

Lifestyles and their Association with Respiratory Diseases

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Abstract

Several respiratory diseases have a serious impact on global morbidity and mortality. Besides chronic diseases like asthma, obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD), and lung cancer, these also include cases of pneumonia. COPD is a progressive and debilitating disease that is linked to recurring respiratory symptoms with frequent exacerbations. The decline in lung function eventually leads to cor pulmonale and respiratory failure. Asthma is a chronic inflammatory disease of the airways that causes wheezing, coughing, chest tightness, and shortness of breath. It significantly impairs life with recurrent bronchial symptoms and frequent rhinitis. OSA is associated with periods of reduced or absence of airflow through mouth or nose resulting in loud snoring, caused by upper respiratory tract airway obstruction during sleep. Due to non-salubrious nocturnal sleep, these patients have excessive daytime sleepiness or fatigue. Lung cancer is common, accounting for an estimated 12% of the global cancer burden. It is extremely lethal, with the five-year relative survival rate being only 19%. Lung cancer deaths account for 1 in 5 cancer deaths worldwide. Pneumonia, both bacterial and viral, also plays a notable role in global morbidity and mortality. Most of these disorders can be substantially reduced in incidence by following healthy day-to-day behaviors. These include abstinence from smoking and alcohol intake, avoiding sedentary life, and partaking in a regular exercise program, a diet that is primarily plant-based, and maintaining normal body weight. Healthy lifestyles also dramatically reduce the impact of these diseases, leading to a better quality of life and a decrease in mortality. This manuscript discusses the relationship between healthy lifestyle behaviors and common respiratory diseases.

Keywords: Smoking, COPD, asthma, obstructive sleep apnea, lung cancer, lifestyles

Introduction

“The WHO mentions several chronic respiratory diseases, and these include bronchiectasis, asthma, pulmonary heart disease and diseases of pulmonary circulation (including pulmonary embolism, pulmonary hypertension, and cor pulmonale), chronic rhinosinusitis, hypersensitivity pneumonitis, lung cancer, and neoplasms of respiratory and intrathoracic organs, lung fibrosis, chronic pleural diseases, pneumoconiosis, pulmonary eosinophilia, chronic obstructive lung disease (including chronic obstructive pulmonary disease (COPD), bronchitis and emphysema), rhinitis, sleep apnea syndrome and sarcoidosis”^[1]. Of these, the most frequent chronic respiratory diseases encountered are COPD, asthma, lung cancer, lung infections, including tuberculosis, and interstitial lung diseases (ILD)^[2]. Obstructive sleep apnea (OSA) is also increasingly being diagnosed^[3]. These diseases inflict a huge morbidity burden globally^[4]. They're also a key factor of death and disability around the world^[5]. They are responsible for about 7.5 million deaths per year and account for approximately 14% of annual deaths worldwide^[6,7]. COPD is a common cause and tobacco smoking is its main underlying cause^[8]. Its global burden is on the increase^[9]. Airflow limitation is a major element in this disease, and this can be diagnosed by an abnormally low forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio¹⁰. The GOLD guidelines are used to classify patients based on their predicted FEV1 percentage: I (mild): FEV1 >80 percent predicted; II (moderate): FEV1=50 percent to 79 percent predicted; III (severe): FEV1=30 percent to 49 percent

predicted; and IV (very severe): FEV1 30 percent predicted^[10]. It causes persistent respiratory symptoms with frequent exacerbations^[11]. It's a debilitating disease that causes lung function to deteriorate, leading to cor-pulmonale and respiratory failure^[11]. “In 2015, COPD was associated with 2-6 percent of Disability-Adjusted Life Years (DALYs) worldwide”^[12]. It eventually causes death^[13]. COPD is the key factor of death over 3 million individual dying each year^[12]. Although asthma is more prevalent worldwide, in 2015, COPD-related deaths were nearly 8 times as common as asthma-related deaths^[12]. COPD is expected to be the 3rd major key factor of death worldwide by 2030, according to the WHO^[14]. Direct and indirect costs related with COPD are estimated to be billions of dollars. Asthma is a usual illness that affects individuals all over the world^[12]. It's a chronic inflammatory disease of the airways^[15]. Asthma affects approximately 8% of the population or about 25 million individuals in the USA^[16]. It is characterized by episodic wheezing, cough, chest tightness, and breathlessness^[17]. Besides the presence of these symptoms, lung function tests (especially using spirometry and peak flow meter (PEF)) help establish a diagnosis and monitoring the disease^[18]. Spirometry is commonly used to diagnose asthma and measures the FEV1 and its reversibility^[18,19]. A good FEV1 is > 80% of predicted^[18]. Airway reversibility is positive when FEV1 increases >12% and >200 ml following treatment^[19]. Regular PEF measurement in asthma patients helps monitor the control of the disease^[20]. Asthma is a serious disease in which bronchial symptoms impair one's quality of life^[21],

while rhinitis co-morbidity impairs one's social life [22]. In 2015, it was responsible for 1.1% of global DALYs [12]. According to the WHO, an estimated 2,50,000 individuals pass away of asthma each year [23]. The upper airway becomes interrupted during sleep, giving rise in obstructive sleep apnea (OSA) [24]. There are periods of reduced or absence of airflow through mouth or nose resulting in loud snoring and the associated hypoxemia is usually terminated by arousal [25]. Despite a 7-9-hour sleep, these patients have excessive daytime sleepiness or fatigue [26]. The STOP-BANG questionnaire and the Epworth Sleepiness Scale (ESS) are frequently used as clinical screening tools for OSA [27, 28]. "The ESS assesses sleepiness as well as the potential of falling asleep, during eight daily activities, and are scored by the patients as never=0; slight=1; moderate=2, high=3, in 8 situations. A total score of >10 is considered abnormal" [27]. "The STOP-BANG survey includes of eight yes/no questions: tired, observed stopped breathing, snore, high BP, BMI >35kg/m², age >50, neck >15.75 inches, and gender=male+" [28]. A high risk for OSA is indicated by a >2 yes response [28]. In the field of diagnostic testing, polysomnography is known as the gold standard [29]. Polysomnography provides an estimate of the apnea-hypopnea index (AHI), which is the proportion number of hypopneas and apneas to total sleep time [30-32]. "The AHI is used to measure the severity of OSA: 5.0-14.9 events per hour=mild OSA, 15-30 events per hour=moderate OSA, and >30 events per hour=severe OSA" [33]. OSA is often associated with several potentially lethal disorders. Further, it may cause poor concentration, cognitive dysfunction, irritability, and depression memory and judgment problems.

Lung cancer is common and lethal [34]. "The American Cancer Society estimates that there were 2.1 million new cases of lung cancer in 2018, and these accounted for 12% of the global cancer burden" [34, 35]. The five-year relative survival rate is dismal, being 19% for all lung cancers [36]. Lung cancer deaths account for 1 in 5 cancer deaths worldwide [34, 35].

In addition to these major conditions, many other respiratory diseases, especially pneumonia, also play a notable role in global morbidity and mortality [37].

Discussion

Unhealthy lifestyles are responsible for over half of global premature deaths [38]. Adherence to five major healthy lifestyles-not smoking, avoiding, or drinking alcohol only in moderation, limiting sedentary behavior and exercising regularly, maintaining an ideal weight, and following a prudent diet, has significant benefits [39, 40]. A study from Harvard University in the USA estimated that at age 50, females can gain 14 extra years of life and males 12.2 more years of life with compliance with all five healthy lifestyles [40]. The impact of these five lifestyle behaviors on major respiratory diseases is discussed in this manuscript.

