

AGING AS A RISK FACTOR FOR NEURODEGENERATIVE DISEASES: INSIGHTS FROM UKRAINE AND THE WORLD

OLES LUHOVYI, MARIA BAYLIAK

Abstract. Aging, often referred to as the autumn of life, is a natural and complex biological process that leads to a progressive decline in physiological functions, increasing susceptibility to various diseases, including neurodegenerative disorders. The neurodegenerative conditions, characterized by the loss of neuronal function and structure, include Alzheimer's disease (AD), Parkinson's disease (PD), and other dementias, which are leading causes of disability and mortality globally, particularly in the elderly. This article explores the most common theories of aging, relationship between aging and neurodegenerative diseases, and molecular and cellular processes underlying neurodegeneration. In particular, we discuss such theories of aging as epigenetic, damage and repair, and metabolic ones, as well as their importance for understanding neurodegenerative processes. At the cellular level, factors such as protein misfolding, mitochondrial dysfunction, and chronic inflammation link aging to neurodegeneration. Using statistical data, we examined the prevalence and mortality associated with these diseases in Ukraine, comparing trends with other countries. In particular, we examined the prevalence and mortality associated with neurodegenerative diseases over the past two decades in Ukraine, in two age groups: 50–69 years and 70+. Comparisons of data from Ukraine with global trends revealed that individuals aged 70+ experience a fourfold higher disease burden, as measured by disability-adjusted life years (DALYs). However, Ukraine demonstrates relatively low mortality rates for these diseases that may reflect underdiagnosis, shorter life expectancy, and unique demographic and socioeconomic factors. The findings emphasize the critical need for improved diagnostics, access to medical care, and population-based prevention strategies to address this growing health burden. Recommendations include early interventions targeting modifiable risk factors, increased research investment into age-related diseases, and the development of robust support systems for elderly populations. These efforts could significantly improve health outcomes, reduce healthcare costs, and enhance quality of life for aging populations.

Keywords: Brain aging; neurodegenerative diseases; Alzheimer's disease; Parkinson's disease; statistics, health.

1. INTRODUCTION

Aging is a natural and multifaceted biological process that involves a progressive age-related decline in physiological functions, increased susceptibility to diseases, and reduced ability to adapt to environmental stressors. At the cellular level, aging is determined by processes such as genomic instability, telomere shortening, and mitochondrial dysfunction, which together contribute to functional decline and age-related pathologies (Consuelo, 2021; Oosterhuis et al., 2022).

A number of studies suggests that aging is influenced by genetic, environmental, and stochastic factors (Gladyshev, 2016; Navarro et al., 2023). The accumulation of cellular damage over time, epigenetic alterations, and systemic changes in inflammatory responses are key contributors. These

processes align with theories like the “hallmarks of aging”, which categorize aging-related mechanisms into cellular and molecular damage and their systemic impacts (Consuelo, 2021).

From an evolutionary perspective, aging is considered a consequence of declining natural selection pressure of post-reproduction. This has led to the development of theories like the disposable soma theory and antagonistic pleiotropy theory, which explain how aging evolved as a trade-off between survival and reproduction (Consuelo, 2021; Bengtson and Settersten, 2019).

2. THEORIES OF AGING

Aging is natural biological process that occurs in all living organisms. However, there is still no consensus among researchers on whether aging leads to impaired health and disease, or whether the accumulation of damage and disease leads to aging. It seems that many factors like biological, environmental and genetic are involved in aging. The exact causes of aging are unknown; therefore, aging is a subject of many competing theories about why and how it happens. Some of these theories we discuss below.

Epigenetic theory of aging

The epigenetic theory of aging suggests that aging does not occur directly due to DNA mutations, but through epigenetic modifications in DNA and histones (Vaiserman et al., 2018). For example, modifications like DNA methylation and histone modifications (acetylation and methylation) may impact gene expression resulting in tissue repair decline and illness resistance (López-Otín et al., 2016). The accumulation of these alterations over time results in cellular dysfunction. Hypomethylation of DNA that occurs with age can lead to chromosomal instability, while hypermethylation of DNA in promoter regions can cause the suppression of certain genes, such as tumor suppressor genes. Furthermore, age-related hyper- or hypomethylation can impair the normal response of genes to environmental stresses, which in turn leads to gradual functional decline and homeostasis (Vaiserman et al., 2018).

Cellular senescence

The theory states that cells usually no longer become malignant after some point, often due DNA damage or stress. These “senescent” cells secrete a cocktail of harmful factors and foster pathogenesis phenotypes (Childs et al., 2015). That the removal of these senescent cells may delay aging (Lushchak et al., 2023).

Damage and repair theory

This theory proposes, that aging is a consequence of the increasing imbalance between the damage to the cells and their capacity of repair. This is a process largely driven by factors such as oxidative stress and mitochondrial dysfunction (Sun et al., 2016). The most popular variant of the damage theory is free radical theory proposed by Harman (Harman, 2006). This theory states that accumulation of oxidative damages to DNA, proteins and other components in cells and tissues leads to aging, diseases, and death (Harman, 2006).

The metabolic control theory

Aging is an immortal metabolism. Overeating of energy-dense foods speeds up biological aging, but lifespan extension and improvement of health span have been demonstrated by calorie restriction (Fontana et al., 2018). This theory claims that age of human organism is as a function of how much energy we consume in food.

3. THE CONCEPT OF NEURODEGENERATIVE DISEASES

Neurodegenerative diseases: features and risk factors

Neurodegenerative diseases are a group of disorders which are characterized by decline in function and structure of neuronal cells, which ultimately leads to their death. Neurodegeneration leads to a range of pathologic changes in the central and peripheral nervous systems, causing cognitive, motoric and behavioral disorders (Kalia & Lang, 2016). Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD) and different types of dementia are typical neurodegenerative diseases. As a leading cause of morbidity and mortality globally, particularly among the elderly, these diseases may sometimes start early in life (Nichols et al. 2019; Heneka et al., 2016). Nowadays, there has been an extension of the perception of neurodegenerative diseases from symptoms-based to pathways and molecular mechanisms behind them as risk factors (Cummings et al., 2023).

Features of neurodegeneration

The insidious onset and relentless progression of loss of function of nervous systems is one of the most prominent characteristics of neurodegeneration. While these conditions may differ in their underlying clinical presentation, they share some common pathological features:

(i) Protein misfolding and aggregation. Key characteristics of protein aggregation is the accumulation of misfolded (pathological) proteins (beta-amyloid in Alzheimer's disease; alpha-synuclein in Parkinson's disease; huntingtin in Huntington's disease) These aggregates perturb the cellular homeostasis and enhance neurotoxicity (Gandhi et al., 2018; Taylor et al., 2016).

