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Current Pharmaceutical Design, 2018, 24, 1-11

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REVIEW ARTICLE

Nutraceutical-based Integrative Medicine: Adopting a Mediterranean Diet Pyramid for Attaining Healthy Ageing in Veterans with DisabilitiesMario Ciccotti^{a,b}, Anna Raguzzini^c, Tommaso Sciarra^a, Giovina Catasta^c, Paola Aiello^c, Cosimo Buccolieri^a, Raffaella Reggi^{b,d}, Maura Palmery^{b,†}, Florio Lista^{e†} and Iliaria Peluso^{c,*}

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Abstract: Veterans with disability represent a big burden worldwide and often require long-term rehabilitation. Unhealthy dietary and lifestyle habits, including smoke and alcohol abuse, are common in veterans. In the context of integrative medicine approaches, the "complementary and alternative medicine" has been suggested for the management of chronic diseases. However, the potential risk of interaction between herbal products, dietary supplements and drugs must be considered in veterans. The Mediterranean diet has been suggested as a natural, non-pharmacological nutraceutical for healthy ageing. Although there is a broad consensus on the positive effect of plant foods consumption, the presence of glucosinolates, flavonoids and furanocoumarins in some plant foods and beverages must be taken into consideration owing to their potential interfering with drugs metabolism and bioavailability. Albeit seasonality could ensure the maintenance of the single dose of phytochemical below that at which adverse effects in some individuals genetically predisposed or unpleasant drug interactions in diseased subjects can occur, a personalized nutrition is recommended in veterans who are under treatment for comorbidities. Furthermore, sports practice can lead veterans with motor disabilities and mental impairments to excel in some disciplines, giving rise to the phenomenon of the Paralympics and the development of "recreational therapy". Moreover, outdoor lifestyle, through vitamin D synthesis, and conviviality, improving socialization, could account for the Mediterranean lifestyle health benefits. In this work, we propose for veterans a Mediterranean Pyramid, which could be the basis for integrative medicine for veterans with disabilities, patient-centered approaches and interprofessional (including physical medicine and rehabilitation clinicians, pharmacists and nutritionists) interventions.

Keywords: Post-traumatic stress disorder, spinal cord injury, rehabilitation, cognition, energy balance, water balance.

ARTICLE HISTORY

Received: September 4, 2018
Accepted: September 28, 2018

DOI:

10.2174/1381612824666181003113444

1. INTRODUCTION

Veterans with disability represent a big burden worldwide, both in developing and in developed countries. Armed conflict generates disabilities due to injuries and/or trauma. For veterans incurring such injuries, the situation is often exacerbated by delays in obtaining emergency health care and long-term rehabilitation. The US Bureau of Census [1] estimated that in 2014 28.8% of veterans (18 years and older) had any type of disability, as defined by the American Community Survey (ACS), and 19.6% of veterans had a Veteran Affairs (VA) service-connected disability rating. In particular, 8.6% of veterans had both a service-connected disability and an ACS-defined disability; service-connected disability in absence of ACS-defined disability was observed in 11% of veterans, while 20.2% of them had no service-connected disability but presented an ACS-defined disability.

Moreover, global ageing has a major influence on disability trends. Both physical disability [2] and psychological [2-5] illnesses, observed in veterans, are negatively associated with successful ageing [6]. Furthermore, subjective age perception is affected by post-traumatic stress disorder (PTSD) [7] and disability

