*Supplementary Material*

**Supplementary Table 1:** **Search strategy**

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| --- | --- |
| Medline  | Result: Number of articles |
| Search strategy: Adult | Results: 169  |
| 1- Adult | n=5,635,715 |
| 2- Adult\* | n= 5,663,949 |
| 3- Young\*  | n=1,340,458 |
| 4- Old adult | n= 493,329  |
| 5- Geriatric | n=72,050 |
| 6- Elderly | n=244,543 |
| 7- 1 or 2 or 3 or 4 or 5 or 6  | n=6,165,535 |
| 8- Limit 7 (English and human and year of publication | n=5,589,271  |
| Search strategy: Depression synonyms |  |
| 9- Depression  | n=385,522 |
| 10- Depression\* | n=385,632 |
| 11- Depress\* | n=520,312 |
| 12- Mood Disorder\* | n=53,143 |
| 13- Dysthymi\* | n=3,533 |
| 15- Depression symptoms  | n=103,746 |
| 14- Adjustment Disorder\* | n= 34,265 |
| 16- Affective Symptoms | n=24,389 |
| 17-8 or 9 or 10 or 11 or 12 or 13 or 14 | n=581,311 |
| 18- Limit 15 (English and human and year of publication  | n=365,802 |
| Search strategy: Vitamin D supplementation |  |
| 19- Vitamin D supplement | n=11,414 |
| 20- Vitamin D | n= 80,737 |
| 21- Vitamin D2 | n=2,132 |
| 22- Vitamin D3\*  | n=988 |
| 23- 1-alpha-hydroxy-vitamin D3  | n=51 |
| 24- 1,25 dihydroxyvitamin D3 | n=6,481 |
| 25- 1,25-dihydroxycholecalciferol | n=1,173 |
| 26- 25 hydroxyvitamin D | n=15,583 |
| 26- Ergocalciferol | n=726 |
| 27- Cholecalciferol | n=8,362 |
| 28- 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 | n=85,696 |
| 29- Limit 27 (English and human and year of publication | n=52,700 |
| Search strategy: Randomized controlled trials |  |
| 30- Clinical trial\* | n=658,649 |
| 31- Trial | n-1,130,713 |
| 32- Intervention | n=897,512 |
| 33- RCT | n=20,849 |
| 34- Placebo  | n=1 |
| 35- Randomized controlled trials  | n=372,163 |
| 36- 30 or 31 or 32 or 33 or 34 or 35 | n=1,858,249 |
| 37- Limit 34 (English and year OF publication | n=1,376,544 |
| **38 – search # 7 AND 16 AND 16 AND 28 AND 35** | **n=169** |
|  |
| PubMed | Result: Number of articles (n=320)  |
|  |  |
| Search strategy: Search adult |  |
| 1- Adult | n=7418591  |
| 2- Adult\* | n=6964852  |
| 3- Young\* | n=648694  |
| 4- Old adult | n=483838 |
| 5- Geriatric\* | n=29575 |
| 6- Elderly | n=238345  |
| 7- 1 or 2 or 3 or 4 or 5 or 6 | n=7781788  |
| 8- Limit 7 (human) | n=7275420  |
|  |  |
| Depression synonyms  |  |
| 9- Depression\*  | n=63473  |
| 10- Depress\* | n=169116  |
| 11- Mood Disorder\* | n=59150 |
| 13- Depression symptoms  | n=3907  |
| 14- Adjustment Disorder\* | n=840 |
| 15- Affective Symptoms | n=4696  |
| 16- Limit (human) 9 or 10 or 11 or 12 or 13 or 14 or 15 | n=189785  |
|  |  |
| Search for: Vitamin D supplement |  |
| 17- Vitamin D supplement | n=258  |
| 18- Vitamin D\* | n=19811  |
| 19- Vitamin D2\* | n=208 |
| 20- 1,25 dihydroxyvitamin D3 | n=481  |
| 21- 1,25-dihydroxycholecalciferol | n=2565  |
| 22- 25 hydroxyvitamin D | n=6713  |
| 23- Ergocalciferol | n=905  |
| 24- Cholecalciferol | n=918  |
| 25- 17 or 18 or 20 or 21 or 22 or 23 or 34 limits (female and male and human) | n=20786  |
|  |  |
| Search strategy: Randomized controlled trials | Results  |
| 26- Randomized controlled trials | n=13432  |
| 27- Trial | n=270086  |
| 28- Intervention | n=151119 |
| 29- RCT | n=7935  |
| 30- 26 OR 27 OR 28 OR 29 limits (Humans; Female; Male | n=379251  |
| **31- search # 8 AND 16 AND 25 AND 30 (Publication dating from 1999/01/01 to 2019/12/31; Humans and female and male)** | **n=320**  |
| Searching in Ovid | Results: Number of articles (n=28) |
|  |  |
| Search strategy: Adult |  |
| 1- Adult\* |  |
| 2- Young\*  |  |
| 3- Elderly |  |
| 4- 1 or 2 or 3 |  |
| Search strategy: Depression  |  |
| 5- Depression\* |  |
| 6- Depress\* |  |
| 7- 5 or 6 |  |
| Search strategy: Vitamin D supplement |  |
| 8- Vitamin D supplement |  |
| 9- RCT |  |
| 10- 4 and 7 and 8 and 9 | Results: Number of articles (n=28)  |
|  |  |
| Search strategy: Searching in Cochrane  | Results: Number of articles (n=182)  |
|  |  |
| Search strategy: Adult |  |
| 1- Adult |  |
| 2- Adult\* |  |
| 3- Young\* |  |
| 4- Old adult |  |
| 5- Geriatrics |  |
| 6- Elderly |  |
| 7- 1 or 2 or 3 or 4 or 5 or 6 |  |
|  |  |
| Search strategy: Depression  |  |
|  |  |
| 8- Depression  |  |
| 9- Depress\* |  |
| 10- Mood disorder |  |
| 11- Dysthymi\* |  |
| 12- Adjustment Disorder\* |  |
| 13- Affective Symptoms |  |
| 14- 8 or 9 or 10 or 11 or 12 or 13  |  |
|  |  |
| Search strategy: Vitamin D supplement |  |
|  |  |
| 15- Vitamin D |  |
| 16- Ergocalciferol  |  |
| 17- Cholecalciferol  |  |
| 18- 1,25 dihydroxyvitamin D3 |  |
| 19- Calcitriol |  |
| 20- 25 hydroxyvitamin D |  |
| 21- 15 or 16 or 17 or 18 or 19 or 20  |  |
|  |  |
| Search strategy: Randomized controlled trials |  |
|  |  |
| 22- Randomized controlled trials |  |
| 23- Clinical trial\* |  |
| 24- Trial |  |
| 25- Intervention  |  |
| 26- RCT |  |
| 27- Placebo |  |
| 28- 22 or 23 or 24 or 25 or 26 or 27 |  |
| 29- search # 7 AND 14 AND 21 AND 28 | n=182 |
| Science Direct Database  |  |
| Adult and depression and vitamin D | n=581 results |

