



REVIEW ARTICLE

The Global Crisis of Parkinson's Disease: Epidemiology and Risk Factors

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ABSTRACT

Parkinson's disease is the second most prevalent neurodegenerative disorder, encompassing sufferers from all races worldwide. With countries around the world transitioning further along their demographics, many developing poor and middle-income countries are falling behind with the required healthcare, education and resources needed to meet the needs of Parkinson's disease patients. We reviewed how demographic transition trends are affecting worldwide Parkinson's disease incidence and prevalence, evaluated the effects of poverty on Parkinson's disease management, reviewed current global initiatives to support Parkinson's disease patients, and proposed factors for the prevention of Parkinson's disease crises in the near future. Parkinson's disease prevalence is increasing due to old age and higher life expectancy. North Americans have higher Parkinson's disease prevalence than Asian and African populations. Parkinson's disease is most prevalent amongst Caucasians in North American and European populations and amongst blacks in African populations. Important Parkinson's disease risk factors include insecticide and heavy metal exposure, welding, antipsychotic medications, and LRRK2 gene mutations. The association of Parkinson's disease and poverty showcases lack of knowledge of Parkinson's disease diagnosis, predominance of care for more pervasive illnesses, limited healthcare facilities, inadequate or no access to care from specialists, and increases in Parkinson's disease-related illnesses. Cost of care can lock up a significant portion of annual income since health insurance may not cover all expenses. These alarming situations may lead to a global Parkinson's crisis. Thus, efforts need to be made to increase the number of training programs for educating caregivers, patients and Parkinson's disease professionals to raise awareness and provide better healthcare and drug and treatment facilities.

Keywords: Epidemiology, Global Crisis, Parkinson's Disease, Risk Factors.

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Introduction

Parkinson's disease (PD) is the second most common progressive neurological disorder worldwide and has a substantial impact on patients' quality of life¹. There are many motor symptoms that characterize PD, including rest tremor, bradykinesia, rigidity, and loss of postural reflexes². Other clinical features include non-motor symptoms such as autonomic dysfunction, cognitive abnormalities, sleep disorders, sensory abnormalities including anosmia, paraesthesia, pain, as well as secondary motor symptoms such as dysarthria, dysphagia, sialorrhoea, micrographia, shuffling gait, dystonia, freezing, and glabellar reflex³.

Old age is an established risk factor for PD development⁴. Less-developed countries are undergoing a demographic transition to aging societies faster than was historically the case for developed countries⁴, and so the rise of age-dependent diseases such as PD in these regions. All races are affected by PD, thus effective management of this chronic disease is expected from the medical and non-medical community worldwide. However, lower and middle income countries may not be able provide the necessary support and treatment for those suffering from PD⁵. These patients are particularly in need of neurologist consultation, medications, and having access to other health professionals such as physiotherapists, speech therapists, dentists, and occupational therapists to manage their symptoms⁶. Also, essential mobility devices such as walkers, proper canes, or wheelchairs may not be readily accessible to this group of patients⁶.

Furthermore, health literacy, attitudes, participation in health education programs, individual beliefs about various health practices have a great impact on management of chronic diseases like PD⁷. Unfortunately, these factors are not spread evenly across various socioeconomic groups, cultures, communities and geographical regions of the world. Not to speak of underdeveloped countries, the indigent and rural populations, immigrants, certain ethnic groups, cultural minorities, those

living in poverty and other small communities in the developed countries lack many resources necessary for day to day care of PD and other chronic illnesses⁸.

For the above reasons, we have decided to further study the world's demographic change in the next decades, and how this trend can affect the incidence and prevalence of PD worldwide. We assess the effects of poverty on the management of PD including the cost of care in different parts of the world, and the resources available to PD patients. Also, the current initiatives to support Parkinson's patients globally are being reviewed. Last but not least, we propose alleviating factors to avoid Parkinson's global crises in the near future.

