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Clinical advances in geriatric psychiatry: a focus on prevention of mood and cognitive disorders

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Abstract

The world's population is ageing in the 21st century at a rate unprecedented in human history, and this will place substantial pressure on health systems across the world along with concurrent rises in chronic diseases. In particular, rates of cognitive disorders and late-life affective disorders are expected to rise. In correlation with ageing, there are robust predictions suggesting rates of age-related cognitive decline and dementia, and geriatric depression, will rise with serious consequences. Clearly innovative prevention and treatment strategies are needed. Here we reviewed the latest promising clinical advances which hold promise for assisting the prevention and treatment of depression and cognitive decline and dementia.

Keywords

Late-life; psychiatry; cognitive decline; mood disorder; depression; prevention; treatment

Introduction

The world's population is ageing in the 21st century at a rate unprecedented in human history, and this will place substantial pressure on health systems across the world along with concurrent rises in chronic diseases. In particular, rates of cognitive disorders and late-life affective disorders are expected to rise. A recent global report [1] suggests the share of older people (aged ≥ 60 years) increased from 9.2 % in 1990 to 11.7 % in 2013 and will continue to grow as a proportion of the world population, reaching 21.1 % by 2050. In correlation with ageing, there are robust predictions suggesting rates of age-related cognitive

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decline and dementia, and geriatric depression, will rise with serious consequences. As of 2013, there were an estimated 44.4 million people worldwide with dementia [2]. This number will increase to an estimated 75.6 million in 2030, and 135.5 million in 2050. The most recent data on geriatric depression [3] identified depressive disorders as a leading cause of burden internationally, and suggested major depressive disorder (MDD) was also a contributor of burden allocated to suicide and ischemic heart disease. Depressive disorders were the second leading cause of years lived with disability (YLD) in 2010 [3].

These large burdens of disease are met by modest efficacies of current therapies and poor access for many. Unfortunately for those with Alzheimer's disease (AD), pharmacological agents temporarily treat symptoms without having an effect on the underlying pathophysiology of the disease [4]. In geriatric depression, a recent meta-analysis of clinical trials suggests a response rate of 48% and a remission rate of 33.7% were found, both very similar to response and remission rates found in adult patients [5]. Clearly innovative prevention and treatment strategies are needed.

Throughout health care, everything we do should be aimed toward prevention. This ranges from preventing the onset of disease in those who are well, through preventing chronicity, disability, and other consequences of disease, to preventing relapses in those in recovery. When conceptualizing approaches in prevention science, the most commonly used models are those of the Institute of Medicine [6] and the World Health Organization's (WHO) framework of levels of prevention (i.e. primary, secondary and tertiary prevention) [7]. A report from the Institute of Medicine [6] suggests prevention may be directed toward the whole population (universal prevention), high-risk groups (selective prevention), or those with subsyndromal symptoms (indicated prevention). The WHO's prevention framework [7] suggests primary prevention involves strategies aimed at preventing the development of disease; secondary prevention involves strategies to diagnose and treat existent disease in early stages before significant morbidity occurs; and, tertiary prevention involves strategies to reduce negative impact of existent disease by restoring function and reducing disease-related complications.

Fortunately there are several innovative prevention and treatment strategies being developed. We focus on several key strategies that include preventive and treatment strategies coming from resilience-building interventions, and complementary, alternative and integrative therapies. Platforms such as telepsychiatry and internet-based interventions are also promising mechanisms to enhance access to therapies.

In this review we outline the latest clinical advances in geriatric psychiatry to the prevention and treatment of mood disorders and cognitive decline. We then explore clinically relevant scientific advances which are underway at present.

Clinical advances in geriatric depression

Preventive interventions for geriatric depression

In this review we will focus on the IOMs framework of prevention: universal, selective and indicated prevention [6]. A critique of prevention in geriatric psychiatry should focus on (1)

feasibility, (2) effectiveness, and (3) ethical and economic considerations [8]. Table 1 outlines these conceptual frameworks of preventive science, as well as clinical examples for the fields of geriatric psychiatry.

With respect to universal prevention, any universal preventative action for geriatric depression should be a 'light' intervention: in terms of cost, effort for patients and in terms of impact (reviewed extensively elsewhere [8]). An example is a public awareness campaign. Cuijpers [9] has described that, even in a disorder like depression which has a relatively high incidence, studies testing universal prevention in depression are not likely to be feasible. Such a study would require too many participants and be costly to be run [8]. Cuijpers suggests 'this does not imply that universal prevention may not be useful, but it does suggest that universal prevention is probably best seen as a 'primer' - a way to prepare the public that depression is a disorder that can be managed, to reduce stigma' [9]. Fortunately, given technological advances and the widespread access to electronic media globally, electronic health preventative interventions for older people are in development [8]. These developments may drive down costs of programs, increase opportunities for and scales of preventive interventions, hence shifting preventative action toward universal programs.

With respect to selective prevention, several tested interventions are available (for review see [8]). They usually involve a way of identifying those at risk, and creating engagement with the intervention itself. Identification of older people at risk and engaging them effectively depends very much on local socio-economic-cultural factors [8]. In high-resource settings with well-developed health services, the more prudent point of contact for selective prevention may be community health services. Encouragingly, epidemiological data showing the vast majority of older people with risk factors for depression do contact their family physician regularly and these doctors have reliable data about many known risk factors [8]. Engaging older people in an intervention who are not clinically depressed is not easy. Complicated factors include a lack of awareness of mental health; lack of trust in interventions; lack of time, trained personnel, and resources to engage in an intervention; and the societal stigma surrounding mental illness [8]. Beekman et al. [8] suggests 'it is possible from an intrapersonal psychological perspective, humans tend to dislike doing things now to avoid harm later – i.e. there is no immediate benefit'. From the intervention perspective, the interventions that have been designed are mostly 'light' versions of robust clinical interventions. This involves versions of cognitive therapy, interpersonal therapy, reminiscence, and problem solving [8]. Often these are modified to cater for people exposed to specific risk factors and circumstances [8]. Other ingredients involve engaging in pleasant activities, physical activity, using nutritional supplements such as vitamin D and fish oils, and exposure to bright light (see for review [10]).