[7]. For this reason, low perceived health and low quality of life are often reported by veterans [8, 9]. In particular, chronic pain [10-12] and chronic fatigue syndrome [13] are common in veterans. Moreover, PTSD is also associated with both the decline in cognitive functioning [14], which is correlated with age and depression [15], and social anxiety disorder in veterans [16]. A meta-regression reported that soldiers and veterans with PTSD benefited less from psychotherapy than non-military subjects [17]. In addition to pharmacotherapy [18-20], meditation [21-23] and psychological programs [20, 24-29], complementary and alternative medicine (CAM), including acupuncture [21, 30], massage [31] and Yoga [32-36], have been suggested for the management of PTSD and chronic diseases in the context of integrative medicine approaches [37-39]. In general, sex, racial/ethnic, socioeconomic and cultural differences have been reported in the prevalence of CAM use [40-42]. Acupuncture, massage, yoga, meditation and spiritual healing are preferentially chosen by women in veterans [43], and meditation and acupuncture are also common in active duty military members [44]. Moreover, CAM has been suggested for the management of chronic pain [32, 33, 45] and it is common among veterans with cancer [45]. A recent meta-analysis has not supported Yoga treatment for chronic pain and has reported limited evidence on the improvement of the quality of life and depression [46]. However, promising results on pain have been recently reported by the Restorative Exercise and Strength Training for Operational Resilience and Excellence (RESTORE) program (9-12 individual yoga sessions for 8 weeks) [47]. Furthermore, meditation programs [22, 23] and mindfulness-based interventions [27-29] have seemed promising for veterans with PTSD [22, 23, 28] and for subjects with

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anxiety [27, 29, 48] and depression [29], potentially reducing suicidal ideation in veterans [29]. PTSD and depression often co-occurred [49] and it has been suggested that depression could be an important factor in the relationship between PTSD and metabolic syndrome [50]. A retrospective study, by the examination of clinical records of Italian soldiers who were admitted during the World War I, confirmed that soldiers engaged in war are at higher risk of developing depression compared to non-deployed soldiers [51]. In Italy the so-called "reconstruction programs" addressed all aspects of rehabilitation (including physiotherapy, curative workshops and vocational therapy) [52]. On the other hand, it has been recently reported that, despite working as a peacekeeper which is associated with the exposure to acute and/or catastrophic events and chronic stressors, Italian peacekeeper soldiers exhibit lower levels of internalizing symptoms (i.e., PTSD, depression, general anxiety, obsessions, and somatization) and have higher levels of quality of life (i.e., higher life satisfaction and lower general stress), as compared to a control group [53]. In this context, in addition to the health property of the Mediterranean lifestyle, Mediterranean diet has been suggested as a natural, non-pharmacological nutraceutical for healthy ageing [54, 55] and metabolic syndrome prevention [56]. Therefore, according to the needs to strengthen and support research on disability, as reported by the World Health Organization [57], the evaluation of the effects of nutraceuticals, lifestyle interventions and environmental factors on military personnel affected by physical and psychological impairment is an interesting topic.

In this work, after discussing the pros and cons of nutraceuticals and supplements, we aim to evaluate the possible use of the Mediterranean pyramid as integrative medicine in veterans (Fig. 1).

2. DIETARY SUPPLEMENTS AND NUTRACEUTICALS: FRIENDS OR FOES?

Bodybuilding, energy and/or weight-loss supplements are used by military personnel [58], and herb and supplement use is common in general population [59], as well as in elderly subjects [60] and in veterans with cancer [45].

Belief in the health effects of nutraceuticals and supplements positively affects the attitude and consumption [61]. In particular, the attitude to use herbal remedies has been ascribed to different factors, including the conviction that they were natural [62] and the dissatisfaction with conventional treatments [63].

On the other hand, in veterans with mental illness, the relationship between CAM use and the perceived effectiveness of conventional treatments (drugs and psychotherapy) is still controversial [64, 65]. However, data from a meta-analysis reported no differences between some CAM (including omega-3 fatty acids, S-adenosyl methionine and *St. John's wort*) and second-generation antidepressants in major depressive disorder [66].

Table 1 summarizes intervention studies [67-82] with supplements and nutraceuticals aimed to evaluate the effects of these treatments on mood, cognition and physical performance.

