

**THE ASSOCIATION BETWEEN POLYPHARMACY,
DEPRESSIVE SYMPTOMS, AND PHYSICAL FRAILTY
STATUS AMONG GERIATRIC PATIENTS AT HOSPITAL
PAKAR UNIVERSITI SAINS MALAYSIA (HPUSM),
KELANTAN**

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**THE ASSOCIATION BETWEEN POLYPHARMACY,
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PAKAR UNIVERSITI SAINS MALAYSIA (HPUSM),
KELANTAN**

by

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requirements for the degree of
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**PERKAITAN ANTARA POLIFARMASI, SIMPTOM
KEMURUNGAN DAN STATUS KELEMAHAN FIZIKAL DALAM
KALANGAN PESAKIT GERIATRIK DI HOSPITAL PAKAR
UNIVERSITI SAINS MALAYSIA (HPUSM), KELANTAN**

ABSTRAK

Polifarmasi, simptom kemurungan dan kelemahan fizikal merupakan isu penting dalam penjagaan geriatrik kerana ia sering berlaku bersama dan boleh menjejaskan kesihatan serta kualiti hidup pesakit warga emas. Kajian ini dijalankan untuk menentukan proporsi polifarmasi, simptom kemurungan dan status kelemahan fizikal serta mengkaji perkaitan antara ketiga-tiganya dalam kalangan pesakit geriatrik di Hospital Pakar Universiti Sains Malaysia (HPUSM), Kelantan. Satu kajian keratan rentas telah dijalankan melibatkan 147 pesakit geriatrik berumur 60 tahun dan ke atas. Data dikumpulkan menggunakan soal selidik piawai bagi menilai status simptom kemurungan (GDS-15-M) dan status kelemahan fizikal (PFFS-M). Daripada 147 responden, 64.6% mempunyai polifarmasi. Simptom kemurungan didapati pada 29.3% responden, dengan majoriti daripadanya mengalami tahap ringan. Bagi status kelemahan fizikal, sebanyak 55.8% responden berada dalam kategori lemah dan 15.6% berisiko lemah. Terdapat perkaitan yang signifikan antara polifarmasi dengan simptom kemurungan ($p=0.018$), polifarmasi dengan status kelemahan fizikal ($p<0.001$), serta simptom kemurungan dengan status kelemahan fizikal ($p<0.001$). Kajian ini menunjukkan bahawa polifarmasi, simptom kemurungan dan kelemahan fizikal saling berkait rapat dalam kalangan pesakit geriatrik dan perlu dinilai bersama dalam penjagaan klinikal.

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ABSTRACT

Polypharmacy, depressive symptoms, and physical frailty are important issues in geriatric care because they often occur together and may affect the health and quality of life of older adults. This study was conducted to determine the proportion of polypharmacy, depressive symptoms and physical frailty status, and to investigate the associations among these three variables among geriatric patients at Hospital Pakar Universiti Sains Malaysia (HPUSM), Kelantan. A cross-sectional study was carried out among 147 geriatric patients aged 60 years and above. Data were collected using standardized questionnaires to assess depressive symptoms status (GDS-15-M) and physical frailty status (PFFS-M). Out of 147 respondents, 64.6% had polypharmacy. Depressive symptoms were found in 29.3% of respondents, with the majority experiencing mild depressive symptoms. For physical frailty status, 55.8% of respondents were classified as frail and 15.6% were classified as at risk of frailty. Significant associations were found between polypharmacy and depressive symptoms ($p=0.018$), polypharmacy and physical frailty status ($p<0.001$), and depressive symptoms and physical frailty status ($p<0.001$). This study shows that polypharmacy, depressive symptoms, and physical frailty are closely related among geriatric patients and should be assessed together in clinical care.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

The trend in aging among the geriatric population in the world and locally has raised a lot of concern about the health concerns of geriatric patients, particularly about polypharmacy, depressive symptoms, and physical frailty status. This study aims to explore the association of these factors among geriatric patients at Hospital Pakar Universiti Sains Malaysia (HPUSM), Kelantan.

Geriatrics refers to the population aged 60 or 65 years and above, and this group is expanding rapidly around the world. Globally, the number of people aged 65 and over is projected to more than double, from 761 million in 2021 to 1.6 billion in 2050. The number of people aged 80 and over is expected to grow even faster, which is expected to triple between 2020 and 2050. (United Nations, 2023; World Health Organization [WHO], 2024). The same is being reflected in Malaysia on a local level. indicated that the proportion of the population at the age of 60 years and above was 7.9% in 2010, and it is projected to increase to 15.3% in 2030 (Department of Statistics Malaysia [DOSM], 2016). The percentage of the population aged 60 and above was projected to increase and this was contributing to the aging population demographic (DOSM, 2016). This demographic shift highlights the necessity to solve the health issues that are specific to geriatric populations in Malaysia, including polypharmacy, symptoms of depression, and frailty.

