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SOCIOECONOMIC INFLUENCE ON BIOLOGICAL AGE: AN OVERVIEW OF CURRENT STUDIES AND ROLE OF ARTIFICIAL INTELLIGENCE

Abstract. *The article is devoted to the analysis and systematization of the relationship between biological aging and the socio-economic status of the population, as well as the use of artificial intelligence (AI) methods to determine biological age. Biological aging is an instrument for determining health status of a person, that is influenced by genetic, environmental, social, economic and other factors. The pace of biological aging is determined using biological age, the definition of which is one of the most pressing issues in Ukraine and the world, as it helps in the diagnosis and prevention of various diseases. Socioeconomic status (SES) is one of the key indicators in analysis of health status of person on scale of groups of people, which includes factors describing the state of education, health care, household income, environmental influences, occupation and mental state. In this work the pace of biological aging is analyzed, as well as influence on it of such factors as wear and tear of body the body due to chronic stress, the presence of various bad habits, the lack of access to quality resources (e.g., food, clean air, etc.) and the deterioration of the psychological state of the population. Results of the conducted research showed that low level of SES significantly accelerates biological aging of a person. The appliance of AI methods in the field of biological aging was analyzed in the following directions: modelling of aging processes, selection of biomarkers, evaluation of biomarker effects and application of automated personalized aging interventions. It is expected that AI methods will be used to analyze large-scale data in order to predict aging a certain region of Ukraine, taking into account various environmental factors and the level of SES. This approach can be invaluable in efficient addressing the most pressing problems of aging and ensuring high quality of life.*

Keywords: *artificial intelligence, biomarkers, biological age, socioeconomic status.*

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СОЦІАЛЬНО-ЕКОНОМІЧНИЙ ВПЛИВ НА БІОЛОГІЧНЕ СТАРІННЯ: ОГЛЯД ПОТОЧНИХ ДОСЛІДЖЕНЬ ТА РОЛЬ ШТУЧНОГО ІНТЕЛЕКТУ

Анотація. *Стаття присвячена аналізу та систематизації зв'язків між біологічним старінням та соціально-економічним статусом населення, а також використання методів штучного інтелекту для визначення біологічного віку. Біологічне старіння це інструмент визначення стану здоров'я людини, на який впливають генетичні, екологічні, соціальні, економічні та інші фактори. Темпи біологічного старіння визначають за допомогою біологічного віку, визначення якого є одним з актуальних питань в Україні та світі, оскільки він допомагає діагностиці та профілактиці різноманітних захворювань. Соціально-економічний статус це один із ключових показників аналізу* *стану здоров'я людини в розрізі груп населення, який включає фактори, що описують стан освіти, охорони здоров'я, дохід домогосподарства, вплив навколишнього середовища, професію та психічний стан людей. У роботі проаналізовано темпи біологічного старіння і впливу на нього таких факторів як зношення організму внаслідок хронічного стресу, наявність різних поганих звичок, відсутності доступу до якісних ресурсів (наприклад, продуктів харчування, чистого повітря тощо) та погіршення психологічного стану населення. Результати проведеного дослідження показали, що низький рівень соціально-економічного статусу значно прискорює біологічне старіння людини. Проаналізовано використання методів штучного інтелекту в області біологічного старіння в наступних направленнях: моделювання процесів старіння, відбір біомаркерів, оцінка ефектів біомаркерів та застосування автоматизованих персоналізованих заходів зі старіння. Очікується, що методи штучного інтелекту будуть використовуватися для аналізу великомасштабних даних з метою прогнозування старіння в певному регіоні України з урахуванням різних факторів навколишнього середовища та рівня соціально-економічного статусу. Цей підхід може виявитися безцінним для ефективного вирішення найнагальніших проблем старіння та забезпечення високої якості життя.*

Ключові слова: *штучний інтелект, біомеркери, біологічний вік, соціально-економічний статус.*