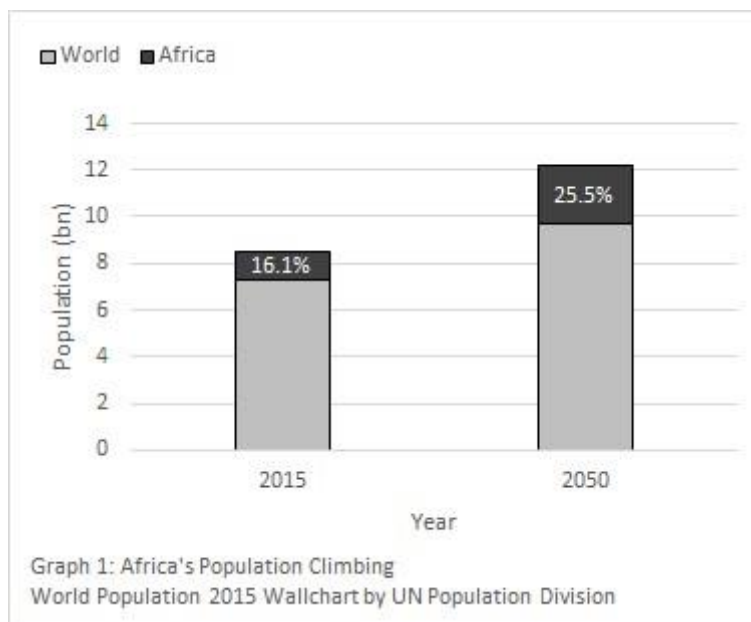
Epidemiology

Considering the recent changes in demographics in Africa, we expect to witness a rise in prevalence of PD in this continent in the near future. Blanckenberg et al. reviewed articles on PD from the entire African continent published over a 60-year period between 1944 and 2004, and revealed only a limited number of published studies on prevalence, incidence and genetics, which revealed a lower prevalence of PD in this continent in comparison to the developed countries⁶. Although PD is thought to be less prevalent in the continent of Africa, it is crucially important to recognize the current changing trends in demographics in this continent. The population in Africa is beginning to see a rise in the number of people above the age of 65 years, as of 2015⁹. This should raise concern since PD most commonly presents itself during the sixth decade of life as old age is an established risk factor for the development of PD. It is predicted that by 2050 there will be about 139 million people aged 60 years and older in Sub-Saharan Africa alone⁴. Africa alone will account for 54.4% of the projected 2.4 billion increase in the global population by 2050, making Africa contain 25.5% of world's population by 2050 in comparison to 16.1% in 2015 (Figure 1)¹⁰. Projections show that the elderly could

account for 4.5% of the population by 2030 from 3.2% in 2010. By 2030, average life expectancy in Africa is projected to reach 64 years, compared to 57 years in 2010¹¹. It is important to note that the rise in life expectancy is expected to be higher for low-income countries in comparison to middle-

and high-income countries. The rise in low-income countries will be 14 years between 1990 and 2030; in middle-income countries, the expected increase is 12 years; and in the upper middle-income countries, the expected increase is only 5 years¹¹.

Figure: 1 Africa's population climbing



In general, PD occurs with a lower frequency in areas of Africa as opposed to Europe. A study reported that about 0.00021% hospitalized Africans were affected compared to 0.001% hospitalized Europeans affected, in the same period⁹. Furthermore, several clinical series studies were conducted in different parts of Africa. A study in Nigeria for the duration of 5 years revealed that out of 1,200 neurological cases, only 20 cases were of PD⁹. Moreover, about 50 cases of PD out of 4,519 neurological cases were documented in a study lasting 10 years, in Senegal⁹. Another study was conducted in South Africa which is a more diverse region in the continent, consisting of many races. The results showed that about 2,638 neurological cases were seen over a span of 7 years which included 1,984 cases amongst Blacks, 395 cases amongst Indians and 259 cases amongst Caucasians. Only 3 (0.2%) cases amongst Blacks, 5 (1.3%) cases amongst Indians and 6 (2.3%) cases amongst Caucasians were of PD⁹. Therefore, it shows that PD follows a racial predominance.

