Review

Food Supplements and Elderly People – Challenges and Risks

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Review

Food Supplements and Elderly People—Challenges and Risks

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Abstract: Polypharmacy and malnutrition are common health issues among older adults. In older people, there is a high prevalence of polypharmacy and malnutrition, and preliminary data also indicates that there is a significant of Food Supplements (FS) use, increasing the risk of duplication of therapies and several adverse reactions and drug-FS and FS-FS interactions. The intervention of health professionals in mitigating these risks is essential. This review not only underscores and discusses the potential association between polypharmacy, malnutrition, and food supplements but also presents current scientific evidence on polypharmacy, malnutrition, and the use of food supplements by the elderly. The work reviews the challenges, advantages and risks of using FS for the elderly who are polymedicated and/or malnourished, focusing on the good practices needed to support healthy ageing. In this regard, the paper intends to help health professionals better deal with the issue of polypharmacy and the use of multiple FS to overcome the malnutrition problem and improve the health and well-being of older adults.

Keywords: food supplements; malnutrition; elderly; polypharmacy; pharmacists

1. Introduction

In 2019, the United Nations (UN) stated that population ageing is about to become one of the most significant social transformations of the 21st century. It is estimated that the number of elderly people aged 60 or over will double by 2050 and more than triple by 2100, rising from 962 million in 2017 to 2.1 billion in 2050 and 3.1 billion in 2100 [1].

By 2024, it is estimated that the population of individuals aged over 65 years will outnumber those under the age of 15 in the World Health Organization European Region [2]. Worldwide, healthy life expectancy at birth has improved by 5.36 years from 58.3 years in 2000 to 63.7 years in 2019 [3].

As Europe's population continues to age, caused by increased life expectancy leads to a rise in age-related diseases. Older adult well-being demands multidisciplinary strategies to support healthy ageing. First, the elderly consume fewer nutrients, leading to a deficiency of essential vitamins and minerals [4]. Second, age-related diseases that result from gradual cellular damage must be addressed. Finally, the prescription and consumption of medicines and other health products have increased among the geriatric population, who take multiple medications. Thus, they are more likely to experience adverse pharmacological events [5–7]. On average, is estimated that one in ten patients is subject to an adverse event while receiving hospital care in high-income countries. [8]

Moreover, the results of the latter investigation suggest an association between malnutrition and polymedication and have been recognised as a global public health problem of adverse events in older adults [1], that could be avoidable.

Therefore, ensuring the best diet possible for older people and using FS to complement the diet is crucial, effectively bridging the gap between malnutrition status and achieving the recommended nutritional intake.

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At the same time, some data leads us to believe that a significant percentage of individuals over 65 consume FS, but little is known about the pattern of FS use in the elderly [9].

The risk of food (which includes FS)-drug interactions should be highlighted, and even the duplication of medicines in a therapeutic regime of 5 or more medicines/day is considerably higher in the elderly. One of the main reasons is that general practitioners and specialist physicians often treat old patients, and since age increases, the prevalence of multiple diseases also increases, which leads to polypharmacy. On the other hand, to obtain well-being, older adults are also easily influenced by friends or television commercials potentiating the consumption of FS. The poor communication between patients and physicians and the lack of health literacy may contribute to unreported FS use. Thus, these interactions are difficult to detect.

European legislation about FS is only partially harmonised. Harmonised legislation regulates the vitamins and minerals and their sources, which can be used in the manufacturing of FS [10]. For other ingredients, the European Commission (EC) has established harmonised rules to protect consumers against potential health risks. FS cannot replace a regular and healthy diet but aims to increase and promote human health [11–13]. When advising their patients on these products, the tools to support health professionals are practically non-existent and most information about FS is obtained from the companies' web pages.

The transposition of European Directive 2002/46/EC into national laws does not guarantee that pharmacists and other health professionals will provide duly informed advice on these products, as happens in Portugal. However, some countries, such as France, Italy, and Belgium, have implemented light procedures that aim to ensure safer advice on these products [11–13].

Nowadays, there is a growing concern about the misuse of FS, their potential for interaction with medicines, and their confusion with them. The misunderstanding starts with the definition of the name of the products. When we talk about medicine, it is medicine in Portugal, France, Spain, Korea, the United States of America (USA) and worldwide. However, a multivitamin can be an FS in Portugal and a Dietary Supplement in the USA. The differences in designations make the research hard. For this investigation, we consider dietary supplements and FS the same, and we will refer to them as FS, as their definitions overlap [11,12,14].