Geriatric diseases have multifaceted health effects. Polypharmacy refers to taking numerous medications at the same time. Polypharmacy is not defined in a standard

manner, but it is typically characterized by the use of five or more medications regularly. This includes patients on prescription drugs and/ or over-the-counter drugs (Halli-Tierney et al., 2019; Masnoon et al., 2017). Polypharmacy is rampant because of the high prevalence of various chronic diseases among the elderly. Polypharmacy leads to higher chances of adverse drug events, functional decline, hospitalization, and mortality (Maher et al., 2014). Research revealed that polypharmacy raises healthcare expenses and is linked to frailty, cognitive loss, depression, and reduced quality of life among older adults (Eyigor et al., 2020). Patients who have multiple prescription medications, such as proton pump inhibitors (PPIs) that impair vitamin B₁₂ absorption leading to neuropsychiatric symptoms, show increased depressive symptoms or depression risk in older adults (Christl et al., 2025; Laudisio et al., 2018; Novotny et al., 2019; Qato et al., 2018; Sahu et al., 2022). The prevalence of depressive symptoms can affect physical and mental health and is linked to negative outcomes, such as frailty and polypharmacy (Eyigor et al., 2020). It has been shown that depressive symptoms in older individuals are predictors of future deterioration in physical performance. Physical frailty is a geriatric syndrome that is defined as reduced strength, endurance, and physiologic functioning that predisposes individuals to stressors and negative health consequences (Apostolo et al., 2017). It is linked to polypharmacy and depression, establishing a multi-layered involvement and, therefore, worsening morbidity among older adults (Eyigor et al., 2020).

Thus, it is pertinent to discover the links between these factors within the Malaysian context, specifically among geriatric patients of Hospital Pakar Universiti Sains Malaysia (HPUSM), Kelantan, to establish evidence-based strategies of geriatric care that meet local demands. The knowledge of these interrelations can help in better management of patients, minimizing their hospitalization, and improving the quality of life of the aging population in Malaysia.

1.2 Problem Statement

An aging population is an issue that is causing serious health challenges to the aging population across the world and in Malaysia, which is straining the available healthcare systems. Elderly must face an increased risk of having various chronic diseases, and therefore, this predisposition to the disease usually results in complicated health conditions that demand numerous drugs, mental frailty, and deterioration (Ghazali et al., 2021; Jaul & Barron, 2017). These are multifactorial problems that increase morbidity and mortality rates of aging populations in global and local settings.

Polypharmacy refers to the simultaneous administration of multiple drugs and is common among the elderly, especially because of their chronic illnesses. According to the study by Lim et al. (2017), polypharmacy rates are estimated at about 45.9% in the community setting, and nearly 50% of the reported falls belong to the polypharmacy group. Polypharmacy trend is growing in the elderly population in most of the countries (Wastesson et al., 2018). According to the systematic review by Chang et al. (2021), the rate of polypharmacy among the elderly population in Malaysia can be between 20.3% to 100%. Polypharmacy is linked to various adverse effects in the elderly, namely, higher hospitalization rates, improper prescription, drug issues, adverse drug events, physical and cognitive functioning, and death (Davies et al., 2020; Wastesson et al., 2018).

The depressive symptoms in the elderly population have a very high prevalence and complicate polypharmacy management further. Depression in older adults is usually manifested in an atypical way, which is why it can be hard to identify, causing underdiagnosis and undertreatment (National Institute on Aging, 2025). Depressive symptoms are linked with poor physical health, including cardiovascular disease, cancer, diabetes, respiratory diseases, and a higher risk of death (National Collaborating Centre

for Mental Health (UK), 2011; WHO, 2025). Additionally, the presence of depressive symptoms will lead to greater disability, social isolation, cognitive impairment, and increased health care costs (Kupferberg and Hasler, 2023; Meshkat et al., 2025). The importance of studying depressive symptoms in geriatrics is to conduct early diagnosis and specific mental healthcare assistance and to lower the overall disability burden.

Physical frailty is a geriatric syndrome that is severe and is defined by the loss of physiological capacities and susceptibility to stressors (Allison II, Assadzandi, and Adelman, 2021). Older adults have frailty as a vulnerable health condition that contributes to a great risk of adverse outcomes, such as functional decline, cognitive impairment, poor quality of life, rise in health care use, potential falls, fractures, hospitalization, disability, and premature mortality (Cunha et al., 2019; Junius-Walker et al., 2018). Alongside these outcomes, another study based on the data of the English Longitudinal Study of Ageing (ELSA) has found that some other factors, including chronic illnesses, allostatic load, low physical activity, depressive symptoms, cognitive impairment, and lack of social support, have a significant effect on increasing the physical frailty in older adults over time (Ding, Kuha, and Murphy, 2017). Frailty, as well as polypharmacy and depressive symptoms, are the areas that should be explored during a thorough geriatric evaluation and proper care planning.