In the "VA homocysteine study" no effects on cognition were observed in chronic kidney disease (CKD) patients after folic acid, vitamin B6 and vitamin B12 supplementation, despite the reduction in homocysteine levels [67]. On the contrary, in the elderly [69, 70], mild cognitive impairment (MCI) patients [77] and subjects with

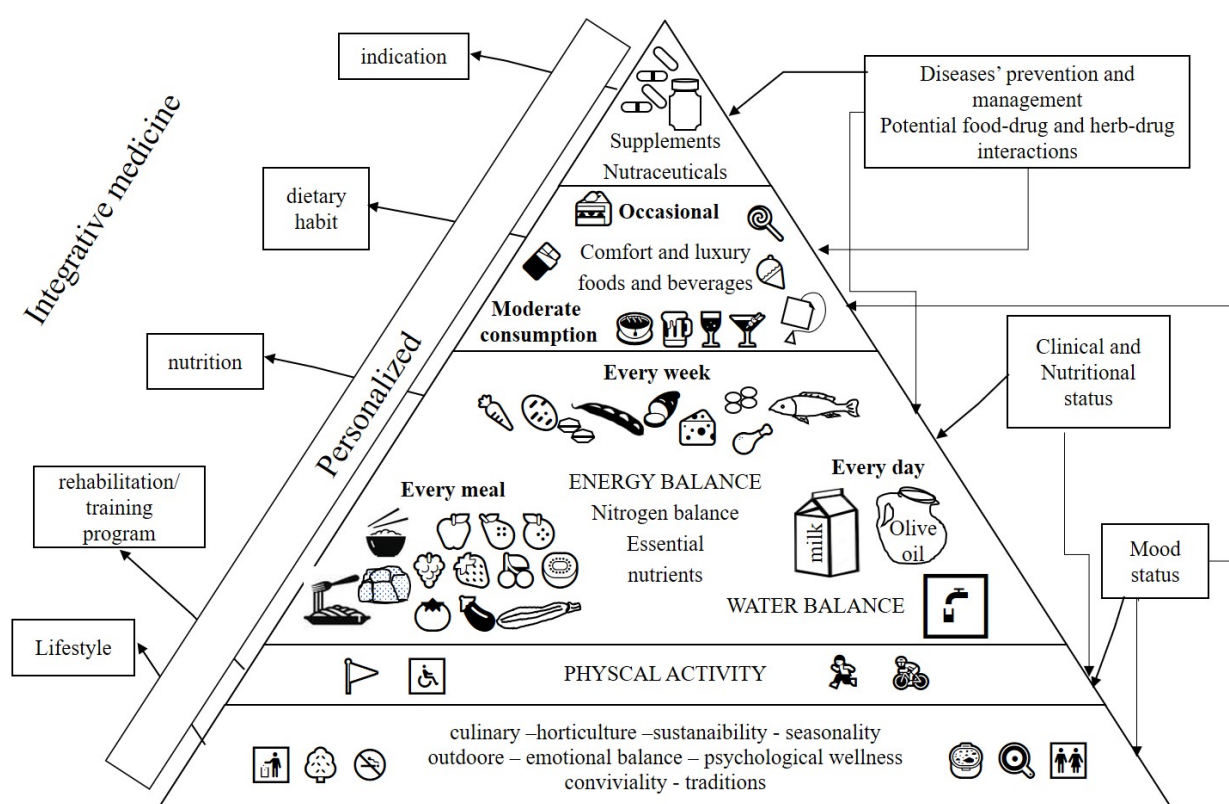


Fig. (1). Mediterranean pyramid for veterans.

Modified from the SENC <http://www.efesalud.com/estilos-de-vida-saludable-nuevas-recomendaciones-de-la-piramide-nutricional-senc-2015/> and the new Mediterranean diet Italian [152] Pyramids.

Table 1. Intervention studies with supplements and nutraceuticals.