Additionally, FS can be sold in pharmacies, dietetic stores, supermarkets, phone sales, catalogues, or on the Internet. This range of points-of-sale raises the problem of a lack of pharmacists' advice.

If the topic alone already generates confusion, when studying the elderly population, in particular, it is more complex. We are even more aware of the importance of this field of study, which should be considered one of the gold standards for healthy ageing.

Last October, the Lisbon Outcome Statement *"Unlocking the future of healthy ageing"* emphasised the need for practices to support healthy ageing and highlighted the importance of a collective effort from all sectors to promote healthy ageing. One of the key priorities focuses on preventing health issues and providing data and evidence to support policy decisions informed by evidence-based practices [15].

This paper aims to comprehensively review the potential association between polypharmacy, malnutrition and FS use in elderly people and emphasise the role of health professionals in facilitating knowledge exchange at regional and global levels to better deal with 1) polypharmacy in the elderly, 2) overcome the malnutrition problem, 3) improve the health and well-being of older people and 4) emphasising the benefits and risks of FS use in this polymedicated age group.

2. Materials and Methods

This review provides an overview of the recent publications on polypharmacy and FS in the elderly. The search in English was performed to identify relevant articles (original research and reviews). We made two searches in parallel. One is in the field of polypharmacy in the elderly, and the other is in the field of consumption of food supplements in the elderly. In both advanced searches, we use PubMed and Web of Science. The keywords used were ((polypharmacy [MeSH Terms]) AND (aged [Mesh Terms)), Filters applied: Systematic Review, in the last 5 years, Humans, English,

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Portuguese, Aged: 65+ years. We obtained 67 results, which we filtered to 2020 – 2023, and we obtained 55 results. In the Scimago platform, we characterised the publications, only selected Q1 and Q2 when relevant, and obtained 35 articles. From these, we selected 8 after reading the abstract. For the second part of the search, we used (food supplement [MeSH Terms]) AND (consumption [MeSH Terms]) AND (aged [MeSH Terms]). Filters applied: in the last 10 years, Humans, English, Portuguese and we obtained 56 results. After selecting the Q1 articles for the title and abstract reading, we obtained 21. Sites such as WHO, EFSA, and other institutional references were also included. The search was done between 19 September and 31 October 2023.

3. Results

3.1. Elderly

Concerning age, the World Health Organization (WHO) considers any individual over 60 an elderly or older person. This definition applies to most industrialised countries and the UN [16]. Nevertheless, in some studies published in the scientific literature, the age of 65 or more is considered, which can bias the results.

The increase in life expectancy has led to a rise in chronic diseases, such as cardiovascular, diabetes, or neurodegenerative conditions, which include an oxidative stress component in the underlying pathological processes [5]. Multimorbidity is associated with an increased risk of death, low quality of life, disabilities, and adverse medicine events and usually requires treatment with multiple medicines [1].

As a consequence of acute and/or chronic disease in combination with age-related degenerative changes, limitations in physical, mental and/or social functions occur. The ability to perform the basic activities of daily living independently is jeopardised or lost. The person is in increased need of rehabilitative, physical, psychological and social care and requires a holistic approach to avoid partial or complete loss of independence [17].

The elderly population has physiological and pharmacologic (pharmacokinetics and pharmacodynamics) changes that make it especially susceptible to presenting secondary or adverse events to medications, even with commonly used medicines [6,7]. Therefore, polypharmacy can put the patient at risk of adverse medicine events and medicine interactions when not used appropriately [1].

It should also be highlighted that adequate nutritional status is essential in preserving health status and preventing or delaying the progression of age-related diseases in older adults.

3.2. Polypharmacy

Polypharmacy is defined by the WHO as "the administration of many drugs at the same time or the administration of an excessive number of drugs" or "the concurrent use of multiple medications" [6,18]. In 2021, a review indicates that one hundred and forty-three definitions of polypharmacy and associated terms were found. Most of them are numerical definitions [6].

Although there is no standard definition, polypharmacy is often defined as the routine use of five or more medications daily. After reviewing definitions, we can say that this is the most commonly used definition for polypharmacy, with 46.4% (n = 51) of studies using this definition [6,19,20]. It includes over-the-counter prescriptions and, in some definitions, also traditional and complementary medicines prescriptions, including FS [18,21].