Indicated prevention engages older people who do have symptoms of depression but who have not developed a diagnosable major mood disorder. They do have symptoms and these symptoms interfere with their well-being and daily functioning. Indeed, older people with subthreshold depressive symptoms are at very high risk to develop diagnosable major mood disorders [11]. A drawback of indicated prevention is that participants need to be diagnosed with 'symptoms but no disorder' [8]. The trials that have been conducted in this area mostly recruited participants through screening [11]. A positive screen implies that some significant

symptoms are present. In a next diagnostic step, the outcome may either 1) a diagnosable major mood disorder or 2) no such disorder. The patient is then referred for treatment or offered a preventive intervention, respectively. A study in the Netherlands by Van Veer-Tazleer et al. [12] tested a program that was organized along the lines of 'stepped care'. In this program all the older participants with "symptoms but major disorder" were offered a choice of educational and self-help interventions first, slowly stepping up the intensity of the intervention if the symptoms remained present. The intervention halved the 12-month incidence of depressive and anxiety disorders, from 0.24 in the usual care group to 0.12 in the stepped-care group (relative risk, 0.49; 95% confidence interval, 0.24 to 0.98).

Resilience building interventions

Advancing age is often associated with increased vulnerability to a unique set of stressors including retirement, medical co-morbidity, loss of loved ones, and the threat of loss of independence. As such, there has been a surge of interest in exploring factors that contribute to older adults aging more successfully. One such aspect of successful aging is the concept of resilience [13].

The critical role of resilience in successful aging has been well-documented [14–16]. Positive constructs such as resilience may be thought of as being complements to traditional medicine in that they emphasize personal strength rather than disease or deficits [17]. The study of resilience coincides with the rising trend towards a strengths-based approach to aging, which is slowly starting to replace or at least complement the traditional negative deficits view of aging (see for review {Jeste, 2013 #73}). One of the goals of positive aging is for individuals to evolve, adapt, and find meaning and purpose in life events. One study found that older adults who were more resilient tended to report fewer adversities and were more likely to use adaptive, solution-driven coping rather than avoidant coping strategies in the face of challenge [18]. Additional individual characteristics that have been viewed as being important contributors to resilience include commitment, dynamism, humor in the face of adversity, optimism, faith, altruism, and perceiving adversity as an opportunity to learn and grow [19].

To our knowledge, there are no published interventions specifically targeting resilience in geriatric mood and cognitive disorders, but there is some data in adults populations. Pedeskey and Mooney [20] describe a four-step Strengths-Based Cognitive Behavioral Therapy Model designed to enhance resilience. The four steps to resilience include: a search for strengths; construction of a personal model of resilience; applying the personal model of resilience to areas of life difficulties; and practicing resilience. In this treatment approach, individuals are supported to search for areas of competence such as good health, positive relationships with others, self-efficacy, emotion regulation skills, and the belief that one's life has meaning. The purpose of this search is based on the notion that all individual possess resilience traits, however they have be unaware of same. A personal model of resilience is created that may then be used by the individual in life situations.

When exploring resilience in older participants, a recent observational study by Jeste and colleagues [21] found significant associations between resilience and self-rated successful aging in a sample of over 1000 community-dwelling older adults. The magnitude of these

effects were reportedly comparable in size to that of physical health. This finding was supported by Manning et al. [22] who reported another observational study, finding high levels of resilience protect against the psychological impact of chronic new conditions in older adults. Some research has suggested that high levels of resilience significantly contribute to longevity and this becomes even more significant at very advanced ages - centenarians being more resilient than any other age group [23]. In a cohort of middle-to-older aged women with breast cancer, Loprinzi et al. [24] demonstrated the possible efficacy of the Stress Management and Resiliency Training (SMART) program in increasing quality of life. In this intervention, participants attended two 90-minute group sessions in which they were taught relaxation techniques, as well as skills to delay judgment and attend to novel aspects of the environment rather than one's thoughts. Participants also learned to adopt a flexible disposition and practice gratitude, compassion, and acceptance. The authors found that relative to the wait-list control group, women who received the SMART intervention reported improved resilience as well as quality of life, anxiety, stress, and fatigue. The evidence of the feasibility of such a brief intervention is promising in the context of adapting programs for older adults.

Complementary, alternative, and integrative therapies for geriatric depression

Complementary and alternative medicine "is a group of diverse medical and health care systems, practices, and products that are not presently considered part of conventional medicine" [25]. Some of these therapies provide promise as novel and effective therapies for treatment and prevention of geriatric psychiatric disorders with generally more modest side-effect profiles [10]. 'Complementary' generally refers to using a non-mainstream approach together with conventional Western medicine. 'Alternative' refers to using a non-mainstream approach in place of conventional Western medicine. 'Integrative medicine' is another term often used when strategy combines alternative and complementary medicine with evidence-based Western medicine. We will refer to such therapies as Complementary, Alternative and Integrative Medicine (CAIM). CAIM interventions have varying levels of efficacy and evidence, they can include mind-body practices, conventional physical activity, dietary interventions, natural products, as well as body-based practices and other medical system practices.

