Chronic obstructive pulmonary disease: Signs and symptoms, diagnosis, treatments, lifestyle risk factors and management

Sook Yee Lim¹, Vaidehi Ulaganathan^{1,*}, Baskaran Gunasekaran¹, Shamala Salvamani^{2,3}, Yee Lian Tiong¹, Siti Madihah Muhammad Royani¹, Kughaneshwary Silvermany¹, Digsha Augundhooa¹ and Mahla Chambari¹

¹Department of Food Science and Nutrition, Faculty of Applied Sciences, Universiti UCSI, 56000 Kuala Lumpur, Malaysia.

²Department of Biotechnology, Faculty of Applied Sciences, Universiti UCSI, 56000 Kuala Lumpur, Malaysia.

³Division of Applied Biomedical Science and Biotechnology, School of Health Sciences, International Medical University, 57000 Bukit Jalil, Kuala Lumpur, Malaysia.

*Correspondence: vaidehi@ucsiuniversity.edu.my

Received: 8 June 2023; Revised: 27 February 2024; Accepted: 3 March 2024; Published: 17 March 2024

DOI https://doi.org/10.28916/lsmb.8.1.2024.123

ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is associated with increased health complications, leading to a rise in mortality rates. COPD remains a significant global health issue, underscoring the importance of recognizing symptoms, facilitating diagnosis, and implementing effective treatment strategies. However, information on lifestyle risk factors and the management of COPD remains fragmented. This review paper aims to understand the clinical pathophysiologic changes triggered by lifestyle practices and their management strategies. It is important to understand its symptoms, diagnostics criteria, and treatment to correlate with lifestyle risk factors and to identify effective lifestyle interventions. Lifestyle practices as defined by dietary practices such being anorexia and low fruit and vegetable intake, smoking habits, alcohol consumption, and physical inactivity have increased the risk of COPD. This review suggested lifestyle approaches for COPD treatment such as regular exercise, a healthy diet, and avoiding smoking. In this case, the development of the guided improved intervention is important for a better understanding of the mechanisms between COPD and its associated lifestyle practices. This information may help clinicians, health practitioners, and dietitians to guide patients to implement improved dietary interventions. To avoid the progression of COPD, lifestyle practice therapy could be the most effective strategies that aid with medications as prescribed by the physicians.

Keywords: Chronic obstructive pulmonary disease; clinical characteristics; health care and lifestyle practices

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), the third most prevalent cause of death globally, led to 3.3 million mortalities in 2019 (Safiri et al., 2022). Sustainable Development Goal 3.4, set for 2030, aims to reduce premature mortality from non-communicable diseases like COPD through prevention and treatment (Singh Thakur et al., 2021) The primary clinical guidelines define COPD based on the presence of chronic, nearly irreversible airflow obstruction (Fazleen & Wilkinson, 2020). A significant criticism directed at these guidelines is

their excessive reliance on forced spirometry values for both the diagnosis and assessment of COPD severity. This emphasis is seen as hindering a thorough evaluation of the diverse modifiable and non-modifiable risk factors of the disease. Considering our current understanding of COPD, it can be asserted that prolonged exposure to smoking fumes or environmental toxins leads to both airflow obstruction and associated damage, including inflammatory responses (Strzelak et al., 2018). However, the contribution of modifiable risk factors, such as lifestyle practices, to predicting the risk and managing COPD remains underexplored and limited in existing knowledge.

COPD commonly results in a decreased body cell mass, a condition more pronounced in end-stage chronic cases, particularly those with emphysema and subsequently those with chronic bronchitis. COPD patients, experiencing substantial fat-free mass depletion, are predisposed to skeletal muscle weakness, irrespective of COPD subtype and airflow obstruction. It has been proven that being underweight, such as having a low body mass index or experiencing extreme weight loss, constitutes independent risk factors for mortality in COPD patients. COPD patients diagnosed with malnutrition often experience a decline during hospitalization (Ayar Karakoç et al., 2016).

Malnourished COPD patients have been associated with increased health complications, leading to consistent adverse effects and a subsequent increase in mortality rates. For example, COPD patients experiencing extreme weight loss or being underweight were more likely to exhibit gas trapping, lower diffusion capacity, and reduced exercise capacity compared to those with COPD but with a normal body mass index (Wada et al., 2021). In COPD, reduction in the mass of the diaphragm and the respiratory muscles is common, indicating the loss of body cell mass, ultimately leading to reduced strength and endurance. Malnutrition-related COPD may compromise the immune system and weaken airway defences, as evidenced by hypercapnic respiratory failure, difficulties in weaning from mechanical ventilation, and increased risk of nosocomial lung infections (Collins et al., 2019).

Although most COPD patients appeared with weight loss, the association between malnutrition and COPD has not been extensively investigated, and the underlying mechanisms remain unclear. Several contributing factors, with a multifactorial effect, have been proposed. These include lifestyle practices such as dietary habits, smoking habits, alcohol consumption, and sedentary behaviour (Ingadottir et al., 2018). As these lifestyle practices are linked to malnutrition, they may be associated with an increased risk of COPD.

SIGNS AND SYMPTOMS OF COPD

The primary signs and symptoms of COPD include dyspnea, particularly on exertion, along with cough and sputum production. COPD shares various signs and symptoms arising from various causes (Vogelmeier et al., 2017). The diagnosis of COPD requires confirmation through spirometry. COPD should be suspected in individuals with reduced exertional activity, particularly those experiencing dyspnea. As patients develop exertional dyspnea, many tend to limit their level or intensity of activity (Hanania & O'Donnell, 2019). COPD can be characterized by cough and sputum production, as well as by airflow limitation. In late COPD patients, the most common signs and symptoms involved the extension of expiratory airflow, signs of chest hyperinflation, and adventitial lung sounds such as rhonchi and wheezes. However, these signs and symptoms of COPD need to be confirmed with spirometry (Sarkar et al., 2019).

Pathological changes in the lungs of COPD patients may lead to changes in lung volumes and capacities. These changes include inflammation and swelling of the peripheral airways, the production and accumulation of excessive mucus, obstruction of the bronchial airway (either due to mucus or the projection of a tumour into a bronchus), and damage and malfunction of the distal airways, involving the constriction of the smooth muscle (bronchospasm) (Vogelmeier et al., 2017).