Overall, geriatric patients are susceptible to polypharmacy, depressive symptoms, and physical frailty. These co-morbidity complications worsen the state of health and raise the burden on the healthcare sector. By focusing on the relationships between these variables, especially in Malaysian contexts like the HPUSM, Kelantan, it will provide information on the localized intervention to be developed to enhance geriatric health outcomes and make the most of the available resources.

1.3 Research Questions

The following questions are sought to be answered at the end of the study:

- I. What is the proportion of polypharmacy among geriatric patients at Hospital Pakar Universiti Sains Malaysia, Kelantan?
- II. What is the proportion of depressive symptoms among geriatric patients at Hospital Pakar Universiti Sains Malaysia, Kelantan?
- III. What is the proportion of physical frailty status among geriatric patients at Hospital Pakar Universiti Sains Malaysia, Kelantan?
- IV. Is there an association between polypharmacy and depressive symptoms among geriatric patients at Hospital Pakar Universiti Sains Malaysia, Kelantan?
- V. Is there an association between polypharmacy and physical frailty status among geriatric patients at Hospital Pakar Universiti Sains Malaysia, Kelantan?
- VI. Is there an association between depressive symptoms and physical frailty status among geriatric patients at Hospital Pakar Universiti Sains Malaysia, Kelantan?

1.4 Research Objectives

1.4.1 *General Objective*

To determine the proportion of polypharmacy, depressive symptoms, and physical frailty status, as well as the association between polypharmacy, depressive symptoms, and physical frailty status among geriatric patients at Hospital Pakar Universiti Sains Malaysia (HPUSM), Kelantan.

1.4.2 *Specific Objectives*

- I. To determine the proportion of polypharmacy among geriatric patients at HPUSM, Kelantan.
- II. To determine the proportion of depressive symptoms among geriatric patients at HPUSM, Kelantan.
- III. To determine the proportion of physical frailty status among geriatric patients at HPUSM, Kelantan.
- IV. To assess the association between polypharmacy and depressive symptoms among geriatric patients at HPUSM, Kelantan.
- V. To assess the association between polypharmacy and physical frailty status among geriatric patients at HPUSM, Kelantan.
- VI. To assess the association between depressive symptoms and physical frailty status among geriatric patients at HPUSM, Kelantan.

1.5 Research Hypothesis

Null Hypothesis (H_0)

- : There is no significant association between polypharmacy and depressive symptoms among geriatric patients at HPUSM, Kelantan.
- : There is no significant association between polypharmacy and physical frailty status among geriatric patients at HPUSM, Kelantan.
- : There is no significant association between depressive symptoms and physical frailty status among geriatric patients at HPUSM, Kelantan.

Alternative Hypothesis (H_1)

- : There is a significant association between polypharmacy and depressive symptoms among geriatric patients at HPUSM, Kelantan.
- : There is a significant association between polypharmacy and physical frailty status among geriatric patients at HPUSM, Kelantan.
- : There is a significant association between depressive symptoms and physical frailty status among geriatric patients at HPUSM, Kelantan.

1.6 Justification of Study

Polypharmacy, depressive symptoms, and physical frailty are among the common and related problems faced by geriatric patients that pose a big problem to the health care sector, not only in Malaysia but globally. Polypharmacy among the Malaysian elderly is very high, with an estimated range of about 39-55% in hospital settings and 45.9% among community-dwelling elderly (Chang et al., 2021; Lim et al., 2017). This polypharmacy is a concern because it is closely associated with adverse drug reactions, poor medication adherence, drug interactions, and is more likely to cause geriatric syndromes (Fauziyah et al., 2017). However, there is limited comprehensive research locally measuring its prevalence and its associations with important geriatric conditions.

The common complementary components of older populations include physical frailty and depressive symptoms. The factors that can lead to frailty and, consequently, preventative measures to combat it concern weight abnormalities and depressive symptoms, which are significant targets (Woods et al., 2005). The elderly are also victims of depression, which has been a factor in increased dysfunction and decreased quality of life. The relation of polypharmacy with these conditions can reveal factors that can be altered to achieve the best geriatric health outcomes.

Although these interrelated issues are evident worldwide, there is limited local information available about Malaysian geriatric patients at the Hospital Pakar Universiti Sains Malaysia (HPUSM) in Kelantan. This study aims to fill that significant gap by determining the proportion of polypharmacy, depressive symptoms, and physical frailty, and assessing the associations among them. The results will offer useful baseline information to clinicians and policymakers to create specific interventions that can

enhance medication management and holistic treatment of the aging population in Malaysia.

Evidence-based strategies to reduce inappropriate polypharmacy while addressing mental health and frailty could improve patient safety, functional ability, and quality of life in such a vulnerable population. The outcomes of this study can also generate subsequent research and guide the reforms in the healthcare delivery to enhance geriatric care delivery in Malaysia.