However, there are some limitations in these definitions. They are unclear as they do not refer to a specific number nor indicate the temporal condition under which polypharmacy is administered simultaneously. Furthermore, the idea of polypharmacy is often confused with inappropriate prescription [21].

Polypharmacy is associated with adverse health outcomes [19,22], including mortality, falls, adverse drug reactions, drug interactions, non-adherence, increased length of stay in hospital, and readmission to hospital soon after discharge [19].

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While in many instances, the use of multiple medicines or polypharmacy may be clinically appropriate, it is crucial to identify patients with inappropriate polypharmacy that may place patients at increased risk of adverse events and poor health outcomes [19].

Interactions between various pharmacologic active substances cannot be excluded, whereas adverse drug reactions could be misdiagnosed. This misinterpretation can lead to the prescription of new drugs, which places the patient at risk of developing additional adverse events. This process is known as the prescribing cascade. Indeed, the effects of medication-related older people can be considered a geriatric syndrome. Mention should be given to potentially inappropriate prescriptions, including drug-drug interactions, disease-drug interactions, under- and over-prescribing, and the prescribing cascade [23].

Polypharmacy is a topic that has generated much concern, having been considered by the WHO as a public health problem of adverse events [18]. WHO launched its third Global Patient Safety Challenge: Medication Without Harm in March 2017 to reduce severe, avoidable medication-related harm worldwide by 50% by 2022 [24]. Every 17th September, the WHO observes World Patient Safety Day to raise awareness about patient safety, involving also their families in safe healthcare policies and practices. The impact in meaningful patient engagement is remarkable, with studies showing a potential reduction in the burden of harm by up to 15%, saving countless lives and billions of dollars each year [25].

3.2.1. Prevalence of polypharmacy

Once prescribing rates continue to increase because of the rise in the older adult population and the availability of many more medications globally, studying the prevalence is essential to support the definition of strategies to fight this global healthcare problem.

Numerous studies assessed and reviewed the prevalence of polypharmacy in elderly people worldwide, and it is important to understand the existing data on populations living in European countries.

It is more objective to study polypharmacy in hospitalised elderly people because, in this context, there is greater control over the pharmacological therapy given to the patient. At home, non-adherence to therapy can be due to forgetfulness.

Some authors (Guillot et al., 2019) concluded, with their research, that the prevalence of polypharmacy is reported between 10 and 90% [26], others between 4 and 96% [27]. The wide range of prevalence is due to different reasons, one of which seems to be related to the different definitions of polypharmacy since there is no harmonised definition within Europe. Nevertheless, age groups and the geographical locations of the data collection should also be considered. A Portuguese study published in 2019 showed that polypharmacy is present in more than 70% of admitted elderly patients [21].

To better understand the prevalence variation in European countries, the data based on the Survey of Health, Aging, and Retirement in Europe (SHARE) database [28], in which polypharmacy is defined as the concurrent use of five or more medications, in people older than 65 years., were evaluated. The results ranged from 26,3% to 39,9%, across 17 European countries plus Israel. Portugal, Israel, and Czechia have, in this study, the highest prevalence of polypharmacy, 36.9%, 37.5% and 39.9% respectively [28]. Across Europe, 32.1% of older adults take 5 or more medications per day [28]. The pooled estimated prevalence of polypharmacy in the 54 studies reporting on polypharmacy in all medication classes was 37% because this analysis included polypharmacy, where 5 or more medications are taken and the group who takes 10 or more medications [22].

Table 1 summarises the relevant studies about polypharmacy prevalence where we can verify the differences between the study designs.

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Table 1. Prevalence of polypharmacy [29–35].

Prevalence of Polypharmacy	Classification of Polypharmacy	Population	Country	References
25,5%	five or more medications	people aged from 65 to 81 years with cardiovascular disease in the population of Lausanne	Switzerland	CoLaus study, 2017 [29]
70,22%	five or more medications daily	patients admitted to geriatric and internal medicine acute care wards of 12 Italian hospitals (mean age 81 years)	Italy	GLISTEN, 2019 [30]
44%	plus 5 drugs	older adults between 2010 and 2013 (aged 65+ years at baseline)	Sweden	2013 [31]
28,6%	4–9 medications	adult electronic primary healthcare records from Scotland, adults aged 60–69 years	Scotland	2014 [32]
51,8%	4–9 medications	people aged 80+ years with cardiovascular disease in the population of Lausanne	Scotland	2014 [32]
6-36%	ten or more medications	older adults (65+ years)	European Union (EU)	SIMPATHY project, 2017 [33]
30,3%	6-9 drugs	2057 older emergency department (65+ years)	Italy	2013 [34]
56%	≥5 prescriptions within six months	elderly 80+years	Poland	Kardas et al. 2018 [35]

The analysis of the population-level data from a prospective survey investigating the biological and genetic determinants of cardiovascular disease in the population of Lausanne revealed that 25,5% of people aged from 65 to 81 years regularly used five or more medications [29].

