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Factors related to delayed initiation of antiretroviral therapy among patients with clinically eligible HIV-infected

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Abstract

Background: Human Immunodeficiency Virus (HIV), namely a virus that reduces the ability of the human immune system, so that sufferers are susceptible to various diseases, the wider scope of ARV administration certainly has a positive impact in reducing mortality and morbidity, improving the quality of life of patients with HIV and AIDS.
Purpose: To determine the factors associated with delayed initiation of antiretroviral therapy in Human Immunodeficiency Virus patients at the VCT (Voluntary Counseling and Testing) Clinic of Pringsewu Hospital in 2022.
Method: This type of quantitative research, using a cross sectional design. The population of this study were HIV positive patients at the Pringsewu Regional General Hospital Clinic, Lampung for the year 2022, namely 174 patients, using the side total technique. Univariate data analysis, bivariate with chi square and multivariate with multiple logistic regression tests.
Results: The result showed that the factors associated with delayed initiation of antiretroviral therapy in Human Immunodeficiency Virus patients at the VCT clinic at Pringsewu General Hospital in 2022 were Socioeconomic Status (p value=0.009), education level (p value=0.001, opportunistic infections (p value= 0.001), HIV/AIDS Stigma (p value=0.003), and Access (p value=0.018). The most dominant factor associated with delayed initiation of antiretroviral therapy in patients with Human Immunodeficiency Virus infection was access (95% CI, p=0.027 and OR; 3.738).
Conclusion: Antiretroviral therapy (ARV) delays in PLWHA are strongly influenced by low socioeconomic status, low education level, presence of opportunistic infections, positive stigma and remote access to healthcare services.
Suggestion: Management at the hospital's VCT clinic is suggested to make guidelines or standardized services, educate about the importance of ARVs, provide motivation, and carry out consistent control of ARV therapy. The management always promotes the importance of awareness and adherence in carrying out ARV therapy which will have many benefits in improving quality of life, healthy behavior, and extending life span.

Keywords: Antiretroviral Therapy; Delayed Initiation; HIV-Infected; Patients

INTRODUCTION

Human Immunodeficiency Virus (HIV) is a retrovirus that belongs to the lentivirus family. There are two genetically different but antigenically related types of HIV, namely HIV-1 and HIV-2, which have been isolated from AIDS patients. HIV-1 is more commonly found in AIDS patients in the United States, Europe, and Central Africa, while HIV-2 is more common in West Africa (Kumar, Lodge, Trudel, Ouellet, Ouellette, & Tremblay, 2010). HIV-1 is more easily transmitted than HIV-2. The period between

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the first infection and the onset of symptoms is longer, and the disease is milder in HIV-2 infections (World Health Organization, 2023).

Human Immunodeficiency Virus (HIV) is a virus that weakens the immune system of humans, making patients susceptible to various diseases (Wibowo, 2015). HIV (Human Immunodeficiency Virus) is an RNA retrovirus that specifically attacks the immune system of the human body. The weakened immune system in HIV-infected individuals makes them susceptible to various infections, which can lead to the development of AIDS (Nuraisyah, Matahari, Isni, & Utami, 2021).

Human Immunodeficiency Virus (HIV) belongs to the lentivirus family. The HIV virus is a group of retroviruses that can utilize its own RNA and host cell DNA to form viral DNA. HIV uses the DNA from CD4+ T cells and lymphocytes to replicate. After formation, the genetic code of the DNA in the form of a double strand enters the cell nucleus. Then, with the help of the enzyme integrase, the viral DNA copy is inserted into the patient's DNA. HIV viruses that successfully enter the patient's body also infect various types of cells, especially monocytes, macrophages, microglia cells in the brain, placental Hofbauer cells, dendritic cells in lymph nodes, epithelial cells in the intestines, and Langerhans cells in the skin (Nuraisyah, Matahari, Isni, & Utami, 2021).

Clinical symptoms resulting from HIV infection are usually realized by patients after some time due to the lack of recovery. HIV-infected patients can remain asymptomatic for years. During the course of the disease, CD4+ T cells decrease in number from 1000/µl before infection to about 200-300/µl after infection within 2-10 years (Kurniawati, 2022).