CAIM interventions have varying levels of efficacy and evidence, they can include mind-body practices, conventional physical activity, dietary interventions, natural products, as well as body-based practices and other medical system practices. Mind-body practices refer to practices where there is both physical and mental activity may be combined during training. These can be more exercise-focused (i.e. yoga, tai chi, qi gong) or more practice and stress-reduction focused (i.e. mindfulness and relaxation). Physical activity refers to any bodily movement produced by skeletal muscles that requires energy expenditure and may include aerobic, resistance, stretching and toning or combination activities. Dietary interventions explore the effect of dietary patterns on health and illness and may include Western, traditional and Mediterranean dietary patterns, as well as caloric restriction, among others. Natural products may include herbs, vitamins, minerals, natural supplements and probiotics. Body-based practices may include spinal manipulation (e.g. chiropractic, osteopathic medicine), aromatherapy and massage therapy. Other medical systems include

traditional Chinese medicine (including acupuncture), Ayurvedic medicine or homeopathy. These CAIM interventions are largely based on therapies, which have been utilized in many civilizations and religions for hundreds and thousands of years. It is not since the past 50 to 100 years that empirical science has begun to explore the evidence behind these therapies.

Clinical importance—There are a number of major reasons why geriatric mental health providers need to recognize the importance of these interventions. (1) *CAIM therapy use is high and rising*. Research suggests 12-month prevalence of any CAIM usage (excluding prayer) in the USA is around 35 – 50%; Baby Boomers (adults born from 1946 to 1964) report significantly higher rates of use than the Silent Generation (born from 1925 to 1945) for chronic conditions [26]. (2) *The global population is aging*. Outlined above. (3) *CAIM therapies are increasingly cited in clinical guidelines*. It is now commonplace to note the use of therapies like conventional exercise in the management of psychiatric conditions. (4) *CAIM therapies are a source for innovative interventions and have a growing, quality empirical research basis*. Empirical research into these therapies are exploring their clinical efficacy in trials and the neurobiological mechanism underlying their effects. (5) *CAIM therapies can help to lower utilization of conventional medicines*. CAIM therapies may be used in replacement of conventional medicines for the management of mild illnesses (e.g. relaxation techniques for mild anxiety instead of benzodiazepines which are known to have adverse effects with elderly populations) [10]. (6) *CAIM therapies can have significant side-effects and CAIM-drug interactions*. With the high use in geriatric populations, this is therefore an important reason why clinicians need to better understand CAIM therapies [10].

Conventional physical activity—Conventional physical exercise has received attention for its potential role in the treatment of geriatric depression. The effects of aerobic exercise on depressed adults (50 years and older) was examined and compared to either monotherapy with sertraline as a standard antidepressant or a combination [27]. The study found that after 16 weeks, all groups demonstrated significant and equivalent reductions in depressive symptoms. Furthermore, a 10-month follow-up study showed participants in the exercise group (who improved to the point of remission during the initial study) showed lower rates of relapse versus antidepressants. Another study of exercise for older adults found 10 weeks of strength-training exercises classes, provided as an adjunctive treatment, lessened depressive symptoms in a group of older adults who failed antidepressant response alone when compared to a health education course [28]. A systematic review [29] examining the role of exercise in the treatment of depression in older adults was published in 2009. This study noted 11 RCTs with a total of 641 participants aged > 60 years. The study noted short-term (0 – 3 months) positive outcomes were found in 9 studies, although there was variation in the type, intensity and duration of exercise. The efficacy of exercise in the medium- and long-term (3 – 12 months and > 12 months, respectively) was less clear. Methodological issues were noted with only 5 studies showing appropriate allocation of concealment, 5 studies showing intention to treat analysis and blinding occurred in 7 studies. From a more real-world perspective, the effectiveness of a number of lifestyle interventions promoting increases in conventional physical exercise were recently reviewed [30]. Interventions were relatively successful in initiating increased levels of physical activity in the short run; however, maintenance of these gains were diminished over time, and there was no

convincing evidence that behavioral reinforcement strategies were beneficial – therefore adherence is a major concern. Another review of exercise interventions found that while many older adults increase activity levels in response to a wide variety of interventions, the amount of increase is seldom enough to impact health outcomes in a positive manner [30].

In conclusion, preliminary evidence points to exercise as having a significant potential to lessen symptoms in depressed older adults, and furthermore, to prevent relapse of depression and/or development of depressive symptoms in older adults experiencing acute stressors associated with aging. Therefore we recommend physical exercise as a stand-alone therapy in the treatment of mild depression, and an adjunct in moderate depression.

Currently, the American College of Sports Medicine [31] recommends that exercise programs for older adults include both aerobic and nonaerobic physical activities, such as resistance training, balance training, and stretching, for optimal general health. See Table 2 for the latest clinical guidelines on physical activity for older adults.

