

HOSPITAL DE CLÍNICAS DE PORTO ALEGRE
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PROGRAMA DE RESIDÊNCIA MÉDICA EM PSIQUIATRIA

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**Suplementação de micronutrientes pode ser uma alternativa para
um melhor tratamento de depressão e ansiedade no SUS?
Uma revisão sistemática dos casos do magnésio e do zinco**

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Orientador:
Dr. Marco Antonio Caldieraro

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1. Depressão. 2. Ansiedade. 3. Micronutrientes. 4. Magnésio. 5. Zinco. I. Caldieraro, Marco Antonio, orient. II. Título.

RESUMO

INTRODUÇÃO: A depressão e a ansiedade causam um importante impacto na vida dos indivíduos diagnosticados e na população como um todo, e a proporção de casos refratários aos tratamentos disponíveis demanda novos tratamentos eficazes. O aumento das publicações sobre micronutrientes, principalmente o magnésio e o zinco, como potenciais tratamentos para essas condições, chama atenção por serem substâncias de fácil acesso, baixo custo e bom perfil de segurança e tolerabilidade.

OBJETIVOS: Neste estudo, desejamos averiguar na literatura quais as evidências de eficácia do magnésio, para tratamento de depressão e ansiedade (diagnóstico e/ou sintoma), e do zinco, para tratamento de ansiedade (diagnóstico e/ou sintoma). Foi optado por não pesquisar as evidências do Zn para tratamento de depressão em função de já haverem revisões recentes de boa qualidade que se prestam à discussão proposta por este estudo.

MÉTODOS: Foi conduzida uma revisão sistemática em cinco bases de dados, acerca do magnésio para tratamento de depressão e ansiedade, e do zinco para tratamento de ansiedade, sem restrição de data ou idioma.

RESULTADOS: Foram encontrados um total de 16.877 registros, dos quais foram selecionados 45 artigos: 8 ECR que estudam suplementação de Mg em indivíduos com diagnóstico de depressão, dos quais 2 apresentaram direção de evidência positiva acompanhada de boa qualidade de evidência e os demais 6 apresentam direções de evidência positivas, negativas ou pouco claras, e baixa qualidade de evidência; um ECR que estuda suplementação de Mg em indivíduos com diagnóstico de ansiedade, cuja direção da evidência é pouco clara; 26 ECR em indivíduos com sintomas de ansiedade e/ou depressão secundários a outras circunstâncias, dos quais 4 apresentaram direção de evidência positiva acompanhada de boa qualidade de evidência. Foram encontrados 2 ECR que estudam suplementação de zinco em indivíduos com diagnóstico de ansiedade, ambos com direção de evidência positiva, mas avaliados como estudos com baixa qualidade de evidência; e 3 ECR em indivíduos com sintomas de ansiedade secundários a outras circunstâncias que apontaram direção de evidência positiva, os três com boa qualidade de evidência.

CONCLUSÃO: Revisões anteriores sugerem que o zinco poderia ser uma boa alternativa como tratamento à depressão, em associação ao tratamento tradicional. Dois novos ECR encontrados por esta revisão sistemática apontam que magnésio também poderia ser uma opção. Urgem mais ensaios clínicos de boa qualidade metodológica que analisem a suplementação de zinco e magnésio em depressão e ansiedade, e mais especificamente na nossa população de pacientes do SUS, uma vez que seriam

especificamente na nossa população de pacientes do SUS, uma vez que seriam tratamentos suplementares com um bom perfil de tolerância e segurança, fácil acesso e uso, e baixo custo.

