- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Assessment of Energy Intake 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

  COPD: Assessment of Energy Intake

  The registered dietitian nutritionist (RDN) should assess the energy intake of adults with COPD. Evidence suggests there was improvement in dyspnea scores with higher energy intakes. In addition, less robust evidence supported a beneficial relationship with functional status, healthcare utilization or duration of illness.

  Rating: Fair
  Imperative

  - Risks/Harms of Implementing This Recommendation

    There are no potential risks or harms associated with the application of the recommendation.

  - Conditions of Application

    There are no conditions which may limit the application of the recommendation.

  - Potential Costs Associated with Application

    Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.

  - Recommendation Narrative

    A total of nine studies were included in the evidence analysis supporting the recommendation:

    - Four randomized controlled trials: One positive-quality (Sugawara et al, 2012), three neutral-quality (Førli and Boe, 2005; Planas et al, 2005; Weekes et al, 2009)
    - Five cross-sectional studies: Three neutral-quality (Lee et al, 2013; Renvall et al, 2009; Yazdanpanah et al, 2010) and two negative-quality (Benton et al 2010; Selvi et al, 2014).

    There was improvement in dyspnea scores with higher energy intakes, with less robust evidence supporting a beneficial relationship with functional status, healthcare utilization or duration of illness.

    - *Respiratory symptoms (three studies):* All three studies found significant associations with dyspnea scores (Lee et al, 2013; Sugawara et al, 2012; Weekes et al, 2009)
    - *Functional status (one study):* The study found a significant association with activities of daily living scores (Weekes et al, 2009)
    - *Healthcare utilization (one study):* The study found a significant association with number of infections requiring antibiotics (Forli and Boe, 2009)
    - *Duration of illness (one study):* The study found a significant association with duration of disease in years (Selvi et al, 2014).

    The findings for the impact of energy intake on exacerbations, quality of life (QoL), weight status and body composition were mixed, with the majority supportive of an association.

    - *Exacerbations (two studies):* One study found a significant association with number of emergency room (ER) visits due to acute exacerbations (AEs) (Lee et al, 2013). One study did not find a association with number of ER visits due to AEs with energy intakes of either 1.7 x or 1.3 x Harris-Benedict Equation (HBE) (Planas et al, 2005).
    - *QoL (three studies):* All three studies found significant associations of Chronic Respiratory Disease Questionnaire (CRQ) scores with energy intakes of 1.3 x HBE (Planas et al, 2005), CRQ scores (Sugawara et al, 2012) and St. George Respiratory Quotient (SGRQ) scores (Weekes et al, 2009). One study did not find significant associations for CRQ scores with energy intakes of 1.7 x HBE (Planas et al, 2005)
    - *Weight status (seven studies)*
      - Six studies found significant associations
        - Weight gain with energy intakes of 1.7 x HBE (Planas et al, 2005)
        - Percentage IBW (Sugawara et al, 2012)
        - Weight gain (Forli and Boe, 2005; Sugawara et al, 2012; Weekes et al, 2009)
        - Body mass index (BMI) (Lee et al, 2013; Renvall et al, 2009).
      - Two studies did not find associations
        - BMI (Benton et al, 2010)
        - BW with energy intakes of 1.3 x HBE (Planas et al, 2005).
    - *Body composition (three studies):* All three studies found significant associations with fat mass (FM), triceps skinfold (TSF) and fat-free mass index (FFMI) with energy intakes of 1.7 x HBE (Planas et al, 2005), FM, fat mass index (Sugawara et al, 2012) and mid-arm circumference and sum of four skinfold thickness measurements (Weekes et al, 2009). All three studies also did not find associations with mid-arm muscle circumference (Weekes et al, 2009), FFMI and arm circumference (Sugawara et al, 2012) or FM, TSF and FFMI with energy intakes of 1.3 x HBE (Planas et al, 2005).

    The evidence for a relationship between energy intake and lung function, systemic inflammation or exercise capacity was inconsistent.

    - *Lung function (five studies):* Two studies found significant associations in forced vital capacity (FVC) and sniff pressure (Weekes et al, 2009) and Pmax inspiratory (PI_{max}) (Sugawara et al, 2012). Three studies did not find associations in FEV in one second (FEV_1) (Lee et al, 2013; Yazdanpanah et al, 2010), FEV_1 with energy intakes of either 1.7 x or 1.3 x HBE (Planas et al, 2005), FVC, FEV_1/FVC, and vital capacity (Yazdanpanah et al, 2010), PI_{max} and Pmax expiratory (PE_{max}) (Weekes et al, 2009) or PE_{max} (Sugawara et al, 2012).
    - *Systemic inflammation (one study):* The study found a significant association with IL-6, but not CRP (Sugawara et al, 2012)
    - *Exercise capacity (five studies):* Three studies found significant associations with upper and lower body strength (Benton et al, 2010) and six-minute walking distance (Benton et al, 2010; Lee et al, 2013; Sugawara et al, 2012). Two studies did not find associations: Handgrip strength (HGS) with energy intakes of either 1.7 x or 1.3 x HBE (Planas et al, 2005) and HGS (Weekes et al, 2009).

    * For Sugawara et al, 2012, the workgroup considered the between-group analysis only in the conclusion statement.

  - Recommendation Strength Rationale

    The conclusion statement supporting the recommendation was Grade II, *Fair.*

  - Minority Opinions

    None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

What association exists between energy intake (e.g., kcal per kg) and outcomes in adults with COPD?

- References

Benton M, Wagner C, Alexander J. Relationship between body mass index, nutrition, strength, and function in elderly individuals with chronic obstructive pulmonary disease. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2010; 30:260-3

Froli L, Boe J. The energy intake that is needed for weight gain in COPD candidates for lung transplantation. *COPD* 2005; 2:405-10

Lee H, Kim S, Lim Y, Gwon H, Kim Y, Ahn J, Park H. Nutritional status and disease severity in patients with chronic obstructive pulmonary disease (COPD). *Archives of Gerontology and Geriatrics* 2013; 56:518-23

Planas M, Alvarez J, García-Peris P, de la Cuerda C, de Lucas P, Castella M, Canseco F, Reyes L. Nutritional support and quality of life in stable chronic obstructive pulmonary disease (COPD) patients. *Clinical Nutrition (Edinburgh, Scotland)* 2005; 24:433-41

Renvall M, Friedman P, Ramsdell J. Predictors of body mass index in patients with moderate to severe emphysema. *COPD* 2009; 6:432-6

Selvi EC, Saikumar P, Kumar N. How to evaluate the risk of malnutrition in patients with COPD?. *Global Journal of Medical Research: F Diseases* 2014; 14:21-25

Sugawara K, Takahashi H, Kashiwagura T, Yamada K, Yanagida S, Homma M, Dairiki K, Sasaki H, Kawagoshi A, Satake M, Shioya T. Effect of anti-inflammatory supplementation with whey peptide and exercise therapy in patients with COPD. *Respiratory Medicine* 2012; 106:1526-34

Weekes C, Emery P, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. *Thorax* 2009; 64:326-31

Yazdanpanah L, Shidfar F, Moosavi A, Heidarnazhad H, Haghani H. Energy and protein intake and its relationship with pulmonary function in chronic obstructive pulmonary disease (COPD) patients. *Acta Medica Iranica* 2010; 48:374-9

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

  None.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Assessment of Body Weight 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

COPD: Assessment of Body Weight Status

The RDN should assess body mass index (BMI) or other measures of body weight in adults with COPD. Strong evidence suggests an association between body weight status and mortality in adults with COPD. The lowest BMI groups had higher mortality rates when compared to higher BMI groups. Furthermore, a BMI classification of approximately 25.0kg/m^2 to 29.99kg/m^2 appeared to lower the risk of mortality when compared to both higher and lower BMI classifications. In unadjusted results, there was fair evidence of a positive association between BMI and FEV_1 percentage predicted. An increasing BMI was also shown to reduce declines in FEV_1 percentage predicted over time in a longitudinal study.

Rating: Strong
Imperative

- Risks/Harms of Implementing This Recommendation

  There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application

  There are no conditions which may limit the application of the recommendation.

- Potential Costs Associated with Application

  Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.

- Recommendation Narrative

  Body Weight

  A total of 22 studies were included in the evidence analysis supporting the recommendation:

  - Eleven prospective cohort studies: Three positive quality (Hallin et al, 2007; Schols et al, 2005; Tsimogianni et al, 2009) and eight neutral quality (Abston et al, 2017; Baccioglu et al, 2014; Galesanu et al, 2014; Koul et al, 2017; Piquet et al, 2013; Pothirat et al, 2007; Qiu et al, 2009; Rutten et al, 2013)
  - Ten neutral quality retrospective cohort studies (Jiang et al, 2017; Lainscak et al, 2011; Lim et al, 2017; Marti et al, 2006; O'Donnell et al, 2011; Ranieri et al, 2008; Slinde et al, 2005; Uh et al, 2011; Yamauchi et al, 2014; Zapatero et al, 2013)
  - One negative quality case-control study (Dimov et al, 2013).

  Body Weight and Lung Function Outcomes

  All studies using FEV_1 % predicted as an outcome found a positive association with BMI or BMI category, and one longitudinal study showing increasing BMI reduced declines in FEV_1 % predicted over time. While these studies appear to indicate that increasing BMI is associated with improvements in FEV_1 % predicted, results did not include adjustment for relevant confounders and should be interpreted with caution. Results for other lung function measures (FEV_1, FVC, FVC % predicted, FEV_1/FVC) were mixed, and therefore, no conclusion can be drawn for these measures.

  - *FEV_1 stratified into quintiles and BMI* (one study): One study (Abston et al, 2017) found BMI was not associated with FEV_1 in the overall group or in any of the FEV_1 quintiles. In each of the FEV1 quintiles, FVC % predicted showed inverse associations with BMI, while FEV_1/FVC showed a positive association with BMI.
  - *BMI stratified into quartiles and FEV_1* (one study): One study (Lainscak et al, 2011) found a positive association between FEV_1 (ml/s) and BMI divided into quartiles in subjects hospitalized for an acute exacerbation of COPD (AECOPD), with FEV_1 increasing as BMI category increased.
  - *BMI and Lung Function (non-adjusted)* (six studies): Six studies (Dimov et al, 2013; Galesanu et al, 2014; Hallin et al, 2007; Lim et al, 2017; O'Donnell et al, 2011; Qiu et al, 2009) found BMI was positively associated with FEV_1 % predicted in analyses, unadjusted for confounding variables. BMI was positively correlated with FEV_1/FVC in two studies (O'Donnell et al; Qiu et al). Qui et al, also found a higher BMI was also associated with a lower decline in lung function over time. Two studies (Galesanu et al

and O'Donnell et al) found that BMI was not associated with FVC. O'Donnell et al found BMI was not associated with FVC % predicted. Galesanu et al found NS association between FEV_1 and BMI, while Lim et al found FEV_1 to be highest in subjects classified as OB by either the WHO or Asian-Pacific methods of BMI. FEV_1 was not reported in four studies (Dimov et al; Hallin et al; O'Donnell et al; Qiu et al).

Body Weight and Mortality Outcomes

The majority of studies comparing BMI (kg/m^2) between survivors and non-survivors with COPD found survivors had a significantly higher BMI. Among studies comparing mortality rates between BMI categories, a lower risk of mortality was found as BMI classification increased. Likewise, those in the lowest BMI groups had higher mortality rates when compared to those in higher BMI groups. In studies evaluating BMI as a predictor of mortality, those in the lowest BMI categories consistently showed higher mortality risk when compared to those in higher BMI classifications. While increasing body weight appeared to be protective when BMI was evaluated as a continuous variable, studies evaluating BMI as a categorical variable found that a BMI of approximately 25.0-29.99 had a lower risk of mortality, when compared to both higher and lower BMI classifications.

- *BMI (mean ±SD) between survivors and non-survivors* (five studies): Five studies evaluated the difference in BMI between survivors and non-survivors with COPD. Four studies (Hallin et al, 2007; Marti et al, 2006; Ranieri et al, 2008; Tsimogianni et al, 2009) found significantly higher BMI in survivors vs. non-survivors. One study (Galesanu et al, 2014) found no differences in BMI between the groups.
- *Differences in Mortality Rates between BMI Categories* (six studies): Two studies (Abston et al, 2017, Lainscak et al, 2011) classified the BMIs of participants into quintiles or quartiles (respectively) and found a lower risk of mortality as BMI categorization increased. In three studies that were unadjusted for confounding variables (Koul et al, 2017; Pothirat, et al, 2007; Uh et al 2011), two studies found higher mortality in the lowest BMI groups (Koul, Pothirat). Koul found higher mortality 2 years after AECOPD in the lowest BMI group compared to the 23-24.9 group. Pothirat found higher mortality in the lowest BMI group compared to the next higher group (both with severe COPD). Uhl found NS differences in cumulative survival rate between all BMI groups. Zapatero found that the OB group (using ICD-9 codes) had a 51% reduction in risk of mortality, compared to NW group after adjusting for possible confounders in patients hospitalized for AECOPD.
- *BMI and weight status as a predictor of mortality* (12 studies):
  - Five studies evaluated BMI (or % reference weight) as a continuous variable as a predictor of mortality in subjects with COPD. Three studies (Galesanau et al, 2014; Ranieri et al, 2008; Schols et al, 2005) found BMI was a predictor of mortality in univariate analyses. Two studies (Jiang et al, 2017; Ranieri et al, 2008) reported BMI was a predictor of mortality in adjusted multivariate analysis. A fourth study (Galesanu et al, 2014) found NS association between BMI and mortality in adjusted multivariate analysis. The fifth study (Slinde et al, 2005) that used % reference weight did not find an association with mortality.
  - Seven studies evaluated BMI as a categorical variable as a predictor of mortality and adjusting for confounding variables (Hallin et al, 2007; Jiang et al, 2017; Marti et al, 2006; Piquet et al, 2013; Rutten et al, 2013, Tsimogianni et al, 2009; Yamauchi et al, 2014). Mortality risk was higher for subjects in the lowest BMI group (ranging from <18.5 to <25) when compared to higher BMI groups. Yamauchi found higher all-cause in-hospital mortality in the lowest BMI group and lower mortality in the higher BMI categories compared to the 18.5-22.9 group in an Asian population. Hallin found higher risk for 2-year mortality after AECOPD in all BMI categories compared to the 25-30 group. Marti found higher risk for both all-cause and respiratory mortality in the lower BMI groups compared to the 25-29.9 group and higher risk for all-cause mortality in the 20-24.9 group compared to the 25-29.9 groups. Piquet found no difference in risk for mortality between the lowest and 20-25 group, but a lower risk for mortality 48 months after AECOPD in the higher BMI categories. Rutten found the highest 2 and 3-year survival in subjects in BMI categories 25-29.99 compared to lower groups as well as those above 30. Jiang found a higher risk of mortality as BMI group classification decreased. Tsimogianni found that a BMI group of <25 had a higher risk of 3-year mortality.

- Recommendation Strength Rationale

  Conclusion statements supporting the recommendation are Grade I, *Good/Strong* and Grade II, *Fair.*

- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  What effect does body weight have on mortality outcomes in adults with COPD?

  What effect does body weight have on lung function outcomes in adults with COPD?

  - References

    Abston E, Comellas A, Reed R, Kim V, Wise R, Brower R, Fortis S, Beichel R, Bhatt S, Zabner J ,Newell J ,Hoffman E, Eberlein M. Higher BMI is associated with higher expiratory airflow normalised for lung volume (FEF25-75/FVC) in COPD. *BMJ Open Respiratory Research* 2017; 4:e000231

    Galesanu R, Bernard S, Marquis K, Lacasse Y, Poirier P, Bourbeau J, Maltais F. Obesity in chronic obstructive pulmonary disease: is fatter really better?. *Canadian Respiratory Journal.* 2014; 21:297-301

    Hallin R, Gudmundsson G, Suppli Ulrik C, Nieminen M, Gislason T, Lindberg E, Brøndum E, Aine T, Bakke P, Janson C. Nutritional status and long-term mortality in hospitalised patients with chronic obstructive pulmonary disease (COPD). *Respiratory Medicine.* 2007; 101:1,954-1,960.

    Jiang J, Zhao J, Yuan Y, Di S. Risk factors associated with acute exacerbation of chronic obstructive pulmonary disease: A retrospective analysis in 4,624 patients. *Biomedical Research.* 2017; 28:3,855-3,859.

    Koul P, Dar H, Jan R, Shah S, Khan U. Two-year mortality in survivors of acute exacerbations of chronic obstructive pulmonary disease: A North Indian study. *Lung India : Official Organ of Indian Chest Society* 2017; 34:511-516

    Lainscak M, von Haehling S, Doehner W, Sarc I, Jeric T, Ziherl K, Kosnik M, Anker S, Suskovic S. Body mass index and prognosis in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. *Journal of Cachexia, Sarcopenia and Muscle.* 2011; 2:81-86.

    Marti S, Muñoz X, Rios J, Morell F, Ferrer J. Body weight and comorbidity predict mortality in COPD patients treated with oxygen therapy. *The European Respiratory Journal.* 2006; 27:689-696.

    Piquet J, Chavaillon J, David P, Martin F, Blanchon F, Roche N. High-risk patients following hospitalisation for an acute exacerbation of COPD. *The European Respiratory Journal* 2013; 42:946-55

    Pothirat C, Phetsuk N, Deesomchok A, Theerakittikul T, Bumroongkit C, Liwsrisakun C, Inchai J. Clinical characteristics, management in real world practice and long-term survival among COPD patients of Northern Thailand COPD club members. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet.* 2007; 90:653-662.

    Ranieri P, Bianchetti A, Margiotta A, Virgillo A, Clini E, Trabucchi M. Predictors of 6-month mortality in elderly patients with mild chronic obstructive pulmonary disease discharged from a medical ward after acute nonacidotic exacerbation. *Journal of the American Geriatrics Society.* 2008; 56:909-913.

