pagepress

COPD patients' pre-flight check: A narrative review

Iqbal Akhtar Khan[1], Paola Pierucci[2], Nicolino Ambrosino[3]

[1]Independent Scholar, Lahore, Pakistan; [2]Cardiothoracic Department, Respiratory and Critical Care Unit, Bari Policlinic University Hospital; Section of Respiratory Diseases, Department of Basic Medical Science Neuroscience and Sense Organs, University of Bari 'Aldo Moro', Bari, Italy; [3]Respiratory Rehabilitation Division, ICS Maugeri IRCCS, Institute of Montescano, Pavia, Italy

Correspondence: Paola Pierucci MD, Cardiothoracic Department, Respiratory and Critical care Unit Bari Policlinic University Hospital; Section of Respiratory Diseases, Dept. of Basic Medical Science Neuroscience and Sense Organs, University of Bari 'Aldo Moro', Bari, Italy.
Tel. +39.080.5591111.
E-mail: paola.pierucci@policlinico.ba.it

Key words: COPD; air travelling; fit to travel; In-flight hypoxemia; narrative review.

Conflict of Interest: All authors declare no conflict of interest in regards to the present manuscript.

Acknowledgement: Dr. Murad Ahmad Khan deserves thanks for his assistance in comprehensive literature search.

Contributions: All authors made substantial contributions to the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article, revising it critically for important intellectual content, and final approval of the version to be submitted and agreed to be accountable for all aspects of the work.

Conflict of interest: The authors declare that they have no direct and indirect financial, commercial, personal/career affiliation with the article, counting any individually held viewpoint that are relevant to their work, to disclose, and all authors confirm accuracy.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Received for publication: 28 February 2022.
Accepted for publication: 8 March 2022.

Monaldi Archives for Chest Disease 2022; 92:2252
doi: 10.4081/monaldi.2022.2252

Abstract

For most of the people with stable and well-controlled chronic obstructive pulmonary disease (COPD), air travel is safe and comfortable, but the flight environment may pose clinical challenges. This narrative review aims to update the requirements for allowance to fly of people with COPD without chronic respiratory failure. A literature review was performed on platforms: PubMed, Scopus and Ovid, for citations in English from 2000 to 2021. The following key words were used: COPD AND: air-travel, in-flight hypoxemia, fitness to air travel. Official regulatory documents and guidelines were also examined. Current air travel statements recommend supplemental oxygen when in flight arterial oxygen tension (PaO_2) is expected to fall below 6.6 or 7.3 kPa. Several lung function variables, prediction equations and algorithms have been proposed to estimate in-flight PaO_2, the need for in-flight supplemental oxygen, and to select individuals needing more advanced pre-flight testing, such as the hypoxia-altitude simulation test. Exercise induced desaturation and aerobic capacity correlate significantly with in-flight PaO_2. COPD patients with late intensification of disease, new changes in medications, recent acute exacerbation/ hospitalization or anticipated emotional and physical stress during the proposed air-travel should be carefully evaluated by the caring family or specialist physician.

"Man must rise above the Earth—to the top of the atmosphere and beyond—for only thus will he fully understand the world in which he lives".
Socrates, 'Plato's Dialogue

Introduction

Air travel is generally safe, but the flight environment poses unique physiologic challenges that may trigger adverse outcomes. Before the COVID-19 pandemic four and half billion passengers flew in 2019 [1]. Given the increase in aged and potentially vulnerable passengers, there are concerns about unrealistic expectations that airlines accept passenger anyone who wishes to fly, independently of their health status [2].

The in-flight medical emergency (IME; a medical occurrence requiring the assistance of the cabin crew) may result from exacerbations of a chronic disease or be an acute event in a previously healthy individual [3]. It has been estimated that 260 to 1,420 IMEs occur daily worldwide [4]. In a study conducted by Martin-

Gill *et al*., on 49,100 IMEs, it was found that syncope or near syncope was the most common (32.7%) followed by gastrointestinal (14.8%), respiratory (10.1%) and cardiovascular (7.0%) symptoms, while cardiac arrest was rare (0.2%) [4]. In-flight respiratory distress was experienced in 18% of individuals with pre-existing respiratory problems, the third most common reason for medical diversion, after cardiac and neurological conditions [5].

Chronic obstructive pulmonary disease (COPD) is the most common diagnosis (39%) amongst individuals with chronic respiratory diseases, referred for pre-flight assessment [5]. For most of the people with stable and well-controlled COPD, air travel is safe and comfortable [6] and they cannot be denied access based on their diagnosis alone. However, these individuals may show various clinical and physiological conditions which might question their safety and comfort during an air travel.

This narrative review aims to update the requirements for people suffering from COPD, to travel by air. It is limited to stable and well controlled individuals, without chronic respiratory failure.