Mind-body practices—Mindful exercise interventions have shown promise in addressing depressive symptoms in older adults. For example, a study of 82 older adult participants with depression randomized to either 16 weeks of qigong practice or newspaper reading groups found that qigong participants showed significantly greater improvements in mood, self-efficacy, and personal well-being [32]. Practice of yoga typically benefits from instruction by expert instructors and requires the dedication by participants to multiple weekly sessions and continual use for maximal benefit. Prior review of published RCTs of yoga for depression in adults revealed that while all trials found benefit trial methodologies have generally been weak with lack of blinding, short duration of the intervention, variable outcome measures, limited information about subjects, randomization procedures, compliance, and dropout rates [33]. Comparative studies of yoga have likewise been limited, with 1 trial demonstrating that yoga was as effective as TCAs and another trial showing that yoga may provide benefit as an augmentation strategy for antidepressant treatment [34]. Yoga is commonly used in combination with other treatments for depression, anxiety, and stress-related disorders. Data on use of yoga for anxiety and depression in older adults are more limited; however, one significant study of 69 older adults in India did compare the impact of yoga to Ayurveda or a wait-list control condition on sleep and depressive symptoms [35]. Participants in the yoga group practiced physical postures, relaxation techniques, regulated breathing, devotional songs, and attended lectures for more than 7 hours a week during the course of the 6-month trial. Practice of yoga significantly impacted quality of sleep and level of depressive symptoms when compared to the two control conditions, neither of which demonstrated significant effects. In particular, depressive symptoms, as measured by the short form of the *Geriatric Depression Scale*, decreased in the yoga group from a baseline average of 10.6 to 8.1 by 3 months and 6.7 by 6 months. The average time to fall asleep decreased in the yoga group by 10 minutes, while total number of hours slept increased by 60 minutes, and resulted in a greater feeling of being rested after 6 months. A recent study by [36] compared the effectiveness of laughter yoga, group exercise therapy and control in decreasing depression in older adult women (60 to 80 years). In this study, seventy depressed women were chosen if their Geriatric Depression Score was > 10. This study went for 10 sessions and found a significant improvement in depression score with both yoga and

group exercise therapy as compared with control. Whilst the evidence supporting the use of these therapies in the treatment of late-life mental illnesses is not strong, there are some interesting early results which require further high-quality research [37].

We recommend the use of mind-body therapies as a stand-alone or adjunctive antidepressant treatment in the management of geriatric depression, based on individual preference and the severity of depression. Further high quality data is needed to further inform these recommendations.

Dietary interventions—Dietary interventions are seen as a promising method to both treat and prevent geriatric depression. When considering the diet composition of older depressed adults, some concerning findings come from a recent cross-sectional study [38]. In this study of 278 older adults (144 with depression; 134 without depression), vitamin C, lutein and cryptoxanthin intakes were significantly lower among depressed individuals than controls. In addition, fruit and vegetable consumption, a primary determinant of antioxidant intake, was lower in depressed individuals. This type of dietary intake may indeed be a risk factor for depression. A recent systematic review [39] addressed associations between dietary patterns and depression in community-dwelling adult populations. A total of 21 studies were identified. Results from 13 observational studies were pooled; from cross-sectional to 15 years prospective. Two dietary patterns were identified. The healthy diet pattern was significantly associated with a reduced odds of depression (OR: 0.84; 95% CI: 0.76, 0.92; $P < 0.001$). No statistically significant association was observed between the Western diet and depression (OR: 1.17; 95% CI: 0.97, 1.68; $P = 0.094$); however, the studies were too few for a precise estimate of this effect. The results suggest that high intakes of fruit, vegetables, fish, and whole grains may be associated with a reduced depression risk.

We are aware of only one RCT currently underway in Australia to explore the effect of dietary interventions on adult depression [40], not specifically in an older-age population. This study is enrolling participants with a current major depressive episode and they are randomized to a dietary intervention group or a social support group. The dietary intervention consists of 7 individual nutrition consulting sessions (60 minutes each) delivered by a dietician. Data will be explored across the 3 month trials and a 6 month follow up. Data on the potential benefits of dietary coaching in the prevention of incident depression for older adults has recently been drawn from a larger randomized depression prevention trial which ran over 2 years [41]. Older adults (n=122) receiving dietary coaching experienced a low incidence of major depressive episodes and exhibited a 40%–50% decrease in depressive symptoms, as well as enhanced well-being, during the initial 6-week intervention; these gains were sustained over 2 years [42]. Clearly the role of dietary intervention is intriguing.

Clinical advances in cognitive decline and dementia

Prevention of cognitive decline and dementia

The rising burden of mental, cognitive and substance use disorders globally [2, 43] supports the need for improved methods to aid prevention and early intervention [44]. Classic risk factor studies in dementia are hampered by the difficult phenotyping of the disease with

large heterogeneity in severity and presentation, and by the fact that once symptomatic, irreversible brain damage is already present. The paradigm shift in medicine towards prevention calls for identification of potentially modifiable factors that affect disease in an earlier stage. The rising burden of cognitive disorders is occurring as our wider understanding of preventive lifestyle modifications and our understanding of the neurobiological underpinnings is rapidly evolving. For example, with AD, a recent study has highlighted the important role of risk factor reduction for reducing AD prevalence [44]. Barnes and Yaffe [44] explored the role of seven potentially modifiable AD risk factors: diabetes, mid-life hypertension, mid-life obesity, smoking, depression, low educational attainment and physical inactivity. They determined these factors contributed to up to half of AD cases globally (17.2 million), and a 10%–25% reduction in all risk factors could potentially prevent as many as 1.1–3.0 million cases. There is now an emerging literature exploring the effect of these risk factors on neurobiology factors. Other lifestyle factors which have been found to reduce the risk of AD include mind-body exercise (e.g. yoga, tai chi, qi gong [45]), conventional physical activity (e.g. aerobic, strength training [45]), supplements (e.g. omega-3 fatty acids, flavanols [46]), stress reduction techniques (e.g. Mindfulness-based Stress Reduction [47]), sleep modification strategies [48], dietary interventions (e.g. fish consumption, Mediterranean diet) [49].

