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ARTICLE

The Predictive Potential of the Kinetic Model of Aging of Living Systems in Demography

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ABSTRACT

An original mathematical model, previously tested by the authors on other non-demographic objects, is proposed for describing and forecasting demographic systems — the population of the countries of the World using the examples of the USA, China and Russia, as well as the number of mice in the "mouse paradise" experiment of the American scientist John Calhoun. The proposed approach allows us to describe the stages and features of this dynamics: population growth in the USA, growth and possible decrease in the population in China, loss of a part of the population of the Russian Empire and the USSR due to two world wars and the collapse of the USSR, biological degradation of the "mouse paradise" up to its complete extinction. The use of the kinetic model of aging of various types of living systems to predict the development of the number of demographic systems is based on the assumptions that the aging and development processes are related to each other and have the same statistical regularity, reflecting the fractal principle of Nature - the unity of structure and function. The results obtained suggest that a person, a population of the World, humanity and other biological species develop and simultaneously age like each other under the conditions of the always existing syndrome of general adaptation (stress) and according to the same pattern corresponding to the mathematical model proposed here.

1. Introduction

The mathematical description and forecasting of population dynamics of the countries of the World is considered in numerous scientific publications. Malthus model of exponential population growth was the result of the assertion that population increases in geometric progression [1]. Verhulst examined population dynamics under the initial assumptions that the rate of population reproduction is proportional to its current base and available resource pool [2]. The author called the solution of the corresponding differential equation as logistic curve. In accordance with empirical "law" of Forester, the hyperbolic growth of Earth's population observed over several millennia is described by function with a singularity point - a point in time when the function goes to infinity [3]. Moreover, according to calculations of Horner, it corresponds to year 2025, and according to Forester - November 13, 2026 [4].

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However, in period 60-90 years of the 20th century, population growth began to decelerate (demographic transition period), hyperbolic growth stopped, and hypothesis appeared about the limit of population growth of humanity. To describe new demographic trends, Kremer introduced in his model of hyperbolic growth additional function of per capita product, that equilibrium value determines equilibrium population size, according to his concept of technological development [5].

S. Kapitsa put forth markedly different concept stated that the change in population over millennia is determined by biological factor, namely by dominant feature of human psychology and information interaction of members of society, and that change is not related to other factors of environment (the principle of demographic imperative) [6,7]. S. Kapitsa modified Forester model, excluding the singularity point, and obtained the equation for dependence of population on reduced time τ in the form of the inverse trigonometric function arcctg(τ). The reduced time τ includes time $t_1 = 2000$ years corresponding to the middle of demographic transition period. Asymptotic stabilization of the population of the Earth corresponds to 12 billion people, while 90% of maximum population, equals to about 11 billion, is expected by 2150.

One of the modern approaches to evaluating trends in demography is solving partial differential equation concerned demographic balance of birth and death rates [8,9]. The most popular databases on demographic prospects of 226 countries and regions of the World are the United States Sensus Bureau (International Database) and the United Nations Population Department (UNPD). UNPD database contains statistics and provides projections of global population changes for the period up to year 2150 - the Global Review and Inventory of Population Policies (GRIPP), and, coordinates the Population Information Network (POPIN) [10-15]. Forecast calculations methods are based on mortality table. Four groups of forecasting methods are used: extrapolation methods, economic and mathematical methods, classification by year of birth and cohort component method, and methods of expert estimates. Unlike extrapolation and analytical methods, cohort component method (classification by year of birth) based on use of demographic balance equation allows to get not only the total population, but also its distribution by sex and age. In practice, several variants of demographic forecasts are always developed. So, e.g., there are three options of forecast by Russian Statistics Agency (ROSSTAT), and by UNPD - eight. Since the future is not exactly known today, the forecast is multi-scenario and is determined, first, by used ideology of forecast model.

In recent decades, reducing the birth rate, which overlaps the simultaneous reducing mortality, has become the prevailing trend in economically developed countries leading to decrease in the growth rate of the population and to change its age composition towards aging the population. Aging process is characterized by increase in the relative share of the elderly population. Part of population aged 60 and over has increased from 8% in year 1950 to 12.3% in year 2015,. by year 2030, it will be 16.5%, by year 2050, it will reach 21.5% of the total World's population [14,15]. The accuracy of population estimates in the census is 5%, and in the long-term forecast, tens and hundreds of % [11,16]. For example, according to the forecasts of demographers from the Expert Council under Russian Government, based on the report of the Higher School of Economics (HSE) "Population of Russia" of 2012, the population of Russia was estimated on 6 scenarios, and by optimistic scenario, in year 2060, population of Russia may be close to 150 million people, and pessimistic - near 70 million people. According to the UN forecast, presented by 9 variants, the population of Russia at the same time was estimated from about 152 million to 110 million [14,15]. At present, population of Russia is about 146.8 million.

Calculation results on 4 options made by experts of HSE Institute for Demography published in Bulletin "Population and Society" No. 371-372 (2009) show wide interval in predicted size of the World population in 2060 ranging from about 27 billion people down to 6 billion people. Currently, total population is approximately equal to 7.7 billion people.

Thus, in highly advanced countries, aging of population and even depopulation has been recorded. However, key challenge remains not clear – what will be the end of this process? Bright hypothetical illustration of negative forecast concerned possible future of mankind may be the results of experiments with mice conducted repeatedly by American scientist John Calhoun in conditions when mice were provided with full availability of space, food, water, favorable physical environmental factors and high hygiene in their crate [17]. The result of same-type experiments was population extinction after a rapid increase in size, hundreds of times higher than the initial cohort (several initial heterosexual couples), due to the gradual stratification of mice society into separate non-interacting and aggressive caste clans, cannibalism, the termination of mating of the opposite sexes, homosexuality, desire for self-sufficiency.

Anyway, mathematical forecast requires not only, and rather, not so much a formal adequacy of the model to previous experimental data but of author's hypothesis about the future, which predicting mathematical result on the base of clear physical idea.

The goal of research is to evaluate the possibility of ap-

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plying mathematical model of aging of various biological species to describe to predict changes in the population of different countries of the World [18].

2. Research Method

Kinetic theory of aging of living systems (LS) considers the human life cycle as time interval during which a biological aging process occurs [19,20]. Aging is characterized numerically by change in the probability of human's death from D = 0 (birth) to D = 1 (the probability of an unavoidable physiological fact of death). Kinetic theory of aging of various biological species is described by mathematical model based on equation (in dimensionless units) [18]:

$$\partial D/\partial \tau = (1\text{-}D)\cdot\{\exp[\mu(\tau)/(1\text{-}\theta\cdot D)] - k\} \quad (1)$$

where D is cumulative function of mortality (CFM) of the living system; $\tau = C \cdot t$ is dimensionless time ($0 \le \tau \le 1$); t is calendar time; C is constant with dimension inverse to calendar time; μ is dimensionless parameter illustrating the "tension" general adaptation syndrome (stress) of the system; k is constant that accounting for adaptation of the system; θ is parameter that taking into account the change in the aging rate with increasing in age of the system. The probability of human death (Dτ), as indicator of the degree of human aging to age τ, is determined statistically by the ratio of the number of people dying in a certain time interval τ to the total number of people of a given generation (generation size). Dimensionless time τ is the ratio of the calendar age t to the life expectancy t_{mb}, i.e., $\tau = t / t_{mb}$. Term "tension" means tension, stress, pressure, load. The term stress was introduced into biology by Canadian physiologist G. Selye in 1936 [21], which later described it as a "general adaptation syndrome", i.e., "A general nonspecific neurohormonal reaction of organism to any requirement claimed to it." The biological role of stress is determined by the strength and duration of stressors, which include all sorts of stimuli, as directly acting on the human body (physical, chemical, mechanical, biological, emotions, pain, hunger, etc.), as well not direct actions on it but potentially dangerous (e.g., seeing of object that poses a threat to humans), There are also irritants that have unexpected character, su ddenly acting on the body, including communicative stressors associated with the activity of 2nd signal system (word power). The indicator of tension Age stress indicator $S = \mu/(1\text{-}\theta\cdot D)$, as the level of the general adaptive syndrome of the body under influence of stressors, increases with increasing in body age D(τ).

Kinetic equation (1) allows obtaining various integral and differential probabilistic indicators of LS aging in dimensionless units: CFM of LS $D(\tau) = \int (\partial D/\partial \tau)\, d\tau$ - probability of system death over a period not exceeding τ; $\partial D/\partial \tau$ - probability density of death; mortality rate $(\partial D/\partial \tau)/(1\text{-}D)$; life duration expectancy:

$$\tau_{mb} = \int_0^1 \partial D / \{(1-D)\cdot[\exp(\mu(\tau)/(1\text{-}\theta\cdot D)) - k]\}. \quad (2)$$

Eq. (1) contains 3 parameters, and each, in its own time interval, affects to the greatest extent on character of time dependence D(τ). These parameters are found as a result of analysis and processing of the experimental statistical dependences D(τ) in accordance with kinetic Eq. (1). Equation is solved numerically to select suitable dimensionless model parameters by comparing with available experimental data. Based on the mathematical analysis of this equation, it follows that the average rate of change of D with time τ in the interval $0.07 \le D \le 0.7$ is determined mainly by parameter μ. Initial interval $0 < D < 0.07$ serves for "correction" of parameter k. In the final interval $1 > D > 0.7$, parameter θ plays key role. Therefore, finding values of parameters begins in a first approximation with estimate of parameter μ using Gompertz distribution, when the experimental data D(τ) are approximated by solving equation $(\partial D/\partial \tau)/(1\text{-}D) \approx A\exp(\alpha\tau)$ in the interval $0.07 \le D \le 0.7$ [18]. Then, the value of parameter k is estimated based on approximation of the experimental data by solving equation (1) D(τ) in interval $0 < D < 0.07$. Finally, parameter θ is estimated similarly in interval $1 > D > 0.7$. After such multiple iterations of approximating the experimental data D(τ) by numerical solutions of Eq. (1) with adjustable parameters, the final choice of parameters is completed by refinement using the least squares method to match the calculations of the experimental dependence D(τ) within an error not exceeding 5% [22,23]. The parameters found in this way are uniquely determined to the extent defined by the convergence of solutions of kinetic equation to experimental results within measurement accuracy.

A human is getting old. Population of the countries of the World is also aging. Obviously, indicators of aging, as also process of increase in age of LS, can be different. To estimate the degree of human aging in kinetic theory, the probability of death is chosen as such indicator. Population growth in highly industrial countries is unambiguously accompanied by its aging - a relative predominant growth in the number of elderly people. Therefore, we choose the ratio of current population size to the maximum possible as indicator of aging population of the countries of the World. The limit of this relationship with increase in calendar time is 1. According to scenarios of

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World forecasts, the maximum possible humanity size can be reached before year 2060, and maybe not. We introduce the dimensionless coordinates. Dimensionless time is defined as the ratio of calendar time from the beginning of the process to time interval corresponding to aging index reaching value of 1. Time at which selected aging index is much less than 1 is taken as the beginning of process. Let's take the previous notations D and τ for these coordinates. These parameters will vary from 0 to 1 accounting for that D(0) is much less than 1. Aging index D(τ) will display the probability of reaching population its maximum value. Under these assumptions, the task of modeling the dynamics of population size is reduced to previous mathematical model of kinetic theory of LS aging – Eq. (1), but with different interpretation of the calculation results. In this case, the previous interpretation of model parameters (1) is retained. Current population N(τ) will be calculated as the product of D(τ) by expected maximum number N_m: $N(\tau) = D(\tau) \cdot N_m$. If, after reaching the maximum, population begins to decrease, this means the transition of aging process to a new phase - the excess of mortality over fertility. For the mathematical description of this phase, function D will be considered as the probability of death of the population, varying from 0 to 1, with 1 corresponding to probability of reaching the maximum number of dead. The maximum number of dead can range from the initial maximum number of 1st stage of aging (e.g., similar to the case of complete degeneration of mice paradise), to level lower than this value (e.g., as in the case of long-time demographic forecast of population size of China). Obviously, to describe the aging process at 2nd stage, the use of the same kinetic Eq. (1) is also valid. Then the total population size at these two stages $N_m(\tau)$ is determined by difference between population size of 1st stage $N_{m1} \times D_1(\tau)$ and number of deaths of 2nd stage $N_{m2} \times D_2(\tau)$, i.e., $N_m(\tau) = N_{m1} \times D_1(\tau) - N_{m2} \times D_2(\tau)$. In general, this process can represent a continuous oscillation of growth and decrease waves with possible difference in amplitudes and duration. Each wave can be described by the same kinetic equation.