    Rutten E, Calverley P, Casaburi R, Agusti A, Bakke P, Celli B, Coxson H, Crim C, Lomas D, Macnee W, Miller B, Rennard S, Scanlon P, Silverman E, Tal-Singer R, Vestbo J, Watkins M, Wouters E. Changes in body composition in patients with chronic obstructive pulmonary disease: do they influence patient-related outcomes?. *Annals of Nutrition & Metabolism.* 2013; 63:239-247.

    Schols A, Broekhuizen R, Weling-Scheepers C, Wouters E. Body composition and mortality in chronic obstructive pulmonary disease. *The American Journal of Clinical Nutrition.* 2005; 82:53-59.

    Slinde F, Grönberg A, Engström C, Rossander-Hulthén L, Larsson S. Body composition by bioelectrical impedance predicts mortality in chronic obstructive pulmonary disease patients. *Respiratory Medicine.* 2005; 99:1,004-1,009.

    Tsimogianni A, Papiris S, Stathopoulos G, Manali E, Roussos C, Kotanidou A. Predictors of outcome after exacerbation of chronic obstructive pulmonary disease. *Journal of*

General Internal Medicine. 2009; 24:1,043-1,048.

Uh S-T, Lee JY, Koo SM, Kim YK, Kim KU, Park JS, Park SW, Jang AS, Kim DJ, Choi JS, Na JO, Suh KH, Kim YH, Park C-S,. The Survival Rate of Korean Patients with COPD with or without Acute Exacerbations. *Tuberculosis and Respiratory Diseases*. 2011; 70:474-481

Yamauchi Y, Hasegawa W, Yasunaga H, Sunohara M, Jo T, Takami K, Matsui H, Fushimi K, Nagase T. Paradoxical association between body mass index and in-hospital mortality in elderly patients with chronic obstructive pulmonary disease in Japan. *International Journal of Chronic Obstructive Pulmonary Disease*. 2014; 9:1,337-1,346.

Zapatero A, Barba R, Ruiz J, Losa J, Plaza S, Canora J, Marco J. Malnutrition and obesity: influence in mortality and readmissions in chronic obstructive pulmonary disease patients. *Journal of Human Nutrition and Dietetics : the Official Journal of the British Dietetic Association* 2013; 26:16-22.

Dimov D, Tacheva T, Koychev A, Ilieva V, Prakova G, Vlaykova T.. Obesity in Bulgarian patients with chronic obstructive pulmonary disease. *Chronic Respiratory Disease*. 2013; 10:215-222.

Lim J, Lee J, Kim J, Hwang Y, Kim T, Lim S, Yoo K, Jung K, Kim Y, Rhee C. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease*. 2017; 12:2,465-2,475.

O'Donnell D, Deesomchok A, Lam Y, Guenette J, Amornputtisathaporn N, Forkert L, Webb K.. Effects of BMI on static lung volumes in patients with airway obstruction. *Chest*. 2011; 140:461-468.

Qiu T, Tang Y, Xu Z, Xu D, Xiao J, Zhang M, Feng Y, Wang K. Association between body mass index and pulmonary function of patients with chronic obstructive pulmonary disease. *Chinese Medical Journal*. 2009; 122:1,110-1,111

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

  None.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Assessment of Energy Needs 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

  COPD: Estimating Resting Metabolic Rate (RMR)

  To calculate RMR in adults with COPD, the RDN may use either the World Health Organization [WHO (including height)] equation or the Harris-Benedict equation (HBE). If body composition is known (fat-free mass, body fat), the RDN may use the Westerterp equation. Limited evidence showed that the Westerterp equation has a prediction accuracy rate of 68%, followed by the WHO (including height; 63%) and Harris-Benedict (61%) equations.

  Rating: Weak
  Conditional

  COPD: Estimating Total Energy Expenditure (TEE)

  To calculate TEE in non-obese adults with COPD, the RDN may use 30kcal per kg body weight (BW) to estimate energy needs. Limited evidence suggests that 30kcal per kg body weight, in non-obese adults with COPD, produced an estimate that was not different from measured values on average, but whose variability was wide, indicating that estimation errors might be common and large.

  Rating: Weak
  Imperative

  - Risks/Harms of Implementing This Recommendation

    Predictive equations may under- or over-estimate energy needs in adults with COPD.

  - Conditions of Application

    - The Westerterp equation requires body composition measurements, fat-free mass (FFM) and body fat (BF), for calculation of RMR. Thus, its utility in clinical care may be limited.
    - The *COPD: Estimating Total Energy Expenditure (TEE)* recommendation applies to non-obese adults with COPD. Clinical judgement should be used in applying the recommendation to individuals with a BMI at or above 30kg/m^2.
    - The RDN should use clinical judgement in determining the body weight value used in calculations. Use of adjustments to body weight for obesity or volume status were not mentioned anywhere in the available studies.
    - For both RMR and TEE predictive equations, errors in individual estimates may be high. Calculation of energy needs (estimation) using a predictive equation is a starting point to determine energy requirements. Changes in body weight should be monitored as an indicator that energy needs should be re-evaluated. Over time, the monitoring of body weight and composition against energy intake is probably the most meaningful expression of energy requirements in COPD. It is important to remember in this type of assessment that if adverse changes in body weight or composition are occurring, equal attention should be paid to the possibility that the patient is not consuming the target intake or that the target intake is not correct.

  - Potential Costs Associated with Application

    Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.

  - Recommendation Narrative

    A total of five studies were included in the evidence analysis supporting the recommendations:

    - Three cross-sectional studies: One positive-quality (Slinde et al, 2011); one neutral-quality (Farooqi et al, 2015); one negative-quality (Ramos et al, 2016)]
    - Two diagnostic, validity or reliability studies: Both neutral-quality (Nordenson et al, 2010; Slinde et al, 2008).

    Predictive Equations for Estimating RMR: A total of 11 equations were tested for validity in predicting RMR in adults with COPD. Two of these [Moore & Angelillo (MAE); Nordenson] were equations developed specifically for COPD patients, while the other equations were developed for healthy adults [Harris-Benedict (HBE); Mifflin St. Jeor (MSJE); Westerterp; de Oliveira; Owen; four variations of Food and Agriculture Organization of the United Nations/World Health Organization/United Nations University (FAO/WHO/UNU)], which were WHO (including height), WHO (omitting height), Nordic Nutrition Recommendation (NNRE) and the Schofield equation. In two of the studies (Farooqi et al, 2015; Slinde et al, 2011) these equations were evaluated as a starting point for estimating total energy expenditure (TEE).

    - *Accuracy:* Four of the 11 equations for predicting RMR were tested for accuracy, but only in one study (Slinde et al, 2008). Slinde et al, 2008, found that the Westerterp

equation yielded an accuracy rate of 68%, followed by the WHO (including height) equation (63%) and HBE (61%). The MAE had the lowest accuracy rate (51%).

- *Limit of Agreement (LOA):* LOA was reported for nine equations. LOA as a percentage of the mean between measured and predicted RMR were -23% to +18% for the Westerterp equation (Slinde et al, 2008), about -28% to +10% for the MAE (in this case, the negative value is an overestimation) (Slinde et al, 2008), less than 25% for WHO (including height) equation and HBE, -45% to +40% for the de Oliveira equation (Ramos et al, 2016), -53% to +33% for the Owen equation (Ramos et al, 2016), -65% to +13% for the MSJE (Ramos et al, 2016), ±19% for the Nordenson equation (Nordenson et al, 2010) and for WHO (omitting height) equation, +18% (Slinde et al, 2011), to as wide as -66% to +24% (Ramos et al, 2016).
- *Bias:* Evidence suggests that the only unbiased estimator of RMR in adults with COPD was the de Oliveira equation. Four other equations were probably[1] unbiased. These included the HBE and Westerterp equations, which might overestimate RMR and the Nordenson and WHO (including height) equations, which might underestimate RMR. Two equations (Owen and MSJE) were biased toward underestimation of RMR. The remaining four equations were probably[1] biased toward overestimation of RMR [MAE, NNRE, Schofield and WHO (omitting height) equations]. Evidence for the WHO (omitting height) equation suggests it might also underestimate RMR in adults with COPD.

  [1]Bias was not reported directly in these studies but is inferred from mean predicted RMR compared to mean measured RMR.

- Thus, the WHO (including height) equation and HBE seem to be equivalent to one another by the parameters of accuracy rate and LOA. If body composition measurements are known, then Westerterp is a better choice for calculation of RMR, because it yields a higher accuracy rate.

Predictive Equations for Estimating TEE: Two studies (Farooqi et al, 2015; Slinde et al, 2011) tested three methods for calculating TEE in adults with COPD. In the first method, a pedometer was used to estimate physical activity to compare against doubly labeled water (DLW) (Farooqi et al, 2015). In this method, a multiplier to RMR was assigned based on the number of steps taken and the multiplier was applied to six RMR equations [WHO (omitting height); Schofield; HBE; MAE; NNRE; Nordenson)]. In the other study, motion and position sensors were used as the criterion method to measure TEE. For prediction purposes, two methods were used: The first was a simple ratio of 30kcal per kg body weight (BW); the second was to compute RMR using the WHO (omitting height) equation and then multiplying by 1.7 to calculate TEE (Slinde et al, 2011).

- *Accuracy:* Only one of the two studies reported accuracy rate (Farooqi et al, 2015). Accuracy rate for the WHO (omitting height) equation x PAL was of 67%, compared to 56% for the Schofield equation x PAL, 50% for HBE x PAL, MAE x PAL and NNRE x PAL, and 21% for the Nordenson equation x PAL.
- *LOA:* The only estimation methods for which LOA was computed were 30kcal per kg and WHO (omitting height) x 1.7 (Slinde et al, 2011). LOA for both of these methods was 956kcal per day (-48; +48% of the mean between predicted and measured TEE)
- *Bias:* The WHO (omitting height) x PAL and the MAE x PAL were probably[2] unbiased, while the Schofield x PAL, HBE x PAL, NNRE x PAL and Nordenson x PAL equations were probably[2] biased (toward underestimation) (Farooqi et al, 2016). An estimate of 30kcal per kg BW yielded a mean difference from measured TEE of 71kcal per day and so was probably unbiased[2], whereas another predictive method of WHO (omitting height) x 1.7 probably[2] was biased toward overestimation, based on a mean difference from measured TEE of 319kcal per day (Slinde et al, 2011).

  [2]Bias was not reported directly in these studies, but is inferred from mean predicted TEE compared to mean measured TEE.

- Recommendation Strength Rationale
  - Conclusion statement supporting the recommendations is Grade III (Limited/Weak)
  - None of the studies evaluating TEE methods were tested more than once
  - Synthesis of results for RMR and TEE was challenging because large gaps exist in the available evidence (small numbers of studies with small sample sizes, inconsistency in the types of statistical treatments from study to study making data difficult to aggregate).
- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  OVERALL: If measurements are not available, what are the best methods to predict energy needs in adults with COPD?

  - References

    Farooqi N, Slinde F, Carlsson M, Håglin L, Sandström T. Predicting energy requirement with pedometer-determined physical-activity level in women with chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease* 2015; 10:1129-37

    Nordenson A, Grönberg A, Hulthén L, Larsson S, Slinde F. A validated disease specific prediction equation for resting metabolic rate in underweight patients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2010; 5:271-6

    Ramos F, Rossato L, Ramires B, Pimentel G, Venâncio L, Orsatti F, de Oliveira E. Comparison of predictive equations of resting energy expenditure in older adults with chronic obstructive pulmonary disease. *Revista Portuguesa de Pneumologia* 2016; 23:40-42

    Slinde F, Svensson A, Gronberg AM, Nordenson N, Hulthen L, Larsson SC. Reproducibility of indirect calorimetry in underweight patients with chronic obstructive pulmonary disease. *European e-Journal of Clinical Nutrition and Metabolism* 2008; 3:40-45

    Slinde F, Gronberg A, Svantesson U, Hulthen L, Larsson S. Energy expenditure in chronic obstructive pulmonary disease-evaluation of simple measures. *European Journal of Clinical Nutrition* 2011; 65:1309-13

  - References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

    None.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Assessment of Serum 25(OH)D Status 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

  COPD: Assessment of Serum 25(OH)D Status

  The RDN should assess serum 25(OH)D levels in adults with COPD as part of a routine nutrition assessment. Evidence from 60% of studies reviewed, found positive associations between serum 25(OH)D and lung function measures.

  Rating: Fair
  Imperative

COPD: Assessment of Exacerbations

If an adult with COPD is having two or more exacerbations per year, the RDN should assess 25(OH)D levels. Limited evidence of vitamin D supplementation in adults with COPD supports improved exacerbation outcomes in those with baseline serum 25(OH)D levels ≤10ng per ml.

Rating: Fair
Conditional

- Risks/Harms of Implementing This Recommendation

  There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application

  - The recommendation *COPD: Assessment of Exacerbations* refers to COPD patients with frequent exacerbations, defined as two or more exacerbations per year (Hurst et al, 2010; Le Rouzic et al, 2018)
  - If necessary data are not available, the RDN should use professional judgment to request or obtain additional data
  - Exacerbations are clinically defined as episodes of increasing respiratory symptoms, particularly dyspnea, cough and sputum production and increased sputum purulence (Wedzicha et al, 2017). The patient perception of an exacerbation is seeking treatment for symptoms; the research criteria is treatment with antibiotics or addition of increased inhaled or systemic steroids.
  - Achievement of normal serum 25(OH)D levels may not be possible in all instances. Therefore, optimizing serum 25(OH)D levels is the goal (Rusinska et al, 2018).

- Potential Costs Associated with Application

  - Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN
  - Costs may be incurred due to initial lab testing to evaluate serum 25(OH)D levels.

- Recommendation Narrative

  COPD: Assessment of Serum 25(OH)D Status

  A total of 29 papers from 28 studies provided evidence supporting the recommendation *COPD: Assessment of Serum 25(OH)D Status*.

  - A total of 14 cross-sectional studies: One positive-quality (Romme et al, 2013), twelve neutral-quality (Azargoon et al, 2011; El-Shafey and El-Srougy, 2014; Hashim Ali Hussein et al, 2015; Janssens et al, 2010; Jolliffee et al, 2018; Mahlin et al, 2014; Mekov et al, 2015; Monadi et al, 2012; Park et al, 2015; Park et al 2016; Persson et al 2012; Shaneen et al 2011) and one negative-quality (Yang et al, 2015)
  - Six prospective cohort studies: Three positive-quality (Kunisaki et al, 2012; Persson et al, 2015; Puhan et al, 2014) and three neutral-quality (Holmgaard et al, 2013; Jung et al, 2015; Quint et al, 2012)
  - Four retrospective cohort studies: Three positive-quality (Berg et al, 2013; Malinovschi et al, 2014; Mekov et al, 2016) and one neutral-quality (Moberg et al, 2014)
  - Two randomized controlled trials (RCT): One positive-quality (Sanjari et al, 2106) and one neutral-quality (Yumrutepe et al, 2015)
  - One neutral-quality before-after study (Said and Abd-Einaeem, 2015)
  - One neutral-quality descriptive study (Gouda et al, 2016)
  - One neutral-quality case-control study (Kunisaki et al, 2011).

  The overall findings were as follows:

  - *Lung Function (LF)* (23 studies): A total of 14 studies found significant relationships between serum 25(OH)D and LF outcomes; i.e., as serum 25(OH)D increased, LF outcomes improved (Azargoon et al, 2011; Berg et al, 2013; El-Shafey and El-Srougy, 2014; Gouda et al, 2016; Janssens et al, 2010; Jolliffee et al, 2018; Jung et al, 2015; Park et al, 2016; Persson et al, 2012; Persson et al, 2015; Romme et al, 2013; Said and Abd-Elnaeem, 2015; Yang et al, 2015; Yumrutepe et al, 2015). Nine studies did not find significant relationships between serum 25(OH)D and LF outcomes (Hashim Ali Hussein et al, 2015; Holmgaard et al, 2013; Kunisaki et al, 2011; Mahlin et al, 2014; Malinovschi et al, 2014; Monadi et al, 2012; Park et al, 2015; Sanjari et al, 2016; Shaheen et al, 2011).
  - *Acute Exacerbations (AE)* (11 studies): Four studies found significant relationships between serum 25(OH)D and AE outcomes; i.e., as serum 25(OH)D increased, AE outcomes improved (Gouda et al, 2016; Malinovschi et al, 2014; Persson et al, 2015; Yang et al, 2015). Seven studies did not find significant relationships between serum 25(OH)D and AE outcomes (Jung et al, 2015; Kunisaki et al, 2011; Mekov et al, 2015; Moberg et al, 2014; Persson et al, 2012; Puhan et al, 2014; Quint et al, 2012).
  - *Mortality* (five studies): NS relationships were found in any of the studies (Holmgaard et al, 2013; Mekov et al, 2016; Moberg et al, 2014; Persson et al, 2015; Puhan et al, 2014).

  COPD: Assessment of Exacerbations

  A total of eight studies were included in the evidence analysis supporting the recommendation *COPD: Assessment of Exacerbations.* Two of the studies evaluated exacerbation outcomes in those with serum 25(OH)D under 10ng per ml.

  - Six RCTs: Four positive-quality (Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Sanjari et al, 2016), one neutral-quality (Khan et al, 2017) and one negative-quality (Zendendel et al, 2015)
  - Two before-after studies: Both neutral-quality (Rezk et al, 2015; Said and Abd-Elnaeem, 2015).

  Seven studies tested oral vitamin D_3 (cholecalciferol) ranging from 1, 200 IU daily for six months; subjects and controls could also take 400 IU vitamin D_3 daily (Rafiq et al, 2017) to 120, 000 IU every two months for 12 months (Martineau et al, 2015). One study administered 200, 000 IU cholecalciferol intramuscularly (IM) every four weeks for six months (Said and Abd-Elnaeem, 2015). All papers either cited the Endocrine Society Clinical Practice Guideline (ESG) (Holick et al, 2011) for serum 25(OH)D classifications or did not define classifications. In addition to the ESG reference, one study (Lehouck et al, 2012) defined "severe" vitamin D deficiency as serum 25(OH)D levels under 10ng per ml.