In Asia, PD has had a lower occurrence in the past as studies have shown minimal cases. For example, a survey conducted in Singapore revealed that 0.33% of Chinese, 0.29% of Malays and 0.28% of Indians out of 15,000 individuals were affected¹². However, this trend is destined to change as there is a continuous rise in the aging population and life expectancy. Despite the faster population growth rate and the presence of half the world's aging population in Asia, few epidemiological studies of PD have been conducted there. Existing reviews of the epidemiology of PD have not focused on Asian countries and have included only a limited number of studies from Asia⁴. As more countries are being developed in Asia, more advancement in treatment and prevention of other diseases emerge. It has been determined that 50% of newborns can expect to live past 100 years of age in the developed countries¹². This shows that the incidence of PD is expected to rise as the population in Asia is expected to live longer. Currently, half of the world's older population lives

in Asia⁴. More than 385.4 million people in Asia are 60 years or older, which accounts for approximately 54.7% of world's population in this age group⁴. As 60% of the world's population resides in this continent, Asia can likely experience the highest number of PD cases in the future.

Incidence of PD is higher in North America and Europe. Studies have shown that an incidence of 224 per 100,000 person-years was documented in people above the age of 65 years in North America¹³. This is estimated to be approximately 81,500 new cases per year. It was determined that the US has a higher incidence than Canada as 160 per 100,000 person-years, approximating 59,000 new cases per year were seen.¹³ Europe on the other hand has reported much higher incidence rates ranging between 410 and 529 per 100,000 person-years. This approximates to be around 171,000 new cases per year¹³.

Overall, in Europe, the United States and Canada the prevalence of PD is projected to increase by about 92% between 2010 and 2050⁶. In contrast, the prevalence of PD in Africa and Asia currently seems to be less in comparison to rest of the world, but by considering the population structure and the current trends, the prevalence rates are expected to rise substantially in the near future in these regions. For example, in Tanzania alone, the prevalence of PD is expected to increase by 200% through 2025.⁶ The rise in aging population and increased life expectancy can be held accountable factors for the expected significant rise in the prevalence of PD in the developing countries.

As discussed earlier, the increased number of PD cases in North America and Europe can be due to a larger Caucasian population. A study conducted in California revealed that out of 588 incident cases per year, approximately 70% consisted of Caucasians and Hispanics while the remaining 30% of cases included Asians and Blacks¹². Although race and ethnicity may play a role in PD, there are other factors that can increase the likelihood of acquiring this disease. These include occupational, environmental factors, nutrition and genetics.

Risk Factors

Numerous studies have reported the associated risk of agricultural chemicals and metal exposure to PD¹⁴. Rotenone, an insecticide, along with MPTP can both damage the dopaminergic neurons in the substantia nigra¹². Exposure to a pesticide known as paraquat can also increase the risk of PD by two-fold^{12,15}. It promotes free radical formation leading to selective damage of the substantia nigra¹². Moreover, it can increase the aggregation of alpha-synuclein which is the major component of Lewy bodies.

Exposure to rotenone and insecticides, particularly in agricultural settings, has been linked to an increased risk of PD¹⁶. Rotenone, a naturally occurring pesticide, can damage dopaminergic neurons by inhibiting mitochondrial complex I, similar to the neurotoxic effects seen in PD^{17,18}. To minimize exposure, individuals should use protective equipment such as gloves and masks, apply insecticides in well-ventilated areas, and prefer less toxic alternatives like kaolin clay or boric acid for pest control^{16,17,18}.

The occupations requiring exposure to heavy metals including copper, lead, iron and manganese have shown an increased risk of PD¹². Manganese and lead are also associated with Parkinsonism^{19,20}. Industrial lead exposure has not been significantly correlated with PD; however, considering the broad availability of sources that may contain lead metal including paint, contaminated soil, and water this correlation may be biased¹⁴.