Let's verify the feasibility of this model by comparing calculations with demographic data.

3. Results and Discussion

In accordance with study objects, the term living system (LS) is understood as population - totality of people of different generations living simultaneously on Earth or within a specific territory - continent, country, region, etc., as well as the group of animals discussed below. Table 1 presents parameters of general kinetic model for all studied LS, formulas and calculation results of population dynamics in the USA (Figure 1), China (Figure 2), Russia (Figure 3) and the demographic experiment "mice paradise" (Figure 4) The calculation results describe the dynamics of the number of individuals in interval of calendar times from 150 years (USA, China) to 218 years (the Russian Empire, the RSFSR, the USSR, the Russian Federation) and 1700 days for the "mice paradise". The population N(t) is calculated according to formulas shown in 7th column of Table 1, in which $D_i(t)$ functions and N_{mi} parameters contribute. Intervals common for determining $D_i(t)$ functions by time t are also indicated. All parameters of the approximating functions (columns 2-5 of) are found by the method indicated above for selecting scenarios that are closest to demographic data. Time intervals for parameters determination is indicated in column 6. The number of time segments of approximation for different countries is determined by the number of function jumps and/or by changing the sign of the first derivative, i.e., the presence of falling part of the function. The population of Russia itself, which by various names was consistently taken up different geographical territories, has suffered three jumps - in years 1914, 1941 and 1991, therefore, it is described

Table 1. Parameters values for modeling population change rates using Eq. (1): for the countries of the World and "mice paradise". Formulas for calculating sizes of biological species N(t) as function of time

	μ	θ	k	$N_m \times 10^6$	t	N(t), size of species
USA	1,520	0,605	4,472	520	1700+400τ, year	$N_m \times D(t)$, years 1900-2050
China	1,539	0,584	4,468	N_{m1}=1570	1850+200τ, year	$N_{m1} \times D_1(t) - N_{m2} \times D_2(t)$, years 1950-2050 $N_{m1} - N_{m2} \times D_2(t)$, years 2050-2100
	1,539	0,584	4,468	N_{m2}=500	1930+200τ, year	
Russian Empire	1,520	0,675	4,472	450	1670+400τ, year	$N_m \times D(t)$ $0,3 \le \tau \le 0,61$, years 1800-1914
RSFSR, USSR	1,520	0,675	4,472	450	1670+400τ, year	$N_m \times [D(t)-0,08]$ $0,62 \le \tau \le 0,677$, years1918-1941
USSR	1,520	0,607	4,472	450	1670+400τ, year	$N_m \times D(t)$ $0,687 \le \tau \le 0,802$, years 1945-1991
Russia	1,520	0,652	4,472	150	1740+300τ, year	$N_m \times D(t)$ $0,837 \le \tau \le 0,923$, years 1991-2018
Mice paradise	1,555	0,550	4,468	N_{m1}=2400	850×τ, days	$N_{m1} \times D_1(t) - N_{m2} D_2(t)$
	1,565	0,510	4,468	N_{m2}=2400	500+1200τ, days	

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by 4 segments of piecewise continuous functions. The population of China and mice paradise are approximated by two functions, due to the decrease in population after passing the maximum.

Data in Table 1 show that taken approach allows to describe in detail stages and features of LS size dynamics. Specifically, this refers to population growth in the USA (Figure 1), growth and possible decrease in population in China (Figure 2), the loss of part of population of the Russian Empire and the USSR due to two World wars and the collapse of the USSR (Figure 3), biological degradation of "mice paradise" up to complete extinction of its members (Figure 4). Discrepancy in results of calculations and experiment does not exceed 5% when varying model parameters for population as follows $\mu = (1.520 - 1.539)$, $\theta = (0.584 - 0.675)$, $k = 4.472$ and 4.468 and for "mice paradise" $\mu = 1.555$ and 1.565, $\theta = 0.550$ and 0.510, $k = 4.468$. Modeling fit can be improved by more careful selection of model parameters, but this task was not considered in this paper.

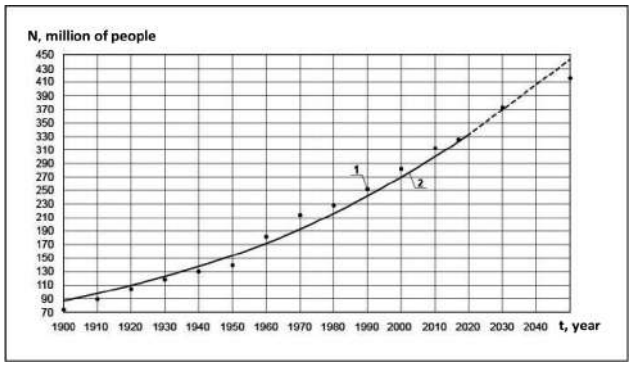

Figure 1. Dependence of the USA population size N on time t. Points – demographic data from [12,13], solid and dash lines – calculation results obtained in frame of current work

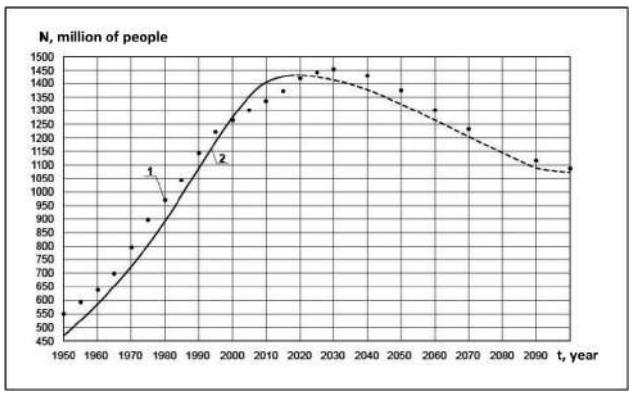

Figure 2. Dependence of China population size N on time t. Points – demographic data from [24,25], solid and dash lines – calculation results obtained in frame of current work

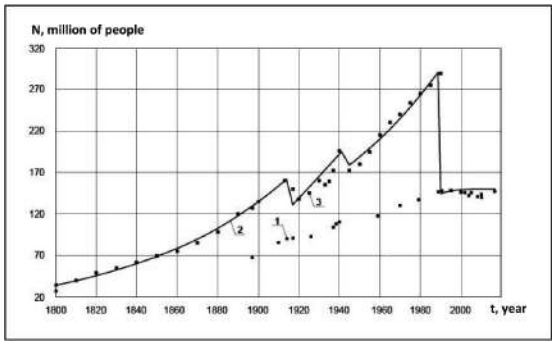

Figure 3. Dependence of population size N on time t of Russian Empire (years 1800-1914), RSFSR (years 1918-1922), USSR (years 1922-1991) and Russia (1991-2018)

Note: Symbols ■ (segment 3) – demographic data from [6,11,26], solid line (segment 2) – calculation results obtained in frame of current work with account of population loss due to 1st and 2nd World wars and collapse of the USSR in year 1991. Symbols ● - demographic data for Russia including being a part of Russian Empire, RSFSR and USSR.

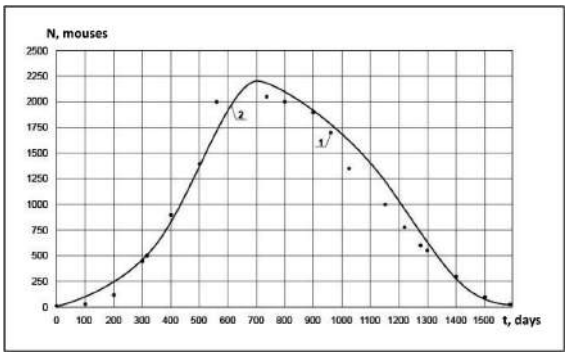

Figure 4. Dependence of "mice paradise" population size N on time t

Note: Points (1) – experimental data from [17], solid line (2) – calculation results obtained in frame of current work.

Figure 5 shows comparison of stress index $S = \mu/(1-\theta D)$ of different LS depending on D value, having in mind that stress in LS increases with increasing in age (1), [27].

Parameters values μ and θ of various LSs used for producing graphs in Figure 5 are given in Table 2.

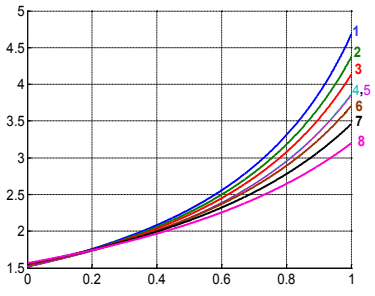

Figure 5. Dependence of stress index $S = \mu/(1-\theta D)$ of different LS on probability D of achieving maximal population size

Note: Life systems names and parameters values μ and θ are given in Table 2.

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Table 2. Parameters values μ and θ of various LSs used for producing graphs in Figure 5

Live system name	μ	θ
1. Russian Empire, RSFSR, USSR (years 1800-1941)	1.520	0.675
2. Russia (years 1991-2018)	1.520	0.652
3. LS [18]	1.520	0.632
4. USSR (years 1945-1991)	1.520	0.607
5. USA (years 1900-2050)	1.520	0.605
6. China (years 1950-2100)	1.539	0.584
7. Mice (population increases)	1.555	0.550
8. Mice (population decreases)	1.565	0.510

Comparing population size changes trends show that the lowest tension (stress) indicator S is observed among the Chinese population, then with small maximum difference (5.5% at D = 1) - among the US population. The greatest tension indicator S is observed among Russian population in the interval from year 1800 to 1941, with maximum increase compared with China by 28% at D = 1. Tension among Indicator S population of the USSR in period from year 1945 to 1991. significantly decreases and practically corresponds to the tension indicator S of the US population. After the collapse of the USSR in year 1991. and till year 2018. the tension among indicator S population of Russia again increases significantly, approaching stress of period 1800-1941 years, exceeding China by about 20% at D = 1. In Russian version, a decrease in the population in 1914-1918, 1941-1945 years and in year 1991 considered as function jumps in where function itself is not defined. Thus, the tension among indicators S population in the Russian Empire, the RSFSR, the USSR and the Russia is different at different stages of life.

It is also interesting to compare (Figure 5) the differences in tension (stress) indicators S of co-existence of people and animals with increase in their numbers and aging [18]. So, for values of parameters averaged over biological species (except for Drosophila) $\mu = 1.520$ [1.517 (rats) $\leq\mu\leq$1.523 (dogs)], $\theta = 0.632$ [0.580 (horses)$\leq\theta\leq$0.665 (rats)] and $k = 4.485$ [4.440 (horses) $\leq k\leq$4.513 (dogs)], average tension indicator S with aging of representatives of biological species is in interval between tension indicator S of China population with increase in its size and Russian population in period from year 1800 to 1941, exceeding the tension among China population by about 13% at D = 1. At the same time, the confidence interval of the aging tension indicators S region of these animals is completely covered interval of changes in the tension indicators S among populations of China, USA and Russia with increase in their size.

Even more interesting are the results of comparing the tension indicators S among mice paradise population (Figure 5): the stress indicators S among mice with increase in number and degeneration of the population residing in comfortable living conditions specially created is less than stress indicator S among population even in China, and stress indicator S of mice during extinction is slightly less than stress indicator S with the growth of population. The parameters of mathematical models describing growth of mice population and its death are close, differing by 0.6% for μ and 7.8% for θ, values of parameter k coincide. For China, kinetic parameters of ascending and descending branches of the population coincide. At the same time, for mice from mice paradise, whose, from the point of view of the experimenter, are in extremely favorable conditions of existence, the tension indicators S among individuals is the smallest among all other cases considered.

Thus, the invariance of the mathematical model of the kinetic theory of aging of living systems for describing and predicting both their aging processes and population development is shown. This invariance can be explained by the possible fractality of life and social systems at all levels-generations, populations, countries of the world, humanity , reflecting the fractal principle of Nature, the unity of structure and function.

According to the biological interpretation of the parameters of the mathematical model adopted in the work from the perspective of G. Selye's theory, a quantitative indicator of the general adaptation syndrome has been introduced, the analysis of the change of which allows us to draw a relationship between the level of development of systems and the values of the indicator determined by the influence stressors.

Here we do not consider the detailed reasons for proximity and difference in tension indicators S of LSs when they are in different conditions, since this task is too complicated from the point of view of classification of stresses and stressors according to G. Selye's theory and requires a special study. However, based on performed analysis, there is reason to believe that humans, humanity and other biological species are developing and aging at the same time: under the influence of always existing tension (stress) and according to one regularity corresponding to the mathematical model presented in article.