COPD symptoms remain asymptomatic until significant lung damage has taken place, and at this stage, it is usually increased in severity, especially among smokers. Another subjectively presented clinical manifestation of COPD includes symptoms such as shortness of breath, particularly while performing physical activities, wheezing, and tightness in the chest (Vogelmeier et al., 2017). COPD may lead to the development of cyanosis, which is presented with blueness of the lips or fingernail beds. COPD patients may experience frequent respiratory infections, swelling in ankles, feet, or legs, unintended weight loss, and lack of energy. COPD patients are mostly presented with episodes called exacerbations, a condition with worsened symptoms with varying intensity and frequency (Vogelmeier et al., 2017).

DIAGNOSTIC CRITERIA FOR COPD

Misdiagnosis of COPD is common, where former smokers are frequently being misdiagnosed with COPD. For instance, it can be challenging to distinguish between symptoms from other respiratory disorders such as asthma and COPD as the similarities between the symptoms make it difficult to differentiate between these two conditions, particularly in smokers and older adults (American Academy of Family Physicians, 2016). Similarly, COPD patients may not be diagnosed until the advanced stage of the disease, when any interventions turn out to be less effective. Physicians are responsible for reviewing the clinical manifestation, assessing the family and

medical history, and any potential hazardous exposure that may lead to lung irritation especially a smoking habit, exposure to second-hand cigarette smoke, or any other pollutants (Gershon et al., 2018). The procedures or tests that need to be taken to diagnose COPD are as follows:

Firstly, the lung (pulmonary) function tests will be conducted to test and quantify the volume of air that can be inhaled or exhaled and the lungs' capacity to deliver enough oxygen to the blood. Next, the diagnosis will be conducted using a spirometry test, the lung function that is frequently used. During the spirometry test, the participant will be asked to blow into a large tube connected to the spirometer. The spirometer measures the amount of air the lungs can hold, and the speed of air able to be blown out of the lung (Bucchieri et al., 2022). The advantage of this test is that a spirometer can detect COPD before the onset of the disease-associated symptoms. Spirometry can be used to track the disease progression and monitoring (Saadeh et al., 2015). The machine often measures the outcomes of the administration of a bronchodilator (Perez-Padilla et al., 2015). The diffusion capacity, pulse oximetry, and lung volume measurements are additional lung function tests (Amalakanti & Pentakota, 2016).

Diagnosis of COPD can also be made via chest X-ray and CT scan, which can show and test for emphysema (van Dort et al., 2018). Arterial blood gas analysis measures the capacity of the lung to transport oxygen into the blood and eliminate carbon dioxide (Bass et al., 2015).

TREATMENT OPTIONS FOR COPD

Medications

The physician may use several types of medications to improve the symptoms and complications of COPD. COPD patients may consume some medications whenever required regularly. For example, bronchodilators lessen the symptoms of airflow obstruction, reduce dyspnea, relax airways and smooth muscle (bronchodilation), and improve the quality of life (Williams & Rubin, 2018). This was mainly used to relax the muscles of the airways and to make breathing easier by relieving coughing and shortness of breath. There are two types of bronchodilators: short-acting bronchodilators which are usually used before activities, and long-acting bronchodilators for daily usage. Some examples of short-acting bronchodilators are albuterol (ProAir HFA and Ventolin HFA), ipratropium (Atrovent) and levalbuterol (Xopenex HFA), while the long-acting bronchodilators include tiotropium (Spiriva), formoterol (Foradil, Perforomist), Salmeterol (Serevent), indacaterol (Arcapta), arformoterol (Brovana) and aclidinium (Tudorza) (Di Marco et al., 2018).

Inhaled corticosteroid medications are mainly used to reduce airway inflammation as well as to avoid exacerbation. However, it is very prone to side effects, including hoarseness, oral infections, and bruising. Fluticasone (Flovent HFA and Flonase) and budesonide (Pulmicort Flexhaler and Uceris) are examples of inhaled steroids that are beneficial for those with frequent exacerbations of COPD (Pavord et al., 2016).

Some inhalers combine inhaled steroids and bronchodilators. Examples of combination inhalers are salmeterol fluticasone (Advair) and formoterol, and budesonide (Symbicort). On the other hand, short courses of oral steroids or corticosteroids, for instance, five days can prevent COPD from getting worse for those who have experienced a moderate or severe acute exacerbation. However, long-term use of steroid inhalers may develop serious adverse effects, including weight gain, osteoporosis, diabetes, cataracts, and a high risk of infection (Hoshino et al., 2015).

Roflumilast (Daliresp) is a new type of medication approved for those diagnosed with severe COPD and severe symptoms of chronic bronchitis. This medication can reduce inflammation and promote relaxation of the airways. However, there are common adverse effects of this drug, such as diarrhea and weight loss (Garnock-Jones, 2015). Theophylline was also used to treat COPD as it is inexpensive and can help improve breathing and prevent exacerbations. Side effects of the consumption of this drug may include fast heartbeats, tremor, nausea, and headache; however, they are dose-related as only low doses are recommended (Devereux et al., 2018).

The symptoms of COPD may become worse for days or weeks, even if the COPD patients are receiving ongoing treatment. This condition is known as an acute exacerbation, which can lead to lung failure if not associated with timely treatment. The main causes of the exacerbations are respiratory infection, air pollution, or other inflammation-triggering factors (Wedzicha et al., 2017). In the event of exacerbations, COPD patients may need to be prescribed additional medications, including antibiotics, steroids, or a combination of both, started with supplemental oxygen therapy or admitted to the hospital for further treatment (Sorge & DeBlieux, 2020).

Antibiotics usage

The symptoms of COPD can be aggravated by respiratory infections, such as acute bronchitis, pneumonia, and influenza. Antibiotics are generally not preventive but can help in the treatment of acute exacerbations. However, recent evidence showed that antibiotic azithromycin could prevent exacerbations which may be because of its antibacterial or anti-inflammatory qualities (Huckle et al., 2018). A network meta-analysis reported that continued use of macrolides, specifically azithromycin, and erythromycin, seemed advantageous in extending the duration between exacerbations, enhancing quality of life, and decreasing the occurrence of severe adverse events (Janjua et al., 2021). A review highlighted that amoxicillin and doxycycline are frequently recommended for treating acute exacerbations of COPD due to their favorable balance of benefits and risks. Prophylactic antibiotics

have been prescribed in specific patients involving severe COPD and frequent exacerbations. The use ofazithromycin on a continuous or intermittent basis has proven effective in reducing the frequency of acute exacerbations of COPD, yet it carries the risk of fostering antibiotic resistance and adverse effects (Al-Hasan, & Al-Jaghbeer, 2020).