**Supplementary Table 2: List of excluded studies (n=8) that presented medians**

|  |  |
| --- | --- |
| **Study** |  **Reason for Exclusion** |
| Jorde [20] 2008 | Reported median rather than mean. Mean is one of the measures of central tendency that can be used to combine studies via meta-analysis to produce a summary estimate, and not the median. Thus, the study could not be added to the meta-analysis |
| Mousa [23] 2018 | Reported median rather than mean. Mean is one of the measures of central tendency that can be used to combine studies via meta-analysis to produce a summary estimate, and not the median. Thus, the study could not be added to the meta-analysis |
| Kjaegaard [24] 2014 | Reported median rather than mean. Mean is one of the measures of central tendency that can be used to combine studies via meta-analysis to produce a summary estimate, and not the median. Thus, the study could not be added to the meta-analysis |
| De Koning [52] 2019 | Reported median rather than mean. Mean is one of the measures of central tendency that can be used to combine studies via meta-analysis to produce a summary estimate, and not the median. Thus, the study could not be added to the meta-analysis |
| Dumville [[53] 2006 | Only provided one mean value (baseline value) for the control and intervention group. As such, the difference in means could not be computed for before and after vitamin D administration. Thus, the study was excluded from the meta-analysis |
| Jorde [54] 2018 | Reported median rather than mean. Mean is one of the measures of central tendency that can be used to combine studies via meta-analysis to produce a summary estimate, and not the median. Thus, the study could not be added to the meta-analysis |
| Lansdowne [55] 1998 | Only provided one mean value (final value) for the control and intervention group. As such, the difference in means could not be computed for before and after vitamin D administration. Thus, the study was excluded from the meta-analysis |
| Sanders [56] 2011 | Both studies by Sanders were excluded, as they did not provide the means for the control group. Therefore, they could not be added to the meta-analysis to calculate a summary estimate |