Complementary, alternative and integrative therapies for cognitive decline and dementia

Conventional physical activity—Conventional physical activity is one of the most promising therapy for the treatment and prevention of cognitive decline and dementia [4]. Importantly, there are a variety of subtypes of physical activity, from aerobic activity, to resistance, to stretching and toning.

A recent RCT [50] examined the efficacy of resistance and aerobic training in the improvement of cognitive functions in subjects with subjective Mild Cognitive Impairment (MCI). The study occurred over 6-months and involved 86 community-dwelling women aged 70 – 80 years.

- Physical activity protocols included twice-weekly resistance training, twice-weekly aerobic training or twice-weekly balance and toning (BAT) training (i.e. control).
- Resistance training improved selective attention, conflict resolution and associated memory compared with BAT.
- In contrast, aerobic physical activity improved general balance and mobility and cardiovascular capacity.
- The study also found aerobic physical activity improved verbal memory and both resistance and aerobic physical activity improved spatial memory.

A recent stringent meta-analysis [51] has examined the efficacy of exercise on cognition in older adults with MCI. MCI was diagnosed on documented criteria or via the Mini-Mental State Exam (MMSE). Fourteen randomized controlled trials (RCTs) with 1,695 participants aged 65–95 years were utilized. These studies had a duration of 6 to 52 weeks. Overall, 42% of effect sizes (ESs) were potentially clinically relevant (ES >0.20) with only 8% of cognitive outcomes statistically significant. The meta-analysis revealed negligible but

significant effects of exercise on verbal fluency (ES: 0.17 [0.04, 0.30]). No significant benefit was found for additional executive measures, memory, or information processing. The authors critically appraised RCT methods and concluded on a moderate quality with the majority of trial samples being too small for sufficient power. There is clearly some effect for exercise at moderate to high levels of exertion. In addition, nowadays there is an emerging evidence for the effect of low levels of physical activity or 'sedentary behaviors' like sitting. Physical inactivity may increase the risk of Alzheimer's disease by 82 % [52]. Approximately 13% of Alzheimer's disease cases worldwide may be attributable to sedentary behaviors [44]. A 25% reduction in sedentary behavior could potentially prevent more than 1 million Alzheimer's disease cases globally [44]. Sedentary behaviors may contribute to risk of Alzheimer's disease and dementia by increased risk of cardiometabolic risk factors – diabetes, hypertension, obesity – diseases associated with increased risk of dementia [53].

Our clinical recommendation is physical activity should be encouraged for all older adults. More work is required to understand if physical activity recommendations or dementia prevention are the same as generic 'healthy aging' recommendations (as in Table 1). While shorter-term interventions are useful in the research setting, care must be taken to ensure a sustained engagement in physical activity. Care must also be taken to create an age- and physical-function appropriate prescription given risks of adverse health effects (e.g. falls, cardiovascular events).

Mindful exercise—A recent meta-analysis [54] critically evaluated the effects of Tai Chi on individuals aged 60 and old with and without cognitive impairment. In this study, 20 eligible studies with a total of 2,553 participants were identified that met inclusion criteria for the systematic review; 11 of the 20 eligible studies were RCTs, one was a prospective non-randomized controlled study, four were prospective non-controlled observational studies, and four were cross-sectional studies. Overall quality of RCTs was modest, with three of 11 trials categorized as high risk of bias. Meta-analyses of outcomes related to executive function in RCTs of cognitively healthy adults indicated a large effect size when Tai Chi participants were compared with non-intervention controls ($g = 0.90$; $P = 0.04$) and a moderate effect size when compared with exercise controls ($g = 0.51$; $P = 0.003$). Meta-analyses of outcomes related to global cognitive function in RCTs of cognitively impaired adults, ranging from mild cognitive impairment to dementia, showed smaller but statistically significant effects when Tai Chi was compared with non-intervention controls ($g = 0.35$; $P = .004$) and other active interventions ($g = 0.30$; $P = .002$).

There is a relative dearth of studies examining yoga and its effects on memory enhancement. One main study of which we are aware explores the effects of yoga and exercise in 135 healthy men and women aged 65 – 85 years [55]. In this study subjects were exposed to 6 months of Hatha yoga classes, walking classes or wait-list control; subjects were screened with a variety of mood and cognition tests (e.g. Stroop test). Interestingly, after the intervention there were no effects from either of the active interventions on any of the cognitive and alertness outcome measures. The yoga intervention produced improvements in physical measures (e.g. timed 1-legged standing, forward flexibility) as well as a number of quality-of-life measures related to sense of well-being and energy and fatigue compared to

controls. This type of study needs to be replicated in populations with MCI to better understand potential effects.

Mind-body practices and stress-reduction techniques—Relaxation techniques, such as breathing exercises, guided imagery, and progressive muscle relaxation, are designed to produce the body's natural relaxation response. These relaxation therapies are shown to lower stress levels in elderly subjects, and so are recommended for clinical use. A recent pilot randomized trial [47] with mindfulness based stress reduction (MBSR) aimed to test the safety and feasibility of MBSR in older adults with MCI. The study found adults with MCI can safely participate and adhere to an MBSR program. The qualitative interviews revealed that most enjoyed the program and described improved mindfulness skills, well-being, inter-personal skills, acceptance/awareness of MCI, and decreased stress reactivity. Most data suggest trend towards improvement for measures of cognition and well-being, however a more formal, large scale RCT is needed.