In 2019, the GLISTEN (Gruppo di Lavoro Italiano Sarcopenia—Trattamento e Nutrizione; Italian working group on sarcopenia—nutrition and treatment) study, the prevalence of polypharmacy (using five or more medications daily) in patients admitted to geriatric and internal medicine acute care ward of 12 Italian hospitals was 70.2% [30].

A large prospective, longitudinal, register-based cohort study in Sweden (N = 1 742 336) specifically analysed the epidemiology of polypharmacy in older adults between 2010 and 2013 in Sweden. This study showed that the prevalence of polypharmacy (plus 5 drugs) was 44% [31].

In a cross-sectional analysis of adult electronic primary healthcare records from Scotland, the prevalence of polypharmacy (the use of 4–9 medications) was 28.6% in adults aged 60–69 years and 51.8% in those aged 80+ years. In this study, the term polypharmacy was not clearly stated. Instead, the "higher" consumption of drugs was categorised into either using 4–9 medications or ten or more [32].

Based on the publication from the EU- funded "Stimulating Innovation in the Management of Polypharmacy and Adherence in the Elderly (SIMPATHY) project", the prevalence of polypharmacy, defined as taking ten or more medications, ranged from approximately 6–36% in older adults. According to this data, deprivation had a profound impact on the prevalence of polypharmacy in all

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age groups. For instance, in people aged 65–69 the prevalence of polypharmacy was about 24% in the most underprivileged vs. around 7% in the least deprived [6,33].

In a large observational cohort study including 2057 older emergency department patients from Ancona in Italy, the prevalence of polypharmacy (the concomitant use of 6–9 drugs in the last 3 months) was 30,3% [34].

In a nationwide assessment in Poland, authors confirmed the prevalence of polypharmacy (≥5 prescriptions within six months) in 56% of elderly aged 80+ [35].

The topic of polypharmacy is also relevant in less developed countries. A study conducted in Ethiopia concluded a prevalence of 33% in polypharmacy [36].

From the data reported in these studies, it is not completely clear that polypharmacy does not include products that are not medicines, such as FS or oral nutritional supplements. This situation is also limiting in data analysis and needs to be improved.

3.3. Malnutrition

ESPEN defines malnutrition as "a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease" [37].

Malnutrition encompasses both overnutrition (i.e., overweight, obesity, and diet-related non-communicable diseases) and undernutrition (i.e., underweight, micronutrient deficiencies, wasting, and stunting) However, in this review, we will focus on undernutrition in older populations, referring to undernutrition as malnutrition throughout because these terms are often used interchangeably in the scientific literature.

It is essential to recognise that older adults face a heightened risk of malnutrition. It is estimated that around a quarter of European older adults (65 years +) are malnourished or at risk of malnutrition [38].

A variety of factors contribute to this, including age-related physiological decline, anorexia, oral health problems, biological changes in the digestive system, chronic diseases, polypharmacy, limited access to nutrient-rich foods and other social conditions. By acknowledging and addressing these risk factors, we can help to ensure that older adults receive the essential nutrients they need to maintain optimal health and well-being.

The cause of malnutrition in older adults is complex and not fully elucidated. A decline in food intake due to acute and chronic disease is typical in older age groups and can manifest with or without inflammation [39]. Malnutrition without disease (non-disease-related malnutrition) can be classified as either hunger-related due to low food availability, which mainly occurs during pandemics or climatic events such as droughts or bushfires, or due to socioeconomic or psychological situations, such as financial hardship, social isolation, marginalisation, food behaviours, cultural factors, low food literacy, and food insecurity [39].

High-income countries, such as Portugal, also report food insecurity in over two-thirds of older populations due to low economic resources, which contributes to the high prevalence of malnutrition [40]. Nutritional status can be significantly affected by ageing, resulting in various complications such as dysphagia, dysgeusia, anorexia, and visual and motor impairment.

