U.S. BURDEN OF NEURODEGENERATIVE DISEASE

Literature Review Summary

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NEURODEGENERATIVE DISEASE

Throughout this review all dollar figures have been adjusted to 2020 USD to allow for overall estimates and comparisons.

Overview

Neurodegenerative disease arises when nerve cells in the brain or other parts of the nervous system lose function and eventually die. Currently available treatments may relieve some of the associated symptoms, but there are no known cures.

Neurodegenerative disease (Alzheimer's disease and related dementias or ADRD, Parkinson's disease and motor neuron diseases including amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy) **collectively affected 4.7 to 6.0 million individuals in the U.S.** between 2016-2017. **These diseases were responsible for 272,644 deaths and 3,011,484 disability adjusted life years in 2016** (Dorsey et al. 2018; Logroscino et al. 2018; Matthews et al. 2019; Nichols et al. 2019; Yang et al. 2020).

The annual cost to the US from Alzheimer's disease and related dementias, Parkinson's disease, amyotrophic lateral sclerosis and spinal muscular atrophy was $655 billion in 2020 USD, including direct medical and non-medical costs and indirect costs from lost productivity and uncompensated caregiving hours (Alzheimer's_Association 2021; Larkindale et al. 2014; Muscular_Dystrophy_Association 2012; Yang et al. 2020).[1]

ALZHEIMER'S DISEASE AND RELATED DEMENTIAS (ADRD)

DISEASE BURDEN

In 2014, **1.6% of the US population was living with Alzheimer's Disease and Related Dementias, 5 million individuals aged 65 and older**. In 2060, **the prevalence is estimated to double to 3.3%, 13.9 million adults**. 11.5% of Medicare beneficiaries had ADRD in 2014: prevalence in this group for men was 9.2%, for women 13.3%, for Blacks 14.7%, for Hispanics 12.9%, for non-Hispanic Whites 11.3%, for American Indians and Alaska natives 10.5% and for Pacific islanders 10.1% (Matthews

[1] Note: Estimate combines costs based on different prevalence years: ADRD from 2021 projection, PD from 2017 and ALS + SMA numbers from 2010. $550 billion is from ADRD alone.

et al. 2019). Black people are 1.5-1.9 times more likely to have an existing or new diagnosis of ADRD than non-Hispanic Whites (Power et al. 2020).

In 2016, ADRD affected 4,029,450 individuals, was responsible for 238,895 deaths, an 11.6% increase from 1990 and 2,473,390 disability adjusted life years, a 3.8% increase since 1990 (Nichols et al. 2019). [Note: total prevalence number disagrees with Mathews 2019 by about ~1 million]

SUBGROUPS AND PROGRESSION:

Among individuals diagnosed with dementia, Alzheimer's disease (AD) represents 60-80% of cases, vascular dementia 5-10%, dementia with Lewy bodies 5% and frontotemporal dementia 3-10%, though over 50% of those with dementia had mixed pathologies (Alzheimer's_Association 2020; Brenowitz et al. 2017; Hogan et al. 2016; Vann Jones and O'Brien 2014). Mild cognitive impairment progresses to AD at a rate of 7-17% per year (Mitchell and Shiri-Feshki 2009; Petersen et al. 2018; Roberts et al. 2014; Thomas et al. 2019; Ward et al. 2013).

NATIONAL ECONOMIC BURDEN

The annual cost to the US from Alzheimer's disease and related dementias was $352 billion in 2021 for medical care and long-term care. $179 billion of this cost was borne by Medicare, $58 billion by Medicaid and $75 billion was in out-of-pocket spending. Informal caregiving was valued at $257 billion in 2021 (adjusted to 2020 USD), from 15.3 billion hours of uncompensated caregiving (Alzheimer's_Association 2020).

The costs of direct medical and long term care to the US Latino population was $13.3 billion and of unpaid informal care $6.8 billion in 2020 (Wu et al. 2020). Costs of direct medical and long term care to the US African American population was $26.7 billion and of unpaid informal care, $49 billion (cost figures updated to 2020 USD) (Gaskin, LaVeist, and Rickard 2013).