Transmission of HIV infection include sexual contact, intravenous drug injection, blood and blood products, and mother-to-child transmission (Ministry of Health of the Republic of Indonesia, 2015).

At the end of the 20th century, the World Health Organization (WHO) reported an epidemic caused by the Human Immunodeficiency Virus (HIV), namely Acquired Immunodeficiency Syndrome (AIDS). Its spread was rapid worldwide. During the period from 1983 to 2011, HIV had infected over 60 million people, with nearly 20 million people suffering from AIDS. This led to over 14,000 new infections every day. Currently, AIDS is the leading cause of death in Africa and a quarter of the world (World Health Organization, 2023).

In Indonesia, the number of new HIV-positive cases increased in 2021, amounting 456,453 individuals, consisting of 320,963 with HIV and 135,490 with AIDS. Among the HIV-positive cases, 9,675 individuals tested positive out of 1,030,793 tested. Among the detected 7,650 HIV-positive cases, 8,232 individuals received antiretroviral treatment (ARV). ARV medication is not meant to eliminate the HIV virus from the body but to suppress its growth, maintaining the health of those who are HIV-positive. Based on age groups, 69.7% of HIV-positive cases found from January to December 2021 were in the 25-49 age group, 16.9% in the 20-24 age group, and 8.1% in the ≥50 age group. HIV-positive cases among infants ≤18 months were 7 out of 287 babies who underwent HIV testing with PCR DNA (EID). In terms of gender, 70% of HIV-positive cases were detected in males and 30% in females (Ministry of Health of the Republic of Indonesia, 2021).

Risk factors for HIV-positive cases detected from January to December 2021 showed that 28% were homosexual, 14.4% heterosexual, 10.3% shared needles, and 40.7% were unknown. Among the 7,650 HIV-positive cases, 2.4% were prostitutes, 26.5% were Gay, 1.1% were transgender individuals, 0.6% were drug users, 1.2% were inmates, 10.0% were pregnant women, 13.0% were TB patients, and 0.8% were sexually transmitted infection (STI) patients. The number of AIDS cases (HIV-positive detected already in the AIDS stage, accompanied by infections related to HIV/AIDS) was 1,677 cases. The provinces with the highest number of AIDS cases in Indonesia were Central Java, North Sumatra, East Java, West Java, East Kalimantan, and Papua (Ministry of Health of the Republic of Indonesia, 2021).

In Lampung Province, Indonesia, in the year 2017, there were 276 HIV/AIDS cases, increasing to 317 cases in 2018, and further rising to 323 cases in 2019. In the period of January to March 2021, there was an additional increase of 124 cases (Health office of Lampung Province, 2021).

Active use of antiretroviral drugs (ARV) has a positive impact on reducing mortality and morbidity,

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and improving the quality of life of people living with HIV and AIDS (PLWHA) (Buchacz, Baker, Moorman, Richardson, Wood, Holmberg, & HIV Outpatient Study (HOPS) Investigators, 2008).

Antiretroviral (ARV) drugs are used to suppress the development of HIV in the body. Some commonly used ARV drugs in Indonesia include Lamivudine and Zidovudine. The use of ARV serves to suppress the replication of HIV, not to eliminate it. ARV therapy should be administered to individuals infected with HIV. If not done, HIV will develop and its levels will increase in the blood. Discontinuing ARV consumption for PLWHA risks the development of resistance to the drug (Mathebula, 2019).

The initiation timing of ARV therapy in HIV patients is closely related to the reduction in mortality and morbidity among PLWHA (Rahayu, Karjadi, & Nelwan, 2016) During the period of 2009 in the United States and South Africa, lower mortality rates and lower HIV infection progression were reported in patients who initiated ARV therapy early after opportunistic infection. Among 283 patients, a higher death rate was found in patients with delayed ARV initiation (24%) compared to those without delay (14%). Some studies also indicated that early initiation of ARV treatment showed a lower death rate (around 1%) compared to those who delayed ARV initiation (5%) (Rahayu, Karjadi, & Nelwan, 2016).