1.7 Conceptual Framework

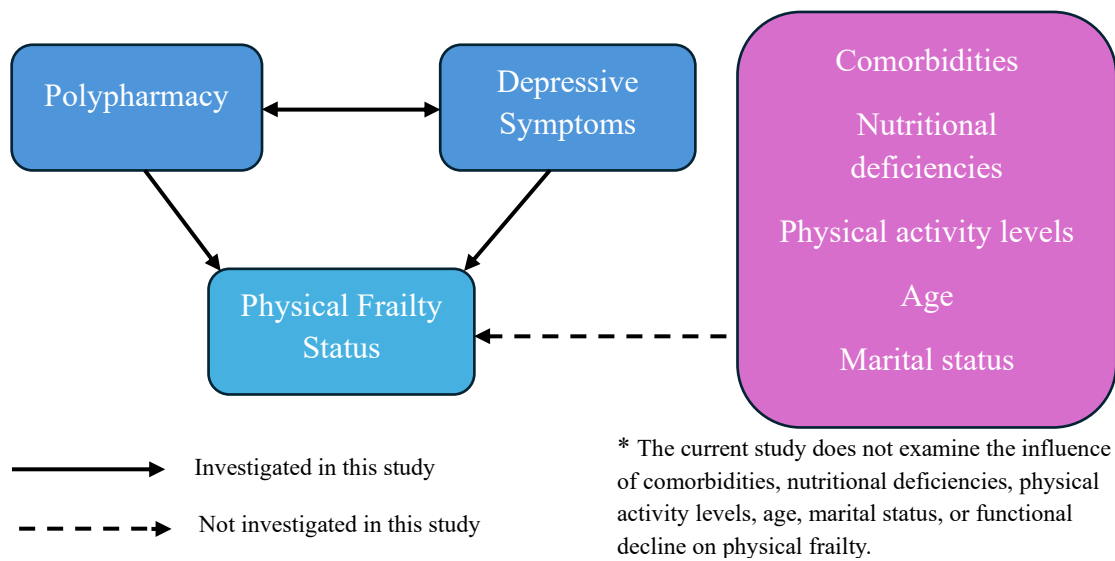


Figure 1.7: Conceptual framework illustrates the relationship between polypharmacy and depressive symptoms (independent variables) affecting physical frailty status (dependent variable) among geriatric patients at Hospital Pakar Universiti Sains Malaysia (HPUSM), Kelantan.

This framework places physical frailty status as the primary outcome of interest, as it is a complex condition that can be affected by various factors (Apóstolo et al., 2018; Fhon et al., 2018). This study focuses on polypharmacy (the use of five or more medications concurrently) and depressive symptoms as key independent variables because they have been reported to have implications on the health and functional status of older adults (Chang et al., 2021; Lim et al., 2017; St. John et al., 2012).

Polypharmacy has been identified as a significant risk factor that can be related to vulnerability to physical frailty because of medication side effects, drug interactions, and a higher risk of falls and hospitalizations (Fauziyah et al., 2017). Depressive symptoms significantly affect the onset and progression of physical frailty status among older adults, which highlights that early intervention must be implemented to reduce the frailty risk (Vaughan et al., 2015). A study reveals that there is a positive relation between polypharmacy and depressive symptoms among geriatric patients, with certain medications being associated with a higher prevalence of depressive symptoms (Leszek et al., 2016).

Although this study will focus on these relationships, it recognizes other uninvestigated factors, including comorbidities, nutritional deficiencies, physical activity levels, age, marital status, and functional decline with age that also play a significant role in frailty development and progression (Apóstolo et al., 2018; Fhon et al., 2018). These other factors underline the multifactorial nature of frailty and the significance of comprehensive assessments in clinical practice.

This study examines the association between polypharmacy, depressive symptoms, and physical frailty status to inform specific interventions to enhance the health outcome and quality of life of geriatric patients in Malaysia.

CHAPTER 2

LITERATURE REVIEW

2.1 Prevalence of Aging Population

Chronological age is the typical definition of the aging population. According to the United Nations and national statistical definitions, the most widely accepted definition is 60 years and older, sometimes 65 years and older (United Nations, 2015). The aging of the population is caused by a decrease in fertility rates and an increase in life expectancy, which leads to a rise in the ratio of the elderly to the general population (World Health Organization, 2024).

The aging population has greatly increased in recent decades across the world. The population of 60 years old and above is expected to rise by 56% between 2015 and 2030, that is, from 901 million to 1.4 billion. This figure is projected to increase more than twice by 2050; it is estimated that the figure will be around 2.1 billion (United Nations, 2015; WHO, 2024). This demographic trend is most evident in developed nations but is also growing at a high rate in low and middle-income nations. The median age of the global population has been rising, and while Europe and North America are already aging, Asia and Latin America are expected to experience the fastest rate of population growth by mid-century (Institute of Medicine (US) Committee on the Long-Run Macroeconomic Effects of the Aging U.S. Population, 2012).