  Seven studies evaluated LF outcomes (Lehouck et al 2012; Martineau et al, 2015; Rafiq et al, 2017; Rezk et al, 2015; Sanjari et al, 2016; Said and Abd-Elnaeem, 2015; Zendedel et al, 2015). Six studies evaluated acute exacerbation (AE) outcomes (Khan et al, 2017; Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Rezk et al, 2015; Zendedel et al, 2015).

  Five studies of vitamin D supplementation included subjects' pre- and post-supplementation levels, allowing changes in vitamin D status due to supplementation to be assessed. Results according to baseline (BL) and post-supplementation improvements in vitamin D status (ESG categories) are as follows:

  - *Deficient to sufficient 25(OH)D:* Supplementation with 1, 200 IU D_3 daily for six months (plus 400 IU daily, if desired) resulted in no impact on LF or AE outcomes (Rafiq et al, 2012). Supplementation with 100, 000 IU D_3 every four weeks over 12 months resulted in a decrease in AE rate in a sub-group of subjects with "*severe deficiency*" [25(OH)D under 10ng per ml] (Lehouck et al, 2012).
  - *Insufficient to sufficient 25(OH)D:* Supplementation with 100, 000 IU D_3 every four weeks over 12 months resulted in no impact on AE or LF outcomes (Lehouck et al, 2012). Supplementation with either 5, 000 IU D_3 or 0.25mcg calcitriol every four weeks over 12 months resulted in no impact on LF outcomes (Sanjari et al, 2016).
  - *Deficient to insufficient 25(OH)D:* Supplementation with 50, 000 IU D_3 per week for eight weeks, then 800 IU daily for 12 months resulted in a decrease in number of AEs and an improvement in maximum voluntary ventilation, but no impact on other LF outcomes in subjects with 25(OH)D under 10ng per ml at BL (Rezk et al, 2015). Supplementation with 120, 000 IU D_3 every two months over 12 months resulted in improvement in AE severity and symptoms, but had no impact on other AE or LF outcomes (Martineau et al, 2015).

  The remaining three studies did not report subjects' post-supplementation vitamin D status. One study (Said and Abd-Elnaeem, 2015) reported BL vitamin D status according to ESG categories, but did not report post-supplementation status. The second study (Khan et al, 2017) reported BL vitamin D status of subjects and controls combined and did not report pre- and post-supplementation status of subjects only. Finally, the last study (Zendedel et al, 2015) did not report either BL or post-supplementation vitamin D status.

  - *Insufficient 25(OH)D (subjects + controls):* Supplementation with 2, 000 IU D_3 per day for six months resulted in reduced AEs (Kahn et al, 2017). Supplementation with 200, 000 IU D_3 IM every four weeks for six months, resulted in no impact in LF outcomes (Said and Abd-Elnaeem, 2015)
  - *Unknown 25(OHD):* Supplementation with 100, 000 IU D_3 every month for six months resulted in improvement in LF outcomes and a reduction in AEs (Zendedel et al, 2015).

- Recommendation Strength Rationale
  - Conclusion statements supporting both recommendations are Grade II, *Fair*
  - For recommendation *COPD: Assessment of Exacerbations*, synthesis of the results was challenging due to lack of consistency in vitamin D dosing, dosing frequency and delivery routes, length of intervention and baseline serum 25(OH)D levels.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  What associations exist between serum 25(OH)D levels and mortality, lung function and exacerbation outcomes in adults with COPD?

  Does vitamin D supplementation improve lung function and exacerbation outcomes in adults with COPD?

  - References

Azargoon AR, Moghadam PK, Shokrollahi S, Ebrahimzadeh F, Pournia Y. . Relationship between FEV1 and 25-hydroxy Vitamin D in patients with chronic obstructive pulmonary disease. *Trends in Medical Research* 2011; 6:184-190

Berg I, Hanson C, Sayles H, Romberger D, Nelson A, Meza J, Miller B, Wouters E, Macnee W, Rutten E ,Romme E, Vestbo J, Edwards L, Rennard S. Vitamin D, vitamin D binding protein, lung function and structure in COPD. *Respiratory Medicine* 2013; 107:1578-88

Basem I, El-Shafey and Hesham A. El-Srougy B. Does serum 25 hydroxy vitamin D level play a role in COPD?. *Egyptian Journal of Chest Diseases and Tuberculosis* 2014; 63:43-47

Essam Gouda, Mohamed Zidan, Gharraf Heba, Doreene Nazeih Younan, Samar Mohamed. Pattern of vitamin D in patients with chronic obstructive pulmonary diseases and in patients with bronchial asthma. *Egyptian Journal of Chest Diseases and Tuberculosis* 2016; 65:389-396

Hashim Ali Hussein S, Nielsen L, Konow Bøgebjerg Dolberg M, Dahl R. Serum magnesium and not vitamin D is associated with better QoL in COPD: A cross-sectional study. *Respiratory Medicine* 2015; 109:727-33

Holmgaard D, Mygind L, Titlestad I, Madsen H, Fruekilde P, Pedersen S, Pedersen C. Serum vitamin D in patients with chronic obstructive lung disease does not correlate with mortality--results from a 10-year prospective cohort study. *PloS One* 2013; 8:e53670

Janssens W, Bouillon R, Claes B, Carremans C, Lehouck A, Buysschaert I, Coolen J, Mathieu C, Decramer M, Lambrechts D. Vitamin D deficiency is highly prevalent in COPD and correlates with variants in the vitamin D-binding gene. *Thorax* 2010; 65:215-20

Jolliffe D, James W, Hooper R, Barnes N, Greiller C, Islam K, Bhowmik A, Timms P, Rajakulasingam R, Choudhury A, Simcock D, Hyppönen E, Walton R, Corrigan C, Griffiths C, Martineau A. Prevalence, determinants and clinical correlates of vitamin D deficiency in patients with Chronic Obstructive Pulmonary Disease in London, UK. *The Journal of Steroid Biochemistry and Molecular Biology* 2018; 175:138-145

Jung J, Kim Y, Kim S, Kim H, Oh Y, Lee S, Seo J, Lee S. Relationship of vitamin D status with lung function and exercise capacity in COPD. *Respirology (Carlton, Vic.)* 2015; 20:782-9

Kunisaki K, Niewoehner D, Singh R, Connett J. Vitamin D status and longitudinal lung function decline in the Lung Health Study. *The European Respiratory Journal* 2011; 37:238-43

Kunisaki K, Niewoehner D, Connett J. Vitamin D levels and risk of acute exacerbations of chronic obstructive pulmonary disease: a prospective cohort study. *American Journal of Respiratory and Critical Care Medicine* 2012; 185:286-90

Måhlin C, von Sydow H, Osmancevic A, Emtner M, Grönberg A, Larsson S, Slinde F. Vitamin D status and dietary intake in a Swedish COPD population. *The Clinical Respiratory Journal* 2014; 8:24-32

Malinovschi A, Masoero M, Bellocchia M, Ciuffreda A, Solidoro P, Mattei A, Mercante L, Heffler E, Rolla G, Bucca C. Severe vitamin D deficiency is associated with frequent exacerbations and hospitalization in COPD patients. *Respiratory Research* 2014; 15:131

Mekov E, Slavova Y, Tsakova A, Genova M, Kostadinov D, Minchev D, Marinova D, Tafradjiiska M. Vitamin D Deficiency and Insufficiency in Hospitalized COPD Patients. *PloS One* 2015; 10:e0129080

Mekov E, Slavova Y, Tsakova A, Genova M, Kostadinov D ,Minchev D, Marinova D, Boyanov M. One-year mortality after severe COPD exacerbation in Bulgaria. *PeerJ* 2016; 4:e2788

Moberg M, Vestbo J, Martinez G, Lange P, Ringbaek T. Prognostic value of C-reactive protein, leukocytes, and vitamin d in severe chronic obstructive pulmonary disease. *The Scientific World Journal* 2014; 2014:140736

Monadi M, Heidari B, Asgharpour M, Firouzjahi A, Monadi M, Ghazi Mirsaied M. Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (COPD). *Caspian Journal of Internal Medicine* 2012; 3:451-5

Park J, Park H, Jung H, Lee S, Koo H. Parathyroid Hormone as a Novel Biomarker for Chronic Obstructive Pulmonary Disease: Korean National Health and Nutrition Examination Survey. *PloS One* 2015; 10:e0138482

Park Y, Kim Y, Kang Y, Shin J, Oh Y, Seo J, Jung J, Lee S. Relationship between vitamin D-binding protein polymorphisms and blood vitamin D level in Korean patients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2016; 11:731-8

Persson L, Aanerud M, Hiemstra P, Hardie J, Bakke P, Eagan T. Chronic obstructive pulmonary disease is associated with low levels of vitamin D. *PloS One* 2012; 7:e38934

Persson L, Aanerud M, Hiemstra P, Michelsen A, Ueland T, Hardie J, Aukrust P, Bakke P, Eagan T. Vitamin D, vitamin D binding protein, and longitudinal outcomes in COPD. *PloS One* 2015; 10:e0121622

Puhan M, Siebeling L, Frei A, Zoller M, Bischoff-Ferrari H, Ter Riet G. No association of 25-hydroxyvitamin D with exacerbations in primary care patients with COPD. *Chest* 2014; 145:37-43

Quint J, Donaldson G, Wassef N, Hurst J, Thomas M, Wedzicha J. 25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease. *BMC Pulmonary Medicine* 2012; 12:28

Romme E, Rutten E, Smeenk F, Spruit M, Menheere P, Wouters E. Vitamin D status is associated with bone mineral density and functional exercise capacity in patients with chronic obstructive pulmonary disease. *Annals of Medicine* 2013; 45:91-6

Said AF and Abd-Elnaeem EA. Vitamin D and chronic obstructive pulmonary disease. *Egyptian Journal of Chest Diseases and Tuberculosis* 2015; 64:67-73

Sanjari M, Soltani A, Habibi Khorasani A, Zareinejad M. The effect of vitamin D on COPD exacerbation: a double blind randomized placebo-controlled parallel clinical trial. *Journal of Diabetes and Metabolic Disorders* 2016; 15:33

Shaheen S, Jameson K, Robinson S, Boucher B, Syddall H, Sayer A, Cooper C, Holloway J, Dennison E. Relationship of vitamin D status to adult lung function and COPD. *Thorax*

2011; 66:692-8

Yang Y, Guo Y, Zhang H, Sun T. Antimicrobial peptide LL-37 circulating levels in chronic obstructive pulmonary disease patients with high risk of frequent exacerbations. *Journal of Thoracic Disease* 2015; 7:740-5

Yumrutepe T, Aytemur Z, Baysal O, Taskapan H, Taskapan C, Hacievliyagil S. Relationship between vitamin D and lung function, physical performance and balance on patients with stage I-III chronic obstructive pulmonary disease. *Revista da Associacao Medica Brasileira (1992)* 2015; 61:132-8

Khan D,Ullah A,Randhawa F,Iqtadar S,Butt N,Waheed K. Role of Vitamin D in reducing number of acute exacerbations in Chronic Obstructive Pulmonary Disease (COPD) patients. *Pakistan journal of medical sciences* 2017; 33:610-614

Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, Decallonne B, Bouillon R, Decramer M, Janssens W. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: a randomized trial. *Annals of Internal Medicine* 2012; 156:105-14

Martineau A, James W, Hooper R, Barnes N, Jolliffe D, Greiller C, Islam K, McLaughlin D, Bhowmik A, Timms P, Rajakulasingam R, Rowe M, Venton T, Choudhury A, Simcock D, Wilks M, Degun A, Sadique Z, Monteiro W, Corrigan C, Hawrylowicz C, Griffiths C. Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease (ViDiCO): a multicentre, double-blind, randomised controlled trial. *The Lancet. Respiratory Medicine* 2015; 3:120-130

Rafiq R, Prins H, Boersma W, Daniels J, den Heijer M, Lips P, de Jongh R. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: a pilot trial. *International Journal of Chronic Obstructive Pulmonary Disease* 2017; 12:2583-2592

Rezk NA, Yehia AA, Hewidy, AA. Effect of vitamin D replacement in chronic obstructive pulmonary disease patients with vitamin D deficiency. *Egyptian Journal of Chest Diseases and Tuberculosos* 2015; 64:353-357

Zendedel A, Gholami M, Anbari K, Ghanadi K, Bachari E, Azargon A. Effects of Vitamin D Intake on FEV1 and COPD Exacerbation: A Randomized Clinical Trial Study. *Global Journal of Health Science* 2015; 7:243-8

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011 Jul; 96 (7): 1, 911-1, 930. doi: 10.1210/jc.2011-0385. Epub 2011 Jun 6. Erratum in: *J Clin Endocrinol Metab.* 2011 Dec; 96 (12): 3, 908. PMID: 21646368.

Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, Miller B, Lomas DA, Agusti A, Macnee W, Calverley P, Rennard S, Wouters EF, Wedzicha JA. Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators. Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med.* 2010 Sep 16; 363 (12): 1, 128-1, 138. doi: 10.1056/NEJMoa0909883. PMID: 20843247.

Le Rouzic O, Roche N, Cortot AB, Tillie-Leblond I, Masure F, Perez T, Boucot I, Hamouti L, Ostinelli J, Pribil C, Poutchnine C, Schück S, Pouriel M, Housset B. Defining the "Frequent Exacerbator" Phenotype in COPD: A Hypothesis-Free Approach. *Chest.* 2018 May; 153 (5): 1, 106-1, 115. doi: 10.1016/j.chest.2017.10.009. Epub 2017 Oct 17. PMID: 29054347.

Rusinska A, Pludowski P, Walczak M, Borszewska-Kornacka MK, Bossowski A, Chlebna-Sokól D, Czech-Kowalska J, Dobrzanska A, Franek E, Helwich E, Jackowska T, Kalina MA, Konstantynowicz J, Ksiazyk J, Lewinski A, Lukaszkiewicz J, Marcinowska-Suchowierska E, Mazur A, Michalus I, Peregud-Pogorzelski J, Romanowska H, Ruchala M, Socha P, Szalecki M, Wielgos M, Zwolinska D, Zygmunt A. Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland - Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies - 2018 Update. *Front Endocrinol (Lausanne).* 2018 May 31; 9: 246. doi: 10.3389/fendo.2018.00246. eCollection 2018. Review. PMID: 29904370.

Wedzicha JA, Miravitlles M, Hurst JR, Calverley PM, Albert RK, Anzueto A, Criner GJ, Papi A, Rabe KF, Rigau D, Sliwinski P, Tonia T, Vestbo J, Wilson KC, Krishnan JA. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. *Eur Respir J.* 2017 Mar 15; 49 (3). pii: 1600791. doi: 10.1183/13993003.00791-2016. Print 2017 Mar. PMID: 28298398.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Medical Nutrition Therapy 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

COPD: Medical Nutrition Therapy (MNT)

The registered dietitian nutritionist (RDN) should provide MNT to adults with COPD to improve patient outcomes. Evidence indicates that MNT intervention provided by an RDN (or international equivalent) as part of a multidisciplinary program was effective in improving body weight status, quality of life, exercise capacity and body composition outcomes in adults with COPD.

Rating: Strong
Imperative

- Risks/Harms of Implementing This Recommendation

  There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application

  There are no conditions that may limit the application of the recommendation.

- Potential Costs Associated with Application

  - Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.
  - For group counseling, such as pulmonary rehabilitation, adequate staffing with expertise in the major component areas of COPD management and adequate space for counseling are required.
  - Cognitive ability and healthy literacy may impact the learning process (Blackstock et al, 2018). Therefore, an understanding of patient needs should be incorporated into the intervention format (Blackstock et al, 2018). Training and educational materials should be appropriate, and culturally relevant for each participant.
  - Absenteeism and attrition may impact the success of counseling. Participation may be limited by the location of counseling (distance from home or workplace), the duration length and frequency of sessions.
  - To optimize outcomes, identification of factors that may hinder learning (e.g., conditions such as anxiety or depression) should be identified and addressed (Blackstock et al, 2018).

- Recommendation Narrative

  A total of six papers reporting the results of five different studies were included in the evidence analysis supporting the recommendation:

  - One positive quality randomized controlled trial (RCT) (van Wetering et al, 2010)
  - Two positive quality papers from one before-after clinical trial [McDonald et al, 2016; McLaughlin et al, 2017 (which was a secondary analysis)]
  - One positive quality non-controlled trial (Farooqi et al, 2011)
  - One neutral quality non-randomized trial (Norrhall et al, 2009)
  - One neutral quality prospective cohort (Gale et al, 2011).

  Studies evaluated COPD subjects receiving MNT intervention by an RDN (or international equivalent), compared to COPD control groups receiving standard or usual care. The studies evaluated multidisciplinary interventions such as pulmonary rehab, which included MNT. All studies included individualized MNT in a one-to-one session (e.g., home visits, nutrition assessment and counseling) and as part of group education.

  MNT and Weight Status, Quality of Life, Exercise Capacity Outcomes

  Post-intervention results from six papers (five studies) (Farooqi et al, 2011; Gale et al, 2011; McDonald et al, 2016; McLoughlin et al, 2017; Norrhall et al, 2009; van Wetering et al, 2010 were as follows:

  - *Weight status* (six papers; five studies): Two papers reported improvements in body weight (Farooqi et al, 2011; McDonald et al, 2016) and percentage ideal body weight (Farooqi et al, 2011). Three papers reported body mass index (BMI) maintenance or improvements in BMI (McDonald et al, 2016; Norhall et al, 2009; van Wetering et al, 2010), while one paper did not report improvements in BMI (Gale et al, 2011). One paper did not find differences in percentage weight change (McLoughlin et al, 2017).
  - *Quality of life (QOL)* (five papers; four studies): Four papers reported improvements in St. George's Respiratory Questionnaire scores (Gale et al, 2011; McDonald et al, 2016; van Wetering et al, 2010) and Three Factor Eating Questionnaire scores (McLoughlin et al, 2017), while one paper did not find significant improvements in Chronic Respiratory Disease Questionnaire scores (Norrhall et al, 2009).
  - *Exercise capacity* (five papers; four studies): All papers reported improvements in quadriceps average power (van Wetering et al, 2010), Short Physical Performance Battery tests (McDonald et al, 2016), total physical activity (McLoughlin et al, 2017), and walking distance, as measured by 6-minute walking distance (6MWD) (McDonald et al, 2016; van Wetering et al, 2010), 12MWD (Farooqi et al, 2011) and incremental shuttle walk test (Gale et al, 2011). One paper reported improvements in hand-grip strength (Farooqi et al, 2011).