Note that sensitivity of LS to stressor intensity is different. For example, chronic X-ray radiation exposition of dogs within range of dose rate changes from 0 to 54 cGr/day results in change in indicator S parameter μ from 4 to 14, while the life expectancy of dogs decreases under effect of radiation from 192 months to 1 month [28]. For human, there is no such data.

We consider that biophysical interpretation of essence of our mathematical model corresponds to the concept of G. Selye [21].

4. Conclusions

(1) There is reason to believe that the aging processes and changes in the number of individuals of living sys-

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tems at all levels are related to each other and have the same mathematical regularity, reflecting the fractal principle of Nature - the unity of structure and function.

(2) The mathematical model of the kinetic theory of aging of living systems, reflecting their fractality, is invariant and can be used to predict the dynamics of the population.

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ARTICLE

How Artificial Intelligence and Virtual Reality Benefit the Elderly and Individuals with Disabilities

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ABSTRACT

The growing and evolving use of emerging technology including Artificial Intelligence (AI) and Virtual Reality (VR), has significantly impacted the lives of two specific groups - the elderly and the disabled. This paper investigates potential reasons for this phenomenon. Clearly, AI and VR Technology alters the everyday lives of people with disabilities and how they navigate the world. Technological developments increasingly work to address the isolation that people with disabilities as well as the elderly experience for they are often unable or limited in how they engage with their communities. This research paper outlines the way technology has improved social communication, information distribution, and day-to-day living for those with disabilities and the elderly. Undoubtedly, the internet has transformed social communication and interaction for most people. Socially isolated individuals with disabilities have gained exposure to social environments through social media. Moreover, the broad range of information available on the internet has increased access to resources such as government services, health services, and social services support. On a related point, assistive devices have enabled disabled people including many seniors to overcome motor, sensory, or cognitive difficulties that may have previously hindered them from performing daily tasks. However, although AI and VR technology has been effectively integrated in the lives of those with disabilities, many such individuals lack access to commonplace technologies, like a personal computer. This paper examines how AI and VR technology has enhanced communication, information access, and everyday activities for the disabled and aging communities despite such socio-economic limitations.

1. Introduction

Disabilities come in different forms such as vision, hearing, and color blindness (to name a few), which means different assistive technologies need to be combined to achieve compliance.

Technology has unequivocally and ubiquitously revolutionized the way we live. Automobiles and flights have transformed the speed and scope of transportation, computers have connected the population with unprecedented efficiency, and social media has overhauled the methods, pace, and transparency of human interaction.

Although historically deemed unable to live productive and independent lives, individuals with disabilities are increasingly enabled by efficient and streamlined tools that

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make life simpler. Technology has enhanced accessibility and empowered people with disabilities to participate in society more completely than ever before. Technological devices allow individuals with disabilities to overcome a multitude of physical, verbal, and mental impairments. The internet, social media in particular, has provided the ability for increased social interactions for people with disabilities and seniors, mitigating social isolation. Communication devices have the potential to improve mental health by allowing others to share experiences and provide catharsis, therefore also alleviating mental and emotional strain. Assistive devices allow people with disabilities and seniors to perform normal day-to-day activities they would be unable to do otherwise—especially with respect to sensory impairments. Technology has served as a boon for the disabled and aging population to realize more fulfilling lives in society.

2. The Use of Artificial Intelligence for Disabilities

2.1 Communication Disorders and Education

Artificial Intelligence has made technological aids more affordable, accessible, and portable to the general public. The World Health Organization has estimated that around one billion people live with a disability, and many of them experience verbal and motor-skill delays and deficits. Because of their language and motor impairment, it is difficult for them to participate in social activities and education. Primary diagnosis such as Autism Spectrum Disorder (ASD), cerebral palsy, and aphasia are the most common disorders accompanied by language and speech impairments. They often find it difficult to express their thoughts and not many people take the time to try to understand and communicate with them. To this population, adaptive applications, commonly known as Augmentative and Alternative Communication (AAC), are necessary [7].

These AAC devices synthesize speech and sound based on the user's selection of words and images. For instance, if a child wants an apple, he can press on a picture of an apple on the device, and the device says the word "apple" out loud. These AAC devices used to be expensive, heavy and bulky, and not easily accessible to the general public, but now they can be easily downloaded on smartphones and tablets. For instance, LIVOX is an Android application that not only functions as an AAC but also allows the user to change the settings to their comfort. The user can customize the number of items on the screen, adjust for repetitive touch behaviors, and change the size of the words and images, in order to meet the needs of the user. Furthermore, the application is self-adaptive and automatically returns to the main page when it detects that the user is done with the sentence. A particular study has shown that when used in different contexts, such as at home, at a school, and in a restaurant, the participants with a communication disorder were able to utilize the AAC application for communication of basic needs and desires, learning letters, interacting in different social contexts, and communicate their routine at home. Indeed, technology has allowed people with language and speech challenges to become better socially integrated by allowing this population to communicate with others in different contexts [7].

2.2 Visual Disabilities

Technology has made significant changes in the lives of people with visual disabilities as well. People who are visually impaired face restrictiveness, since they need manual information about their environment, while carrying out daily tasks like eating and walking. For instance, there is an application called Object Recognition, which uses the smartphone camera to take pictures, convert the image into HSI (Hue Saturation Intensity), and detect what the object is. There are also applications that assist with speech synthesis and text recognition. It recognizes the text from a document or a pdf file and reads it out loud to the person; other applications can recognize text from images and convert it to speech [8].

Many different AI companies are working on wearable technology that can meet the needs of people who are visually impaired. For instance, a company called Navcog has recently invented a software which uses someone's smartphone camera and Bluetooth technology in order to provide live directions to the user [9]. The camera converts the images into a 3D map and provides auditory directions through earphones for the user. Similarly, a company called MyEye is working on a finger-sized device that one can attach to a pair of glasses, which can identify objects, people, and obstacles [9]. It is important to note that many companies are recognizing the impact technology can have on those with impairments and are working on ways to incorporate technology to augment people's lives and independence [8].

2.3 Smart Homes and Independent Living

Devices such as the Amazon Echo, Google Home, and Apple HomePod has reshaped the lives of many senior citizens and people with disabilities and has started promoting more independence [16]. These are voice-activated smart speakers, which can act like an "assistant" for things around the house. For instance, one can turn on household lights, turn on the heat or air conditioning,

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change the TV channel, and even start the robotic vacuum cleaner by telling the device to do so. The smart devices allow people to communicate and perform tasks easily, as well as improve the safety of senior citizens and people with disabilities who live alone. When they fall or start having medical emergencies, they can easily speak out loud and tell the device to call emergency services or a family member for assistance [17]. More recently, companies have updated their artificial intelligence technologies to assist people who are blind, deaf, or who have motor impairments. They are continuing to improve their technology in computer vision and voice recognitions [16].

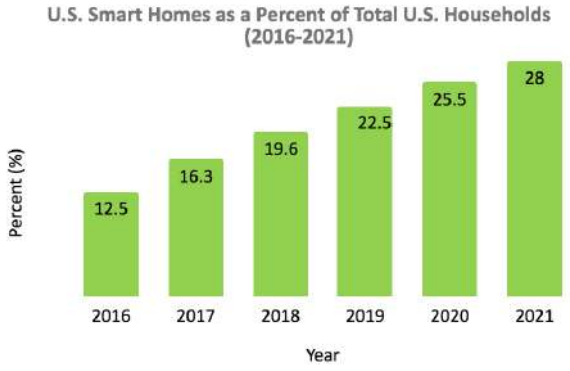

Figure 1. This graph shows the steady, projected increase of smart home usage, from 2016 to 2021 in the United States

2.4 Accessibility and Self-Driving Cars

Self-driving cars is another example of AI that can tremendously affect the lives of people with disabilities [17]. The ability to leave the house and drive yourself to a market when you need something is a basic yet overlooked skill in people with disabilities. However, technology advancements in the automobile industry shows promising hope to further assist people with disabilities. Tesla, for example, has an automated driving mode, called autopilot mode, that requires very minimal control from the driver. The automobile also has a self-park option as well as a "summon" feature, where the car moves autonomously for a few feet in the driveway or parking lot, to make it easier for passengers to get in. This new technology also has many safety features, such as automatic emergency braking, side collision warnings, and blind spot warnings [18]. The cars also utilize AI for depth perception, to interpret what objects and people are in front of the car. The development of AI technology in automobiles dissolve the barrier of transportation and accessibility for people going to work, meet friends, and perform daily activities [17].

3. Utilization of Virtual Reality for Disabilities

3.1 Overcoming Social and Emotional Barriers with Virtual Reality

Virtual Reality Exposure Therapy (VRET) is often used for people with underlying conditions such as depression, anxiety, ASD, and social anxiety. VRET can be used as an alternative to the traditional exposure-based therapy and is more immersive to the actual environment, because it allows sensory stimulation. A meta-analysis concluded that VRET is highly effective in treating anxiety disorders, including post-traumatic stress disorder, panic disorder, and specific phobias from a simulated exposure to the stimuli [11].

Furthermore, people with underlying conditions such as ASD, mental disorders such as depression, and learning disabilities are more likely to experience discrimination, isolation, and social anxiety. Social situations can be stressful, in addition to excessive stimulation such as light, background noise, and crowds of people. These daily-life simulations may be stressful and become a huge sensory barrier on this population for independent living. Using smartphones and affordable VR headsets, it is possible to use VR as a form of exposure therapy in order to help this population better prepare for certain social situations, also known as Virtual Reality Exposure Therapy (VRET) [12]. One specific application focuses on interactions at the Aberdeen International Airport. Through the VR interaction, users can gain exposure to the entrance and check-in gates, bathrooms at the airport, a coffee shop, and the boarding gate. The user can line up at a crowded check-in gate and become more familiarized with the noise, lighting, and the layout. They can also rehearse their interactions with workers as well as adjust their expectations for the real situation [12].

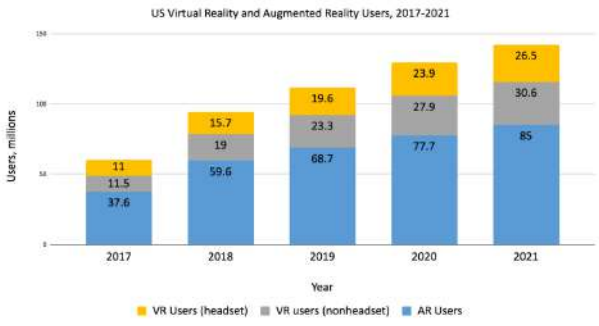

Figure 2. This graph shows the steady increase of VR and AR usage, from 2017 to 2021 in the United States

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3.2 Virtual Reality for Intellectual Disabilities

The utilization of VR technologies for people with Intellectual Disability (ID) is starting to become recognized. VR training uses VR environments to explain and teach certain skills, or independent living skills, to this population. This training allows learning skills in a safe environment and generalization into real life. One study examined the effects of a VR application on a tablet, which provides information on general knowledge and family orientation, simulation of taking the right medications at the right time, practicing packing a suitcase for a trip, buying the things on a grocery list at the supermarket. Adolescents and adults with ID showed significant improvements in functional living skills. Through VR training, that was easily managed at home, the skills that they acquired were effectively generalized into the real-life situation. VR training is beneficial not only due to its easy directions but also because it may allow remote rehabilitation of people with ID, without a presence of a supervisor or a behavior therapist.

3.3 Overcoming Physical Disabilities

Cerebral Palsy (CP) is a congenital condition that causes motor function followed by paralysis and disturbances in sensation [13]. Oftentimes, a patient with CP either exhibits impaired body structure and function, such as involuntary spasms, hypertonicity, and muscle weakness. They have poor, delayed fine motor skills and have restrictions in their daily activities [13]. VR applications, such as Xbox Kinect or the Wii, can be utilized as an interactive simulation for a patient with CP to practice and perform functional activities. VR provides an ecologically accurate environment for CP patients to perform task-specific practices. It also incorporates a social play component and encourages interaction with friends and family. Studies have shown that children with CP experienced improvements in ambulation, posture control, and arm function. Although a professional, engineer-built VR system often has a better effect, commercially available VR systems can be a good alternative and have a significant effect on mobilization improvements for this population [14].