Most PD patients do not live in industrial settings; therefore, the role of metal toxin exposure in urban and non-urban areas needs to be investigated. The study of Willis et al. demonstrates a relation between community metal release and an increase in urban PD incidence rates using over 35,000 of neurologist-diagnosed PD cases. Africa, and especially Sub-Saharan Africa, has experienced an unprecedented rate of urban growth, outpacing other regions. The expected migration flows from rural areas present challenges for development of infrastructure and basic service needs. Central Africa is projected to remain the least urbanized region and North Africa the most urbanized¹¹.

Welding has been established as a potential hazard of Parkinsonism²¹. However, little is being done to increase welders' awareness of health hazards and their adherence to the safety regulations in African countries²². A study from China assessed the practice of safety regulations amongst welders in the region, and found that the health-related quality of life of welders is significantly affected and currently there is little being done to improve these safety regulations²³.

Some of the other PD risk factors include the role of anti-psychotic medication's adverse effects in the emergence of Parkinsonism which has long been a well-established contributing issue. Specifically, first generation (typical) anti-psychotics have a higher propensity for causing Parkinson manifestations. Little is known on regulation and patient education programs regarding these medications in Africa. Also, several research groups discovered that mutations in the LRRK2 gene, a gene that enhances the development of PD and may lead to an earlier onset of symptoms, accounted for 10% of autosomal dominant and 4% of sporadic cases of PD worldwide¹³. Mutations in the LRRK2 gene are rather rare among both familial and sporadic Indian PD populations²⁴.

Association with Poverty

Due to poverty and poor access to health care, it has been difficult to monitor PD occurrence in these areas. In Africa for example, there are limited neurologists and specialized institutions which only exist in urban areas. One of the major obstacles in managing and diagnosing PD in sub-Saharan Africa is the lack of sufficient numbers of neurologists, particularly movement disorder specialists⁶. The median number of neurologists available to people in sub-Saharan Africa is only 3 per 10 million people²⁵. Involvement of neurologists care in management of PD patients in the United States significantly improves outcomes²⁶. In a study using Medicare data, Racette and Willis found that neurologist treatment reduced overall hospitalization rate, skilled nursing

facility days, and health care costs, as well as a reduction in PD-related illness such as psychosis, depression, urinary tract infection, and traumatic injury but not general medical illnesses such as diabetes or hypertension²⁶. This suggests a specific nature of the role of neurologist in the care of PD patients and managing their symptoms¹⁴. In Africa, a large portion of the population residing in rural areas with a lower socioeconomic status will have restricted access to care. Furthermore, a prevalence study in Tanzania revealed that many individuals with signs of PD had never been diagnosed and were oblivious to the existence of this medical condition⁶. Another study in old age homes in India showed that approximately 96% were unaware of presence of PD and were never treated for it²⁷.

More common diseases in Africa such as HIV/AIDS and Malaria have overshadowed PD. This has left PD in an unknown territory with limited diagnostic knowledge amongst health care workers. It is estimated that more than 218 million people live in extreme poverty just in Sub-Saharan Africa, which has a total population of 800 million people²⁸. This area consists of the world's largest density of poor people and the incidence of poverty is rising faster than the population. Furthermore, a very small percentage of health care is funded by the government. For example, a gross domestic product of 4.3% is spent towards health care in Tanzania which is the poorest country in Africa⁶. To make matters worse, only half of this percentage is government-funded. As a result, treatment for PD has become unaffordable as people have to prioritize their spending on food and access to clean water.