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BIBLIOGRAFIA

1. World Health Organization. Depression [Internet]. 2022 [cited 2022 Nov 1]. Available from: <https://www.who.int/news-room/fact-sheets/detail/depression>
2. Rush JA, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report. *Am J Psychiatry* [Internet]. 2006;163(11):1905–17. Available from: <http://ajp.psychiatryonline.org.proxy.hsl.ucdenver.edu/doi/pdf/10.1176/ajp.2006.163.11.1905>
3. Malhi GS, Mann JJ. Depression. *Lancet*. 2018;392(10161):2299–312.
4. American Psychological Association. Clinical practice guideline for the treatment of depression across three age cohorts. 2019;(February). Available from: <https://www.apa.org/depression-guideline>
5. Wang J, Um P, Dickerman BA, Liu J. Zinc, magnesium, selenium and depression: A review of the evidence, potential mechanisms and implications. *Nutrients*. 2018;10(5):1–19.
6. Schefft C, Kilarski LL, Bschor T, Köhler S. Efficacy of adding nutritional supplements in unipolar depression: A systematic review and meta-analysis. *Eur Neuropsychopharmacol*. 2017;27(11):1090–109.
7. Yosae S, Clark CCT, Keshtkaran Z, Ashourpour M, Keshani P, Soltani S. Zinc in depression: From development to treatment: A comparative/ dose response meta-analysis of observational studies and randomized controlled trials. *Gen Hosp Psychiatry* [Internet]. 2020;74(January):110–7. Available from: <https://doi.org/10.1016/j.genhosppsych.2020.08.001>
8. Da Silva LEM, De Santana MLP, Costa PRDF, Pereira EM, Nepomuceno CMM, Queiroz VADO, et al. Zinc supplementation combined with antidepressant drugs for treatment of patients with depression: A systematic review and meta-analysis. *Nutr Rev*. 2020;0:1–12.
9. World Health Organization. Micronutrients [Internet]. [cited 2022 Sep 10]. Available from: <https://www.who.int/health-topics/micronutrients>
10. Aliasgharpour Mehri. Trace Elements in Human Nutrition (II) – An Update. *Int J Prev Med*. 2020;
11. Kraemer K, Badham J, Parul C, Jee Hyun R. Micronutrients, Macro Impact: The story of vitamins and a hungry world. *Sight Life* [Internet]. 2012;8–146. Available from: <http://www.sightandlife.org/library.html>

12. International Food Policy Research Institute, Concern Worldwide, Welthungerhilfe. Global Hunger Index - The Challenge of Hidden Hunger. FIEP Bull On-line [Internet]. 2014;80(0):1–56. Available from: https://www.ifpri.org/sites/default/files/ghi/2014/feature_1818.html
13. Pochwat B, Szewczyk B, Sowa-Kucma M, Siwek A, Doboszewska U, Piekoszewski W, et al. Antidepressant-like activity of magnesium in the chronic mild stress model in rats: Alterations in the NMDA receptor subunits. *Int J Neuropsychopharmacol.* 2014;17(3):393–405.
14. Levenson CW. Zinc: The new antidepressant? *Nutr Rev.* 2006;64(1):39–42.
15. Vink R, Nechifor M. Magnesium in the Central Nervous System. University of Adelaide Press; 2011.
16. King DE, Mainous AG, Geesey ME, Woolson RF. Dietary Magnesium and C-reactive Protein Levels. *J Am Coll Nutr.* 2005;24(3):166–71.
17. Leonard B, Maes M. Mechanistic explanations how cell-mediated immune activation, inflammation and oxidative and nitrosative stress pathways and their sequels and concomitants play a role in the pathophysiology of unipolar depression. *Neurosci Biobehav Rev [Internet].* 2012;36(2):764–85. Available from: <http://dx.doi.org/10.1016/j.neubiorev.2011.12.005>
18. Mocchegiani E, Costarelli L, Giacconi R, Malavolta M, Basso A, Piacenza F, et al. Micronutrient – gene interactions related to inflammatory / immune response and antioxidant activity in ageing and inflammation . A systematic review. *Mech Ageing Dev [Internet].* 2014; Available from: <http://dx.doi.org/10.1016/j.mad.2013.12.007>
19. Młyniec K, Davies CL, De Agüero Sánchez IG, Pytka K, Budziszewska B, Nowak G. Essential elements in depression and anxiety. Part I. *Pharmacol Reports.* 2014;66(4):534–44.
20. Boyle NB, Lawton C, Dye L. The effects of magnesium supplementation on subjective anxiety and stress - a systematic review. *Nutrients.* 2017;9(5).
21. Schiopu C, Ștefănescu G, Diaconescu S, Bălan GG, Gimiga N, Rusu E, et al. Magnesium Orotate and the Microbiome–Gut–Brain Axis Modulation: New Approaches in Psychological Comorbidities of Gastrointestinal Functional Disorders. *Nutrients.* 2022;14(8).
22. de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: Implications for health and disease. *Physiol Rev.* 2015;95(1):1–46.
23. Szewczyk B. Antidepressant activity of zinc and magnesium in view of the current hypotheses of antidepressant action. *Pharmacol Reports.* 2008;60:588–99.
24. Olza J, Aranceta-bartrina J, Gonz M, Ortega RM. Reported Dietary Intake, Disparity between the Reported Consumption and the Level Needed for Adequacy and Food Sources of Calcium, Phosphorus, Magnesium and Vitamin D in the Spanish Population: Findings from the ANIBES Study. *Nutrients.* 2017;168:1–17.
25. Jähnen-dechent W, Ketteler M. Magnesium basics. *Clin Kidney J.* 2012;5(1):i3–14.
26. Murck H. Magnesium and affective disorders. *Nutr Neurosci.* 2002;5(6):375–89.
27. Elin RJ. Magnesium: The fifth but forgotten electrolyte. *Am J Clin Pathol.* 1994;102(5):616–22.
28. Shayganfar M. Are Essential Trace Elements Effective in Modulation of Mental Disorders? Update and Perspectives. *Biol Trace Elem Res.* 2021;1032–59.
29. Volpe SL. Magnesium in disease prevention and overall health. *Adv Nutr.* 2013;4(3):378–83.
30. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and Human Health: Perspectives and Research Directions. *Int J Endocrinol.* 2018;2018.
31. Departamento de Informática em Saúde, Escola Paulista de Medicina. Tabela de