Surgery

COPD patients with severe emphysema will be optioned for surgery as the medications do not help much in relieving the symptoms (Bollmeier & Hartmann, 2020). Lung volume reduction surgery involves the removal of small wedges of lung tissue that have been damaged from the upper lungs. This may create extra space in the chest cavity to allow the remaining healthier lung tissue to expand and the diaphragm to function more efficiently. This surgery may improve the quality of life and the survival rate (Deslée et al., 2016). Lung transplants are only conducted in certain people who meet the specific criteria. This step can improve the ability to breathe and to be active. However, the surgery involves significant risk, which may cause organ rejection or lifelong dependence on immune-suppressing medications (Siddiqui & Diamond, 2018). Bullectomy is the removal of the formation of large air spaces (bullae) in the lungs to improve the airflow. This is an effective option if the walls of the air sacs are damaged. These bullae may increase in size and cause breathing complications (Marchetti & Criner, 2015).

PATHOPHYSIOLOGIC CHANGES OF LIFESTYLE RISK FACTORS IN COPD

Diet plays an important role in maintaining good health. Anorexia and decreased dietary intake are common among COPD patients. Severe food intake limitation leads to complex alterations in metabolism resulting in inflammation, hypoxia, hypercapnia, nutritional deprivation, and pharmacologic therapy. Anorexia may also induce stressors such as nosocomial infection, worsening the condition by enhancing hypermetabolism (Calder et al., 2017). Severe anorexic patients often deteriorate, and numerous systemic comorbidities are correlated with chronic inflammation associated with COPD (Dubé & Laveneziana, 2018; Gea et al., 2014; Global Initiative for Chronic Obstructive Lung Disease, 2022). Anorexia is linked to augmented breathing work and an elevated inflammatory status associated with exacerbations of COPD symptoms. This directly affects muscle function and raises the possibility of hospitalization due to exacerbations (Gea et al., 2018). In COPD patients, the clinical phenotype varies from mild weight loss with anorexia, inflammation, and signs of muscle wasting to severe weight loss with noticeable muscle depletion (sarcopenia), fatigue, and diminished physical performance leading toward frailty (Collins et al., 2019). An extreme lack of food activates the catabolic state and the ubiquitin-proteasome pathway, further accelerating the breakdown of muscle proteins. Prolonged anorexia may lead to the development of cachexia, weakness, and wasting of the body. In the inflammatory state, anorexic patients may develop cytokinemediated cachexia, comparable to other syndromes of end-stage organ failure, potentially inducing COPD in those patients (Abdulai et al., 2018). COPD in anorexic patients is commonly presented with elevated concentrations of soluble tumor necrosis factor receptors, as well as with acute-phase proteins (Chen et al., 2019). In addition, steroid therapy for anorexic patients may further induce proteolysis and enhance gluconeogenesis by inhibiting both protein synthesis and the transportation of amino acids into the muscle (Mondello et al., 2015). In anorexiamediated COPD, conditions such as derangement of hormones and activation of the inflammatory immune system. As severe and prolonged anorexia contributes to the development of cachexia, appetite-stimulating therapy may serve as a novel therapeutic option in COPD patients (Acanfora et al., 2018).

Fruits and vegetables are known to be rich in antioxidants. A study showed that the higher the antioxidant capacity of fruits and vegetables, the lower might be the reduction of the plasma concentration of high-sensitivity C-reactive protein. This action may be a valid reason for the obvious reduction in antioxidant capacity in COPD patients (Kaluza et al., 2017). A higher intake of vegetables and fruits was linked with a low death rate among COPD patients and associated with the reduction of COPD symptoms, such as cough with phlegm which potentially may block the airways. For instance, consumption of fruits, and vegetables rich in dietary fibers, vitamins C and E, polyphenols, and β-carotene were individually associated with a lower risk of COPD, compared to the intake of processed meat which was linked to a higher risk of COPD (van Iersel et al., 2022). Besides, consuming a high amount of vegetables and fruits, evidences showed that COPD's risk could be reduced even among smokers (Kaluza et al., 2018). For instance, the high antioxidant content present in fruits and vegetables may shield the lungs from tobacco smoke's oxidative damage and even avert the development of COPD, indicating that each serving per day increased intake of total fruit and vegetables significantly decreases the risk of COPD by 8% among current smokers and by 4% among ex-smokers (Kaluza et al., 2018). Moreover, long-term intake of high dietary fiber was associated with a 30% lower incidence of COPD, specifically fiber sources such as cereal and fruit fiber among current and ex-smokers (Szmidt et al., 2020). An augmented intake of micronutrients such as calcium, phosphorus, iron, selenium, and vitamin C from dried fruits was associated with decreased odds of COPD, hence dried fruits can help to prevent the development of COPD (Fekete et al., 2023). A meta-analysis showed that individuals with a high consumption of both fruits and vegetables have a reduced risk of COPD by 25%. Individually, a high consumption of fruits reduced the risk of COPD by 28%, and a high consumption of vegetables reduced the risk by 24% (Zhai et al., 2020). A systematic review revealed that high consumption of fruit and

vegetables, directly increases dietary fibers, vitamins C and E, polyphenols, and β -carotene. Individually, these components were found to reduce the risk of COPD (van Iersel et al., 2022).

Smoking habit

Smokers were found to have significantly declined lung function and a higher chance of developing chronic bronchitis. Smoking habits may induce oxidative stress, which plays an important role in developing COPD (Dransfield et al., 2017). Previous evidence showed that smoking habit might lead to 80-90% of COPD patients, especially among females. However, recent evidence showed that only 50% of the smoking population would develop COPD (He et al., 2023). This observation might be since smoking-related COPD may also be affected by other factors, including environmental exposures or pollution (Murgia & Gambelunghe, 2022). Independently, environmental exposure has contributed to 20% of COPD patients. There is also consistent evidence that smoking cessation lowers the risk of mortality due to COPD (Karpman et al., 2018).