Tobacco smoking exposes the primary smoker to almost 70 carcinogens [41]. Unfortunately, non-smokers, involuntarily, become exposed to second-hand and third hand smoke [42, 43]. "Second-hand smoke is a mixture of the smoker's exhaled smoke and side-stream smoke from the cigarette's burning edge" [42]. Smoke pollutants that fall on skin, hair, clothing, furniture, carpets, etc., are inhaled when airborne and constitute third hand smoke [43]. Alcohol has cardiovascular benefits in low to moderate intake [44] but is harmful if imbibed in excess [45]. "Moderate alcohol consumption is defined as two standard drinks a day for men and one standard drink a day for women" [46, 47]. There's a relation

between drinking too much alcohol and getting a lung infection [48]. Activity guidelines are listed by several professional health organizations [49], and impart several benefits, both in morbidity and mortality, across a wide array of diseases [50]. "BMI is determined, By dividing a person's weight by the square of their height in meters" [51]. Anthropometric measurements can also determine a person's visceral obesity [52]. These include waist circumferences of <88cm in women and <102cm in men, waist-hip ratios of 0.85 or less in female and 0.9 or less in male, and a weight-height ratio of 0.5 in both men and women. [52]. Diet has a major effect on human physiology and should be of appropriate calories to prevent weight gain [53]. It should also be rich in non-starchy whole grains, legumes, vegetables and fruits, with limited to moderate consumption of lean meats, nuts, seafood, rich in mono and polyunsaturated fats, low-fat dairy products, and vegetable oil [54, 55]. It should avoid trans-fats and be limited in the consumption of fried foods, saturated fats, red meat, excess sodium, sugar-sweetened beverages and refined carbohydrates [54, 55]. Two popular diets, DASH diet and Mediterranean diet are healthy diets to follow [56, 57]. All these health behaviors, if improperly adhered to, have detrimental effects on several major respiratory diseases.

Exercise

Several systematic review meta-analyses and Cochrane analysis have been recorded the merits of exercise training in COPD patients [58, 59]. Exercise is beneficial in these patients independent of gender, age, disease severity or level of dyspnea [60]. Both aerobic [61] and resistance [62] "workouts help alleviate dyspnea, improve exercise tolerance (6-minute walk test) and, health-related life quality in patients with mild-to-severe COPD" [63, 64]. Respiratory muscle training helps [65]. Besides a reduction in exercise-induced hyperinflation, there is an increase in muscle function with exercise training [66]. Yoga [67] and qigong [68] exercises in these patients help COPD-related anxiety and depression [69]. Exercise also helps COPD associated co-morbidities [70], such as musculoskeletal or neurological disorders, chronic heart disease, metabolic syndrome, and some cancers [71]. Studies suggest that exercise improves exercise-induced asthma [72], decreases asthma-related symptoms [73], reduces asthma exacerbations in adults, and aids in the improvement of these patients' quality of life (QOL) [74]. Exercise in asthma improves cardiopulmonary fitness, with an increase in maximal oxygen consumption [75]. It also helps the airway smooth muscle [76]. Exercise reduces bronchial hyperresponsiveness [77, 78] and serum pro-inflammatory cytokines [78, 79]. Exercise also helps to reduce weight in these patients [80]. Physical activity and exercise are also beneficial for OSA [81-84]. Exercise in these patients reduces AHI, improves sleep efficiency, and reduces daytime sleepiness [85-89]. Besides the benefit of exercise on weight loss [90], exercise can help these patients by reducing fluid buildup in the neck, increasing upper airway dilator muscle tone, lowering inflammatory responses, and improving slow-wave sleep [91]. Exercise may also help the disturbed sympathetic nervous system and increased oxidative stress often seen in these patients [92]. Exercise training is also beneficial in interstitial lung disease [93-95]. They are less breathless, do better on the 6MWT, and have a better QOL [93-95]. "Exercise training improves right ventricular function in patients with pulmonary arterial hypertension" [96]. Exercise has significant beneficial effects on lung cancer [97]. A reduction of risk of 20-50% in men and 20-30% in women is generally found [97].

Preoperative exercises improve pulmonary function before lung resection surgery and reduce complications and hospital stay in these patients [98]. Postoperatively, exercise is related with a notable reformation in the QOL [99]. Exercise in patients with lung cancer may also help reduce brain metastasis [100].

Obesity

Obesity and COPD frequently coexist [101]. Obese COPD patients, especially those with severe disease [102, 103], usually demonstrate improved survival [104, 105] when compared to those with low or normal BMI [106]. This association is paradoxical to that seen with obesity and many other health conditions [107]. However, this obesity paradox has been questioned, as when CO₂ levels, muscle mass, and exercise capacity are looked at, there appears to be no obesity paradox in these patients [108]. It has therefore been suggested that exercise therapies may be considered in COPD patients that encourage weight loss without sacrificing lean body mass [109-111]. Since COPD patients are more likely to develop obesity associated diseases like cardiovascular disease [112], diabetes mellitus [113], and metabolic syndrome [114], the weight loss should also help mitigate these co-morbid conditions. Obesity raises the asthma risk in children [115]. "Obesity and weight gain in the mother during pregnancy are both interconnected to a 15-30 percent increased risk of asthma in the offspring" [116]. Obese children have more severe asthma, less disease control, and a lower life quality [117]. Obese adults also have a higher risk of incident asthma [118]. Beuther and Sutherland in a meta-analysis of many researches, including over 300,000 adults, estimated that when compared to lean people, the odd ratio for asthma in overweight people was 1.5, and 1.9 in obese people [118]. Obesity appears to have a more impact on asthma in female than in male [119]. Obese asthma patients experience a reduced response to asthma medications, a low life quality, and a higher level hospitalization risk [120, 121]. Weight loss helps these patients improve clinically [122, 123]. Obesity, especially visceral or central obesity, is a strong predictor of OSA [124]. Weight loss helps reduce OSA [125]. "Weight loss through lifestyle modification is recommended by the American Academy of Sleep Medicine as a treatment option for improving the apnea-hypopnea index (AHI) in obese OSA patients" [126]. A 10% decrease in BMI corresponds to a 30% decrease in AHI [127-129]. Several mechanisms are involved. Obesity is associated with incensement in the size of soft tissue structures within and around the airway. [130]. Further, Obesity can cause a reduction in lung volume due to a combination of increased abdominal fat mass [131] and abnormal neuroanatomic interactions [132]. The relation between lung cancer and obesity remains controversial [133]. Some studies report an opposite relationship between lung cancer and obesity [134, 135]. Abdominal or central obesity, even with a normal BMI, may be related to a high lung cancer risk [136-138]. However, a study among 162,679 American adults failed to find a relation between WC and BMI with the lung cancer risk [139]. Carreras-Torres *et al.*, using Mendelian randomization, recently reported that genetically predicted BMI, weight-height ratio, and insulin resistance, increased the potential lung cancer risk, especially for small cell and squamous cell lung cancers [140]. Obesity raises the potential of a variety of cancers [141], and therefore a higher lung cancer risk in obese patients is more likely-more studies must confirm this association. There also appears to be an obesity paradox with

lung cancer [142] and the involved mechanisms behind this are not well understood [143].

Smoking

The most significant key component for COPD is cigarette smoking [144]. Almost 20% of smokers develop COPD [145]. Current smokers are approximately 30% more prone to create COPD than former smokers [146]. Women highly susceptible to COPD as a result of tobacco smoke exposure [147, 148]. Inhaling secondhand smoke is also linked to a high level risk of COPD [149]. Smoking cessation is beneficial in COPD patients [150-154]. It decreases disease progression [151], improves symptoms [152], and reduces mortality [153, 154]. Smoking-related COPD patients also exhibit higher risk of lung cancer, diabetes, and CVD, and smoking cessation should also help mitigate these [155-157]. Smoking raises the risk for asthma in children [158]. Smoking results in poor control with frequent exacerbations [159] and raises the risk of the development of COPD [160]. Second hand-smoke exposure also exacerbates asthma symptoms [160, 161]. Several earlier researches describe a strong relation between OSA and cigarette smoking [162-164]. However, after controlling for BMI, age, and sex, a recent study discovered no relation between OSA and smoking [165]. Tobacco smoke is highly carcinogenic [166]. Most lung cancers are causally related to smoking [167]. Cigarette smokers face a 20-fold higher risk of developing lung cancer [168-170]. This increase in risk has also been noted with cigars and water-pipe smoking [171]. Tobacco smoke exposure has no safe level, especially when it comes to cancer. Even lung cancer risk is increased by 25% when secondhand smoke is inhaled [172]. Smoking cessation is beneficial, although an excess risk of cancer remains throughout life after quitting [173].

