

**Evidence Analysis Library: Chronic Obstructive Pulmonary Disease (COPD)  
Micronutrients**

**Does vitamin D supplementation improve outcomes in adults with COPD?  
What serum level of 25(OH) vitamin D improves outcomes in adults with COPD?**

**List of Excluded Articles (N=53)**

Article	Reason for Exclusion <sup>1</sup>
Al-Azzawi MA, Ghoneim AH, Elmadbouh I. Evaluation of Vitamin D, Vitamin D Binding Protein Gene Polymorphism with Oxidant – Antioxidant Profiles in Chronic Obstructive Pulmonary Disease, <i>J Med Biochem</i> 2017; 36 (4), 331-340. doi: <a href="https://doi.org/10.1515/jomb-2017-0012">https://doi.org/10.1515/jomb-2017-0012</a>	No outcomes of interest reported; evaluated the association of plasma vitamin D level and COPD category (mild, moderate, severe), but not specific FEV <sub>1</sub> values.
Andersson I, Gronberg A, Slinde F, Bosaeus I, Larsson, S. Vitamin and mineral status in elderly patients with chronic obstructive pulmonary disease. <i>Clin Respir J</i> 2007; 1(1), 23-29. PMID: 20298274 doi:10.1111/j.1752-699X.2007.00003.x	Not relevant to research question; evaluated vitamin D/calcium intake but no serum vitamin D levels reported or supplements.
Bjerk SM, Edgington BD, Rector TS, Kunisaki KM. Supplemental vitamin D and physical performance in COPD: A pilot randomized trial. <i>Inter J of Chron Obstructive Pulmonary Disease</i> , 2013; 8, 97-104. doi:10.2147/COPD.S40885 [doi] PMID: 23430315	No outcomes of interest; primary outcome was short physical performance battery test, SGRQ scores.
Black, P. N., & Scragg, R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey. <i>Chest</i> , 2005. 128(6), 3792-3798. doi: S0012-3692(15)49620-5 [pii] PMID: 16354847	Population based study (NHANES); did not separate out COPD subjects in reporting.
Calder PC, Laviano A, Lonnqvist F, Muscaritoli M, Öhlander M, Schols A. Targeted medical nutrition for cachexia in chronic obstructive pulmonary disease: a randomized, controlled trial. <i>J Cachexia Sarcopenia Muscle</i> . 2018 Feb;9(1):28-40. doi: 10.1002/jcsm.12228. Epub 2017 Sep 10. PMID: 28891198	Evaluated vitamin D + PUFA supplement; did not separately report vitamin D results; no outcomes of interest reported.
Datta, Priyanka & Singh, Kriti & Belle, Vijetha & Prabhu, Krishnananda. (2017). A Pilot Study on Vitamin D and Respiratory Diseases in Southern Part of India. <i>Int J Current Res Review</i> . 9. 15-18.	Not relevant to research question; no outcomes of interest reported. Compares vitamin D levels in asthma and COPD groups.
de Batlle J, Romieu I, Antó JM, Mendez M, Rodríguez E, Balcells E, Ferrer A, Gea J, Rodríguez-Roisin R, García-Aymerich J; PAC-COPD Study Group. Dietary habits of firstly admitted Spanish COPD patients. <i>Respir Med</i> . 2009 Dec; 103(12): 1904-10. doi: 10.1016/j.rmed.2009.06.001. Epub 2009 Jun 28. PMID: 19564102	Not relevant to research question; examined dietary intakes of vitamin D compared to the recommended amounts.
Forli L, Bjortuft O and Boe J. Vitamin D status in relation to nutritional depletion and muscle function in patients with advanced pulmonary disease. <i>Exp Lung Res</i> . 2009;35(6):524-38. PMID: 19842836.	Data on COPD subjects were not separated from other pulmonary disease in results.
Franco CB, Paz-Filho G, Gomes PE, Nascimento VB, Kulak CA, Boguszewski CL, Borba VZ. Chronic obstructive pulmonary disease is associated with osteoporosis and low levels of vitamin D. <i>Osteoporos Int</i> . 2009 Nov;20(11):1881-7. doi: 10.1007/s00198-009-0890-5. Epub 2009 Mar 20. PMID: 19300892	No outcomes of interest reported; primary outcome was oxygen saturation.
