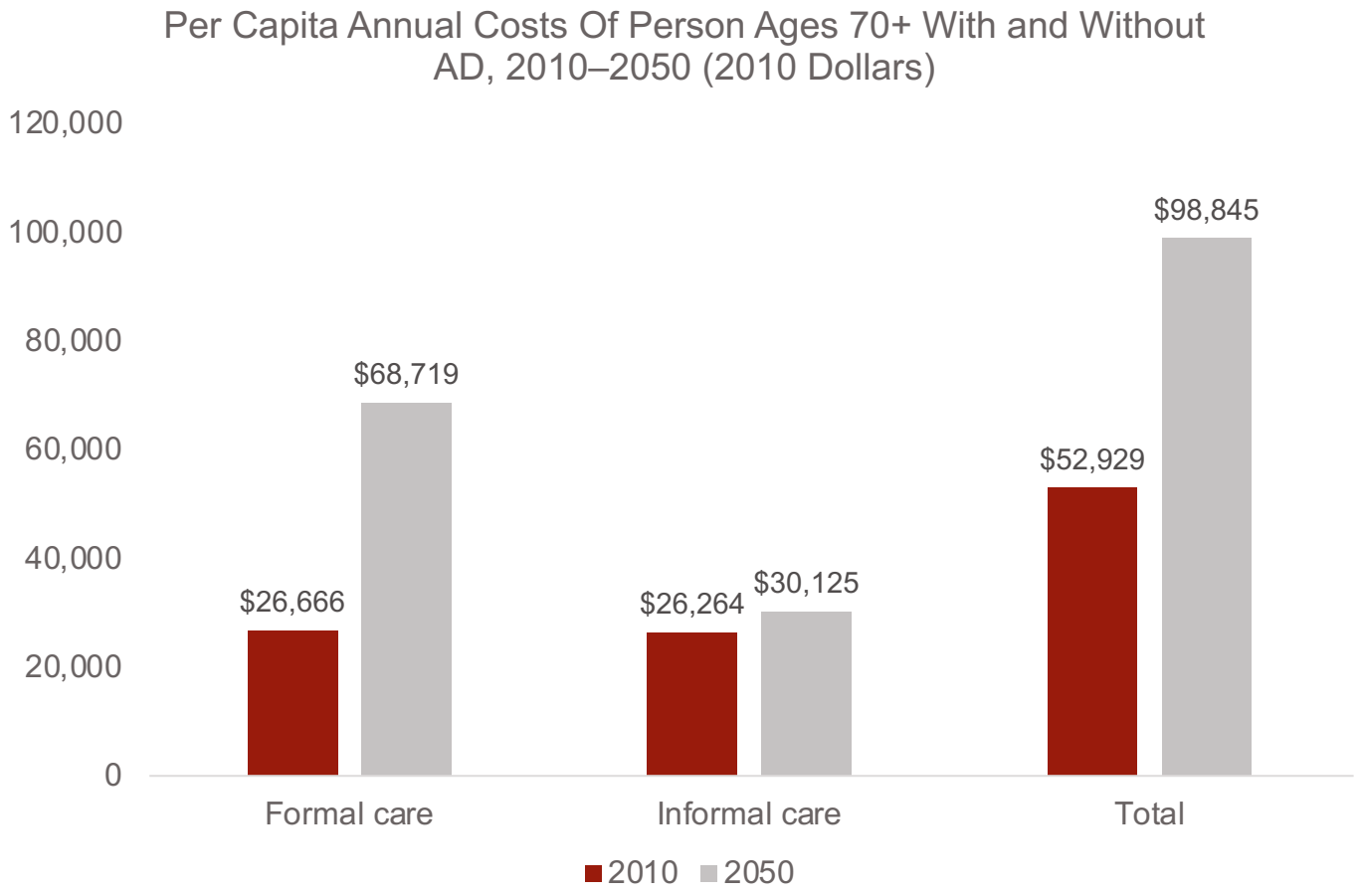
What about neurodegenerative disorders?

- **Select results using the FEM to study Alzheimer's disease (AD)**
  - **FEM estimates of the annual per-patient cost of treatment for patients with AD**
    - **Based on data through 2010 and projected in 2050**
    - **Cost broken down into formal medical spending and the cost of informal care**
  - **Simulated policy experiment:**
    - **Suppose a treatment was developed that delayed onset by 1 or 5 years**

Projected change in the lifetime burden of AD



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Simulated benefits of delayed onset of AD

Per-Capita Health Effects and Treatment Costs Of 70–74 Year Olds			
	At baseline	*Change with delayed onset*	
		1-year delay	5-years delay
Total life years remaining	15.6	+1.0	+2.7
Years without AD	9.8	+1.7	+4.8
Years in a nursing home	1.94	-0.13	-0.35
Treatment cost			
Formal	493,837	6,419	17,721
Informal	218,315	-19,518	-49,580

Source: Zissimopoulos, Julie, Eileen Crimmins, and Patricia St. Clair. "The value of delaying Alzheimer's disease onset." In *Forum for Health Economics and Policy*, vol. 18, no. 1, pp. 25-39. De Gruyter, 2015.

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A comprehensive approach is needed to understand the returns to innovations that improve patient outcomes

- **Need to look beyond line-item accounting of cost savings**
  - Consider *total spending*, including hospitalizations, outpatient services, medication as well as social services, etc.
  - Use *forward-looking measures* that consider the lifetime effects on patients
  - Measure both *direct and indirect effects*
    - Labor market productivity, correctional facility spending, caregiver burden, etc.
- **More research and data are needed to support ROI measurement**
  - Data that spans different systems
  - Research that includes objective measures of outcomes spanning the full range of potential costs and benefits

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Data collection should include more than just clinical endpoints

Data Elements Used in the FEM/FAM		
Health	Chronic conditions	ADRD, cancers, congestive heart failure, diabetes, heart attack, heart disease, hypertension, COPD, stroke, pain
	Functional limitations	Activities of daily living, instrumental activities of daily living
	Mental health	Depressive symptoms
	Mortality	Death
	Risk factors	BMI, exercise, smoking
Life events		Widowhood, nursing home entry
Economic	Employment status	Working for pay
	Health insurance	Health insurance type
	Income and assets	Capital income, earnings, wealth
	Public program participation	OASI, DI, SSI, other transfers

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Data collection should include more than just clinical endpoints

Data Elements Used in the FEM/FAM		
Medical cost and use	Individual	Drug $, out of pocket $
	Medicaid	Eligibility, $
	Medicare	Total $, Part A $, Part B $
	Total expenditures	$
	Utilization	Doctor visits, hospital encounters, hospital nights
	Informal care	Spousal care hours, non-spousal care hours
Taxes paid		Federal $, state $, property
Subjective well-being		Life satisfaction, quality-adjusted life years (EQ5D, HUI3), self-reported health
Government transfers		OASI benefits, SSDI benefits, SSI benefits, others government transfers

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Summary and conclusions

- **Central nervous system disorders impose significant lifetime burden for patients**
  - **But scientific and economic hurdles lead to inadequate private R&D spending**
  - **Investment through CIRM and other public funding sources can provide significant societal value through promoting innovation**

- **Microsimulation and other economic modelling techniques provide a useful framework for helping stakeholders assess the return that this investment provides**
  - **But to do so requires collecting data on patient outcomes that are often not included in clinical trials**
  - **Funders should consider the potential benefits of encouraging investigators to include these types of data in their research protocols**

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