1. Introduction

Biological aging is a measure of accumulated health issues through life of individual [1], regardless of origin of those issues. Commonly used chronological age could vary from biological age, showing only time spent alive. People of same chronological age could be very different regarding their health status, so it isn't really representative in scope of problems of aging or other problems regarding health. Therefore, specialists in leading Ukrainian scientific medical and technical institutions conduct work on predicting and assessment of the biological age of various organs and systems to identify problematic areas for early diagnosis of diseases and preventive measures [3-6]. Most Ukrainian works in field of biological aging are focused on analysis of dependency of biological age on physiological indicators of body of a person, but not on analysis of connections between biological age and socioeconomic factors. Therefore, the study of the influence of SES on biological aging of the human body in Ukrainian context is relevant.

Taking in account everything else except genetic factors, person health mostly connected with their socioeconomic status (SES), as it directly shows their financial, medical and social possibilities and highlights stress of having low SES [2]. SES is composed of variety of factors, which include education, health care, household income, exposure to environment, occupation and factors connected with mental state. For regional analysis of biological aging SES could be used as tool for mass analysis, as it requires fewer medical data and produces precise enough output for modelling health statuses on regional scale for different SES levels. For analysis on higher scale it is crucial to consider factor of urban and rural regions, as latter ones have much more obstacles regarding accessing medical services, getting a full range of nutrients and other challenges. The aim of this overview was to analyze different aspects of biological age assessment, based on biomarkers, SES, environmental, particularly regional factors and outline a role of AI-driven models in aging calculation, biomarker selection and large-scale analysis of socioeconomic data to predict aging trajectories with emphasis on Ukrainian reality, and to explore on different perspective findings in this field.

2. Methods

This overview was reported using a systematic approach to identify, analyze, synthesize relevant literature on matter of socioeconomic factors of biological aging, role of AI in assessment of it and with focus on Ukraine.

Literature search. PubMed, Scopus, Web of Science and Google Scholar databases were searched to identify latest findings in field. Key words and terms that were used for search are following: "biological aging", "epigenetics", "socioeconomic status", "artificial intelligence", "deep learning", "Ukraine", "war" and "health disparities". Mostly, excluding specific Ukrainian social studies, articles were limited to be published in English. No strict time restrictions were applied to articles publications, to give more historical context, but studies regarding appliance of artificial intelligence and epigenetic clocks were more likely to be chosen if they recently published. Inclusion criteria for searched studies were following: highlighting relationship between SES and biological aging, exploring application of AI in biological aging analysis, study focused on Ukrainian population SES or relevant to Ukraine data.

Limitations. The review is limited by the availability of studies that specifically address Ukrainian population in the context of biological aging and SES.

Synthesis. Data from selected articles was extracted for further analysis. Extracted data includes findings in connection between SES and biological aging, description of used epigenetic clock models, their efficiency and dataset contents, application in AI in field of biological age, regional assessment of SES in Ukraine with its influence on expected longevity. Further, extracted data was synthesized into review categories that address overview objectives.

3. Links between Socioeconomic Status and Biological Aging

There are many aspects of connection between SES and biological aging, which influence how accelerated biological aging of individual becomes. Further section describes a list of factors that are studied on this matter. Schematically different factors are presented on figure 1.