Literature research

A comprehensive literature review was performed on electronic platforms: PubMed, Scopus and Ovid, for publications in English, from 2000 to 2021. The following key words, in pairs, were used: COPD AND: air travel, in-flight hypoxemia, fitness to air travel respectively. The results were cumulated to get the final list of citations. Additionally, the retrieved articles were tracked down looking for other relevant studies or reviews (Figure 1). Furthermore, the sources of official regulatory documents and guidelines were investigated in order to extract relevant material on technical and legal issues [2,7-18]. There was no quality evaluation as this was a narrative review.

Physiology of air flight

Altitude is the distance above sea level and is defined as [18]:

- High (4,921 – 11,483 feet/1,500-3,500 meters)
- Very high (11,483 - 18,045 feet/3,500-5,500 meters)
- Extremely high (>18,045 feet/>5,500 meters)

In aircraft cabin environment, the passengers may eventually face lower air pressure, humidity, and sub-optimal air quality [19]. Increasing altitude indeed may result in decreasing inspired oxygen partial pressure (PiO_2), arterial oxygen tension (PaO_2), and saturation (SaO_2). The difference between PiO_2 and PaO_2 depends also on time of exposure (residents, acclimatization *vs* acute vs subacute exposure), and it reduces at high altitude because of increased minute ventilation (VE), SaO_2 is maintained while awake until over 9,843 feet (3,000 meters) of real pressure altitude [20,21]. Atmospheric pressure estimated PiO_2 and equivalent inspiratory oxygen fraction (FiO_2) at sea level according to altitude is shown in Table 1.

The typical "cruising altitude" – that is, the usual highest altitude reached during commercial flights and sustained between take-off and landing – is around 38,000 feet (11,582 meters). In cabins the Environmental Control System maintains the air pressure, expressed as a "pressure altitude equivalent" versus real pressure altitude, defined as the distance above sea level at which the atmosphere exerts the same pressure as the actual pressure in the aircraft cabin [16]. The regulatory agencies require that an aircraft should be capable of maintaining a minimal cabin pressure equivalent to an altitude of 8,000 feet (2,438 meters) under normal operating conditions [13]. The baseline threshold of altitude-induced hypoxemia is generally considered to be 3,300 feet (1,006 meters); the choice of maintaining a pressure altitude equivalent of 8,000 feet (2,438 meters) in the

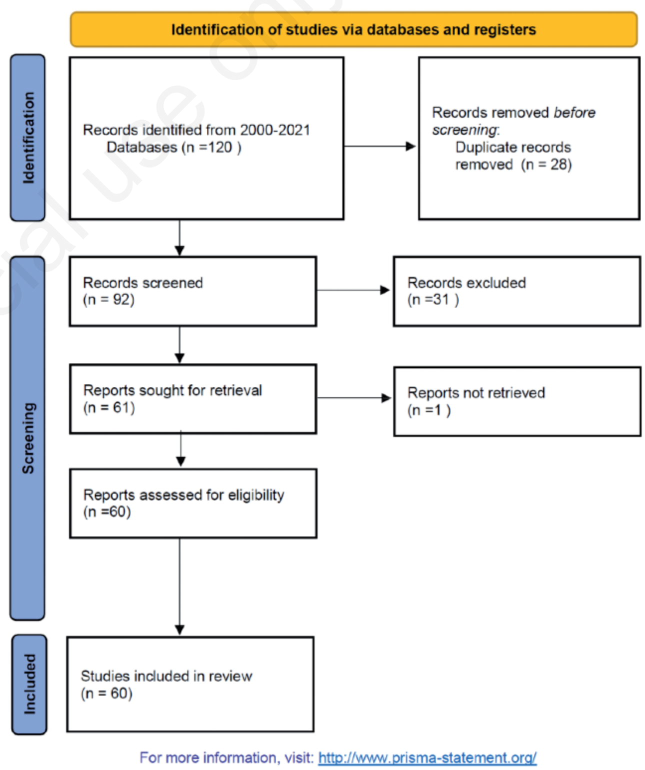

Figure 1. Flow diagram for new systemic reviews which included searches of databases and registers only.

Table 1. Estimated PiO_2 and equivalent FiO_2 at sea level.

	Meters	Feet	Pa, mmHg	PiO_2, mmHg	SL equivalent FiO_2
	Sea level	Sea level	796.6	149.1	0.209
High	1,500	4,921	640.8	124.3	0.174
	3,500	11,483	505.4	95.9	0.135
Very high	5,500	18,045	393.9	72.6	0.102
Extremely high	10,000	32,808	215.2	35.2	0.049

Pa, atmospheric pressure; PiO_2, Partial pressure of inspired oxygen; FiO_2, inspiratory oxygen fraction; SL, sea level.

cabin is because up to that level, SaO_2 normally remains above 90% in average healthy individual [7]. Therefore, it would be highly advisable for those with COPD, to limit their in-flight movements, to minimise the risk of desaturation.