The aging population is increasing at a rate never seen in the Asian context. In 2050, the proportion of the Asian population aged 60 years and above is expected to rise to a quarter, and the elderly population is projected to triple to 1.3 billion people (UNFPA Asia and the Pacific, 2025). China and Japan are among the nations with serious demographic issues due to the declining number of individuals in the working-age

population and the increasing percentage of the aged demographic, which will affect their economic growth and social welfare systems (Wang, 2026).

Locally, Malaysia is becoming an aging nation. According to the Department of Statistics Malaysia (DOSM), the proportion of people aged 65 and above increased to approximately 8.0% of the total population in 2025 (Department of Statistics Malaysia, 2025). Long-term population projections indicate that the percentage of Malaysians aged 65 and over is expected to nearly triple by 2060 compared with 2020, rising from about 6.8% to 18.3%, reflecting rapid population ageing (Department of Statistics Malaysia, 2025). In Kelantan, the elderly population (aged 60 and above) comprises 6.4% of the population, according to the DOSM Kawasanku dashboard (Department of Statistics Malaysia, 2025). Kelantan is also showing a similar trend, with the proportion of aging people projected to exceed 15% by 2032, primarily driven by declining fertility rates and rising life expectancy (Lembaga Penduduk dan Pembangunan Keluarga Negara [LPPKN], 2025). Life expectancy in Malaysia is expected to reach around 75 years in 2024, further exacerbating the growth of the aging population (Amri, 2025).

The population ageing in Malaysia and Kelantan is caused by the falling number of children per woman and an increase in the life expectancy due to the improved health conditions and standards of living (Amri, 2025; LPPKN, 2025). In 2014, the fertility rate in Kelantan was 3.6, but in 2023, it was 2.7 (LPPKN, 2025). This change in demographic is also being affected by economic transformation, urbanization, and a shift in social structure.

In summary, population aging is a major and fast-increasing demographic trend not only worldwide, but also in Asia and Malaysia. It poses challenges and opportunities to the healthcare, economic, and social systems, which must be addressed and planned.

2.2 Risk Factors of Aging

Aging is a complicated interaction between biological, lifestyle, environmental, chronic disease, and psychosocial factors. Biologically, genetic factors do play a major part in lifespan and aging patterns. Recent studies have estimated that genetic factors account for up to 50% of human lifespan and affect important aging characteristics such as frailty and muscle strength (Dean, 2025; Maldonado et al., 2023; Tenchov et al., 2023). Other important biological contributors to aging include shortening of telomeres, epigenetic alterations, and mitochondrial dysfunction (Maldonado et al., 2023; Tenchov et al., 2023).

One of the determinants of aging that is important and can be altered is lifestyle. Eating fruits, vegetables, whole grains, and lean protein and physically exercising have been linked to greater longevity and less frailty (Fadnes et al., 2023; Fekete et al., 2022; Zhou et al., 2021). On the other hand, smoking, alcoholism, and a sedentary lifestyle make an individual age faster and predispose them to the risk of chronic disease (WHO, 2024). A research carried out in ASEAN nations, including Malaysia, established that healthy lifestyles and more active behaviors among the elderly led to a better chance of active aging (Tiraphat et al., 2021).

There are also environmental factors, including exposure to pollution, housing, and socioeconomic status, which impact aging. Urbanization in Malaysia has caused disparities in access to healthcare and the quality of the environment, which affects the elderly population, especially in rural regions, where the shortage of food and inadequate transportation options worsen the state of health (Abdullah, Ismail, & Yusoff, 2024). Research has found that the development of age-friendly environments can enhance the mental health and physical functioning of older Malaysians (Tan, 2022).

Functional impairments and decline may also be caused by chronic illnesses, thus increasing the aging process (Hu et al., 2024; Zhang et al., 2023). Multimorbidity, the presence of two or more chronic diseases, is extremely widespread among older adults and is associated with indicators of aging acceleration (Zhang et al., 2023). The presence of common chronic diseases like diabetes, cardiovascular disease, arthritis, and cognitive decline also makes the process of aging more complicated (WHO, 2024). Moreover, numerous chronic diseases can be related to chronic inflammation, which is also characteristic of aging itself, which is called inflammaging. This chronic inflammation leads to the damage of cells and may increase the development of other age-related diseases (Ferrucci & Fabbri, 2018).

