

**The Burden of Neurological Disease in the United States:
A Summary Report and Call to Action**

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Abstract

The United States carries a substantial fiscal burden resulting from the nearly 100 million Americans with neurological disease. The combined annual costs of Alzheimer's and other dementias, low back pain, stroke, traumatic brain injury, migraine, epilepsy, multiple sclerosis, spinal cord injury and Parkinson's disease totals nearly 800 billion dollars and is rapidly rising due to the aging of the U.S. population. We provide a summary overview of the substantial current and future economic impact of neurological disease, and provide an action plan for reducing this burden through neurological research and enhanced clinical management of neurological disorders in the United States.

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COMMON NEUROLOGICAL DISEASES: Prevalence and Costs

INTRODUCTION

As the expense of healthcare in the United States rises towards unsustainable levels, we have entered a new age of cost justification in which the prevalence, morbidity and disability of the diseases we treat are becoming critical to the continued allocation of fiscal resources towards neurological care and research. The return on the considerable investments in cardiovascular disease and cancer research over the last few decades has yielded remarkable therapeutic benefits for those diseases, dramatically increasing overall health and survival. However, less investment has been made in overcoming neurological disorders and, therefore, therapeutic gains have been correspondingly limited. Ironically, the burgeoning number of elderly citizens resulting from decreases in the mortality of cardiovascular disease and cancer is producing unprecedented numbers of people affected by neurological disease, because neurological disease is so much more prevalent in the elderly [1]. As of 2011, nearly 100 million Americans are afflicted by at least one of the more than 1,000 neurological diseases [2-4]. Though mortality is often the primary outcome measure in many research studies, the cost and societal impact of diseases are largely determined by the disability they cause; consequently, nearly 50% of the total health burden in the U.S. is due to morbidity and disability. This is particularly true of neurological disorders, and the years lost to disability from neurological and musculoskeletal disorders is greater than that of all other categories of disease.[5, 6]

In this paper, we provide a summary overview of the substantial current and future economic impact of neurological disease, and provide an action plan for reducing this burden through neurological research and enhanced clinical management of neurological disorders in the United States.

COMMON NEUROLOGICAL DISEASES: Prevalence and Costs

After a detailed review of the world literature, we chose the most prevalent and costly neurological diseases in the U.S. for analysis, focusing on those prevalence and cost estimates we considered the most comprehensive and accurate. Using this strategy, Alzheimer's and other dementias, chronic low back pain, stroke, traumatic brain injury, migraine headache, epilepsy, multiple sclerosis, spinal cord injury and Parkinson's disease emerged as the key disorders and are presented below in order of most to least costly (Figure 1). We excluded many other disorders, which often have mixed etiologies beyond primary nervous system injury (e.g. depression, chronic pain, etc.) to be as conservative as possible, even though these diseases are commonly managed by neurologists. A full accounting of all neurological disorders would, of course, push cost estimates substantially higher.

Alzheimer's Disease and Other Dementias

The prevalence of Alzheimer's dementia (AD) in the U.S. is commonly cited at 5.3 million, with an additional 2.2 million having other forms of dementia, for a total of about 7.5 million, or 2.4% of the general population.[7] The risk of dementia increases exponentially with age, reaching 13.9% for those 71 and over, with disproportionate effects on women and disadvantaged ethnic minorities (especially Blacks and Hispanics), as well as those with lower educational achievement. As the population ages further and as overall life expectancy continues to increase, dementia will become increasingly prevalent, and approximately 8.4 million Americans over 65 will have AD or another dementia by 2030, less than 15 years from now [8]. The cost of dementia is dramatically increased by the disability it causes, and the high levels of daily care, supervision and assistance it necessitates. The total annual cost of purchased care and informal home care for each patient ranges from \$45,805 to \$61,525, depending on how caregiving time is calculated (e.g. replacement cost vs. forgone wages, care purchased in the market place and informal home care, etc.) [9]. The lower annual cost estimate for AD and other dementias is \$243 billion, using the most conservative per person cost of \$45,805. Seventy percent of all dementias in the U.S. are caused primarily by AD, accounting for \$170 billion of the \$243 billion total cost, while [10, 11] 30% are non-AD dementias, account for the remaining \$73 billion.