Subjects	Treatment, duration	Outcomes	Refs.
CKD (n = 659) treated with dialysis and advanced CKD (n = 423) (creatinine clearance of 30 mL/min or less).	Multivitamin [folic acid (40 mg) + vitamin B6 (100 mg) + of vitamin B12 (2 mg)] or placebo, 1 year.	↔ Cognition	[67]
Depression (n=57)	<i>R. rosea</i> SHR-5 powdered extract (340 mg; standardized to a content of rosavin 3.07%/rhodioloside 1.95%) sertraline or placebo, 12 weeks	↔ versus placebo (less antidepressant effect versus sertraline)	[68]
Elderly (n = 101)	Pycnogenol (150 mg), or placebo, 3 months	↑ Cognition	[69]
Elderly (n = 54)	<i>Bacopa monnieri</i> whole plant standardized dry extract (300 mg/day) or a placebo, 12 weeks.	↑ Cognition	[70]
Elderly (n = 80)	<i>Centella asiatica</i> extract (250, 500 and 750 mg), or placebo, 90 days.	↑ Physical performance	[71]
Elderly undergoing major elective operations requiring ICU (n = 325)	L-tryptophan (1 g orally three/day) or placebo, after surgery and for up to 3 days postoperatively	↔ Incidence or duration of postoperative delirium	[72]
GAD (n = 10)	<i>Rhodiola rosea</i> herbal extract (340 mg), 10 weeks	↓ Anxiety	[73]
GAD (n=72)	<i>Manasamitra Vataka</i> tablets (100 mg twice daily). <i>Manasamitra Vataka</i> tablets + <i>Shirodhara</i> (therapy involving dripping of medicated oil [Brahmi tail] over the forehead) treatment for the first 7 days. or clonazepam, 30 days	↓ Anxiety (all treatments)	[74]
GWI (disabling fatigue, widespread pain, and cognitive dysfunction) (n = 25)	L-carnosine (B-alanyl-L-histidine) (500, 1000, and 1500 mg increasing at 4 weeks intervals) or placebo, 12 weeks	↑ Cognition ↔ Fatigue, pain, hyperalgesia	[75]
Major depression (n = 72)	<i>Nepeta menthoides</i> Boiss. & Buhse freeze-dried aqueous extract or sertraline, 4 weeks	↓ Depression (versus sertraline)	[76]
MCI (n=95)	<i>Dangguijagyag-san</i> (DJS, angelica and peony formula 1.875 g twice/d), 12 weeks, follow-up 1 year	↑ Cognition	[77]
MDD (n = 92)	<i>Chlorella vulgaris</i> extract (CVE) (1800 mg/day; n=42) or continued standard antidepressant therapy alone, 6 weeks.	↓ Anxiety and Depression	[78]
Schizophrenia and tardive dyskinesia (n = 152)	Ginkgo biloba extract (EGb) 240 mg/d, 12 weeks or placebo	↓ Tardive dyskinesia symptoms	[79]
Veterans (elderly) with baseline 25(OH)D ≤ 30 ng/mL (n = 130)	Vitamin D 4,000 IU or placebo, 9 months	↔ Physical performance	[80]
Veterans with chronic pain and baseline 25(OH)D ≤ 30 ng/mL (n = 28)	Vitamin D 1200 IU daily if serum 25(OH)D was 20 to 29 ng/mL or 50,000 IU weekly if serum 25(OH)D <20 ng/mL 3 months	↓ pain ↑ sleep duration ↑ general health ↑ vitality ↑ social functioning	[81]
Veterans with PTSD (n = 21)	Sentra AM: Choline bitartrate (250mg), Cocoa extract (6% Theobromine) (70mg), L-Glutamic acid (40mg), Acetyl-L-carnitine (40mg), <i>Ginkgo biloba</i> (25mg), <i>Hawthorne crataegus</i> spp. (15mg) and minerals (calcium and magnesium). Sentra PM: Sentra AM + <i>Griffonia</i> extract (5.5mg). Two capsules (950 mg) of Sentra AM in the morning and two capsules (961 mg) of Sentra PM at bedtime, 30 days.	↓ PTSD symptoms ↔ Physical health (trend ns increase)	[82]

25(OH)D: 25-hydroxyvitamin D; CKD: Chronic kidney disease; GAD: Generalized anxiety disorder; GWI: Gulf War illness; ICU: intensive care unit; MCI: Mild cognitive impairment; MDD: Major depressive disorder; PTSD: posttraumatic stress disorder.