Data from scientific studies in Europe have highlighted unfavourable intakes by older adults of total and saturated fat, sugar, salt and dietary fibre with low intakes and suboptimal status of crucial micronutrients such as vitamins D, B_2, B_{12}, folate and calcium [41].

Malnutrition predisposes older adults to an increased risk of adverse clinical outcomes such as frailty, osteoporosis, muscle wastage, and mortality [39]. Physically, a better nutritional status is associated with better cognitive function and functional capacity in the elderly [42]. Furthermore, we found a positive association between polypharmacy and malnutrition, but this relationship is not fully delineated [20,43]. A recent meta-analysis demonstrated a statistically significant association between polypharmacy and malnutrition. However, the authors state that future research is required to determine the magnitude of the effect of the increased number of drugs, in combination with the type of drugs, on the risk of malnutrition [44].

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The relationship between polypharmacy and malnutrition is based on several mechanisms. Long-term use of multiple drugs leads to anorexia, which is generally a mild or more serious impairment of the digestive system. Additionally, many drugs have the potential to negatively affect nutritional status by altering the sensory perception of taste, intestinal absorption, and metabolism or inducing the elimination of essential vitamins and minerals. More than 250 drugs have been reported to have adverse effects on the patient's nutritional status [45].

Age-related physiologic, pathologic, and environmental changes also place older adults at increased risk of polypharmacy and malnutrition. These changes include the increased prevalence of chronic medical conditions, as said before, as well as reduced senses of thirst and taste, which can increase the risk of fluid and electrolyte imbalances and dry mouth. Moreover due to disability and food deserts (because of environmental changes), accessing a nutritionally adequate diet is more challenging [20].

Moreover, older patients are at even greater risk of adverse effects due to decreased renal and hepatic function, lower lean body mass, and reduced hearing, vision, cognition, and mobility [19,46].

Hence, nutritional status needs to be assessed before prescribing medications. In elderly perioperative patients with cancer, a multidisciplinary team comprising physicians, pharmacists, nutritionists, and other professionals should know the potential effects of individual drugs and polypharmacy on perioperative nutritional status and seek to reduce negative impacts [45]. We also verified with this review that some diseases more clearly reflect the consequences of polypharmacy associated with malnutrition, namely sarcopenia. So, subjects with sarcopenia had a greater prevalence of malnutrition, and the researchers hypothesise that the association between polypharmacy and sarcopenia might be mediated by other conditions, in particular malnutrition [47].

3.3.1. Malnutrition – What to do!

Given the significant prevalence of polypharmacy among the elderly population and the evidence indicating its potential impact on malnutrition, it is possible to pursue two complementary strategies to combat this issue. First, an assessment of a more rational prescription, and second, the improvement patient's nutritional status. A healthy personalised diet is fundamental but may not be enough, and in these situations, physicians, pharmacists and nutritionists have to resort to FS or oral nutritional supplements. Oral nutritional supplements are *food for particular medical purposes' means food specially processed or formulated and intended for the dietary management of patients, including infants, to be used under medical supervision; it is intended for the exclusive or partial feeding of patients with a limited, impaired or disturbed capacity to take, digest, absorb, metabolise or excrete ordinary food or certain nutrients contained therein, or metabolites, or with other medically-determined nutrient requirements, whose dietary management cannot be achieved by modification of the regular diet alone* [48]. These products are usually presented in 200/300ml bottles, so any similarity with the FS classification is pure distraction. Additionally, they are products with a relevant caloric value (up to 50kcal), reinforcing integration into a specific class that excludes FS [49].

3.4. Food Supplements

As said before, one of the aims of this review is to contextualise and frame the opportunities and risks of the consumption of FS by the elderly. For a better understanding, it is essential first to consider its definition and, second, to be aware of the lack of European legislation about FS.

FS are concentrated sources of nutrients or other substances with a nutritional or physiological effect, which are marketed in small "dose" form (tablets, liquids in measured doses, etc). A wide range of nutrients and other ingredients might be present in its composition, including micronutrients, amino acids, fibre, plants and herbal extracts, and others. They are intended to correct nutritional deficiencies, maintain an adequate intake of certain nutrients, or support specific physiological functions. They are not medicines, so they cannot exert a pharmacological, immunological, or metabolic action. Therefore, their use is neither intended to treat or prevent human diseases nor to modify physiological functions. The European Union regulates FS as food [11–13].