(ii) Selective vulnerability. Selective neuronal populations are more vulnerable to degeneration. To use an example, dopaminergic neurons in substantia nigra are the primarily degenerated type of neurons in PD whereas loss of focal cortical and hippocampal neurons is a characteristic of AD (Alzheimer's Association., 2022).

(iii) Neuroinflammation. Excessive activation of microglia and astrocytes causes an inflammatory environment, which in turn adversely affects neuron functioning and further damages nerves (Taylor et al., 2016; Alami et al., 2024).

(iv) Mitochondrial dysfunction and oxidative stress. Disturbances in energy production with reactive oxygen species (ROS) and antioxidant imbalance is considered as a factor in neuronal damage and aggravation of neurodegeneration (Lushchak et al., 2021; Alami et al., 2024; Pajares et al., 2020).

Main neurodegenerative diseases are Alzheimer's disease and Parkinson's disease. Alzheimer's disease (AD) is the most common neurodegenerative disorder, which comprises memory loss and cognitive decline (Ross & Tabrizi, 2011). The pathological components are the intracellular neurofibrillary tangles which contain amyloid plaques and hyperphosphorylated tau proteins (Gandhi et al. 2018; Taylor et al., 2016). Parkinson's disease (PD) predominantly dysregulates motor control by death of dopaminergic neurons in black substance. The disease is related to intraneuronal accumulations of α -synuclein-rich inclusions (Pringsheim et al., 2019; Klemmensen et al., 2023).

The risk of neurodegenerative diseases is an age-related health problem that is increasingly recognized as an important global health issue related to population aging (Dabir et al. 2006; Ascherio & Schwarzschild, 2016). Although the exact cause is not known, neurodegenerative diseases occur through common risk factors — genetic susceptibility, environmental factors, e.g.,

low physical activity, diets high in refined carbohydrates, and other comorbidities such as diabetes or heart disease (Ascherio & Schwarzschild, 2016; Gitler, Dhillon & Shorter, 2017).

Recent studies have also emphasized the importance of genetic mutations (e.g., APOE ϵ 4 in AD, LRRK2 in PD) and epigenetic changes in disease susceptibility (Yuan, 2021; Hou et al. 2019). Common environmental toxins like pesticides and heavy metals have been recognized as contributing factors to diseases like PD (Ascherio & Schwarzschild, 2016; Hou 2019).

Pathophysiological insights and implications for therapeutics

The neurodegenerative diseases concept has changed from exclusively clinical to primarily molecular and systems-based. Recent studies in biomarker research (CSF, neuroimaging) have resulted in the potential for early detection and downstream monitoring of these diseases (Pajares et al. 2020; Brown, Al-Chalabi, 2017) Moreover, mechanistic processes (e.g., autophagy and extracellular vesicles) are contributing to the understanding of how diseases initiate and progress at a cellular level (Alami et al., 2024; Przedborski et al., 2018).

Although we have come a long way in terms of understanding of underlying mechanisms, therapeutic developments are still lacking. Current treatment focuses mainly on symptomatic management and secondary prevention of disease progression (Nguyen et al., 2020; Sen, Thummer, 2022). At the same time, there are some emerging approaches (e.g., gene editing such as CRISPR-Cas9, immune therapies directed against protein aggregates, and regenerative strategies consisting of stem cell therapy) which may change disease outcome (Sen, Thummer, 2022; Valiukas et al., 2022).

Thus, neurodegenerative diseases are complex and poly-factorial conditions, with enormous societally and economic burdens. Knowledge of common mechanisms and distinct modifiers of these diseases will advance our understanding concerning pathogenesis and may serve as therapeutic targets. Research in molecular principles of neuroimmunology and preventive medicine is important to address the problem that is exacerbated by these conditions (Valiukas et al., 2022; Martínez-Cué, Rueda, 2020).

4. CONNECTION BETWEEN NEURODEGENERATIVE DISEASES AND AGING

Among various risk factors linked to neurodegenerative diseases, age has consistently been recognized as the most significant (Armstrong, 2019; Henderson, 1988). Furthermore, direct evidence suggesting that neurodegenerative diseases may represent an accelerated form of aging is most prominently provided by Alzheimer's disease (Cholerton et al., 2013) and Parkinson's disease (Collier et al. 2011; Dugger et al., 2014). Most, if not all, of the neuropathological changes associated with AD (Hyman et al., 2012; Montine et al., 2012) are also observed in the brains of normally aged individuals (Bennett et al., 2012). Therefore, in cognitively normal brains, age-related changes include a reduction in volume and mass, enlargement of the ventricles, and a loss of synapses and dendrites in specific regions (Imhof et al., 2007).

Environmental and human genetic factors determine the progression of neurodegenerative disease. Therefore, neurodegenerative diseases are considered as a manifestation of accelerated aging. On the other hand, aging is a major risk factor for neurodegeneration (Wyss-Coray, 2016). Parkinson's disease, one of the most common neurodegenerative diseases, is predominantly observed in elderly individuals, and the risk of this disease increases with age (Hou, 2019) (Fig. 1).