- Composição Química dos Alimentos [Internet]. [cited 2022 Nov 1]. Available from: <https://tabnut.dis.epm.br/alimento>
- 32. <https://www.hsph.harvard.edu/nutritionsource/magnesium/> [Internet]. Available from: <https://www.hsph.harvard.edu/nutritionsource/magnesium/>
 - 33. Guyton, A.C. and Hall JE. Textbook of Medical Physiology. 11th Editi. Saunders E, editor. Amsterdam; 2006.
 - 34. A. S. Fauci, D. L. Kasper, D. L. Longo, E. Braunwald, S. L. Hauser JLJ and JL. Harrison's Internal Medicine. 17th editi. 2008.
 - 35. Lowe NM. The global challenge of hidden hunger: Perspectives from the field. *Proc Nutr Soc.* 2021;80(3):283–9.
 - 36. Seelig MS. Consequences of magnesium deficiency on the enhancement of stress reactions; Preventive and therapeutic implications (A review). *J Am Coll Nutr.* 1994;13(5):429–46.
 - 37. Takeda A. Zinc signaling in the hippocampus and its relation to pathogenesis of depression. *Mol Neurobiol.* 2011;44(2):166–74.
 - 38. Zheltova AA, Kharitonova M V., Iezhitsa IN, Spasov AA. Magnesium deficiency and oxidative stress: An update. *Biomed.* 2016;6(4):8–14.
 - 39. Libigerova E. Changes in visual evoked potentials after magnesium in anxiety disorders. Cambridge Univ Press. 2002;
 - 40. Barragán-Rodríguez L, Rodríguez-Morán M, Guerrero-Romero F. Efficacy and safety of oral magnesium supplementation in the treatment of depression in the elderly with type 2 diabetes: A randomized, equivalent trial. *Magnes Res.* 2008;21(4):218–23.
 - 41. Bambling M, Parham SC, Coulson S, Vitetta L. S-adenosylmethionine (SAMe) and Magnesium Orotate as adjunctives to SSRIs in sub-optimal treatment response of depression in adults: A pilot study. *Adv Integr Med* [Internet]. 2015;2(1):56–62. Available from: <http://dx.doi.org/10.1016/j.aimed.2015.04.003>
 - 42. Rajizadeh A, Mozaffari-Khosravi H, Yassini-Ardakani M, Dehghani A. Effect of magnesium supplementation on depression status in depressed patients with magnesium deficiency: A randomized, double-blind, placebo-controlled trial. *Nutrition* [Internet]. 2017;35:56–60. Available from: <http://dx.doi.org/10.1016/j.nut.2016.10.014>
 - 43. Mehdi SMA, Atlas SE, Qadir S, Musselman D, Goldberg S, Woolger JM, et al. Double-blind, randomized crossover study of intravenous infusion of magnesium sulfate versus 5% dextrose on depressive symptoms in adults with treatment-resistant depression. *Psychiatry Clin Neurosci.* 2017;71(3):204–11.
 - 44. Tarleton EK, Littenberg B, MacLean CD, Kennedy AG, Daley C. Role of magnesium in the treatment of depression. *PLoS One* [Internet]. 2017;12(6 e0180067):1–15. Available from: <https://pubmed.ncbi.nlm.nih.gov/28654669/>
 - 45. Ryszewska-Pokraśniewicz B, Mach A, Skalski M, Januszko P, Wawrzyniak ZM, Poleszak E, et al. Effects of magnesium supplementation on unipolar depression: A placebo-controlled study and review of the importance of dosing and magnesium status in the therapeutic response. *Nutrients.* 2018;10(8):1–14.
 - 46. Abiri B, Sarbakhsh P, Vafa M. Randomized study of the effects of vitamin D and/or magnesium supplementation on mood, serum levels of BDNF, inflammation, and SIRT1 in obese women with mild to moderate depressive symptoms. *Nutr Neurosci* [Internet]. 2021;0(0):1–13. Available from: <https://doi.org/10.1080/1028415X.2021.1945859>
 - 47. Afsharfar M, Shahraki M, Shakiba M, Asbaghi O, Dashipour A. The effects of magnesium supplementation on serum level of brain derived neurotrophic factor (BDNF) and depression status in patients with depression. *Clin Nutr ESPEN* [Internet]. 2021;42:381–6. Available from: <https://doi.org/10.1016/j.clnesp.2020.12.022>