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Moreover, studies on the prevalence of FS consumption by the elderly in Europe are scarce, and this food category is excluded from European guidelines for malnutrition. Therefore, we present below some pertinent information and studies conducted worldwide. We also resorted to some older studies due to the lack of more recent robust studies.

3.4.1. Food Supplements - Reflection on Consumption Data

As far as we know, we have data from a study performed in 2015 that disclosed that the use of FS was reported by 26.6% of the Portuguese population and is higher in females, adults and elderly individuals. In this age group, the prevalence is 28.4% [50].

In 2014 in Belgium, 38.3% of the population (3-64 years) consumed a FS during the year. More women (47.0%) than men (29.1%) consume FS. No information has been collected for people over 64 years old [51].

Data on the consumption of FS in Europe is scarce and not recent; however, what exists shows the high use of these products.

FS use is also common in the USA. Survey results suggest that the prevalence of regular FS use among adults in USA is about 50%, but the overall prevalence of FS use may be closer to two-thirds of the adult population. FS use in adults has been consistently reported to increase with age, income, and education, and within each age group, women are also more likely to use FS than men [52]. Data from the National Health and Nutrition Examination Survey estimates FS use among USA adults increases with age, overall, and in both sexes and was highest among women aged 60 and over (80.2%). From 2007–2008 through 2017–2018, the prevalence of FS use increased in all age groups among USA adults. The most common types of FS used by all age groups were multivitamin-mineral supplements, followed by vitamin D and omega-3 fatty acid supplements[53].

As people age, earn more, and have higher education levels, they use FS more frequently. Additionally, women use FS more than men across all age groups [51–54]. The increased rates of FS use among women could be partially attributed to the increased use of calcium and vitamin D supplements to maintain bone health throughout their lifespan and prevent the onset of osteoporosis during ageing [52]. In 2023, in a cohort study of 15,732 community-dwelling healthy older adults in Australia and the USA, 66.2% reported the use of one or more FS or complementary and alternative medication in the past month before the questionnaire. Female sex, USA residency, higher education, polypharmacy, and frailty were associated with self-reported use and the most commonly utilised were vitamin D, fish oil, calcium, and multivitamin [54].

3.4.2. Food Supplements Efficacy

Eating a healthy, varied diet is essential to an optimal nutritional status, but the ability of individuals to achieve this varies considerably depending on income, disability, food access, attitudes, cooking skills and knowledge. Scientific evidence combined with economic impact studies reveals that topping up diets with supplemented nutrients prevents nutritional deficiency and could lead to significant health savings due to the beneficial impact on chronic disease risk.

Supplementation is an effective way of bridging the gap between current status and optimal intakes. Indeed, this is already recognised for certain nutrients, as illustrated by the example of vitamin D supplementation, which is now recommended across the EU due to the approval of health claims for vitamin D [55–57].

The Dietary Guidelines for Americans 2015-2020 and 2020-2025 state that nutrient needs should be met primarily from nutrient-dense foods. Nevertheless, it also states that in some instances, fortified foods and FS may be helpful [58,59].

Some professionals and researchers have also addressed the issue of the efficacy of oral supplementation through FS. As is well known, how this type of product is placed on the market does not require efficacy (or safety) tests [60]. In addition, the European legislation mandates the use of health claims that have been approved by EFSA. A health claim is any allegation that states, suggests, or implies the existence of a relationship between a food category, a food (e.g. micronutrient or bioactive), or one of its constituents and health. In this sense, when there is a health claim, the

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efficacy and safety of the claimed active substance are done. When there is no health claim, doubts persist [56,61].

There are scientific studies that support FS efficacy. In a study on the impact of FS on eye health, researchers concluded that, in the light of published reports and despite many well-conducted trials, the scientific evidence is scarce. It is impossible to establish a clear benefit over a placebo of FS containing vitamins, minerals, and fish oil substances to prevent, relieve, or effectively treat ocular conditions. There are currently only two exceptions: 1) for treatment of the high-risk stage of age-related maculopathy to delay but not prevent progression to late-stage age-related macular degeneration and 2) to reduce the risk of age-related macular degeneration in a sub-group of people having a genetically determined family history of the condition [62].