Generali JA, Cada DJ, Vitamin D: Exacerbations in Chronic Obstructive Pulmonary Disease (COPD) Volume: 47 issue: 10, page(s): 766-768; October 1, 2012. <a href="https://doi.org/10.1310/hpj4710-766">https://doi.org/10.1310/hpj4710-766</a>	Review article; hand searched for relevant primary research.
Ginde AA, Mansbach JM, Camargo CA Jr. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. <i>Arch Intern Med</i> . 2009 Feb 23;169(4): 384-90. doi: 10.1001/archinternmed.2008.560. PMID: 19237723	Lung condition that is not COPD; upper respiratory tract infection study. COPD is covariate not separate analyzed population.
Gold DR, Manson JE. Severe vitamin D deficiency: a prerequisite for COPD responsiveness to vitamin D supplementation? <i>Ann Intern Med</i> . 2012 Jan 17; 156(2):156-7. doi: 10.7326/0003-4819-156-2-201201170-00013. No abstract available. PMID: 22250148	Study protocol.
Graat-Verboom L, Smeenk FW, van den Borne BE, Spruit MA, Donkers-van Rossum AB, Aarts RP, Wouters EF. Risk factors for osteoporosis in caucasian patients with moderate chronic obstructive pulmonary disease: A case control study. <i>Bone</i> , 2012; 50(6), 1234-1239. doi:10.1016/j.bone.2012.02.638 [doi] PMID: 22426499	Not relevant to research question; vitamin D levels were treated as a characteristic of the groups; no real analysis done on effect of vitamin D on outcomes of interest.
Graat-Verboom L, Smeenk FW, van den Borne BE, Spruit MA, Jansen FH, van Enschoot JW & Wouters EF. Progression of osteoporosis in patients with COPD: A	Not relevant to research question; risk factors for osteoporosis evaluated.

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3-year follow up study. <i>Resp Med</i> , 2012; 106(6), 861-870. doi: 10.1016/j.rmed.2011.12.020 [doi] PMID: 22369986	
Heidari B, Javadian Y, Monadi M, Dankob Y, Firouzjahi A. Vitamin D status and distribution in patients with chronic obstructive pulmonary disease versus healthy controls. <i>Caspian J Intern Med</i> . 2015 Spring; 6(2):93-7. PMID: 26221507	Not relevant to research question; descriptive study only of vitamin D status in COPD subjects vs. controls. Effect of vitamin D was not evaluated and no outcomes reported.
Hendryx, M., & Luo, J. (2015). A test of vitamin D benefits on respiratory health mediated through inflammatory markers. <i>Chron Respir Dis</i> , 12(1), 24-30. doi:10.1177/1479972314556086 [doi] PMID:25336462	Not relevant to research question; NHANES data; does not relate vitamin D status to outcomes in a population with COPD.
Heulens N, Korf H, Janssens W. Innate immune modulation in chronic obstructive pulmonary disease: moving closer toward vitamin D therapy. <i>J Pharmacol Exp Ther</i> . 2015 May;353(2):360-8. doi: 10.1124/jpet.115.223032. Epub 2015 Mar 9. Review. PMID: 25755208	Review article; hand searched for relevant primary research.
Horadagoda C, Dinihan T, Roberts M, Kairaitis K. Body composition and micronutrient deficiencies in patients with an acute exacerbation of chronic obstructive pulmonary disease. <i>Intern Med J</i> . 2017 Apr 12. doi: 10.1111/imj.13453. [Epub ahead of print] PMID: 28401645	Not relevant to research question; evaluated vitamin D deficiency and BMI during acute exacerbations but did not separate out effects of vitamin D alone.
Hornikx M, Van Remoortel H, Lehouck A, Mathieu C, Maes K, Gayan-Ramirez G, Decramer M, Troosters T, Janssens W. Vitamin D supplementation during rehabilitation in COPD: a secondary analysis of a randomized trial. <i>Respir Res</i> . 2012 Sep 25;13:84. doi: 10.1186/1465-9921-13-84. PMID: 23006613	No outcomes of interest; primary outcomes were MIP and MEP.