Similarly, VR therapy can be used to help patients with stroke with their balance and gait ability [15]. Stroke patients are heavily affected by motor impairment, especially in the legs. Their balance and walking ability is negatively affected, as they experience muscle weakness. Impaired gait and balance can lead to future falls and injuries, especially dangerous for older patients. In the past, rehabilitation therapy involved high-intensity, repetitive tasks. VR intervention allows clients to play games that incorporate components of physical therapy. Studies on virtual reality rehabilitation therapy reveal that VR training has a stronger effect on balance and gait improvement than conservative therapy [15]. VR allows stroke patients to repetitively train themselves without any additional equipment, which may have contributed to the improvement in outcome. Furthermore, because VR therapy is more fun and enjoyable, due to the "play" nature of the therapy, participants were more likely to be motivated to participate in the intervention [15].

4. The Role of AI in Web-based ADA Compliance

A data obtained from recent research analyzing 10 million web pages shows a very low level of Americans with Disabilities Act(ADA) compliance globally. Some of the key takeaways include:

(1) 98% of websites failed to satisfy the requirements relating to menus;

(2) 52% of websites failed to implement proper alt attributes for images (actually deemed a decent percentage);

(3) 89% of websites failed to meet the minimum compliance level of popups (considering popups break the entire compliance level of a website, this is pretty bad);

(4) 71% of websites failed to make sure forms are accessible;

(5) 83% of websites failed to have WCAG compliant buttons, largely due to missing tags;

(6) 22% of websites failed to comply with link requirements — by far the most compliant group of website elements, mainly due to default browser settings.

Those are just some of the more noticeable accessibility requirements websites must include to be compliant. The research paints a grim picture of the current state of ADA, stemming from either lack of focus or unawareness of the severity of the issue.

5. Web Content Accessibility Guidelines (WCAG) 2.2 in Development

Arguably the best way to prepare a website accessibility is to design and build with web accessibility in mind. However, in the majority of cases, that's not effective because a foundation is already set and achieving accessibility manually is near impossible due to the sheer scope of requirements.

This is where AI steps in. There are a few services that specialize in this area, powered by machine learning technologies that scan and analyze every aspect of a site's design. The Accessibility Guidelines Working Group (AGWG) has published a First Public Working Draft of

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WCAG 2.2. Additional success criteria in development for 2.2 address the needs of people with cognitive or learning disabilities, users of mobile devices, and users of ebooks.

To understand how artificial intelligence can help, we first need to get a glimpse of WCAG 2.0 and WCAG technical standards. They are organized under four principles: perceivable, operable, understandable, and robust. Simplified, a website needs to be/have:

(1) Easy to navigate using keyboard-only commands besides simple mouse navigation;

(2) The information presented easy to find and process;

(3) Adjustable to evolving needs of the users;

(4) Easy to comprehend.

It's a lot of ground to cover. As expected, automated testing allows for a quicker discovery and resolution of potential interference and issues. However, an AI-powered solution differs from its more basic automated testing counterparts due to its ability to mimic a browser. It can thoroughly understand a website's structure and the role of its various elements, particularly those that are hidden and only show up upon action.

6. Digital Disparity

Developments in technology have improved the expectations of those with disabilities by enhancing their capacities and optimizing their quality of life. Technology has provided individuals with verbal disabilities a chance to communicate, with audial disabilities a chance to hear, with mobile restrictions a chance to explore. When people are more exposed to social environments, they can experience higher levels of social and personal growth, as well as the ability to make impactful contributions. Such technological advances are increasingly allowing people with physical disabilities to live a more participatory and stimulating lifestyle.

Previous data suggests a large correlation between certain socioeconomic factors and the use of technology. Unfortunately, many individuals with disabilities do not have personal computers with internet connection in their household, or lack access to resources that can provide such technology. As resources evolve and improve, this lack of accessibility creates a digital divide in societal systems. Understanding the relationship between social status and access to technology is essential in this research.

People who live in neighborhoods of above average socioeconomic status have greater access to technology. Those who live in neighborhoods of lower than average socioeconomic status may have limited access to technology. This creates a digital divide between subpopulations of people with disabilities. This research examines strategies to eliminate digital disparity and provide technology for all individuals with disabilities.

7. The Internet and Global Connectivity

The invention of the internet has transformed modern society, changing the way people obtain information, interact with others, shop for products, and consume media. For individuals with disabilities, the internet provides an escape from isolation. Internet access has greatly improved communication for individuals with disabilities, in addition to enhancing their independence and self-sufficiency. Improved physical and mental health outcomes have also been reported as a result of internet use.

The internet encourages people with disabilities to be more visible and participate more fully in society. However, before people with disabilities can use the internet for communicating, learning, or working, they must be able to gain access to it. This often requires additional assistance by other people or by modified hardware and software. Those with disabilities are less likely to live in households with computers that are connected to the internet and are therefore less likely to be online. Even if they do have access to computers with an internet connection, they may need the assistance of adaptive hardware and software. For example, a text reader is necessary for someone who is blind, and a speech-to-text program is required for someone with mobility issues that limit typing.

Developing standard adaptive hardware and software is often difficult due to the broad range of disabilities. An individual with hearing disabilities may solely require hearing aids, while others may require a sign language interpreter. Universally, closed captions for video and audio material are key to successfully navigate and interact. Adaptive hardware and software are also necessary for individuals with vision disabilities. For those with reduced vision, a screen magnifier may suffice. However, for individuals with more significant visual loss, a screen reader that converts text to speech output may be required. In addition, braille readers that convert text to braille may be helpful.

People with physical disabilities are often unable to use a standard keyboard. In such cases, alternative keyboards with larger keys, different key arrangements, touchscreens, or speech recognition software using voice command may be warranted. Some individuals may have poor hand or voice control, such as in severe cases of stroke or multiple sclerosis. Assistive technologies exist and continue to emerge, allowing individuals to utilize their head, mouth, or eye movements as alternatives to a traditional mouse or keyboard.

For those with speech impairment, communication through discussion boards, blogs, and other social net-

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working tools can be beneficial. Communication with speech output can be used when speech is necessary. For people with cognitive impairments such as learning disabilities, technology plays a large role in increasing or maintaining their independence. Tools such as a spell checker, grammar checker, word prediction, and voice recognition programs are valuable.

Many people with disabilities use the internet for social interactions and cathartic support. We increasingly use the internet to develop and sustain relationships, as exemplified by the dominance of Facebook, Twitter, and other social networks and dating sites. In addition, there are many online resources to assist individuals if they need information about their disabilities.

Given the benefits of internet use, efforts to increase access to computers with internet connection in disabled communities should be a priority. These social connection points can be a source of support, and further support can be found on informative sites relating to disabilities that assist in understanding, awareness, and even solutions to minimize the impact of disabilities.

Table 1. Percentage of all US adults and seniors over 65 who go online each year, from 2000 to 2012

Year	% of all adults 18+ who go online	% of seniors who go online
2000	50	14
2002	59	19
2004	62	22
2006	74	35
2008	75	35
2010	79	41
2012	86	59

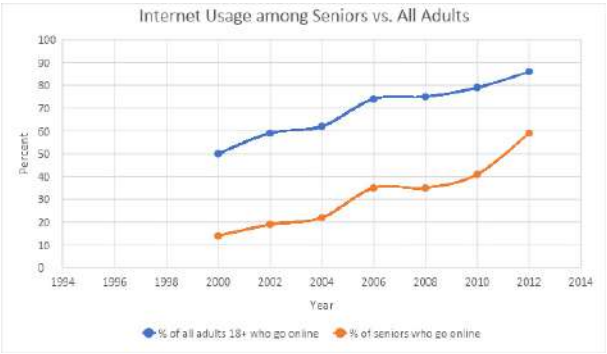

Figure 3. This graph shows the steady increase of adults and seniors who use the internet from 2000 to 2012

An increasing number of seniors are adapting to technology. As shown in Table 1 and 3, only 14% of seniors were internet users in 2000. In 2012, however, 59% of seniors adopted technology and became internet users. While still significantly below the national average, internet usage among seniors is steadily rising. This shows potential for seniors to adopt technology that will assist them in their day-to-day lives.

8. Assistive Devices

Advances in technology support the independence and security of seniors and those with disabilities. Assistive devices are used to compensate for motor, sensory, or cognitive difficulties in disabled and aging populations. Some of these difficulties include the inability to make continuous motions, lack of coordination, and hindrances in visual and auditory abilities. Such physical impairments make it difficult for people with disabilities and seniors to operate within the home. Assistive devices such as powered wheelchairs and stair climbers help individuals with limited motor functions become more mobile. Cognitive orthotics, including simple reminder systems and interactive robotic assistants, serve as technological support for cognitive aging.

Cognitive orthotics provide technological support in two different dimensions. The first dimension relates to executive function, or information processing. This function controls planning, task prioritization, self-monitoring, and problem solving, as these are related to memory, attention, and orientation. The second-dimension concerns attempts to strengthen intrinsic abilities (rehabilitation technologies) or to provide extrinsic support (compensation technologies). Cognitive orthotics requires monitoring of one's environment, as tracking one's actions is the best method of assessing health and independence.

The purpose of technological aids involves maintaining independent functionality, security, autonomy, and safety, as well as to provide both synchronous and asynchronous means of connecting with distant family members and friends. Overall, technology can facilitate the security of people with disabilities and seniors to compensate for age and disease-related problems. Technology can help older adults delay and possibly avoid a decline in function while maximizing their ability to live independently. Technology related to living environments of the disabled and aging populations can provide cognitive assistance, monitoring, and social communication.

Technological advancements such as security systems, webcams, and built-in communication systems allow people with disabilities and seniors to feel protected from intruders and other safety issues. These advances also allow family members to feel more secure about leaving a senior at home alone. Moreover, in terms of home health and wellness, systems such as health management apps help ensure the elderly family member or person with dis-

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abilities takes his or her medication and is self-sufficient. One example of a health management app is MHealth, which also helps the elderly and people with disabilities to track their overall wellness with other family members.

9. Discussion

Technological innovation can break traditional barriers that exist for people with disabilities while diminishing their exclusion and marginalization. Information and Communication Technology (ICT) devices and services can provide opportunities for people with disabilities to access lifelong education, skills development, and employment while facilitating communication and information distribution. According to a recent survey of 150 experts, websites and mobile devices can contribute to the social inclusion of people with disabilities. Text-to-speech, voice recognition, ability to change contrast and color schemes, touch and gesture input, and screen magnification features are already available

It is crucial to understand the disability divide as about 15 percent of the world's population lives with one or more disabilities. Discrimination exists in employing those with disabilities, which is illustrated by employment rates. The employment rate of people with disabilities are a third to half of the rate for those without disabilities. The unemployment rate among people with disabilities is as high as 80 to 90 percent in developed and developing economies. Unfortunately, lower education and lower productivity in the workplace results in a wage disparity among those with disabilities as compared to individuals without disabilities. Implementing community programs that help those with disabilities learn workplace technology will lessen the high rate of unemployment.

However, there are several barriers and challenges that people with disabilities and seniors face when using new technologies. These include physical challenges to using technology due to disability, handicap, or chronic disease, as well as skepticism about the benefits of technology and difficulties learning to use new technologies. Financial barriers can also influence the accessibility to these technologies. Individuals with disabilities and seniors should increase their engagement with technology and the digital world, so companies and innovators should focus on how to make alternative technology more affordable. It is important to overcome the difficulties and learn how to use technology as there are many benefits to their mental health, daily life, and professional life. Communication channels also allow them to connect with more people and maintain relationships with them. In addition, it allows them to find large amounts of health-related information beneficial to their health. It is imperative to address such issues and find ways for more seniors and those with disabilities to embrace technology.

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ARTICLE

PARK16 rs708730 Polymorphism Decreases Parkinson's Disease Risk in European Ancestry Population: A Meta-analysis

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PARK16 rs708730 polymorphism

ABSTRACT

Parkinson's disease (PD) is a complex fatal chronic neurodegenerative disease most common in elderly people. The early genome-wide association studies (GWAS) found that the minor allele variant of PARK16 rs708730 polymorphism is a significant protective factor for PD in Caucasian populations. However, these results cannot be repeated by the following studies in Caucasian populations and other populations. We considered that the inconsistency of the findings may be caused by the small-scale samples or the heterogeneity among di□erent populations. Therefore, in this study, we synthesized the previous related GWAS studies through three authoritative sources, and used the large-scale samples (10,645 PD cases and 30,499 controls) to reevaluate the association between rs708730 polymorphism and PD. The results showed that there is no association between them in Asian ancestry population. While, in European ancestry population, we found that the minor allele variant (G) of rs708730 polymorphism is significantly associated with a decreased risk of PD. Collectively, our findings further verified the association of rs708730 with PD and show its genetic heterogeneity among different populations, which can help to develop a better understanding of the PD's pathogenesis.