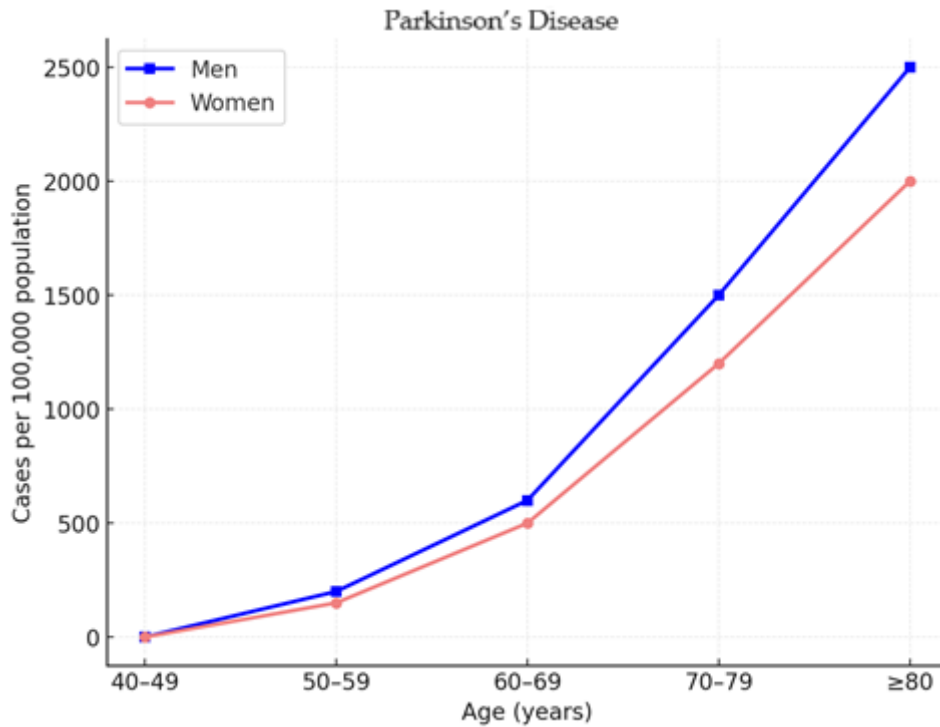


Figure 1. Prevalence of Parkinson's disease per 100,000 men and women by age globally (Nussbaum & Ellis, 2003; Poewe et al., 2017) (Mod. Hou et al., 2019).

Aging is a major risk factor for many neurodegenerative diseases (e.g., AD, PD and amyotrophic lateral sclerosis (ALS)). With age, biological processes in the brain get dysregulated and this leads to the following types of disease, that occur with increasing age. This is largely due to accumulation of misfolded proteins, which can disrupt normal cellular structure and cause ultimately toxicity leading to cell death. Age-related neurodegenerative disease is a typical example of this, simply because protein plaques and tau tangles block neural communication and impair brain functioning (Fontana et al., 2010; Frontiers, 2021).

Another important mediator that links aging with neurodegeneration is mitochondria dysfunction. We know that over time cells become more inefficient in energy production leading to oxidative stress (Lushchak et al., 2021). This causes brain cell death and results in diseases such as Parkinson's disease which is characterized by mitochondrial impairment (Mattson & Arumugam, 2018).

Inflammation is also a feature connecting aging with neurodegeneration. Neurodegeneration occurs with age as inflammation becomes more prevalent, at least low level chronic (inflammation), and potentiates neurodegenerative processes. It destroys the blood-brain barrier and creates an unfavorable environment for neurons (Franceschi et al., 2018).

Recent studies have also underscored that impaired protein quality control mechanisms play a role in neurodegeneration and aging. Aging compromises the efficiency of these systems, like autophagy which is supposed to clear dysfunctional proteins and organelles. This defect is associated with the formation of toxic protein aggregates, which, in particular, are observed in Huntington's disease (Rubinsztein et al., 2011).

Perhaps a unique insight into the future treatment may involve elucidation of common pathways between aging and neurodegenerative diseases. Inhibition of age-related pathways by improving

mitochondrial function or decreased inflammation may slow disease progression and improve quality of life (Fontana et al., 2010; Frontiers, 2021).

5. PREVALENCE OF NEURODEGENERATIVE DISEASES IN UKRAINE

According to data from Alzheimer's Disease International in 2019, more than 50 million people worldwide are living with dementia, with 62% of these cases being Alzheimer's disease, 17% vascular dementia, 10% a combination of Alzheimer's disease and vascular dementia, and the remaining cases are due to other causes (Armstrong, 2020). Neurodegenerative diseases, along with cardiovascular and oncological diseases, are among the leading causes of disability and mortality in the elderly across various countries, including Ukraine (Lukyanova, 2022) (Table 1).

Table 1. The leading types of neurological disorders responsible for a substantial number of deaths in Ukraine's population (*reproduced from Public Health Center of the Ministry of Health of Ukraine*)

	Men	Women
1	Alzheimer's disease and other dementias	Alzheimer's disease and other dementias
2	Parkinson's disease	Parkinson's disease
3	Epilepsy	Multiple sclerosis
4	Other neurological disorders	Epilepsy
5	Multiple sclerosis	Other neurological disorders
6	Motor neuron disease	Motor neuron disease

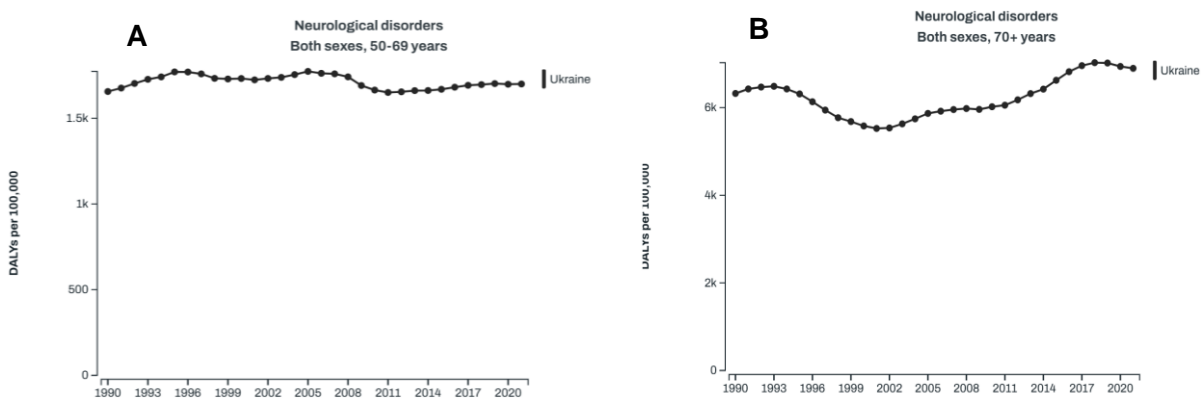


Figure 2. Distribution of neurological disorders between both sexes in Ukraine. A. 50-69 years, B. 70+ years, DALYs per 100,000 in Ukraine. (Mod. from Institute for Health Metrics and Evaluation (IHME), 2021)

The main factor in the development of neurodegenerative diseases is the accelerated process of aging. According to Institute for Health Metrics and Evaluation (IHME, 2021) the incidence of neurodegenerative diseases in people aged 50 to 69 years as of 2021 is 1,700.56 DALYs (Disability-

Adjusted Life Years) per 100000 (Fig 2, A), in people aged 70+ as of 2021 is 6,897.08 DALYs per 100000 (Fig 2, B). According to these data, people aged 70+ get sick 4 times more often than people aged 50–69, which confirms that the incidence of neurodegenerative diseases increases with age.

