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Review article

The role of vitamin D in the prevention of late-life depression

Olivia I. Okereke [a,b,c,*], Ankura Singh [a]

[a] Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, United States
[b] Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA 02115, United States
[c] Department of Psychiatry, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 02115 United States

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ABSTRACT

Background: In this article, we review current evidence regarding potential benefits of vitamin D for improving mood and reducing depression risk in older adults. We summarize gaps in knowledge and describe future efforts that may clarify the role of vitamin D in late-life depression prevention.
Methods: MEDLINE and PsychINFO databases were searched for all articles on vitamin D and mood that had been published up to and including May 2015. Observational studies and randomized trials with 50 or more participants were included. We excluded studies that involved only younger adults and/or exclusively involved persons with current depression.
Results: Twenty observational (cross-sectional and prospective) studies and 10 randomized trials (nine were randomized placebo-controlled trials [RCTs]; one was a randomized blinded comparison trial) were reviewed. Inverse associations of vitamin D blood level or vitamin D intake with depression were found in 13 observational studies; three identified prospective relations. Results from all but one of the RCTs showed no statistically significant differences in depression outcomes between vitamin D and placebo groups.
Limitations: Observational studies were mostly cross-sectional and frequently lacked adequate control of confounding. RCTs often featured low treatment doses, suboptimal post-intervention changes in biochemical levels of vitamin D, and/or short trial durations.
Conclusion: Vitamin D level-mood associations were observed in most, but not all, observational studies; results indicated that vitamin D deficiency may be a risk factor for late-life depression. However, additional data from well-designed RCTs are required to determine the impact of vitamin D in late-life depression prevention.

Contents

* Corresponding author at: Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, United States.
E-mail address: ookereke@partners.org (O.I. Okereke).

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1. Background

1.1. PART 1: overview

1.1.1. The problem of late-life depression and the need to identify risk factors and prevention strategies

Depression is the leading cause of disease burden in developed regions, responsible for between 5% and 8% of the total disability-adjusted life years (DALYs) in countries considered to be middle- or high-income (WHO, 2008). In the United States, the burden of depression in late-life is expected to increase, as the proportion of the population aged over 65 years continues to rise rapidly (Djernes, 2006; Mathers and Loncar, 2006). It is estimated that major depressive disorder (MDD) currently affects approximately 2% of older adults living in the community and 6.5–9% of elderly patients of primary care clinics (Beekman et al., 1999; Katon et al., 2003; Steffens et al., 2009). Clinically relevant depressive symptoms are even more common among older adults than MDD *per se*: between 8% and 20% of older adults in the community, and it has been estimated that over 30% of those seen in primary care settings, suffer from clinically relevant depressive symptoms (i.e., this may include minor depression, major depression or dysthymia) (Steinman et al., 2007). Despite its high prevalence, however, depression among older adults tends to be under-recognized and under-treated (Mulsant and Ganguli, 1999; Steinman et al., 2007; Unützer et al., 2000). Importantly, although the incidence of depression and/or clinically relevant depressive symptoms is lower in older adults than in young and middle-aged persons, these observed rates (about 20–25 cases/1,000 person-years) (Luijendijk et al., 2008; Norton et al., 2006; Paĺsson et al., 2001) are comparable to those of other major illnesses among older adults – such as cardiovascular disease (Ridker et al., 2005) and breast cancer (Cook et al., 2005).

Costs of depression include both direct medical costs and indirect costs resulting from reduced productivity (Greenberg et al., 2003). Depressive symptoms have been linked to impaired daily functioning (Beekman et al., 2002), an outcome that can translate into diminished work productivity among younger adults and still-working older adults alike. However, there are important ways in which costs of depression can become exaggerated among older compared to younger adults. First, adult caregivers of older adults with depression often experience high levels of caregiver burden and psychological distress (Martire et al., 2010; Scazufca et al., 2002), which may result in lost productivity among stressed carers – potentially further contributing to workplace-related costs. Second, as a large proportion of older adults are retired from work, healthcare costs make up much of the economic burden of late-life depression (Greenberg et al., 2003; Romeo et al., 2011). In addition to having a role in increasing disability and reducing overall well-being and quality of life, depression is associated with considerable costs among older adults (Beekman et al., 2002; Katon et al., 2003). In a study (Katon et al., 2003) of approximately 9,000 elderly patients recruited from primary care clinics, outpatient costs were 43% to 52% higher among depressed versus non-depressed elderly patients, even after adjustment for medical comorbidities; the increased cost burden was observed broadly across health care, and only a small proportion of increased costs was specifically due to mental health or depression treatment. Notably, the authors did not find that there were costs differences among elderly patients with subthreshold depressive syndromes compared with those with DSM-IV-based depressive disorders – highlighting the importance for older persons of preventing occurrence of even milder depressive syndromes.

The development of strategies to prevent late-life depression is necessary to reduce its impact on disease burden and associated costs. If investigators are able to identify key risk factors for depression in older persons – especially those that are modifiable – then interventions can be targeted at high-risk groups, and a substantial amount of morbidity may be prevented (Okereke et al., 2013). Indeed, the combination of low recognition/under-treatment, high morbidity and disability burden, and high cost speaks strongly to an imperative for prevention of late-life depression (Reynolds, 2008).

1.1.2. Concepts of dietary/nutritional factors in depression risk

Given the strong need for late-life depression prevention, increasing attention has turned to readily addressable risk factors. Dietary modification may be a highly feasible means of intervention for reducing depression risk among older adults. The potential influence of diet on mood has emerged as a major research interest in recent years (Freeman, 2010; Soh et al., 2009). A number of potential diet-related risk factors for late-life depression have been identified: examples range from micronutrient intakes and/or deficiencies to adherence to certain dietary patterns (Bertone-Johnson et al., 2011; Rienks et al., 2013; Skarupski et al., 2010a, 2010b, 2013; Vashum et al., 2014). The use of nutritional supplements has been gaining popularity in recent years as a possible method of improving mood outcomes, although intervention studies that have involved vitamin supplementation to prevent and/or treat depression have had inconsistent results (Lavretsky, 2009). As few randomized placebo-controlled trials (RCTs) that examine the relationship between vitamin D treatment and depressive symptoms in older adults have been carried out to date, the impact of vitamin D on late-life depression prevention remains unclear. Thus, as described in this review, while biologic evidence and observational data are compelling, further clinical trial evidence is needed to confirm whether or not this link exists in older populations. We conclude this review by discussing key attributes that future clinical trials should possess in order to provide a highly informative picture of the role of vitamin D in late-life depression prevention.

1.2. PART 2: basics of vitamin D

1.2.1. Key concepts in vitamin D biology and relevance to late-life depression

Vitamin D refers to a group of closely related secosteroid hormones (Holick, 2007; Norman, 2008). Vitamin D is obtained as vitamin D2 or D3 from diet or supplements, or as D3 (cholecalciferol) from conversion of 7-dehydrocholesterol in the skin by ultraviolet B radiation (Holick, 2007; Norman, 2008), and is synthesized in the liver to 25-hydroxyvitamin D [25(OH)D], the major