Firm clinical recommendations for these activities are not possible given the paucity of sufficient evidence at this stage. However, we would recommend mind-body therapies as useful stand-alone or adjunctive therapies for the management of mild neuropsychiatric symptoms (e.g. cognitive impairment and psychological distress) and physical health (e.g. balance, strength, co-ordination). Care must be taken to create an age-, physical- and mental-function appropriate prescription [56]. There recommendations are based from clinical experience, emerging evidence and the safe nature of these activities.

Dietary interventions—Examining the effect of nutrition on cognitive decline is a new area of research showing favorable results. Two significant studies are outlined below to illustrate the latest and most significant developments in this area. A recent analysis of the Australian Imaging, Biomarkers and Lifestyle Study of ageing explores the association of three well-recognized dietary patterns with cognitive change over a 3-year follow up period. In this study 527 healthy older participants (age 69.3+/− 6.4) were enlisted and they underwent dietary analysis using a food frequency question, as well as neuropsychological analyses at baseline, 18 and 36 months. Three dietary patterns were discerned including the Australian-style Mediterranean diet (AusMeDi), western diet and the prudent diet. The principal aspects of this AusMeDi diet include proportionally high consumption of olive oil, legumes, unrefined cereals, fruits, and vegetables, moderate to high consumption of fish, moderate consumption of dairy products (mostly as cheese and yogurt), moderate wine consumption, and low consumption of meat and meat products. Western diets are characterized by high intakes of red meat, sugary desserts, high-fat foods, and refined grains. It also typically contains high-fat dairy products, high-sugar drinks, and higher intakes of processed meat. The prudent diet was characterized by high intakes of green leafy vegetables, fruits, nuts, grains, low-fat foods and protein. Higher baseline adherence to the AusMeDi was associated with better performance in the executive function cognitive domain after 36 months in apolipoprotein E (APOE) ε4 allele carriers ($P<0.01$). Higher baseline western diet adherence was associated with greater cognitive decline after 36 months in the visuospatial cognitive domain in APOE ε4 allele non-carriers ($P<0.01$). All

other results were not significant. Systematic reviews of observation studies show similar results [57].

We are only aware of one RCT exploring the role of diet in the prevention of cognitive impairment. This study was a multicenter, randomized, primary prevention trial named Prevención con Dieta Mediterránea (PREDIMED) [58] and assessed the effects of a nutritional intervention using the MeDi (supplemented with either extra-virgin olive oil (EVOO) or mixed nuts) in comparison with a low-fat control diet. This study assessed 522 participants at high vascular risk (age 74.6+/−5.7) and examined cognitive performance (MMSE and Clock Drawing Test (CDT)) after 6.5 years of nutritional intervention. After full adjustment, the MeDi EVOO group showed higher mean MMSE and CDT scores versus control (adjusted differences: +0.62 95% CI +0.18 to +1.05, p=0.005 for MMSE, and +0.51 95% CI +0.20 to +0.82, p=0.001 for CDT). Similarly, the MeDi+Nuts group showed higher mean MMSE and CDT scores (adjusted differences: +0.57 (95% CI +0.11 to +1.03), p=0.015 for MMSE and +0.33 (95% CI +0.003 to +0.67), p=0.048 for CDT) versus control. Clearly further RCTs are needed in this field to improve the quality of the field.

From a clinical perspective, we recommend the population in general adhere as close as possible to the Mediterranean and healthy diets. Further clinical trials are needed to understand the best diet(s) for maintaining brain health.

Natural products—Natural products may include herbs, minerals, natural supplements, vitamins and probiotics. A range of these products have been explored with regards to the treatment and prevention of cognitive impairment. There are too many of these products to thoroughly review here, so only the main products, with a larger body of research and/or epidemiological usage, are reviewed here with further reading recommended.

Omega-3 polyunsaturated fatty acid supplements—One of the most widely utilized therapies is Ω3 polyunsaturated fatty acids (PUFAs). Over 37% of individuals who reported using a non-vitamin, non-mineral natural product in the 2007 NHIS reported using Ω3 PUFAs [59]. Oily fish, such as salmon, mackerel, herring and sardines are a rich source of Ω3 PUFA which are essential for brain development. It is thought that Ω3 PUFAs may benefit neurodegenerative disorders due to anti-oxidant and anti-inflammatory effects [60]. Previous research from observational studies has suggested that increased consumption of fish oils rich in Ω3 PUFA may reduce the chance of developing dementia. A recent Cochrane Database systematic review [60] explored the effects of Ω3 PUFAs on the prevention of dementia and cognitive decline in cognitively healthy older people. Information was available from 3 RCTs including 3536 participants in total. This meta-analysis found no evidence to support a preventative effect following 24 or 40 months of intervention. RCTs suggest that selected patients with a MMSE score >27 were more likely to identify a positive effect of Ω-3 PUFA supplementation. It appears studies of longer duration are required to further explore this area. Our clinical recommendation emphasizes clinician-patient discussions of evidence. Care must be taken with potential side effects of mild nausea, mild increased bleeding and a fishy aftertaste.

For further details on other utilized CAIM therapies for the treatment and prevention of cognitive decline, please see Table 3.

Potential side effects and CAIM-drug interactions—As eluded to above, when encountering natural products in a clinical environment, it is important to consider potential side effects and CAIM-drug interactions. In Table 4 we outline an array of clinical findings and potential pitfalls of natural products. It is important to note that CAIM use may exacerbate polypharmacy in the elderly, which is a risk factor for drug interactions, medication errors and hospitalization. A survey of 271 British seniors found a mean of 5.91 (range 4 – 7) herbal and nutritional supplements and 2.26 prescription drugs [61].