The analysis of data on the prevalence of neurological diseases in Ukraine in the 1990–2020 (Fig. 3) in two age groups (50–69 years and 70+) allows us to come to several conclusions.

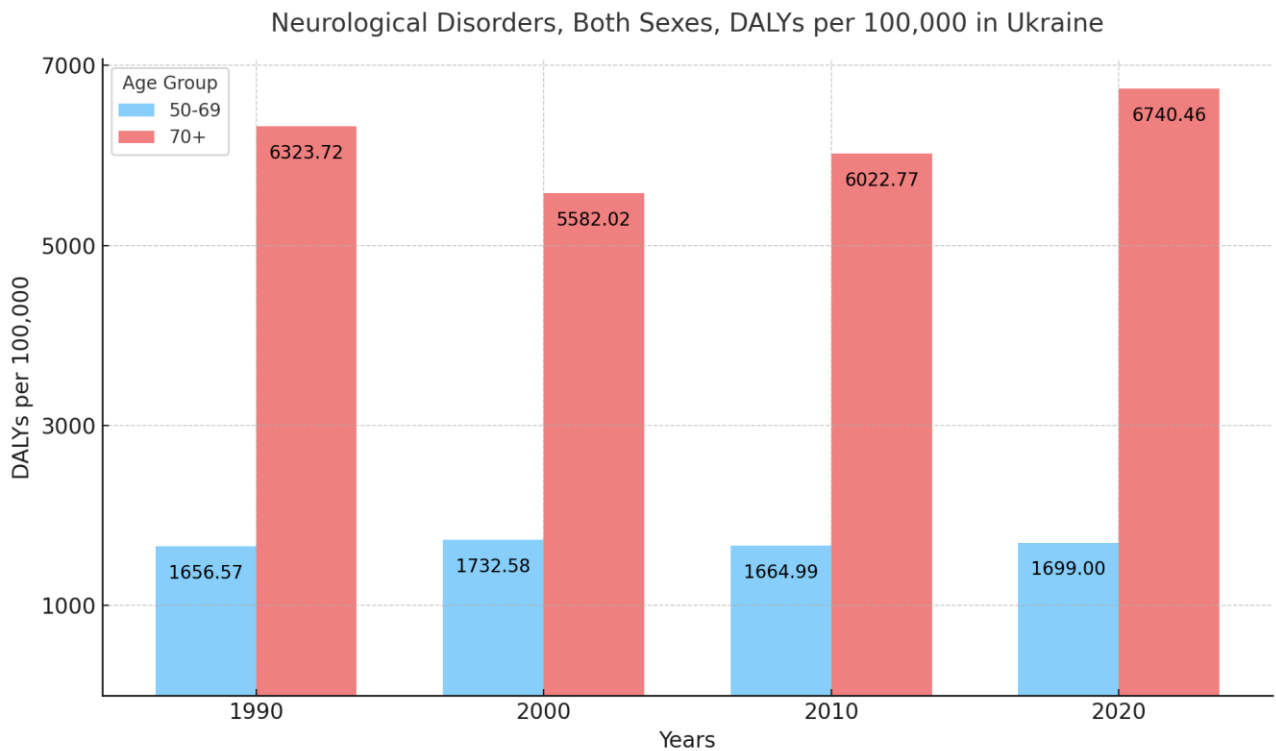


Figure 3. Neurological disorders in both sexes in terms of DALYs per 100000 in Ukraine (Mod. from Institute for Health Metrics and Evaluation (IHME), 2021)

First, the DALYs (disability and mortality) in the 70+ age group are significantly higher than in the 50–69 age group. This indicates that neurological diseases are becoming more prevalent over time. For 70+ the DALY values were between 6324 in 1990 and 6740.46 in 2020 showing a slight increase over the past 20 years. In the 50–69 age group, the DALY values are from 1656.57 in 1990 to 1699 in 2020 that seem relatively stable with negligible increase only.

Second, dynamics of DALYs is age-specific. In the period from 1990 to 2000, there was a slight increase in DALYs (from 1656.57 to 1732.58) in the 50–69 age group. This can be explained either by increasing a number of diagnosed cases or both, an increase in cases and diagnosis, to be precise. The ranking dropped to 1664.99 in 2010 which could be considered as the health stabilization of that age group. This was followed by a further slight increase to 1,699 in 2011. In the group 70+, DALYs peaked at an all-time high since 1990 (6,323.72 in 1990) and dropped to 5,582 by 2000. This may be due either to improvements in the provision of healthcare or changes in the demographic profile, or both. In 2010, there was a new rise to 6,022.77 cases, and by 2020, this number had risen even higher to 6,740.46. This could be the result of an aging population, improved diagnosis or an increase in the incidence of diseases such as dementia and stroke.

Third, the main trend in the 70+ age group is the increase in DALYs modeled to 2020 that may be a function of changing demographics due to population aging (deaths among those under 70 is declining faster than among older people). The decrease in DALYs during 1990–2000 for age 70+

could mean that the prevention or treatment of neurological diseases had improved. The stability of DALYs in the age band of 50–69 seems to be among risks that remain relevant for this category, e.g., lifestyle or access to healthcare.

Thus, most of the neurological disease burden is among people aged 70+ and will only increase with the population aging. There is evidence to support the need to focus on population-based prevention and treatment of neurological diseases at the younger age to morbidity later in life.

The primary risk factors contributing to premature death from neurological disorders in Ukraine are high body mass index, smoking, elevated blood glucose levels, and alcohol consumption. Reducing these key risk factors among the population could help decrease the burden of neurological disorders in Ukraine and lower the incidence of premature death.

Neurological disorders are now widely recognized as a major cause of death and disability worldwide. In 2019 alone, they were responsible for 2.22 million deaths. In the European Union, neurological conditions ranked third among leading causes of death, following cardiovascular and cancer-related diseases, accounting for 19.5% of all deaths in 2017 (Public Health Center of the Ministry of Health of Ukraine, 2024).

In Ukraine, neurological disorders are the fourth leading cause of mortality, with 21,644 deaths annually, accounting for 3.1% of all deaths. Over the past 29 years, this number has increased by 34%, from 14,214 deaths (or 2.2% of total deaths) in 1990 (Public Health Center of the Ministry of Health of Ukraine, 2024). The mortality rate from neurological disorders in Ukraine is moderate compared to other countries in the world. Mortality rates from neurological disorders in different countries, documented from 1990 to 2021, is shown in Fig.4.

