

Multimorbidity in older patients – practical approach to the diagnosis and management

Wielochorobowość u osób starszych – praktyczne aspekty diagnostyki i postępowania klinicznego

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Abstract

The article explains the notion and definition of multimorbidity, showing how multimorbidity can be measured in clinical practice and research. Moreover, we present the epidemiology and patterns of multimorbidity, listing the most important consequences of multimorbidity for patients, caregivers, and healthcare systems. Lastly, practical approach to the diagnosis and management of multimorbidity is described. (Gerontol Pol 2023; 31; 258-268) doi: 10.53139/GP.20233137

Keywords: *ultimorbidity, older patients, diagnosis, management*

Streszczenie

Artykuł wyjaśnia pojęcie i definicję wielochorobowości i prezentuje w jaki sposób można ją definiować w praktyce klinicznej i badaniach naukowych. Analizowana jest epidemiologia wielochorobowości oraz najważniejsze jej konsekwencje dla pacjentów, opiekunów i systemów opieki zdrowotnej. W podsumowaniu przedstawione zostało także praktyczne podejście do diagnozowania i leczenia wielochorobowości. (Gerontol Pol 2023; 31; 258-268) doi: 10.53139/GP.20233137

Słowa kluczowe: *wielochorobowość, starsi pacjenci, diagnoza, postępowanie*

Introduction

Chronic conditions account for most healthcare services and are the leading cause of death globally [1]. An extended life expectancy and the aging of populations are the two main reasons for the increasing prevalence of chronic conditions. Moreover, unfavorable lifestyle factors, such as tobacco and alcohol use, physical inactivity, and unhealthy diet are behind the increasing prevalence of non-communicable diseases, such as cardiovascular diseases, diabetes, obesity, or cancer [2].

Currently, it is common for one person to live with several chronic conditions – a state termed multimorbidity. Multimorbidity is associated with a substantial disease burden for patients and their caregivers but has also become a major challenge for healthcare systems. In this review, we explain the notion and definition of

multimorbidity, showing how multimorbidity can be measured in clinical practice and research. Moreover, we present the epidemiology and patterns of multimorbidity, listing the most important consequences of multimorbidity for patients, caregivers, and healthcare systems. Lastly, we suggest a practical approach to the diagnosis and management of multimorbidity.

Notion of multimorbidity

The notion of multimorbidity highlights the importance of understanding how different chronic conditions interplay with one another to affect the patient as a whole. Importantly, multimorbidity does not give priority to any of the many conditions a person may live with. In addition, multimorbidity is patient-centered, underlying

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the need for a holistic approach that considers the patient's needs and values on a par with treatment algorithms. Multimorbidity is contrasted with the notion of co-morbidity, which prioritizes one index condition, seeing the remaining conditions as somehow less important. This perspective is common in secondary clinical practice in which specialist clinicians focus on one condition in their field of expertise, failing to notice how all the conditions interplay and disturb the patient's well-being. Similarly, treatment guidelines are often created solely for single diseases even when a considerable proportion of patients with a given disease may have other chronic conditions.

Definition of multimorbidity

Although there is no universally accepted definition of multimorbidity, the World Health Organization's (WHO) definition is widely used. According to this definition, multimorbidity refers to the presence of two or more chronic conditions in the same person. [3]. The inclusion of any two chronic conditions has been criticized because some chronic conditions may have no noticeable effect on patients, such as well-controlled hypertension or hypercholesterolemia. Therefore, some investigators prefer to define multimorbidity as chronic conditions affecting three or more organ systems (complex multimorbidity), which should help identify those patients who receive care from different specialist clinicians [4]. However, despite some critique, the WHO's definition is broadly endorsed. For example, the Academy of Medical Sciences agrees that multimorbidity should be defined as the co-existence of two or more chronic conditions in the same person, with each of the conditions being either: (1) a physical non-communicable disease of long duration, such as a cardiovascular disease or cancer, (2) a mental health condition of long duration, such as a mood disorder or dementia, or (3) an infectious disease of long duration, such as human immunodeficiency virus (HIV) infection or hepatitis C [5]. Likewise, in a Delphi consensus study, 150 expert researchers and 25 people with multimorbidity agreed that multimorbidity should be defined as two or more chronic conditions in the same person [6]. According to this consensus, to be included, the condition must demonstrate one of the following characteristics: currently active; permanent in their effects; requiring current treatment, care, or therapy; requiring surveillance; or relapsing-remitting conditions requiring ongoing care.