According to the Minister of Health of the Republic of Indonesia Decree No. HK.01.07/Menkes/90/2019 on the National Guidelines for HIV Medical Services, ARV therapy must be provided to all individuals with HIV/AIDS regardless of clinical stage and CD4 count. For asymptomatic PLWHA, ARV therapy should start within 7 days after a positive HIV diagnosis and clinical examination (Alen, Agresa, & Yuliandra, 2017).

In 2009, research in Nigeria, which has the second highest number of HIV/AIDS patients after South Africa, found a proportion of 26% delayed ARV therapy initiation. Delayed initiation of ARV therapy in PLWHA could be related to factors such as high CD4 count, low functional status, and low body mass index (BMI) (Arisudhana, & Artati, 2022).

A study of 444 patients starting ARV therapy for the first time showed that 107 patients (24.1%) experienced delayed ARV initiation, while 337 patients (75.9%) did not experience delay. Among the statistically significant variables were opportunistic infection (Sutini, Cahyarti, Rahayu, Sofro, Fahanah, Pramudo, & Riyadi, 2020). Risk factors associated with delayed ARV initiation were age > 30 years (pooled OR = 1.46, 95% CI 1.09-1.94), male gender (pooled OR = 1.22, 95% CI 1.01-1.48), long distance to the clinic (pooled OR = 2.02, 95% CI 1.20-3.40), and fear of confidentiality breach (pooled OR = 2.72, 95% CI 1.00-7.44) (Sari, Jannah, Tahlil, & Susanti, 2022).

Research conducted at Amertha Bali Clinic concluded that factors influencing PLWHA to initiate ARV therapy include gender (PR = 1.21), education (PR = 1.22), marital status, insurance ownership (PR = 1.17), knowledge (PR = 1.55), perceived barriers (PR = 1.33), guideline-based counseling (PR = 1.42), and social support (PR = 1.24) (Yuliyatni, 2015).

In Indonesia, a total of 49,217 PLWHA received ARV therapy from all 34 provinces. In Lampung Province, 319 PLWHA received ARV therapy, individuals with Human Immunodeficiency Virus infection.

Ministry of Health Decree No. 451/MENKES/SK/XII states that there are 358 referral hospitals for PLWHA. These designated hospitals are required to provide comprehensive health services to PLWHA, including services related to HIV/AIDS, such as Voluntary Counseling and Testing (VCT), ARV, Prevention of Mother-to-Child Transmission (PMTCT), treatment for opportunistic infections, and support services (Ministry of Health of the Republic of Indonesia, 2021).

In 2016, there were a total of 3,771 HIV testing services in operation, yet there remained a significant gap between the number of individuals who needed testing and the number of tests conducted. Additionally, nearly half of those who ever received ARV treatment couldn't maintain it due to death or loss to follow-up. The under-utilization of available HIV/AIDS healthcare services may result in program failure to prevent HIV/AIDS transmission, leading to increased HIV rates and higher morbidity and mortality rates for affected individuals (World Health Organization, 2023).

Pringsewu Regional General Hospital is a designated HIV/AIDS referral hospital until

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September 2022. In the VCT Clinic section that administers ARV therapy, there are 174 individuals. Based on preliminary surveys conducted in October 2021, among the seven PLWHA utilizing healthcare services at the VCT Clinic, some had higher education but did not adhere well to ARV therapy (experienced loss to follow-up), four out of seven PLWHA, or 57.1%. Among these seven PLWHA, five of them, or 71.4%, had good family support, and their knowledge of HIV/AIDS was good. From an organizational perspective, feedback showed that five individuals, or 71.4%, rated healthcare worker behavior as friendly and responsive, six individuals, or 85.7%, rated the facilities as adequate, but data indicated that service utilization was not yet optimal.

There are factors related to delayed ARV initiation in PLWHA at the VCT Clinic of Pringsewu Regional General Hospital that are causing the therapy program to not function as intended. This study aims to examine the factors related to delayed ARV initiation in PLWHA. The basic concept of this behavior refers to the health belief model (HBM) theory (Setiyaningsih, Tamtomo, & Suryani, 2016). Each individual has an assessment of belief in their vulnerability and severity levels, which influences preventive efforts against diseases (Glanz, Rimer, & Viswanath, 2008; Rosenstock, 1974). The health belief model concept can provide insight into healthy behavior for ARV therapy at an individual level. Thus, factors related to belief and motivation for ARV therapy can be obtained.