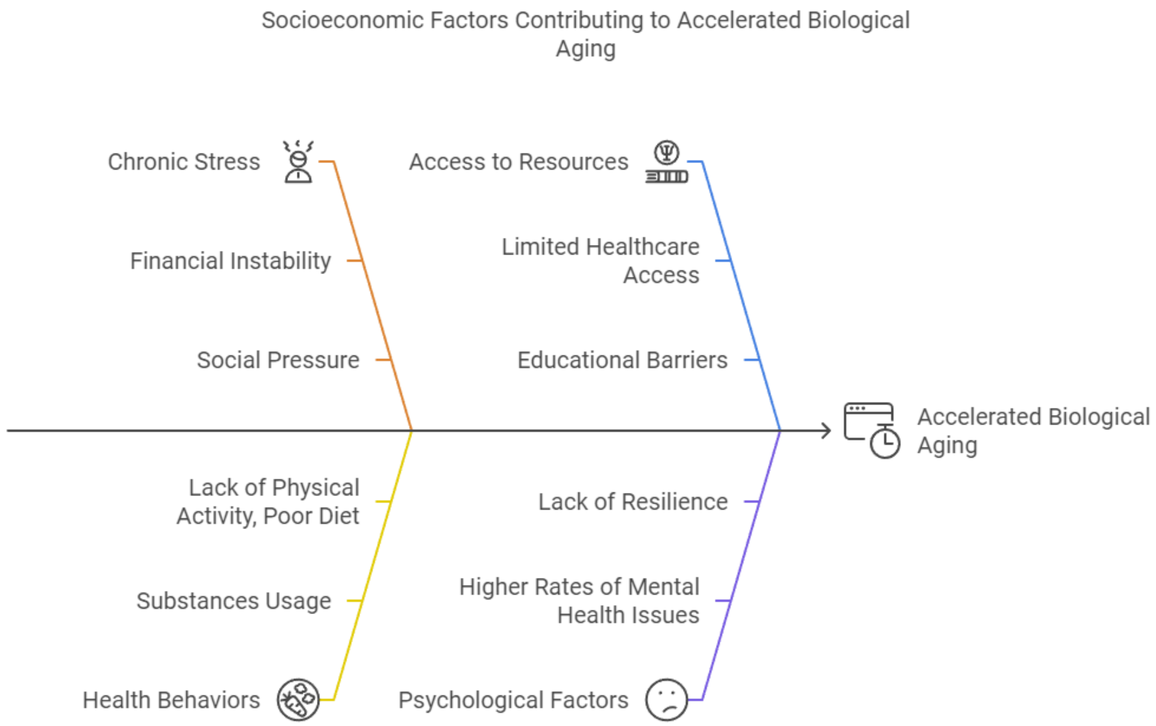

Fig. 1. SES factors

Allostatic Load. This is the “wear and tear” of the person’s body that is accumulated trough lifespan under higher stress levels. Lower SES is a mark of social deprivation, financial insecurity and other problems that creates pressure on a person and causes their body to activate compensatory mechanisms that accelerate biological aging. Studies show that prolonged exposure to social disadvantage accumulates poorer health, giving a solid estimation of potential problems and lifespan expectations [7]. Combining study of allostatic load and usage of biomarkers, provides an extent analysis of health status and can be used to prescribe medicine for improved health and lifespan expectancy in advance.

Chronic stress. Lower SES causes person to be under constant stress and that leads to higher risks of chronic illnesses. The stress produced by lower SES is constant, so exposure to it can last years, starting to alter human body and decision making [8]. Study shows that chronic stress could lead to promotion of proinflammatory phenotype characterized by immune cells mounting exaggerated cytokine responses to challenge and being less sensitive to inhibitory signals [9].

Another aspect of chronical stress it that individual can get into a loop of stress-leading behavior. If life of a person is stressful, for example, many situations with bad outcome happened to them, where they had no control, like bad childhood, it could lead to development of coping strategies that are aimed not to resolve problems, but to avoid stress of dealing with them [10]. Development of such strategies only accumulates more problems and leads to more stress.

Regarding Ukraine, factors of stress from lower SES only becomes more acute, as people rate themselves as poor even if they have moderate income. Study shows that compared to proclaimed 30% of people being poor, 38 out of 50 questioned people with incomes from lower to higher bracket claimed to be poor [11].

Health Behaviors. Lower SES leads to a chain of factors that result in bad habits. As poor SES is associated with bad life conditions, it leads to higher stress levels, which leads to worse self-control caused by poor work of reflective system and stressed impulsive system, leading to higher estimations from small and immediate rewards and lower estimations of larger postponed rewards. Those processes are associated with practice of unhealthy behaviors. Bad health behaviors, associated with poor SES are following: usage of tobacco, poor diet, no physical activity [12]. Those studies show that SES influences behaviors of people, making them acquire bad habits and showing that this problem should be addressed.