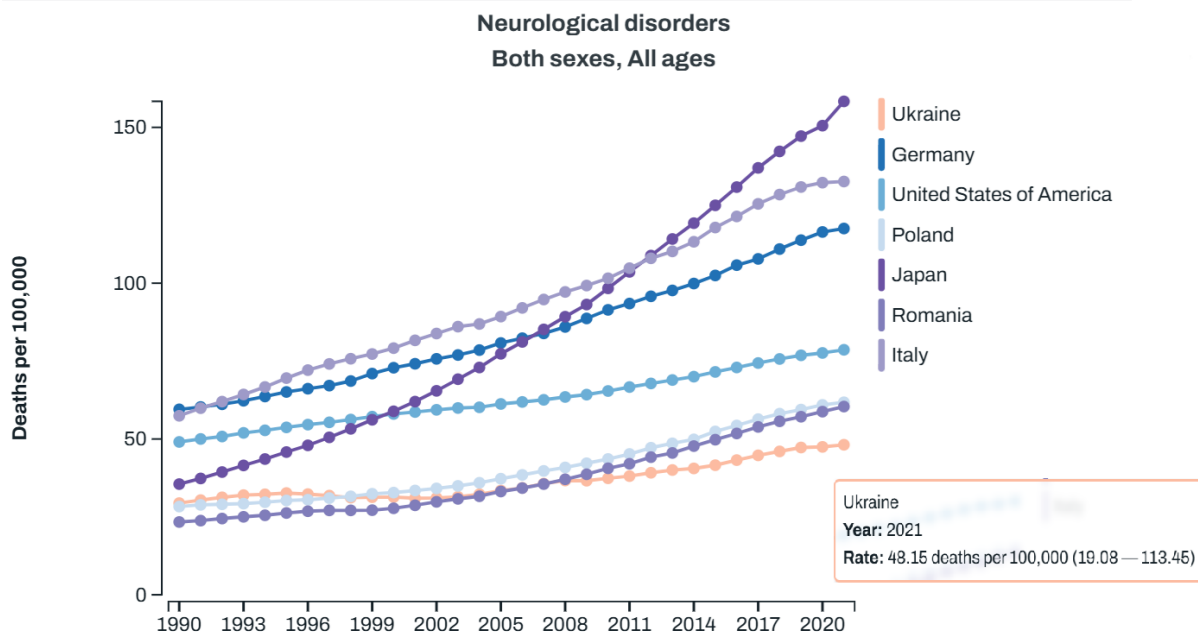


Figure 4. Deaths from neurological disorders (per 100 000, both sexes combined, all ages) in different countries from 1990 to 2021 (reproduced from Institute for Health Metrics and Evaluation (IHME), 2021).

Analyzing data on mortality from neurological disorders in Ukraine for the period 1990–2021 in all ages, several conclusions can be drawn. In particular, from 1990 to 2021, Ukraine demonstrated

the lowest mortality rates from neurological diseases among the analyzed countries. In 2021, this rate was 48.15 deaths per 100,000 population. Potential reasons for low mortality rates may include younger population, shorter life expectancy, and low diagnostic rates. Compared to many developed countries, Ukraine has a lower percentage of elderly people, the demographic most vulnerable to neurological disorders. Increased mortality rates from other causes, such as cardiovascular diseases, injuries, and infectious diseases, may prevent many individuals from reaching the age where neurological conditions become more prevalent. Ukraine is a country with a less developed healthcare system compared to European countries, so neurological diseases, particularly chronic ones, may be underdiagnosed or overlooked.

We can also summarize the following trends in Ukraine regarding neurodegenerative diseases. Mortality rates in Ukraine *is* increasing more slowly than in other countries. This trend can be attributed to minimal demographic changes and lifestyle and socioeconomic factors. The proportion of elderly individuals in Ukraine has been growing more gradually than in countries like Italy or Germany. Unique aspects of lifestyle, healthcare standards, and economic conditions in Ukraine influence the patterns and structure of disease prevalence.

General recommendations for prevention and management of neurodegenerative diseases

Strengthening prevention programs can be one of the most effective measures. Implementation of interventions to minimize risk factors before 50–69 years can substantially reduce the proportion of severe diseases in the future. Ensuring the quality health care for the elderly, especially those aged among 70 and above, is a prerequisite for improving health outcomes for the older group. Investing in neurological research, particularly for age-related diseases such as dementia and stroke will speed up medical interventions and treatments. Improving social support systems for the elderly, including services in rehabilitation and psychological care programs will improve the life support and general wellbeing of elderly people.

Recommendations for Ukraine

1. *Diagnostics* of neurological disorders, especially in the elderly, must be improved. Good diagnosis would boost data quality and give a hand to develop personalized intervention programs.
2. Emergence of neurological diseases are multifactorial and require neurologists along with psychologists and physiotherapists for the management. Ensuring access to these services, particularly in more remote areas, is important.
3. Preventive strategies should focus on the risk factors such as hypertension, diabetes and obesity that lead to strokes and other preventable neurological disorders.
4. There is a need for support for the elderly and annual medical and social support, given the growing number of aging people in Ukraine.
5. Raising public awareness through widespread educational campaigns should be aimed at identifying symptoms of neurological diseases and emphasizing the benefits of early diagnosis and treatment.

Conclusions

Aging is a primary risk factor for neurodegenerative diseases, with individuals aged 70+ being disproportionately affected. Analysis of Ukrainian data reveals a gradual increase in disability-adjusted life years (DALYs) for the elderly, signaling an urgent need for improved healthcare access

and diagnostics. Comparisons with other countries show that underdiagnosis and shorter life expectancy might contribute to Ukraine's relatively low neurodegenerative disease mortality rates. Prevention strategies focusing on modifiable risk factors, such as obesity and hypertension, could significantly reduce future disease burden. Enhancing social and medical support systems for the elderly and investing in neurological research are critical to mitigating the societal and economic impacts of these diseases.

Declaration of competing interest

The authors declare no competing interests.

Acknowledgements: This work was supported by a grant from the Ministry of Education and Science of Ukraine [grant number 0123U101790]. The authors are grateful to the heroic armed forces of Ukraine for their protection and the opportunity to work and study.