Airways wall thickness or luminal area of sub-segmental and specific segmental bronchi is a biomarker for the COPD diagnosis quantifiable by CT as a screening method for inspiratory lung. Among smokers, the thickening of the airway walls may be due to a combination of inflammatory changes and remodeling, which may lead to the further development of COPD (Dransfield et al., 2017).

Alcohol consumption

Alcohol, specifically ethanol, was attributed to developing acute intoxication which affects judgment and motor skills (Wetherbee et al., 2015). Besides, alcohol was well known for its deleterious effects on vital organ function, including heart, liver, pancreas, and brain. However, recently, alcohol consumption was also related to the deformity of lung function, which may contribute to COPD (Singh et al., 2016). The effect of alcohol consumption on the risk of COPD was not independent. The effect of alcohol can only be observed in smoking-associated COPD which presents oxidative stress. However, in the event of chronic alcohol consumption, reducing or stopping alcohol consumption may improve COPD symptoms (Wetherbee et al., 2015).

Chronic alcohol consumption may profound antioxidant glutathione deficiency in the lungs which generates a marked susceptibility towards COPD and acute respiratory distress syndrome (ARDS) (Singh et al., 2016). Chronic alcohol consumption also may develop pulmonary dysfunction, gradual decline in total lung capacity, diffusing capacity, forced vital capacity, and residual volume, for example, the amount of leftover air in the lungs after maximum exhalation of the lungs (Wetherbee et al., 2015). Chronic alcohol consumption declines the mucus-clearing ability and increases the rate of death among COPD victims by worsening the lung function outcomes. With alcohol abstinence, the lungs' diffusing capacity may be replaced but it does not improve the airway obstruction in COPD (Singh et al., 2016).

Alcohol consumption may interfere with the intake of certain medications and reduce the effectiveness of that medication. On the other hand, consumption of certain medications together with alcohol may intoxicate and slowly reduce breathing. For instance, all opioids, namely morphine, methadone, oxycodone, fentanyl, and hydrocodone when combined with alcohol, have an increased risk of an overdose that results in death by suppressing the brain's respiratory centers. Moreover, buprenorphine in combination with alcohol results in hypotension, respiratory depression, profound sedation, and coma (US Food and Drug Administration, 2021). Prolonged exposure to these substances to this condition may develop severe lung disease or COPD (Singh et al., 2016).

In conclusion, alcohol consumption may lead to lung irritation and increase the risk of COPD by (1) inhibiting cells that are responsible for killing bacteria in the lung, (2) preventing the immune system from protecting the body from infections including pneumonia against body infection, (3) preventing mucus production from trapping and eliminating toxins, and (4) reducing the breathing rate by increasing the buildup of carbon dioxide.

Physically inactive

Being physically active may improve pulmonary rehabilitation, further improve the quality of life and symptoms as well as reduce the risk of COPD exacerbation (Maltais et al., 2016). Having a higher physical activity level may lower the risk of hospital admissions and death among patients with COPD. Exercise capacity is frequently reduced among COPD patients as a result of physiological dysfunction (Troosters et al., 2018). A cross-sectional study reported that the daily physical activity among COPD patients was significantly lower compared to controls (4095 steps vs. 6734 steps). The study also reported that daily physical activity COPD was associated with the level of breathlessness and the frequency of exacerbations (Albarrati et al., 2020) and the survival rates of COPD patients were significantly predicted to increase at approximately 7500 steps per day (Lee et al., 2019). A longitudinal study reported that moderate to vigorous PA significantly declines the force expiratory volume, forced vital capacity, and diffusion capacity of the lung for carbon monoxide in COPD patients (Demeyer et al., 2019).

LIFESTYLE APPROACH FOR COPD MANAGEMENT

Smoking cessation is the foremost strategy required in COPD therapy. It is the most effective way to prevent COPD from worsening and improve the lung function (Doo et al., 2023). However, this therapy is not easy to implement. In some cases, attempting to quit may worsen the condition if the COPD patient fails. COPD patients may consult their physician for nicotine replacement therapy in the form of a product or medication, which has consistently helped people quit smoking and avoid complications (Saeed et al., 2020). The physician may also recommend participation in a support group for those deciding to quit smoking. For non-smoking COPD patients, it is advisable to avoid exposure to second-hand smoke (Dransfield et al., 2017).

Physicians or respiratory therapists may advise COPD patients on techniques for breathing more efficiently throughout the day. The discussion will mainly focus on breathing positions and relaxation techniques, especially when experiencing shortness of breath. In COPD, mucus tends to collect in the air passages and can be difficult to clear. Adopting habits like controlled coughing, maintaining high water consumption, and using a humidifier may successfully alleviate symptoms (Murphy et al., 2017). In the event of exacerbations, COPD patients may benefit from quitting smoking, using long-acting bronchodilators, inhaled steroids, or other medications, and avoiding air pollution, which may speed up the recovery process (Putcha & Wise, 2018).

COPD patients often find it difficult to exercise, especially when experiencing trouble breathing. Regular exercises can improve their strength, and endurance and enhance the strength of their respiratory muscles. However, any activities need to be discussed with the physician to avoid further complications (Maltais et al., 2016). A healthy diet may enhance the strength of COPD patients as well. In the case of being underweight, nutritional supplements can be recommended. However, for overweight COPD patients, losing weight may significantly improve their breathing, especially during exertion (Kaluza et al., 2018). Besides avoiding smoking, it is important to avoid exposure to other smoke, such as second-hand cigarette smoke, which may further damage the lungs. Additionally, other types of air pollutants may also irritate the lungs (Murphy et al., 2017).

CONCLUSION

Understanding and addressing lifestyle factors are integral parts of COPD prevention, management, and overall healthcare. Lifestyle modifications, in conjunction with medical interventions, can significantly improve the quality of life for individuals living with COPD. Yet, longitudinal studies are needed across various populations, taking into account the synergic and additive effect of these factors on COPD or the disease progression. This information may help the clinician, health practitioners, and dietitian guide the patients to implement improved lifestyle practices including dietary, smoking, alcohol consumption, physical activities as well as environmental exposure. In the event of emphysema (severe COPD), malnutrition is often irreversible, even with lifestyle modification. Although there is no definite cure for COPD, the introduction of many effective medications and therapy options has improved the possibility of total management of COPD and maintained normal. To avoid the progression of COPD, lifestyle practice therapy could be the most effective strategies aid with medications as prescribed by the physicians.