Diet

A calorie-restricted diet, in concert with exercise, helps weight reduction, and this also benefits respiratory diseases [174]. The quality of diet also appears to influence COPD [175-177]. A COPD healthy diet reduces the development of COPD from 25% to 54% [177-179]. COPD healthy diet is related with a raised intake of vegetables and fruits [180], fish [181], and a lower consumption of processed meats [182, 183]. The benefits of fruits and vegetables have been attributed to the presence of several micronutrients in these foods [184], a reduction in inflammation, and lower oxidative stress [184, 185]. Higher fruit intake has an inverse relationship with COPD-related mortality [186]. Obesity is harmful in asthma patients [187, 188]. A weight-reducing diet is therefore beneficial [189]. Asthma is primarily an inflammatory disease [190]. Fruits and vegetables, help lower airway inflammation [191, 192]. "A diet high in saturated fats, desserts and sweets, refined grains, processed and red meats, fried foods, and high-fat dairy products, combined with a low intake of vegetables and fruits, has been connected to asthma, particularly in children" [193-198]. OSA is beneficially affected by the Mediterranean diet [199]. Broccoli and other cruciferous vegetables, are rich in isothiocyanates, and have cancer-preventive effects [200]. The lung cancer risk does not appear to be increased by a higher consumption of total or saturated fat, as a pooled analysis of eight cohort studies showed [201]. However, high levels of nitrosamines (formed during cooking) in well-done or fried red meat, appear to raise the risk of cancer. [202, 203].

Alcohol

There is no certain relation between COPD and alcohol intake [204]. There is some suggestion that alcohol intake may decrease COPD-related death [205], and a heavy intake of alcohol may increase COPD risk [206], suggesting a possible U-shaped relationship [207]. Alcohol may induce asthma, but the literature on this relationship is limited [208]. The triggers include alcohol related acetaldehyde, sulfite additives and salicylates [209, 210]. However, alcohol may also be a treatment for asthma [211]. It relaxes airway smooth muscle tone and is an effective bronchodilator [211]. Its association with lung cancer is confounded by frequent smoking in alcohol consumers [212-214]. However, even after ruling out this confounding factor, heavy alcohol intake appears to increase lung cancer risk [212-214]. Moderate to heavy alcohol intake, is also known to increase the frequency of OSA [215]. AUD patients appear more susceptible to pneumonia because of *Klebsiella pneumoniae* and *Streptococcus pneumoniae* [216-220], and progression to bacteremia, sepsis, septic shock, and acute respiratory distress syndrome [221-222]. They are also more prone to pulmonary tuberculosis [223] and respiratory syncytial virus infection [224]. Acute lung injury is also seen more commonly in alcoholics after major trauma [225, 226].

Conclusion

The main five modifiable behaviors, namely smoking, diet, alcohol intake, exercise, and Obesity is a key factor in the evolution and advancement of most respiratory illness. The impact is especially severe in COPD, asthma, pneumonia, and lung cancer-respiratory diseases that are responsible for high mortality and morbidity, worldwide. It is therefore essential to avoid smoking and drinking alcohol, keep active and exercise regularly, while following a prudent and calorie-appropriate diet. The benefits of healthy behaviors also spill over to many comorbid diseases that are common in these patients. The result is a healthier and long life.

References

1. https://www.who.int/gard/publications/chronic_respiratory_diseases.pdf.
2. Wassim W Labaki, MeiLan K Han. Chronic respiratory diseases: a global view. *Lancet*. 2020; 8(6):531-533. Doi: [https://doi.org/10.1016/S2213-2600\(20\)30157-0](https://doi.org/10.1016/S2213-2600(20)30157-0).
3. Benjafield AV, Ayas NT, Eastwood PR *et al*. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *The Lancet Respir Med*. 2019; 7(8):687-698.
4. Soriano JB, Kendrick P, Paulson K, Gupta V, Vos T. Prevalence and attributable health burden of chronic respiratory diseases from 1990-2017: a systematic analysis from the Global Burden of Disease Study 2017. *Lancet Respir Med*. 2020.
5. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med*. 2020; 8(6):585-596. Doi: 10.1016/S2213-2600(20)30105-3.
6. Noncommunicable Diseases Country Profile. Geneva: World Health Organization, 2018, 223. Available online: <https://www.who.int/nmh/publications/ncd-profiles-2018/en>.
7. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med*. 2020; 8(6):585-596. Doi: 10.1016/S2213-2600(20)30105-3.
8. Salvi S. Tobacco smoking and environmental risk factors for chronic obstructive pulmonary disease. *Clin Chest Med*. 2014; 35(1):17-27. Doi: 10.1016/j.ccm.2013.09.011.
9. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*. 2007; 370(9589):765-73. Doi: 10.1016/S0140-6736(07)61380-4.
10. Rabe KF, Hurd S, Anzueto A *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2007; 176:532-555.
11. Demoule A, Brochard L, Dres M *et al*. How to ventilate obstructive and asthmatic patients. *Intensive Care Med*. 2020; 46(12):2436-2449. Doi: 10.1007/s00134-020-06291-0.
12. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med*. 2017; 5(9):691-706. Doi: 10.1016/S2213-2600(17)30293-X.
13. WHO. Chronic Obstructive Pulmonary Disease (COPD), 2017. Available from: [https://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)). Accessed December 2, 2018.
14. WHO. Chronic Obstructive Pulmonary Disease (COPD), 2017. Available from: [https://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)), 2018.
15. Mims JW. Asthma: definitions and pathophysiology. *Int Forum Allergy Rhinol*. 2015; 5(1):S2-6. Doi: 10.1002/alr.21609.
16. CDC-Asthma-Most recent asthma data. 2018. Available at: https://www.cdc.gov/asthma/most_recent_data.htm. Accessed September 4, 2021.
17. <https://www.cdc.gov/asthma/faqs.htm> - accessed, 2021.
18. <https://www.lung.org/lung-health-diseases/lung-disease-lookup/asthma/diagnosing-treating-asthma/how-is-asthma-diagnosed>.
19. Pellagrino R, Viegi G *et al*. Interpretative strategies for lung function tests. *Eur Respir J*. 2005; 26:948-968.
20. National Heart, Lung, and Blood Institute. Expert panel report 3 (EPR-3): Guidelines for the diagnosis and management of asthma-Full Report, 2007. Accessed 11/12/14 at: <http://www.nhlbi.nih.gov/files/docs/guidelines/asthgdln.pdf>.
21. Wilson SR, Rand CS, Cabana MD, Foggs MB, Halterman JS, Olson L *et al*. Asthma outcomes: Quality of life. *J Allergy Clin Immunol*. 2012; 129:S88-123.
22. Boulet LP, Boulay MÈ. Asthma-related comorbidities. *Expert Rev Respir Med*. 2011; 5(3):377-93. Doi: 10.1586/ers.11.34.
23. https://www.who.int/gard/publications/chronic_respiratory_diseases.pdf.
24. Qaseem A *et al*. Diagnosis of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2014; 161(3):210-220.