Chronic Low back pain

Chronic low back pain (CLBP) is the second leading cause of adult disability in the U.S. Though 80% of U.S. citizens will experience acute low back pain in their lifetimes, a significant minority will have symptoms persisting more than three months, becoming chronic low back pain (CLBP) [12]. Though the prevalence of all CLBP for ages 24-39 is 4.2%, the prevalence progressively increases with age, reaching 19.6% when patients through age 59 are included [13]. Because of the methodological challenges of quantitating severe CLBP and the differing definitions used in different studies, prevalence estimates vary, but were estimated at 10.2% in one well executed state-wide study [12]. Using this estimate and extrapolating to the entire U.S. population, 32 million Americans are estimated to suffer from CLBP. As per patient direct medical incremental costs are estimated at \$1,843 in 2014 dollars [14], the aggregate direct medical costs attributable to CLBP total \$59 billion. Indirect costs, consisting primarily of lost work and lost wages, are twice as high as direct costs at nearly \$120 billion [15], producing a total annual economic burden of approximately \$177 billion.

Stroke

Stroke affects 6.8 million people over the age of 20 in the United States (2.8%) and disproportionately affects the elderly, as well as disadvantaged ethnic minorities (especially non-Hispanic Blacks) and those with lower educational achievement [16]. The total direct medical cost of stroke alone in the United States was estimated at \$75.2 billion for the year 2013. This estimate included the costs of physicians and other health professionals, medications and other medical durables as well as acute and long term

care, but excluded the cost of other cardiovascular diseases and allied conditions [17]. Lost productivity due to stroke morbidity and mortality added an additional \$34.4 billion in indirect costs, yielding an annual total of \$109.6 billion in 2014 dollars. By 2030, 3.9% of adults will be living with stroke and total direct costs are forecast to increase by 157% and indirect costs by 68%, driven largely by the aging of the population [17].

Traumatic Brain Injury

The annual incidence of traumatic brain injury (TBI) in the U.S. ranges from 1.4 to 1.7 million [24, 25], resulting in 12,000 deaths and causing long-term disability in a cumulative 3.32 million [18]. Almost 10% of these injuries occur in those age 65 and over, most commonly due to falls and motor vehicle accidents [19]. Recovery from TBI in the elderly is poor, more likely to result in hospitalization, and is associated with higher treatment costs, therefore the burden imposed by TBI will increase with the aging of the U.S. population in the immediate future. The economic costs of TBI in the U.S. are estimated at \$86 billion annually (2014 dollars), with indirect costs, (lost wages, lost productivity, and nonmedical expenditures) accounting for over 85% of the total.[20-22]

Migraine Headache

Headache is one of the most common of human afflictions. Migraine and severe headache affect up to 72 million Americans (22.7% of the general population) according to the National Health and Nutrition Examination Survey (NHANES) [23], which also estimated the prevalence of migraine alone at 16.2% in adults [23, 24]. Migraine is most prevalent in younger patients, particularly women (26.1%), though it is still very common in the elderly (18.7% of those age 65-74), and in the economically disadvantaged [23]. Most studies have focused on the economic burden of migraine alone, which causes substantial disability and lost work productivity because it strikes most frequently during the prime working years [24-27]. The American Migraine Prevalence and Prevention (AMPP) study calculated the cost of migraine by estimating the cost of chronic and episodic migraine separately. The total annual cost per chronic migraine (CM) sufferer was estimated at \$9,364 in 2014 dollars [24] (with indirect costs including lost productivity accounting for nearly 70 percent of that total), while the total per person cost for episodic migraine (EM) sufferers was estimated at \$2,158. A second, more recent study estimated lower annual cost for CM (\$8,414) but higher costs for EM (\$2,706) in 2014 dollars; using these data and the prevalence estimates from the NHANES, the total estimated cost of all migraine headaches amounts to \$78 billion per year.

Epilepsy

Epilepsy affects approximately 2.8 million Americans, approaching 1% of the general population,[28] disproportionately affecting the elderly, as well as Blacks, especially black men [29]. Despite its high

prevalence, the economic burden of epilepsy has been less well studied than that of other neurological diseases. One paper estimated direct medical costs in both children and adults in the year 2004, but did not estimate full indirect costs [30]. Assuming static disease prevalence from 2004 to 2014 and adjusting to 2014 dollars and using the Bureau of Labor Statistics medical price index, the direct medical costs of epilepsy for 2014 are estimated at \$13.4 billion [31]. However, indirect costs for epilepsy patients are quite substantial, accounting for 66% of total cost for adults, and 20% of total cost for children.[32] Taking into account that 85% of patients are adults, while 15% are children [31], the total cost burden (direct and indirect) is estimated at \$36.8 billion.