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1. Introduction

Parkinson's disease (PD) is a chronic progressive complex neurodegenerative disorder, and it is common in elderly people [1,2]. Particularly, the prevalence of PD in the people aged above 60 years is more than three times that in entire population [2]. Another study further showed a rising popularizing rate of PD with age (425 per 100,000 in individuals aged 60-69 years, 1087 in 70-79 years, and 1903 in aged above 80 years) [3]. PD is characterized by the dopaminergic neurons prominent death in substantia nigra and Lewy body formation [4,5]. A previous study predicted that the newly diagnosed PD patients are expected to reach as many as 8.7-9.3 million by 2030 from 4.1-4.6 million in 2005 around the 15 most populous nations [6].

The variants in a specific gene region, which is designated as PARK16 (1q32), are considered to play an important role in pathogenesis of PD [7-9]. In this region, the single nucleotide polymorphism (SNP) rs708730 (G < A) was identified significantly associated with PD in Caucasian populations by a large-scale genome-wide association studies (GWAS) [10]. Particularly, Sanchez et al. collected and analyzed 14,075 Caucasian individuals (including 5,272 PD patients and 8,803 controls) from USA, Germany and UK by GWAS. They found that the rs708730 polymorphism minor allele variant (G) can reduce the risks of PD (odds ratio (*OR*)=0.90, $P=1.59\times10^{-3}$) [10].

However, the consistent and inconsistent results for the effect of rs708730 variant on PD in USA, UK, China, Japan and Korea populations have been reported by the subsequent studies. For example, by analyzing 2,000 PD and 1986 control Caucasian subjects from USA, Hamza et al. also found that the rs708730 polymorphism minor allele variant is a protective factor for PD (*OR*=0.87, *P*=0.03) [11]. While according to the results of two independent studies, the rs708730 is found not associated with PD in UK (*OR*=0.98, *P*=0.82) [12] and China populations (*OR*=0.81, *P*=0.19) [13], respectively. Further, Satake et al. and Chung et al. selected 20,392 (including 2,011 PD patients and 18,381 controls) and 2,244 (including 1,036 PD patients and 1,208 controls) individuals from Japan and Korea, respectively, and they found that the minor allele of rs708730 are associated with an increased risk of PD (*OR*=1.33 and $P=2.43\times10^{-8}$ for Japan population [14]; *OR*=1.22 and *P*=0.008 for Korea population [15]).

We considered that the inconsistency of the findings may be caused by the small-scale samples or the heterogeneity among dierent populations. To overcome these defects and enhance reliability of the results, we selected a more complete sample set by searching the PubMed, ClinicalKey and Google Scholar databases. The large-scale samples include 10,645 PD patients and 30,499 controls from nine related GWAS studies, which are involved in European and Asian ancestry populations. Then, according to the method used in the previous studies [16-24], we conducted a meta-analysis to reevaluated the association between rs708730 polymorphism and PD. Further, we explored the heterogeneity among different populations and assessed the association between rs708730 and PD in Asian and European ancestry populations, respectively.

2. Methods

2.1 Literatures Acquisition and Studies Selection

We selected all the possible studies by searching PubMed (http://www.ncbi.nlm.nih.gov/pubmed) and ClinicalKey (https://www.clinicalkey.com/) databases, respectively, using the keywords: "Parkinson's disease" and "rs708730", or "Parkinson's disease" and "PARK16". We collected all these literatures from the two databases before the last update on September 25 2018. And then, the Google Scholar (http://scholar.google.com/) was further used to query all the references of the studies and the articles citing these studies identified from PubMed and ClinicalKey databases.

After that, the appropriate studies were identified according to the following criteria: (1) The study is designed according to the case-control strategy. (2) The study evaluates the association of rs708730 polymorphism and PD. (3) The study provides the number of cases and controls. (4) The ethnicity of each individual in the study was presented clearly. (5) The number of rs708730 genotypes both in cases and controls are provided by the study or it provides enough data to calculate these. (6) The *OR* value with 95% confidence interval (*CI*) and the *P* value are provided by the study or it provides enough data to calculate these.

2.2 Data Extraction

The following information from each of the selected studies was extracted: (1) The publication year and the first author of these studies. (2) The ethnicity and population of the participants in these studies. (3) The number of PD patients and healthy controls in these studies. (4) The genotype information of rs708730 both in the PD patients and healthy controls. (5) The association analysis results (*OR* value with 95%*CI* and *P* value) in these studies. (6) The genotyping platforms. For the genotypes, *OR* value

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and the 95%*CI* as well as the corresponding *P* value, we worked them out using R program (http://www.r-project.org/) if these informations didn't be provided directly.

2.3 Genetic Model Choice

Among the two alleles G and A of the rs708730 polymorphism, G was the minor allele. According to the previous studies [25-29], the allele model (A allele versus G allele), the dominant model (AG+GG versus AA), the recessive model (GG versus AA+AG), and the additive model (AA versus GG) are the common genetic model for the association analysis. Given that only the genotyping data of A allele versus G allele are provided from the selected studies (shown in Table 1), the allele model was used to analyze the association between rs708730 polymorphism and PD in this study.

2.4 Heterogeneity Test

We chose the two common quantities, Cochran's Q and I^2, to measure the heterogeneity among the di erent ethnic groups in this study. Cochran's Q approximately follows a chi-squared distribution whose degrees of freedom is k-1 (where k is the number of studies), and the I^2 value is calculated through Cochran's $Q\left(I^2 = \frac{Q-(k-1)}{Q}\times 100\%\right)$, which ranges from 0 to 100%. Usually, the low, moderate, high and extreme heterogeneity are tentatively assigned to the I^2 value of <25%, 25-50%, 50-75% and >75%, respectively. According to previous studies, when the I^2>50% and P<0.01, the heterogeneity among different ethnic groups is deemed significant in this study [25-29].

2.5 Meta-analysis and Subgroup Analysis

Usually, there are two models (fixed e ect model and random e ect model) used for meta-analysis. According to the results of heterogeneity test, we used the random and the fixed e ect model in the meta-analysis when heterogeneity is significant or not, respectively [30]. In meta-analysis, we calculated the pooled *OR* value and its 95%*CI* as well as the corresponding *P* value to measure the association between the rs708730 polymorphism and PD based on the Z test. The meta-analysis was performed by the R package 'meta' (http://cran.r-project.org/web/packages/meta/index.html). By most criteria, the threshold of significant association was set as 95%*CI* of *OR* value do not include 1 and. And then, we further split the original samples into European and Asian ancestry populations, and performed the meta-analyses in each subgroup, respectively.

2.6 The Sensitivity and Publication Bias Analysis

By most criteria, we used the two methods, Begg's test [60] and Egger's test [61], to evaluate the publication bias in this allele model. When the *P* values are less than 0.05, we deemed the publication bias is significant. Then, the funnel plot was drawn to show the results of the publication bias analysis based on its asymmetry. Finally, we performed the sensitivity analyses. For this purpose, each of the selected studies was excluded from the whole sample orderly to assess the influence of these studies one by one.

3. Results

3.1 Study Collection and Data Acquisition

Through the keyword search in PubMed and ClinicalKey databases and the filtration according to these criteria (see Methods for details), we identified a total 5 articles and corresponding 9 studies in them which include 10,645 PD cases and 30,499 controls from European and Asian ancestry populations. Moreover, another related study involved in Asian ancestry population was further obtained by checking the citation using Google Scholar. The workflow was shown in Figure 1. Then, we extracted the characteristics of these 9 studies, and the main contents were exhibited in Table 1. Finally, we counted the rs708730 polymorphism genotype data of each study for the following meta-analysis (Table 2).

Figure 1. The flow chart of studies selection for re-evaluating the association of SNP rs708730 with PD

Table 1. The main contents in the selected studies for this meta-analysis

Study	Year	Country	Ethnicity	No. of cases	No. of controls	Genotyping platform	Kind of genotype
Sanchez *et al.*(Stage I)	2009	USA and Germany	European	1,063	3,071	HumanHap550	G/A
Sanchez *et al.*(Stage II)	2009	USA, UK and Germany	European	3,452	4,756	Illumina	G/A
Pankratz *et al.*	2009	UK	European	857	867	Illumina	G/A
Hamza *et al.*	2010	USA	European	2,000	1,986	Illumina	G/A
Yan *et al.*	2011	China	Asian	226	230	ABI 3100 automated sequencer	G/A
Satake *et al.*(Stage I)	2009	Japan	Asian	1,078	2,628	Illumina	G/A
Satake *et al.*(Stage II)	2009	Japan	Asian	612	14,139	VeraCode	G/A
Satake *et al.*(Stage III)	2009	Japan	Asian	321	1,614	TaqMan	G/A
Chung *et al.*	2013	Korea	Asian	1,036	1,208	Sequenom MassARRAY system	G/A
All				10,645	30,499		

Note: "G/A" means that the data of genotypes G and A are provided by the study both in cases and controls.

Table 2. the genotype information of the selected studies

Study	Year	Ethnicity	Minor allele	MAF in case/control	PD.G	TOTAL.G	PD.A	TOTAL.A
Sanchez *et al.*(Stage I)	2009	European	G	0.15/0.17	319	1363	1807	6905
Sanchez *et al.*(Stage II)	2009	European	G	0.16/0.17	1105	2722	5799	13694
Pankratz *et al.*	2009	European	G	0.17/0.17	291	586	1423	2862
Hamza *et al.*	2010	European	G	0.16/0.17	640	1315	3360	6657
Yan *et al.*	2011	Asian	G	0.19/0.23	87	192	365	720
Satake *et al.*(Stage I)	2009	Asian	G	0.14/0.18	302	1248	1854	6164
Satake *et al.*(Stage II)	2009	Asian	G	0.15/0.17	1040	25077	184	4991
Satake *et al.*(Stage III)	2009	Asian	G	0.12/0.18	565	3212	77	658
Chung *et al.*	2013	Asian	G	0.19/0.22	1678	3563	394	925

Note: MAF: Minor allele frequency

3.2 Heterogeneity Test

Given that only the genotyping data of G and A allele are provided from the 9 studies, we first tested the heterogeneity of all these samples based on the allele model. We found a significant genetic heterogeneity of rs708730 polymorphism among these selected samples (I^2=83% and P<0.01). Therefore, according to the ethnicity of these samples, we further tested the rs708730 polymorphism heterogeneity in European and Asian ancestry populations, respectively. We also found a significant genetic heterogeneity of rs708730 polymorphism among Asian ancestry populations using the allele model (I^2=90% and P<0.01). However, we did not identify the significant genetic heterogeneity among the European ancestry populations (I^2=0 and P=0.63).

3.3 Meta-analysis and Subgroup Analysis

Because we observed a significant heterogeneity for all these samples, we performed a meta-analysis to assess the association between rs708730 polymorphism and PD using the random e ect model. We have not found a significant association for the comprehensive population based on the allele model (*OR*=0.989, 95% *CI*=0.878-1.115, *P*=0.875). The corresponding forest plot was described in Figure 2. Given that the genetic heterogeneity of rs708730 polymorphism in the comprehensive population is significant, we further divided these samples into Asian and European ethnicity subgroups. According to the results of heterogeneity, we performed the meta-analyses using the fixed e ect and random e ect model for the European and Asian ancestry populations, respectively. Still, we have not observed a significant association between rs708730 polymorphism and PD in the Asian ancestry population (*OR*=1.055, 95% *CI*=0.811−1.372, *P*=0.689) (Figure 3a). However, the significant association was identified in the European ethnicity subgroups. Particularly, we found that the minor allele G of rs708730 polymorphism is significantly associated with a reduced risk of PD in European ancestry population

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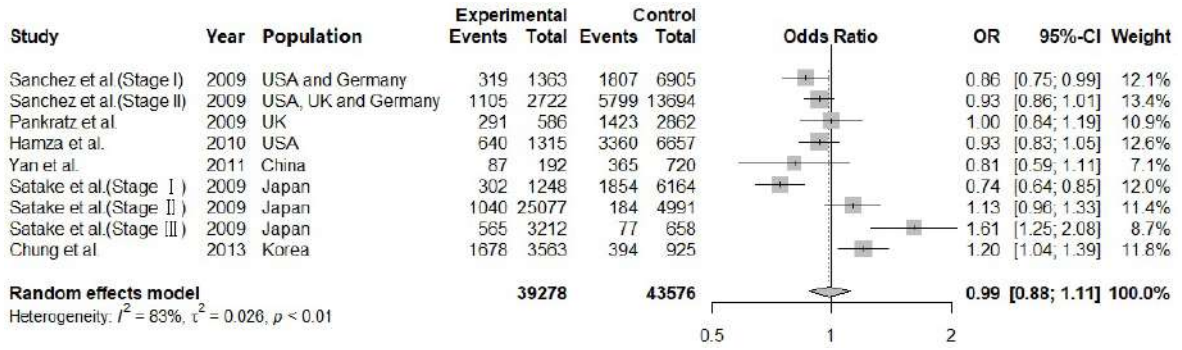

Figure 2. The forest plot showing the results of the meta-analysis in allele model.