48. Chouinard G, Beauclair L, Geiser R, Etienne P. A pilot study of magnesium aspartate hydrochloride (Magnesiocard®) as a mood stabilizer for rapid cycling bipolar affective disorder patients. *Prog Neuropsychopharmacol Biol Psychiatry*. 1990;14(2):171–80.
49. Facchinetto F, Borella P, Sances G, Fioroni L, Nappi RE, Genazzani AR. Oral magnesium successfully relieves premenstrual mood changes. *Obstet Gynecol*. 1991;78(2):177–81.
50. Borrello G, Mastroroberto P, Curcio F, Chello M, Zofrea S, Mazza ML. The effect of magnesium oxide on mild essential hypertension and quality of life. *Curr Ther Res*. 1996;57(10):767–74.
51. Walker AF, De Souza MC, Marakis G, Robinson PA, Morris AP, Bolland KM. Unexpected benefit of sorbitol placebo in Mg intervention study of premenstrual symptoms: Implications for choice of placebo in RCTs. *Med Hypotheses*. 2002;58(3):213–20.
52. Phelan D, Molero P, Martínez-gonzález MA, Molendijk M. Magnesium and mood disorders : systematic review and meta-analysis. 2018;167–79.
53. Khine K, Rosenstein DL, Elin RJ, Niemela JE, Schmidt PJ, Rubinow DR. Magnesium (Mg) Retention and Mood Effects After Intravenous Mg Infusion in Premenstrual Dysphoric Disorder. *Biol Psychiatry [Internet]*. 2006;74(5):826–32. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3624763/pdf/nihms412728.pdf>
54. Quaranta S, Buscaglia MA, Meroni MG, Colombo E, Cella S. Pilot study of the efficacy and safety of a modified-release magnesium 250mg tablet (Sincromag®) for the treatment of premenstrual syndrome. *Clin Drug Investig*. 2007;27(1):51–8.
55. Poikolainen K, Alho H. Magnesium treatment in alcoholics: A randomized clinical trial. *Subst Abus Treat , Prev , Policy*. 2008;12:1–12.
56. BARWOOD N, WALKER S, SHANLEY T. Once-weekly encapsulated magnesium sulfate— an effective, new strategy for the management of chronic constipation. *J Gastroenterol Hepatol*. 2009;24(2).
57. Fathizadeh N, Ebrahimi E, Valiani M, Tavakoli N, Yar MH. Evaluating the effect of magnesium and magnesium plus vitamin B6 supplement on the severity of premenstrual syndrome. *Iran J Nurs Midwifery Res [Internet]*. 2010;15(Suppl 1):401–5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22069417%0Ahttp://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&term=PMC3208934>
58. Ebrahimi E, Khayati Motlagh S, Nemati S, Tavakoli Z. Effects of magnesium and vitamin b6 on the severity of premenstrual syndrome symptoms. *J caring Sci [Internet]*. 2012;1(4):183–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25276694%0Ahttp://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&term=PMC4161081>
59. Abbasi B, Kimiagar M, Shahidi S, Shirazi M, Sadeghniait K, Payab M, et al. Effect of Magnesium Supplementation on Mental Health in Elderly Subjects with Insomnia: A Double-blind Randomized Clinical Trial. *Iran J Psychiatry Clin Psychol*. 2013;19(1):9–19.
60. Bagis S, Karabiber M, As I, Tamer L, Erdogan C, Atalay A. Is magnesium citrate treatment effective on pain, clinical parameters and functional status in patients with fibromyalgia? *Rheumatol Int*. 2013;33(1):167–72.
61. Fischer SGL, Collins S, Boogaard S, Loer SA, Zuurmond WWA, Perez RSGM. Intravenous magnesium for chronic complex regional pain syndrome type 1 (CRPS-1). *Pain Med (United States)*. 2013;14(9):1388–99.
62. Gendle MH, Hara KPO. Oral Magnesium Supplementation and Test Anxiety in University Undergraduates. *J Artic Support Null Hypothesis [Internet]*. 2015;11(2):21–