25. Maspero C, Giannini L, Galbiati G, Rosso G, Farronato G. Obstructive sleep apnea syndrome: a literature review. *Minerva Stomatol.* 2015; 64(2):97-109.
26. Patel SR. Obstructive Sleep Apnea. *Ann Intern Med.* 2019; 171(11):ITC81-ITC96. Doi: 10.7326/AITC201912030.
27. Chervin RD, Aldrich MS. The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnea. *Neurology.* 1999; 52(1):125-131.
28. Chung F, Yegneswaran B, Liao P *et al.* STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008; 108(5):812-821.
29. Iber C, Ancoli-Israel S, Chesson A, Quan SF for the American Academy of Sleep and Medicine. The ASSM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications 1st ed Winchester, IL: American Academy of Sleep Medicine, 2007.
30. Naughton MT. Sleep disorders in patients with congestive heart failure. *Curr Opin Pulm Med.* 2003; 9(6):453-458. <http://dx.Doi.org/10.1097/00063198-200311000-00001>.
31. Pham LV, Schwartz AR. The pathogenesis of obstructive sleep apnea. *J Thorac Dis.* 2015; 7(8):1358-1372.
32. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. *Lancet.* 2014; 383(9918):736-747. [http://dx.Doi.org/10.1016/S0140-6736\(13\)60734-5](http://dx.Doi.org/10.1016/S0140-6736(13)60734-5).
33. Naughton MT. Sleep disorders in patients with congestive heart failure. *Curr Opin Pulm Med.* 2003; 9(6):453-458. <http://dx.Doi.org/10.1097/00063198-200311000-00001>;
34. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clin.* 2018; 68(2018):394-424.
35. American Cancer Society. Global Cancer Facts & Figures 4th Edition. Atlanta: American Cancer Society, 2018.
36. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin.* 2019; 69:7-34.
37. https://www.who.int/gard/publications/The_Global_Impact_of_Respiratory_Disease.pdf.
38. Martin Loef, Harald Walach. The combined effects of healthy lifestyle behaviors on all-cause mortality: A systematic review and meta-analysis. *Preventive Medicine.* 2012; 55(3):163-170. <https://Doi.org/10.1016/j.ypmed.2012.06.017>.
39. Yanping Li, An Pan, Dong D, Wang *et al.* Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population. *Circulation.* 2018; 138:345-355. <https://Doi.org/10.1161/CIRCULATIONAHA.117.032047>.
40. Hoffmann D, Hoffmann I. The changing cigarette: Chemical studies and bioassays. In: Risks Associated with Smoking Cigarettes with Low Machine-Measured Yields of Tar and Nicotine (Smoking and Tobacco Control Monograph No. 13; NIH Publ. No. 02-5074), Bethesda, MD, National Cancer Institute, 2001, 59-191.
41. Braun M, Klingelhöfer D, Oremek GM, Quarcoo D, Groneberg DA. Influence of Second-Hand Smoke and Prenatal Tobacco Smoke Exposure on Biomarkers, Genetics and Physiological Processes in Children-An Overview in Research Insights of the Last Few Years. *Int J Environ Res Public Health.* 2020; 17(9):3212.
42. Kuo HW, Rees VW. Third-hand smoke (THS): What is it and what should we do about it? *J Formos Med Assoc.* 2019; 118(11):1478-1479. Doi: 10.1016/j.jfma.2019.08.025.
43. Kolovou GD, Salpea KD, Anagnostopoulou KK, Mikhailidis DP. Alcohol use, vascular disease, and lipid-lowering drugs. *J Pharmacol Exp Ther.* 2006; 318(1):1-7. Doi: 10.1124/jpet.106.102269.
44. Beyer FR, Campbell F, Bertholet N, Daeppen JB, Saunders JB, Pienaar *et al.* The Cochrane 2018 Review on Brief Interventions in Primary Care for Hazardous and Harmful Alcohol Consumption: A Distillation for Clinicians and Policy Makers. *Alcohol Alcohol.* 2019; 54(4):417-427.
45. Weber MA, Schiffrin EL, White WB *et al.* Clinical practice guidelines for the management of hypertension in the community: A statement by the American Society of Hypertension and the International Society of Hypertension. *Journal of Clinical Hypertension (Greenwich).* 2014; 16(1):14-26.
46. Xi B, Veeranki SP, Zhao M, Ma C, Yan Y, Mi J. Relationship of Alcohol Consumption to All-Cause, Cardiovascular, and Cancer-Related Mortality in U.S. Adults. *J Am. Coll Cardiol.* 2017; 70:913-922. Doi: 10.1016/j.jacc.2017.06.054.
47. Kershaw CD, Guidot DM. Alcoholic lung disease. *Alcohol Res Health.* 2008; 31(1):66-75.
48. World Health Organization Global action plan on physical activity 2018-2030: more active people for a healthier world. Geneva: World Health Organization, 2018, 2021.
49. <https://www.cdc.gov/physicalactivity/basics/pa-health/index.htm> - accessed, 2021.
50. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser.* 1995; 854:1-452.
51. Wakabayashi Ichiro. Necessity of Both Waist Circumference and Waist-to-Height Ratio for Better Evaluation of Central Obesity. *Metabolic Syndrome and Related Disorders.* 2013; 11(3):189-194. Doi: 10.1089/met.2012.0131.
52. Kim JY. Optimal Diet Strategies for Weight Loss and Weight Loss Maintenance. *J Obes Metab Syndr.* 2021; 30(1):20-31. Doi: 10.7570/jomes20065.
53. Kesteloot H. Nutrition and health. *Eur Heart J.* 1992; 13:120-128.
54. U.S. Department of Health and Human Services and the U.S. Department of Agriculture Dietary Guidelines for Americans, 2015-2020. <https://health.gov/dietaryguidelines/2015/guidelines/>.
55. Neelakantan N, Koh WP, Yuan JM, Van Dam RM. Diet-Quality Indexes Are Associated with a Lower Risk of Cardiovascular, Respiratory, and All-Cause Mortality among Chinese Adults. *J Nutr.* 2018; 148(8):1323-1332. Doi: 10.1093/jn/nxy094.
56. Dobrosielski DA, Papandreou C, Patil SP, Salas-Salvadó J. Diet and exercise in the management of obstructive sleep apnoea and cardiovascular disease risk. *Eur Respir Rev.* 2017; 26(144):160110. Doi: 10.1183/16000617.0110-2016.
57. O'Donoghue G, Blake C, Cunningham C, Lennon O, Perrotta C. What exercise prescription is optimal to improve body composition and cardiorespiratory fitness in adults living with obesity? A network meta-analysis. *Obes Rev.* 2021; 22(2):e13137. Doi: 10.1111/obr.13137.

58. Posadzki P, Pieper D, Bajpai R *et al.* Exercise/physical activity and health outcomes: an overview of Cochrane systematic reviews. *BMC Public Health*. 2020; 20(1):1724. Doi: 10.1186/s12889-020-09855-3.
59. Emtner M, Wadell K. Effects of exercise training in patients with chronic obstructive pulmonary disease--a narrative review for FYSS (Swedish Physical Activity Exercise Prescription Book). *Br J Sports Med*. 2016; 50(6):368-71. Doi: 10.1136/bjsports-2015-095872.
60. Leung RW, Alison JA, McKeough ZJ, Peters MJ. Ground walk training improves functional exercise capacity more than cycle training in people with chronic obstructive pulmonary disease (COPD): a randomised trial. *J Physiother*. 2010; 56(2):105-12. Doi: 10.1016/s1836-9553(10)70040-0.
61. Mador MJ, Bozkanat E, Aggarwal A, Shaffer M, Kufel TJ. Endurance and strength training in patients with COPD. *Chest*. 2004; 125(6):2036-2045.
62. Butts JF, Belfer MH, Gebke KB. Exercise for patients with COPD: an integral yet underutilized intervention. *Phys Sportsmed*. 2013; 41(1):49-57. Doi: 10.3810/psm.2013.02.1999.
63. Beauchamp MK, Nonoyama M, Goldstein RS, Hill K, Dolmage TE, Mathur S *et al.* Interval versus continuous training in individuals with chronic obstructive pulmonary disease--a systematic review. *Thorax*. 2010; 65(2):157-164. Doi: 10.1136/thx.2009.123000.
64. Sturdy G, Hillman D, Green D, Jenkins S, Cecins N, Eastwood P *et al.* Feasibility of high-intensity, interval-based respiratory muscle training in COPD. *Chest*. 2003; 123(1):142-150.
65. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y *et al.* Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2015; (2):CD003793.
66. Selman L, McDermott K, Donesky D, Citron T, Howie-Esquivel J. Appropriateness and acceptability of a Tele-Yoga intervention for people with heart failure and chronic obstructive pulmonary disease: qualitative findings from a controlled pilot study. *BMC Complement Altern Med*. 2015; 15:21.
67. Leung RW, McKeough ZJ, Peters MJ, Alison JA. Short-form Sun-style t'ai chi as an exercise training modality in people with COPD. *Eur Respir J*. 2013; 41(5):1051-1057.
68. Li Z, Liu S, Wang L, Smith L. Mind-Body Exercise for Anxiety and Depression in COPD Patients: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2019; 17(1):22. Doi: 10.3390/ijerph17010022.
69. Negewo NA, Gibson PG, McDonald VM. COPD and its comorbidities: Impact, measurement and mechanisms. *Respirology*. 2015; 20(8):1160-71. Doi: 10.1111/resp.12642.
70. Mantoani LC, Dell'Era S, MacNee W, Rabinovich RA. Physical activity in patients with COPD: the impact of comorbidities. *Expert Rev Respir Med*. 2017; 11(9):685-698. Doi: 10.1080/17476348.2017.1354699.
71. Côté A, Turmel J, Boulet LP. Exercise and Asthma. *Semin Respir Crit Care Med*. 2018; 39(1):19-28. Doi: 10.1055/s-0037-1606215.
72. Carson KV, Chandratilleke MG, Picot J, Brinn MP, Esterman AJ, Smith BJ *et al.* Physical training for asthma. *Cochrane Database Syst Rev*. 2013; (9):CD001116.
73. França-Pinto A, Mendes FA, De Carvalho-Pinto RM *et al.* Aerobic training decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. *Thorax*. 2015; 70:732-9.
74. Heikkinen SAM, Quansah R, Jaakkola JJK, Jaakkola MS. Effects of regular exercise on adult asthma. *Eur J Epidemiol*. 2012; 27:394-407. Doi: 10.1007/s10654-012-9684-8.
75. Lucas SR, Platts-Mills TA. Activity and exercise in asthma: relevance to etiology and treatment. *J Allergy Clin Immunol*. 2005; 115:928-934. Doi: 10.1016/j.jaci.2005.01.033.
76. Hewitt M, Estell K, Davis IC, Schwiebert LM. Repeated bouts of moderate-intensity aerobic exercise reduce airway reactivity in murine asthma model. *Am J Respir Cell Mol Biol*. 2010; 42:243-249. Doi: 10.1165/rcmb.2009-0038OC.
77. França-Pinto A, Mendes FA, De Carvalho-Pinto RM *et al.* Aerobic training decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. *Thorax*. 2015; 70:732-9.
78. Silva RA *et al.* Aerobic training reverses airway inflammation and remodelling in asthma murine model. *Eur Respir J*. 2010; 35:994-1002. Doi: 10.1183/09031936.00049509.
79. Freitas PD *et al.* The role of exercise in a weight-loss program on clinical control in obese adults with asthma: a randomized controlled trial. *Am J Respir Crit Care Med*. 2017; 195:32-42. Doi: 10.1164/rccm.201603-0446OC.
80. Peppard PE, Young T. Exercise and sleep-disordered breathing: an association independent of body habitus. *Sleep*. 2004; 27:480-484.
81. Quan SF, O'Connor GT, Quan JS *et al.* Association of physical activity with sleep-disordered breathing. *Sleep Breath*. 2007; 11:149-157. <http://dx.Doi.org/10.1007/s11325-006-0095-5>.
82. Sengul YS, Ozalevli S, Oztura I, Itil O, Baklan B. The effect of exercise on obstructive sleep apnea a randomized and controlled trial. *Sleep Breath*. 2011; 15(1):49-56. <http://dx.Doi.org/10.1007/s11325-009-0311-1>.
83. Awad KM, Malhotra A, Barnet JH, Quan SF, Peppard PE. Exercise is associated with a reduced incidence of sleep-disordered breathing. *Am J Med*. 2012; 125(5):485-490. <http://dx.Doi.org/10.1016/j.amjmed.2011.11.025>.
84. Norman JF, Von Essen SG, Fuchs RH, McElligott M. Exercise training effect on obstructive sleep apnea syndrome. *Sleep Res Online*. 2000; 3(3):121-129.
85. Kline CE, Crowley EP, Ewing GB, Burch JB, Blair SN, Durstine JL *et al.* The effect of exercise training on obstructive sleep apnea and sleep quality a randomized controlled trial. *Sleep*. 2011; 34(12):1631-1640. <http://dx.Doi.org/10.5665/sleep.1422>.
86. Servantes DM, Pelcerman A, Salvetti XM, Salles AF, De Albuquerque PF, De Salles FC *et al.* Effects of home-based exercise training for patients with chronic heart failure and sleep apnoea a randomized comparison of two different programmes. *Clin Rehabil*. 2012; 26(1):45-57. <http://dx.Doi.org/10.1177/0269215511403941>.
87. Aiello KD, Coughy WG, Nelluri B, Sharma A, Mookadam F, Mookadam M *et al.* Effect of exercise training on sleep apnea A systematic review and meta-