Ishii, T., Motegi, T., Kamio, K., Gemma, A., & Kida, K. (2014). Association of group component genetic variations in COPD and COPD exacerbation in a Japanese population. <i>Respirology</i> (Carlton, Vic.), 19(4), 590-595. doi:10.1111/resp.12277 [doi] PMID: 24735339	Not relevant to research question; evaluated genetic components of vitamin D metabolism.
Jackson AS, Shrikishna D, Kelly JL, Kemp SV, Hart N, Moxham J, Polkey MI, Kemp P, Hopkinson NS. Vitamin D and skeletal muscle strength and endurance in COPD. <i>Eur Respir J</i> . 2013 Feb;41(2):309-16. doi: 10.1183/09031936.00043112. Epub 2012 May 3. Erratum in: <i>Eur Respir J</i> . 2013 Apr;41(4):998. Kemp, Samuel V [added]. PMID: 22556020	No outcomes of interest; primary outcome was quad muscle strength, HGS.
Khawar A, Mukhtar A, Khan RMA, Prevalence of risk factors leading to osteoporosis in chronic obstructive pulmonary disease (COPD) <i>Medical Forum Monthly - Volume 28, Issue 10, pp. 68-72 - published 2017-01-01</i>	Evaluated risk factors of osteoporosis; no outcomes of interest reported.
Kim C, Jung JY, Kim YS, Lee JS, Rhee CK, Lee JH, Lee JH, Kim TH, Lim SY, Sheen SS, Yoo KH, Seo JB, Oh YM, Lee SD, Park YB. Vitamin D Deficiency Is Associated with Rapid Decline in Exercise Capacity in Male Patients with Chronic Obstructive Pulmonary Disease. <i>Respiration</i> . 2016;91(5):351-8. doi: 10.1159/000445266. Epub 2016 Apr 23. PMID: 27105006	Not relevant to research question; investigated effects of vitamin D deficiency on change in exercise capacity in COPD patients. No evaluation of vitamin D status and outcomes of interest.
Kokturk N, Baha A, Oh YM, Young Ju J, Jones PW. Vitamin D deficiency: What does it mean for chronic obstructive pulmonary disease (COPD)? a comprehensive review for pulmonologists. <i>Clin Respir J</i> . 2016 Dec 7. doi: 10.1111/crj.12588. [Epub ahead of print] Review. PMID: 27925404	Review article; hand searched for relevant primary research.
Kunisaki, K. M., & Rector, T. S. (2011). Vitamin D and responses to inhaled fluticasone in severe chronic obstructive pulmonary disease. <i>Int J Chron Obstr Pulm Dis</i> , 6, 29-34. doi:10.2147/COPD.S15358 [doi] PMID:21311691	Not relevant to research question; primary outcome was lung function in response to inhaled corticosteroids.
Laudisio A, Costanzo L, Di Gioia C, Delussu AS, Traballese M, Gemma A, Antonelli Incalzi R. Dietary intake of elderly outpatients with chronic obstructive pulmonary disease. <i>Arch Gerontol Geriatr</i> . 2016 May-Jun;64:75-81. doi: 10.1016/j.archger.2016.01.006. Epub 2016 Jan 14. PMID: 26952380	Not relevant to research question; evaluated diet quality compared to recommended needs; no vitamin D-specific information related to COPD outcomes of interest.
Lee PH, Kok VC, Chou PL, Ku MC, Chen YC, Horng JT. Risk and clinical predictors of osteoporotic fracture in East Asian patients with chronic obstructive pulmonary disease: a population-based cohort study. <i>PeerJ</i> . 2016 Oct 27;4: e2634. eCollection 2016. PMID: 27812429	Not relevant to research question; population-based study. No information on serum levels or actual use of vitamin D supplements.
Matkovic Z, Cvetko D, Rahelic D, Esquinas C, Zarak M, Miravitlles M, Tudoric N. Nutritional Status of Patients with Chronic Obstructive Pulmonary Disease in Relation to their Physical Performance. <i>COPD</i> . 2017 Dec;14(6):626-634. doi: 10.1080/15412555.2017.1386643. Epub 2017 Nov 3. PMID: 29099635	Not relevant to research question; vitamin D was not evaluated related to COPD outcomes of interest.