Note: Because the genetic heterogeneity of rs708730 polymorphism in the comprehensive population is significant, we used the random effect model to perform the meta-analysis of all 9 selected studies in the allele contrast (G versus A)

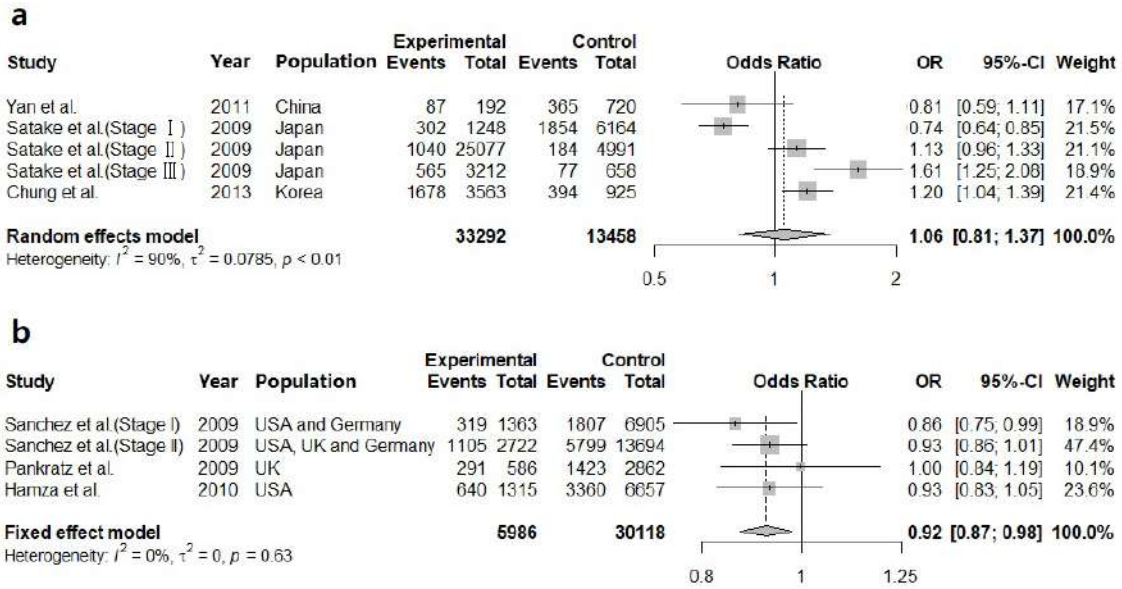

Figure 3. The forest plot showing the results of the meta-analysis in subgroups.

Note: (a) In Asian ancestry population, the significant association between rs708730 polymorphism and PD is not observed. While, (b) the minor allele variant (G) of rs708730 polymorphism is significantly associated with a reduced risk of PD in European ancestry population.

(*OR*=0.924, 95% *CI*=0.872−0.979, *P*=0.007) (Figure 3b).

3.4 The Sensitivity and Publication Bias Analysis

After the Egger's test and Begg's test, we found no significant publication bias in all these studies based on the allele model (Egger's test, *P*=0.393, and Begg's test, *P*=0.404). The results were described in a funnel plot (Figure 4). Moreover, we further excluded each study orderly to perform the sensitivity analysis. The results showed that the heterogeneity and the association between rs708730 polymorphism and PD have not changed significantly when excluding any of the studies from the whole. The detailed information was shown in the Table 3.

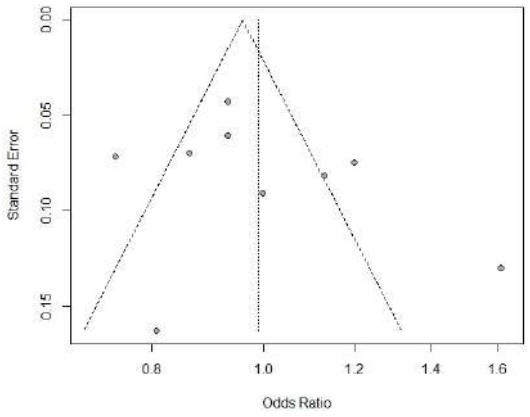

Figure 4. The funnel plot showing the results of the publication bias analysis.

Note: The allele genetic model is used for the association assessment between rs708730 polymorphism and PD.

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Table 3. The result of Sensitivity Analysis in allele model

The omitted study	Year	OR	95% CI	p-value	tau^2	I^2
Sanchez *et al.*(Stage I)	2009	1.0087	[0.8824; 1.1531]	0.8989	0.0292	84.00%
Sanchez *et al.*(Stage II)	2009	1.0005	[0.8624; 1.1608]	0.9945	0.0373	84.70%
Pankratz *et al.*	2009	0.9889	[0.8659; 1.1294]	0.8688	0.0292	84.80%
Hamza *et al.*	2010	0.9993	[0.8685; 1.1497]	0.9921	0.0326	84.80%
Yan *et al.*	2011	1.005	[0.8865; 1.1393]	0.9384	0.0267	84.50%
Satake *et al.*(Stage I)	2009	1.0266	[0.9152; 1.1515]	0.6546	0.0198	78.20%
Satake *et al.*(Stage II)	2009	0.9723	[0.8553; 1.1053]	0.6679	0.0265	83.20%
Satake *et al.*(Stage III)	2009	0.9449	[0.8516; 1.0484]	0.2852	0.0161	76.40%
Chung *et al.*	2013	0.9626	[0.8530; 1.0863]	0.5367	0.0227	80.60%

4. Discussion

PD is characterized by the Lewy body formation and dopaminergic neurons death in substantia nigra, and is most seen in elderly people [1-5]. The previous studies reported that a specific gene region, PARK16 (1q32), plays a key role in PD's pathogenesis [7-9]. And then, the subsequent GWAS studies found that the SNP rs708730 is in PARK16 and its minor allele variant (G) is a protective factor for PD in Caucasian populations [11,10]. However, these results cannot be repeated in China (*OR*=0.81, *P*=0.19) [13], Japan (*OR*=1.33, *P*=2.43×10^{-8}) [14], Korea (*OR*=1.22, *P*=0.008) [15] and another Caucasian population (*OR*=0.98, *P*=0.82) [12]. We considered that the inconsistency of the findings may be caused by the small-scale samples or the heterogeneity among di erent populations. Therefore, after selecting and summarizing the related studies, the larger scale samples and more comprehensive population were used to explore the association between rs708730 polymorphism and PD.

In this study, 9 related GWAS studies (involving in a total 10,645 PD cases and 30,499 controls from USA, UK, Germany, China, Japan and Korea) were selected through three authoritative public databases. Then, we re-evaluated the association between rs708730 polymorphism and PD in European and Asian ancestry ethnicity, respectively. The results showed that there is no association between rs708730 polymorphism and PD in Asian ancestry population (*OR*=1.005, 95% *CI*=0.811−1.372 *P*=0.689). While, in European ancestry population, we found that the minor allele variant (G) of rs708730 polymorphism is significantly associated with a reduced risk of PD (*OR*=0.924, 95% *CI*=0.872−0.979 *P*=0.007). Moreover, we found that genetic heterogeneity of rs708730 polymorphism is significant on the whole (I^2=83% and *P*<0.01). When we split the original samples into European and Asian ancestry populations, the genetic heterogeneity is still significant in Asian (I^2=90% and *P*<0.01) but not European ancestry populations (I^2=0 and *P*=0.63). So, the more similar association studies should be performed in more subgroups of Asian ancestry population.

To our knowledge, this meta-analysis selected the most comprehensive samples by far to explore the association between the PARK16 rs708730 polymorphism and PD. Our findings reveal a significant protective function of rs708730 minor allele variant for PD in European but not Asian ancestry populations, which have further verified the association between rs708730 and PD and also show its genetic heterogeneity among different populations. In summary, the findings of this study would help deepen cognition about pathogenesis of PD.

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ARTICLE

Telepsychiatry: The Evaluation and Treatment of Seniors in Rural Retirement Communities

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ABSTRACT

Few studies examine the benefits from geriatric telepsychiatry in rural retirement communities. **Objectives:** 1. To demonstrate that using telepsychiatry (a) standard approaches to psychiatric evaluation would yield diagnoses in Diagnostic and Statistical Manual of Mental Disorders (DSM-V); (b) psychotherapies and pharmacotherapy could be effectively administered. 2. To examine the relationships among cognition, mood, agitation and functions at baseline and the response to treatment over time. **Design:** Prospective longitudinal study. **Measures:** Geriatric Depression scale (GDS), Mini Mental State Exam (MMSE), Barthel Index (BI), Pittsburgh Agitation Scale (PAS). **Setting:** Video Teleconferencing. **Interventions:** Psychotherapy, psychopharmacology. **Participants:** 428 Seniors over 55, met criteria for at least one DSM-V diagnosis. **Results:** Treatments were administered for a full range of psychiatric diagnoses and age-related medical conditions. The most frequently prescribed pharmacological agents were: antidepressants (78%) antipsychotics (64%), memory enhancers (38%). Participants (66%) received psychotherapy: individual (31%), couple (7%), family (13%). Variation in the MMSE scores were observed: 55% remained stable, 11% declined, 18% improved. GDS Scores improved from baseline to 26 weeks (p=0.02, d=0.99: 95% CI 0.39-1.56). PAS scores declined from baseline to 52 weeks (McNemar's S= 11.27, p=0.0008, d=1.17: 95% CI 0.63-1.68). Function (BI) at week 26 was not statistically significantly different from baseline (t(26)=1.66, p=0.11, d=0.65: 95%CI -0.16-1.42). Participants maintained independence (64.5%) at 52 weeks (McNemar's S = 6.23, p=0.013, d=0.79: 95%CI 0.19-1.36) Conclusion: This study demonstrates the feasibility and benefit of providing a full complement of services via telepsychiatry to seniors and provides a rationale for more comprehensive reimbursement plans .

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Susanne Inez Steinberg and Robert Gallop have nothing to disclose

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1. Introduction

Telepsychiatry has proven feasible in a wide range of settings, across a complement of psychiatric treatments and in different ethnic groups [1,2]. Diagnoses can be made reliably using a variety of assessment measures [2]. Comparisons with in-person care (IP) report benefits attributed to telepsychiatry: shortened hospitalization, better medication adherence, symptom reduction from treatment with evidenced based therapies [3,4].

With respect to geriatric telepsychiatry, a recent systematic review described 68 publications which reflect the current state of knowledge [5]. Of these, 35% investigated neuropsychological testing, had small sample sizes [6,7] with a few exceptions [8,9] confirmed feasibility, satisfaction and correlation between in person (IP) and videoconferencing (VC). Another focus (26%) was clinical diagnosis and treatment of dementia in community dwelling patients using a variety of study designs (one randomized controlled trial (RCT), three crossover, four prospective, six descriptive and two non-controlled feasibility studies). The reliability of the clinical diagnosis of dementia via VC was not inferior to IP [10]. There was a high degree of compliance and satisfaction in the VC group. RCT found comparable improvement in cognition for both groups [11]. Only 10% studied nursing homes for a total of 367 participants. Telepsychiatry in a rural setting was more cost effective for the physician in terms of time and travel than IP consultation [12]. Outpatient studies reported increased expenditures for both modalities [13] and even found VC to be more costly than IP due to the lack of collaboration of local physicians with follow up care [14]. Mixed results reflect different measurements, different venues, cultural variation and the general trend of increasing health care costs. Few papers provide results of psychotherapy: behavioral activation via VC was not inferior to IP (N = 241) [15], improvements gained by problems solving therapy for the depressed and low income persisted longer for VC than IP care (n=158) [16] and cognitive behavioral therapy improved sleep and mood (N=5) [17].