Health in older age is also affected by psychological and social factors. Older adults might have their physical and mental health deteriorated by loneliness, depression, lack of social support, and deprivation of social status (Apalasamy et al., 2024; Hussein & Mohd Sahardi, 2025; WHO, 2023). Studies in Malaysia highlight that social isolation and psychological distress are common among older adults and significantly impact their quality of life (Apalasamy et al., 2024; Lim et al., 2023). Healthy aging is based on maintaining strong social networks and reducing stigma associated with aging.

In summary, age is predetermined by genetic vulnerability, which, in turn, depends on lifestyle, environmental factors, persistent health conditions, and psychosocial factors. These risk factors are important to be understood in detail to establish effective interventions to facilitate healthy aging in the world and Malaysia.

2.3 Consequences and Healthy Effects of Aging

Aging is associated with a range of consequences and health impacts that affect physical, cognitive, emotional, and functional well-being. Physiologically, the elderly are more susceptible to chronic diseases, including hypertension, diabetes, osteoarthritis, and respiratory diseases, which can lead to sensory impairment, including vision and hearing loss (Haron et al., 2024; WHO, 2024). Sensory deterioration may affect the quality of daily functioning and social isolation (Xiao et al., 2021).

Aging is the most significant risk of dementia and other neurodegenerative illnesses, and the process of cognitive deterioration is a vital issue. Between 60-70% of individuals older than 65 will experience any type of dementia, and the most prevalent one will be Alzheimer's disease (Colita et al., 2024; WHO, 2025). Cognitive impairment includes memory loss, decreased executive function, and slowed processing speed, which may have a prominent influence on independence and quality of life (Colita et al., 2024).

Older adults are likely to be affected by emotional and mental health problems, including depression, anxiety, and loneliness due to several factors, which include loss of loved ones, declining health, and social isolation. These mental and social issues are often accompanied by a worsening physical and cognitive condition, which further increases their effect on well-being (Guarnera, Yuen, & Macpherson, 2023; Puyané et al., 2025). Older adults with depression are known to have a high morbidity and mortality rate, which is why it needs specific focus (Sekhon, Patel, & Sapra, 2025).

The disability of the functional performance of activities of daily living (ADLs) and instrumental activities of daily living (IADLs) is functional impairment caused by aging and comorbidity, and results in greater dependency on caregivers (Balasubramanian et al., 2024; Edemekong et al., 2025; Souto et al., 2024). This functional impairment not

only affects the autonomy of the person but is also a significant predictor of hospitalization and institutionalization (Souto et al., 2024).

The utilization of healthcare and its costs are also increasing exponentially as the population ages. This is mainly because it requires chronic disease management, rehabilitation, and long-term care. In Malaysia, elderly healthcare is expected to burden the economy of this country as the population is aging and the prevalence of chronic diseases is on the rise (Haron et al., 2024). This is highly problematic for the healthcare systems, which will be required to adjust service delivery and financing to suitably adjust to an aging population.

In summary, the effects of aging are complex and affect physical health, cognitive ability, mental health, and functional capacity. With the increasing demands of healthcare and costs, this highlights the importance of policies and interventions to promote healthy aging.

2.4 Polypharmacy in Geriatrics

The general definition of polypharmacy in geriatrics is based on the concurrent use of 5 or more prescription drugs and/ or over-the-counter medications (Halli-Tierney et al., 2019; Masnoon et al, 2017). This indicates the multifaceted management of various chronic conditions, which are prevalent among older adults (Halli-Tierney et al., 2019; Masnoon et al, 2017). Polypharmacy allows the effective treatment of various chronic diseases among the elderly, enhancing the control of the disease and its symptoms, as well as the overall quality of life through the appropriately selected and monitored medications (Jandu et al., 2024; Kurczewska-Michalak et al., 2021). Polypharmacy is required in most

cases but may also cause the inappropriate use of medication that may result in adverse outcomes.

Globally, the prevalence of polypharmacy in the general population is 37%, with higher rates among older people (45%), outpatients (48%), and inpatients (52%). The prevalence was higher in North America (52%) than in Asia (36%) and Europe (36%). Polypharmacy is most common in Europe (68%) and in hospital settings (71%), with a prevalence of 59% among frail elderly people (Kim et al., 2024). According to the systematic review by Chang et al. (2021), the prevalence of polypharmacy among the Malaysian aging population may range from 20.3% to 100%. The significant variation is due to the disparate definitions of polypharmacy. Older adults with more than one disease often take more than one medicine. Based on a research shows that almost half of the older people in Malaysia were taking more than one medication (Chang et al., 2021). Such high prevalence emphasizes the necessity to implement strict pharmaceutical review and management for the aging population (Ministry of Health Malaysia, 2024).