- analysis. *Respir Med.* 2016; 116:85-92. <http://dx.Doi.org/10.1016/j.rmed.2016.05.015>.
88. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T *et al.* Progression and regression of sleep-disordered breathing with changes in weight the Sleep Heart Health Study. *Arch Intern Med.* 2005; 165(20):2408-2413.
 89. Andrade FM, Pedrosa RP. The role of physical exercise in obstructive sleep apnea. *J Bras Pneumol.* 2016; 42(6):457-464. Doi: 10.1590/S1806-37562016000000156.
 90. Ramos-Barrera GE, DeLucia CM, Bailey EF. Inspiratory muscle strength training lowers blood pressure and sympathetic activity in older adults with OSA: a randomized controlled pilot trial. *J Appl Physiol.* 1985, 2020; 129(3):449-458. Doi: 10.1152/jappphysiol.00024.2020.
 91. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C *et al.* An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am. J. Respir. Crit. Care Med.* 2013; 188: e13-64.
 92. Holland AE, Hill CJ, Conron M, Munro P, McDonald CF. Small changes in six-minute walk distance are important in diffuse parenchymal lung disease. *Respir. Med.* 2009; 103:1430-5.
 93. Dowman LM, McDonald CF, Hill CJ, Lee AL, Barker K, Boote. The evidence of benefits of exercise training in interstitial lung disease: a randomised controlled trial. *Thorax.* 2017; 72:610-9.
 94. Ehlken N, Lichtblau M, Klose H *et al.* Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial. *Eur. Heart J.* 2015; 37:35-44.
 95. Emaus A, Thune I. Physical activity and lung cancer prevention. *Recent Results Cancer Res.* 2011; 186:101-33. Doi: 10.1007/978-3-642-04231-7_5.
 96. Sebio Garcia R, Yáñez Brage MI, Giménez Moolhuyzen E, Granger CL, Denehy L. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: a systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg.* 2016; 23(3):486-97. Doi: 10.1093/icvts/ivw152.
 97. Jones LW, Eves ND, Peterson BL *et al.* Safety and feasibility of aerobic training on cardiopulmonary function and quality of life in postsurgical non small cell lung cancer patients: a pilot study. *Cancer.* 2008; 113(12):3430-9. Doi: 10.1002/cncr.23967.
 98. Wolff G, Davidson SJ, Wrobel JK, Toborek M. Exercise maintains blood-brain barrier integrity during early stages of brain metastasis formation. *Biochem. Bioph. Res. Co.* 2015; 463:811-817.
 99. Franssen FM, O'Donnell DE, Goossens GH, Blaak EE, Schols AM. Obesity and the lung: 5. Obesity and COPD. *Thorax.* 2008; 63(12):1110-1117.
 100. Landbo C, Prescott E, Lange P, Vestbo J, Almdal TP. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1999; 160(6):1856-1861.
 101. Huber MB, Kurz C, Kirsch F, Schwarzkopf L, Schramm A, Leidl R. The relationship between body mass index and health-related quality of life in COPD: real-world evidence based on claims and survey data. *Respir Res.* 2020; 21(1):291. Doi: 10.1186/s12931-020-01556-0.
 102. Yamauchi Y, Hasegawa W, Yasunaga H *et al.* Paradoxical association between body mass index and in-hospital mortality in elderly patients with chronic obstructive pulmonary disease in Japan. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2014; 9:1337-46.
 103. Lainscak M, Von Haehling S, Doehner W *et al.* Body mass index and prognosis in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. *J Cachexia Sarcopenia Muscle.* 2011; 2(2):81-86.
 104. Cao C, Wang R, Wang J *et al.* Body mass index and mortality in chronic obstructive pulmonary disease: a meta-analysis. *PLoS One.* 2012; 7(8):e43892.
 105. World Health Organization Obesity and overweight. 2013. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html.
 106. Marquis K, Debigare R, Lacasse Y *et al.* Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2002; 166(6):809-813.
 107. Ramachandran K, McCusker C, Connors M, Zuwallack R, Lahiri B. The influence of obesity on pulmonary rehabilitation outcomes in patients with COPD. *Chron Respir Dis.* 2008; 5(4):205-209.
 108. Sava F, Laviolette L, Bernard S, Breton MJ, Bourbeau J, Maltais F *et al.* The impact of obesity on walking and cycling performance and response to pulmonary rehabilitation in COPD. *BMC Pulm Med.* 2010; 10:55.
 109. Greening NJ, Evans RA, Williams JE, Green RH, Singh SJ, Steiner MC *et al.* Does body mass index influence the outcomes of a waking-based pulmonary rehabilitation programme in COPD? *Chron Respir Dis.* 2012; 9(2):99-106.
 110. Mannino DM, Thorn D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J.* 2008; 32(4):962-969.
 111. Feary JR, Rodrigues LC, Smith CJ, Hubbard RB, Gibson JE. Prevalence of major comorbidities in subjects with COPD and incidence of myocardial infarction and stroke: a comprehensive analysis using data from primary care. *Thorax.* 2010; 65(11):956-962.
 112. Park SK, Larson JL. Metabolic syndrome and associated factors in people with chronic obstructive pulmonary disease. *West J Nurs Res.* 2013.
 113. Gilliland FD, Berhane K, Islam T, McConnell R, Baderman WJ, Gilliland SS *et al.* Obesity and the risk of newly diagnosed asthma in school-age children. *Am J Epidemiol.* 2003; 158:406-15.
 114. Dumas O, Varraso R, Gillman MW, Field AE, Camargo CA. Jr Longitudinal study of maternal body mass index, gestational weight gain, and offspring asthma. *Allergy.* 2016; 71:1295-304.
 115. Arismendi E, Bantulà M, Perpiñá M, Picado C. Effects of Obesity and Asthma on Lung Function and Airway Dysanapsis in Adults and Children. *J Clin Med.* 2020; 9(11):3762. Doi: 10.3390/jcm9113762.
 116. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med.* 2007; 175:661-6.