This study seeks to describe the components of HBM, which include beliefs that represent an individual's perception of a condition. Thus far, the Health Belief Model is the most commonly used theory in health education and promotion (Glanz, Rimer, & Viswanath, 2008). This theory was chosen because HBM is a cognition-based theory that combines knowledge, opinions, and actions taken by individuals related to their health condition. There is a close relationship between beliefs and healthy behavior.

The situational presence of a pandemic poses a threat (perceived threat of injury or illness) as well as advantages and disadvantages (benefits and costs). This basic concept guides behavior to initiate a process.

Based on the initial survey results, support from experts, and existing health policies, the phenomenon of delayed ARV initiation in PLWHA at the VCT Clinic of Pringsewu Regional General Hospital is assumed to be related to individual characteristics (age, gender, education, marital status, opportunistic infection status, perception of HIV stigma, experience of discrimination, knowledge, family support, and social environment support) and organizational characteristics (healthcare worker behavior, healthcare worker human resources, and service facilities).

RESEARCH METHOD

This research is of a quantitative nature and employs a Cross-Sectional approach. The subjects of this study are HIV-positive patients (UPT HIV) at the VCT Clinic of Pringsewu Regional General Hospital, Lampung Province in the year 2022, totaling 174 patients.

The object of this research is the delay in initiating antiretroviral therapy in patients diagnosed with HIV, where patients who should have received immediate treatment experience delays in their therapeutic process. This study is divided into two groups: less than 7 days and more than 7 days. The factors include socioeconomic status, education level, opportunistic infection, HIV stigma, and access to facility. Socioeconomic status is divided into high income (>IDR 1,581,000) and low income (<IDR 1,581,000). Education level is divided into high school graduate or above (>senior high school) and less than high school graduate (<senior high school). Opportunistic infection factors categorize those infected and those not infected, including ARI, Diarrhea, Candidiasis, and TB.

The factors influencing stigma HIV/AIDS are divided into positive and negative groups, based on a questionnaire consisting of five statements. Each statement is scored from 1 to 3, with the total score ranging from 5 to 15. Stigma is considered positive if the total score is above the mean and negative if it is below the mean.

The access to facility factor is divided based on the distance to the clinic: far (>4km) and close (≤4km). The research was conducted from March to October 2023. The study obtained ethical approval from the University of Malahayati's Research Ethics Commission with ethical certificate no. 3405/EC/KEP-UNIMAL/V/2023, dated May 3, 2023.

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RESEARCH RESULT

Table 1. Characteristic of Respondent (N=174)

Variables	Results
Age (Mean ±SD) (Range) (Year)	**(33.39±0.677) (18-56)**
Gender (n/%)	
Male	154/88.5
Female	20/11.5
Delayed Initiation of Antiretroviral Therapy (n/%)	
≤7	48/27.6
≥8 days	126/72.4
Socioeconomic (n/%)	
High	40/23.0
Low	134/77.0
Education level (n/%)	
University	59/33.9
High school	115/66.1
Opportunistic Infection (n/%)	
Infection	117/67.2
No infection	57/32.8
Stigma of HIV/AIDS (n/%)	
Potisive	75/43.1
Negative	99/56.9
Access to Healthcare Services (n/%)	
Far	37/21.3
Near	137/78.7

In Table 1, the average age of 174 respondents shows a mean of 33.39 with a standard deviation of 0.677 with an age range of 18 to 56 years. Meanwhile, based on gender, the majority are male, namely 88.5%.

Based on the table above, the majority of respondents have delayed initiation of antiretroviral therapy for more than 7 days, amounting to 72.4%. Furthermore, the majority of respondents have a low socioeconomic status, comprising 77.0%, while the majority have an education level less than high school graduate (<senior high school), at 66.1%. Additionally, the majority of respondents have opportunistic infections, totaling 67.2%. Negative stigma is prevalent among the majority of respondents, accounting for 56.9%, and most respondents have access to clinics nearby, constituting 78.7%.