Access to Resources. Different socioeconomic possibilities of people lead to inequality of access to medical services, that has direct impact on a health status. There is direct correlation between elder people's health, their healthcare access and their SES. Issue of not accessible healthcare is worsened by the fact, that people with lower SES tend to demand more medical help and stay longer in hospitals, spending more money [13]. It has to be considered, but access to a variety of foods is also crucial for healthy aging.

Psychological Factors. Psychological pressure that, on first sight, seems not really important in overall study, turns out to be highly influential factor for estimation of biological aging. Those negative psychological condition include prolonged loneliness, general feel of unhappiness, which may seem not critical in comparison to bad habits. Different states of mind, especially of seniors' mind, could provoke higher aging acceleration than smoking, living area, biological sex, etc., and can add up to 1.65 years of aging [14].

On the other hand, psychological ageing changes behavior of an individual in different ways, creating hostile, dependence and constructive attitudes towards self and others. Also ageing reduces ability of a person to learn new skills, adapt to new situations, cognitive and intellectual functions may suffer as well, reduced levels of perceived information and altered way of processing the information. Addressing biological aging tacking into account both psychological and biological factors, all psychological processes lead to molecular changes that can be empirically inspected and using this tool of analysis, longevity can be greatly improved [15].

Other findings. A study, conducted on data collected from elder people, their SES level and DNA-methylation using different clocks used for calculation of biological aging, concluded that elders with lower SES are likely to have lower memory capabilities and higher rates of memory declination [16].

Socioeconomic disadvantage at early age, in childhood, leads to higher in DNA-methylation that can be measured. Children in environment of low SES begin to develop bad habits, higher body mass index, faster pubertal development that influence DunedinPoAm that can be measured and be marker of faster aging [17]. A child, whose parents never attended college had telomere shorter by 1178 base pairs, that corresponds to approximately 6 years of aging, compared to children with at least one parent, who college-educated [39].

4. Artificial intelligence in Studying Biological Aging

Biological age is a complex estimation of health status of a person that can consist of hundreds of biomarkers and environmental factors. At the beginning of study of biological aging, biomarkers where analyzed using regression models. Having very complex models and big sets of parameters that can influence each other not only in linear way, usage of artificial intelligence (AI) and deep learning models was necessary for efficient analysis of data and estimation of biological age acceleration. Data for biological age estimation consists of qualitative and quantitative parts, and there are models that are either of those types.

Traditional methods of assessment of biological age using AI consist of deep learning models, where learning process automatically determines useful features [18]. There are few types of deep learning models: deep neural networks (DNN), convolutional neural networks (CNN) and recurrent neural networks (RNN).

Deep neural networks consist of multiple layers of neurons that are interconnected, creating a complex system, that can process data in a non-linear way. There are several types of layers: input layer, that receives input information, multiple hidden layers for feature extraction and output layer, that holds the output data after procession [18]. In scope of biological aging, this type of neural networks models is very widely used for different tasks in predictive modelling, as it is good in determination of feature value, that is crucial on big dataset that consists of biomarkers, environmental factors, etc. Other task for DNN is analysis of feature importance, as it can output weights and activations in trained models, providing insight on each feature usage.

Convolutional neural networks are the class of deep neural networks that is mostly used for image processing [19]. CNNs mostly consist of input, hidden and output layers, but have special types of hidden layers: convolutional – layer that convolves the input and passes it further, pooling – layer that combines local clusters, fully connected layers – layer that is has fully connected neurons to other for classifications and normalization layers. As part of biological aging analysis CNN are used for image processing, for example facial features or different type of CT scanning, etc., to find biomarkers of aging.