117. Akinbami LJ, Fryar CD. NCHS data brief, no 239. Hyattsville, MD: National Center for Health Statistics. Asthma prevalence by weight status among adults: United States, 2001-2014. NCHS Data Brief. Hyattsville, MD: National Center for Health Statistics, 2016.
118. Boulet LP, Franssen E. Influence of obesity on response to fluticasone with or without salmeterol in moderate asthma. *Respir. Med.* 2007; 101:2240-2247. Doi: 10.1016/j.rmed.2007.06.031.
119. Scott HA, Gibson PG, Garg ML, Pretto JJ, Morgan PJ, Callister R *et al.* Dietary restriction and exercise improve airway inflammation and clinical outcomes in overweight and obese asthma: A randomized trial. *Clin. Exp. Allergy.* 2013; 43:36-49. Doi: 10.1111/cea.12004.
120. Scott HA, Gibson PG, Garg ML, Pretto JJ, Morgan PJ, Callister R *et al.* Dietary restriction and exercise improve airway inflammation and clinical outcomes in overweight and obese asthma: A randomized trial. *Clin. Exp. Allergy.* 2013; 43:36-49. Doi: 10.1111/cea.12004.
121. Van Huisstede A, Rudolphus A, Cabezas MC *et al.* Effect of bariatric surgery on asthma control, lung function and bronchial and systemic inflammation in morbidly obese subjects with asthma. *Thorax.* 2015; 70:659-667. Doi: 10.1136/thoraxjnl-2014-206712.
122. Peppard PE, Young T, Palta M *et al.* Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA.* 2000; 284:3015-3021.
123. Schwartz AR, Gold AR, Schubert N *et al.* Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1991; 144:494-498.
124. Epstein LJ, Kristo D, Strollo PJ *et al.* Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med.* 2009; 5:263-276.
125. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA.* 2000; 284(23):3015-3021. <http://dx.doi.org/10.1001/jama.284.23.3015>.
126. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T *et al.* Progression and regression of sleep-disordered breathing with changes in weight the Sleep Heart Health Study. *Arch Intern Med.* 2005; 165(20):2408-2413. <http://dx.doi.org/10.1001/archinte.165.20.2408>.
127. Dobrosielski DA, Patil S, Schwartz AR, Bandeen-Roche K, Stewart KJ. Effects of exercise and weight loss in older adults with obstructive sleep apnea. *Med Sci Sports Exerc.* 2015; 47(1):20-26. <http://dx.doi.org/10.1249/MSS.0000000000000387>.
128. Resta O, Foschino-Barbaro MP, Legari G *et al.* Sleep-related breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. *Int J Obes Relat Metab Disord.* 2001; 25:669-75.
129. Isono S. Obesity and obstructive sleep apnoea: mechanisms for increased collapsibility of the passive pharyngeal airway. *Respirology.* 2012; 17:32-42.
130. Polotsky M, Elsayed-Ahmed AS, Pichard L *et al.* Effects of leptin and obesity on the upper airway function. *J Appl Physiol.* 2012; 112:1637-43.
131. Ardesch FH, Ruiter R, Mulder M, Lahousse L, Stricker BHC, Kiefte-de Jong JC. The Obesity Paradox in Lung Cancer: Associations with Body Size versus Body Shape. *Front Oncol.* 2020; 10:591110. Doi: 10.3389/fonc.2020.591110.
132. Duan P, Chunhui H, Quan C, Yi X, Zhou W, Yuan M *et al.* Body mass index and risk of lung cancer: Systematic review and dose-response meta-analysis. *Sci Rep.* 2015; 5:16938. 10.1038/srep16938.
133. Hidayat K, Du X, Chen G, Shi M, Shi B. Abdominal Obesity and Lung Cancer Risk: Systematic Review and Meta-Analysis of Prospective Studies. *Nutrients.* 2016; 8(12):810. 10.3390/nu8120810.
134. Yu D, Zheng W, Johansson M *et al.* Overall and Central Obesity and Risk of Lung Cancer: A Pooled Analysis. *J Natl Cancer Inst.* 2018; 110(8):831-842. Doi:10.1093/jnci/djx286.
135. Patel AV, Carter B, Stevens V, Gaudet M, Campell P, Gapstur S *et al.* The relationship between physical activity, obesity, and lung cancer risk by smoking status in a large prospective cohort of US adults. *Cancer Causes Control.* 2017; 28(12):1357-68. 10.1007/s10552-017-0949-0.
136. Carreras-Torres R, Johansson M, Haycock PC *et al.* Obesity, metabolic factors and risk of different histological types of lung cancer: A Mendelian randomization study. *PLoS One.* 2017; 126:e0177875.
137. Bharkaran K, Douglas I, Forbes H, Dos-Santos-Silva I, Leon D, Smeeth L *et al.* Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5-24 million UK adults. *Lancet.* 2014; 384(9945):755-65. 10.1016/S0140-6736(14)60892-8.
138. Leung CC, Lam TH, Yew WW, Chan WM, Law WS, Tam CM *et al.* Lower lung cancer mortality in obesity. *Int J Epidemiol.* 2011; 40(1):174-82. Doi: 10.1093/ije/dyq134.
139. Zhang X, Liu Y, Shao H, Zheng X. Obesity Paradox in Lung Cancer Prognosis: Evolving Biological Insights and Clinical Implications. *J Thorac Oncol.* 2017; 12(10):1478-1488. Doi: 10.1016/j.jtho.2017.07.022.
140. Rennard SI, Vestbo J. Natural histories of chronic obstructive pulmonary disease. *Proc Am Thorac Soc.* 2008; 5(9):878-83. 10.1513/pats.200804-035QC.
141. Løkke A, Lange P, Scharling H, Fabricius P, Vestbo J. Developing COPD: a 25 year follow up study of the general population. *Thorax.* 2006; 61(11):935-939. Doi:10.1136/thx.2006.062802.
142. Kamal R, Srivastava AK, Kesavachandran CN. Meta-analysis approach to study the prevalence of chronic obstructive pulmonary disease among current, former and non-smokers. *Toxicol Reports.* 2015; 2:1064-74.
143. Aryal S, Diaz-Guzman E, Mannino DM. COPD and gender differences: an update. *Transl Res.* 2013; 162:208-218.
144. Jenkins C. More action to address the impact of smoking in women. *Am J Respir Crit Care Med.* 2017; 195:1132-1134.
145. Diver WR, Jacobs EJ, Gapstur SM. Secondhand smoke exposure in childhood and adulthood in relation to adult mortality among never smokers. *Am J Prev Med.* 2018; 55:345-52. 10.1016/j.amepre.2018.05.005.
146. Berry CE, Wise RA. Mortality in COPD: causes, risk factors, and prevention. *Copd.* 2010; 7(5):375-382. Doi:10.3109/15412555.2010.510160.
147. Scanlon PD, Connett JE, Waller LA *et al.* Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease. The Lung Health Study. *Am J Respir Crit Care Med.* 2000; 161161(2):381-390. Doi: 10.1164/ajrccm.161.2.9901044.