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Table 2. Some factors in Delayed Initiation of Antiretroviral Therapy

Variables	Delayed Initiation of Antiretroviral Therapy		p-value	OR 95% CI
	≤7 days (n=48)	≥8 days (n=126)		
Socioeconomic Status (n/%)				
High	18/37.5	22/17.5	0.009	2.83 (1.34-5.96)
Low	30/62.5	104/82.5		
Education level (n/%)				
University	26/54.2	33/26.2	0,001	3,33 (1,66-6,65)
High School	22/45.8	93/73.8		
Opportunistic Infection (n/%)				
Infection	20/41.7	97/77.0	0,000	4,68 (2,30-9,50)
No Infection	28/58.3	29/23.0		
Stigma (n/%)				
Positive	30/62.5	45/35.7	0,003	3,00 (1,50-5,97)
Negative	18/37.5	81/64.3		
Access to Healthcare Services (n/%)			0,018	3,90 (1,30-11,7)
Far	4/8.3	33/26.2		
Near	44/91.7	93/73.8		

Based on the table above, the results of bivariate analysis reveal relationships with p-values as follows: socioeconomic status shows a p-value of 0.009, education p-value of 0.001, opportunistic infection p-value of 0.000, HIV stigma p-value of 0.003, and access to facility p-value of 0.018, in relation to the delay in initiating antiretroviral therapy in Human Immunodeficiency Virus patients.

Bivariate analysis results indicate that out of the 48 respondents who initiated antiretroviral therapy within 7 days, those with a high socioeconomic status comprise 37.5%, while those with a low socioeconomic status constitute 62.5%. Additionally, among the 126 respondents who initiated antiretroviral therapy after 7 days, those with a high socioeconomic status make up 17.5%, while those with a low socioeconomic status account for 82.5%.

Regarding the factor of education level, those with an education level above high school (>senior high school) are 54.2%, while those with an education level below high school (<senior high school) are 45.8%. Among the 126 respondents who initiated antiretroviral therapy after 7 days, those with an education level above high school (>senior high school) are 26.2%, while those with an education level below high school (<senior high school) are 73.8%.

For the factor of opportunistic infection, respondents with an opportunistic infection make up 41.7%, while those without an opportunistic infection account for 58.3%. Among the 126 respondents who initiated antiretroviral therapy after 7 days, those with an opportunistic infection are 77.0%, while those without an opportunistic infection are 23.0%.

Regarding the stigma factor, respondents with a positive stigma are 62.5%, while those with a negative stigma are 37.5%. Among the 126 respondents who initiated antiretroviral therapy after 7 days, those with a positive stigma are 35.7%, while those with a negative stigma are 64.3%.

Finally, for the access to facility factor, respondents with distant access to facility are 8.3%, while those with close access to facility are 91.7%. Among the 126 respondents who initiated antiretroviral therapy after 7 days, those with distant access to facility are 26.2%, while those with close access to facility are 73.8%.

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Table 3. Final Model after Interaction

Variables	B	*p*	Exp (B)	95 % CI for Exp (B)	
				Lower	*Upper*
Education level	1,119	,005	3,061	1,397	6,706
Opportunistic infection	1,165	,004	3,017	1,466	7,016
Stigma	,895	,026	2,447	1,111	5,391
Access to healthcare services	1,318	,027	3,738	1,160	12,042
Constant	-1,084	,008	,338		

Based on the table above, after removing the interaction variable, the four variables above have p-values ≤ 0.05, and no more variables are eliminated, thus considered the final model, concluding the multivariate modeling. In the final stage, there are four variables significantly related to the delay in initiating antiretroviral therapy: education, opportunistic infection, stigma, and access to the service facilities. The final multivariate results indicate that out of these four factors related to the delay in initiating antiretroviral therapy, the access to the service facilities variable is the most dominant factor (p=0.027 and OR; 3.738).

DISCUSSION

Socioeconomic status

Based on this explanation, individuals with a lower socioeconomic status tend to have lower levels of compliance with ARV therapy. This is due to limited financial resources, which are associated with treatment costs, transportation, healthcare facility accommodations, and social support..