INDIVIDUAL COSTS

The **lifetime cost of care for an individual with dementia was estimated at $350,228, $200,811 greater than lifetime costs for individuals without dementia** (Jutkowitz et al. 2017). From age 65 to death, individuals with a diagnosis of dementia spend $45,940 more than individuals without a dementia diagnosis on medical and long term care costs, over 98% of which was in nursing home costs (Hudomiet, Hurd, and Rohwedder 2019). The five-year incremental cost to Medicare of dementia was $17,139 per patient compared to patients without dementia (White et al. 2019). Individuals with dementia spent more (32%) on out of pocket medical expenses than individuals without

dementia (11%) as a fraction of total household wealth measured 5 years before death, and this fraction was larger for Black people (48%), people without a high school education (48%) and widowed or unmarried women (58%) (Kelley et al. 2015). Women diagnosed with ADRD have 16% higher incremental Medicare costs and 70% higher incremental Medicaid costs than male patients with ADRD (Yang and Levey 2015).

PROGRESSION AND SUBGROUPS:

In early stages of ADRD, total costs per year in medical expenses and informal caregiving were $53,664 for patients with mild dementia and $35,616 for individuals with mild cognitive impairment. The largest drivers of costs were direct medical costs (39%) for the mild cognitive impairment group and informal caregiving (45.1%) for the mild dementia group (Robinson et al. 2020).

The per beneficiary annual cost of persons with dementia to California Medicare in 2015 was $19,590, compared to $7,050 for beneficiaries without dementia. Alzheimer's dementia carried the lowest per-person cost ($16,185), followed by frontotemporal dementia ($17,251), vascular dementia ($24,393) and the most expensive subtype, Lewy body dementia ($26,149) (Chen et al. 2019).

COSTS TO CAREGIVERS:

Seventy percent of the lifetime cost of care of individuals with dementia is borne by their families in unpaid caregiver hours and out of pocket expenses (Jutkowitz et al. 2017). Caregivers for adults with dementia had twice the out of pocket expenses as those caring for adults without dementia (Skufca, Rainville, and Mehegan 2016). A female family member of a male patient diagnosed with ADRD carries a lifetime cost of informal care six times greater than a male family member of a female patient with ADRD (Yang and Levey 2015).

PARKINSON'S DISEASE

DISEASE BURDEN

The number of individuals with **Parkinson's disease (PD) was estimated between 0.7 and 1.04 million adults in 2016-2017**, depending on whether epidemiological studies or survey data was used (Dorsey et al. 2018; Yang et al. 2020). **About 20% of adults with PD are thought to be undiagnosed** (Schrag, Ben-Shlomo, and Quinn 2002). The disease is more prevalent in older age groups: 0.07% in adults under 65 and 1.69% in adults 65 and over (Yang et al. 2020). Compared with women, **men are at twice the risk of being diagnosed with Parkinson's** (Miller and Cronin-Golomb 2010).

Some studies report that the disease is more prevalent in Hispanic and non-Hispanic white groups than in Black groups (Dahodwala et al. 2009; Van Den Eeden et al. 2003; Wright Willis et al. 2010) but the association between race and PD is still unclear (Ben-Joseph et al. 2020).

PD caused 26,117 deaths in 2016, a 22.4% increase from 1990 **and accounted for 355,735 disability adjusted life years,** a 15% increase since 1990 (Dorsey et al. 2018).

NATIONAL ECONOMIC BURDEN

Based on a prevalence of 1.04 million individuals with PD, the **US economic burden of Parkinson's disease was $54.7 billion in 2017**: **direct medical costs of $26.8 billion** and **$27.9 billion in indirect and non-medical costs**. This $27.9 billion includes an indirect cost of $15 billion (persons with Parkinson's and caregiver burden of future earnings lost, reduced employment, absenteeism, presenteeism, productivity losses in unpaid work), non-medical costs of $7.9 billion, and $5.1 billion due to disability income received by persons with Parkinson's. Of this $27.9 billion in indirect and non-medical costs, $21 billion were direct costs to individuals with Parkinson's and the remaining $6.9 billion was due to productivity losses from informal caregiving (Yang et al. 2020).

Total direct and indirect costs were projected to rise to $57.1 billion in 2018 and $83.4 billion in 2037 (based on an estimated 1.09 million and 1.64 million individuals with Parkinson's in 2018 and 2037 respectively). The largest drivers of this increase are likely to be direct medical costs, social productivity loss, disability income, long-term care costs and caregiver productivity loss (Yang et al. 2020).