  MNT and Body Composition and Lung Function Outcomes

  Post-intervention results of four papers (three studies) (McDonald et al, 2016; McLaughlin et al, 2017; Norrhall et al, 2009; van Wetering et al, 2010) were as follows:

  - *Body composition* (three papers; two studies): All reported improvements in body fat mass (McDonald et al, 2016), fat-free mass (van Wetering et al, 2010), percentage body fat (McDonald et al, 2016), waist circumference (McLaughlin et al, 2017) and waist to hip ratio (McDonald et al, 2016). One study did not find differences in skeletal muscle mass or appendicular skeletal muscle mass index (McDonald et al, 2016).
  - *Lung function or respiratory impairment* (three studies): One study reported improvements in maximum inspiratory mouth pressure (PI_{max}) (van Wetering et al, 2010), one study reported improvements in forced vital capacity (FVC) (McDonald et al, 2016), while one study did not find improvements in FVC (Norhall et al, 2009). Studies did not show improvements in forced expiratory volume in 1 minute (FEV_1) (McDonald et al, 2016; Norrhall et al, 2009) and FEV_1/FVC, functional residual capacity, residual volume, expiratory reserve volume, or total lung capacity (McDonald et al, 2016). No negative outcomes in lung function parameters were found.

- Recommendation Strength Rationale

  - Conclusion statements supporting the recommendation are Grade I, *Good/Strong* (body weight status, QOL, exercise capacity outcomes) and Grade II, *Fair* (lung function, body composition outcomes).
  - All studies were conducted outside the U.S.

- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  What is the effectiveness of medical nutrition therapy as part of a multidisciplinary program on body weight, quality of life and exercise capacity outcomes in adults with COPD?

  What is the effectiveness of medical nutrition therapy as part of a multidisciplinary program on body composition and lung function outcomes in adults with COPD?

  - References

    Farooqi N, Nordström L, Lundgren R, Sandström T, Håglin L. Changes in body weight and physical performance after receiving dietary advice in patients with chronic obstructive pulmonary disease (COPD): 1-year follow-up. *Archives of Gerontology and Geriatrics* 2011; 53:70-5

    Gale N, Duckers J, Enright S, Cockcroft J, Shale D, Bolton C. Does pulmonary rehabilitation address cardiovascular risk factors in patients with COPD?. *BMC Pulmonary Medicine* 2011; 11:20

    McDonald V, Gibson P, Scott H, Baines P, Hensley M, Pretto J, Wood L. Should we treat obesity in COPD? The effects of diet and resistance exercise training. *Respirology (Carlton, Vic.)* 2016; 21:875-82

    McLoughlin RE, McDonald VM, Gibson PG, Scott HA, Hensley MJ, MacDonald-Wicks L, and Wood LG. The Impact of a Weight Loss Intervention on Diet Quality and Eating Behaviours in People with Obesity and COPD. *Nutrients* 2017; 9:1147

    Norrhall M, Nilsfelt A, Varas E, Larsson R, Curiac D, Axelsson G, Månsson J, Brisman J, Söderström A, Björkelund C, Thorn J. A feasible lifestyle program for early intervention in patients with chronic obstructive pulmonary disease (COPD): a pilot study in primary care. *Primary Care Respiratory Journal* 2009; 18:306-12

    van Wetering C, Hoogendoorn M, Broekhuizen R, Geraerts-Keeris G, De Munck D, Rutten-van Mölken M, Schols A. Efficacy and costs of nutritional rehabilitation in muscle-wasted patients with chronic obstructive pulmonary disease in a community-based setting: a prespecified subgroup analysis of the INTERCOM trial. *Journal of the American Medical Directors Association* 2010; 11:179-87

  - References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

    Blackstock FC, Lareau SC, Nici L, ZuWallack R, Bourbeau J, Buckley M, Durning SJ, Effing TW, Egbert E, Goldstein RS, Kelly W, Lee A, Meek PM, and Singh S; on behalf of the American Thoracic Society, Thoracic Society of Australia and New Zealand, Canadian Thoracic Society, and British Thoracic Society. Chronic Obstructive Pulmonary Disease Education in Pulmonary Rehabilitation. An Official American Thoracic Society/Thoracic Society of Australia and New Zealand/Canadian Thoracic Society/British Thoracic Society Workshop Report. 2018. *Ann Am Thorac Soc* Vol 15, No 7, 769–784, Jul 2018.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Energy Prescription 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

COPD: Energy Prescription

For adults with COPD, the RDN should individualize the calorie prescription based on a nutrition assessment of energy intake, body weight and estimated energy needs to achieve and maintain an optimal weight status. Strong evidence indicates that the lowest body mass index (BMI) groups had higher mortality rates when compared to higher BMI groups. A BMI classification of approximately 25.0kg/m^2 to 29.99kg/m^2 appeared to lower risk of mortality when compared to both higher and lower BMI classifications. Furthermore, fair evidence suggests that higher energy intakes improved dyspnea scores and also showed a beneficial but less robust relationship with functional status, healthcare utilization or duration of illness. In unadjusted results, fair evidence suggests a positive association between BMI and FEV_1 percentage predicted. In addition, an increasing BMI was also shown to reduce the longitudinal decline in FEV_1 percentage predicted over time.

Rating: Fair
Imperative

- Risks/Harms of Implementing This Recommendation

  There are no potential risks or harms associated with the application of the recommendation.

- Conditions of Application

  - The RDN should use clinical judgement in providing a calorie prescription. Calculation of energy needs (estimation) using a predictive equation is a starting point to determine energy requirements. Changes in body weight (BW) should be monitored as an indicator that energy needs should be re-evaluated. Over time, the monitoring of BW and composition against energy intake is probably the most meaningful expression of energy requirements in COPD. It is important to remember in this type of assessment that, if adverse changes in BW or composition are occurring, equal attention should be paid to the possibility that the patient is not consuming the target intake, or that the target intake is not correct.
  - An optimal body weight goal should be individualized for each patient.

- Potential Costs Associated with Application

  Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.

- Recommendation Narrative

  Body Weight

  A total of 22 studies were included in the evidence analysis supporting the recommendation:

  - A total of 11 prospective cohort studies: Three positive-quality (Hallin et al, 2007; Schols et al, 2005; Tsimogianni et al, 2009) and eight neutral-quality (Abston et al, 2017; Baccioglu et al, 2014; Galesanu et al, 2014; Koul et al, 2017; Piquet et al, 2013; Pothirat et al, 2007; Qiu et al, 2009; Rutten et al, 2013)
  - A total of 10 neutral-quality retrospective cohort studies (Jiang et al, 2017; Lainscak et al, 2011; Lim et al, 2017; Marti et al, 2006; O'Donnell et al, 2011; Ranieri et al, 2008; Slinde et al, 2005; Uh et al, 2011; Yamauchi et al, 2014; Zapatero et al, 2013)
  - One negative-quality case-control study (Dimov et al, 2013).

  Body Weight and Lung Function Outcomes
  All studies using FEV_1 percentage predicted as an outcome found a positive association with BMI or BMI category and one longitudinal study showed increasing BMI reduced declines in FEV_1 percentage predicted over time. While these studies appear to indicate that increasing BMI is associated with improvements in FEV_1 percentage predicted, results did not include adjustment for relevant confounders and should be interpreted with caution. Results for other lung function measures (FEV_1, FVC, FVC percentage predicted, FEV_1/FVC) were mixed and, therefore no conclusion can be drawn for these measures.

  - *FEV_1 stratified into quintiles and BMI (one study):* One study (Abston et al, 2017) found BMI was not associated with FEV_1 in the overall group or in any of the FEV_1 quintiles. In each of the FEV1 quintiles, FVC percentage predicted showed inverse associations with BMI, while FEV_1/FVC showed a positive association with BMI.
  - *BMI stratified into quartiles and FEV_1 (one study):* One study (Lainscak et al, 2011) found a positive association between FEV_1 (ml per second) and BMI divided into quartiles in subjects hospitalized for an acute exacerbation of COPD (AECOPD), with FEV_1 increasing as BMI category increased.
  - *BMI and lung function (non-adjusted) (six studies):* Six studies (Dimov et al, 2013; Galesanu et al, 2014; Hallin et al, 2007; Lim et al, 2017; O'Donnell et al, 2011; Qiu et al, 2009) found BMI was positively associated with FEV_1 percentage predicted in analyses, unadjusted for confounding variables. BMI was positively correlated with FEV_1/FVC in two studies (O'Donnell et al, 2011; Qiu et al, 2009). Qui also found a higher BMI was also associated with a lower decline in lung function over time. Two studies (Galesanu et al, 2014; O'Donnell et al, 2011) found that BMI was not associated with FVC. O'Donnell found BMI was not associated with FVC percentage predicted. Galesanu found NS association between FEV_1 and BMI, while Lim found FEV_1 to be highest in subjects classified as OB by either the WHO or Asian-Pacific methods of BMI. FEV_1 was not reported in four studies (Dimov et al; Hallin et al; O'Donnell et al; Qiu et al).

  Body weight and mortality outcomes
  The majority of studies comparing BMI (kg/m^2) between survivors and non-survivors with COPD found survivors had a significantly higher BMI. Among studies comparing mortality rates between BMI categories, a lower risk of mortality was found as BMI classification increased. Likewise, those in the lowest BMI groups had higher mortality rates when compared to those in higher BMI groups. In studies evaluating BMI as a predictor of mortality, those in the lowest BMI categories consistently showed higher mortality risk when compared to those in higher BMI classifications. While increasing body weight appeared to be protective when BMI was evaluated as a continuous variable, studies evaluating BMI as a categorical variable found that a BMI of approximately 25.0 to 29.99 had a lower risk of mortality, when compared to both higher and lower BMI classifications.

  - *BMI (mean ±SD) between survivors and non-survivors (five studies):* Five studies evaluated the difference in BMI between survivors and non-survivors with COPD. Four studies (Hallin et al, 2007; Marti et al, 2006; Ranieri et al, 2008; Tsimogianni et al, 2009) found significantly higher BMI in survivors vs. non-survivors. One study (Galesanu et al, 2014) found no differences in BMI between the groups.
  - *Differences in mortality rates between BMI categories (six studies):* Two studies (Abston et al, 2017, Lainscak et al, 2011) classified the BMIs of participants into quintiles or quartiles (respectively) and found a lower risk of mortality as BMI categorization increased. In three studies that were unadjusted for confounding variables (Koul et al, 2017; Pothirat, et al, 2007; Uh et al 2011), two studies found higher mortality in the lowest BMI groups (Koul, Pothirat). Koul found higher mortality two years after AECOPD in the lowest BMI group compared to the 23-24.9 Group. Pothirat found higher mortality in the lowest BMI group compared to the next higher group (both with severe COPD). Uhl found NS differences in cumulative survival rate between all BMI groups. One study (Zapatero et al, 2013) found that the OB Group (using ICD-9 codes) had a 51% reduction in risk of mortality, compared to NW Group, after adjusting for possible confounders in patients hospitalized for AECOPD.
  - *BMI and weight status as a predictor of mortality (12 studies):*
    - Five studies evaluated BMI (or percentage of reference weight) as a continuous variable as a predictor of mortality in subjects with COPD. Three studies (Galesanau et al, 2014; Ranieri et al, 2008; Schols et al, 2005) found BMI was a predictor of mortality in univariate analyses. Two studies (Jiang et al, 2017; Ranieri et al, 2008) reported BMI was a predictor of mortality in adjusted multivariate analysis. A fourth study (Galesanu et al, 2014) found NS association between BMI and mortality in adjusted multivariate analysis. The fifth study (Slinde et al, 2005) that used percentage of reference weight did not find an association with mortality.
    - Seven studies evaluated BMI as a categorical variable as a predictor of mortality and adjusting for confounding variables (Hallin et al, 2007; Jiang et al, 2017; Marti et al, 2006; Piquet et al, 2013; Rutten et al, 2013, Tsimogianni et al, 2009; Yamauchi et al, 2014). Mortality risk was higher for subjects in the lowest BMI group (ranging from less than 18.5 to 25) when compared to higher BMI groups. Yamauchi found higher all-cause in-hospital mortality in the lowest BMI group and lower mortality in the higher BMI categories, compared to the 18.5-22.9 Group in an Asian population. Hallin found higher risk for two-year mortality after AECOPD in all BMI categories, compared to the 25-30 Group. Marti found higher risk for both all-cause and respiratory mortality in the lower BMI groups, compared to the

25-29.9 Group and higher risk for all-cause mortality in the 20-24.9 Group, compared to the 25-29.9 Groups. Piquet found no difference in risk for mortality between the lowest and 20-25 Group, but a lower risk for mortality 48 months after AECOPD in the higher BMI categories. Rutten found the highest two- and three-year survival in subjects in BMI categories 25-29.99, compared to lower groups as well as those above 30. Jiang found a higher risk of mortality as BMI group classification decreased. Tsimogianni found that a BMI group of less than 25 had a higher risk of three-year mortality.

Energy Intake

A total of nine studies were included in the evidence analysis supporting the recommendation:

- Four randomized controlled trials: One positive-quality (Sugawara et al, 2012), three neutral-quality (Førli and Boe, 2005; Planas et al, 2005; Weekes et al, 2009)
- Five cross-sectional studies: Three neutral-quality (Lee et al, 2013; Renvall et al, 2009; Yazdanpanah et al, 2010) and two negative-quality (Benton et al 2010; Selvi et al, 2014).

There was improvement in dyspnea scores with higher energy intakes, with less robust evidence supporting a beneficial relationship with functional status, healthcare utilization or duration of illness.

- *Respiratory symptoms (three studies):* All three studies found significant associations with dyspnea scores (Lee et al, 2013; Sugawara et al, 2012; Weekes et al, 2009)
- *Functional status (one study):* The study found a significant association with activities of daily living scores (Weekes et al, 2009)
- *Healthcare utilization (one study):* The study found a significant association with number of infections requiring antibiotics (Forli and Boe, 2009)
- *Duration of illness (one study):* The study found a significant association with duration of disease in years (Selvi et al, 2014).

The findings for the impact of energy intake on exacerbations, quality of life (QoL), weight status and body composition were mixed, with the majority supportive of an association.

- *Exacerbations (two studies):* One study found a significant association with number of emergency room (ER) visits due to acute exacerbations (Lee et al, 2013). One study did not find an association with number of ER visits due to AEs with energy intakes of either 1.7x or 1.3 x Harris-Benedict Equation (HBE) (Planas et al, 2005).
- *QoL (three studies):* All three studies found significant association of Chronic Respiratory Disease Questionnaire (CRQ) scores with energy intakes of 1.3 x HBE (Planas et al, 2005), CRQ scores (Sugawara et al, 2012) and St. George Respiratory Quotient scores (Weekes et al, 2009). One study did not find significant associations for CRQ scores with energy intakes of 1.7 x HBE (Planas et al, 2005).
- *Weight status (seven studies)*
  - Six studies found significant associations
    - Weight gain with energy intakes of 1.7 x HBE (Planas et al, 2005)
    - Percentage of ideal body weight (Sugawara et al, 2012)
    - Weight gain (Forli and Boe, 2005; Sugawara et al, 2012; Weekes et al, 2009)
    - BMI (Lee et al, 2013; Renvall et al, 2009).
  - Two studies did not find associations
    - BMI (Benton et al, 2010)
    - BW with energy intakes of 1.3 x HBE (Planas et al, 2005).
- *Body composition (three studies):* All studies found significant associations with fat mass (FM), triceps skinfold (TSF) and fat-free mass index (FFMI) with energy intakes of 1.7 x HBE (Planas et al, 2005), FM, fat mass index (Sugawara et al, 2012) and mid-arm circumference and sum of four skinfold thickness measurements (Weekes et al, 2009). All three studies also did not find associations with mid-arm muscle circumference (Weekes et al, 2009), FFMI and arm circumference (Sugawara et al, 2012) or FM, TSF and FFMI with energy intakes of 1.3 x HBE (Planas et al, 2005).

The evidence for a relationship between energy intake and lung function, systemic inflammation or exercise capacity was inconsistent.

- *Lung function (five studies):* Two studies found significant associations in forced vital capacity (FVC) and sniff pressure (Weekes et al, 2009) and Pmax inspiratory (PI_{max}) (Sugawara et al, 2012). Three studies did not find associations in FEV in one second (FEV_1) (Lee et al, 2013; Yazdanpanah et al, 2010), FEV_1 with energy intakes of either 1.7 x or 1.3 x HBE (Planas et al, 2005), FVC, FEV_1/FVC, and vital capacity (Yazdanpanah et al, 2010), PI_{max} and Pmax expiratory (PE_{max}) (Weekes et al, 2009) or PE_{max} (Sugawara et al, 2012).
- *Systemic inflammation (one study):* The study found a significant association with Interleukin-6, but not C-reactive protein (Sugawara et al, 2012)
- *Exercise capacity (five studies)*
- Three studies found significant associations with upper and lower body strength (Benton et al, 2010) and six-minute walking distance (Benton et al, 2010; Lee et al, 2013; Sugawara et al, 2012). Two studies did not find associations for handgrip strength (HGS) with energy intakes of either 1.7 x or 1.3 x HBE (Planas et al, 2005) and HGS (Weekes et al, 2009).

* For Sugawara et al, 2012, the workgroup considered the between-group analysis only in the conclusion statement.

- Recommendation Strength Rationale

  - Conclusion statements supporting the recommendation are Grade I, *Good/Strong* (Body Weight and Mortality) and Grade II, *Fair* (Body Weight and Lung Function; Energy Intake)
  - For energy intake, outcomes varied among the studies, making synthesis of the findings challenging.

- Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

What association exists between energy intake (e.g., kcal per kg) and outcomes in adults with COPD?

What effect does body weight have on mortality outcomes in adults with COPD?

What effect does body weight have on lung function outcomes in adults with COPD?

- References

Benton M, Wagner C, Alexander J. Relationship between body mass index, nutrition, strength, and function in elderly individuals with chronic obstructive pulmonary disease. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2010; 30:260-3

Froli L, Boe J. The energy intake that is needed for weight gain in COPD candidates for lung transplantation. *COPD* 2005; 2:405-10

Lee H, Kim S, Lim Y, Gwon H, Kim Y, Ahn J, Park H. Nutritional status and disease severity in patients with chronic obstructive pulmonary disease (COPD). *Archives of Gerontology and Geriatrics* 2013; 56:518-23

Planas M, Alvarez J, García-Peris P, de la Cuerda C, de Lucas P, Castella M, Canseco F, Reyes L. Nutritional support and quality of life in stable chronic obstructive pulmonary disease (COPD) patients. *Clinical Nutrition (Edinburgh, Scotland)* 2005; 24:433-41

Renvall M, Friedman P, Ramsdell J. Predictors of body mass index in patients with moderate to severe emphysema. *COPD* 2009; 6:432-6

Selvi EC, Saikumar P, Kumar N. How to evaluate the risk of malnutrition in patients with COPD?. *Global Journal of Medical Research: F Diseases* 2014; 14:21-25

Sugawara K, Takahashi H, Kashiwagura T, Yamada K, Yanagida S, Homma M, Dairiki K, Sasaki H, Kawagoshi A, Satake M, Shioya T. Effect of anti-inflammatory supplementation with whey peptide and exercise therapy in patients with COPD. *Respiratory Medicine* 2012; 106:1526-34

Weekes C, Emery P, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. *Thorax* 2009; 64:326-31

Yazdanpanah L, Shidfar F, Moosavi A, Heidarnazhad H, Haghani H. Energy and protein intake and its relationship with pulmonary function in chronic obstructive pulmonary disease (COPD) patients. *Acta Medica Iranica* 2010; 48:374-9

Abston E, Comellas A, Reed R, Kim V, Wise R, Brower R, Fortis S, Beichel R, Bhatt S, Zabner J ,Newell J ,Hoffman E, Eberlein M. Higher BMI is associated with higher expiratory airflow normalised for lung volume (FEF25-75/FVC) in COPD. *BMJ Open Respiratory Research* 2017; 4:e000231

Galesanu R, Bernard S, Marquis K, Lacasse Y, Poirier P, Bourbeau J, Maltais F. Obesity in chronic obstructive pulmonary disease: is fatter really better?. *Canadian Respiratory Journal.* 2014; 21:297-301

Hallin R, Gudmundsson G, Suppli Ulrik C, Nieminen M, Gislason T, Lindberg E, Brøndum E, Aine T, Bakke P, Janson C. Nutritional status and long-term mortality in hospitalised patients with chronic obstructive pulmonary disease (COPD). *Respiratory Medicine.* 2007; 101:1,954-1,960.

Jiang J, Zhao J, Yuan Y, Di S. Risk factors associated with acute exacerbation of chronic obstructive pulmonary disease: A retrospective analysis in 4,624 patients. *Biomedical Research.* 2017; 28:3,855-3,859.

Koul P, Dar H, Jan R, Shah S, Khan U. Two-year mortality in survivors of acute exacerbations of chronic obstructive pulmonary disease: A North Indian study. *Lung India : Official Organ of Indian Chest Society* 2017; 34:511-516

Lainscak M, von Haehling S, Doehner W, Sarc I, Jeric T, Ziherl K, Kosnik M, Anker S, Suskovic S. Body mass index and prognosis in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. *Journal of Cachexia, Sarcopenia and Muscle.* 2011; 2:81-86.

Marti S, Muñoz X, Rios J, Morell F, Ferrer J. Body weight and comorbidity predict mortality in COPD patients treated with oxygen therapy. *The European Respiratory Journal.* 2006; 27:689-696.

Piquet J, Chavaillon J, David P, Martin F, Blanchon F, Roche N. High-risk patients following hospitalisation for an acute exacerbation of COPD. *The European Respiratory Journal* 2013; 42:946-55

Pothirat C, Phetsuk N, Deesomchok A, Theerakittikul T, Bumroongkit C, Liwsrisakun C, Inchai J. Clinical characteristics, management in real world practice and long-term survival among COPD patients of Northern Thailand COPD club members. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet.* 2007; 90:653-662.

Ranieri P, Bianchetti A, Margiotta A, Virgillo A, Clini E, Trabucchi M. Predictors of 6-month mortality in elderly patients with mild chronic obstructive pulmonary disease discharged from a medical ward after acute nonacidotic exacerbation. *Journal of the American Geriatrics Society.* 2008; 56:909-913.

Rutten E, Calverley P, Casaburi R, Agusti A, Bakke P, Celli B, Coxson H, Crim C, Lomas D, Macnee W, Miller B, Rennard S, Scanlon P, Silverman E, Tal-Singer R, Vestbo J, Watkins M, Wouters E. Changes in body composition in patients with chronic obstructive pulmonary disease: do they influence patient-related outcomes?. *Annals of Nutrition & Metabolism.* 2013; 63:239-247.

Schols A, Broekhuizen R, Weling-Scheepers C, Wouters E. Body composition and mortality in chronic obstructive pulmonary disease. *The American Journal of Clinical Nutrition.* 2005; 82:53-59.

Slinde F, Grönberg A, Engström C, Rossander-Hulthén L, Larsson S. Body composition by bioelectrical impedance predicts mortality in chronic obstructive pulmonary disease patients. *Respiratory Medicine.* 2005; 99:1,004-1,009.

Tsimogianni A, Papiris S, Stathopoulos G, Manali E, Roussos C, Kotanidou A. Predictors of outcome after exacerbation of chronic obstructive pulmonary disease. *Journal of General Internal Medicine.* 2009; 24:1,043-1,048.

Uh S-T, Lee JY, Koo SM, Kim YK, Kim KU, Park JS, Park SW, Jang AS, Kim DJ, Choi JS, Na JO, Suh KH, Kim YH, Park C-S,. The Survival Rate of Korean Patients with COPD with or without Acute Exacerbations. *Tuberculosis and Respiratory Diseases.* 2011; 70:474-481

Yamauchi Y, Hasegawa W, Yasunaga H, Sunohara M, Jo T, Takami K, Matsui H, Fushimi K, Nagase T. Paradoxical association between body mass index and in-hospital mortality in elderly patients with chronic obstructive pulmonary disease in Japan. *International Journal of Chronic Obstructive Pulmonary Disease.* 2014; 9:1,337-1,346.

Zapatero A, Barba R, Ruiz J, Losa J, Plaza S, Canora J, Marco J. Malnutrition and obesity: influence in mortality and readmissions in chronic obstructive pulmonary disease patients. *Journal of Human Nutrition and Dietetics : the Official Journal of the British Dietetic Association* 2013; 26:16-22.

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

  None.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Macronutrient Composition 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

  COPD: Macronutrient Composition (Percentage Distribution)

  The RDN should individualize the macronutrient composition of the diet based on nutrition assessment. Limited evidence examining the impact of macronutrient distribution did not confirm an ideal percentage distribution of carbohydrates, protein and fat, or if macronutrient distribution should be different for adults with COPD.

  Rating: Fair
  Imperative

  - Risks/Harms of Implementing This Recommendation

    There are no potential risks or harms associated with the application of this recommendation.

  - Conditions of Application

    - Comorbid conditions such as cardiovascular disease, diabetes, etc. should be considered when individualizing the macronutrient distribution
    - Lifestyle, financial barriers and personal preferences should be considered when individualizing the macronutrient distribution.

  - Potential Costs Associated with Application

    Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.

  - Recommendation Narrative

One negative-quality non-randomized trial (Tümer et al, 2009) was included in the evidence analysis supporting the recommendation.

The study provided a comparison between COPD subjects' post-acute exacerbation (N=30 men) who consumed ~1, 800kcals [28% carbohydrate (CHO), 50% fat, 16% protein)] and COPD controls who consumed ~1, 800kcals (57% CHO, 30% fat, 16% protein). After 10 days, subjects showed an improvement in forced vital capacity (P=0.033) and tidal volume (P=0.002), and the change was not significant in the controls. Neither group experienced significant differences in forced expiratory volume in one second or vital capacity change after 10 days.

- Recommendation Strength Rationale
  - Conclusion statement supporting the recommendation is Grade III, *Limited/Weak*
  - One study (all men) of short duration.
- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  Does the macronutrient composition (percentage distribution) of the diet have an effect on outcomes in adults with COPD?

  - References

    Tümer G, Mercanligil SM, Uzun O, Aygün C. . The Effects of a High-Fat, Low-Carbohydrate Diet on the Prognosis of Patients with an Acute Attack of Chronic Obstructive Pulmonary Disease. *Turkiye Klinikleri J Med Sci* 2009; 29:895-904

  - References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

    None.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Vitamin D Supplementation 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

  COPD: Vitamin D Supplementation for Serum 25(OH)D Levels 10ng/ml or Lower

  If an adult with COPD has serum 25(OH)D levels ≤10ng per ml, the RDN should advise vitamin D supplementation to optimize serum 25(OH)D status. Limited evidence of vitamin D supplementation in adults with COPD supports improved exacerbation outcomes in those with baseline serum 25(OH)D levels 10ng per ml or lower.

  Rating: Fair
  Conditional

  COPD: Vitamin D Supplementation for Serum 25(OH)D Levels 11-29ng/ml

  If an adult with COPD has serum 25(OH)D levels 11ng to 29ng per ml, the RDN should consider vitamin D supplementation to optimize serum 25(OH)D status. While vitamin D is important for health, evidence indicates that vitamin D supplementation may or may not improve lung function or reduce exacerbations in adults with COPD who have baseline serum levels within this range. Evidence related to the effect of vitamin D supplementation on lung function and exacerbation outcomes yielded mixed findings and depended upon on dosing, dosing frequency and delivery routes, length of intervention and baseline serum 25(OH)D levels.

  Rating: Fair
  Conditional

  - Risks/Harms of Implementing This Recommendation

    There are no potential risks or harms associated with the application of this recommendation.

  - Conditions of Application
    - The recommendation *COPD: Vitamin D Supplementation for Serum 25(OH)D Levels 10ng per ml or Lower* applies to those with serum 25(OH)D levels ≤10ng per ml
    - The recommendation *COPD: Vitamin D Supplementation for Serum 25(OH)D Levels 11ng to 29ng per ml* applies to those with serum 25(OH)D levels that are insufficient (21ng to 29ng per ml) or deficient (less than 20ng per ml)
    - Coordination with the prescribing provider may be required for vitamin D supplement orders
    - Achievement of normal serum 25(OH)D levels may not be possible in all instances. Therefore, optimizing serum 25(OH)D levels is the goal (Rusinska et al, 2018).

  - Potential Costs Associated with Application
    - Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN
    - Costs may be incurred related to the purchase of over-the-counter vitamin D supplements or co-pays.
  - Recommendation Narrative

    A total of eight studies were included in the evidence analysis supporting the recommendations:

    - Six randomized controlled trials (RCTs) [four positive-quality (Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Sanjari et al, 2016), one neutral-quality (Khan et al, 2017) and one negative-quality (Zendendel et al, 2015)]
    - Two before-after studies [both neutral-quality (Rezk et al, 2015; Said and Abd-Elnaeem, 2015)].

    Seven studies tested oral vitamin D_3 (cholecalciferol) ranging from 1, 200 IU daily for six months; subjects and controls could also take 400 IU vitamin D_3 daily (Rafiq et al, 2017) to 120, 000 IU every two months for 12 months (Martineau et al, 2015).

    - One study administered 200, 000 IU cholecalciferol intramuscularly (IM) every four weeks for six months (Said and Abd-Elnaeem, 2015)
    - All papers either cited the Endocrine Society Clinical Practice Guideline (ESG) (Holick et al, 2011) for serum 25(OH)D classifications or did not define classifications. In addition to the ESG reference, one study (Lehouck et al, 2012) defined “severe” vitamin D deficiency as serum 25(OH)D levels under 10ng per ml.

Seven studies evaluated lung function (LF) outcomes (Lehouck et al 2012; Martineau et al, 2015; Rafiq et al, 2017; Rezk et al, 2015; Sanjari et al, 2016; Said and Abd-Elnaeem, 2015; Zendedel et al, 2015). Six studies evaluated acute exacerbation (AE) outcomes (Khan et al, 2017; Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Rezk et al, 2015; Zendedel et al, 2015).

Five studies of vitamin D supplementation included subjects' pre- and post-supplementation levels, allowing changes in vitamin D status due to supplementation to be assessed. Results according to baseline (BL) and post-supplementation improvements in vitamin D status (ESG categories) are as follows:

- *Deficient to sufficient 25(OH)D:* Supplementation with 1, 200 IU D_3 daily for six months (plus 400 IU daily, if desired) resulted in no impact on LF or AE outcomes (Rafiq et al, 2012). Supplementation with 100, 000 IU D_3 every four weeks over 12 months resulted in a decrease in AE rate in a sub-group of subjects with "*severe deficiency*" [25(OH)D under 10ng per ml] (Lehouck et al, 2012).
- *Insufficient to sufficient 25(OH)D:* Supplementation with 100, 000 IU D_3 every four weeks over 12 months resulted in no impact on AE or LF outcomes (Lehouck et al, 2012). Supplementation with either 5, 000 IU D_3 or 0.25mcg calcitriol every four weeks over 12 months resulted in no impact on LF outcomes (Sanjari et al, 2016).
- *Deficient to insufficient 25(OH)D:* Supplementation with 50, 000 IU D_3 per week for eight weeks, then 800 IU daily for 12 months resulted in a decrease in number of AEs and an improvement in MVV, but no impact on other LF outcomes in subjects with 25(OH)D under 10ng per ml at BL (Rezk et al, 2015). Supplementation with 120, 000 IU D_3 every two months over 12 months resulted in improvement in AE severity and symptoms, but had no impact on other AE or LF outcomes (Martineau et al, 2015).

The remaining three studies did not report subjects' post-supplementation vitamin D status. One study (Said and Abd-Elnaeem, 2015) reported BL vitamin D status according to ESG categories, but did not report post-supplementation status. The second study (Khan et al, 2017) reported BL vitamin D status of subjects and controls combined and did not report pre- and post-supplementation status of subjects only. Finally, the last study (Zendedel et al, 2015) did not report either BL or post-supplementation vitamin D status.

- *Insufficient 25(OH)D (subjects + controls):* Supplementation with 2, 000 IU D_3 per day for six months resulted in reduced AEs (Kahn et al, 2017). Supplementation with 200, 000 IU D_3 IM every four weeks for six months resulted in no impact in LF outcomes (Said and Abd-Elnaeem, 2015).
- *Unknown 25(OHD):* Supplementation with 100, 000 IU D_3 every month for six months resulted in improvement in LF outcomes and a reduction in AEs (Zendedel et al, 2015).

- Recommendation Strength Rationale

  - Conclusion statements supporting the recommendations are Grade II, *Fair*
  - Synthesis of the results was challenging due to lack of consistency in vitamin D dosing, dosing frequency and delivery routes, length of intervention and baseline serum 25(OH)D levels.

- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  Does vitamin D supplementation improve lung function and exacerbation outcomes in adults with COPD?

  - References

    Khan D,Ullah A,Randhawa F,Iqtadar S,Butt N,Waheed K. Role of Vitamin D in reducing number of acute exacerbations in Chronic Obstructive Pulmonary Disease (COPD) patients. *Pakistan journal of medical sciences* 2017; 33:610-614

    Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, Decallonne B, Bouillon R, Decramer M, Janssens W. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: a randomized trial. *Annals of Internal Medicine* 2012; 156:105-14

    Martineau A, James W, Hooper R, Barnes N, Jolliffe D, Greiller C, Islam K, McLaughlin D, Bhowmik A, Timms P, Rajakulasingam R, Rowe M, Venton T, Choudhury A, Simcock D, Wilks M, Degun A, Sadique Z, Monteiro W, Corrigan C, Hawrylowicz C, Griffiths C. Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease (ViDiCO): a multicentre, double-blind, randomised controlled trial. *The Lancet. Respiratory Medicine* 2015; 3:120-130

    Rafiq R, Prins H, Boersma W, Daniels J, den Heijer M, Lips P, de Jongh R. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: a pilot trial. *International Journal of Chronic Obstructive Pulmonary Disease* 2017; 12:2583-2592

    Rezk NA, Yehia AA, Hewidy, AA. Effect of vitamin D replacement in chronic obstructive pulmonary disease patients with vitamin D deficiency. *Egyptian Journal of Chest Diseases and Tuberculosos* 2015; 64:353-357

    Said AF and Abd-Elnaeem EA. Vitamin D and chronic obstructive pulmonary disease. *Egyptian Journal of Chest Diseases and Tuberculosis* 2015; 64:67-73

    Sanjari M, Soltani A, Habibi Khorasani A, Zareinejad M. The effect of vitamin D on COPD exacerbation: a double blind randomized placebo-controlled parallel clinical trial. *Journal of Diabetes and Metabolic Disorders* 2016; 15:33

    Zendedel A, Gholami M, Anbari K, Ghanadi K, Bachari E, Azargon A. Effects of Vitamin D Intake on FEV1 and COPD Exacerbation: A Randomized Clinical Trial Study. *Global Journal of Health Science* 2015; 7:243-8

  - References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

    Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011 Jul; 96 (7): 1, 911-1, 930. doi: 10.1210/jc.2011-0385. Epub 2011 Jun 6. Erratum in: *J Clin Endocrinol Metab.* 2011 Dec; 96 (12): 3, 908. PMID: 21646368.

    Jolliffe DA, Greenberg L, Hooper RL, Mathyssen C, Rafiq R, deJongh RT, Camargo C, Griffiths CJ, Janssens W, Martineau AR. Vitamin D to prevent exacerbations of COPD: systematic review and meta-analysis of individual participant data from randomised controlled trials. *Thorax.* Published Online First: 10 January 2019. doi: 10.1136/thoraxjnl-2018-212092.