Measurement of multimorbidity

Condition catalogues

While there is agreement among most investigators that multimorbidity refers to the presence of two or more medical conditions in a single person, the lack of consensus on which conditions to include is hindering research on the topic. A systematic review of over 500 studies on multimorbidity found that the condition catalogues listed from as few as two to as many as 285 conditions (median 17) [7]. In that systematic review, the following condition groups were included in over 80% of the studies: cardiovascular, metabolic-endocrine, respiratory, musculoskeletal, and mental health conditions [7]. Moreover, only eight individual diseases were found in over half of the studies: diabetes, stroke, cancer, chronic obstructive pulmonary disease (COPD), hypertension, coronary heart disease, chronic kidney disease, and heart failure [7]. This variability in measuring multimorbidity makes it difficult to compare results from different studies.

Simple counts and weighted indices

Multimorbidity can be measured with two types of indices: simple condition counts and weighted indices, which consider the severity of each condition. Condition counts are suitable for estimating the prevalence and for examining the patterns of multiple chronic conditions. However, simple counts fail to notice that various chronic conditions may be associated with different burdens. In contrast, weighted indices of multimorbidity assign weights that link a condition to an outcome of interest, such as mortality, physician-rated health, or risk of hospital admission [8]. For example, in the Charlson Comorbidity Index (CCI), which predicts death, a condition with an increased mortality risk, such as malignancy, is assigned a greater weight (2 points) than a more benign condition, such as a well-controlled diabetes (1 point) [9].

The weighted multimorbidity indices can be broadly classified based on the information source used to obtain condition names and on the type of outcome used for weighting. Figure 1 shows the divide between indices that use direct information on diagnoses, e.g., from patients or their records, or indirect information based on medication use. Further subclassification depends on the type of outcomes used for weighting, with the most popular outcomes being mortality, hospital admission, and physician-rated health. Below, we briefly describe a few of such indices.

The CCI and the Elixhauser Comorbidity Index (ECI) are the two most popular indices that predict mortality [1]. Although the CCI lists 17 comorbidities, compared to 30 comorbidities in the ECI, both indices include the most common physical and mental condition groups [10]. A direct comparison between the two indices found that the ECI performed better than the CCI at predicting in-hospital death in the elderly [11].

The Cumulative Illness Rating Scale for Geriatrics (CIRS-G) was developed to measure disease severity in the elderly. With this index, the clinician rates a person's health across 14 condition groups, including both physical and psychiatric conditions, assigning each condition group a score of 0 (no problems), 1 (mild problems – no treatment needed), 2 (moderate problems – active treated needed), 3 (severe problem – constant disability), or 4 (extremely severe – urgent clinical problem) [3]. Higher CIRS-G scores are associated with increased mortality, hospitalization risk, and disability [12].

The Geriatric Index of Comorbidity (GIC) is another index developed to predict mortality in elderly people based on the number and severity of the most common diseases of old age. The GIC lists 15 conditions, including several cardiovascular diseases, diabetes, anemia, gastrointestinal diseases, neurologic diseases, musculoskeletal diseases, and cancer [13]. The severity of each condition is graded by the clinician on a scale from 0 (absence of disease) to 4 (life-threatening disease). Subsequently, patients are classified into four classes of disease severity, from Class 1 (diseases with severity grades of no greater than 1) to Class 4 (at least one con-

dition with a severity grade of 4 or two diseases with a grade of 3). In a validation study of the GIC, 12 months after hospital discharge, the survival rates were ~95% for Class 1, ~85% for Class 2, ~75% for Class 3, and less than 50% for Class 4 [13].

The weighted Functional Comorbidity Index (w-FCI) may be used to predict functional status at hospital discharge. The w-FCI includes 18 diagnoses, such as cardiovascular diseases, bone diseases, respiratory diseases, neurologic diseases, and psychiatric diseases. The severity of each of the 18 diagnoses is scored by the physician as 0 (no influence on functional status), 1 (partial influence), or 2 (severe influence) [14]. In a study among elderly patients, the w-FCI predicted mobility after rehabilitation better than the CCI [15].