Multiple Sclerosis

Multiple sclerosis (MS) affects approximately 400,000 to 600,000 people in the U.S., or 0.2% of the general population [33]. Women are two to three times more likely to develop MS and it is more common in younger adults, peaking around age 30, the beginning of the most productive work and family years. Direct medical costs were estimated at \$26,631 per MS patient for the year 2011, but may be much higher now, as considerably more expensive drugs have been developed and deployed widely over the last five years [34]. Indirect costs, consisting primarily of lost productivity, amount to an additional \$21,854 per patient. [35]. Using the mid-range prevalence estimate of 500,000 patients, direct and indirect costs together total \$24.2 billion annually in the United States. Even in this 2011 analysis, drugs accounted for nearly 40% of direct medical costs and were a major contributor to the increasing costs of MS care.

Traumatic Spinal Cord Injury

The prevalence of traumatic spinal cord injury (TSCI) in the United States ranges from 240,000 to 337,000 [36], and these injuries are primarily the result of motor vehicle accidents and falls. TSCI disproportionately affects males (80%) and 53% of injuries result in partial or complete quadriplegia, with 37% causing partial or complete paraplegia. There is a 3-year cumulative incidence rate of 56.4 per million, with a higher cumulative incidence among older adults of 79.4 per million [37]. As with traumatic brain injury, older patients have a higher risk of death, as well as a higher rate of placement in chronic care than do younger patients [37]. The direct medical costs associated with TSCI vary significantly with the severity of the injury, but average \$29,183 (2014 dollars) [38]. The estimated average indirect costs per patient (lost wages, fringe benefits, and lost productivity) are \$71,961 [36]. Using the most conservative estimates, the total annual economic burden associated with TSCI approaches \$18.5 billion [39].

Parkinson's disease

Parkinson's disease (PD) is estimated to affect 630,000 to 1,000,000 people in the U.S., or 0.3% of the general population, and these numbers are projected to approximately double by 2050 [40]. It disproportionately affects men (2:1) and those over 50 [41]. Direct costs are estimated at \$13,786 per patient, for an aggregate direct medical cost of \$8.1 billion, including institutional care, outpatient care, retail prescriptions, equipment and supplies [40]. Indirect costs, are \$10,816 per patient, or \$6.8 billion in aggregate, including reduced employment, workdays lost due to illness, reduced household income, higher disability payments, adult day care, other formal care, and miscellaneous household expenditures. Together, direct and indirect costs for PD total \$15.5 billion per year.

Less common neurological diseases

Individually, less common neurological diseases do not have a major economic impact, but collectively these disorders cause substantial burden. The Rare Diseases Act of 2002 defines a rare disease as one affecting fewer than 200,000 Americans. More than 6,000 diseases meet this definition, affecting 25 million Americans in total, and approximately 360 of these rare diseases are primarily neurological, including amyotrophic lateral sclerosis and Huntington's disease (18,000 to 30,000 each), frontotemporal dementia (48,000) and myasthenia gravis (64,000), among many others [42, 43] [44]. The epidemiology and total costs of rare neurological diseases are poorly characterized, and no well-developed estimates are available. However, given the severity of many of these disorders and their aggregate burden, it is reasonable to assume substantial direct and indirect medical expenditures. However, in this era in which expenditure is so carefully weighed against group benefit, there must also be a place for individuals with less common diseases, for whom there is a humanitarian, rather than purely economic rationale. Furthermore, given the pathophysiological mechanisms of neurodegeneration shared by many common and uncommon neurological diseases, many research advances made in rarer conditions will likely have much more widespread application to other, much more prevalent disorders.

DISCUSSION

The current estimated annual cost to American society of just nine common neurological diseases is staggering, totaling nearly 0.8 trillion dollars (789 billion in 2014 dollars; Figure 1). This cost will increase even further over the coming years as the elderly segment of the population nearly doubles, increasing from 43.1 million as of 2011, to 83.7 million by 2050 [45, 46]. The costs of dementia and stroke alone are projected to total over 600 billion by 2030 (calculated in 2014 dollars; not adjusted for projected inflation). The growing costs of healthcare for neurological and other diseases were the major impetus for the implementation of the Affordable Care Act, but it is not clear the proposed measures of this program will be sufficient to meet the daunting fiscal challenges of the near future. Given the extraordinary and rapidly growing costs of neurological disorders themselves, a concrete strategy is urgently needed to reduce the burden of neurological disease. We propose the following steps.