Gulf War illness (GWI) [75], improved cognition has been observed after treatment with *Bacopa monnieri* extract [70], *Danggui-jagyag-san* [77], pycnogenol [69] and L-carnosine [75], but the latter one did not affect fatigue, pain and hyperalgesia (Table 1).

Pain reduction, as well as improved general health, was observed in veterans with chronic pain and low baseline 25-hydroxyvitamin D (25(OH)D) after vitamin D supplementation [81]. However, such supplementation did not improve physical performance [80].

On the other hand, *Centella asiatica* extract increased physical performance in the elderly [71].

Concerning anxiety and depression, improvements have been found in the majority of studies with nutraceuticals and herbal extracts [73, 74, 76, 78]. Furthermore, two nutraceuticals, containing amino acids, minerals and extracts (cocoa, *Ginkgo biloba*, *Hawthorne crataegus* spp. with or without *Griffonia*), reduced PTSD symptoms in veterans [82].

Despite the potential therapeutic effects of medicinal herbs and phytochemicals on depression [83] and neurodegeneration [84], self-prescription and potential adverse effects must be taken into account.

In a retrospective study, 10 out of 20 (50%) patients with fulminant hepatic failure were recent or active users of potentially hepatotoxic supplements or herbs [85].

The use and self-prescription of nutritional supplements and herbal extracts are common in veterans [86-88]. In addition to the risk of medication substitution [87], it has been reported that veterans with dementia and/or depression who used herbal products were also taking potentially interacting drugs [89].

The potential risk of interaction between a dietary supplement and prescription medication was also identified in veterans with cancer taking supplementations [90].

Polypharmacy (five or more daily drugs) is common in older people for managing comorbidities [91-93] and is a well-known problem in the management of the psychiatric elderly [95], and an independent risk factor for delirium in older patients after emergency admission [96].

Inappropriate prescriptions [97-100] and potential prescription omissions [98] have also been documented. Moreover, multiple medications are frequently used in patients with PTSD and traumatic brain injury [101, 102], as well as in the management of chronic pain [103-106].

In general, multimorbidity and polypharmacy are associated with malnutrition [107], as well as to the occurrence of adverse drug reactions [99, 108, 109], and Central Nervous System Polypharmacy is associated with drug/alcohol overdose and suicide in veterans [110], among whom prevalence of depression [111] and alcohol use disorders [112] are higher. Therefore, veterans, like the elderly, are a clinically vulnerable group which is worth monitoring carefully for potential herb- and nutraceutical-drug interactions [113-116].

Particular attention requires the use of green tea catechins [115-118], both in form of extract and tea infusion, and *Hypericum perforatum* [119, 120]. Therefore, herbal infusion should not be considered as a water equivalent for water balance (Fig. 1).

Possible interactions with drugs have also been suggested for mineral-fortified foods and fruit juices [121-123]. In this context, the Spanish Society of Community Nutrition (SENC) included some concerns about supplementation and nutraceuticals as personalized option in the pyramid for the 2016 Dietary Guidelines for general population [124] (Fig. 1).

3. HEALTHY DIET FOR VETERANS

Malnutrition is associated with higher mortality rates in veterans [125], in particular in the elderly [126], and food insecurity affects the

low diet quality in veterans [127-129]. In overweight and obese veterans, low fruit and vegetable consumption is often associated with tobacco use [130]. Unhealthy dietary and lifestyle habits, including smoke, are common in veterans [131-133], increasing the risk of cancer and cardiovascular diseases (CVD) [134].