148. Kanner RE, Connett JE, Williams DE *et al.* Effects of randomized assignment to a smoking cessation intervention and changes in smoking habits on respiratory symptoms in smokers with early chronic obstructive pulmonary disease: the Lung Health Study. *Am J Med.* 1999; 106(5):675-679.
149. Anthonisen NR, Skeans MA, Wise RA *et al.* The effects of a smoking cessation intervention on 145-year mortality: a randomized clinical trial. *Ann Intern Med.* 2005; 142(4):233-239. Doi: 10.7326/0003-4819-142-4-200502150-00005.
150. Berry CE, Wise RA. Mortality in COPD: causes, risk factors, and prevention. *Copd.* 2010; 7(5):375-382. Doi:10.3109/15412555.2010.510160.
151. Koshiol J, Rotunno M, Consonni D *et al.* Chronic obstructive pulmonary disease and altered risk of lung cancer in a population-based case-control study. *PLoS One.* 2009; 4(10):e7380. Doi: 10.1371/journal.pone.0007380.
152. Chen W, Thomas J, Sadatsafavi M, FitzGerald JM. Risk of cardiovascular comorbidity in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Lancet Respir Med.* 2015; 3(8):631-639.
153. Khateeb J, Fuchs E, Khamaisi M. Diabetes and Lung Disease: A Neglected Relationship. *Rev Diabet Stud.* 2019; 15:1-15. Doi: 10.1900/RDS.2019.15.1.
154. Simons E, To T, Moineddin R, Stieb D, Dell SD. Maternal second-hand smoke exposure in pregnancy is associated with childhood asthma development. *J Allergy Clin Immunol Pract.* 2014; 2:201-207.
155. Hollenbach JP, Schifano ED, Hammel C, Cloutier MM. Exposure to secondhand smoke and asthma severity among children in Connecticut. *PLoS One.* 2017; 12:0.
156. Guerra S, Stern DA, Zhou M, Sherrill DL, Wright AL, Morgan WJ *et al.* Combined effects of parental and active smoking on early lung function deficits: a prospective study from birth to age 26 years. *Thorax.* 2013; 68:1021-1028.
157. López Blázquez M, Pérez Moreno J, Vigil Vázquez S, Rodríguez Fernández R. Impact of passive smoking on lung function and asthma severity in children. *Arch Bronconeumol.* 2018; 54:436-437.
158. Kashyap R, Hock LM, Bowman TJ. Higher prevalence of smoking in patients diagnosed as having obstructive sleep apnea. *Sleep Breath.* 2001; 5(4):167-172. Doi: 10.1007/s11325-001-0167-5.
159. Wetter DW, Young TB, Bidwell TR *et al.* Smoking as a risk factor for sleep-disordered breathing. *Arch Intern Med.* 1994; 154(19):2219-2224. Doi: 10.1001/archinte.154.19.2219.
160. Dicipinigitis PV. Cough reflex sensitivity in cigarette smokers. *Chest.* 2003; 123(3):685-688. Doi: 10.1378/chest.123.3.685.
161. Hsu WY, Chiu NY, Chang CC, Chang TG, Lane HY. The association between cigarette smoking and obstructive sleep apnea. *Tob Induc Dis.* 2019; 17:27. Doi:10.18332/tid/105893.
162. Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. *Ann N Y Acad Sci.* 2012; 1248:107-123.
163. American Cancer Society. Cancer Facts & Figures 2019. Atlanta: American Cancer Society, 2019.
164. U.S. Department of Health and Human Services. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General, 2014. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.
165. Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines; Chest 2013; 143:e1S-e29S.
166. Peto J. That the effects of smoking should be measured in pack-years: misconceptions 4. *Br J Cancer.* 2012; 107:406-407.
167. Malhotra J, Borron C, Freedman ND, Abnet CC, Van den Brandt PA, White E *et al.* Association between Cigar or Pipe Smoking and Cancer Risk in Men: A Pooled Analysis of Five Cohort Studies. *Cancer Prev Res (Phila).* 2017; 10:704-709.
168. Kim AS, Ko HJ, Kwon JH, Lee JM. Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies. *Int J Environ Res Public Health.* 2018, 15.
169. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoke. In: Tobacco smoke and involuntary smoking. Lyon, World Health Organization/IARC, 2004; 83:51-1187.
170. Jessri M, Wolfinger RD, Lou WY, L'Abbe MR. Identification of dietary patterns associated with obesity in a nationally representative survey of Canadian adults: Application of a priori, hybrid, and simplified dietary pattern techniques. *Am J Clin Nutr.* 2017; 105:669-684. Doi: 10.3945/ajcn.116.134684.
171. Van de Boel C, Mattijssen-Verdonschot C, Van Melick PP *et al.* Quality of dietary intake in relation to body composition in patients with chronic obstructive pulmonary disease eligible for pulmonary rehabilitation. *Eur J Clin Nutr.* 2014; 68(2):159-165.
172. Scoditti E, Massaro M, Garbarino S, Toraldo DM. Role of Diet in Chronic Obstructive Pulmonary Disease Prevention and Treatment. *Nutrients.* 2019; 11(6):1357. Doi: 10.3390/nu11061357.
173. Shaheen SO, Jameson KA, Syddall HE *et al.* The relationship of dietary patterns with adult lung function and COPD. *Eur Respir J.* 2010; 36(2):277-284.
174. Tabak C, Smit HA, Heederik D, Ocke MC, Kromhout D. Diet and chronic obstructive pulmonary disease: independent beneficial effects of fruits, whole grains, and alcohol (the MORGEN study) *Clin Exp Allergy.* 2001; 31(5):747-755.
175. Varraso R, Fung TT, Barr RG, Hu FB, Willett W, Camargo CA *et al.* Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women. Am J Clin and forced expiratory volume in 1 s decline: the health, aging and body composition study. *Eur Respir J Nutr.* 2007; 86(2):488-495.
176. Bentley AR, Kritchevsky SB, Harris TB *et al.* Dietary antioxidants. 2012; 39(4):979-984.
177. Tabak C, Feskens EJ, Heederik D, Kromhout D, Menotti A, Blackburn HW *et al.* Fruit and fish consumption: a possible explanation for population differences in COPD mortality (the Seven Countries Study) *Eur J Clin Nutr.* 1998; 52(11):819-825.
178. Tabak C, Feskens EJ, Heederik D, Kromhout D, Menotti A, Blackburn HW *et al.* Fruit and fish consumption: a possible explanation for population differences in COPD