INDIVIDUAL COSTS

The **mean annual direct medical costs for Medicare beneficiaries with PD were $24,000-26,000 per person** between 2013-2015 and costs increased with disease severity (Dahodwala et al. 2020; Mantri et al. 2019; Yang et al. 2020). The biggest cost drivers for medical costs were hospital inpatient services and institutional care followed by outpatient visits and prescription medication. Patients who were diagnosed with Parkinson's disease psychosis had annual direct medical costs ~$33,000 higher than patients with Parkinson's disease without psychosis and the largest driver of this cost difference was use of long-term care (Hermanowicz and Edwards 2015). Direct medical costs were also lower in prescription compliant patients with PD, the increased drug cost offset by lower costs in inpatient and emergency department visits (Davis, Edin, and Allen 2010; Richy et al. 2013). Direct medical costs increase by 16.7% per year post diagnosis (Johnson et al. 2013). **Mean annual indirect costs were $26,935 per person**, mainly driven by productivity loss and nonmedical care (Yang 2020). Persons with Parkinson's experience higher lifetime income loss the earlier they are diagnosed:

$686,669 if diagnosed at age 45, $226,771 if diagnosed at age 55, $42,682 if diagnosed at age 65 and $2947 if diagnosed at age 75 (Johnson et al. 2011).

COSTS TO CAREGIVERS:

Compared to caregivers with non-Parkinson's dependents, Parkinsons's caregivers had higher first-year total all-cause insurer costs ($10,727 vs $8484) and medical costs ($8441 vs $6637). They also had higher prescription costs, out of pocket costs, indirect costs and income loss (Martinez-Martin et al. 2019). Caregivers spent a mean of 22 hours per week on unpaid informal care (Whetten-Goldstein et al. 1997).

MOTOR NEURON DISEASES

DISEASE BURDEN

Motor neuron diseases (amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy) **affected 62,531 individuals in the USA in 2016**, a 3.4% prevalence increase from 1990 to 2016. It caused 7,632 deaths in the same year, a 27.9% increase from 1990 and accounted for 182,359 disability adjusted life years, a 14.3% increase since 1990 (Logroscino et al. 2018).

ALS: There were **21,835 people in the US diagnosed with ALS in 2015** and this is projected to increase to 29,306 in 2040, a 34% increase. The global number of ALS cases is projected to increase from 222,801 in 2015 to 376,674 in 2040, a 69% increase (Arthur et al. 2016).

SMA: In 2017, there were between **8,526-10,333 individuals in the US diagnosed with Spinal Muscular Atrophy** (SMA) types I,II or III (Lally et al. 2017).

NATIONAL ECONOMIC BURDEN

ALS: The US economic burden of ALS was estimated between $1210-1213 million per year in total direct and indirect costs (Muscular_Dystrophy_Association 2012; Larkindale et al. 2014).

SMA: The annual national burden for early onset SMA was $809 million and for other SMA subtypes $323 million(Muscular_Dystrophy_Association 2012).

INDIVIDUAL COSTS

ALS: **Annual per patient direct medical costs for a patient with ALS in 2010 were ~$41,000-$42,000**. Direct nonmedical costs were $21,164 and indirect costs were $17,370. The biggest cost component of medical costs was outpatient care and for nonmedical costs, loss in productivity, paid caregiving and specific housing needs (Larkindale et al. 2014; Muscular_Dystrophy_Association 2012).

A study that tracked a **single patient with ALS over a 10-year period from diagnosis until death found that total direct costs over the disease duration were $2,016,803** of which 85% was paid by insurance, 9% by family and 6% by charities. The largest cost components were for in-home caregivers (46.3%), ventilation (14.7%) and hospital care (7.9%) (Obermann and Lyon 2015).

SMA: **Annual mean direct medical costs for individuals with SMA were $153,916 for early childhood onset SMA and $24,316 for SMA other types**. Inpatient care was the main cost driver for early onset SMA while outpatient care was the major expense for other SMA subtypes. **Direct nonmedical costs were $61,122 for early childhood onset SMA and $16,912 for SMA other types**. Annual family income loss was $21,010 for early-onset SMA and $15,678 for other SMA types (Muscular_Dystrophy_Association 2012).

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