Mental illness is also related with poor nutrition [132, 133] and both PTSD and depression are associated with binge eating disorders in veterans [135]. Data from meta-analysis indicated that subjects with PTSD had a high risk of developing impaired memory [136], Type 2 diabetes mellitus [137], CVD [138] and metabolic syndrome [139]. In this context, it must be taken into account that the anthropometric parameters in injured veterans are not comparable to able-bodied people. In particular, erroneous estimations of anthropometric measurements can occur in amputees classifying unilateral amputees as thinner and the bilateral ones more obese than they actually are [140]. Moreover, it has been suggested that subjects with spinal cord injury have distinct physiological characteristics from the able-bodied adults, making difficult the estimate of the prevalence of carbohydrates and lipid disorder, of the potential impact of exercise and of the pharmacological therapies and dietary interventions [141]. Contrary to the mindfulness-based stress reduction, which did not improve dietary habit in veterans [142], integrated approaches, such as "Lifestyle Balance" (modified from the Diabetes Prevention Program) [143], gave promising results. The weight management MOVE! included a self-management support of both physical activity and dietary habit [144, 145]. In obese veterans with schizophrenia, treated with clozapine, an intervention including both dietary control, with a reduction of 200-300 Kcal/day (1600-1800 Kcal/day men and 1300-1500 Kcal/day women), and regular physical activity (walking and walking stairs for 60 min. 3days a week used approximately 600-750 kcal per week) reduced body weight, insulin metabolic profile and triglyceride, compared to the controls [146].

On the other hand, it is well recognized the role of dietary habits in metabolic control in veterans [147] and that plant foods consumption is associated with high cognitive performance [148, 149].

The potential of the Mediterranean diet in disease prevention has been related to the favorable effect of a balanced ratio of omega 6 and omega-3 polyunsaturated fatty acids and of high amounts of fiber and polyphenols found in fruit, vegetables and olive oil [56, 150]. Non-linear relationships are often observed between plant foods consumption and cognitive function. Increasing cognitive performance with increasing intakes of potatoes or grain products reached a plateau or started to decrease at about 100-150 g/d [149]. The associations between cognition and combined intake of fruit and vegetables were strongest, with a marked dose-dependent relationship up to about 500 g/d [149]. In particular, the favorable effects of just taking vegetable reached a maximum at a dose of about 150-200 g/d and for fruit at around 300 g/d [149]. Therefore, the fruit/vegetables intake probably should range between the 400g/d suggested by the WHO [151] (i.e. 5 servings of 80g) and up to 3 servings of 150/200g as suggested by Vitiello et al. in the new Mediterranean diet Italian Pyramid [152].

On the other hand, it has been reported that a high intake (10 servings daily) of fruit and vegetable, including cruciferous vegetables (broccoli, cabbage, and daikon radish sprouts), soy foods (soy milk, veggies slices, tofu, and roasted soy nuts), and citrus fruits (grapefruit and orange juices, orange/grapefruit segments, and dried orange peel) affected the pharmacokinetic of paracetamol [153]. Therefore, the presence of glucosinolates, flavonoids and furanocoumarins in some plant foods and beverages must be taken into consideration owing to their potential interfering with drugs metabolism and bioavailability, despite the positive association between cognitive function and consumption of cruciferous vegetables and citrus fruits [149]. Interactions between drugs and natural fruit juices have been reported, especially grapefruit juice [154, 155] but also cranberry [156] and pomegranate [157] juices, a quercetin containing muscadine grape [158] and soy protein [159]. Accordingly, considering the high content of bioactive compounds and phytochemicals in plant

foods [160], a personalized nutrition (Figure 1) should take into account potential food-drug interactions in veterans who are in treatment for comorbidities. In agreement, dietetic interventions based on personalized dietary advice have also been suggested for old subjects [161], in order to avoid potential food-drug interactions [162-170]. In particular, the effect of high-protein, low-carbohydrate diets on warfarin efficacy should be taken into consideration [169, 170]. In this context, nitrogen balance should be the aim of dietary regimes (Fig. 1) even when dietetic restriction is required for the weight management.