31. Available from: <http://www.jasnh.com/pdf/Vol11-No2-article2.pdf>
63. Park H, Qin R, Smith TJ, Atherton PJ, Barton DL, Sturtz K, et al. North Central Cancer Treatment group N10C2 (Alliance): A double-blind placebo-controlled study of magnesium supplements to reduce menopausal hot flashes. *Menopause.* 2015;22(6):627–32.
64. Fard FE, Mirghafourvand M, Mohammad-Alizadeh Charandabi S, Farshbaf-Khalili A, Javadzadeh Y, Asgharian H. Effects of zinc and magnesium supplements on postpartum depression and anxiety: A randomized controlled clinical trial. *Women Heal.* 2017;57(9):1115–28.
65. Kovacevic G, Stevanovic D, Bogicevic D, Nikolic D, Ostojic S, Tadic BV, et al. A 6-month follow-up of disability, quality of life, and depressive and anxiety symptoms in pediatric migraine with magnesium prophylaxis. *Magnes Res.* 2017;30(4):133–41.
66. Maor NR, Alperin M, Shturman E, Khairaldeen H, Friedman M, Karkabi K, et al. Effect of magnesium oxide supplementation on nocturnal leg cramps: A randomized clinical trial. *JAMA Intern Med.* 2017;177(5):617–23.
67. Pouteau E, Kabir-Ahmadi M, Noah L, Mazur A, Dye L, Hellhammer J, et al. Superiority of magnesium and vitamin B6 over magnesium alone on severe stress in healthy adults with low magnesemia: A randomized, single-blind clinical trial. *Clin Nutr.* 2018;37:S289–90.
68. Skalski M, Mach A, Januszko P, Ryszewska-Pokraśniewicz B, Biernacka A, Nowak G, et al. Pharmaco-electroencephalography-based assessment of antidepressant drug efficacy—the use of magnesium ions in the treatment of depression. *J Clin Med.* 2021;10(14).
69. Jaripur M, Ghasemi-Tehrani H, Askari G, Gholizadeh-Moghaddam M, Clark CCT, Rouhani MH. The effects of magnesium supplementation on abnormal uterine bleeding, alopecia, quality of life, and acne in women with polycystic ovary syndrome: a randomized clinical trial. *Reprod Biol Endocrinol [Internet].* 2022;20(1):1–11. Available from: <https://doi.org/10.1186/s12958-022-00982-7>
70. Randomized FA, Macian N, Dual C, Voute M, Leray V, Courrent M, et al. Short-Term Magnesium Therapy Alleviates Moderate Stress in Clinical Trial. 2022;
71. Russo AJ. Decreased Zinc and Increased Copper in Individuals with Anxiety. *Nutr Metab Insights.* 2011;4:1–5.
72. Afzali A, Vakili Z, Goli S, Bagheri H, Mirhosseini S, Ebrahimi H. A Randomized Clinical Trial of the Effect of Zinc Supplement on Depression and Anxiety in the Elderly. *Open Public Health J.* 2021;14(1):537–44.
73. Katz R, C K, Hurley L, Glader J, Lett IF, Kellams-harrison KM. Zinc deficiency in anorexia nervosa. *J Adolesc Heal Care.* 1987;8(5):400–6.
74. Üçkardeş Y, Kültür SEÇ, Özmet EN, Ünal F, Yurdakök K. THE EFFECT OF ZINC SUPPLEMENTATION ON THE ANXIETY SYMPTOMS OF PRI- MARY SCHOOL CHILDREN FROM LOW SOCIOECONOMIC LEVEL. *Rev Saúde Ment Infant e Juv.* 2009;16(3):137–44.
75. Sawada T, Yokoi K. Effect of zinc supplementation on mood states in young women: A pilot study. *Eur J Clin Nutr [Internet].* 2010;64(3):331–3. Available from: <http://dx.doi.org/10.1038/ejcn.2009.158>
76. Verma DK, Das B, Khanra S. EFFECT OF ZINC SUPPLEMENTATION ON ANTIDEPRESSANT THERAPY AND SERUM ZINC LEVEL IN UNIPOLAR DEPRESSION: A DOUBLE-BLIND RANDOMIZED CONTROLLED STUDY. *Int J Sci Res.* 2020;9(2):28–32.
77. Ahmadi M, Khansary S, Parsapour H, Alizamir A, Pirdehghan A. The Effect of Zinc Supplementation on the Improvement of Premenstrual Symptoms in Female