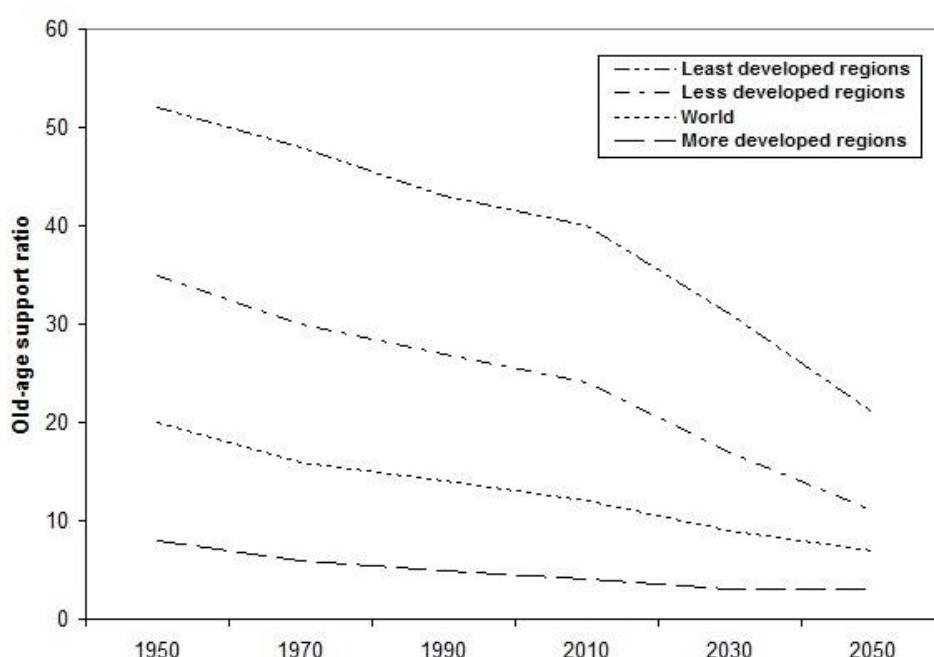
Asia is also experiencing severe poverty with nearly 920 million people living below the poverty line which consists of a \$1.25 USD/day consumption rate⁴. With a total population of nearly 4.5 billion people, it is estimated that over 65% of the world's poor people reside here⁴. Due to a lack of clean water supply and sanitation, it is evident that people must be suffering from many other infectious diseases caused by malnutrition. Therefore, a disease like Parkinson's becomes unknown and

tough to manage when someone actually acquires it. The major crises being faced by this region is the recent onset of devastating earthquakes and tsunamis which have wiped out large areas of infrastructure. In the case of PD, the loss of limited health care facilities and manpower will further deprive Asia from managing this condition⁴.

Also, as a result of the region's aging population, the old-age support ratio, which is the number of persons aged 15 to 64 years per person aged 65 or older, has decreased in the region from 12.1 in

1980 to 9.1 in 2013 and is expected to be at 3.7 in 2050. East and Northeast Asia have the lowest old-age support ratio. The old-age support ratio is expected to decrease globally, with the highest decline rates in the least developed countries (Figure 3)¹¹. Low old age support ratios are expected to have several economic and social implications, such as negative impact on pension schemes when a shrinking working population has to finance the pensions of an increasing number of older persons.

Figure: 2 Old age support ration



Graph 2: Old-age Support Ratio: a rough comparison
Source: United Nations, Department of Economic and Social Affairs Population Division

Although North America has had a successful economy, there are still certain rural areas and ethnic groups facing poverty. About 15.5% of the population equalling 49 million face poverty in US²⁹. Moreover, nearly 4 million people face poverty in Canada which approximates 9% of the population³⁰. Individuals who belong to a lower income class will find it very difficult to afford the high costs of care for PD. Furthermore, people residing in the outskirts and more remote areas not only face poverty but also have poor access to health care. These factors raise concern as PD occurs with a higher prevalence in North America³⁰.

Poverty in Europe has been at a minimum as 16.4% of the population comprising of 80 million people are considered under the poverty threshold.³¹ The area of concern is the disparity amongst the poverty threshold between European countries. For example, the Romanian poverty threshold is 176 Euro/month per person while the British is set at 853 Euro/month per person.³¹ In the case of PD, this can serve as a major issue as treatment or care available in one country may not be affordable by another country. The wealthier countries in Europe are more inclined to possess health care facilities and treatments for PD which may not be affordable by the others³¹.