Acceleration of Translational Research in Preventative and Disease-Modifying Therapy

Effective preventative strategies employed before disease onset can have substantial impact. The per capita risk of stroke has already been dramatically reduced since the 1970s, first by charting the pathophysiology of atherosclerosis, then by designing and deploying strategies to control its major risk factors (e.g. hypertension, hypercholesterolemia, atrial fibrillation etc.). Implementation of antihypertensive and statin therapy, among other measures, reduced the incidence of ischemic stroke by 40% between 1988 and 2008 [47] and the deployment of warfarin and other anticoagulant therapies has significantly reduced the incidence of embolic stroke.[48] Even those new therapies which are only disease-modifying and not curative can produce dramatic savings. For example, as Alzheimer's disease typically starts late in life, a new treatment delaying its onset by only 5 years would effectively eliminate 50% of cases, while a delay of onset by 10 years would spare 75% of patients symptomatic disease, potentially saving over 175 billion dollars annually [49].

Unfortunately, there has been a crisis in neurological research funding in the United States which, along with Japan, had the lowest growth rate in brain research worldwide in 2013 [50]. NIH funding has been under pressure throughout the years of the American recession, with significant short and long term consequences on research infrastructure, workforce and productivity. In addition, over the last decade, progressive reductions in clinical reimbursement across the board have eliminated what was traditionally a major source of cross-subsidization for funding research into new therapies in humans (most especially critical Phase I and II studies). A comprehensive plan of accelerated re-investment by the federal government to offset this serious decline in funding for translational research is desperately needed.[51]

Enhanced Outcome and Comparative Effectiveness Research

Investment in outcomes and comparative effectiveness research into current treatments to determine which are most effective and cost efficient is also of critical importance, particularly as the medical system moves away from fee-for-service paradigms towards quality-based population management. Initiatives such as the Patient Centered Outcomes Research Initiative (PCORI) provide a start, but are currently insufficiently funded to enable meaningful progress, even in the most common of neurological disorders. Research such as this will not be funded by private industry, as it may run counter to drug and device company business strategy. However, such studies have the potential to rapidly impact cost, morbidity and mortality in substantive ways, and funding should be expanded to include a meaningful level of research into at least the most common and costly of neurological diseases.

Comprehensive Databasing and Tracking of Neurological Disease

A comprehensive means of national data collection quantitating the clinical features, response to therapies and ongoing burden of neurological disease and its economic impact is critical. Such databases are not only important for assessment of the status quo, but also to accurately track the success of new strategies to improve health and reduce costs, as many seemingly logical strategies may not prove successful in actual implementation. It is also important to confirm the projected impact of successful new preventative and treatment strategies. Tracking, database, and “big data” management strategies are currently being designed in a global way, but realistic and rapidly implementable approaches are needed, and aggressive measures are necessary to break down formidable existing barriers (e.g. competitive lack of electronic health record system interoperability; payment to health systems for dedicated and trained data entry personnel, etc.).

Taking Advocacy to the Next Level

Given the present environment of constrained resources and fiercely competing priorities, coordinated advocacy efforts at the individual, institutional, organizational, local, state and federal government levels are essential to encourage prioritization, funding and implementation for the above initiatives.

Organizations such as the American Neurological Association, the American Academy of Neurology and the Society for Neuroscience, as well as our subspecialty organizations, and individual neurologists and neuroscientists must work together to coordinate their advocacy efforts more aggressively than ever before. The very future of the neurological sciences and the patients we serve is now at stake, and the welfare of generations yet to come hangs upon the success of our efforts.

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All authors contributed to the conception and design, data acquisition and analysis, and drafting the text or preparing the figure for this manuscript.

Potential Conflicts of Interest:

The authors have nothing to disclose.

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FIGURE LEGENDS

Figure 1: Annual Costs of Major Neurological Diseases

Costs of Alzheimer’s and other dementias, chronic low back pain, stroke, traumatic brain injury, migraine headache, epilepsy, multiple sclerosis, spinal cord injury and Parkinson’s disease. Dollar figures were converted into 2014 values using the all items consumer price index for non-medical (indirect) costs. Direct costs were converted using the medical price index.