Recurrent neural networks are used to analyze sequential, dynamic types of data that contains recurrent latent, or hidden, state that changes and develop each layer of network [20]. Typical usage for RNN is analysis of video, audio, speech. Stand out advantage of RNN is sequential inputs and storing data states. Appliance of RNN in scope of biological aging is connected with different prolonged in time measurements. For instance, tracking biological aging in time to model further aging trajectory, or reading vital signs during training to analyze how they are changed in time of body stress to predict further aging.

There is a list of main areas of application of AI below.

Predictive modelling. Having complex set of data that describes biomarkers of a person, opens a possibility to create an AI model to predict biological ageing for preventive measures to improve health and longevity. Study shows that using AI can not only give precise model, that performs better than traditional regression model [4], it is also can reduce number of biomarkers to optimize efforts of estimation of biological age. DNNs show high precision in modelling aging, outperformed linear models on biomarkers that being collected regularly in clinics, showing much more consistent correlation coefficients: linear – 0.831, DNN – 0.988 and AI model output 1.6 stronger linear relationship than traditional statistics methods [21]. Flexibility of AI technology allows creation of models, that are more suitable to particular set of biomarkers. In the article [3] use biomarkers of human blood to determine biological age.

Other significant factor of using AI for biological aging and potential illnesses prediction is that it can process alternative sources of information very efficiently. Using multimodal Transformer AI model that on basis combination of photos of face, tongue and retina could output accurate biological age predictions and detect disease on basis of calculated age [22]; based only on human lens photographs, deep learning clock was created, that precisely predicts aging and eye diseases [23]; based on chest x-ray, CXR-Age was implemented that predicts all-cause and cardiovascular mortality

[24]; based on ECG, multiple AI models were implemented that predict morbidity and mortality [25]. All that gives opportunity not only to analyze alternative biomarkers instead of usual, like blood samples, it is efficient in processing pictures on mass scale and that could potentially change usual clocks like Horvath's clock.

Epigenetic Analysis. Epigenetics is aging changes in human body. Performing analysis of different biomarkers to find epigenetic marks is a base of biological aging calculation. However, even with many successful studies in field of predicting different cardiovascular, cancer and other internals diseases of human, mechanism and correlation between epigenetics and genetics is poorly understood [40]. Usage of complex AI machine learning models eliminates problem of not understanding the whole mechanism of epigenetics, as it successfully predicts epigenetic states based on samples collected [26].

Deep learning AI models are used with massive datasets of DNA-methylation, that is considered a biomarker of aging, however not all DNA methylation is responsible for aging. Conducted study on DNA methylation with usage of AI showed that there is methylation that is indeed detrimental methylations and adaptive methylations, that shows not only damage done to human body, but beneficial changes too, introducing two new separate clocks: DamAge – showcasing harmful methylations and AdaptAge – tracking helpful methylations, respectively [27].

Biomarker Identification. Capabilities of AI are suitable for analysis of big data sets, that consist of hundreds of parameters. Thus, it opens a possibility of modelling biological aging on basis of biomarkers that were not considered before due to different reasons. Since Horvath's aging clock, that is based on DNA methylation, publication, many studies were conducted on matter of biological aging and DNA methylation showing that different datasets output reasonable accuracy. AI powered search of new aging and disease markers have shown it efficiency in deep aging clocks that are predicting biological age more efficiently than traditional learning algorithms based on discovered biomarkers, reducing cost and time [28]. AI based study open possibility to predict biological aging on basis of hematological parameters, transcriptomic and proteomic data to promote more omics data for biological aging analysis that hard to explore in scope of traditional statistics. An AI driven approach from opposite direction of finding healthy biomarkers to identify helpful therapeutic practices is also potentially useful direction of creating new approaches for longevity [29].

AI models have broad field of appliance, machine learning models are able to not only identify biomarkers, but they can help evaluate them. For instance, study conducted in field of brain aging and Alzheimer's disease, highlights brain-age delta as a non-invasive marker of aging and different influences of individuals' sex on it [30].