4. PHYSICAL ACTIVITY FOR VETERANS

Exercise capacity is inversely related to mortality in older veterans [171] and there is wide agreement on the importance of physical activity programs in veterans [172-174], in order to improve mobility in frail elders [175] and to reduce obesity [145, 176] and mortality in hypertensive veterans [145, 177], as documented by the STRIDE program [178] and the Project LIFE [179]. In particular, cardio-respiratory fitness has been suggested as one of the factors involved in the obesity paradox (i.e. higher BMI associated with better survival) [180, 181]. However, physical inactivity can be imposed by pathological conditions, such as lower extremity amputation, and it has been underlined that over half of overweight and obese veterans reported the intention to lose weight, but only a few reported having followed a complete weight loss path, highlighting an unsatisfied need to draw on an external support of psychological and physical nature during their program [182].

In addition to the adoption of diets and eating habits, veterans have also been involved in sports during their rehabilitation processes, with the resulting evidence that sports practice in association with a proper food intake can lead individuals with motor disabilities and mental impairments to excel in some disciplines in order to achieve elite levels, giving rise to the phenomenon of the Paralympics and the development of "recreational therapy" [183].

Low physical activity has also been suggested as one of the factors involved in the high prevalence of osteoporosis and osteopenia in overweight/obese veterans with a sedentary lifestyle [184]. However, in the management of veterans unable to walk should be considered some characterizing aspects and risks, such as the possibility of fractures occurring. Falls are strongly associated with benzodiazepines, neuroleptics, antidepressants and anti-hypertensives [108]. Therefore, polypharmacy and mental health can affect the risk of fracture. On the other hand, in hospitalized people or in nursing homes the presence of fractures of the hip was related to an insufficient intake of vitamin D or to an incorrect reintegration of vitamin D [185-188]. This problem was found in association with an incorrect diagnosis of osteoporosis and an inadequate recognition of the problem at the time of patient acceptance in the nursing home. The scientific evidence highlights the need to develop adequate vitamin D integration protocols in those patients with reduced mobility, who are therefore subjected to treatments that include hospitalization in healthcare facilities and not. Investigating the incidence of hip fractures in the lower limbs or hip with the administration of vitamin D or calcium supplements, some studies have highlighted that a preventive intake of supplements, such as calcium and vitamin D, before hospitalization of patients leads to a lower risk of fracture development [189-191]. These studies have showed how the lifestyle of these people, often subjected to wheelchair ambulation, exposed them to greater risks of fractures, which may occur during the transfer phases to and from wheelchairs. The same studies have found a relationship between vitamin D deficiency and diseases, such as hypertension, cancer, CVD and diabetes mellitus. Other causes involved in low vitamin D levels included the admission in nursing homes and consequent not adequate exposure to sunlight, comorbidity and physiological decrease of vitamin D due to age. In this context, it has been suggested that outdoor lifestyle, through vitamin D synthesis, could account for Mediterranean lifestyle health benefits [192] (Fig. 1). Furthermore, it has been reported

that older adults with high adherence to Mediterranean diet had faster walking speed and were more likely to have a greater physical activity [193, 194] which was associated with a higher cognitive function [195].

5. LIFESTYLE AND ENVIRONMENTAL FACTORS

It has been suggested that both physical and cognitive activity components should be taken into consideration in lifestyle interventions for veterans [196].

There is a broad consensus that adherence to Mediterranean diet, particularly in conjunction with social interaction and physical activity, prevents cognitive frailty in the elderly [194, 197-200], as well as depression [195, 201].

Physical activity and plant foods intake are within the major recommendations in graphical representations of healthy diet worldwide [202, 203], as well as in the Double Pyramid Model and in the Iberoamerican Nutrition Foundation (FINUT) pyramid of healthy lifestyles [204], considering also the dietary environmental impact [205], which could have a positive influence on veterans. In this context, in veterans with mental illness lifestyle changes, such as exercise, diet, relaxation, time in nature, relationships and service to others, improve quality of life, weight loss and diastolic blood pressure [133]. Moreover, non-pharmacological intervention programs which have been suggested for cognitive impairment and depression, with promising results in the elderly [205] or veterans [207], include pet of insects [206] and horticultural therapy [207].