Mekov E, Slavova Y, Tsakova A, Genova M, Kostadinov D, Minchev D, Marinova D. Metabolic syndrome in hospitalized patients with chronic obstructive pulmonary disease. <i>PeerJ</i> . 2015 Jul 2;3:e1068. doi: 10.7717/peerj.1068. eCollection 2015. PMID: 26157632	Not relevant to research question; all outcomes were related to metabolic syndrome; not vitamin D status. No outcomes of interest.

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Moberg M, Elango P, Ferrucci L, Spruit MA, Wouters EF, Rutten EP. Vitamin D deficiency and airflow limitation in the Baltimore Longitudinal Study of Ageing. <i>Eur J Clin Invest</i> . 2015 Sep;45(9):955-63. doi: 10.1111/eci.12498. Epub 2015 Aug 7. PMID: 26173468	Lung condition that is not COPD; general population.
Moberg, M., Ringbaek, T., Roberts, N. B., & Vestbo, J. (2014). Association between vitamin D status and COPD phenotypes. <i>Lung</i> , 192(4), 493-497. doi: 10.1007/s00408-014-9582-9 [doi] PMID:24748443	Not relevant to research question; evaluated phenotypes on outcomes; vitamin D level and 6-MWD; no outcomes of interest.
Ng TP, Niti M, Yap KB, Tan WC. Dietary and supplemental antioxidant and anti-inflammatory nutrient intakes and pulmonary function. <i>Public Health Nutr</i> . 2014 Sep;17(9):2081-6. doi: 10.1017/S1368980013002590. Epub 2013 Sep 27. PMID: 24074036	Not relevant to research question; no serum vitamin D levels and supplement amounts. Not COPD population.
Odler, B., Ivancso, I., Somogyi, V., Benke, K., Tamasi, L., Galffy, G. Szalay B, Muller, V. (2015). Vitamin D deficiency is associated with impaired disease control in asthma-COPD overlap syndrome patients. <i>Int J Chron Obstruct Pulmon Dis</i> 10, 2017-2025. doi:10.2147/COPD.S91654 [doi] PMID: 26451099	Not relevant to research question; aim was to assess the levels of serum vitamin D its correlation with clinical parameters.
Persson LJ, Aanerud M, Hardie JA, Miodini Nilsen R, Bakke PS, Eagan TM, Hiemstra PS. Antimicrobial peptide levels are linked to airway inflammation, bacterial colonisation and exacerbations in chronic obstructive pulmonary disease. <i>Eur Respir J</i> . 2017 Mar 15;49(3). pii: 1601328. doi: 10.1183/13993003.01328-2016. Print 2017 Mar. PMID: 28298400	No outcomes of interest; primary outcome was antimicrobial peptide.
Piazzolla G, Castrovilli A, Liotino V, Vulpi MR, Fanelli M, Mazzocca A, Candigliota M, Berardi E, Resta O, Sabbà C, Tortorella C. Metabolic syndrome and Chronic Obstructive Pulmonary Disease (COPD): The interplay among smoking, insulin resistance and vitamin D. <i>PLoS One</i> . 2017 Oct 24;12(10): e0186708. doi: 10.1371/journal.pone.0186708. eCollection 2017. PMID: 29065130	Evaluated metabolic syndrome, C-peptide and vitamin D status but no outcomes of interest were reported.
Rafiq R, Aleva FE, Schruppf JA, Heijdra YF, Taube C, Daniels JM, Lips P, Bet PM, Hiemstra PS, van der Ven AJ, den Heijer M, de Jongh RT. Prevention of exacerbations in patients with COPD and vitamin D deficiency through vitamin D supplementation (PRECOVID): a study protocol. <i>BMC Pulm Med</i> . 2015 Sep 23;15:106. doi: 10.1186/s12890-015-0101-4. PMID: 26399451	Study protocol; no results reported.