Data availability

Data supporting this study are openly available from Institute for Health Metrics and Evaluation (IHME) (2021). GBD Compare Data Visualization; IHME, University of Washington, Seattle, WA, USA at <http://vizhub.healthdata.org/gbd-compare> and from Public Health Center of the Ministry of Health of Ukraine, 2024 at <https://phc.org.ua>

REFERENCES

- Alami M., Fulop T., Boumezough K., Khalil A., Zerif E. & H. Berrougui H. (2024). Oxidative Stress in Neurodegenerative Diseases. *Biomarkers of Oxidative Stress*, pp 71–102. https://doi.org/10.1007/978-3-031-69962-7_4
- Alzheimer's Association. (2022). Alzheimer's disease facts and figures. *Alzheimer's & Dementia*, 18(4), 700–789. <https://doi.org/10.1002/alz.12638>
- Armstrong R.A. (2019). Risk factors for Alzheimer's disease. *Folia Neuropathol*, 57: 87-105. <https://doi.org/10.5114/fn.2019.85929>
- Armstrong R.A. (2020) What causes neurodegenerative disease? *Folia Neuropathol*, 58(2):93–112. <https://doi.org/10.5114/fn.2020.96707>
- Ascherio, A., & Schwarzschild, M. A. (2016). The epidemiology of Parkinson's disease: Risk factors and prevention. *The Lancet Neurology*, 15(12), 1257–1272. [https://doi.org/10.1016/S1474-4422\(16\)30230-7](https://doi.org/10.1016/S1474-4422(16)30230-7)
- Bengtson V.L., Settersten R.A. (2019). Emerging theory on aging as a lifelong process. *The Gerontologist*, Volume 55, Issue Suppl_2, Page 791. <https://doi.org/10.1093/geront/gnv424.06>
- Bennett D.A., Wilson R.S., Boyle P.A., Buchman A.S., Schneider J.A. (2012). Relation of neuropathology to cognition in persons without cognitive impairment. *Ann Neurol*, 728: 599-609. <https://doi.org/10.1002/ana.23654>
- Brown, R. H., & Al-Chalabi, A. (2017). Amyotrophic lateral sclerosis. *The New England Journal of Medicine*, 377(2), 162–172. <https://doi.org/10.1056/NEJMra1603471>

- Childs, B. G., Baker, D. J., Wijshake, T., Conover, C. A., Campisi, J., & van Deursen, J. M. (2015). Cellular senescence in aging and age-related disease: From mechanisms to therapy. *Nature Medicine*, 21(12), 1424–1435. <https://doi.org/10.1038/nm.4000>
- Cholerton B., Larson E.B., Baker L.D., Craft S., Crane P.K., Millard S.P., Sonnen J.A., Montine T.J. (2013). Neuropathologic correlates of cognition in a population-based sample. *Journal of Alzheimer's Disease*, 36: 699- 709. <https://doi.org/10.3233/JAD-130281>
- Collier T.J., Kanaan N.M., Kordower J.H. (2011). Ageing as a primary risk factor for Parkinson's disease: evidence from studies of non-human primates. *Nature Reviews Neuroscience*, 12: 359-366. <https://doi.org/10.1038/nrn3039>
- Consuelo B.B. (2021). The Challenge of Unlocking the Biological Secrets of Aging. *Specialty grand challenge*, sec. Molecular Mechanisms of Aging Volume 2. <https://doi.org/10.3389/fragi.2021.676573>
- Cummings J., Zhou Y., Lee G., Zhong K., Fonseca J., Cheng F., (2023). Alzheimer's drug development pipeline: 2023. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, Volume 9, Issue 2. <https://doi.org/10.1002/trc2.12385>
- Dabir D.V., Robinson M.B., Swanson E., Zhang B., Trojanowski J.Q, Lee V. M.-Y. and Forman M. S. (2006). Impaired glutamate transport in a mouse model of tau pathology in astrocytes. *Journal of Neuroscience*, 26 (2) 644-654. <https://doi.org/10.1523/JNEUROSCI.3861-05.2006>
- Dugger B.N., Adler C.H., Shell H.A., Caviness J., Jacobsen S., DriverDinckey E., Beach T.G. (2014). Concomitant pathologies among a spectrum of parkinsonian disorders. *Parkinsonism & Related Disorders*, 20: 525-529. <https://doi.org/10.1016/j.parkreldis.2014.02.012>
- Fontana, L., Partridge, L., & Longo, V. D. (2010). Extending healthy life span—from yeast to humans. *Science*, 328(5976), 321–326. <https://doi.org/10.1126/science.1172539>
- Franceschi C., Garagnani P., Parini P., Giuliani C., & Santoro A. (2018). Inflammaging: A new immune–metabolic viewpoint for age-related diseases. *Nature Reviews Endocrinology*, 14(10), 576–590. <https://doi.org/10.1038/s41574-018-0059-4>
- Frontiers. (2021). Aging and neurodegeneration in the brain. Frontiers Research Topic. Retrieved from <https://www.frontiersin.org/research-topics/38651/aging-and-neurodegeneration-in-the-brain>
- Gandhi J., Antonelli A., Afridi A., Vatsia S., Joshi G., Romanov V., Murray I.V.J. and Sardar Khan A. (2018). Protein misfolding and aggregation in neurodegenerative diseases: a review of pathogenesis, novel detection strategies, and potential therapeutics. *Reviews in the Neurosciences*. <https://doi.org/10.1515/revneuro-2016-0035>
- Gitler, A. D., Dhillon, P., & Shorter, J. (2017). Neurodegenerative disease: Models, mechanisms, and a new hope. *Dis Model Mechanisms*, 10 (5): 499–502. <https://doi.org/10.1242/dmm.030205>
- Gladyshev V.N. (2016). Aging: progressive decline in fitness due to the rising deleteriome adjusted by genetic, environmental, and stochastic processes. *Aging Cell*. 2016 Aug;15(4):594-602. <https://doi.org/10.1111/accel.12480>. PMID: 27060562; PMCID: PMC4933668.
- Harman D. (2006). Free radical theory of aging: an update: increasing the functional life span. *Ann N Y Acad Sci.*, 1067:10-21. <https://doi.org/10.1196/annals.1354.003>. PMID: 16803965
- Henderson A.S. (1988). The risk factors for Alzheimer's disease: a review and a hypothesis. *Acta Psychiatr Scand*, 78: 257-275. <https://doi.org/10.1111/j.1600-0447.1988.tb06336.x>