Education level

The statistical test results yielded a p-value of 0.001, indicating a relationship between education level and the delay in initiating antiretroviral therapy in patients with HIV infection. The OR value of 3.33 indicates that respondents with an education level above high school (>senior high school) are 3.33 times more likely to initiate antiretroviral therapy within 7 days compared to respondents with an education level below high school (<senior high school).

Based on this explanation, the education factor influences the delay in ARV therapy initiation. There are several ways to address the impact of education on the delay of ARV therapy, such as providing comprehensive and easily accessible knowledge to all PLWHA. Additionally, involving social workers, counselors, and trained medical teams is necessary to assist low-educated PLWHA individuals in addressing issues according to ARV therapy procedures.

Opportunistic infection

The statistical test results yielded a p-value of 0.000, indicating a relationship between opportunistic infections and the delay in initiating antiretroviral therapy in patients with HIV infection. The OR value of 4.68 indicates that respondents without opportunistic infections are 4.68 times more likely to initiate antiretroviral therapy within 7 days compared to respondents with opportunistic infections.

Based on this explanation, opportunistic infections can hinder ARV therapy in HIV/AIDS patients. Several factors contribute to this, such as treatment complexity. The treatment process for PLWHA patients with opportunistic infections becomes complex and intensive, especially when involving additional medications with strict schedules. This can complicate the management and adherence to the ARV therapy process. Additionally, drug interactions for treating opportunistic infections can interact with ARV drugs. Drug interactions may affect the effectiveness of ARV or increase the risk of unwanted side effects..

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Stigma

The statistical test results yielded a p-value of 0.003, indicating a relationship between HIV/AIDS stigma and the delay in initiating antiretroviral therapy in patients with HIV infection. The OR value of 3.00 indicates that respondents experiencing positive HIV/AIDS stigma are 3.00 times more likely to initiate antiretroviral therapy within 7 days compared to respondents experiencing negative HIV/AIDS stigma.

It can be concluded that stigma causes PLWHA to tend to conceal their identity, especially regarding their HIV-positive status. This can affect HIV prevention efforts, behavior in seeking HIV treatment, as well as the quality of care and treatment provided to PLWHA. Stigma worsens the quality of life for PLWHA, necessitating efforts to combat societal stigma against them.

Access to healthcare services

The statistical test results yielded a p-value of 0.018, indicating a relationship between healthcare access and the delay in initiating antiretroviral therapy in patients with HIV infection. The OR value of 3.90 indicates that respondents with close access are 3.9 times more likely to initiate antiretroviral therapy within 7 days compared to respondents with distant access.

Based on the research findings, in the context of HIV/AIDS, adequate access to comprehensive healthcare services, including diagnosis, treatment, monitoring and support, is crucial for achieving the success of ARV therapy in improving the quality of life for PLWHA. Efforts must be made to ensure that comprehensive and affordable healthcare services are available to all individuals with HIV who are in need.

The dominance of the healthcare access variable over other variables is due to its smallest obtained p-value and the largest OR value. This can be interpreted as respondents with close access are 3 times more likely to initiate antiretroviral therapy within 7 days (without delay) compared to respondents with distant access.

There is a connection between healthcare access and the delay in ARV therapy among individuals with HIV. ARV drugs are used to treat HIV and prevent the virus from progressing to AIDS. Delays or difficulties in accessing healthcare services that provide ARV therapy can lead to several negative consequences. For instance, if a person with HIV doesn't receive timely ARV therapy, the HIV virus can continue to replicate in the body, damaging the immune system, and causing serious health complications, particularly immune system decline. Additionally, delays in starting ARV therapy can result in decreased immune function, making the body more vulnerable to infections and other diseases, viral transmission, and the health deterioration of untreated individuals with HIV.

CONCLUSION

The delay of ARV therapy in PLWHA is greatly influenced by low socioeconomic status, low education level, the presence of opportunistic infections, positive stigma, and the distance of healthcare access from the community health center.

SUGGESTION

The management at the VCT clinic of the hospital should establish guidelines or service standardizations, educate about the importance of ARV, provide motivation, and consistently monitor ARV therapy. Management consistently promotes the importance of awareness and adherence to ARV therapy, which will bring numerous benefits in enhancing quality of life, promoting healthy behaviors, and extending lifespan.

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