    Rusinska A, Pludowski P, Walczak M, Borszewska-Kornacka MK, Bossowski A, Chlebna-Sokól D, Czech-Kowalska J, Dobrzanska A, Franek E, Helwich E, Jackowska T, Kalina MA, Konstantynowicz J, Ksiazyk J, Lewinski A, Lukaszkiewicz J, Marcinowska-Suchowierska E, Mazur A, Michalus I, Peregud-Pogorzelski J, Romanowska H, Ruchala M, Socha P, Szalecki M, Wielgos M, Zwolinska D, Zygmunt A. Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland - Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies - 2018 Update. *Front Endocrinol (Lausanne).* 2018 May 31; 9: 246. doi: 10.3389/fendo.2018.00246. eCollection 2018. Review. PMID: 2990437.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Monitor and Evaluate Energy Intake and Body Weight for Energy Needs 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

COPD: Monitor and Evaluate Energy Intake and Body Weight for Energy Needs

For adults with COPD, the RDN should routinely monitor and evaluate body weight (BW) status and energy intake and adjust the estimated calorie prescription to achieve or maintain an optimal weight. Evidence suggests an association between BW status and both mortality and lung function in adults with COPD. Strong evidence indicates that the lowest BMI groups had higher mortality rates when compared to higher BMI groups. Furthermore, a BMI classification of approximately 25.0kg/m^2 to 29.99kg/m^2 appeared to lower risk of mortality when compared to both higher and lower BMI classifications. In unadjusted results, fair evidence indicates that BMI was positively associated with FEV_1 percentage predicted. Fair evidence was also found showing improvement in dyspnea scores with higher energy intakes.

Rating: Fair
Imperative

- Risks/Harms of Implementing This Recommendation

  There are no potential risks or harms associated with the application of this recommendation.

- Conditions of Application

  - Over time, the monitoring of BW against energy intake is probably the most meaningful expression of energy requirement in COPD. If adverse changes in body weight or composition are occurring, equal attention should be paid to the possibility that the patient is not consuming the target intake or that the target intake is not correct.
  - An optimal body weight goal should be individualized for each patient.

- Potential Costs Associated with Application

  Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN.

- Recommendation Narrative

  Energy Intake

  A total of nine studies were included in the evidence analysis supporting the recommendation:

  - Four randomized controlled trials: One positive-quality (Sugawara et al, 2012), three neutral-quality (Førli and Boe, 2005; Planas et al, 2005; Weekes et al, 2009)
  - Five cross-sectional studies: Three neutral-quality (Lee et al, 2013; Renvall et al, 2009; Yazdanpanah et al, 2010) and two negative-quality (Benton et al 2010; Selvi et al, 2014).

  There was improvement in dyspnea scores with higher energy intakes, with less robust evidence supporting a beneficial relationship with functional status, healthcare utilization or duration of illness.

  - *Respiratory symptoms (three studies):* All three studies found significant associations with dyspnea scores (Lee et al, 2013; Sugawara et al, 2012; Weekes et al, 2009)
  - *Functional status (one study):* The study found a significant association with activities of daily living scores (Weekes et al, 2009)
  - *Healthcare utilization (one study):* The study found a significant association with number of infections requiring antibiotics (Forli and Boe, 2009).
  - *Duration of illness (one study):* The study found a significant association with duration of disease in years (Selvi et al, 2014).

  The findings for the impact of energy intake on exacerbations, quality of life (QoL), weight status and body composition were mixed, with the majority supportive of an association.

  - *Exacerbations (two studies):* One study found a significant association with number of emergency room (ER) visits due to acute exacerbations (AEs) (Lee et al, 2013). One study did not find a association with number of ER visits due to AEs with energy intakes of either 1.7 x or 1.3 x Harris-Benedict Equation (HBE) (Planas et al, 2005).
  - *QoL (three studies):* All three studies found significant associations of Chronic Respiratory Disease Questionnaire (CRQ) scores with energy intakes of 1.3 x HBE (Planas et al, 2005), CRQ scores (Sugawara et al, 2012) and St. George Respiratory Quotient (SGRQ) scores (Weekes et al, 2009). One study did not find significant associations for CRQ scores with energy intakes of 1.7 x HBE (Planas et al, 2005).
  - *Weight status (seven studies)*
    - Six studies found significant associations
      - Weight gain with energy intakes of 1.7 x HBE (Planas et al, 2005)
      - Percentage IBW (Sugawara et al, 2012)
      - Weight gain (Forli and Boe, 2005; Sugawara et al, 2012; Weekes et al, 2009)
      - Body mass index (BMI) (Lee et al, 2013; Renvall et al, 2009).
    - Two studies did not find associations
      - BMI (Benton et al, 2010)
      - BW with energy intakes of 1.3 x HBE (Planas et al, 2005).
  - *Body composition (three studies):* All three studies found significant associations with fat mass (FM), triceps skinfold (TSF) and fat-free mass index (FFMI) with energy intakes of 1.7 x HBE (Planas et al, 2005), FM, fat mass index (Sugawara et al, 2012) and mid-arm circumference and sum of four skinfold thickness measurements (Weekes et al, 2009). All three studies also did not find associations with mid-arm muscle circumference (Weekes et al, 2009), FFMI and arm circumference (Sugawara et al, 2012) or FM, TSF and FFMI with energy intakes of 1.3 x HBE (Planas et al, 2005).

  The evidence for a relationship between energy intake and lung function, systemic inflammation or exercise capacity was inconsistent.

  - *Lung function (five studies):* Two studies found significant associations in forced vital capacity (FVC) and sniff pressure (Weekes et al, 2009) and Pmax inspiratory (PI_{max}) (Sugawara et al, 2012). Three studies did not find associations in FEV in one second (FEV_1) (Lee et al, 2013; Yazdanpanah et al, 2010), FEV_1 with energy intakes of either 1.7 x or 1.3 x HBE (Planas et al, 2005), FVC, FEV_1/FVC and vital capacity (Yazdanpanah et al, 2010), PI_{max} and Pmax expiratory (PE_{max}) (Weekes et al, 2009) or PE_{max} (Sugawara et al, 2012).
  - *Systemic inflammation (one study):* The study found a significant association with IL-6, but not CRP (Sugawara et al, 2012)
  - *Exercise capacity (five studies):* Three studies found significant associations with upper and lower body strength (Benton et al, 2010) and six-minute walking distance (Benton et al, 2010; Lee et al, 2013; Sugawara et al, 2012). Two studies did not find associations: Handgrip strength (HGS) with energy intakes of either 1.7 x or 1.3 x HBE (Planas et al, 2005) and HGS (Weekes et al, 2009).

  * For Sugawara et al, 2012, the workgroup considered the between-group analysis only in the conclusion statement.

  Energy Needs

  A total of five studies were included in the evidence analysis supporting the recommendation:

  - Three cross-sectional studies: One positive-quality (Slinde et al, 2011), one neutral-quality (Farooqi et al, 2015), one negative-quality (Ramos et al, 2016)
  - Two diagnostic, validity or reliability studies: Both neutral-quality (Nordenson et al, 2010; Slinde et al, 2008).

  Predictive equations for estimating RMR: A total of 11 equations were tested for validity in predicting RMR in adults with COPD. Two of these [Moore & Angelillo (MAE), Nordenson] were equations developed specifically for COPD patients, while the other equations were developed for healthy adults [Harris-Benedict (HBE), Mifflin St. Jeor (MSJE), Westerterp, de Oliveira, Owen and four variations of Food and Agriculture Organization of the United Nations/World Health Organization/United Nations University (FAO/WHO/UNU)], which were WHO (including heigheight), WHO (omitting heigheight), Nordic Nutrition Recommendation (NNRE) and the Schofield equation. In two of the studies (Farooqi et al, 2015; Slinde et al, 2011) these equations were evaluated as a starting point for estimating total energy expenditure (TEE).

  - *Accuracy:* Four of the 11 equations for predicting RMR were tested for accuracy, but only in one study (Slinde et al, 2008). Slinde found that the Westerterp equation yielded an accuracy rate of 68%, followed by the WHO (including heigheight) equation (63%) and HBE (61%). The MAE had the lowest accuracy rate (51%).

- *Limit of agreement (LOA):* LOA was reported for nine equations. LOA as a percentage of the mean between measured and predicted RMR were -23% to +18% for the Westerterp equation (Slinde et al, 2008), about -28% to +10% for the MAE (in this case the negative value is overestimation) (Slinde et al, 2008), less than 25% for WHO (including height) equation and HBE, -45% to +40% for the de Oliveira equation (Ramos et al, 2016), -53% to +33% for the Owen equation (Ramos et al, 2016), -65% to +13% for the MSJE (Ramos et al, 2016), ±19% for the Nordenson equation (Nordenson et al, 2010) and for WHO (omitting height) equation, +18% (Slinde et al, 2011), to as wide as -66% to +24% (Ramos et al, 2016).
- *Bias:* Evidence suggests that the only unbiased estimator of RMR in adults with COPD was the de Oliveira equation. Four other equations were probably[1] unbiased. These included the HBE and Westerterp equation, which might overestimate RMR and the Nordenson and WHO (including height) equations, which might underestimate RMR. Two equations (Owen and MSJE) were biased toward underestimation of RMR. The remaining four equations were probably[1] biased toward overestimation of RMR [MAE, NNRE, Schofield and WHO (omitting height) equations]. Evidence for the WHO (omitting height) equation suggests it might also underestimate RMR in adults with COPD.

  [1]Bias was not reported directly in these studies but is inferred from mean predicted RMR compared to mean measured RMR.

- Thus, the WHO (including height) equation and HBE seem to be equivalent to one another by the parameters of accuracy rate and LOA. If body composition measurements are known, then Westerterp is a better choice for calculation of RMR, because it yields a higher accuracy rate.

Predictive equations for estimating TEE: Two studies (Farooqi et al, 2015; Slinde et al, 2011) tested three methods for calculating TEE in adults with COPD. In the first method, a pedometer was used to estimate physical activity to compare against doubly labeled water (DLW) (Farooqi et al, 2015). In this method, a multiplier to RMR was assigned based on the number of steps taken and the multiplier was applied to six RMR equations [WHO (omitting height), Schofield, HBE, MAE, NNRE, Nordenson)]. In the other study, motion and position sensors were used as the criterion method to measure TEE. For prediction purposes, two methods were used. The first was a simple ratio of 30kcal per kg body weight (BW). The second was to compute RMR using the WHO (omitting height) equation and then multiplying by 1.7 to calculate TEE (Slinde et al, 2011).

- *Accuracy:* Only one of the two studies reported accuracy rate (Farooqi et al, 2015). Accuracy rate for WHO (omitting height) equation x PAL was of 67%, compared to 56% for Schofield equation x PAL, 50% for HBE x PAL, MAE x PAL, and NNRE x PAL, and 21% for the Nordenson equation x PAL
- *LOA:* The only estimation methods for which LOA was computed were 30kcal per kg and WHO (omitting height) x 1.7) (Slinde et al, 2011). LOA for both of these methods was 956kcal per day (-48%; +48% of the mean between predicted and measured TEE).
- *Bias:* The WHO (omitting height) x PAL and the MAE x PAL were probably[2] unbiased, while the Schofield x PAL, HBE x PAL, NNRE x PAL and Nordenson x PAL equations were probably[2] biased (toward underestimation) (Farooqi et al, 2016). An estimate of 30kcal per kg BW yielded a mean difference from measured TEE of 71kcal per day and so was probably unbiased[2], whereas another predictive method of WHO (omitting height) x 1.7 probably[2] was biased toward overestimation, based on a mean difference from measured TEE of 319kcal per day (Slinde et al, 2011).

  [2]Bias was not reported directly in these studies but is inferred from mean predicted TEE compared to mean measured TEE.

Body Weight

A total of 22 studies were included in the evidence analysis supporting the recommendation:

- 11 prospective cohort studies: Three positive-quality (Hallin et al, 2007; Schols et al, 2005; Tsimogianni et al, 2009) and eight neutral-quality (Abston et al, 2017; Baccioglu et al, 2014; Galesanu et al, 2014; Koul et al, 2017; Piquet et al, 2013; Pothirat et al, 2007; Qiu et al, 2009; Rutten et al, 2013)
- 10 neutral-quality retrospective cohort studies (Jiang et al, 2017; Lainscak et al, 2011; Lim et al, 2017; Marti et al, 2006; O'Donnell et al, 2011; Ranieri et al, 2008; Slinde et al, 2005; Uh et al, 2011; Yamauchi et al, 2014; Zapatero et al, 2013)
- One negative-quality case-control study (Dimov et al, 2013).

Body weight and lung function outcomes

All studies using FEV_1 percentage predicted as an outcome found a positive association with BMI or BMI category and one longitudinal study showing increasing BMI reduced declines in FEV_1 percentage predicted over time. While these studies appear to indicate that increasing BMI is associated with improvements in FEV_1 percentage predicted, results did not include adjustment for relevant confounders and should be interpreted with caution. Results for other lung function measures (FEV_1, FVC, FVC percentage predicted, FEV_1/FVC) were mixed and therefore, no conclusion can be drawn for these measures.

- *FEV_1 stratified into quintiles and BMI (one study):* One study (Abston et al, 2017) found BMI was not associated with FEV_1 in the overall group or in any of the FEV_1 quintiles. In each of the FEV1 quintiles, FVC percentage predicted showed inverse associations with BMI, while FEV_1/FVC showed a positive association with BMI.
- *BMI stratified into quartiles and FEV_1 (one study):* One study (Lainscak et al, 2011) found a positive association between FEV_1 (ml per second) and BMI divided into quartiles in subjects hospitalized for an acute exacerbation of COPD (AECOPD), with FEV_1 increasing as BMI category increased
- *BMI and lung function (non-adjusted) (six studies):* Six studies (Dimov et al, 2013; Galesanu et al, 2014; Hallin et al, 2007; Lim et al, 2017; O'Donnell et al, 2011; Qiu et al, 2009) found BMI was positively associated with FEV_1 percentage predicted in analyses, unadjusted for confounding variables. BMI was positively correlated with FEV_1/FVC in two studies (O'Donnell et al; Qiu et al). Qui also found a higher BMI was also associated with a lower decline in lung function over time. Two studies (Galesanu et al; O'Donnell et al) found that BMI was not associated with FVC. O'Donnell found BMI was not associated with FVC percentage predicted. Galesanu found NS association between FEV_1 and BMI, while Lim found FEV_1 to be highest in subjects classified as OB by either the WHO or Asian-Pacific methods of BMI. FEV_1 was not reported in four studies (Dimov et al; Hallin et al; O'Donnell et al; Qiu et al).

Body weight and mortality outcomes

The majority of studies comparing BMI (kg/m^2) between survivors and non-survivors with COPD found survivors had a significantly higher BMI. Among studies comparing mortality rates between BMI categories, a lower risk of mortality was found as BMI classification increased. Likewise, those in the lowest BMI groups had higher mortality rates when compared to those in higher BMI groups. In studies evaluating BMI as a predictor of mortality, those in the lowest BMI categories consistently showed higher mortality risk when compared to those in higher BMI classifications. While increasing body weight appeared to be protective when BMI was evaluated as a continuous variable, studies evaluating BMI as a categorical variable found that a BMI of approximately 25.0 to 29.99 had a lower risk of mortality when compared to both higher and lower BMI classifications.

- *BMI (mean ±SD) between survivors and non-survivors (five studies):* Five studies evaluated the difference in BMI between survivors and non-survivors with COPD. Four studies (Hallin et al, 2007; Marti et al, 2006; Ranieri et al, 2008; Tsimogianni et al, 2009) found significantly higher BMI in survivors vs. non-survivors. One study (Galesanu et al, 2014) found no differences in BMI between the groups.
- *Differences in mortality rates between BMI categories (six studies):* Two studies (Abston et al, 2017, Lainscak et al, 2011) classified the BMIs of participants into quintiles or quartiles (respectively) and found a lower risk of mortality as BMI categorization increased. In three studies that were unadjusted for confounding variables (Koul et al, 2017; Pothirat, et al, 2007; Uh et al 2011), two studies found higher mortality in the lowest BMI groups (Koul, Pothirat). Koul found higher mortality two years after AECOPD in the lowest BMI group, compared to the 23-24.9 Group. Pothirat found higher mortality in the lowest BMI group compared to the next higher group (both with severe COPD). Uhl found NS differences in cumulative survival rate between all BMI groups. One study (Zapatero et al, 2013) found that the OB Group (using ICD-9 codes) had a 51% reduction in risk of mortality, compared to the NW Group after adjusting for possible confounders in patients hospitalized for AECOPD.
- *BMI and weight status as a predictor of mortality (12 studies)*
  - Five studies evaluated BMI (percentage reference weight) as a continuous variable as a predictor of mortality in subjects with COPD. Three studies (Galesanau et al, 2014; Ranieri et al, 2008; Schols et al, 2005) found BMI was a predictor of mortality in univariate analyses. Two studies (Jiang et al, 2017; Ranieri et al, 2008) reported BMI was a predictor of mortality in adjusted multivariate analysis. A fourth study (Galesanu et al, 2014) found NS association between BMI and mortality in adjusted multivariate analysis. The fifth study (Slinde et al, 2005) that used percentage reference weight did not find an association with mortality.
  - Seven studies evaluated BMI as a categorical variable as a predictor of mortality and adjusting for confounding variables (Hallin et al, 2007; Jiang et al, 2017; Marti et al, 2006; Piquet et al, 2013; Rutten et al, 2013, Tsimogianni et al, 2009; Yamauchi et al, 2014). Mortality risk was higher for subjects in the lowest BMI group (ranging from under 18.5 to 25) when compared to higher BMI groups. Yamauchi found higher all-cause in-hospital mortality in the lowest BMI group and lower mortality in the higher BMI categories, compared to the 18.5-22.9 Group in an Asian population. Hallin found higher risk for two-year mortality after AECOPD in all BMI categories compared to the 25-30 Group. Marti found higher risk for both all-cause and respiratory mortality in the lower BMI groups compared to the 25-29.9 Group and higher risk for all-cause mortality in the 20-24.9 Group compared to the 25-29.9 Groups. Piquet found no difference in risk for mortality between the lowest and 20-25 Group, but a lower risk for mortality 48 months after AECOPD in the higher BMI categories. Rutten found the highest two- and three-year survival in subjects in BMI categories 25 to 29.99 compared to lower groups as well as those above 30. Jiang found a higher risk of mortality as BMI group classification decreased. Tsimogianni found that a BMI group of less than 25 had a higher risk of three-year mortality.