Personalized aging interventions. AI is a powerful tool in scope of processing big amounts of data. As biological aging is composed of multiple biological and environmental factors, each person needs personal amendments in lifestyle and medical prescription. Study shows that even if aging process is similar between organisms, it is still asynchronous and to eliminate that problem, AI is used to develop organism-specific aging clocks to produce more precise analysis [31].

Table 1 highlights differences between AI models in usage and outputs. Studied models cover different sets of biomarkers, output precision and different aspects of health status predictions.

New approach in study of biological aging is elimination of black box problem and creation of explainable artificial intelligence models. Those models stand out from Machine Learning, exactly by producing not only usual aging prediction, but metrics of that assessment too. That change opens a possibility for analysis of different tracks of aging and personalized prescriptions. A study conducted on 26 variables has shown that it is enough for determination of personalized physiological age and prediction of chronic diseases and mortality [32].

Not only analysis is important for intervention, but process of aging intervention itself important as well. Using AI with Internet of Things (IoT) technology can eliminate routine work of measurement and making amendments into health programs, it can replace work of personal coach, that has to make adjustments into trainings all the time for healthy aging and reducing costs of operation [38].

Table 1

AI models comparison

AI analysis method	Biomarkers	Upsides	Downsides
Multimodal Transformer-based [22]	Retina, tongue, facial images	Non-invasiveness, easy-to-collect data, high correlation of BA acceleration and unhealthy patients.	Sometimes data collected from one organ (mainly retina) can be misleading, therefore there used tree features to mitigate that. Ethical concerns due to processing facial images.
LensAge [23]	Human lens photographs	Non-invasiveness, data could be collected even from smartphones, acceptable correlation between BA and CA with mean absolute error of 4.5 years.	Limitations due to different retinal diseases. Different obstacles in clear photo taking. Decent accuracy but not perfect, compared to invasive data collection.
CXR-Age [24]	Chest x-ray (CXR) image	Non-invasiveness, output data highlights mortality rate and cardio-vascular mortality rate in the next 5 years. Elimination of “black-box” problem by highlighting problematic spots on CXR and specifying risk factors.	Samples limited to 224 by 224 resolution images, due to limitations of the processing unit. Also training data isn’t sufficient enough (lacking usual epigenetic clocks dataset), so model predicts mortality better than chronological age.
AI-ECG [25]	Electrocardiogram (ECG)	Non-invasiveness, affordability. Potential integration to smartphones and wearable technology. Good and predicting different cardio-vascular diseases and difference between CA and BA.	This model suffers from “black box” problem, lacking trust from patient and physicians. AI-ECG is better at predicting mortality, different diseases that calculating age, it produces deviations from CA, not standalone BA. Current usage of this model is more of an addition to other models than solitary usage.
Explainable machine learning framework [32]	26 biological markers	High precision, versatility for different data sets, used data set was chosen by optimization of used dataset from NHANES. Explainable metrics, that output aging trajectories and different health aspects.	Dataset is quite extensive, demanding many samples collection from patient. This study is conducted on basis of USA national data collection, so it reflects certain SES and population cohort, demanding separate validation for different populations.

5. Socioeconomic Situation in Ukraine

As it was established previously, SES has big impact on predicted aging trajectories and expected longevity. Socioeconomic situation in Ukraine is worsened by war, however the economic disparity in Ukraine is point of discussion many years now.

Regional studies. Study shows that for two decades, the economic gap between regions and Kyiv only grown (based on GRP growth 2004-2020) [33]. Such difference and inequal distribution between the capital and the regions causes big SES difference between population of Ukraine. In general disparity between regional policies, development and management led to shortage of life expectancy on regional level, as men in South and East regions are expected to have it on level of 61.8 years and 61.2 years respectively, when on West part of Ukraine their life expectancy is around 64.0 years [34].

Current state of war led to lowered levels of GDP per capita due to occupation of different regions and worsening economic situation in general, and lower GDP per capita is directly associated SES , however, it isn't an ultimate estimate of all social and economic factors, as many ecological, social, economic factors outweigh it on individual and higher levels [35].