The Health Impact Index (HII) was validated against a self-rated state of health, ranging from poor (1 point) to very good (4 points). In total, 19 conditions were included in the HII, with weights ranging from 1 (e.g. psoriasis) to 13 (Parkinson's disease) [16].

The Seattle Index of Comorbidity (SIC) considers age, smoking status, and a history of myocardial infarction, cancer, lung disease, heart failure, diabetes, pneumonia, and stroke to predict both mortality and hospital admissions. A SIC score of 7-8 is associated with a six-fold increase in mortality and a 50% increase in hospital admission risk compared to SIC scores of 0 – 4 [17].

The Modified-Chronic Disease Score uses prescription data to predict 1-year mortality. In this tool, medications are assigned to groups of conditions, which then are given different weights depending on the risk of de-

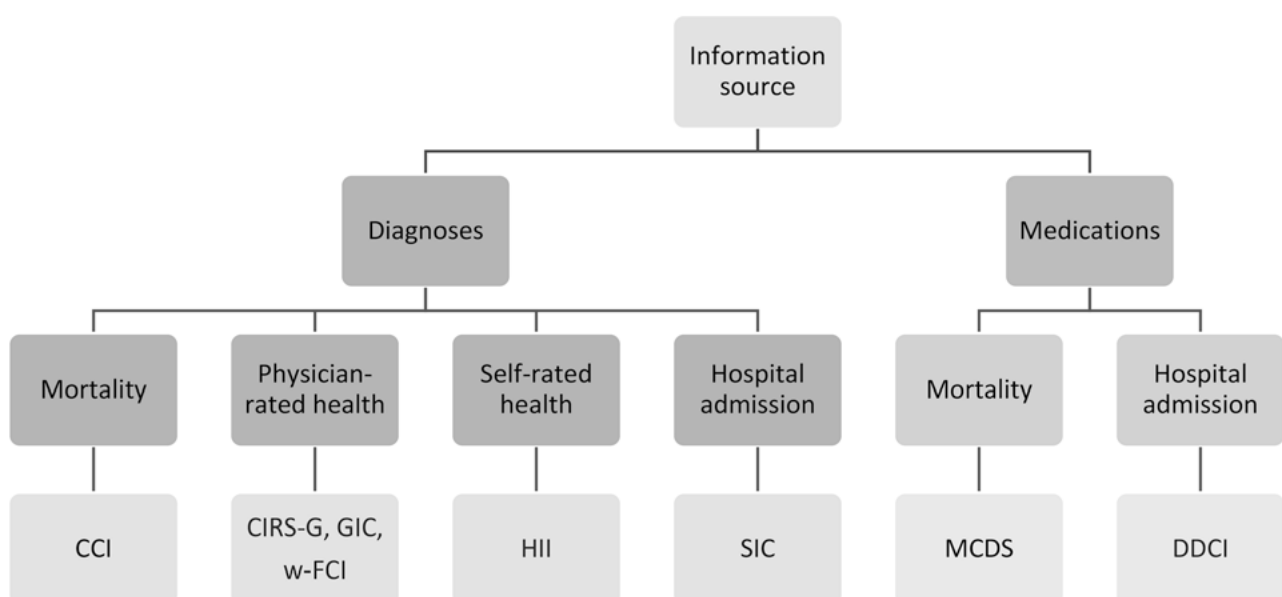


Figure 1. Classification of multimorbidity indices depending on the information source used to obtain conditions and on the type of outcome. CCI, Charlson Comorbidity Index; ECI, Elixhauser Comorbidity Index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; GIC, Geriatric Index of Comorbidity; w-FCI, weighted Functional Comorbidity Index; HII, Health Impact Index; SIC, Seattle Index of Comorbidity; MCDS, Modified-Chronic Disease Score; DDCI, Drug Derived Complexity Index

ath (e.g., cancer, 10 points; dementia, 2 points) [18]. The Drug Derived Complexity Index uses a similar approach to estimate the risks of death and unplanned hospital admissions [19].