Cost of Care

The burden people face in Africa is not only the high cost of treatment but also the availability of medications. It is estimated that only 12.5% of the population has access to these medications³². The current annual cost to treat one PD patient is approximately \$400 USD.³² This is highly unaffordable as an average person has an income of \$60-\$70 USD per month³². Treatment with PD medications such as Levodopa/Carbidopa at 100mg on a course of three times per day costs nearly \$60 USD per month³². This suggests that a PD patient in Africa spends 571% of their income

on average on the medications alone (Table 1). The health insurance in Africa only covers a selective amount of medications which adds to the problem. Furthermore, the high costs of neuroimaging make it impossible to determine if surgical treatment is required. An average cost of \$200-\$300 USD is needed for a brain CT scan while a brain MRI costs nearly \$400-\$800 USD³². This is why people in Africa have resorted to the traditional "smell test" as an inexpensive and efficient diagnostic tool, which is non-specific, cannot differentiate LRRK2 mutation-induced PD from idiopathic PD, and hence may provide misleading results³²⁻³⁴.

Table-1: Comparison between the costs of medication to the average income per continent.

	Average Income (USD)	Cost of Medication (USD)	Percentage (%)
Africa	70	400	571
Asia	406	203	50
Europe	36,000	4,000	11
USA	27,000	12,800	47

Source: Cilia et al., 2011; Dodel et al., 2008; Rektorova et al., 2011; Ragothaman et al., 2006; & Journal of Economic Notes; U.S. Census Bureau – U.S Department of Commerce.

Note: 1. Monthly values are shown 2. Average monthly income of the European Union countries ranges from \$416 in Romania to \$3987 in Luxembourg. We chose \$3000 as an arbitrary average monthly income. 3. Percentage represents the cost of medication alone in relation to the average income.

The developing countries in Asia are also struck with the high costs of treatment for PD. For example, India has a gross national income averaging \$450-\$540 USD annually³⁵. There were 176 consecutive PD cases reviewed and it was discovered that nearly half of the patients had an annual salary of less than \$1,148.63 USD³⁵. Approximately 16% to 41.7% of the gross national income was spent on medications³⁵. With medical insurance covering only 3% of the entire population, it is very difficult to manage PD. The average cost of hospitalization ranges from \$162-\$214 USD which includes a stay between 1-78 days³⁵. Furthermore, home-nursing costs about \$86 USD per month. The annual cost of medications is about \$203 USD which is nearly half of the salaries of most people³⁵. This suggests that a PD patient in Asia spends 50% of their income on average on the medications alone (Table 1). Dopaminergic agonist treatment is the

most expensive as it ranges from \$109-\$128 USD per year, while Levodopa can start from \$35 USD and increase to \$121 USD per year, based on the severity of the disease³⁵. Other medicines including selegiline, amantadine and ropinirole range from \$4.36-\$8.63 USD per year³⁵. Costs for consultation with a neurologist average about \$23.6 USD, which exclude the expense of travel at approximately \$27.3 USD³⁵. Lastly, the expenditure for neuroimaging including brain MRI and CT scans average about \$63.8 USD³⁵.

Costs of PD in Europe are substantial as they approximate to be around 13.9 billion Euros annually³⁶. The expenses vary amongst the European countries and become higher as the disease progresses. For example, Germany has an annual expenditure of 18,660 Euros per person for PD at stages 1-2³⁶. This expense rises to 31,660

Euros per person as the stages progress to 2-5³⁶. A study conducted in 145 PD patients across the European countries revealed an annual cost averaging 20,860 Euros per person³⁷. This amount consisted of 3,840 Euros in medicine costs per person annually with dopaminergic agonist drugs accounting for 65% of the total³⁷. This suggests that a PD patient in Europe spends 11% of its income on average on the medications alone (Table 1). Furthermore, hospitalization costs were approximately 1,420 Euros per person annually. Physiotherapy, inpatient rehabilitation and diagnostic procedures each cost nearly 1,000 Euros per person annually³⁷. Moreover, supportive devices such as walkers, canes and wheelchairs also cost about 1,000 Euros per person annually³⁷. The indirect costs of 6,360 Euros included consultation with psychiatrists, disability payments, early retirement from work and home re-building³⁷. Although the health insurance covers most of the expenses of individuals who pay tax, however, it excludes people who are unemployed and living in poverty.