- Recommendation Strength Rationale

One conclusion statement supporting the recommendation is Grade I, *Good/Strong* and two conclusion statements are Grade II, *Fair.*

- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  OVERALL: If measurements are not available, what are the best methods to predict energy needs in adults with COPD?

  What association exists between energy intake (e.g., kcal per kg) and outcomes in adults with COPD?

  What effect does body weight have on mortality outcomes in adults with COPD?

  - References

    Farooqi N, Slinde F, Carlsson M, Håglin L, Sandström T. Predicting energy requirement with pedometer-determined physical-activity level in women with chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease* 2015; 10:1129-37

    Nordenson A, Grönberg A, Hulthén L, Larsson S, Slinde F. A validated disease specific prediction equation for resting metabolic rate in underweight patients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2010; 5:271-6

    Ramos F, Rossato L, Ramires B, Pimentel G, Venâncio L, Orsatti F, de Oliveira E. Comparison of predictive equations of resting energy expenditure in older adults with chronic obstructive pulmonary disease. *Revista Portuguesa de Pneumologia* 2016; 23:40-42

    Slinde F, Svensson A, Gronberg AM, Nordenson N, Hulthen L, Larsson SC. Reproducibility of indirect calorimetry in underweight patients with chronic obstructive pulmonary disease. *European e-Journal of Clinical Nutrition and Metabolism* 2008; 3:40-45

    Slinde F, Gronberg A, Svantesson U, Hulthen L, Larsson S. Energy expenditure in chronic obstructive pulmonary disease-evaluation of simple measures. *European Journal of Clinical Nutrition* 2011; 65:1309-13

    Benton M, Wagner C, Alexander J. Relationship between body mass index, nutrition, strength, and function in elderly individuals with chronic obstructive pulmonary disease. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2010; 30:260-3

    Froli L, Boe J. The energy intake that is needed for weight gain in COPD candidates for lung transplantation. *COPD* 2005; 2:405-10

    Lee H, Kim S, Lim Y, Gwon H, Kim Y, Ahn J, Park H. Nutritional status and disease severity in patients with chronic obstructive pulmonary disease (COPD). *Archives of Gerontology and Geriatrics* 2013; 56:518-23

    Planas M, Alvarez J, García-Peris P, de la Cuerda C, de Lucas P, Castella M, Canseco F, Reyes L. Nutritional support and quality of life in stable chronic obstructive pulmonary disease (COPD) patients. *Clinical Nutrition (Edinburgh, Scotland)* 2005; 24:433-41

    Renvall M, Friedman P, Ramsdell J. Predictors of body mass index in patients with moderate to severe emphysema. *COPD* 2009; 6:432-6

    Selvi EC, Saikumar P, Kumar N. How to evaluate the risk of malnutrition in patients with COPD?. *Global Journal of Medical Research: F Diseases* 2014; 14:21-25

    Sugawara K, Takahashi H, Kashiwagura T, Yamada K, Yanagida S, Homma M, Dairiki K, Sasaki H, Kawagoshi A, Satake M, Shioya T. Effect of anti-inflammatory supplementation with whey peptide and exercise therapy in patients with COPD. *Respiratory Medicine* 2012; 106:1526-34

    Weekes C, Emery P, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. *Thorax* 2009; 64:326-31

    Yazdanpanah L, Shidfar F, Moosavi A, Heidarnazhad H, Haghani H. Energy and protein intake and its relationship with pulmonary function in chronic obstructive pulmonary disease (COPD) patients. *Acta Medica Iranica* 2010; 48:374-9

    Abston E, Comellas A, Reed R, Kim V, Wise R, Brower R, Fortis S, Beichel R, Bhatt S, Zabner J ,Newell J ,Hoffman E, Eberlein M. Higher BMI is associated with higher expiratory airflow normalised for lung volume (FEF25-75/FVC) in COPD. *BMJ Open Respiratory Research* 2017; 4:e000231

    Galesanu R, Bernard S, Marquis K, Lacasse Y, Poirier P, Bourbeau J, Maltais F. Obesity in chronic obstructive pulmonary disease: is fatter really better?. *Canadian Respiratory Journal.* 2014; 21:297-301

    Hallin R, Gudmundsson G, Suppli Ulrik C, Nieminen M, Gislason T, Lindberg E, Brøndum E, Aine T, Bakke P, Janson C. Nutritional status and long-term mortality in hospitalised patients with chronic obstructive pulmonary disease (COPD). *Respiratory Medicine.* 2007; 101:1,954-1,960.

    Jiang J, Zhao J, Yuan Y, Di S. Risk factors associated with acute exacerbation of chronic obstructive pulmonary disease: A retrospective analysis in 4,624 patients. *Biomedical Research.* 2017; 28:3,855-3,859.

    Koul P, Dar H, Jan R, Shah S, Khan U. Two-year mortality in survivors of acute exacerbations of chronic obstructive pulmonary disease: A North Indian study. *Lung India : Official Organ of Indian Chest Society* 2017; 34:511-516

    Lainscak M, von Haehling S, Doehner W, Sarc I, Jeric T, Ziherl K, Kosnik M, Anker S, Suskovic S. Body mass index and prognosis in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. *Journal of Cachexia, Sarcopenia and Muscle.* 2011; 2:81-86.

    Marti S, Muñoz X, Rios J, Morell F, Ferrer J. Body weight and comorbidity predict mortality in COPD patients treated with oxygen therapy. *The European Respiratory Journal.* 2006; 27:689-696.

    Piquet J, Chavaillon J, David P, Martin F, Blanchon F, Roche N. High-risk patients following hospitalisation for an acute exacerbation of COPD. *The European Respiratory Journal* 2013; 42:946-55

    Pothirat C, Phetsuk N, Deesomchok A, Theerakittikul T, Bumroongkit C, Liwsrisakun C, Inchai J. Clinical characteristics, management in real world practice and long-term survival among COPD patients of Northern Thailand COPD club members. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet.* 2007; 90:653-662.

    Ranieri P, Bianchetti A, Margiotta A, Virgillo A, Clini E, Trabucchi M. Predictors of 6-month mortality in elderly patients with mild chronic obstructive pulmonary disease discharged from a medical ward after acute nonacidotic exacerbation. *Journal of the American Geriatrics Society.* 2008; 56:909-913.

    Rutten E, Calverley P, Casaburi R, Agusti A, Bakke P, Celli B, Coxson H, Crim C, Lomas D, Macnee W, Miller B, Rennard S, Scanlon P, Silverman E, Tal-Singer R, Vestbo J, Watkins M, Wouters E. Changes in body composition in patients with chronic obstructive pulmonary disease: do they influence patient-related outcomes?. *Annals of Nutrition & Metabolism.* 2013; 63:239-247.

    Schols A, Broekhuizen R, Weling-Scheepers C, Wouters E. Body composition and mortality in chronic obstructive pulmonary disease. *The American Journal of Clinical Nutrition.* 2005; 82:53-59.

    Slinde F, Grönberg A, Engström C, Rossander-Hulthén L, Larsson S. Body composition by bioelectrical impedance predicts mortality in chronic obstructive pulmonary disease

patients. *Respiratory Medicine.* 2005; 99:1,004-1,009.

Tsimogianni A, Papiris S, Stathopoulos G, Manali E, Roussos C, Kotanidou A. Predictors of outcome after exacerbation of chronic obstructive pulmonary disease. *Journal of General Internal Medicine.* 2009; 24:1,043-1,048.

Uh S-T, Lee JY, Koo SM, Kim YK, Kim KU, Park JS, Park SW, Jang AS, Kim DJ, Choi JS, Na JO, Suh KH, Kim YH, Park C-S,. The Survival Rate of Korean Patients with COPD with or without Acute Exacerbations. *Tuberculosis and Respiratory Diseases.* 2011; 70:474-481

Yamauchi Y, Hasegawa W, Yasunaga H, Sunohara M, Jo T, Takami K, Matsui H, Fushimi K, Nagase T. Paradoxical association between body mass index and in-hospital mortality in elderly patients with chronic obstructive pulmonary disease in Japan. *International Journal of Chronic Obstructive Pulmonary Disease.* 2014; 9:1,337-1,346.

Zapatero A, Barba R, Ruiz J, Losa J, Plaza S, Canora J, Marco J. Malnutrition and obesity: influence in mortality and readmissions in chronic obstructive pulmonary disease patients. *Journal of Human Nutrition and Dietetics : the Official Journal of the British Dietetic Association* 2013; 26:16-22.

Baccioglu A, Gulbay B, Acican T. Body composition in patients with stable chronic obstructive pulmonary disease: comparison with malnutrition in healthy smokers. *The Eurasian Journal of Medicine* 2014; 46:169-175

Dimov D, Tacheva T, Koychev A, Ilieva V, Prakova G, Vlaykova T.. Obesity in Bulgarian patients with chronic obstructive pulmonary disease. *Chronic Respiratory Disease.* 2013; 10:215-222.

Lim J, Lee J, Kim J, Hwang Y, Kim T, Lim S, Yoo K, Jung K, Kim Y, Rhee C. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease.* 2017; 12:2,465-2,475.

O'Donnell D, Deesomchok A, Lam Y, Guenette J, Amornputtisathaporn N, Forkert L, Webb K.. Effects of BMI on static lung volumes in patients with airway obstruction. *Chest.* 2011; 140:461-468.

Qiu T, Tang Y, Xu Z, Xu D, Xiao J, Zhang M, Feng Y, Wang K. Association between body mass index and pulmonary function of patients with chronic obstructive pulmonary disease. *Chinese Medical Journal.* 2009; 122:1,110-1,111

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

  None.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Monitor and Evaluate Serum 25(OH)D Status 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

  COPD: Monitor and Evaluate Serum 25(OH)D Levels

  The RDN should periodically check serum 25(OH)D levels in adults with COPD as part of a routine nutrition monitoring and evaluation. Evidence from 60% of studies reviewed found positive associations between serum 25(OH)D and lung function measures.

  Rating: Fair
  Imperative

  - Risks/Harms of Implementing This Recommendation

    There are no potential risks or harms associated with the application of this recommendation.

  - Conditions of Application

    If necessary data are not available, the RDN should use professional judgment to request or obtain additional data.

  - Potential Costs Associated with Application

    - Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN
    - Costs may be incurred due to lab testing to evaluate serum 25(OH)D levels.

  - Recommendation Narrative

    A total of 29 papers from 28 studies provided evidence supporting the recommendation.

    - A total of 14 cross-sectional studies: One positive-quality (Romme et al, 2013), twelve neutral-quality (Azargoon et al, 2011; El-Shafey and El-Sougy, 2014; Hashim Ali Hussein et al, 2015; Janssens et al, 2010; Jolliffee et al, 2018; Mahlin et al, 2014; Mekov et al, 2015; Monadi et al, 2012; Park et al, 2015; Park et al, 2016; Persson et al, 2012; Shaneen et al, 2011) and one negative-quality (Yang et al, 2015)
    - Six prospective cohort studies: Three positive-quality (Kunisaki et al, 2012; Persson et al, 2015; Puhan et al, 2014) and three neutral-quality (Holmgaard et al, 2013; Jung et al, 2015; Quint et al, 2012)
    - Four retrospective cohort studies: Three positive-quality (Berg et al, 2013; Malinovschi et al, 2014; Mekov et al, 2016) and one neutral-quality (Moberg et al, 2014)
    - Two randomized controlled trials (RCT): One positive-quality (Sanjari et al, 2106) and one neutral-quality (Yumrutepe et al, 2015)
    - One neutral-quality before-after study (Said and Abd-Einaeem, 2015)
    - One neutral-quality descriptive study (Gouda et al, 2016)
    - One neutral-quality case-control study (Kunisaki et al, 2011).

    The overall findings were as follows:

    - *Lung Function (LF)* (23 studies): A total of 14 studies found significant relationships between serum 25(OH)D and LF outcomes; i.e., as serum 25(OH)D increased, LF outcomes improved (Azargoon et al, 2011; Berg et al, 2013; El-Shafey and El-Sougy, 2014; Gouda et al, 2016; Janssens et al, 2010; Jolliffee et al, 2018; Jung et al, 2015; Park et al, 2016; Persson et al, 2012; Persson et al, 2015; Romme et al, 2013; Said and Abd-Elnaeem, 2015; Yang et al, 2015; Yumrutepe et al, 2015). Nine studies did not find significant relationships between serum 25(OH)D and LF outcomes (Hashim Ali Hussein et al, 2015; Holmgaard et al, 2013; Kunisaki et al, 2011; Mahlin et al, 2014; Malinovschi et al, 2014; Monadi et al, 2012; Park et al, 2015; Sanjari et al, 2016; Shaheen et al, 2011).
    - *Acute Exacerbations (AE)* (11 studies): Four studies found significant relationships between serum 25(OH)D and AE outcomes; i.e., as serum 25(OH)D increased, AE outcomes improved (Gouda et al, 2016; Malinovschi et al, 2014; Persson et al, 2015; Yang et al, 2015). Seven studies did not find significant relationships between serum 25(OH)D and AE outcomes (Jung et al, 2015; Kunisaki et al, 2011; Mekov et al, 2015; Moberg et al, 2014; Persson et al, 2012; Puhan et al, 2014; Quint et al, 2012).
    - *Mortality* (five studies): NS relationships were found in any of the studies (Holmgaard et al, 2013; Mekov et al, 2016; Moberg et al, 2014; Persson et al, 2015; Puhan et al,

2014).

- Recommendation Strength Rationale
  - Conclusion statement supporting the recommendation is Grade II, *Fair*.
  - Synthesis of results was challenging due to lack of consistency in vitamin D dosing, dosing frequency and delivery routes, length of intervention and baseline serum 25(OH)D levels.
- Minority Opinions

  None.

- Supporting Evidence

  The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

  What associations exist between serum 25(OH)D levels and mortality, lung function and exacerbation outcomes in adults with COPD?

  - References

    Azargoon AR, Moghadam PK, Shokrollahi S, Ebrahimzadeh F, Pournia Y. . Relationship between FEV1 and 25-hydroxy Vitamin D in patients with chronic obstructive pulmonary disease. *Trends in Medical Research* 2011; 6:184-190

    Berg I, Hanson C, Sayles H, Romberger D, Nelson A, Meza J, Miller B, Wouters E, Macnee W, Rutten E ,Romme E, Vestbo J, Edwards L, Rennard S. Vitamin D, vitamin D binding protein, lung function and structure in COPD. *Respiratory Medicine* 2013; 107:1578-88

    Basem I. El-Shafey and Hesham A. El-Srougy B. Does serum 25 hydroxy vitamin D level play a role in COPD?. *Egyptian Journal of Chest Diseases and Tuberculosis* 2014; 63:43-47

    Essam Gouda, Mohamed Zidan, Gharraf Heba, Doreene Nazeih Younan, Samar Mohamed. Pattern of vitamin D in patients with chronic obstructive pulmonary diseases and in patients with bronchial asthma. *Egyptian Journal of Chest Diseases and Tuberculosis* 2016; 65:389-396

    Hashim Ali Hussein S, Nielsen L, Konow Bøgebjerg Dolberg M, Dahl R. Serum magnesium and not vitamin D is associated with better QoL in COPD: A cross-sectional study. *Respiratory Medicine* 2015; 109:727-33

    Holmgaard D, Mygind L, Titlestad I, Madsen H, Fruekilde P, Pedersen S, Pedersen C. Serum vitamin D in patients with chronic obstructive lung disease does not correlate with mortality--results from a 10-year prospective cohort study. *PloS One* 2013; 8:e53670

    Janssens W, Bouillon R, Claes B, Carremans C, Lehouck A, Buysschaert I, Coolen J, Mathieu C, Decramer M, Lambrechts D. Vitamin D deficiency is highly prevalent in COPD and correlates with variants in the vitamin D-binding gene. *Thorax* 2010; 65:215-20

    Jolliffe D, James W, Hooper R, Barnes N, Greiller C, Islam K, Bhowmik A, Timms P, Rajakulasingam R, Choudhury A, Simcock D, Hyppönen E, Walton R, Corrigan C, Griffiths C, Martineau A. Prevalence, determinants and clinical correlates of vitamin D deficiency in patients with Chronic Obstructive Pulmonary Disease in London, UK. *The Journal of Steroid Biochemistry and Molecular Biology* 2018; 175:138-145

    Jung J, Kim Y, Kim S, Kim H, Oh Y, Lee S, Seo J, Lee S. Relationship of vitamin D status with lung function and exercise capacity in COPD. *Respirology (Carlton, Vic.)* 2015; 20:782-9

    Kunisaki K, Niewoehner D, Singh R, Connett J. Vitamin D status and longitudinal lung function decline in the Lung Health Study. *The European Respiratory Journal* 2011; 37:238-43

    Kunisaki K, Niewoehner D, Connett J. Vitamin D levels and risk of acute exacerbations of chronic obstructive pulmonary disease: a prospective cohort study. *American Journal of Respiratory and Critical Care Medicine* 2012; 185:286-90

    Måhlin C, von Sydow H, Osmancevic A, Emtner M, Grönberg A, Larsson S, Slinde F. Vitamin D status and dietary intake in a Swedish COPD population. *The Clinical Respiratory Journal* 2014; 8:24-32

    Malinovschi A, Masoero M, Bellocchia M, Ciuffreda A, Solidoro P, Mattei A, Mercante L, Heffler E, Rolla G, Bucca C. Severe vitamin D deficiency is associated with frequent exacerbations and hospitalization in COPD patients. *Respiratory Research* 2014; 15:131