- mortality (the Seven Countries Study) *Eur J Clin Nutr.* 1998; 52(11):819-825.
179. De Batlle J, Mendez M, Romieu I *et al.* PAC-COPD Study Group. Cured meat consumption increases risk of readmission in COPD patients. *Eur Respir J.* 2012; 40(3):555-60. Doi: 10.1183/09031936.00116911.
 180. Scoditti E, Massaro M, Garbarino S, Toraldo DM. Role of diet in Chronic Obstructive Pulmonary Disease prevention and treatment. *Nutrients.* 2019; 11:1357. Doi: 10.3390/nu11061357.
 181. De Batlle J, Barreiro E, Romieu I *et al.* Dietary modulation of oxidative stress in chronic obstructive pulmonary disease patients. *Free Radic Res.* 2010; 44(11):1296-1303.
 182. Walda IC, Tabak C, Smit HA *et al.* Diet and 20-year chronic obstructive pulmonary disease mortality in middle-aged men from three European countries. *Eur J Clin Nutr.* 2002; 56(7):638-643.
 183. Peters JI, McKinney JM, Smith B, Wood P, Forkner E *et al.* Impact of obesity in asthma: Evidence from a large prospective disease management study. *Ann. Allergy Asthma Immunol.* 2011; 106:30-35. Doi: 10.1016/j.anai.2010.10.015.
 184. Forno E, Celedon JC. The effect of obesity, weight gain, and weight loss on asthma inception and control. *Curr. Opin. Allergy Clin. Immunol.* 2017; 17:123-130. Doi: 10.1097/ACI.0000000000000339.
 185. Okoniewski W, Lu KD, Forno E. Weight Loss for Children and Adults with Obesity and Asthma. A Systematic Review of Randomized Controlled Trials. *Ann Am Thorac Soc.* 2019; 16(5):613-625. Doi: 10.1513/AnnalsATS.201810-651SR.
 186. Crespo A, Giner J, Torrejon M *et al.* Clinical and inflammatory features of asthma with dissociation between fractional exhaled nitric oxide and eosinophils in induced sputum. *J Asthma.* 2016; 53:459-464. Doi: 10.3109/02770903.2015.1116086.
 187. Alwarith J, Kahleova H, Crosby L, Brooks A, Brandon L, Levin SM *et al.* The role of nutrition in asthma prevention and treatment. *Nutr Rev.* 2020; 78(11):928-938. Doi: 10.1093/nutrit/nuaa005.
 188. Romieu I, Barraza-Villarreal A, Escamilla-Nunez C *et al.* Dietary intake, lung function and airway inflammation in Mexico City school children exposed to air pollutants. *Respir. Res.* 2009; 10:122. Doi: 10.1186/1465-9921-10-122.
 189. Wood LG, Garg ML, Powell H, Gibson PG. Lycopene-rich treatments modify noneosinophilic airway inflammation in asthma: Proof of concept. *Free Radic. Res.* 2008; 42:94-102. Doi: 10.1080/10715760701767307.
 190. Berthon BS, Macdonald-Wicks LK, Gibson PG, Wood LG. Investigation of the association between dietary intake, disease severity and airway inflammation in asthma. *Respirology.* 2013; 18:447-454. Doi: 10.1111/resp.12015.
 191. Scott HA, Gibson PG, Garg ML, Pretto JJ, Morgan PJ, Callister R *et al.* Dietary restriction and exercise improve airway inflammation and clinical outcomes in overweight and obese asthma: A randomized trial. *Clin. Exp. Allergy.* 2013; 43:36-49. Doi: 10.1111/cea.12004.
 192. Hu FB. Dietary pattern analysis: A new direction in nutritional epidemiology. *Curr. Opin. Lipidol.* 2002; 13:3-9. Doi: 10.1097/00041433-200202000-00002.
 193. Berentzen NE, Van Stokkom VL, Gehring U *et al.* Associations of sugar-containing beverages with asthma prevalence in 11-year-old children: The PIAMA birth cohort. *Eur. J Clin. Nutr.* 2015; 69:303-308. Doi: 10.1038/ejcn.2014.153.
 194. Castro-Rodriguez JA, Ramirez-Hernandez M, Padilla O *et al.* Effect of foods and Mediterranean diet during pregnancy and first years of life on wheezing, rhinitis and dermatitis in preschoolers. *Allergol. Immunopathol. (Madr).* 2016; 44:400-409. Doi: 10.1016/j.aller.2015.12.002.
 195. Dobrosielski DA, Papandreou C, Patil SP, Salas-Salvadó J. Diet and exercise in the management of obstructive sleep apnoea and cardiovascular disease risk. *Eur Respir Rev.* 2017; 26(144):160110. Doi: 10.1183/16000617.0110-2016.
 196. Lam TK, Gallicchio L, Lindsley K *et al.* Cruciferous vegetable consumption and lung cancer risk: a systematic review. *Cancer Epidemiol Biomark Prev.* 2009; 18:184-195.
 197. Smith-Warner SA, Ritz J, Hunter DJ *et al.* Dietary fat and risk of lung cancer in a pooled analysis of prospective studies. *Cancer Epidemiol Biomark Prev.* 2002; 11:987-99257.
 198. Sinha R, Kulldorff M, Curtin J *et al.* Fried, well-done red meat and risk of lung cancer in women (United States). *Cancer Causes Control.* 1998; 9:621-630.
 199. Sinha R, Kulldorff M, Swanson CA *et al.* Dietary heterocyclic amines and the risk of lung cancer among Missouri women. *Cancer Res.* 2000; 60:3753-3756.
 200. Kaluza J, Harris HR, Linden A, Wolk A. Alcohol Consumption and Risk of Chronic Obstructive Pulmonary Disease: A Prospective Cohort Study of Men. *Am J Epidemiol.* 2019; 188(5):907-916. Doi: 10.1093/aje/kwz020.
 201. Tabak C, Smit HA, Heederik D, Ocke MC, Kromhout D. Diet and chronic obstructive pulmonary disease: independent beneficial effects of fruits, whole grains, and alcohol (the MORGEN study) *Clin Exp Allergy.* 2001a; 31:747-755.
 202. Sisson JH. Alcohol and airways function in health and disease. *Alcohol.* 2007; 41(5):293-307. Doi: 10.1016/j.alcohol.2007.06.003.
 203. Tabak C, Smit HA, Räsänen L *et al.* Alcohol consumption in relation to 20-year COPD mortality and pulmonary function in middle-aged men from three European countries. *Epidemiology.* 2001; 12(2):239-45. Doi: 10.1097/00001648-200103000-00018.
 204. Fujimura M, Myou S. Alcohol-induced asthma. *Intern Med.* 2001; 40(7):557-8. Doi: 10.2169/internalmedicine.40.557;
 205. Vally H, De Klerk N, Thompson PJ. Alcoholic drinks: important triggers for asthma. *J Allergy Clin Immunol.* 2000; 105:462-467.
 206. Shimoda T, Kohno S, Takao A *et al.* Investigation of the mechanism of alcohol-induced bronchial asthma. *J Allergy Clin Immunol.* 1996; 97:74-84.
 207. Vally H, De Klerk N, Thompson PJ. Alcoholic drinks: important triggers for asthma. *J Allergy Clin Immunol.* 2000; 105:462-467.
 208. Sisson JH. Alcohol and airways function in health and disease. *Alcohol.* 2007; 41(5):293-307. Doi: 10.1016/j.alcohol.2007.06.003.
 209. Bandera EV, Freudenheim JL, Vena JE. Alcohol consumption and lung cancer a review of the

- epidemiologic evidence. *Cancer Epidemiol Biomark Prev.* 2001; 10:813-821.
- 210.Korte JE, Brennan P, Henley SJ *et al.* Dose-specific meta-analysis and sensitivity analysis of the relation between alcohol consumption and lung cancer risk. *Am J Epidemiol.* 2002; 155:496-506.
- 211.Freudenheim JL, Ritz J, Smith-Warner SA *et al.* Alcohol consumption and risk of lung cancer: a pooled analysis of cohort studies. *Am J Clin Nutr.* 2005; 82:657-667.
- 212.Scanlan MF, Roebuck T, Little PJ, Redman JR, Naughton MT. Effect of moderate alcohol upon obstructive sleep apnoea. *Eur Respir J.* 2000; 16(5):909-13. Doi: 10.1183/09031936.00.16590900.
- 213.Garcia-Vidal C, Ardanuy C, Tubau F, Viasus D, Dorca J, Liñares J *et al.* Pneumococcal pneumonia presenting with septic shock: host-and pathogen-related factors and outcomes. *Thorax.* 2010; 65:77-81.
- 214.Mehta AJ, Guidot DM. Alcohol abuse, the alveolar macrophage and pneumonia. *American Journal of the Medical Sciences.* 2012; 343(3):244-247.
- 215.Happel KI, Nelson S. Alcohol, immunosuppression, and the lung. Proceedings of the American Thoracic Society. 2005; 2(5):428-432.
- 216.Perlino CA, Rimland D. Alcoholism, leukopenia, and pneumococcal sepsis. *The American Review of Respiratory Disease.* 1985; 132(4):757-760.
- 217.Jong GM, Hsiue TR, Chen CR *et al.* Rapidly fatal outcome of bacteremic Klebsiella pneumoniae pneumonia in alcoholics. *Chest.* 1995; 107(1):214-217.
- 218.Plevneshi A, Svoboda T, Armstrong I, Tyrrell GJ, Miranda A, Green K *et al.* Population-based surveillance for invasive pneumococcal disease in homeless adults in Toronto. *PLoS One.* 2009; 4:e7255.
- 219.Moss M, Bucher B, Moore FA, Moore EE, Parsons PE. The role of chronic alcohol abuse in the development of acute respiratory distress syndrome in adults. *JAMA.* 1996; 275:50-54.
- 220.Borgdorff MW, Veen J, Kalisvaart NA, Nagelkerke N. Mortality among tuberculosis patients in the Netherlands in the period 1993-1995. *European Respiratory Journal.* 1998; 11(4):816-820.
- 221.Jerrells TR, Pavlik JA, DeVasure J *et al.* Association of chronic alcohol consumption and increased susceptibility to and pathogenic effects of pulmonary infection with respiratory syncytial virus in mice. *Alcohol.* 2007; 41(5):357-369.
- 222.Moss M, Burnham EL. Chronic alcohol abuse, acute respiratory distress syndrome, and multiple organ dysfunction. *Critical Care Medicine.* 2003; 31(4):S207-S212.
- 223.Liffner G, Bak Z, Reske A, Sjöberg F. Inhalation injury assessed by score does not contribute to the development of acute respiratory distress syndrome in burn victims. *Burns.* 2005; 31:263-268.