- Heneka, M. T., et al. (2015). Neuroinflammation in Alzheimer's disease. *The Lancet Neurology*, 14(4):388-405. [https://doi:10.1016/S1474-4422\(15\)70016-5](https://doi:10.1016/S1474-4422(15)70016-5).
- Hou Y., Dan X., Babbar M., Wei Y., Hasselbalch S. G., Croteau D. L., & Bohr, V. A. (2019). Ageing as a risk factor for neurodegenerative disease. *Nature Reviews Neurology*, 15(10), 565–581. <https://doi.org/10.1038/s41582-019-0244-7>
- Hou, Y., et al. (2019). Ageing as a risk factor for neurodegenerative diseases. *Nature Reviews Neurology*, 15(10), 565–581. <https://doi.org/10.1038/s41582-019-0244-7>
- Hyman B.T., Phelps C.H., Beach T.G., Bigio E.H., Cairns N.J., Carrillo M.C., Dickson D.W., Duyckaerts C., Frosch M.P., Masliah E., Mirra S.S., Nelson P.T., Schneider J.A., Thal D.R., Thies B., Trojanowski J.Q., Vinters H.V., Montine T.J. (2012). National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. *Alzheimer's Dementia*, 8: 1-13. <https://doi.org/10.1016/j.jalz.2011.10.007>
- Imhof A., Kovari E., von Gunten A., Gold G., Rivara C.B., Herrmann F.R., Hof P.R., Bouras C., Glanakiopoulos P. (2007). Morphological substrates of cognitive decline in nonagenarians and centenarians: A new paradigm? *Journal of the Neurological Science*, 257: 72-79. <https://doi.org/10.1016/j.jns.2007.01.025>
- Institute for Health Metrics and Evaluation (IHME) (2021). GBD Compare Data Visualization; *IHME*, University of Washington, Seattle, WA, USA. <http://vizhub.healthdata.org/gbd-compare>
- Kalia, L. V., & Lang, A. E. (2016). Parkinson's disease. *The Lancet*, 386(9996), 896–912. [https://doi.org/10.1016/S0140-6736\(14\)61393-3](https://doi.org/10.1016/S0140-6736(14)61393-3)
- Klemmensen M.M., Borrowman S.H., Pearce C., Pyles B., Chandra Bh., (2023). Mitochondrial dysfunction in neurodegenerative disorders. *Neurotherapeutics*, 19;21(1): e00292. <https://doi.org/10.1016/j.neurot.2023.10.002>.
- López-Otín C., Blasco M. A., Partridge L., Serrano M., & Kroemer, G. (2013). The hallmarks of aging. *Cell*, 153(6), 1194–1217. <https://doi.org/10.1016/j.cell.2013.05.039>
- Lukyanova E. (2022). *Dissertation* "The role of endothelial dysfunction in the mechanisms of the development of scopolamine- and nitrite-induced alzheimer's-type dementia in rats"
- Lushchak O., Schosserer M., Grillari J. (2006). Senopathies-Diseases Associated with Cellular Senescence. *Biomolecules.*, 8;13(6):966. <https://doi:10.3390/biom13060966>. PMID: 37371545; PMCID: PMC10296713.
- Lushchak V.I., Duszenko M., Gospodaryov D.V., Garaschuk O. (2021). Oxidative Stress and Energy Metabolism in the Brain: Midlife as a Turning Point. *Antioxidants (Basel).*, 28;10(11):1715. <https://doi:10.3390/antiox10111715>. PMID: 34829586; PMCID: PMC8614699.
- Martínez-Cué C., Rueda N. (2020). Cellular senescence in neurodegenerative diseases. *Front Cell Neurosci*, Sec. Cellular Neuropathology ,Volume 14 - 2020. <https://doi.org/10.3389/fncel.2020.00016>
- Mattson M. P., & Arumugam T. V. (2018). Hallmarks of brain aging: Adaptive and pathological modification by metabolic states. *Cell Metabolism*, 27(6), 1176–1199. <https://doi.org/10.1016/j.cmet.2018.05.011>
- Montine T.J., Phelps C.H., Beach T.G., Bigio E.H., Cairns N.J., Dickson D.W., Duyckaerts C., Frosch M.P., Masliah E., Mirra S.S., Nelson P.T., Schneider J.A., Thal D.R., Trojanowski J.Q., Vinters H.V., Hyman B.T., National Institute on Aging, Alzheimer's Association (2012). National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of

- Alzheimer's disease: a practical approach. *Acta Neuropathol*, 23: 1-11. <https://doi.org/10.1007/s00401-011-0910-3>
- Navarro C., Salazar J., Díaz M.P., Chacin M., Santeliz R., Vera I.D., Marco L., Parra H., Bernal M.C., Castro A., Escalona D., García-Pacheco H., Bermúdez V. (2023). Intrinsic and environmental basis of aging: A narrative review. *Heliyon*. 18;9(8):e18239. <https://doi:10.1016/j.heliyon.2023.e18239>. PMID: 37576279; PMCID: PMC10415626.
- Nguyen H., Zarriello S., Coats A., Nelson C., Kingsbury C., Gorsky A., Rajani M., Neal E.G., Borlongan C.V. (2019). Stem cell therapy for neurological disorders: A focus on aging. *Neurobiology of Disease*, Volume 126, Pages 85-104. <https://doi.org/10.1016/j.nbd.2018.09.011>
- Nichols, E., et al. (2019). Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Neurology*, 18(1), 88–106. [https://doi.org/10.1016/S1474-4422\(18\)30403-4](https://doi.org/10.1016/S1474-4422(18)30403-4)
- Nussbaum R. L. & Ellis C. E. (2003). Alzheimer's disease and Parkinson's disease. *The New England Journal of Medicine*, 348:1356-1364. <https://doi.org/10.1056/NEJM2003ra020003>
- Oosterhuis E.J., Slade K., May P.J.C. and Nuttall H.E. (2022). Toward an Understanding of Healthy Cognitive Aging: The Importance of Lifestyle in Cognitive Reserve and the Scaffolding Theory of Aging and Cognition. *The Journals of Gerontology, Series B*, Volume 78, Issue 5, Pages 777–788. <https://doi.org/10.1093/geronb/gbac197>
- Pajares M., Rojo A.I., Manda G., Boscá L., Cuadrado A. (2020). The role of inflammation in Parkinson's disease. *Cells*, 14;9(7):1687. <https://doi.org/10.3390/cells9071687>
- Poewe W., Seppi K., Tanner C.M., Halliday G.M., Brundin P., Volkman J., Schrag A-E., Lang A.E. (2017). Parkinson disease. *Nature Reviews Disease Primers*, 3:17013. <https://doi.org/10.1038/nrdp.2017.13>
- Pringsheim, T., et al. (2019). The incidence and prevalence of Huntington's disease: A systematic review and meta-analysis. *Movement Disorders*, 34(12), 1823–1831. <https://doi.org/10.1002/mds.25075>
- Przedborski, S., Vila, M., & Jackson-Lewis, V. (2003). Neurodegeneration: What is it and where are we? *The Journal of Clinical Investigation*, 111(1):3-10. <https://doi.org/10.1172/JCI17522>
- Public Health Center of the Ministry of Health of Ukraine, 2024. <https://phc.org.ua>
- Ross, C. A., & Tabrizi, S. J. (2011). Huntington's disease: From molecular pathogenesis to clinical treatment. *The Lancet Neurology*, 10(1):83-98. [https://doi.org/10.1016/S1474-4422\(10\)70245-3](https://doi.org/10.1016/S1474-4422(10)70245-3)
- Rubinsztein D. C., Mariño G., & Kroemer G. (2011). Autophagy and aging. *Cell*, 146(5), 682–695. <https://doi.org/10.1016/j.cell.2011.07.030>
- Sen T., Thummer R.P. (2022). CRISPR and iPSCs: Recent Developments and Future Perspectives in Neurodegenerative Disease Modelling, Research, and Therapeutics. *Neurotoxicity Research*, Volume 40, pages 1597–1623. <https://doi.org/10.1007/s12640-022-00564-w>
- Sen, P., Shah, P. P., Nativio, R., & Berger, S. L. (2016). Epigenetic mechanisms of longevity and aging. *Cell*, 166(4), 822–839. <https://doi.org/10.1016/j.cell.2016.07.050>
- Sun, N., Youle, R. J., & Finkel, T. (2016). The mitochondrial basis of aging. *Molecular Cell*, 61(5), 654–666. <https://doi.org/10.1016/j.molcel.2016.01.028>
- Taylor, J. P., Brown, R. H., & Cleveland, D. W. (2016). Decoding ALS: From genes to mechanism. *Nature*, 539(7628), 197–206. <https://doi.org/10.1038/nature20413>