**Supplementary Table 3: Characteristics of excluded trials (*n*=36)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author, Year** | **Title** | **Objective** | **Exclusion Reason** | **Comment** |
| **Sharifi, A. [21] 2019** | Vitamin D decreases the Beck Depression Inventory (BDI) score in patients with mild to moderate ulcerative colitis | To assess the effect of vitamin D on the BDI score in ulcerative colitis patients. | Population | Population group included ulcerative colitis patients to assess the effect of vitamin D on their BDI scores. These patients were assigned to receive a single injection of 300,000 IU vitamin D3 or 1 ml normal saline as a placebo.  |
| **Alavi, N.M. [39] 2018** | Effect of vitamin D supplementation on depression in elderly patients: A randomized clinical trial | To investigate the effect of vitamin D supplementation on the severity of depression in an elderly population. | Population  | Included patients aged over 60 years who were under treatment for depression. |
| **Yalamanchili, V. [44] 2018** | Randomized, controlled clinical trial | To examine the effect of one year of treatment with several doses of vitamin D on the Geriatric Depression Score (GDS) in older Caucasian and African American women. | Control group | Both studies by Yalamanchili were excluded, as they either did not have a control group (only using an intervention group), or did not provide a mean in their paper for the control group, making it impossible to add these to the meta-analysis. |
| **Aucoin, M. [57] 2018** | Adjunctive vitamin D in the treatment of non-remitted depression: Lessons from a failed clinical trial | To complete a randomized, controlled trial (RCT) using vitamin D as an adjunctive therapy in patients with non-remitted depression to see if any relief of depression will occur. |  Sample size  | The sample size of enrolled participants (7/125, 5.6%) lacks power to conduct a full assessment of findings. |
| **Tartagni, M. [58] 2016**  | Vitamin D supplementation for premenstrual syndrome-related mood disorders in adolescents with severe hypovitaminosis D | To assess whether administration of vitamin D (200,000 IU at first, followed by 25,000 IU every 2 weeks) for a 4-month period will lessen the appearance and intensity of mood disorders associated with PMS in young girls with severe hypovitaminosis D. | Population  | The sample size included 158 young girls (15-21 years old). |

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| **Ghaderi, A. [59] 2017** | Clinical trial of the effects of vitamin D supplementation on psychological symptoms and metabolic profiles in maintenance methadone treatment patients | To determine the effect of vitamin D supplementation on psychological symptoms and metabolic profiles in MMT patients. | Population | Patients used methadone treatment. Methadone is an opioid. |
| **Stein, M.S. [60] 2011** | A randomized controlled trial of high-dose vitamin D2 followed by intranasal insulin in Alzheimer's disease | To examine the effect of high-dosage vitamin D, followed by nasal insulin, on memory and disability in mild-moderate AD. | Population & outcome | Primary outcome measures were Alzheimer's disease assessment scale-cognitive subscale (ADAS-cog) and Disability Assessment in Dementia. |
| **Jalali-Chimeh, F**. **[61] 2019** | Effect of vitamin D therapy on sexual function in women with sexual dysfunction and vitamin D deficiency | To investigate the effect of vitamin D therapy on sexual function in women with low vitamin D levels and sexual dysfunction. | Outcome  | Primary outcome investigated the effect of vitamin D therapy on sexual function.  |
| **Kenny, A.M. [62] 2003**  | Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men | To study the effects of vitamin D supplementation in healthy male populations. | Outcome  | Depression scale not used in this trial. |
| **Kopp, B.T. [63] 2016** | Pilot trial of light therapy for depression in hospitalized patients with cystic fibrosis | To examine bright-light therapy during hospitalisation, in order to ascertain whether it augments anti-depressant regimens and reduces length of stay (LOS) in depressed non-CF patients. | Study design & intervention  | Pilot trial and participants not taking vitamin D supplement.  |
| **Williams, J.A. [64] 2016**  | Vitamin D levels and perinatal depressive symptoms in women at risk: A secondary analysis of the mothers, omega 3, and mental health study | To evaluate whether low maternal vitamin D levels are associated with depressive symptoms in pregnancy. | Intervention & population  | Participant not taking vitamin D supplement. Study included pregnant women.  |