Our prospective longitudinal study collected data from all consecutive referrals meeting eligibility criteria. The assessments and treatment approaches are consistent with best practices in geriatric psychiatry.

2. Objectives

The study goals are: (1) to examine the characteristics and diagnoses of the population referred for telepsychiatry, (2) to determine what types of interventions could feasibly be provided to the participants via this venue, (3) to examine the relationships between cognitive status, mood, agitation and level of independence at baseline and over the period of observation.

3. Methods

3.1 Videoconferencing Telepsychiatry

Forefront Telecare (FT) Inc. delivers behavioral health HIPAA-compliant TeleCare services to rural retirement facilities using high definition monitors and web cam. FT uses 13 technology products for its websites including WordPress (website construction), Vimeo (refined video production) and PHP (embedded server-side scripting ensuring maximum performance and non-interruptible functioning). FT identified the facilities in need of remote services, introduced the psychiatrist (SS) to their teams (nursing, social workers, internal medicine physicians and management) prior to scheduling the resident's appointments for telepsychiatry in order to establish a collaborative model of care known to improve outcomes [18]. Clinical care was scheduled in response to resident needs at the request of onsite physicians and their colleagues. Prior to consultations, the in-house teams provided the psychiatrist with information about the resident's medical health (lab results, imaging reports). The telepsychiatry sessions were staffed by an on-site social worker who accompanied the patient and family to the designated room for sessions with the "TV Doc." and remained throughout the interview. New evaluations required 90 minutes and follow up sessions 30 minutes. The psychiatrist would make recommendations for treatment and the onsite team would implement them. The research assessments were fixed at certain intervals as described in the measures section.

3.2 Participants

Participants were recruited and referred from 9 facilities in central and northern Pennsylvania for psychiatric evaluation and treatment via telepsychiatry all completed by the first author (SS). Baseline and follow up visits occurred from 2012 to 2015. Involvement was discontinued for the following reasons: 16 were discharged (4%), 7 had a lateral transfer to community care as telepsychiatry was ineffective (1.6%), 155 had a consultation only (36%) and 87 died (20%). After these exclusions the final cohort was N=428. The Crozer Keystone Institutional Review Board approved the study and all participants, or their representatives provided informed consent.

3.3 Eligibility Criteria

The participants were eligible if they were age 55 or over and included regardless of race, socioeconomic group,

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or pre-existing medical conditions. Participants were excluded if they were receiving face-to-face therapy in their local community.

3.4 Measures

The measures supplemented a complete psychiatric evaluation using Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria. The measures selected are widely used, well validated, brief, and were administered at baseline and every 6 months thereafter by the psychiatrist (SS).

Geriatric Depression Scale (GDS) The 15-item version Geriatric Depression Scale (GDS) was administered with a cut point of ≥5 suggesting depression. Remission was considered when the score was <5 or 50% of the baseline value.

Mini-mental State Examination (MMSE) The Mini-Mental State Exam is a test of global cognitive function. Scores range from 0-30. Commonly used cut scores for severity: normal 27-30; mild 21-26, moderate >10-20 and severe ≤ 10.

Pittsburgh Agitation Scale (PAS) [19] tests four groups of behaviors: aberrant vocalizations, aggression, resisting care and agitation rated on a four point Likert scale with a maximum total score of 16. Participants with scores of 8 or more required treatment. Remission was defined as a 50% or more decrease from baseline.

Barthel Index (Activities of Daily Living) [20] is a measure of activities of daily living (ADLs) scored from 0-100. A clinically significant decline in independence was defined as a change from independence (≥50) to dependence (<50) or a decline of 10% in the mean score from baseline.

3.5 Statistical Analysis

The analysis consists primarily of descriptives (i.e. means with standard deviation and frequencies/percent). Parametric analyses included t-test for comparison of a binary and continuous measures, ANOVA for comparison of a categorical and a continuous measure. To assess for relationships over repeated time points, we used the paired t-test for continuous measures, McNemar's test for binary measures. Cohen's d Effect sizes with 95% confidence intervals are derived for all continuous measures. For binary measures, odds ratio and chi-square tests are converted into Cohen's d per Chinn S (2000) [21], which allow the use of Cohen's guidelines of 0.2, 0.5 and 0.8 to classify the effect size as small, medium or large for clinical interpretation [22]. All analyses are two tailed with type I error <0.05. All analyses were performed using SAS, version 9.4 [23].

4. Results

4.1 Characteristics of the Study Population

The mean age of the cohort at baseline (N=428) was 80.4 (sd = 9.6; range 55-102). Women constituted 64% of the sample. The population was 99% Caucasian, reflecting the demographics of the region. The majority was single (68%). Most participants (75%) had been skilled or unskilled laborers. Although they were living in retirement facilities, their level of independence varied. Most required long-term care (71%). Others had short stays for rehabilitation (12%) or lived relatively independently in apartments or cottages (7%). Few facilities had dementia units and only 11% of the participants resided there. (Table 1)

Table 1. Characteristics of the Population*

Characteristic	Number	Percentage
Age, years		
55-64	28	7
65-84	236	54
85-99	161	38
100+	3	1
Gender		
Female	273	64
Race		
Caucasian	425	99
Education, years		
< 12	164	39
12-16	243	57
>16	18	4
Marital Status		
Married	136	32
Single	44	10
Divorced	44	10
Widowed	204	48
Children		
Yes	346	81
Occupation		
Management	38	9
Professional	38	9
Sales	31	7
Clerical	60	14
Skilled Laborer	43	10
Laborer	145	34
Homemaker	50	12
Not in workforce	22	5
Residence		
Dementia Unit	47	11
Assisted/Independent	28	7
Long Term Care	302	71
Short Term Care	51	12
Primary Payer		
Medicare	166	39
Medicaid	146	34
Commercial	58	14
Private pay	54	13

Note: * N = 428

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4.2 Psychiatric Disorders

Psychiatric history was present in 219 (51%). In Figure 1, some disorders have been clustered due to the sample size. For example, mood disorders include major depressive and bipolar disorders. Mood/Anxiety disorders due to a general medical condition were common 54(13%). Anxiety disorders 32(8%) include generalized anxiety disorder and panic disorder. Schizophrenia includes schizoaffective disorders, diagnosed in 23(5%). Adjustment disorders 53 (12%) include the different subtypes: anxiety, depression and conduct. Some disorders are noteworthy. Persistent Complex Bereavement Disorder occurred in 38 (9%) of participants. Personality Disorders 17 (4%), Alcohol Use Disorder 32(8%), Other Substance Use Disorder 3(0.7%) and Gambling Disorder 1 (0.2%) continue in late life. Hoarding Disorder was diagnosed in 5 (1%) of participants.

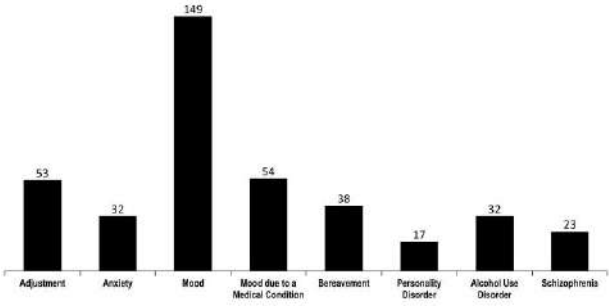

Figure 1. Psychiatric Disorders (N)

Major 218 (51%) and mild 102 (24%) neurocognitive disorders were present. Of these 67 (16%) were unable to complete the MMSE. The neurocognitive disorders were due to Alzheimer's 114 (27%), Vascular 71(17%), Lewy Body Disease 16(4%), Parkinson's 47(11%), Frontal Temporal Lobar Degeneration (FTLD) 8(2%) and a mixed group 53 (12%). The mixed group of neurocognitive disorders included: infections (Creutzfeldt Jacob Disease-CJD), Huntington's disease (Figure 2). Those who met criteria for a major neurocognitive disorder were significantly more likely to have a psychiatric history (X^2 =30.5, df = 1, p < 0.0001, d=0.53: 95%CI 0.33-0.72).

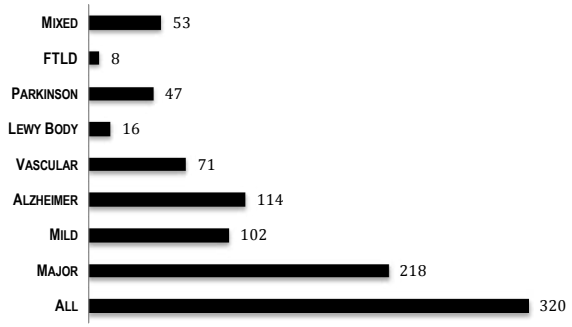

Figure 2. Neurocognitive Disorders (N)

Abbreviations: FTLD: Frontotemporal Lobar Degeneration

4.3 Medical Conditions

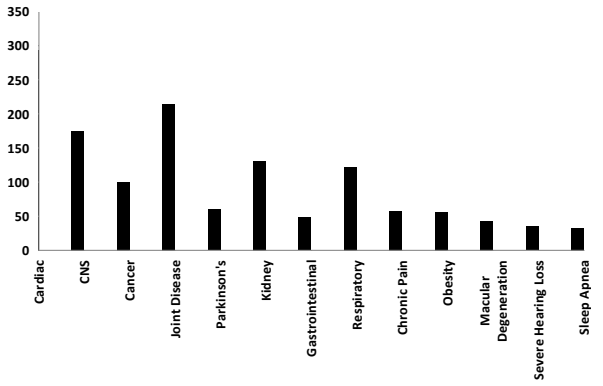

Figure 3. Pharmacotherapy (N)

The most common systems affected by moderate to severe pathology were Central Nervous System (CNS) 175 (41%), cardiac 294 (64%), renal 131(31%), rheumatologic 214 (50%), respiratory 122 (29%), gastrointestinal disease 48(21%). Specific medical conditions observed included chronic pain 58 (14%), cancer 100 (23%), macular degeneration 43 (10%), severe hearing loss 34 (8%), Parkinson's Disease 60 (14%), obesity 56 (13%) sleep apnea 33 (7.7%), hematological conditions requiring blood transfusions 10 (2%), pseudobulbar affect 4 (1%), restless leg syndrome 16 (4%) and normal pressure hydrocephalus 9 (2%). Four or more co-morbid medical conditions were present in109 subjects (25%) (Figure 3).

4.4 Correlations with Medical Conditions

Participants with macular degeneration were more likely to be agitated as measured by higher scores on the PAS (X^2 5.2, df =1 p = 0.02, d=0.22: 95%CI 0.03-0.41). In fact, 42.9% of those with macular degeneration were agitated compared to 26.2% without macular degeneration. The strongest correlation with macular degeneration was with increasing age (t = -5.3, df = 426 p < 0.0001, d=0.51: 95% CI 0.32-0.71) with their mean age being 87.6 (sd=6.92) for those with macular degeneration compared to a mean age of 79.6 (sd=9.54) for this without. Participants with severe hearing impairment were more likely to be agitated as measured by higher scores on the PAS (X^2 4.9, df =1 p = 0.03, d=0.21: 95%CI 0.02-0.40) and performed below the norm on the MMSE (X^2 3.8, df =1; p = 0.05, d=0.19: 95%CI 0.00-0.38). Those suffering chronic pain also performed below the norm on the MMSE (X^2 5.7, df =1; p = 0.02, d=0.23: 95%CI 0.03-0.42).

4.5 Reasons for Referral

The common reasons for referral were behavioral disturbances 173 (40%), depression 149 (35%), altered mental

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status 77 (18%), psychotic symptoms (hallucinations or delusions) 72 (18%), adjustment to loss and change 42 (10%) and anxiety 33 (8%). The prominent behavioral disturbances were: unrelenting vocalizations 25 (6%), aggression or abuse 100 (23%), intrusive wandering 33 (8%), agitation 72 (17%), inappropriate sexual behavior 23 (5%) and resisting care 40 (9%).

4.6 Treatments

Pharmacotherapy

The psychiatrist (SS), introduced to participants already receiving a myriad of psychotropic medications, took an active role in medication adjustments.