The Korea National Health and Nutrition Survey 2018–2020 (2478 people aged ≥65 years) showed a cross-section of insufficient and excessive nutritional status through food intake and multivitamins and mineral supplements (MVMS) in older Korean adults. When they consumed most micronutrients only with conventional food ingestion, the intake of most nutrients was less than recommended. However, the intake of a single MVMS helped improve their micronutrient intake, refining their nutritional status. The authors concluded that elderly Koreans should receive education on proper vitamin and mineral intake through a proper diet and, if necessary, MVMS [46].

3.4.3. Cost-effectiveness Evaluation

It should be noted that the majority of data on FS intake by the elderly are gathered through research on the economic benefit of preventing certain diseases through FS use.

The Achmea Health Database (AHD), which contains anonymised medical information of 4.2 million individuals of all ages in the Netherlands, was used to investigate the economic consequence of osteoporosis. [63]. This study encompassed a total of 108,013 individuals who had a history of fractures. In this particular population, 59 193 patients used anti-osteoporotic medication, while 86 776 used preventive supplements. In the Netherlands, individuals over 50 are typically prescribed vitamin D and calcium supplements by their general practitioner and usually get them from pharmacies [63].

Thus, the reimbursement data of the AHD shows the primary use of vitamin D and FS by people older than 50. The costs of over-the-counter sales are small, so this study does not consider them. This might have led to a slight underestimation of the costs of vitamin D and FS[63]. There is a lack of information regarding the doses of Vitamin D and calcium to confirm if the researchers are evaluating costs with FS our medication [63].

Another example is the supplementation of vitamin D (800 UI) and calcium (1000 mg) study for both women and men with osteoporosis aged over 60. It concludes that it is cost-effective and should be administered concomitantly with other osteoporosis treatments

The recommendation of the European Society for Clinical and Economic Aspects of Osteoporosis working group for vitamin D and calcium supplementation in patients with osteoporosis older than 65 is justified based on its cost-effectiveness [64].

Vitamin D supplementation was also analysed in the prevention of falls. The conclusion was that, with only reference to fall prevention, the provision of empiric cholecalciferol therapy to all older adults in the United Kingdom (UK) offers considerable cost-saving to the UK National Health System over a 5-year horizon. Besides such financial benefits, a reduction in attributable premature mortality and an increase in quality-adjusted life years could also be expected [65].

And what about the gains of probiotic supplementation for the elderly? In France, researchers concluded that the effect of probiotics on common respiratory tract infections is significant for public health and budget in a country like France and shows positive consequences to all economic agents. It benefits the National Health System, the society, and the family. Children and people living in the community have higher incremental benefits because of their higher exposure to respiratory viruses and a declining immune system (elderly) [66].

Another topic of debate that has recently begun to be more studied is the cost of malnutrition. In practice, the aim is to assess whether it is more beneficial to intervene to prevent malnutrition,

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using funds for supplementation, or to intervene medically only after diagnosis. Unfortunately, this study highlighted in our research only uses oral nutritional supplements and excludes FS as an option for intervention [67].

3.4.4. FS Interactions

Healthcare professionals have the information and the knowledge that FS contains vitamins and minerals and herbal plants or extracts that have a high potential to interact with medicines. Nevertheless, FS use is not shared with healthcare professionals despite the increased risk of herb-drug interactions, and there are very few scientific studies evaluating the use of FS in older people besides its relevance.

Points for improvement in patient care include intensifying communication between patients and healthcare professionals. For example, patients sometimes do not know why they have to use certain drugs or experience side effects, such as loss of taste and deviating from the prescription, whether consciously or not, or eating less. Furthermore, the cooperation and communication between the various healthcare professionals is not always optimal. There may be no agreements between physicians and pharmacists about the performance of drug checks. And it is imperative that both reach a mutual agreement on drug checks. Any disagreement on this matter can pose a significance threat of patient safety and optimising the exchange of information between healthcare professionals involved about which drugs have been prescribed, changed, or stopped is recommended as an intervention [44].

A relevant study made in 2006 aimed to describe the users of herbal medicine products and FS in a community in the southeast of Sweden (aged 60+). This study concluded that physicians must consider the extensive use of herbal medicine products and FS among elderly patients when making treatment decisions. Because its use is reported independently of conventional medicine and since more than half of the users do not discuss their use with their physician [68].

Older adults who routinely utilise non-prescription therapies, including FS or complementary and alternative medication, are at increased risk of severe drug interactions, a risk that increases with increasing age and use of specific concomitant therapies, including warfarin and aspirin. The findings of this study emphasise the importance of healthcare providers actively assessing the use of FS/complementary and alternative medication in healthy older adults [54].