AUTHOR CONTRIBUTIONS

Sook Yee Lim and Vaidehi Ulaganathan worked on the conception or design of the work. Sook Yee Lim, Vaidehi Ulaganathan, and Baskaran Gunasekaran prepared the original draft writing. All authors; Shamala Salvamani, Yee Lian Tiong, Siti Madihah Muhammad Royani, Kughaneshwary Silvermany, Digsha Augundhooa, Mahla Chambari contributed to revising it critically for important intellectual content. All authors approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are well addressed.

ETHICS APPROVAL

Not applicable.

FUNDING

This work was funded by a Research Excellence and Innovation Grant (REIG-FAS-2020-008) supported by UCSI University.

CONFLICTS OF INTEREST

The authors declare no conflict of interest in this work.

ACKNOWLEDGEMENTS

The authors would like to express their sincere gratitude to team members of the Nutrition and Biotechnology Research in Genetics and Genomics (nBRG2) research group for their valuable contributions during the preparation of this review paper.

REFERENCES

Abdulai, R. M., Jensen, T. J., Patel, N. R., Polkey, M. I., Jansson, P., Celli, B. R., & Rennard, S. I. (2018). Deterioration of limb muscle function during acute exacerbation of chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, 197(4), 433–449.

https://doi.org/10.1164/rccm.201703-0615CI

Acanfora, D., Scicchitano, P., Carone, M., Acanfora, C., Piscosquito, G., Maestri, R., Zito, A., Dentamaro, I., Longobardi, M., Casucci, G., Antonelli-Incalzi, R., & Ciccone, M. M. (2018). Relative lymphocytes count as an indicator of 3-year mortality in elderly people with severe COPD. *BMC Pulmonary Medicine*, 18(1), 116.

https://doi.org/10.1186/s12890-018-0685-6

Albarrati, A. M., Gale, N. S., Munnery, M. M., Cockcroft, J. R., & Shale, D. J. (2020). Daily physical activity and related risk factors in COPD. *BMC Pulmonary Medicine*, 20(1), 60.

https://doi.org/10.1186/s12890-020-1097-y

Amalakanti, S., & Pentakota, M. R. (2016). Pulse oximetry overestimates oxygen saturation in COPD. Respiratory Care, 61(4), 423–427.

https://doi.org/10.4187/respcare.04435

American Academy of Family Physicians. (2016). COPD and Asthma, Differential Diagnosis.

https://www.aafp.org/dam/AAFP/documents/news/COPD-Asthma_Phys_Ed_Booklet.pdf

Ayar Karakoç, G., Ernam, D., Aka Aktürk, Ü., Öztaş, S., Oğur, E., & Kabadayı, F. (2016). The evaluation of nutritional status of stable COPD patients and to investigate the effect of nutritional status on perception of dyspnea, exercise capacity, body composition, hospitalisation and life quality. *Tuberkuloz ve toraks*, 64(2), 119–126. https://doi.org/10.5578/tt.20998

Bass, C. M., Sajed, D. R., Adedipe, A. A., & West, T. E. (2015). Pulmonary ultrasound and pulse oximetry versus chest radiography and arterial blood gas analysis for the diagnosis of acute respiratory distress syndrome: A pilot study. *Critical Care (London, England)*, 19(1), 282.

https://doi.org/10.1186/s13054-015-0995-5

Bollmeier, S. G., & Hartmann, A. P. (2020). Management of chronic obstructive pulmonary disease: A review focusing on exacerbations. *American Journal of Health-System Pharmacy: AJHP: Official Journal of the American Society of Health-System Pharmacists*, 77(4), 259–268.

https://doi.org/10.1093/ajhp/zxz306

Bucchieri, S., Alfano, P., Audino, P., Fazio, G., Marcantonio, S., & Cuttitta, G. (2022). Airway obstruction in primary care patients: Need for implementing spirometry use. *Diagnostics* 12(11).

https://doi.org/10.3390/diagnostics12112680

Calder, P. C., Bosco, N., Bourdet-Sicard, R., Capuron, L., Delzenne, N., Doré, J., Franceschi, C., Lehtinen, M. J., Recker, T., Salvioli, S., & Visioli, F. (2017). Health relevance of the modification of low-grade inflammation in ageing (inflammageing) and the role of nutrition. *Ageing Research Reviews*, 40, 95–119. https://doi.org/10.1016/j.arr.2017.09.001

Chen, Y.-P., Chan, A. T. C., Le, Q.-T., Blanchard, P., Sun, Y., & Ma, J. (2019). Nasopharyngeal carcinoma. *The Lancet*, 394(10192), 64–80.

https://doi.org/10.1016/S0140-6736(19)30956-0

Collins, P. F., Yang, I. A., Chang, Y.-C., & Vaughan, A. (2019). Nutritional support in chronic obstructive pulmonary disease (COPD): an evidence update. *Journal of Thoracic Disease*, 11(S17), S2230–S2237. https://doi.org/10.21037/jtd.2019.10.41

Dal Negro, R. W. (2019). COPD: The annual cost-of-illness during the last two decades in Italy, and its mortality predictivity power. *Healthcare (Basel, Switzerland)*, 7(1), 35.

https://doi.org/10.3390/healthcare7010035

Demeyer, H., Donaire-Gonzalez, D., Gimeno-Santos, E., Ramon, M. A., DE Battle, J., Benet, M., Serra, I., Guerra, S., Farrero, E., Rodriguez, E., Ferrer, J., Sauleda, J., Monso, E., Gea, J., Rodriguez-Roisin, R., Agusti, A., Antó, J. M., & Garcia-Aymerich, J. (2019). Physical activity is associated with attenuated disease progression in chronic obstructive pulmonary disease. *Medicine and Science in Sports and Exercise*, *51*(5), 833–840.

https://doi.org/10.1249/MSS.000000000001859

Deslée, G., Mal, H., Dutau, H., Bourdin, A., Vergnon, J. M., Pison, C., Kessler, R., Jounieaux, V., Thiberville, L., Leroy, S., Marceau, A., Laroumagne, S., Mallet, J. P., Dukic, S., Barbe, C., Bulsei, J., Jolly, D., Durand-Zaleski, I., & Marquette, C. H. (2016). Lung volume reduction coil treatment vs usual care in patients with severe emphysema: The REVOLENS randomized clinical trial. *JAMA*, 315(2), 175–184.