Epidemiology of multimorbidity

According to a meta-analysis of studies enrolling over 15 Million people from 54 countries, nearly 4 in 10 people (37%) globally have multimorbidity (South America, 46%; North America 43%; Europe, 39%; Asia, 35%) [20]. Among people aged 60 years or more, over half (51%) have two or more chronic conditions [20].

Age is the strongest epidemiological predictor of multimorbidity. In the general population, between the ages of 50 and 80 years, the prevalence of multimorbidity increases linearly from 20% to 80%, which amounts to an increase of about 10% per 5 years [21]. However, in absolute numbers, there are more middle-aged than elderly people with multimorbidity owing to a larger proportion of the former age group in the general population [21,22]. By 2050, the proportion of people aged 60 years or older is expected to triple worldwide, making the elderly the largest age group affected by multimorbidity [23]. Although the existing research on multimorbidity concerns predominantly adult populations, more and more chronic conditions are being diagnosed before adulthood. However, more research is needed to characterize both the prevalence and patterns of multimorbidity in children and adolescents [24].

Multimorbidity is more prevalent in women than men, with most studies reporting a difference in prevalence of about 10% between the two sexes [25,26]. Multimorbidity is also more common in people with a low socioeconomic status, which is characterized by, among other things, lower education, high unemployment, and low income [21,27,28]. The prevalence of multimorbidity varies across countries: multimorbidity is most prevalent in low and middle-income countries, which suffer from poverty, environmental pollution, and poorly developed healthcare services [29]. In contrast, in high-income countries, multimorbidity is driven primarily by lifestyle factors such as chronic stress, poor sleep, physical inactivity, and smoking [30].

Patterns of multimorbidity

Patients with multimorbidity are heterogeneous, with a multitude of possible combinations of chronic conditions. A systematic review of 23 observational studies of multimorbidity found 165 different combinations of two

diseases [31]. Certain health conditions are more likely to occur together than others. For example, a middle-aged person from a developed country with diabetes is more likely to also have obesity rather than an HIV infection. Similarly, an elderly patient with Parkinson's disease is more likely to have dementia than asthma. To provide better care, we need to understand which conditions commonly occur together. It is therefore more important to identify multimorbidity patterns than just counting individual diseases. Understanding these patterns can help develop relevant treatment guidelines and characterize patient profiles. However, there is limited evidence on multimorbidity patterns due to most studies analyzing co-morbidities associated with a single index condition. Recently, however, studies have used statistical methods like cluster analysis or factor analysis to identify multimorbidity patterns.

The multi-country Study on Global AGEing and Adult Health (SAGE, China, Ghana, India, Mexico, Russia, and South Africa) and the Collaborative Research on Ageing in Europe (COURAGE) survey (Finland, Poland, and Spain) analyzed the co-occurrence of the twelve most common conditions: angina, arthritis, asthma, cataract, COPD, depression, diabetes, edentulism, hypertension, cognitive impairment, obesity, and stroke [32]. Using exploratory factor analysis, the study found three major multimorbidity patterns: cardio-respiratory (angina, asthma, and COPD), metabolic (diabetes, obesity, and hypertension), and mental-articular (arthritis and depression). The cardio-respiratory and metabolic patterns were seen across the included countries, whereas the mental-articular pattern was found in India, Ghana, and China [32].

In line with the SAGE and COURAGE surveys, a systematic review of 14 studies found that the three most common multimorbidity patterns were cardiometabolic diseases, mental health diseases, and musculoskeletal diseases [33]. Likewise, another systematic review of 39 studies from twelve countries found the three following patterns to be most common: osteoarthritis, cardiovascular diseases, and metabolic conditions [26].

Across different studies, the cardiometabolic and mental health condition patterns seem most replicable [34,35]. A cross-sectional study among nearly two million people from the general population reported that physical and mental conditions co-existed in over 10% of the population [21].

Further research is necessary to better understand multimorbidity patterns across age groups, sexes, and races. For example, the patterns of multimorbidity in children and adolescents vary substantially from those found in adults [36].

Consequences of multimorbidity

Multimorbidity is associated with a substantial burden for patients, their caregivers, and healthcare systems. For example, patients with multimorbidity are at an increased risk of death, hospital admission, polypharmacy, frailty, and poor quality of life compared with people without multimorbidity [37,38].