Polypharmacy is commonly caused by various chronic conditions, including diabetes, hypertension, cardiovascular disease, and psychiatric disorders that involve taking several medications (Cho et al., 2022). Additionally, being male, older, having insurance, and using healthcare services were all linked to a higher chance of polypharmacy (Cho et al., 2022). Polypharmacy can also be caused by prescribing cascades, in which the side effects of one medication trigger further prescriptions (Halli-Tierney et al., 2019; Tejani & Perry, 2025). The risk factors linked to polypharmacy include adverse drug reactions, drug-drug interactions, falls, cognitive impairment, hospitalization, and healthcare expenditure (Davies et al., 2020; Varghese, 2024). Adverse drug reactions are unintended, harmful events caused by medicines that can contribute to or occur during many unscheduled hospital admissions, whereas drug-drug interactions

are when two or more medications are administered concurrently, which can result in unintended effects, toxicity or a lack of efficacy (Jutley et al., 2024). Older adults are the group most vulnerable to preventable adverse drug events and require continuous evaluation of the suitability of medications (Halli-Tierney et al., 2019).

There are a few tools that can be used to assess and optimize polypharmacy. The Beers Criteria are a widely recognized list of potentially inappropriate medication use in older adults. Evidence-based tools that can be used to detect potentially harmful medications and treatment omissions, respectively, are the STOPP (Screening Tool in Older Adults) and START (Screening Tool in Reminding Right Treatment) criteria (Halli-Tierney et al., 2019; Keche et al., 2022; Ministry of Health Malaysia, 2024; Sadia et al., 2025). These tools, which have recently been revised to capture the emerging clinical evidence, are essential in reducing prescribing and enhancing the safety of medication in older adults within the country and the entire world.

2.5 Depressive Symptoms among Geriatric

Depressive symptoms in older adults tend to be different as compared to younger individuals. Older adults are often affected by anhedonia, sleep disorders, cognitive dysfunction, and somatic symptoms such as lack of appetite and fatigue despite not exhibiting classic signs and symptoms of major depressive disorder, such as sadness or irritability (Devita et al., 2022; Sözeri-Varma, 2012). The absence of interest, sleeping difficulties, hopelessness, lack of appetite, and suicidal thoughts without apparent depression are the features of one of the subtypes of depression known as “depression without sadness” (Devita et al., 2022).

Depression among older adults has varied causes that include biological, psychological, and social factors. Neurochemical changes, inflammation, and dysregulation of the brain-derived neurotrophic factors are examples of biological factors (Szymkowicz et al., 2023; Zenebe et al., 2021). Cognitive decline and lack of coping mechanisms are among the psychological factors, and loneliness, bereavement, social deprivation, and low socioeconomic status are among the social factors (Remes et al., 2021; Zenebe et al., 2021). Depression is much higher in rural older adults with low health literacy levels and high comorbidities in Malaysia (Azhar et al., 2025).

Older adults with depression are characterized by high morbidity and suicide risk, cognitive impairment, poor physical functioning, and higher health care use (Maier et al., 2021; WHO, 2023). Dementia and death are also highly predicted by late-life depression, which highlights the necessity of early diagnosis and treatment (Maier et al., 2021).

Screening tools such as the 15-item Geriatric Depression Scale (GDS-15) and the Patient Health Questionnaire-9 (PHQ-9) have been validated and widely used to assess depressive symptoms in older adults (Costa et al., 2016). Both tools have proven to be sensitive and specific in the detection of major depressive episodes in older adults across diverse settings, including Malaysia (Azhar et al., 2025; Costa et al., 2016). These tools are simple to administer, and they help in early diagnosis to allow early management.

In summary, geriatric depression is a complicated disorder that is characterized by unique clinical features and complex etiologies. Routine screening with a validated instrument (the GDS-15 and PHQ-9) and individual interventions based on the Malaysian context should be justified due to their considerable influence on health outcomes.

2.6 Physical Frailty in Geriatrics

Physical frailty in geriatrics is a clinical syndrome that is defined by the increased susceptibility to stressors because of reduced physiological reserves and functioning of multiple organ systems (Nordin et al., 2021). In general, conceptual models define frailty as a multidimensional concept including physical, cognitive, psychological, and social determinants, with the best-known one being the somatic phenotype model developed by Fried et al. (2001), comprising unintentional weight loss, muscle weakness, fatigue, slow walking speed, poor endurance, and low physical activity as its criteria (Allison II et al., 2021; Nordin et al., 2025).

The prevalence of frailty varies globally, ranging from approximately 6% to over 76% among older adults, depending on the population and the assessment tool used (Shaharudin & Abd Rahman, 2022). In Malaysia, frailty rates have been reported to be between 5.7% and 56.5%, with more than half of older adults having pre-frailty, which shows high heterogeneity (Embong et al., 2021; Shaharudin & Abd Rahman, 2022). The factors that affect this variation include living in an urban or rural area, socioeconomic status, and comorbidity burden.