Furthermore, even conviviality and culinary activities are included in the new Mediterranean diet pyramid [208, 209] and in the FINUT pyramid [210]. In particular, it has been suggested that conviviality, improving socialization, could be one of the determining factors in the health benefits of Mediterranean lifestyle [192]. In addition to conviviality, the SENC included the emotional balance in the pyramid [124]. In this context, in veterans with spinal cord injury, marital status and living arrangement are positively related to higher self-care behaviors [211] and a family focused therapy has been suggested for rehabilitation of veterans with traumatic brain injury [212].

On the other hand, loneliness has been identified as an important factor involved in depression and suicidal ideation in veterans [213]. In addition to PTSD, delayed-onset (>6 months) PTSD was almost twice in veterans compared to non-professional victims [214]. Post-trauma, low social and family supports are both associated with the PTSD occurrence [215] and veterans exposed to wartime combat are more susceptible to subsequent stressors [216], in particular during ageing [217, 218]. For this reason, we have integrated in the suggested Mediterranean pyramid for veterans (Fig. 1), starting from the base, the previous indications of emotional balance, traditions, conviviality, frugality, sustainability and seasonality with culinary and horticultural activities, outdoor live and psychological wellness. The latter one is strictly connected to physical activity and physical performance. Recommendation for physical activity range at least between 30 [152] and 60 (SENC) per day. However, the evaluation of mood, clinical and nutritional status should drive personalized lifestyle and rehabilitation/training programs in veterans with disabilities (Fig. 1), including training for Paralympics competitions [183].

As previously suggested, seasonality implies the "intermittent" consumption of different foods, which contain a variable mix of bioactive molecules, and it allows to prevent the onset of phenomena of tolerance that might otherwise occur with the chronic intake of a single flavonoid or with a same food source of flavonoids. Although variability could also ensure the maintenance of the single dose of flavonoid below that at which adverse effects in some individuals genetically predisposed or unpleasant drug interactions in diseased subjects may occur [219], probably the avoidance of foods and beverages with high content of phytochemicals [117, 149, 153-159] could be recommended in subjects under polypharmacy regimes. In

these patients, plant foods should be chosen within those containing low phytochemicals and high micronutrients. If this aim is difficult to reach, vitamins and/or minerals supplementation can be indicated (top of the Pyramid) (Fig. 1).

In the middle of the pyramid, there are energy, nitrogen and water balance, as well as nutrient requirement coverage (Fig. 1). Although the frequency of consumption should be (every meal: cereals, vegetables and fruit; every day: milk or yogurt and olive oil; every week: meat, fish, eggs, cheese, pulses, potatoes, carrots and nuts) similar to the previously indicated ones [152], non-nutrient herbs and spices to flavor dishes and herbal infusions have been added to comfort and luxury foods and beverages (sweet, cocoa, coffee, tea, beer and wine). Occasional and/or moderate consumption should be suggested for this category, taking also into account potential interactions of phytochemicals with drugs and the effects on water and energy balance. However, the potential effects on mood should also be considered [220, 221].

CONCLUSION

Veterans with multimorbidity often identified specific self-care approaches for disease management, including both medication, healthy lifestyle practices and CAM [222].

The role of pharmacists in the elderly with polypharmacy has been previously suggested [223-225]. In this context, personalized nutrition could also have a role in the prevention of drug-food interactions [226] and in the plan of integrating programs for healthy ageing in veterans with disabilities.

In conclusion, although the Mediterranean Pyramid could be the basis for integrative medicine for veterans with disabilities, patient-centered approaches and interprofessional (including physical medicine and rehabilitation clinicians, pharmacists and nutritionists) interventions could be useful.

LIST OF ABBREVIATIONS

25(OH)D =	25-hydroxyvitamin D
ACS =	American Community Survey
CAM =	complementary and alternative medicine
CKD =	Chronic kidney disease
CVD =	cardiovascular diseases
GWI =	Gulf War illness
MCI =	Mild cognitive impairment
PTSD =	post-traumatic stress disorder
SENC =	Spanish Society of Community Nutrition

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

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