Increased mortality

People with multimorbidity are at an increased risk of death compared with the general population. A meta-analysis of longitudinal studies reported that multimorbidity was associated with a 50% increased risk of death [39]. Another study estimated that, on average, each additional chronic condition reduces life expectancy by about two years; thus, someone with five conditions will die nearly ten years earlier than a person without any such conditions [40]. However, not all multimorbidity patterns have the same risk of death. A nationwide Danish study found that having cancer, a neurological condition, a mental health condition, or a lung condition was associated with the greatest risk of long-term death, whereas the lowest risk was seen for musculoskeletal diseases, gastroenterological diseases, and kidney diseases [41]. In a similar study from the USA, complex cardiometabolic morbidity was associated with the greatest mortality followed by cognitive impairment and respiratory diseases [42].

High hospitalization risk

Having many chronic conditions puts people at risk of in-hospital treatment. A study carried out in 16 European countries found that multimorbidity was associated with a substantially increased risk of being admitted to hospital and with a longer hospital stay [43]. Likewise, in a population-based study in China, multimorbidity was associated with twice the odds of hospital admission compared with the general population [44]. Similarly, a meta-analysis of 33 studies found that multimorbidity was associated with over twice the odds of being admitted to hospital; however, the evidence linking multimorbidity with prolonged hospital stay was inconsistent [45]. The patterns of multimorbidity associated with the greatest risk of hospital admission may include cardiovascular diseases, anemia combined with dementia, psychiatric disorders, and metabolic conditions [46].

Polypharmacy

Polypharmacy is the prescription of too many medications to one patient. Some investigators distinguish between appropriate and inappropriate polypharmacy, with the latter defined as the use of multiple medications that put the patient at an increased risk of unfavorable health outcomes. Although there is no clear cutoff for the number of prescriptions that constitute polypharmacy, for practical purposes, the most commonly accepted definition of polypharmacy is the regular use of five or more medications [47]. Indeed, of 81 studies using a count-based definition of polypharmacy, 51 used the cutoff of 5 or more medications [48]. Using this definition, a meta-analysis of studies enrolling over 50 million people reported that polypharmacy is used in nearly half of people aged 65 years or older [49]. The risk factors for polypharmacy include specialist care provided by multiple physicians, chronic mental conditions, and residing in a long-term care facility [50]. The negative consequences of polypharmacy are many, such as decreased quality of life, impaired mobility, increased mortality, an increased risk of falls, frailty, prescribing errors, and medication non-adherence [50].

Frailty

Frailty, which may co-exist with multimorbidity, is associated with a substantial disease burden. There might be a bidirectional causal relationship between multimorbidity and frailty: frailty may predispose to the development of multiple chronic diseases, but it may also result from multimorbidity. Frailty is defined as a reduced capacity of older people to cope with daily or acute stressors caused by an aged-associated decline in physiological reserve. The frailty phenotype is diagnosed in people who demonstrate at least three of the following physical components: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity [51]. A meta-analysis of 25 studies reported that frailty is seen in 16% of patients with multimorbidity, but over 70% of people with frailty have multimorbidity [52]. A study from Spain found that, between the ages of 65 and 80 years, the prevalence of multimorbidity did not change substantially (~90% of people), but the prevalence of frailty increased linearly from 20% to 80% [53].

Decreased quality of life

Measuring quality of life is important to assess the disease and treatment burdens from the patient's perspective. Unsurprisingly, living with many chronic conditions

reduces health-related quality of life. Studies carried out to date have consistently found a reduced quality of life in patients with multimorbidity [54,55]. Moreover, in a meta-analysis of 39 studies, quality of life decreased significantly with each additional chronic condition in both the physical and mental domains [55]. Of note, mental health conditions may reduce quality of life more than do cardiovascular conditions [54].

Burden on caregivers

People with multimorbidity often rely on friends and family members for day-to-day care [56]. People who provide daily care to patients with multimorbidity experience a hard burden in the physical, emotional, and financial domains. One study found that the burden might be the greatest for spousal caregivers [57]. Importantly, one person with multimorbidity may require the care of many informal caregivers. A community-based study of nearly eight Million people with multimorbidity reported that, on average, one person with multimorbidity required the help of two informal caregivers [58]. The challenges for caregivers include managing multiple specialists, appointments, and medications and their adverse effects [59].