The total annual costs of PD in US are approximately \$14.4 billion USD and the estimated PD-related medical expenses are \$12,800 USD per patient^{26,38}. This suggests that a PD patient in US spends 47% of their income on average on the medications alone (Table 1). These account for medical expenses which are about \$8.1 billion and non-medical expenses which are estimated at \$6.3 billion USD annually³⁸. A considerable amount is spent on nursing home care as more than \$5 billion USD accounts for about 15% of PD patients annually. The average annual cost incurred by a patient is \$22,800 USD which includes medical expenses of \$12,800 USD and non-medical expenses of \$10,000 USD³⁸. Outpatient medical care including physiotherapy, occupational therapy and assisted equipment (wheelchairs, walkers, canes) cost nearly \$5,472 USD annually³⁸. Furthermore, the cost for hospitalization is around \$3,420 USD and the medication expenses are approximately \$3,192 USD annually. A large expenditure of about \$10,716 USD is allotted towards long-term care including nursing homes and other rehabilitation

facilities³⁸. Although Medicare and Medicaid insurance cover many of the expenses associated with PD, it has to be obtained through an employer-assisted program. People with low-income and those who are unemployed will not benefit from the insurance coverage and will be faced with a crises³⁸.

Canada has a lower degree of costs associated with PD compared to US. The total annual figure approximates \$447 million CAD which include \$202 million CAD of direct and \$245 million of indirect costs³⁹. The direct costs consist of hospital expenditures at \$89 million CAD, pharmacologic therapy at \$99 million CAD and physician consultations at \$14 million CAD³⁹. A significant portion of the indirect costs are associated with early retirement and lost productivity and treatment of co-morbidities associated with PD such as depression and psychosis³⁹. The health insurance in Canada will cover most expenses associated with this condition; however, the outpatient services such as physiotherapy will require employer-assisted coverage.

What can be done?

Considering the expected global rise in prevalence of PD, especially in the developing-regions, more training programs need to be available to educate new neurologists and caregivers. More educational and rehabilitation programs need to be implemented. The importance of educating caregiver and patients themselves should not be underestimated. A task force has been created in Africa to overcome the lack of awareness and training of health professionals for PD. Considering the economic burden of many developing-countries, more volunteering and cultural programs are suggested to be initiated to help improve the general understanding of PD and to alleviate the current deficiency in health care of PD patients. The Parkinson's and Related Movement Disorders Association of South Africa has taken a pivotal role in raising awareness in Africa.

Furthermore, the economic disadvantages associated with lost productivity and early

retirement demonstrates the need for implementing appropriate prevention plans that would include a substantial reduction in environmental risk factors. The International Parkinson and Movement Disorder Society's Asian and Oceanic Section organizes programs that take place in different parts of Asia.

In Canada, the World Parkinson's Program founded in 2008 by senior Canadian neurologist Dr. A. Q. Rana, provides free Parkinson's medications globally, PD educational literature in more than 20 languages used in more than 50 countries, walking devices in addition to other beneficial activities for patients, caregivers and PD professionals. Despite the various programs designed to raise awareness, train healthcare professionals, and fundraising to help PD patients globally, the expected global rise in prevalence and incidence of PD in the near future verifies the vital role of new research to be inevitable for successfully managing Parkinson's global crises.

Conclusion

The burden of PD represents a significant and growing global health challenge, particularly in developing regions where demographic shifts

towards older populations and limited healthcare resources compound its impact. Our study highlights the critical need for comprehensive strategies that include better training for healthcare professionals, increased awareness, and improved access to essential healthcare services and medications. Environmental factors such as exposure to pesticides and heavy metals have been identified as significant contributors to PD risk, emphasizing the need for stricter regulations and protective measures. By addressing these issues through coordinated global efforts and targeted interventions, we can mitigate the rising prevalence of PD and enhance the quality of life for those affected by this debilitating disease.

Conflict of Interest:

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