Tele-psychiatry and internet-based approaches for older adults

Due of the low rates of receiving adequate treatment among older adults, and the intrinsic and extrinsic barriers to mental health care, it is important to develop evidence-based treatments which are easily accessible for patients, and which keep time and costs low [62]. Telemedicine and Internet-based treatments have been proposed to be such interventions helpful for the above issues [63–65]. Internet-guided and telepsychiatry interventions may save costs and time from patients and therapists, they may reach depressed older adults who are not reached with traditional therapies, solve transportation problems, stimulate empowerment of patients, and reduce the stigma associated with mental illness [62].

Internet-based therapies can be seen as a specific type of guided self-help intervention (for review see [62]). A self-help intervention can be defined as a psychological treatment, where the patient or client takes home a standardized treatment and works through it more or less independently [66, 67]. In the standardized psychological treatment, the patient can follow step-by-step instructions on what to do in applying a generally accepted psychological treatment. The standardized psychological treatment can be written down in hard copy print, but it can also be made available through other media, such as a personal computer, television, video or the internet. Contact with therapists is not a necessity for the completion of the self-help therapy; if contact with a therapist takes place, it should only be for support or facilitation. Contact is not aimed at developing a traditional relationship between therapist and patient, and is only meant to support the carrying out of the psychological treatment. Interaction between patient and therapist can take place through face-to-face contact, by telephone, by email, or any other communication method.

Although a growing number of studies has examined the effects of Internet-based interventions and telephone-supported interventions, few have examined these in older adults [67]. However, research shows that these interventions are promising and there is no reason to assume that they are not effective in older adults. Concerns may include lesser proficiency with information technology in old age, and concerns with lesser visual acuity. More research is needed, especially since technological developments are rapidly occurring and innovative types of interventions and new possibilities to reduce the disease burden are required

Summary

A number of major factors coalesce to drive the need for innovation in geriatric psychiatry. Firstly the global population is aging. Secondly age-related cognitive decline, dementia and depression have a large burden. Thirdly the current treatment options for these conditions are modest. Finally there is a relative poor lack of access in low and middle income environments. In this review we have outlined some promising advances in geriatric psychiatry which include preventive resilience building interventions and complementary, alternative and integrative therapies, brain stimulation techniques. Platforms such as telepsychiatry and internet-based interventions are also promising mechanisms to enhance access to therapies.

Promising research agendas

In addition to these current clinical advances there are a range of research advances which may pave the way for future clinical innovations. These research advances include:

- *Geroscience*: Geroscience is an interdisciplinary field that aims to understand the relationship between ageing and age-related diseases [68]. In geroscience, researchers in a variety of disciplines may work together, sharing data and ideas, with a common goal of explaining and intervening in age-related diseases. ‘Compression of morbidity’ is a major focus of geroscience research. ‘Compression of morbidity’ is a concept whereby scientists discover ways to decrease the period of an individual’s life where there is poor health. With this aim, individuals hope to postpone and reduce disease onset, disability, dependency and suffering. The exact mechanisms of aging are still under debate, however there are a number of mechanisms which are generally agreed upon (see for discussion [69]). The mechanisms include genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, mitochondrial dysfunction, cellular senescence and chronic inflammation.
- *Health neuroscience*: Health neuroscience was coined by Erickson et al. [70] is at the interface of health psychology and neuroscience. It is concerned with the interplay between the brain and physical health over the life span. A chief goal of health neuroscience is to characterize bidirectional and dynamic brain-behavior and brain-physiology relationships that are determinants, markers, and consequences of physical-health states across the life span. The motivation behind this goal is that a better understanding of these relationships will provide mechanistic insights into how the brain links multilevel genetic, biological, psychological, behavioral, social, and environmental factors with physical health—especially vulnerability to and resilience against clinical illnesses.
- *Convergence medicine*: Convergence medicine is a novel derivative of convergence science and refers to the discipline of how societal health can be optimized by the cross-pollination of clinical medical practice with non-clinical fields (e.g. engineering, information technology, entrepreneurship, public health, business, finance, management, journalism, politics, law and the arts) [71]. The aim is for

health innovation based on interdisciplinary team work and multidisciplinary mindsets.

Conclusion

Major problems are faced in the field of geriatric psychiatry. Here we reviewed the latest promising clinical advances which hold promise for assisting the prevention and treatment of depression and cognitive decline and dementia.

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Key points

- World population ageing in the 21st century is unprecedented in human history, and will place substantial pressure on health systems across the world with concurrent rises in chronic diseases, particularly cognitive disorders and late-life affective disorders.
- Prevention of mood and cognitive disorders is of utmost importance to reduce morbidity and mortality and the high costs of health care to the patients and the society
- We discuss recent data and innovative preventive interventions involving lifestyle, resilience-building, and complementary, alternative and integrative medicine for treatment and prevention of geriatric mood and cognitive disorders
- We discuss the clinical challenges and future directions for research

Table 1

Clinical implications of preventive science frameworks in geriatric psychiatry

Data from Refs [4, 6, 7, 72–74]