Healthcare costs

Multimorbidity is responsible for 65% of healthcare spending in developed countries [60], increasing total healthcare spending, hospital costs, care transition costs, primary care use, dental care use, emergency department use, and hospitalizations [61]. In the US Medicare system, 80% of all healthcare costs are spent on people with four or more chronic conditions [62]. Similarly, 80% of all primary consultations in the United Kingdom are provided for patients with multimorbidity [63]. A study from 16 European countries found that each additional chronic condition was associated with a greater cost of healthcare in both primary and secondary settings [43]. A meta-analysis of 51 studies from developed countries reported that the annual costs of multimorbidity per person ranged from \$800 to \$150,000, depending on disease combinations, country, and cost ingredients [64].

Diagnosis of multimorbidity

Because multimorbidity is the co-existence of two conditions, diagnosing multimorbidity is simple. It is difficult, however, to decide when multimorbidity becomes relevant and requires a shift from the single-disease perspective to a holistic approach. The National Institu-

te for Health and Care Excellence (NICE) recommends that multimorbidity-oriented care be considered when the patient requests such care or has any of the following: finding it difficult to manage treatment or usual activities; receiving care from multiple services; having both physical and mental health chronic conditions; frequently seeking unplanned or emergency care; taking multiple medicines; or having frailty [65,66]. Importantly, the condition and treatment burdens are greater in patients who require multidirectional treatment. For example, a person with ischemic heart disease and diabetes would benefit from the same lifestyle modifications, such as regular physical activity. In contrast, someone with ischemic heart disease and arthritis might find it difficult to take regular exercise, which is recommended for the prevention of cardiovascular diseases. Similarly, the management of hypertension and ischemic heart disease has largely the same goals, whereas managing hypertension and asthma may require the use of counteracting treatments, such as beta-mimetics and beta-blockers.

Management of multimorbidity

Most healthcare is single-disease-centered, which interferes with providing comprehensive management for individual patients. Patients with multimorbidity who receive single-disease-centered care for each of their conditions suffer from a high treatment burden due to frequent visits, examinations, and multiple medications. Recommendations from different secondary care clinicians may be contradictory, like reducing physical exercise for osteoarthritis and increasing it for cardiovascular conditions. Already 20 years ago, investigators noticed that adhering to disease-specific treatment guidelines in older patients with multiple chronic conditions could lead to unfavorable health outcomes [67]. This observation underscored the need to establish treatment guidance for patients with multimorbidity. In 2018, a panel of 18 multidisciplinary experts from seven countries established the following aspects of the care of patients with multimorbidity [68]:

1. Interaction assessment.
2. Eliciting patients' preferences and sharing realistic treatment goals.
3. Individualized management.
4. Monitoring and follow-up.

Interaction assessment involves the identification of specific diseases, the patient's functional status, and pharmacological and non-pharmacological treatments to see how these elements might interact and impact the

patient. When assessing interactions, it is important to consider risks that may arise from a patient's treatment. For example, a patient who frequently falls and suffers from depression may be taking warfarin alongside a selective serotonin reuptake inhibitor (SSRI), which could cause a decreased warfarin metabolism. In such cases, it may be necessary to reconsider the use of warfarin or choose a different anticoagulant that does not interact with the SSRI.

To ensure patient satisfaction, clinicians should encourage patients to express their values and priorities when making treatment decisions. This approach helps to increase adherence and facilitate shared decision-making. For example, an elderly patient may find it preferable to engage in regular walks rather than frequent physical therapy sessions. Similarly, when treating a patient with dementia and incontinence with donepezil and oxybutynin, respectively, it is important to ask which condition has a greater impact. Knowing this can help determine which of the two antagonistic drugs to discontinue.

Individualized management aims to consider the treatment burden when prescribing medications and other interventions. In particular, clinicians should try to reduce polypharmacy. Deprescribing should include prioritization of medicines to be discontinued and stopping one medication at a time. The medication classes that clinicians should consider stopping in elderly patients with multimorbidity include benzodiazepines, proton pump inhibitors, glucose-lowering medications, antidepressants, and anti-hypertensives. Discontinuing or reducing the doses of some of these medications might reduce the risks of falls and resulting fractures, death, and hospitalization and improve cognitive function [69].