- University Students: a Randomized Clinical Trial Study. *Biol Trace Elem Res.* 2022;(0123456789).
- 78. Ghosh S, Ghosh UK, Ghosh M, Rahman AS, Dewan ZF. Effect of Zinc Supplementation on Depression in Selective Serotonin Reuptake Inhibitors-Treated Major Depressive Disorder Patients. *KYAMC J.* 2022;13(1):18–23.
 - 79. Hamedifard Z, Farrokhan A, Reiner Ž, Bahmani F, Asemi Z, Ghotbi M, et al. The effects of combined magnesium and zinc supplementation on metabolic status in patients with type 2 diabetes mellitus and coronary heart disease. *Lipids Health Dis.* 2020;19(1):1–9.
 - 80. Bhudia SK, Cosgrove DM, Naugle RI, Rajeswaran J, Lam BK, Walton E, et al. Magnesium as a neuroprotectant in cardiac surgery: A randomized clinical trial. *J Thorac Cardiovasc Surg.* 2006;131(4).
 - 81. Murck H. Ketamine, magnesium and major depression - From pharmacology to pathophysiology and back. *J Psychiatr Res [Internet].* 2013;47(7):955–65. Available from: <http://dx.doi.org/10.1016/j.jpsychires.2013.02.015>
 - 82. Górska N, Cubała WJ, Słupski J, Gałuszko-Węgielnik M. Ketamine and magnesium common pathway of antidepressant action. *Magnes Res.* 2018;31(2):33–8.
 - 83. Cheungpasitporn W, Thongprayoon C, Mao MA, Srivali N, Ungprasert P, Varothai N, et al. Hypomagnesaemia linked to depression: A systematic review and meta-analysis. *Intern Med J.* 2015;45(4):436–40.
 - 84. Yary T, Lehto SM, Tolmunen T, Tuomainen TP, Kauhanen J, Voutilainen S, et al. Dietary magnesium intake and the incidence of depression: A 20-year follow-up study. *J Affect Disord [Internet].* 2016;193:94–8. Available from: <http://dx.doi.org/10.1016/j.jad.2015.12.056>
 - 85. Aucoin M, Lachance L, Naidoo U, Remy D, Shekdar T, Sayar N, et al. Diet and anxiety: A scoping review. *Nutrients.* 2021;13(12).
 - 86. Elin RJ. Magnesium Metabolism and Disease. *Disease-a-Month.* 1988;34(April):161–218.
 - 87. Sarris J, Ravindran A, Yatham LN, Marx W, Rucklidge JJ, McIntyre RS, et al. Clinician guidelines for the treatment of psychiatric disorders with nutraceuticals and phytoceuticals: The World Federation of Societies of Biological Psychiatry (WFSBP) and Canadian Network for Mood and Anxiety Treatments (CANMAT) Taskforce. *World J Biol Psychiatry [Internet].* 2022;0(0):1–32. Available from: <https://doi.org/10.1080/15622975.2021.2013041>