Not only economic damage is being done, mental health is being damaged as well. A study, conducted on students of adolescent age, shows that individuals from region in active war state like Donetsk region report many dangerous mental states like PTSD, depression, anxiety as a result of witnessing armed attacks, being victims of violence and being forced to leave their homes [36].

Healthcare system factors influencing SES in Ukraine.

Ukrainian healthcare system suffers from different policies and obstacles that generally lower SES of people. Most of state medical facilities are underfunded and situated somewhere in economical centers, creating imparity between rural and urban regions in healthcare access. Generally low staff payment in medical field due to system of "free" medicine leads to low motivation of medical workers and out-of-pocket expenses of service receivers, that add up to 53% of total costs [37].

6. Discussion

Findings of this overview highlight correlation between SES and biological aging, including Ukrainian statistics. Analyzed literature outlined strong association of low SES to accelerated aging with impact that can be measured by different biomarkers, like telomere length, DNA methylation or cortisol level in scalp hair. But on the other hand, multiple environmental and biological may overlap in a way, which couldn't be precisely analyzed with linear models, and to overcome this particular issue, deep learning models of epigenetic clocks are really suitable.

Regional analysis of SES in rural and urban regions shows that Ukraine still suffers from centralization policies in the past. Many rural regions lack of proper health care systems and access to different recourses in general due to bad development in past. Ukrainian economics still in development, and new entrepreneurships in rural regions only beginning to develop, creating workplaces and local economy growth. Disparity of budgeting, development, ecology in regions of Ukraine is clearly traceable on statistics of GDP per capita and longevity expectancy. Aggravation of situation with SES levels, mental health due to war is studied as well, to be addressed so management of crisis situation is appropriate. Regarding overall policies of SES improvement, income disparity itself is not so impactful as prosperity and corruption levels, so rather than eliminating disparity of income per household trough some social policies, general policies should be implemented to lower corruption levels and to develop region in general, like promotion of entrepreneurship, promotion of decentralization to create local growth.

Artificial intelligence is being widely used in field of biological ageing for different aspects of predicting aging trajectories: modelling aging itself, biomarkers selection, biomarkers influence assessment, applying automated personalized aging interventions. In Ukraine some aspects of AI can be very fruitful when applied, as some models that abased on non-invasive biomarkers collection, such as photographs of retina, or ECG of chest combined with general data like age, sex, height, weight, blood pressure, etc., is cheap to collect and precise enough in comparison to expensive-to-apply epigenetic clocks like Horvath's clock that are based on invasive sample collection. Other factor is analysis of large-scale data to predict aging trajectories in region depending on different environmental factors and SES levels to efficiently address most impactful issues.

In field of public health, biological aging shows that there is direct impact of bad habits like substance usage, exposure to tobacco, bad diet, lower physical activity on aging acceleration. Additionally, to lifestyle factors, mental health is crucial factor too, in cases of longer solitude, it can be more impactful that tobacco usage. To address those issues, public guidelines should outline impacts of lifestyle on longevity and address psychological issues with full extent of seriousness.

Future research should be focused on studying application of AI models to predict aging trajectories, based on SES levels in Ukraine. It should be based on longitudinal track of SES data and biomarkers data to analyze aging over time in specific to Ukraine conditions, so it could be used to predict regional life expectancy in future and can outline specific to each region factors to address. AI based tool is crucial to this task, as work with multi-dimensional large-scale dataset is highly optimized and far more efficient than using traditional statistics methods.

7. Conclusion

To summarize, in the review it is highlighted that the role of SES application in aging predictions models is crucial on regional-based analysis of aging trajectories and it can be used on individual scale as well. Ukrainian regional data correlates with expectations based on SES. Usage of AI in aging studies provides many possibilities of yielding predictions and optimizing the process, as well as analyzing alternative sources of data and larger scales of data for regional analysis. Addressing socioeconomic disparities is important for regional development in Ukraine and further creation of healthy aging policies.

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