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| **Vafa, M. [41] 2019** | Comparing the effectiveness of vitamin D plus iron vs vitamin D on depression scores in anemic females: Randomized triple-masked trial | To evaluate the effects of iron-vitamin D co-supplementation versus vitamin D alone on depression scores in anaemic females with low levels of serum 25-hydroxyvitamin D. | Intervention  | A combination of vitamin D3, with iron.  |
| **Bahrami, A. [65] 2018** | High dose vitamin D supplementation is associated with a reduction in depression score among adolescent girls: A nine-week follow-up study | To evaluate the effectiveness of high-dose vitamin D supplementation on depression and aggression scores in adolescent girls. | Population  | Participants not meeting inclusion criteria age <18 years old.  |
| **Hogie-Lorenzen, T.L. [66] 2003** | The relationship between depression levels and vitamin D status among older adults in eastern South Dakota | To indicate that depressive behaviours are related to a drop in an individual's vitamin D status, as measured from serum 25-hydroxyvitamin D (25[OH]D) concentrations. | Intervention | Individuals randomized to receive Vitamin-D fortified cheese. Intervention not vitamin D supplement.  |
| **Belcaro, G. [67] 2010** | MF Afragil(R) in the treatment of 34 menopause symptoms: A pilot study | To determine the effects of a combination of calcium, vitamin D3, lycopene, astaxantin and citrus bioflavonoid in reducing symptoms of climacteric status. | Intervention  | A combination of vitamin D3, with calcium, lycopene, astaxantin and Citrus bioflavonoid (MF Afragil[R]). |
| **Khoraminya, N. [68] 2013** | Therapeutic effects of vitamin D as an adjunctive therapy to fluoxetine in patients with major depressive disorder | To compare the therapeutic effects of vitamin D3 plus fluoxetine and fluoxetine alone in patients with major depressive disorder. | Intervention & population  | Intervention (vitamin D3) combined with an anti-depressant. Study also involved depressed participants taking fluoxetine (anti-depressant). |
| **Hogberg, G. [69] 2012** | Depressed adolescents in a case-series were low in vitamin D and depression was ameliorated by vitamin D supplementation | To find the relationship between depression in adolescents and vitamin D. | Population | Study population consisted of depressed adolescent aged 10-19 years (mean age: 16, SD 1.8).  |

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| --- | --- | --- | --- | --- |
| **Gloth, F.M. [70] 1999** | Vitamin D vs. broad spectrum phototherapy in the treatment of seasonal affective disorder (SAD) | To examine the correlation between vitamin D deficiency and SAD. | Intervention | Comparator subjects received phototherapy. Trial was conducted in a group of 15 subjects with SAD. Eight subjects received 100,000 IU of vitamin D and seven subjects received phototherapy. |
| **Focker, M., et al. [71] 2018** | Effect of vitamin D deficiency on depressive symptoms in children and adolescent psychiatric patients - a randomized controlled trial: Study protocol | To investigate the effect of vitamin D deficiency on inpatient psychiatric treatment of depressive symptoms in children and adolescents. | Population  | The population of this trial comprised psychiatric patients (children and adolescents). |
| **Okereke, O.I. [72] 2018** | Vitamin D and omega-3 trial depression endpoint prevention (VITAL-DEP) | To determine effects on the prevention of depression and on the trajectory of mood symptoms in long-term supplementation with vitamin D and marine omega-3 fatty-acids.  | Intervention | Vitamin D supplementation (vitamin D3 2000IU/day) combined with marine omega-3 fatty-acids (eicosapentaenoic acid + docosahexaenoic acid, 1g/day), in a 2x2 factorial design. |
| **Raygan, F. [73] 2018** | The effects of vitamin D and probiotic co-supplementation on mental health parameters and metabolic status in type 2 diabetic patients with coronary heart disease | To evaluate the effects of vitamin D and probiotic co-supplementation on mental health parameters and metabolic status in diabetic patients with coronary heart disease (CHD).  | Intervention | Vitamin D combined with probiotic co-supplementation. |
| **Stokes, C.S. [74] 2016** | Vitamin D supplementation reduces depressive symptoms in patients with chronic liver disease (CLD) | To investigate whether vitamin D replacement ameliorates depressive symptoms in CLD patients. | Population | Patients with CLD were assessed for vitamin D deficiency and depressive symptoms. |
| **Zanetidou, S. [75] 2011** | Vitamin D supplements in geriatric major depression | To evaluate the safety and efficacy of vitamin D supplementation among older patients with major depression. | Intervention and study design  | Non-randomized trial. Vitamin D was additionally given to the routine anti-depressant study group.  |
| **Vaziri, F. [76] 2016** | A randomized controlled trial of vitamin D supplementation on perinatal depression: In Iranian pregnant mothers | To evaluate the effect of vitamin D3 supplementation on perinatal depression scores. | Population | Effect of vitamin D supplementation on depressive symptoms in pregnant women was examined. |
| **Yalamanchili, V. [77] 2012** | Treatment with hormone therapy and calcitriol did not affect depression in older postmenopausal women | To examine the effect of hormone therapy and calcitriol on depression in elderly postmenopausal women and to determine whether the response was associated with polymorphisms of estrogen receptor-alpha and vitamin D receptors. | Intervention | Intervention of calcitriol combined with hormone therapy. |
| **Shipowick, C.D. [[78] 2009** | Vitamin D and depressive symptoms in women during the winter: A pilot study | To indicate that vitamin D supplementation may decrease depressive symptoms during the winter months. | Study design and population  | A pilot study and study group consisting of children and adolescents.  |
| **Wang, Y. [79] 2016** | Efficacy of high-dose supplementation with oral vitamin D3 on depressive symptoms in dialysis patients with vitamin D3 insufficiency | To evaluate whether high-dose vitamin D3 (VD3) supplementation has beneficial effects on depressive symptoms in dialysis patients. | Population | Study population consisted of dialysis patients.  |
| **Zhang, M. [80] 2011** | Vitamin C provision improves mood in acutely hospitalized patients | To investigate the effect of deficiencies of vitamin C and D in acute hospitalized patients. | Intervention  | Vitamin D supplement combined with vitamin C. |
| **Ostadmohammadi, V. [81] 2019** | Vitamin D and probiotic co-supplementation affects mental health, hormonal, inflammatory and oxidative stress parameters in women with polycystic ovary syndrome (PCOS) | To determine the effect of vitamin D and probiotic co‐administration on mental health, hormonal, inflammatory and oxidative stress parameters in women with PCOS. | Intervention  | Vitamin D combined with probiotic co-supplementation. |