Anexo I

ESTRATÉGIAS

PubMed - 3262 resultados

(Anxiety/diet therapy[mh] OR Anxiety/drug therapy[mh] OR Anxiety/drug effects[mh] OR Anxiety Disorders/diet therapy[mh] OR Anxiety Disorders/drug therapy[mh] OR Mood Disorders/diet therapy[mh] OR Mood Disorders/drug therapy[mh] OR Stress, Psychological/drug effects[mh] OR Stress, Psychological/diet therapy[mh] OR Stress, Psychological/drug therapy[mh] OR Trauma and Stressor Related Disorders/diet therapy[mh] OR Trauma and Stressor Related Disorders/drug therapy[mh] OR Depression/drug effects[mh] OR Depression/drug therapy[mh] OR Depression/diet therapy[mh] OR Antidepressive Agents/therapeutic use[mh] OR Angst[tiab] OR Hypervigilan*[tiab] OR Nervousness[tiab] OR Anxiet*[tiab] OR Anxious*[tiab] OR Agoraphobi*[tiab] OR Panic[tiab] OR Phobi*[tiab] OR Claustrophobi*[tiab] OR Obsessive-Compulsive[tiab] OR OCD[tiab] OR Hoarding[tiab] OR Adjustment Disorder*[tiab] OR Reactive Disorder*[tiab] OR Psychological Trauma*[tiab] OR Sexual Trauma*[tiab] OR Sexual Abuse Trauma*[tiab] OR Post-Traumatic Stress Disorder*[tiab] OR Posttraumatic Stress Disorder*[tiab] OR PTSD[tiab] OR Psychological Stress*[tiab] OR Psychologic Stress*[tiab] OR Emotional Stress*[tiab] OR Life Stress*[tiab] OR Mental stress*[tiab] OR Burnout[tiab] OR Mood*[tiab] OR Depress*[tiab] OR Cyclothymi*[tiab] OR Dysthymi*[tiab] OR Affective[tiab])