Scheduling regular follow-up visits is crucial for the assessment of adverse effects of treatment to make any necessary adjustments.

Comprehensive geriatric assessment

In elderly or frail patients with multimorbidity, the comprehensive geriatric assessment (CGA) model has proven useful in providing patient-centered care. According to the CGA (figure 2), clinicians need to assess the five following domains of health [70]:

1. Physical health conditions.
2. Mental health conditions.
3. Functional status.
4. Social circumstances.
5. Environment.

When assessing physical health in frail people with multimorbidity, clinicians should identify all the patient's diseases and medications, trying to find unfavorable interactions between them. At this stage, deprescribing should be considered. In addition, the assessment of physical health should include the evaluation of nutritional status, which is crucial for overall health. Assessing mental health is just as important because mental disorders found frequently in frail people, such as dementia, depression, and anxiety, substantially worsen the well-being of patients and reduce treatment adherence. People who have both mental and physical health conditions experience a greater disease burden than those with physical health problems only [5]. Assessing a patient's functional status is crucial in determining if they face mobility issues, falls, or trouble with daily tasks. Addressing such problems, whether by providing walking aids or assistance with meal preparation, can greatly enhance treatment outcomes. It is also important to consider a patient's social circumstances, including their financial resources and support network, as shortco-

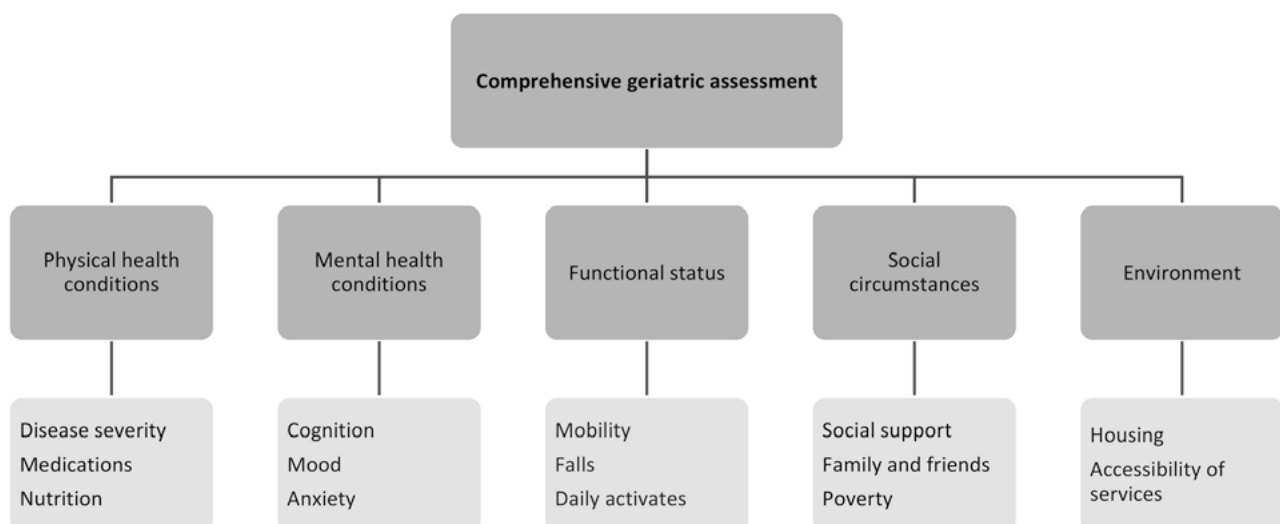


Figure 2. Comprehensive geriatric assessment for elderly or frail people with multimorbidity

mings in these areas can be addressed by involving social workers or prescribing more affordable medications. Evaluating a patient's environment can also help identify needs, such as improved housing or transportation for follow-up visits.

Conclusions

Multimorbidity is a growing global challenge owing to the aging of populations and unfavorable lifestyle chan-

ges. Globally, the burden of multimorbidity is expected to rise considerably [71]. As the number of people with multimorbidity is expected to increase in the coming years, we need to create patient-centered treatment guidelines relevant to people with multimorbidity. Moreover, healthcare systems worldwide need to establish effective models of care for patients with multimorbidity to adapt to the increasing burden of multimorbidity.

Conflict of interest

None

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