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| **Penckofer, S. [82] 2017** | Vitamin D supplementation improves mood in women with type 2 diabetes (T2DM) | To determine the effect of vitamin D supplementation on improving mood (depression and anxiety) and health status (mental and physical) in women with T2DM. | Population  | No control groups; all participants take vitamin D supplements.  |
| **Harris, S. [83] 1993** | Seasonal mood changes in 250 normal women | To examine the effects of supplementation with vitamin D on overall and seasonal rates of bone loss. | Population  | No control groups; all participants take vitamin D supplements. |
| **Marsh, W.K. [84] 2017** | Vitamin D supplementation in bipolar depression: A double-blind placebo-controlled trial | To examine the efficiency of vitamin D in reducing bipolar depression symptoms. | Population  | Included patients under treatment for depression. |
| **Rolf, L. [85] 2017** | Vitamin D3 supplementation in multiple sclerosis (MS): Symptoms and biomarkers of depression | Vitamin D3 supplementation reduces depressive symptoms in MS via its immunomodulatory properties. | Study design  | A pilot study.  |
| **Sepehrmanesh, Z. [86] 2016** | Vitamin D supplementation affects BDI, insulin resistance, and biomarkers of oxidative stress in patients with major depressive disorder: A randomized, controlled clinical trial | To assess whether vitamin D supplementation can reduce symptoms of depression, metabolic profiles, serum high-sensitivity C-reactive protein (hs-CRP), and biomarkers of oxidative stress in patients with major depressive disorder (MDD). | Outcome and population | **1 – Primary** **outcome:** BDI for depressive symptoms and **secondary outcome:** Glucose homeostasis variables, lipid profiles, hs-CRP, and biomarkers of oxidative stress outcomes assessed.**2 – Population** on psychiatry medication. |
| **Vieth, R. [87] 2004** | Randomized, controlled clinical trial | To compare the effects of these doses on biochemical responses and the sense of well-being. | Control group | Both studies by Vieth were excluded from the meta-analysis, as these only used an intervention group, with no control group for comparison. |

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| --- | --- | --- | --- | --- |
| **Rajabi-Naeeni, et al.** **[88] 2019**  |  2 × 2 factorial, triple-blind, randomized, placebo-controlled, clinical trial | To determine the effects of these two supplements on fasting blood sugar, other cardio-metabolic risk factors, and psychological distress in reproductive-aged women with prediabetes and hypovitaminosis D. | Intervention | Vitamin D combined with omega 3 supplementation. |

*Supplementary Figure Legends*

**Supplementary Figure 1:** Funnel plots of publication bias for vitamin D supplementation and depressive symptoms. The blue dots represent the studies; the solid vertical line represents the log odds ratio for the pooled estimate obtained from the meta-analysis, and the dashed diagonal lines represent the 95% confidence limits around the pooled estimate

**Supplementary Figure 1**

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