At baseline the majority were taking antidepressants 335 (78%). Antipsychotic agents were prescribed to 272 (64%). Participants on antipsychotic agents were more likely to die (X^2 = 8.5, df 1, p = 0.004, d=0.28: 95%CI 0.09-0.47) than those who were not. This pattern was not observed with opioid analgesia (X^2 = 0.69, df 1, p = 0.40, d=0.08: 95%CI -0.11-0.27). Mood stabilizers 65(15%) were useful for participants with bipolar disorders and for behavior disorders that were refractory to second-generation antipsychotics. The memory enhancers 162 (38%) were less often prescribed. 'Sleep Aids' 47 (11%) included trazodone, mirtazapine, melatonin. Only if these failed, non-benzodiazepine hypnotics were prescribed. Medications specific for neurological conditions were also administered: Seizure Disorder 29 (7), Parkinson's disease 45 (11) and Restless Leg Syndrome 22(5). (Figure 4).

Psychotherapy

Participants could engage in the individual therapy 132 (31%)

(e.g. supportive/educational, cognitive behavioral, insight oriented, interpersonal psychotherapy). Couples were treated 29 (7%). Families received interventions 56 (13%). All team members used behavioral modification 171(40%). Most participants received a psychotherapeutic intervention 284 (66%).

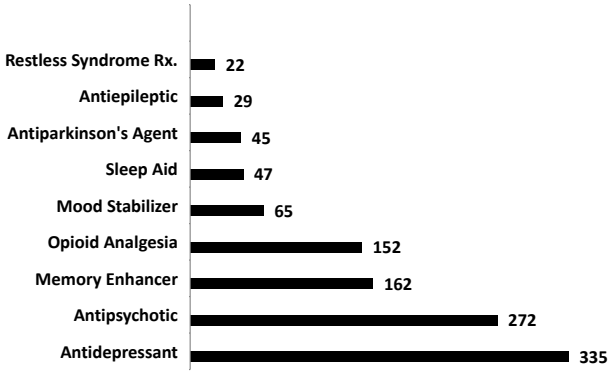

Figure 4. Pharmacotherapy (N)

4.7 Correlations of Cognitive Status, Mood, Agitation and Function

The participants with major neurocognitive disorder were more likely to be dependent (Mean 37, sd=24.8) compared to those without impairment (Mean 57, sd=27.8 p < 0.0001, d=0.76: 95%CI -0.56-0.96). A similar pattern was observed for agitation. Participants with major neurocognitive disorder were more likely to be agitated (Mean 6.4, sd=5.4) than those who were normal or only mildly impaired (Mean 2.1, sd=3.8 p < 0.0001; d=0.92: 95%CI 0.72-1.12). Participants with major neurocognitive disorder were also more likely to be depressed (Mean 7.3, sd=5.8) than those who were normal or only mildly impaired (Mean 5.9, sd=4.4, p=0.003, d=0.27: 95%CI 0.08-0.46).

4.8 Cognitive Status At Baseline and Change Over Time (MMSE)

Baseline MMSE scores for the cohort were normal 65 (16%), mild 134 (32%), moderate 136 (32%), severe 18 (4%) and so severe that the MMSE could not be completed 67(16%). The mean score was 20.9 (N =353, sd=5.96). The McNemar's test was used to assess if the proportion of patients impaired varied significantly at different time points when compared to baseline. While a significant difference from baseline was observed at 26 weeks (McNemar's S=4.00, p=0.046, d=0.58: 95%CI 0.01-1.14), (N=26), this effect was driven by 4 patients with normal MMSE scores who declined. This change was not observed at 52 or 78 weeks. Since it is well known that

Table 2. Cognitive Transitions: Weeks 26 & 52 vs. Baseline Using MMSE Categories*

Baseline	Week 26	%	Baseline	Week 52	%
Normal	Stable	34	**Normal**	Stable	46
	Mild	54		Mild	36
	Moderate	17		Moderate	18
	Severe	0		Severe	0
Mild	Stable	67	**Mild**	Stable	50
	Moderate	22		Normal	20
	Severe	11		Moderate	25
Moderate	Stable	50		Severe	5
	Mild	**30**	**Moderate**	Stable	47
	Severe	20		**Normal**	**6**
Severe	Stable	100		Mild	29
				Severe	18

Note: * Mini-Mental State Exam (MMSE) Scores range from 0-30. Here are the commonly used cut scores for severity: normal 27-30; mild 21-26, moderate >10-20 and severe ≤ 10. Improvement is highlighted in grey.

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change in cognitive function occurs gradually, we elected to search for patterns in the data descriptively. This inspection revealed that most seniors remain stable (55%). Some become severely impaired overtime (11%) and 18% improved. (Table 2).

4.9 Geriatric Depression Scale Scores at Baseline and Overtime

As many as 173 (48%) had scores >5 on the GDS with mean =6.35, sd = 4.11. For the 26 patients with both baseline and 26 weeks, using the continuous scale, we recorded a significant reduction in GDS scores from baseline (mean=6.35, sd=4.11) to 26 weeks (mean=4.50, sd=3.64) (t(25)=2.48, p=0.02, d=0.99: 95%CI 0.39-1.56). Of depressed individuals only 35% improved over a 6-month period. At weeks 52 and 78, no further improvement was observed.

4.10 Pittsburgh Agitation Scale Scores at Baseline and Overtime

The frequency of agitation at baseline was 117 (27.9%). By week 26, 80% of the agitated patients transitioned to a non-agitated state, scores below 4 on the PAS or a 50% reduction from baseline (McNemar's S= 12.0, p=0.0005, d=1.20: 95%CI 0.66-1.71). Similarly by week 52 McNemar's S= 12.0, p=0.0005,d=1.20,95%CI 0.66-1.71 and 78, 100% of the agitated patients transitioned to a non-agitated state (McNemar's S= 11.27, p=0.0008, d=1.17: 95%CI 0.63-1.68). For the 34 patients with both baseline and 26 weeks, using the continuous scale, there was a significant reduction in PAS scores from baseline (mean=5.38, sd=4.95) to 26 weeks (mean=2.97, sd=3.91) (t(33)=3.00, p=0.005, d=1.04: 95%CI 0.51-1.54).

4.11 Barthel Index Scores: Activity of Daily Living at Baseline and Overtime

Of the 414 participants, the mean score on the Barthel Index was 47, sd=28 with 48.3% of the cohort being independent. A subset of the population was followed over time with mean scores of 41.4 (sd=32.39, 44.8 (sd=32.03), and 40.3 (sd=20.59) over weeks 26, 52, and 78 respectively. Decline in function at week 26 was not statistically significantly different (t(26)=1.66, p=0.11, d=0.65: 95%CI -0.16-1.42) but at 52 and 78 was statistically significant (t(48)=3.00, p=0.0042, d=0.87: 95%CI 0.26-1.45; t(35)=4.24, p=.0002, d=1.43: 95%CI 0.77-2.04) Focusing on independent status when compared to baseline, by week 52, 35.5% (McNemar's S = 6.23, p=0.013, d=0.79: 95%CI 0.19-1.36) and by week 78, 59.1% transitioned to a dependent state (McNemar's S = 13.00, p=0.0003, d=1.04: 95%CI 0.42-1.62).

4.12 Reimbursement for Telepsychiatry Services

The participants paid for the services primarily through state or federal funding (75%). Two other sources of payment were personal health insurance (13.5%) or private pay (12.2%).

5. Discussion

Telepsychiatric evaluation using DSM-V criteria supplemented by assessment tools yielded a full range of diagnoses and revealed interactions with medical comorbidities similar to office practice. The frequency of the various neurocognitive disorders in our cohort followed the same pattern reported in the literature: Alzheimer's Disease, cerebrovascular disorders, lewy body spectrum disorders and FTLD [24-26]. Rare causes of neurocognitive disorders were also diagnosed: CJD [27] and Huntington Disease [28]. Notable interactions with co-morbid medical conditions include a higher levels of agitation in participants with macular degeneration and severe hearing impairment. Those with chronic pain and hearing impairment performed below the norm on the MMSE.

Telepsychiatry permitted our participants to receive a variety of therapies with or without medication management. Individuals and couples responded to an eclectic approach to psychotherapies dependent on their needs (cognitive behavioral, interpersonal, insight oriented and supportive/educational). Family interventions varied from a single consultation to facilitate treatment post discharge to more commonly assisting families to manage caretaker burden. Psychopharmacology lends itself well to telepsychiatry. We used an evidence-based approach (reference to recent scientific publications, participants' medical records, laboratory and imaging) to plan treatment. For example, acetylcholinesterase inhibitors have been reported to be more effective in mild neurocognitive disorders [29]. Improved diagnostic precision resulted in a change of treatment for pseudobulbar affect [30]. The prescription of second-generation antipsychotics in seniors increases mortality rate. However, untreated psychosis in patients with Alzheimer's disease is strongly associated with nursing home admission and time to death when untreated [18]. The FDA Summary Basis of Approval reports for 28 pharmacological agents approved between 1990 and 2011 found that overall mortality risk was significantly associated with psychiatric diagnosis but was not further increased when patients were assigned to psychotropic agents versus placebo [31]. The current treatment recommendation for psychosis and agitation in late life remains antipsychotics

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[32]. Similar to our study, antidepressants were the most frequently prescribed psychotropic medication [33].

Lower scores on the MMSE were associated with depression, agitation, and dependence at baseline confirming earlier research. MMSE scores over time did not yield clear evidence of change in this 3-year study using standard statistical tools. In one study, the mean age at which the cognitively unimpaired transition to subjective memory complaints was 81.5 years. 55% of that cohort were diagnosed with mild cognitive impairment over a further 9 year period [34]. When we applied a purely descriptive approach to our data, variations were identified. In fact, most participants remained stable, some became severely impaired and some improved. Cognitive status shows variation even during this relatively short time span and allows an opportunity for intervention. The reasons for the improvements require research confirmation: treating the underlying medical condition, refinement of medication regime, reduction in agitation, decrease in family dysfunction, improved mood.

Depression was common in our cohort. GDS scores decreased significantly from baseline to 26 weeks but not beyond. Only 35% of depressed individuals responded to treatment over 6 months replicating findings reported from the face-to-face Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT) [35]. The latter study provides an alternative health care approach (family physician and nurse manager) effective in decreasing depressed mood, suicidal ideas, morbidity and mortality [35-37].

Agitation at baseline affected 28% of participants. By 52weeks, 100% had significantly reduced PAS scores. Agitation is one of the variables found to most impact caretaker burden [38] and therefore a modifiable factor preventing or postponing admission to a retirement facilities.

Dependence at baseline was common. Further decline in activities of daily living was particularly noticeable at 52 and 78 weeks. Maintenance of mobility is another possible modifiable factor that may allow seniors to remain in the community. Research has demonstrated that vigorous physical activity improves memory and protects against cardiovascular risk factors; whereas a sedentary lifestyle is associated with decline in executive function [39].

One study reported that a telemedicine program received comparable insurance reimbursement to in-person care with a mixture of 45% private, 50% medicare, and 5% self-pay [40]. In our study, insurance reimbursement for IP and telepsychiatry was similar, but most of the burden was on government payers.

Strengths: (1) This is a prospective longitudinal cohort study of 428 seniors using telepsychiatry to recreate best geriatric psychiatry office practices for those underserved in rural areas. (2) The same psychiatrist completed the evaluations and scored the instruments, which avoided problems arising from poor inter-rater reliability. (3) These results are generalizable to seniors in other settings with similar demographics. Generalizability was further improved by the adoption of non-restrictive eligibility criteria. (4) Our results treating seniors via telepsychiatry are often consistent with the literature involving participants seen face-to-face.

Limitations: The study does not include a control group nor measure cost effectiveness nor does it examine the efficacy of any specific psychotherapeutic intervention. Brenes et al. 2015 addressed both these limitations in her a randomized control study comparing "telephone" delivered cognitive behavior therapy (CBT) with non-directive supportive therapy for older adults with generalized anxiety disorder with CBT proving superior [41]. The attrition of subjects over time due to death, discharge and significant physical decompensation resulted in smaller sample sizes by study year 3.

6. Conclusions

To our knowledge this the first longitudinal study of adults in late life living in rural retirement communities that demonstrates the feasibility of offering a full complement of geriatric psychiatry services via telepsychiatry. This study contributes to our understanding of the correlation of cognitive status, mood, agitation and dependence. It highlights the need for a new approach to health care delivery (i.e. telepsychiatry) to stem the decline in dependence, manage refractory depression and maintain cognitive resilience for seniors who are underserviced both in rural or urban areas with the aim of extending their community living. This study argues for further research evaluating cost effectiveness of Telepsychiatry in seniors to support demands for a more inclusive payment policy from both managed care and government funding bodies.

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Presentation

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