Ringbaek, T., Martinez, G., Durakovic, A., Thogersen, J., Midjord, A. K., Jensen, J. E., & Lange, P. (2011). Vitamin d status in patients with chronic obstructive pulmonary disease who participate in pulmonary rehabilitation. <i>J Cardiopulm Rehabil Prev</i> , 31(4), 261-267. doi:10.1097/HCR.0b013e31821c13aa [doi] PMID: 21623214	Not relevant to research question; primary outcome was risk of dropping out from pulmonary rehab program; no outcomes of interest.
Sanket S, Madireddi J, Stanley W, Sura P, Prabhu M. Relation between Vitamin D Deficiency and Severity of Chronic Obstructive Pulmonary Disease-A Case Control Study. <i>J Clin Diagn Res</i> . 2016 Jan;10(1):OC16-9. doi: 10.7860/JCDR/2016/15404.7097. Epub 2016 Jan 1. PMID: 26894108	Not relevant to research question; primary outcome was BMI; COPD was associated with higher risk of vitamin D deficiency and higher GOLD classification.
Skaaby T, Husemoen LL, Thuesen BH, Pisinger C, Jørgensen T, Fenger RV, Linneberg A. Vitamin D status and chronic obstructive pulmonary disease: a prospective general population study. <i>PLoS One</i> . 2014 Mar 4;9(3):e90654. doi: 10.1371/journal.pone.0090654. eCollection 2014. PMID: 24594696	Not relevant to research question; primary outcome was prevalence and incidence of COPD in the general population.
Sluyter JD, Camargo CA, Waayer D, Lawes CMM, Toop L, Khaw KT, Scragg R. Effect of Monthly, High-Dose, Long-Term Vitamin D on Lung Function: A Randomized Controlled Trial. <i>Nutrients</i> . 2017 Dec 13;9(12). pii: E1353. doi: 10.3390/nu9121353. PMID: 29236049	Combined asthma and COPD subjects in all analyses; data on COPD subjects were not separated.
Solidoro P, Belloccchia M, Facchini F. The immunobiological and clinical role of vitamin D in obstructive lung diseases. <i>Minerva Med</i> . 2016 Jun;107(3 Suppl 1):12-9. Review. PMID: 27424501	Review article; hand searched for relevant primary research.
van de Bool C, Rutten EPA, van Helvoort A, Franssen FME, Wouters EFM, Schols AMWJ. A randomized clinical trial investigating the efficacy of targeted nutrition as adjunct to exercise training in COPD. <i>J Cachexia Sarcopenia Muscle</i> . 2017 Jun 12. doi: 10.1002/jcsm.12219. [Epub ahead of print] PMID: 28608438	Not relevant to research question; did not separate out effects of vitamin D alone; vitamin D was part of an oral nutrition supplement.
van de Bool C, Mattijssen-Verdonschot C, van Melick PP, Spruit MA, Franssen FM, Wouters EF, Schols AM, Rutten EP. Quality of dietary intake in relation to body composition in patients with chronic obstructive pulmonary disease eligible for pulmonary rehabilitation. <i>Eur J Clin Nutr</i> . 2014 Feb;68(2):159-65. doi: 10.1038/ejcn.2013.257. Epub 2013 Dec 11. PMID: 24327123	No outcomes of interest reported; evaluated diet quality in relation to body composition, not vitamin D alone.
Wood AM, Bassford C, Webster D, Newby P, Rajesh P, Stockley RA, Thickett DR. Vitamin D-binding protein contributes to COPD by activation of alveolar	Does not specify with or without COPD in study group reporting; study evaluated vitamin D binding protein

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macrophages. <i>Thorax</i> . 2011 Mar;66(3):205-10. doi: 10.1136/thx.2010.140921. Epub 2011 Jan 12. PMID: 21228423	and vitamin D levels in four groups; results for FEV <sub>1</sub> are not reported for COPD subjects separately.
Wright, R. J. (2005). Make no bones about it: Increasing epidemiologic evidence links vitamin D to pulmonary function and COPD. <i>Chest</i> , 128(6), 3781-3783. doi: S0012-3692(15)49614-X [pii] PMID:16354841	Review article.