A prospective study was conducted in ambulatory patients with cancer treated with oral and/or intravenous drugs in Costa Rica. We identified that 50.3% of patients treated with anticancer agents were at risk of herbal drug interactions due to herbal supplements (FS with herbs or herbal extracts). This study showed that a program of medication surveillance in patients with cancer led by clinical pharmacists could prevent a relatively high proportion of patients from experiencing the potentially adverse clinical consequences of herbal drug interactions [69].

In 2021, a study was published to bring forth an up-to-date overview of the essential knowledge involving the interactions between FS and medicines relevant to awareness by healthcare professionals. Drugs used to treat cardiovascular, autoimmune, nervous, and oncological diseases commonly involve significant clinical interactions with FS, several with a narrow therapeutic margin [70].

4. SWOT Analyses

Considering the potential toxicity of these drugs and to enable evidence-based advice, healthcare professionals need to increase their knowledge of user populations [68] .

To summarise and make a reflection on this topic more pragmatic, we carried out a SWOT analysis on "Food supplements and elderly people – challenges and risks", shown in Table 2.

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Table 2. SWOT analysis on "Food supplements and elderly people – challenges and risks".

Frames of Swot Analysis	Points of reflection
Strengths	- Awareness and information of misguided FS use. -Eliminate adverse health effects/risks with FS. -Contribute to the success of pharmacological therapies. -Promote the safety of polymedicated older patients and healthy ageing. - Educate or inform patients and families of patient safety incidents that cause (or could have caused) inadvertent harm. -Strength high-quality integrated healthcare. -Contribute to cost-effective treatment of older persons.
Weakness	-Gaps in the FS regulatory framework. -Lack of rigour in the distinction between FS and oral nutritional supplements. -Inadequate safety evaluation of FS. -Lack of communication between patients and healthcare professionals. -Lack of data on FS consumption in the EU. -High complexity in establishing FS consumption patterns in older people.
Opportunities	- Inclusion in the review of the guidelines on malnutrition and the use of FS. - Improvement of safe health care. - Eliminate avoidable harm in health care. - Improvement of teamwork and communication in protecting patients from harm. -Assure elderly health and economic benefits. -Mitigate adverse health effects due to FS. -Create a digital database on food supplements to support health professionals' advice. -Strength collaboration between Academia, health professionals and industry.
Threatens	-Lack of robust FS legislation. -Lack of a harmonised definition of polypharmacy. -Unclear if polypharmacy includes or does not FS or oral nutritional supplements. -Difficulty of comparable prevalence data. -Hinders the definition of guidelines and health policies. -Unsafety and lack of quality of FS.

5. Conclusions

Concern about a healthy ageing population is increasingly present in civil society, but also in political institutions around the world. It is known that malnutrition is more prevalent among polymedicated seniors, and this review confirms the high prevalence of polypharmacy in older people and concomitant FS use that strongly impacts several health-related outcomes.

The concerns of healthy ageing often led older people to take other health products, such as FS, on their initiative. However, taking medicines concomitantly with FS can trigger significant adverse reactions. On the other hand, FS use is important to treat nutritional deficiencies and increase the nutritional status of old persons, allowing for healthier ageing. Scientific evidence shows that food supplements help prevent some diseases and have health and economic benefits. So, health professionals have a pivotal role in identifying the use of FS and assessing the potential risk to the patient's pharmacological treatment.

Another significant contribution of the current work is improving the awareness of health professionals and communication with patients. These interactions are rarely included or

misdiagnosed in the assessment and evaluation of treatment plans but are essential for successful pharmacological and nutritional therapies.

In order to reduce the risk of inappropriate drug use and prevent adverse reactions in older patients, it is important to implement educational interventions and regulatory measures. This approach aligns with the Global Patient Safety Action Plan 2021-2030, which aims to minimize preventable patient harm and ensure patient safety. The use of FS is complex, and we think it is crucial to develop guidelines and other tools to improve FS use in the elderly and to assess these risks more quickly and practically.

All these data reinforce the crucial importance of improving the regulation of FS by regulatory affairs specialists, industry pharmacists in developing and producing safer FS and community pharmacists in counselling and dispensing them.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org., Table S1: Prevalence of polypharmacy, Table S2: SWOT analysis on "Food supplements and elderly people – challenges and risks.

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