    Mekov E, Slavova Y, Tsakova A, Genova M, Kostadinov D, Minchev D, Marinova D, Tafradjiiska M. Vitamin D Deficiency and Insufficiency in Hospitalized COPD Patients. *PloS One* 2015; 10:e0129080

    Mekov E, Slavova Y, Tsakova A, Genova M, Kostadinov D ,Minchev D, Marinova D, Boyanov M. One-year mortality after severe COPD exacerbation in Bulgaria. *PeerJ* 2016; 4:e2788

    Moberg M, Vestbo J, Martinez G, Lange P, Ringbaek T. Prognostic value of C-reactive protein, leukocytes, and vitamin d in severe chronic obstructive pulmonary disease. *The Scientific World Journal* 2014; 2014:140736

    Monadi M, Heidari B, Asgharpour M, Firouzjahi A, Monadi M, Ghazi Mirsaied M. Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (COPD). *Caspian Journal of Internal Medicine* 2012; 3:451-5

    Park J, Park H, Jung H, Lee S, Koo H. Parathyroid Hormone as a Novel Biomarker for Chronic Obstructive Pulmonary Disease: Korean National Health and Nutrition Examination Survey. *PloS One* 2015; 10:e0138482

    Park Y, Kim Y, Kang Y, Shin J, Oh Y, Seo J, Jung J, Lee S. Relationship between vitamin D-binding protein polymorphisms and blood vitamin D level in Korean patients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2016; 11:731-8

    Persson L, Aanerud M, Hiemstra P, Hardie J, Bakke P, Eagan T. Chronic obstructive pulmonary disease is associated with low levels of vitamin D. *PloS One* 2012; 7:e38934

    Persson L, Aanerud M, Hiemstra P, Michelsen A, Ueland T, Hardie J, Aukrust P, Bakke P, Eagan T. Vitamin D, vitamin D binding protein, and longitudinal outcomes in COPD. *PloS One* 2015; 10:e0121622

    Puhan M, Siebeling L, Frei A, Zoller M, Bischoff-Ferrari H, Ter Riet G. No association of 25-hydroxyvitamin D with exacerbations in primary care patients with COPD. *Chest* 2014; 145:37-43

    Quint J, Donaldson G, Wassef N, Hurst J, Thomas M, Wedzicha J. 25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease. *BMC Pulmonary Medicine* 2012; 12:28

    Romme E, Rutten E, Smeenk F, Spruit M, Menheere P, Wouters E. Vitamin D status is associated with bone mineral density and functional exercise capacity in patients with chronic obstructive pulmonary disease. *Annals of Medicine* 2013; 45:91-6

    Said AF and Abd-Elnaeem EA. Vitamin D and chronic obstructive pulmonary disease. *Egyptian Journal of Chest Diseases and Tuberculosis* 2015; 64:67-73

    Sanjari M, Soltani A, Habibi Khorasani A, Zareinejad M. The effect of vitamin D on COPD exacerbation: a double blind randomized placebo-controlled parallel clinical trial. *Journal of*

Diabetes and Metabolic Disorders 2016; 15:33

Shaheen S, Jameson K, Robinson S, Boucher B, Syddall H, Sayer A, Cooper C, Holloway J, Dennison E. Relationship of vitamin D status to adult lung function and COPD. *Thorax* 2011; 66:692-8

Yang Y, Guo Y, Zhang H, Sun T. Antimicrobial peptide LL-37 circulating levels in chronic obstructive pulmonary disease patients with high risk of frequent exacerbations. *Journal of Thoracic Disease* 2015; 7:740-5

Yumrutepe T, Aytemur Z, Baysal O, Taskapan H, Taskapan C, Hacievliyagil S. Relationship between vitamin D and lung function, physical performance and balance on patients with stage I-III chronic obstructive pulmonary disease. *Revista da Associacao Medica Brasileira (1992)* 2015; 61:132-8

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011 Jul; 96 (7): 1, 911-1, 930. doi: 10.1210/jc.2011-0385. Epub 2011 Jun 6. Erratum in: *J Clin Endocrinol Metab.* 2011 Dec; 96 (12): 3, 908. PMID: 21646368.

Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, Miller B, Lomas DA, Agusti A, Macnee W, Calverley P, Rennard S, Wouters EF, Wedzicha JA. Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators. Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med.* 2010 Sep 16; 363 (12): 1, 128-1, 138. doi: 10.1056/NEJMoa0909883. PMID: 20843247.

Le Rouzic O, Roche N, Cortot AB, Tillie-Leblond I, Masure F, Perez T, Boucot I, Hamouti L, Ostinelli J, Pribil C, Poutchnine C, Schück S, Pouriel M, Housset B. Defining the "Frequent Exacerbator" Phenotype in COPD: A Hypothesis-Free Approach. *Chest.* 2018 May; 153 (5): 1, 106-1, 115. doi: 10.1016/j.chest.2017.10.009. Epub 2017 Oct 17. PMID: 29054347.

Rusinska A, Pludowski P, Walczak M, Borszewska-Kornacka MK, Bossowski A, Chlebna-Sokól D, Czech-Kowalska J, Dobrzanska A, Franek E, Helwich E, Jackowska T, Kalina MA, Konstantynowicz J, Ksiazyk J, Lewinski A, Lukaszkiewicz J, Marcinowska-Suchowierska E, Mazur A, Michalus I, Peregud-Pogorzelski J, Romanowska H, Ruchala M, Socha P, Szalecki M, Wielgos M, Zwolinska D, Zygmunt A. Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland - Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies - 2018 Update. *Front Endocrinol (Lausanne).* 2018 May 31; 9: 246. doi: 10.3389/fendo.2018.00246. eCollection 2018. Review. PMID: 29904370.

Wedzicha JA, Miravitlles M, Hurst JR, Calverley PM, Albert RK, Anzueto A, Criner GJ, Papi A, Rabe KF, Rigau D, Sliwinski P, Tonia T, Vestbo J, Wilson KC, Krishnan JA. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. *Eur Respir J.* 2017 Mar 15; 49 (3). pii: 1600791. doi: 10.1183/13993003.00791-2016. Print 2017 Mar. PMID: 28298398.

- Chronic Obstructive Pulmonary Disease
- Chronic Obstructive Pulmonary Disease (COPD) Guideline (2019)

Quick Links

Recommendations Summary

COPD: Monitor and Evaluate Effect of Vitamin D Supplementation 2019

Click here to see the explanation of recommendation ratings (Strong, Fair, Weak, Consensus, Insufficient Evidence) and labels (Imperative or Conditional). To see more detail on the evidence from which the following recommendations were drawn, use the hyperlinks in the Supporting Evidence Section below.

- Recommendation(s)

COPD: Monitor and Evaluate Effect of Vitamin D Supplementation

In adults with COPD who are receiving vitamin D supplementation, the RDN should monitor and evaluate the effect of the supplementation regimen on serum 25(OH)D levels. If baseline serum 25(OH)D levels were ≤10ng per ml, the RDN should also evaluate the frequency of exacerbations to measure the effectiveness of supplementation. Limited evidence of vitamin D supplementation in adults with COPD supports improved exacerbation outcomes in those with baseline serum 25(OH)D levels 10ng per ml or lower. While vitamin D is important for general health, vitamin D supplementation in those with baseline serum 25(OH)D levels 11ng to 29ng per ml may or may not improve lung function or reduce exacerbations in adults with COPD.

Rating: Fair
Conditional

- Risks/Harms of Implementing This Recommendation

  There are no potential risks or harms associated with the application of the recommendation.

- Conditions of Application

  - The recommendation applies to adults with COPD with baseline (BL) serum 25(OH)D levels less than 29ng per ml and in whom vitamin D supplements have been initiated, and in COPD patients with BL serum 25(OH)D levels ≤10ng per ml who may also have frequent exacerbations. Frequent exacerbations are defined as two or more exacerbations per year (Hurst et al, 2010; Le Rouzic et al, 2018).
  - Coordination with the prescribing provider may be required for recommended changes to vitamin D supplementation and physician orders
  - Exacerbations are clinically defined as episodes of increasing respiratory symptoms, particularly dyspnea, cough and sputum production and increased sputum purulence (Wedzicha et al, 2017). The patient perception of an exacerbation is seeking treatment for symptoms; the research criteria is treatment with antibiotics or addition of increased inhaled or systemic steroids.
  - Achievement of normal serum 25(OH)D levels may not be possible in all instances. Therefore, optimizing serum 25(OH)D levels is the goal (Rusinska et al, 2018).
  - Frequency of monitoring serum 25(OH)D levels post-supplementation should be at three-month intervals (Rusinska et al, 2018).

- Potential Costs Associated with Application

  - Costs may include expenses related to medical nutrition therapy (MNT) visits from an RDN
  - Costs may be incurred related to the purchase of over-the-counter vitamin D supplements or co-pays
  - Costs may be incurred due to lab testing to evaluate serum 25(OH)D levels.

- Recommendation Narrative

  A total of eight studies were included in the evidence analysis supporting the recommendation:

  - Six randomized controlled trials (RCTs) [four positive-quality (Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Sanjari et al, 2016), one neutral-quality (Khan et al, 2017) and one negative-quality (Zendendel et al, 2015)]
  - Two before-after studies [both neutral-quality (Rezk et al, 2015; Said and Abd-Elnaeem, 2015)].

  Seven studies tested oral vitamin D_3 (cholecalciferol) ranging from 1, 200 IU daily for six months; subjects and controls could also take 400 IU vitamin D_3 daily (Rafiq et al, 2017) to 120, 000 IU every two months for 12 months (Martineau et al, 2015).

  - One study administered 200, 000 IU cholecalciferol intramuscularly (IM) every four weeks for six months (Said and Abd-Elnaeem, 2015)
  - All papers either cited the Endocrine Society Clinical Practice Guideline (ESG) (Holick et al, 2011) for serum 25(OH)D classifications or did not define classifications. In

addition to the ESG reference, one study (Lehouck et al, 2012) defined "severe" vitamin D deficiency as serum 25(OH)D levels under 10ng per ml.

Seven studies evaluated lung function (LF) outcomes (Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Rezk et al, 2015; Sanjari et al, 2016; Said and Abd-Elnaeem, 2015; Zendedel et al, 2015). Six studies evaluated acute exacerbation (AE) outcomes (Khan et al, 2017; Lehouck et al, 2012; Martineau et al, 2015; Rafiq et al, 2017; Rezk et al, 2015; Zendedel et al, 2015).

Five studies of vitamin D supplementation included subjects' pre- and post-supplementation levels, allowing changes in vitamin D status due to supplementation to be assessed. Results according to baseline (BL) and post-supplementation improvements in vitamin D status (ESG categories) are as follows:

- *Deficient to sufficient 25(OH)D:* Supplementation with 1, 200 IU D_3 daily for six months (plus 400 IU daily, if desired) resulted in no impact on LF or AE outcomes (Rafiq et al, 2012). Supplementation with 100, 000 IU D_3 every four weeks over 12 months resulted in a decrease in AE rate in a sub-group of subjects with "*severe deficiency*" [25(OH)D under 10ng per ml] (Lehouck et al, 2012).
- *Insufficient to sufficient 25(OH)D:* Supplementation with 100, 000 IU D_3 every four weeks over 12 months resulted in no impact on AE or LF outcomes (Lehouck et al, 2012). Supplementation with either 5, 000 IU D_3 or 0.25mcg calcitriol every four weeks over 12 months resulted in no impact on LF outcomes (Sanjari et al, 2016).
- *Deficient to insufficient 25(OH)D:* Supplementation with 50, 000 IU D_3 per week for eight weeks, then 800 IU daily for 12 months resulted in a decrease in number of AEs and an improvement in MVV, but no impact on other LF outcomes in subjects with 25(OH)D under 10ng per ml at BL (Rezk et al, 2015). Supplementation with 120, 000 IU D_3 every two months over 12 months resulted in improvement in AE severity and symptoms, but had no impact on other AE or LF outcomes (Martineau et al, 2015).

The remaining three studies did not report subjects' post-supplementation vitamin D status. One study (Said and Abd-Elnaeem, 2015) reported BL vitamin D status according to ESG categories, but did not report post-supplementation status. The second study (Khan et al, 2017) reported BL vitamin D status of subjects and controls combined and did not report pre- and post-supplementation status of subjects only. Finally, the last study (Zendedel et al, 2015) did not report either BL or post-supplementation vitamin D status.

- *Insufficient 25(OH)D (subjects + controls):* Supplementation with 2, 000 IU D_3 per day for six months resulted in reduced AEs (Kahn et al, 2017). Supplementation with 200, 000 IU D_3 IM every four weeks for six months resulted in no impact in LF outcomes (Said and Abd-Elnaeem, 2015).
- *Unknown 25(OHD):* Supplementation with 100, 000 IU D_3 every month for six months resulted in improvement in LF outcomes and a reduction in AEs (Zendedel et al, 2015).

- Recommendation Strength Rationale
  - Conclusion statement supporting the recommendation is Grade II, *Fair*
  - Synthesis of results was challenging due to lack of consistency in vitamin D dosing, dosing frequency and delivery routes, length of intervention and baseline serum 25(OH)D levels.
- Minority Opinions

  None.

- Supporting Evidence

The recommendations were created from the evidence analysis on the following questions. To see detail of the evidence analysis, click the blue hyperlinks below (recommendations rated consensus will not have supporting evidence linked).

Does vitamin D supplementation improve lung function and exacerbation outcomes in adults with COPD?

- References

Khan D,Ullah A,Randhawa F,Iqtadar S,Butt N,Waheed K. Role of Vitamin D in reducing number of acute exacerbations in Chronic Obstructive Pulmonary Disease (COPD) patients. *Pakistan journal of medical sciences* 2017; 33:610-614

Lehouck A, Mathieu C, Carremans C, Baeke F, Verhaegen J, Van Eldere J, Decallonne B, Bouillon R, Decramer M, Janssens W. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease: a randomized trial. *Annals of Internal Medicine* 2012; 156:105-14

Martineau A, James W, Hooper R, Barnes N, Jolliffe D, Greiller C, Islam K, McLaughlin D, Bhowmik A, Timms P, Rajakulasingam R, Rowe M, Venton T, Choudhury A, Simcock D, Wilks M, Degun A, Sadique Z, Monteiro W, Corrigan C, Hawrylowicz C, Griffiths C. Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease (ViDiCO): a multicentre, double-blind, randomised controlled trial. *The Lancet. Respiratory Medicine* 2015; 3:120-130

Rafiq R, Prins H, Boersma W, Daniels J, den Heijer M, Lips P, de Jongh R. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: a pilot trial. *International Journal of Chronic Obstructive Pulmonary Disease* 2017; 12:2583-2592

Rezk NA, Yehia AA, Hewidy, AA. Effect of vitamin D replacement in chronic obstructive pulmonary disease patients with vitamin D deficiency. *Egyptian Journal of Chest Diseases and Tuberculosos* 2015; 64:353-357

Said AF and Abd-Elnaeem EA. Vitamin D and chronic obstructive pulmonary disease. *Egyptian Journal of Chest Diseases and Tuberculosis* 2015; 64:67-73

Sanjari M, Soltani A, Habibi Khorasani A, Zareinejad M. The effect of vitamin D on COPD exacerbation: a double blind randomized placebo-controlled parallel clinical trial. *Journal of Diabetes and Metabolic Disorders* 2016; 15:33

Zendedel A, Gholami M, Anbari K, Ghanadi K, Bachari E, Azargon A. Effects of Vitamin D Intake on FEV1 and COPD Exacerbation: A Randomized Clinical Trial Study. *Global Journal of Health Science* 2015; 7:243-8

- References not graded in Academy of Nutrition and Dietetics Evidence Analysis Process

Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011 Jul; 96 (7): 1, 911-1, 930. doi: 10.1210/jc.2011-0385. Epub 2011 Jun 6. Erratum in: *J Clin Endocrinol Metab.* 2011 Dec; 96 (12): 3, 908. PMID: 21646368.

Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, Miller B, Lomas DA, Agusti A, Macnee W, Calverley P, Rennard S, Wouters EF, Wedzicha JA. Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators. Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med.* 2010 Sep 16; 363 (12): 1, 128-1, 138. doi: 10.1056/NEJMoa0909883. PMID: 20843247.

Le Rouzic O, Roche N, Cortot AB, Tillie-Leblond I, Masure F, Perez T, Boucot I, Hamouti L, Ostinelli J, Pribil C, Poutchnine C, Schück S, Pouriel M, Housset B. Defining the "Frequent Exacerbator" Phenotype in COPD: A Hypothesis-Free Approach. *Chest.* 2018 May; 153 (5): 1, 106-1, 115. doi: 10.1016/j.chest.2017.10.009. Epub 2017 Oct 17. PMID: 29054347.

Rusinska A, Pludowski P, Walczak M, Borszewska-Kornacka MK, Bossowski A, Chlebna-Sokól D, Czech-Kowalska J, Dobrzanska A, Franek E, Helwich E, Jackowska T, Kalina MA, Konstantynowicz J, Ksiazyk J, Lewinski A, Lukaszkiewicz J, Marcinowska-Suchowierska E, Mazur A, Michalus I, Peregud-Pogorzelski J, Romanowska H, Ruchala M, Socha P, Szalecki M, Wielgos M, Zwolinska D, Zygmunt A. Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland - Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies - 2018 Update. *Front Endocrinol (Lausanne).* 2018 May 31; 9: 246. doi: 10.3389/fendo.2018.00246. eCollection 2018. Review. PMID: 29904370.

Wedzicha JA, Miravitlles M, Hurst JR, Calverley PM, Albert RK, Anzueto A, Criner GJ, Papi A, Rabe KF, Rigau D, Sliwinski P, Tonia T, Vestbo J, Wilson KC, Krishnan JA. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. *Eur Respir J.* 2017 Mar 15; 49 (3). pii: 1600791. doi: 10.1183/13993003.00791-2016. Print 2017 Mar. PMID: 28298398.