Xiaomei W, Hang X, Lingling L, Xuejun L. Bone metabolism status and associated risk factors in elderly patients with chronic obstructive pulmonary disease (COPD). <i>Cell Biochem Biophys</i> . 2014 Sep;70(1):129-34. doi: 10.1007/s12013-014-9868-9. PMID: 24633456	Not relevant to research question; evaluation of characteristics between COPD and control groups; risk factors of bone disease in COPD.
Yang H, Long F, Zhang Y, Yu R, Zhang P, Li W, Li S, Jin X, Xia J, Dong L, Zhu N, Huang Y, Gong Y, Chen X. 1 $\alpha$ ,25-Dihydroxyvitamin D <sub>3</sub> Induces Neutrophil Apoptosis through the p38 MAPK Signaling Pathway in Chronic Obstructive Pulmonary Disease Patients. <i>PLoS One</i> . 2015 Apr 23;10(4):e0120515. doi: 10.1371/journal.pone.0120515. eCollection 2015. PMID: 25905635	Not relevant to research question; did not report vitamin D levels; evaluated effect of vitamin D on neutrophil apoptosis rate in COPD subjects.
Zhang L, Yuan QY. Vitamin D should be supplemented more actively in elderly patients with coronary heart disease combined with COPD. <i>Int J Chron Obstruct Pulmon Dis</i> . 2016 Jun 21;11:1359-65. doi: 10.2147/COPD.S105671. eCollection 2016. PMID: 27382272	Not relevant to research question; authors obtained serum vitamin D levels but did not associate vitamin D status with an outcome of interest.
Zhang LL, Gong J, Liu CT. Vitamin D with asthma and COPD: not a false hope? A systematic review and meta-analysis. <i>Genet Mol Res</i> . 2014 Feb 13;13(3):7607-16. doi: 10.4238/2014.February.13.10. Review. PMID: 24615096	Review article; hand searched for relevant primary research.
Zhao G, Ford ES, Tsai J, Li C, Croft JB. Low concentrations of serum 25-hydroxyvitamin D associated with increased risk for chronic bronchitis among US adults. <i>Br J Nutr</i> . 2012 May;107(9):1386-92. doi: 10.1017/S0007114511004417. Epub 2011 Sep 8. PMID: 21899806	Lung condition that is not COPD; evaluated vitamin D levels and risk of chronic bronchitis.
Zhou X, Han J, Song Y, Zhang J, Wang Z. Serum levels of 25-hydroxyvitamin D, oral health and chronic obstructive pulmonary disease. <i>J Clin Periodontol</i> . 2012 Apr;39(4):350-6. doi: 10.1111/j.1600-051X.2012.01852.x. Epub 2012 Feb 1. PMID: 22296704	No outcomes of interest reported; primary outcome was periodontal disease. After stratified by smoking status, serum vitamin D concentrations were positively correlated with FEV <sub>1</sub> /FVC among non-smokers.
Zhu B, Zhu B, Xiao C, Zheng Z. Vitamin D deficiency is associated with the severity of COPD: a systematic review and meta-analysis. <i>Int J Chron Obstruct Pulmon Dis</i> . 2015 Sep 11;10:1907-16. doi: 10.2147/COPD.S89763. eCollection 2015. Review. PMID: 26392765	Review article; hand searched for relevant primary research.
Zilz C, Blaas SH, Pfeifer M, Jörres RA, Budweiser S. Mental health, serum biomarkers and survival in severe COPD: a pilot study. <i>Multidiscip Respir Med</i> . 2016 Jan 18;11:3. doi: 10.1186/s40248-016-0041-8. eCollection 2015. PMID: 26788321	No outcomes of interest reported; evaluated vitamin D and serum biomarkers.

<sup>1</sup>**Abbreviations:** 6-MWD=6-minute walking distance; BMI=body mass index; COPD=chronic obstructive pulmonary disease; FEV<sub>1</sub>=forced expiratory volume in 1 second; FVC=forced vital capacity; GOLD=Global Initiative for Chronic Obstructive Lung Disease; HGS=hand grip strength; MEP=maximal expiratory pressure; MIP=maximal inspiratory pressure; NHANES=National Health and Nutrition Examination Survey; PUFA=polyunsaturated fatty acid; SGRQ=St George's Respiratory Questionnaire.