Frailty can be caused and contributed by chronic diseases such as cardiovascular disease, diabetes, and arthritis, as well as malnutrition and physical inactivity (Liu et al., 2024; Wei et al., 2018). Malnutrition, which is common among about two-thirds of the older population, aggravates muscle weakness and functional impairments and is closely related to the development of frailty (Norazman et al., 2020). Frailty is further promoted by physical inactivity in enhancing muscle weakness and sarcopenia (Liu et al., 2024).

Physical frailty is related to several health risks, such as the risk of falls, hospitalization, prolonged recovery, disability, and death (Hu et al., 2021; Nordin et al.,

2025; Rivas-González et al., 2025). Frail individuals are at high risk of falls and injuries, and have a longer hospitalization, resulting in higher healthcare expenses and reduced quality of life (Hu et al., 2021).

Frailty assessment tools that are commonly used include the Fried Frailty Criteria and the FRAIL scale. The Fried Phenotype provides an objective assessment based on indicators of physical function, while the FRAIL scale is a simple questionnaire that assesses fatigue, resistance, mobility, illness, and weight loss, suitable for use in both clinical and community settings (Allison II et al., 2021; NSW Aged Care Health Network, 2020). Both tools have shown good reliability and predictive validity for adverse outcomes and would be useful in the routine screening and intervention programs. Moreover, the Pictorial Fit-Frail Scale (PFFS) is also a simple, feasible, and reliable tool in identifying the frailty among patients, caregivers, and health practitioners in clinical settings (McGarrigle et al., 2019; Theou et al., 2019).

2.7 Association between Polypharmacy and Depressive Symptoms

Polypharmacy, which is generally referred to as taking five or more drugs at once, is becoming linked with adverse mental health outcomes, especially depressive symptoms, among older adults. It has been found that there is a positive relationship between polypharmacy and depression, and various studies have found a positive correlation between the number of medications taken and the severity of depression symptoms (Alsulami et al., 2024; Leszek et al., 2016). This association could be explained by the difficulty of dealing with complicated medication schedules and the side effects of specific drugs that are known to influence mood.

This study indicates that the complicated interactions between polypharmacy and clinically significant drug-drug interactions (DDIs) and adverse drug reactions (ADRs) in older Chinese adults with cancer are emphasized by Yan et al. (2025), with a specific focus on sex and depression. Even though the presence of DDIs and polypharmacy was closely linked with an increased risk of ADRs, the correlation between these variables appeared to be more significant in individuals with depressive symptoms (Yan et al., 2025).

Previous studies indicate that depressive symptoms could be the cause as well as the effect of polypharmacy. As an example, in the case of older adults, depression is usually accompanied by additional comorbidities and necessitates multiple medications. Polypharmacy in itself can also worsen depression due to pharmacodynamic effects and a higher risk of adverse drug reactions (Cheng & Bai, 2022; Palapinyo et al., 2021). These findings reveal the bidirectional and complex relationship between polypharmacy and depression.

Medication reconciliation and prescription reduction interventions of polypharmacy have demonstrated the capability to mitigate the medication burden, enhance adherence, and improve the quality of life, thereby alleviating depressive symptoms (Alsulami et al., 2024; Palapinyo et al., 2021). This is to underscore the significance of a comprehensive care approach to the physical and mental health of older adults with polypharmacy.

2.8 Association between Polypharmacy and Physical Frailty Status

Polypharmacy and physical frailty are related conditions that are common among elderly people. Research has shown that frailty is closely related to the number of

medications taken, and their frequency or intensity. The study conducted by Alqahtani (2023) established that polypharmacy, which is defined as taking five or more medications daily, was still considerably correlated with frailty among older adults living in the community even after adjusting for possible confounding factors, such as age, sex, body mass index (BMI), and comorbidities.

The possible links between polypharmacy and frailty are medication side effects, including weight loss, issues with balance, malnutrition, and cognitive impairment, which are primary characteristics of frailty (Alqahtani, 2023; Ekram et al., 2022). Furthermore, polypharmacy may exacerbate frailty through cumulative anticholinergic effects and drug interactions that result in adverse drug reactions (Umegaki, 2025). While the prevalence of multiple chronic conditions partially explains the overlap between polypharmacy and frailty, there is evidence that polypharmacy independently contributes to the development of frailty beyond the burden of disease (Alqahtani, 2023; Ekram et al., 2022).

The clinical implication of this relationship is that close attention to medication in frail elderly patients is necessary to minimize the probability of further impairment of functional status, hospitalization, and poor outcomes. The safer medication regimens and general care can be influenced by prescription reduction programs and frailty screening tools, such as the Fried Frailty Phenotype and the FRAIL Scale (Alqahtani, 2023). Malaysian data are consistent with the global trends, with the observation that polypharmacy is strongly linked to increased prevalence of frailty among older people in rural and institutionalized settings, which is the reason why the specific intervention measures are required (Hasan et al., 2017).

In summary, polypharmacy is a common and modifiable factor associated with physical frailty in older adults. It is important to address polypharmacy by ensuring that