Preventive approach	Definition and explanation	Clinical examples for geriatric depression	Clinical examples for cognitive decline
Universal	Strategies that involve the whole population. Provided without screening.	Environmental design and modification (e.g. green space development, walkway modification, food access, health communities); cross-governmental initiatives; internet-based promotions; informational programs for the general public.	
Selective	Strategies that involve targeted subpopulations whose risk of developing a disorder is above average. Involves identified exposure to specific risk factors.	Risk factors: • Pre-existing disease: e.g. psychiatric illness (e.g. anxiety disorder, age-related cognitive dysfunction, substance-related disorders); general medical conditions (e.g. cardiovascular disease, obesity, diabetes) • Health related behaviors: e.g. psychological stress; physical inactivity; alcohol, tobacco and other drugs; sleep disruption; dietary factors. Biological factors	
Indicated	Strategies aimed at subjects who have early and sub-threshold symptoms and signs of illness. Involves a screening process.	Sub-threshold; early intervention.	
Primary	Strategies to avoid occurrence of disease.	As per universal and selective approaches.	
Secondary	Strategies to diagnose and treat existent disease in early stages before significant morbidity occurs.	Relapse prevention; attenuation of episode duration and severity of episode; early intervention.	Early intervention to prevent conversion to
Tertiary	Strategies to reduce negative impact of existent disease by restoring function and reducing disease-related complications.	Prevention of cognitive decline; prevention of psychotropic drug use and therefore reduced side effects; prevention of catatonia; prevention of adverse effects of illness on social and occupational functioning.	

Table 2

Clinical suggestions for geriatric populations

Adapted from the Centers for Disease Control and Prevention Report ‘Physical activity is essential to healthy aging’. How much physical activity do older adults need? 2014. Accessed 10/28/14; with permission.

If 65 years or older, generally fit, and have no limiting health conditions. • At least 150 minutes of moderate-intensity aerobic activity (i.e. brisk walking) every week and muscle-strengthening activities on 2 or more days a week that work all major muscle groups (i.e. legs, hips, back, abdomen, chest, shoulders and arms). OR • 75 minutes of vigorous-intensity aerobic activity (i.e. jogging or running) every week and muscle-strengthening activities on 2 or more days a week that work all major muscle groups. OR • An equivalent mix of moderate- and vigorous-intensity aerobic activity and muscle-strengthening activities on 2 or more days a week that work all major muscle groups.
Other comments: • If there is a limiting condition, it is recommended the health professional and patient consult a qualified exercise physiologist. • 10 minutes at a time is fine for physical activity. • The following activities count as muscle-strengthening activities: yoga, heavy gardening.

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Table 3

Other natural products and supplements suggested for the treatment of cognitive impairment

Data from Refs[76–82]

Herb/Supplement	Suggested Dose	Possible Mechanism of Action	Evidence Base	Side Effects
Bacopa monniera	300 mg/day	An Ayurvedic medicinal plant that acts as a free radical scavenger and in animal models reduces Aβ; may also boost cholinergic function	No convincing evidence: 9 RCTs; 518 subjects in meta-analysis. Limited evidence given poor study design.	GI upset
Curcumin (yellow curry)	2,000–8,000 mg/day	Antioxidant, anti-inflammatory, induces heat shock proteins; anti-amyloid effects in animals	Mixed results; no convincing evidence: 2 studies find no effect; 1 study finds beneficial effect.	GI upset
Dehydroepiandro- sterone (DHEA)	100 mg/day	Adrenal steroid that declines with aging, is lower in Alzheimer's disease patients, and is neurotrophic in animals	No convincing evidence of benefit. 3 RCTs	Acne, balding, insulin resistance, dyslipidemia, mood changes, hepatic dysfunction, possible effects on hormone- sensitive cancers
Hydergine	3 mg/day	Combination of 4 ergot derivatives with vasodilatory effects and possible effect on mono-amine and cholinergic transmission	2000 Cochrane meta-analysis of 19 trials found some evidence of modest efficacy but many trials conducted before standardized criteria for diagnosing dementia	GI upset, psychosis, flushing, blood pressure changes
Lecithin	3,600 mg/day	An acetylcholine precursor	Review of 11 randomized trials showed no consistent benefit	GI upset, rash, headache, dizziness
Resveratrol	Unknown (phase 1 trials 2,500–5,000 mg/day)	Polyphenol in the skin of red grapes and red wine with antioxidant and anti-amyloid properties in animals	Clinical trial linking to increased cerebral blood flow. Needs further study on cognitive effects	Possible estrogen-like effects, as its chemical structure is similar to phytoestrogens
Vitamin E	800 – 2000 IU/day	Free radical scavenging	No convincing evidence. Cochrane review – 3 studies.	High dose increases all-cause mortality.

D, Alzheimer's disease; ChAT, choline acetyl transferase (the enzyme that synthesizes acetylcholine); GI, gastrointestinal; RCT, randomized controlled trial.

Table 4

Potential CAIM-drug interactions between natural products and prescription medications

Herb/Supplement	Prescription Drug(s)	Possible Interaction
Chamomile	Sedatives (or alcohol)	Oversedation
Garlic extract	Protease inhibitors	Decreased efficacy against HIV
Ginkgo biloba	Anticoagulants Omeprazole (CYP2C19 substrates) Antipsychotic	Excessive bleeding Decreased drug levels (2C19 induction) Priapism
Ginseng	Anticoagulants Monoamine Oxidase Inhibitors Sulfonylureas, Insulin Stimulants	Excessive bleeding Mania, Hypertension, Headache Hypoglycemia Insomnia, Anxiety, Mania
Kava	Sedatives (or alcohol) Levodopa	Oversedation Increased Parkinsonism
Omega-3 fatty acids	Warfarin	Excessive bleeding
St. John’s wort	Protease inhibitors Cyclosporine Serotonergicantidepressants Oral contraceptives Tetracycline	Decreased efficacy against HIV Organ rejection Serotonin syndrome Ineffective contraception Photosensitivity
Valerian	Sedatives (or alcohol) CYP3A4 substrates	Oversedation Increased drug levels (3A4 inhibition)
Vitamin E	Anticoagulants	Excessive bleeding