https://doi.org/10.1001/jama.2015.17821

Devereux, G., Cotton, S., Fielding, S., McMeekin, N., Barnes, P. J., Briggs, A., Burns, G., Chaudhuri, R., Chrystyn, H., Davies, L., De Soyza, A., Gompertz, S., Haughney, J., Innes, K., Kaniewska, J., Lee, A., Morice, A., Norrie, J., Sullivan, A., ... Price, D. (2018). Effect of theophylline as adjunct to inhaled corticosteroids on exacerbations in patients with COPD: A randomized clinical trial. *JAMA*, 320(15), 1548–1559.

https://doi.org/10.1001/jama.2018.14432

Di Marco, F., Sotgiu, G., Santus, P., O'Donnell, D. E., Beeh, K.-M., Dore, S., Roggi, M. A., Giuliani, L., Blasi, F., & Centanni, S. (2018). Long-acting bronchodilators improve exercise capacity in COPD patients: a systematic review and meta-analysis. *Respiratory Research*, 19(1), 18.

https://doi.org/10.1186/s12931-018-0721-3

Doo, J. H., Kim, S. M., Park, Y. J., Kim, K. H., Oh, Y. H., Kim, J. S., & Park, S. M. (2023). Smoking cessation after diagnosis of COPD is associated with lower all-cause and cause-specific mortality: a nationwide population-based cohort study of South Korean men. *BMC Pulmonary Medicine*, 23(1), 237.

https://doi.org/10.1186/s12890-023-02533-1

Dransfield, M. T., Kunisaki, K. M., Strand, M. J., Anzueto, A., Bhatt, S. P., Bowler, R. P., Criner, G. J., Curtis, J. L., Hanania, N. A., Nath, H., Putcha, N., Roark, S. E., Wan, E. S., Washko, G. R., Wells, J. M., Wendt, C. H., & Make, B. J. (2017). Acute exacerbations and lung function loss in smokers with and without chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, 195(3), 324–330.

https://doi.org/10.1164/rccm.201605-10140C

Dubé, B.-P., & Laveneziana, P. (2018). Effects of aging and comorbidities on nutritional status and muscle dysfunction in patients with COPD. *Journal of Thoracic Disease*, 10(S12), S1355–S1366. https://doi.org/10.21037/jtd.2018.02.20

Fazleen, A., & Wilkinson, T. (2020). Early COPD: current evidence for diagnosis and management. *Therapeutic Advances in Respiratory Disease*, 14, 1753466620942128.

https://doi.org/10.1177/1753466620942128

Fekete, M., Csípő, T., Fazekas-Pongor, V., Fehér, Á., Szarvas, Z., Kaposvári, C., Horváth, K., Lehoczki, A., Tarantini, S., & Varga, J. T. (2023). The effectiveness of supplementation with key vitamins, minerals, antioxidants, and specific nutritional supplements in COPD-A review. *Nutrients*, *15*(12).

https://doi.org/10.3390/nu15122741

Garnock-Jones, K. P. (2015). Roflumilast: A review in COPD. *Drugs*, 75(14), 1645–1656. https://doi.org/10.1007/s40265-015-0463-1

Gea, J., Martínez-Llorens, J., & Barreiro, E. (2014). Nutritional abnormalities in chronic obstructive pulmonary disease. *Medicina Clínica*, 143(2), 78–84.

https://doi.org/10.1016/j.medcli.2013.05.040

Gea, J., Sancho-Muñoz, A., & Chalela, R. (2018). Nutritional status and muscle dysfunction in chronic respiratory diseases: stable phase versus acute exacerbations. *Journal of Thoracic Disease*, 10(S12), S1332–S1354. https://doi.org/10.21037/jtd.2018.02.66

Gershon, A. S., Thiruchelvam, D., Chapman, K. R., Aaron, S. D., Stanbrook, M. B., Bourbeau, J., Tan, W., & To, T. (2018). Health services burden of undiagnosed and overdiagnosed COPD. *Chest*, 153(6), 1336–1346. https://doi.org/10.1016/j.chest.2018.01.038

Global Initiative for Chronic Obstructive Lung Disease. (2022). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease.

https://goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf

Hanania, N. A., & O'Donnell, D. E. (2019). Activity-related dyspnea in chronic obstructive pulmonary disease: physical and psychological consequences, unmet needs, and future directions. *International Journal of Chronic Obstructive Pulmonary Disease*, 14, 1127–1138.

https://doi.org/10.2147/COPD.S188141

He, Y., Qian, D. C., Diao, J. A., Cho, M. H., Silverman, E. K., Gusev, A., Manrai, A. K., Martin, A. R., & Patel, C. J. (2023). Prediction and stratification of longitudinal risk for chronic obstructive pulmonary disease across smoking behaviors. *Nature Communications*, *14*(1), 8297.

https://doi.org/10.1038/s41467-023-44047-8

Hoshino, M., Ohtawa, J., & Akitsu, K. (2015). Comparison of airway dimensions with once daily tiotropium plus indacaterol versus twice daily Advair® in chronic obstructive pulmonary disease. *Pulmonary Pharmacology & Therapeutics*, 30, 128–133.

https://doi.org/10.1016/j.pupt.2014.08.002

Huckle, A. W., Fairclough, L. C., & Todd, I. (2018). Prophylactic antibiotic use in COPD and the potential anti-inflammatory activities of antibiotics. *Respiratory Care*, *63*(5), 609–619.

https://doi.org/10.4187/respcare.05943

Ingadottir, A. R., Beck, A. M., Baldwin, C., Weekes, C. E., Geirsdottir, O. G., Ramel, A., Gislason, T., & Gunnarsdottir, I. (2018). Two components of the new ESPEN diagnostic criteria for malnutrition are independent predictors of lung function in hospitalized patients with chronic obstructive pulmonary disease (COPD). *Clinical Nutrition (Edinburgh, Scotland)*, 37(4), 1323–1331.