- Vaiserman A., Koliada A., Lushchak O. (2018). Developmental programming of aging trajectory. *Ageing Res Rev.*, 47:105-122. <https://doi:10.1016/j.arr.2018.07.007>. PMID: 30059788.
- Valiukas Z., Ephraim R., Tangalakis K., Davidson M., Apostolopoulos V., Feehan J. (2022). Immunotherapies for Alzheimer's Disease—A Review. *Vaccines (Basel)*, 10(9):1527. <https://doi.org/10.3390/vaccines10091527>
- Wyss-Coray T., 2016. Ageing, neurodegeneration and brain rejuvenation. *Nature*, 539(7628):180-186. <https://doi.org/10.1038/nature20411>
- Yuan Q., Li X., Zhang S., Wang H., Wang Y. (2021). Extracellular vesicles in neurodegenerative diseases: Insights and new perspectives. *Genes & Diseases*, Volume 8, Issue 2, Pages 124-132. <https://doi.org/10.1016/j.gendis.2019.12.001>

Oles Luhovyi, PhD student, Department of Biochemistry and Biotechnology Vasyl Stefanyk Precarpathian National University, Ivano-Frankivsk, **Ukraine**;
ORCID ID: 0009-0009-7863-9860

Maria Bayliak, Professor, Doctor of Science, Department of Biochemistry and Biotechnology Vasyl Stefanyk Precarpathian National University, Ivano-Frankivsk, Ukraine;
ORCID ID: 0000-0001-6268-8910

Address: Oles Luhovyi, Maria Bayliak, Vasyl Stefanyk Precarpathian National University, 57 Shevchenko Str., Ivano-Frankivsk, 76018 Ukraine.

E-mail: oles.luhovyi.23@pnu.edu.ua, maria.bayliak@pnu.edu.ua.

Луговий Олес, Байляк Марія. Старіння як фактор ризику нейродегенеративних захворювань: Аналіз даних з України та світу. *Журнал Прикарпатського університету імені Василя Стефаника. Біологія*, Том 11 (2024), С.78-С92.

Анотація. Старіння, яке часто називають осінню життя, є природним і складним біологічним процесом, що призводить до прогресивного зниження фізіологічних функцій, підвищуючи сприйнятливості до різних захворювань, включаючи нейродегенеративні розлади. До таких станів, що характеризуються втратою функцій і структури нейронів, належать хвороба Альцгеймера (ХА), хвороба Паркінсона (ХП) та інші деменції, які є основними причинами інвалідності та смертності в усьому світі, особливо серед людей похилого віку. У цій статті аналізуються найпоширеніші теорії старіння, також взаємозв'язок між старінням і нейродегенеративними захворюваннями, а також молекулярні та клітинні процеси, що лежать в основі нейродегенерації. Зокрема, в цій статті розглядаються такі теорії старіння, як епігенетична, репарації та пошкоджень та метаболічна, а також їх значення для розуміння нейродегенеративних процесів. На клітинному рівні такі фактори, як порушення структури білків, дисфункція мітохондрій і хронічне запалення, пов'язують старіння з нейродегенерацією. Використовуючи статистичні дані, ми проаналізували поширеність і смертність від нейродегенеративних захворювань в Україні, порівнюючи тенденції з іншими країнами. На основі даних з України нами проаналізовано поширеність та смертність від нейродегенеративних захворювань за останні два десятиліття у двох вікових групах: 50-69 років та 70+. Порівняння з глобальними тенденціями показує, що люди віком 70+ в Україні відчують вчетверо вищий тягар хвороб, що вимірюється роками життя, скоригованими на втрату працездатності. Однак відносно низькі показники смертності від цих захворювань в Україні можуть бути наслідком недостатньої діагностики, коротшої тривалості життя, а також унікальних демографічних та соціально-економічних чинників. Результати дослідження підкреслюють гостру потребу в покращенні діагностики, доступу до медичної

допомоги та стратегій профілактики, орієнтованих на населення, для подолання цього зростаючого тягаря для здоров'я. Рекомендації включають ранні втручання, спрямовані на зменшення впливу факторів ризику, збільшення інвестицій у дослідження вікових захворювань і розробку надійних систем підтримки для людей похилого віку. Ці зусилля можуть значно покращити стан здоров'я, зменшити витрати на охорону здоров'я та підвищити якість життя людей похилого віку.

Ключові слова: старіння мозку; нейродегенеративні захворювання; хвороба Альцгеймера; хвороба Паркінсона, статистика, здоров'я.