AND

(Magnesium/administration and dosage[mh] OR Magnesium/therapeutic use[mh] OR Magnesium Chloride/therapeutic use[mh] OR Magnesium Chloride/administration and dosage[mh] OR Magnesium compounds/administration and dosage[mh] OR Magnesium compounds/therapeutic use[mh] OR Zinc/administration and dosage[mh] OR Zinc/therapeutic use[mh] OR Zinc Compounds/administration and dosage[mh] OR Zinc Compounds/therapeutic use[mh] OR Magnesium[tiab] OR Zinc[tiab] OR Asbesto*[tiab] OR Talc*[tiab] OR Struvit*[tiab])

Embase - 4094 resultados (1351 resumos de congressos + 2743 artigos)

('anxiety'/exp OR 'anxiety disorder'/exp OR 'mood disorder'/exp OR 'mental stress'/exp OR 'posttraumatic stress disorder'/exp OR 'depression'/exp) AND ('diet therapy'/exp OR 'drug therapy'/de OR 'drug effect'/de) OR 'antidepressant agent'/exp OR (Angst OR Hypervigilan* OR Nervousness OR Anxiet* OR Anxious* OR Agoraphobi* OR Panic OR Phobi* OR Claustrophobi* OR 'Obsessive-Compulsive' OR OCD OR Hoarding OR 'Adjustment Disorder*' OR 'Reactive Disorder*' OR 'Psychological Trauma*' OR 'Sexual Trauma*' OR 'Sexual Abuse Trauma*' OR 'Post-Traumatic Stress Disorder*' OR 'Posttraumatic Stress Disorder*' OR PTSD OR 'Psychological Stress*' OR 'Psychologic Stress*' OR 'Emotional Stress*' OR 'Life Stress*' OR 'Mental stress*' OR Burnout OR Mood* OR Depress* OR Cyclothymi* OR Dysthymi* OR Affective):ti,ab,kw)

AND

('magnesium'/exp OR 'magnesium sulfate'/exp OR 'magnesium chloride'/exp OR 'magnesium derivative'/exp OR 'magnesium hydroxide'/exp OR 'magnesium oxide'/exp OR 'magnesium silicate'/exp OR 'asbestos'/exp OR 'talc'/exp OR 'struvite'/exp OR 'zinc'/exp OR 'zinc oxide'/exp OR 'zinc sulfate'/exp OR (Magnesium OR Zinc OR Asbesto* OR Talc* OR Struvit*):ti,ab,kw)

AND

[embase]/lim NOT ([embase]/lim AND [medline]/lim)

PsycInfo - 620 resultados

((IndexTermsFilt: ("Anxiety") OR IndexTermsFilt: ("Anxiety Sensitivity") OR IndexTermsFilt: ("Climate Anxiety") OR IndexTermsFilt: ("Computer Anxiety") OR IndexTermsFilt: ("Death Anxiety") OR IndexTermsFilt: ("Health Anxiety") OR IndexTermsFilt: ("Mathematics Anxiety") OR IndexTermsFilt: ("Performance Anxiety") OR IndexTermsFilt: ("Social Anxiety") OR IndexTermsFilt: ("Speech Anxiety") OR IndexTermsFilt: ("Test Anxiety") OR IndexTermsFilt: ("Travel Anxiety") OR IndexTermsFilt: ("Anxiety Disorders") OR IndexTermsFilt: ("Anxiety Management") OR IndexTermsFilt: ("Generalized Anxiety Disorder") OR IndexTermsFilt: ("Panic") OR IndexTermsFilt: ("Panic Attack") OR IndexTermsFilt: ("Panic Disorder") OR IndexTermsFilt: ("Phobias") OR IndexTermsFilt: ("Posttraumatic Stress") OR IndexTermsFilt: ("Stress") OR IndexTermsFilt: ("Affective Disorders") OR IndexTermsFilt: ("Depression (Emotion)") OR IndexTermsFilt: ("Cyclothymic Disorder") OR IndexTermsFilt: ("Major Depression") OR IndexTermsFilt: ("Atypical Depression") OR IndexTermsFilt: ("Endogenous Depression") OR IndexTermsFilt: ("Late Life Depression") OR IndexTermsFilt: ("Postpartum Depression") OR IndexTermsFilt: ("Reactive Depression") OR