https://doi.org/10.1016/j.clnu.2017.05.031

Janjua, S., Mathioudakis, A. G., Fortescue, R., Walker, R. A., Sharif, S., Threapleton, C. J., & Dias, S. (2021). Prophylactic antibiotics for adults with chronic obstructive pulmonary disease: a network meta-analysis. *The Cochrane Database of Systematic Reviews*, 1(1), CD013198.

https://doi.org/10.1002/14651858.CD013198.pub2

Kaluza, J., Harris, H. R., Linden, A., & Wolk, A. (2018). Long-term consumption of fruits and vegetables and risk of chronic obstructive pulmonary disease: a prospective cohort study of women. *International Journal of Epidemiology*, 47(6), 1897–1909.

https://doi.org/10.1093/ije/dyy178

- Kaluza, J., Larsson, S. C., Orsini, N., Linden, A., & Wolk, A. (2017). Fruit and vegetable consumption and risk of COPD: a prospective cohort study of men. *Thorax*, 72(6), 500–509. https://doi.org/10.1136/thoraxinl-2015-207851
- Karpman, M. D., Eldridge, R., Follis, J. L., Etzel, C. J., Shete, S., & El-Zein, R. A. (2018). Chronic obstructive pulmonary disease among lung cancer-free smokers: The importance of healthy controls. *Respiratory Investigation*, 56(1), 28–33. https://doi.org/10.1016/j.resinv.2017.11.002
- Lee, I.-M., Shiroma, E. J., Kamada, M., Bassett, D. R., Matthews, C. E., & Buring, J. E. (2019). Association of step volume and intensity with all-cause mortality in older women. *JAMA Internal Medicine*, 179(8), 1105–1112. https://doi.org/10.1001/jamainternmed.2019.0899
- Maltais, F., Hamilton, A., Trampisch, M., Tafur, C., & Troosters, T. (2016). Effect of Once-daily tiotropium and olodaterol, alone and combined with exercise training, on two measures of walking capacity in patients with COPD. *Chest*, *150*, 853A. https://doi.org/10.1016/j.chest.2016.08.953
- Marchetti, N., & Criner, G. J. (2015). Surgical approaches to treating emphysema: lung volume reduction surgery, bullectomy, and lung transplantation. *Seminars in Respiratory and Critical Care Medicine*, *36*(4), 592–608. https://doi.org/10.1055/s-0035-1556064
- Mondello, P., Mian, M., Aloisi, C., Famà, F., Mondello, S., & Pitini, V. (2015). Cancer cachexia syndrome: pathogenesis, diagnosis, and new therapeutic options. *Nutrition and Cancer*, 67(1), 12–26. https://doi.org/10.1080/01635581.2015.976318
- Murgia, N., & Gambelunghe, A. (2022). Occupational COPD-The most under-recognized occupational lung disease? *Respirology* (*Carlton, Vic.*), 27(6), 399–410. https://doi.org/10.1111/resp.14272
- Murphy, P. B., Rehal, S., Arbane, G., Bourke, S., Calverley, P. M. A., Crook, A. M., Dowson, L., Duffy, N., Gibson, G. J., Hughes, P. D., Hurst, J. R., Lewis, K. E., Mukherjee, R., Nickol, A., Oscroft, N., Patout, M., Pepperell, J., Smith, I., Stradling, J. R., ... Hart, N. (2017). Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial. *JAMA*, *317*(21), 2177–2186. https://doi.org/10.1001/jama.2017.4451
- Pavord, I. D., Lettis, S., Locantore, N., Pascoe, S., Jones, P. W., Wedzicha, J. A., & Barnes, N. C. (2016). Blood eosinophils and inhaled corticosteroid/long-acting β-2 agonist efficacy in COPD. *Thorax*, 71(2), 118–125. https://doi.org/10.1136/thoraxjnl-2015-207021
- Perez-Padilla, R., Wehrmeister, F. C., Montes de Oca, M., Lopez, M. V., Jardim, J. R., Muino, A., Valdivia, G., Pertuze, J., & Menezes, A. M. B. (2015). Instability in the COPD diagnosis upon repeat testing vary with the definition of COPD. *PloS One*, 10(3), e0121832.

https://doi.org/10.1371/journal.pone.0121832

- Putcha, N., & Wise, R. A. (2018). Medication regimens for managing COPD exacerbations. *Respiratory Care*, 63(6), 773–782. https://doi.org/10.4187/respcare.05912
- Saadeh, C., Saadeh, C., Cross, B., Gaylor, M., & Griffith, M. (2015). Advantage of impulse oscillometry over spirometry to diagnose chronic obstructive pulmonary disease and monitor pulmonary responses to bronchodilators: An observational study. SAGE Open Medicine, 3, 2050312115578957. https://doi.org/10.1177/2050312115578957
- Saeed, M. I., Sivapalan, P., Eklöf, J., Ulrik, C. S., Pisinger, C., Lapperre, T., Tønnesen, P., Hoyer, N., Janner, J., Karlsson, M. L., Bech, C. S., Marså, K., Godtfredsen, N., Brøndum, E., Munk, B., Raaschou, M., Browatzski, A., Lütken, P., & Jensen, J.-U. S. (2020). TOB-STOP-COP (TOBacco STOP in COPd trial): study protocol—a randomized open-label, superiority, multicenter, two-arm intervention study of the effect of "high-intensity" vs. "low-intensity" smoking cessation intervention in active smokers with chronic obstructive pulmonary disease. *Trials*, *21*(1), 730. https://doi.org/10.1186/s13063-020-04653-z
- Safiri, S., Carson-Chahhoud, K., Noori, M., Nejadghaderi, S. A., Sullman, M. J. M., Ahmadian Heris, J., Ansarin, K., Mansournia, M. A., Collins, G. S., Kolahi, A.-A., & Kaufman, J. S. (2022). Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. *BMJ (Clinical Research Ed.)*, 378, e069679. https://doi.org/10.1136/bmj-2021-069679
- Sarkar, M., Bhardwaz, R., Madabhavi, I., & Modi, M. (2019). Physical signs in patients with chronic obstructive pulmonary disease. *Lung India: Official Organ of Indian Chest Society*, *36*(1), 38–47. https://doi.org/10.4103/lungindia.lungindia 145 18
- Siddiqui, F. M., & Diamond, J. M. (2018). Lung transplantation for chronic obstructive pulmonary disease: past, present, and future directions. *Current Opinion in Pulmonary Medicine*, 24(2), 199–204. https://doi.org/10.1097/MCP.0000000000000452
- Singh, G., Zhang, W., Kuo, Y.-F., & Sharma, G. (2016). Association of psychological disorders with 30-day readmission rates in patients with COPD. *Chest*, *149*(4), 905–915. https://doi.org/10.1378/chest.15-0449
- Singh Thakur, J., Nangia, R., & Singh, S. (2021). Progress and challenges in achieving noncommunicable diseases targets for the sustainable development goals. *FASEB BioAdvances*, *3*(8), 563–568. https://doi.org/10.1096/fba.2020-00117
- Sorge, R., & DeBlieux, P. (2020). Acute exacerbations of chronic obstructive pulmonary disease: A primer for emergency physicians. *The Journal of Emergency Medicine*, *59*(5), 643–659. https://doi.org/10.1016/i.jemermed.2020.07.001
- Strzelak, A., Ratajczak, A., Adamiec, A., & Feleszko, W. (2018). Tobacco smoke induces and alters immune responses in the lung triggering inflammation, allergy, asthma and other lung diseases: A mechanistic review. *International Journal of Environmental Research and Public Health*, 15(5). https://doi.org/10.3390/ijerph15051033

- Szmidt, M. K., Kaluza, J., Harris, H. R., Linden, A., & Wolk, A. (2020). Long-term dietary fiber intake and risk of chronic obstructive pulmonary disease: a prospective cohort study of women. *European Journal of Nutrition*, *59*(5), 1869–1879. https://doi.org/10.1007/s00394-019-02038-w
- Troosters, T., Maltais, F., Leidy, N., Lavoie, K. L., Sedeno, M., Janssens, W., Garcia-Aymerich, J., Erzen, D., De Sousa, D., Korducki, L., Hamilton, A., & Bourbeau, J. (2018). Effect of bronchodilation, exercise training, and behavior modification on symptoms and physical activity in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, 198(8), 1021–1032.

https://doi.org/10.1164/rccm.201706-12880C

- US Food and Drug Administration. (2021). Sublocade (buprenorphine extended-release) injection, for subcutaneous use. https://www.accessdata.fda.gov/Drugsatfda_docs/Label/2021/209819s018lbl.Pdf#page=45
- van Dort, M. J., Romme, E. A. P. M., Smeenk, F. W. J. M., Geusens, P. P. P. M., Wouters, E. F. M., & van den Bergh, J. P. (2018). Diagnosis of vertebral deformities on chest CT and DXA compared to routine lateral thoracic spine X-ray. *Osteoporosis International: A Journal Established as Result of Cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, 29(6), 1285–1293. https://doi.org/10.1007/s00198-018-4412-1
- van Iersel, L. E. J., Beijers, R. J. H. C. G., Gosker, H. R., & Schols, A. M. W. J. (2022). Nutrition as a modifiable factor in the onset and progression of pulmonary function impairment in COPD: a systematic review. *Nutrition Reviews*, 80(6), 1434–1444. https://doi.org/10.1093/nutrit/nuab077
- Vogelmeier, C. F., Criner, G. J., Martinez, F. J., Anzueto, A., Barnes, P. J., Bourbeau, J., Celli, B. R., Chen, R., Decramer, M., Fabbri, L. M., Frith, P., Halpin, D. M. G., López Varela, M. V., Nishimura, M., Roche, N., Rodriguez-Roisin, R., Sin, D. D., Singh, D., Stockley, R., ... Agusti, A. (2017). Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: gold executive summary. *The European Respiratory Journal*, 49(3). https://doi.org/10.1183/13993003.00214-2017
- Wada, H., Ikeda, A., Maruyama, K., Yamagishi, K., Barnes, P. J., Tanigawa, T., Tamakoshi, A., & Iso, H. (2021). Low BMI and weight loss aggravate COPD mortality in men, findings from a large perspective cohort: the JACC study. *Scientific Reports*, 11(1), 1531.

https://doi.org/10.1038/s41598-020-79860-4

Wedzicha, J. A. E. C.-C., Miravitlles, M., Hurst, J. R., Calverley, P. M. A., Albert, R. K., Anzueto, A., Criner, G. J., Papi, A., Rabe, K. F., Rigau, D., Sliwinski, P., Tonia, T., Vestbo, J., Wilson, K. C., & Krishnan, J. A. A. C.-C. (2017). Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. *The European Respiratory Journal*, 49(3).

https://doi.org/10.1183/13993003.00791-2016

- Wetherbee, E. E., Niewoehner, D. E., Sisson, J. H., Lindberg, S. M., Connett, J. E., & Kunisaki, K. M. (2015). Self-reported alcohol intake and risk of acute exacerbations of chronic obstructive pulmonary disease: a prospective cohort study. *International Journal of Chronic Obstructive Pulmonary Disease*, 10, 1363–1370. https://doi.org/10.2147/COPD.S86572
- Williams, D. M., & Rubin, B. K. (2018). Clinical Pharmacology of bronchodilator medications. *Respiratory Care*, 63(6), 641–654. https://doi.org/10.4187/respcare.06051
- Zhai, H., Wang, Y., & Jiang, W. (2020). Fruit and vegetable intake and the risk of chronic obstructive pulmonary disease: a dose-response meta-analysis of observational studies. *BioMed Research International*, 2020, 3783481. https://doi.org/10.1155/2020/3783481

Citation:

Lim, S. Y., Ulaganathan, V., Gunasekaran, B., Salvamani, S., Tiong, Y. L., Muhammad Royani, S. M., Silvermany, K., Augundhooa, D., & Chambari, M. (2024). Chronic obstructive pulmonary disease: Signs and symptoms, diagnosis, treatments, lifestyle risk factors and management. *Life Sciences, Medicine and Biomedicine*, 8(1). https://doi.org/10.28916/lsmb.8.1.2024.123



Life Sciences, Medicine and Biomedicine ISSN: 2600-7207

Copyright © 2024 by the Author(s). Life Sciences, Medicine and Biomedicine (ISSN: 2600-7207) Published by Biome Journals - Biome Scientia Sdn Bhd. Attribution 4.0 International (CC BY 4.0). This open access article is distributed based on the terms and conditions of the Creative Commons Attribution license https://creativecommons.org/licenses/by/4.0/