Physiology of COPD

Chronic obstructive pulmonary disease leads to symptoms and functional limitations with airflow obstruction, increased load on breathing and abnormalities in gas exchange [6]. As the aircraft environment is designed for people without oxygenation problems, the cabin pressure allowing acceptable oxygenation in individuals with normal lung function may be not enough for people with COPD [22]. A healthy adult, at altitude of 8,000 feet (2,438 meters], will desaturate to approximately 92-93%, whereas an individual with COPD, may reach approximately 82% and might experience hypoxic symptoms [23]. In individuals with COPD, the ability to increase VE in response to hypoxia is limited and the presence of an alteration in perfusion/ventilation ratio makes it often difficult for them to maintain adequate oxygenation during the flight. As a result, these individuals may have a higher risk for significant hypoxemia during air travel [24]. The effects of high altitude on individuals with COPD were studied during a commercial flight with a mean cabin pressure equivalent to an altitude of 6,000 feet (1,829 meters) [25]. The subjects were tested both when seated and when walking along the aisle. In the pre-flight evaluation all of them had been found fit for air travel without supplemental oxygen. The mean pre-flight pulse oximetry (SpO_2) at sea level fell from 96% to 94% after one hour of flight at cruising altitude, while seated. However, it decreased significantly to 87% when walking [25-26]. Therefore, it would be advisable that airflight's clients with COPD should remain seated while flying to prevent hypoxia.

Oxygenation

The blood oxygenation and by extension, the risk of tissue hypoxia is most commonly monitored non-invasively by SpO_2, despite the limitations of this approach. More accurate assessments can be obtained by arterial blood gas analysis (ABG). For adequate tissue oxygenation, first the blood must contain normal haemoglobin (Hb) concentration which should be >95 % saturated with oxygen in arterial blood [27], the second element necessitating attention being Hb concentration, which must be enough to carry the oxygen to tissues.

Pre-flight screening

Air travelling for most of the people with stable and well-controlled COPD is a safe activity. However, for those with more advanced and unstable disease, the guidelines of Aerospace Medical Association [17], American Thoracic Society [15] and British Thoracic Society [14] suggest that they should undergo a clinical and functional evaluation for "Fit to Fly", before the planned departure. The examining physician needs a detailed history examination and physical examination to critically evaluate health status of the intending traveller. Any previous flying history should be explored, so that relevant events during the flight and after the travel could be critically analysed. The notable issues would be to ascertain the nature and extent of

1. New co-morbidities.
2. Intensification of pre-existing medical conditions.
3. Changes in medications.
4. Acute exacerbation/ hospitalization.
5. Anticipated emotional and physical stress during the proposed air travel.

Of note, each case, for further work up, should be evaluated on its peculiarities and the custom of "One-Size-Fits-All" should not be practised. The advanced COPD is a systemic disease with pulmonary and extra-pulmonary manifestations. Which of the following commonly employed tests, for pre-flight screening, needs to be done cannot be generalised. The decision should be individualised. Ideally, individuals with COPD especially those with more advanced and unstable disease should undergo an evaluation before a planned flight [28] to rule out any contraindication to travel before planning the trip [29]. It is of utmost importance, for the attending physician (GP; Primary Care Physician/Specialist) to conduct detailed history and physical examination to evaluate the health status of the intending traveller. If there is a history of travel problems in previous air trips, the details of the events should be explored. Moreover, it is necessary to check the COPD status with particular attention on recent exacerbation and therapy correct use. Furthermore, it is important to perform several test to identify potential onset of respiratory problems during the flight, therefore, in the following paragraphs all the necessary and available tests in clinical practice will be detailed.

Hypoxia Altitude Simulation Test (HAST)

Several lung function variables, prediction equations and algorithms have been proposed to estimate in-flight PaO_2, the need for in-flight supplemental oxygen, and to select individuals needing more advanced pre-flight testing, such as the hypoxia-altitude simulation test (HAST) [14,30,31,32]. Prediction equations, sea level PaO_2 and spirometer values alone have proven not to be reliable tool for estimating the risk of severe in-flight hypoxemia [14,25,30,31].

The results of HAST are reasonably comparable with conditions at commercial flight cruising altitudes and this still test is considered as the "clinical gold standard" to identify the need for supplemental in-flight oxygen [30-33]. However, HAST is time consuming and not widely available, therefore it is really important to minimize its costs by correctly screening individuals needing it. Under ECG and SpO_2 monitoring, the intending traveller is required to breathe a mixture of 15% oxygen and 85% nitrogen, from a Douglas bag, through a mouthpiece or a facial mask, connected to a two-way valve [34]. Arterial blood gases are sampled pre and post-test [35]. The interpretation of the test is that an individual needs in-flight oxygen if PaO_2 falls below 6.6 Kpa (50 mmHg) after the test or if SpO_2 falls below 85% [29-36].

Pulse oximetry

The pulse oximeter is a non-invasive, readily available, simple to use and inexpensive device. In individuals with COPD, breathing room air at sea level, and normoxemic at rest, the results may be interpreted as follows:

- SpO_2 >95% - To be accepted as fit to fly, without further work up. No need of in-flight supplemental oxygen [29].
- Although a SpO_2 ≥92% indicates that hypoxemia may be not present [37-38], values between 92% and 95% are considered as an alert and further evaluations such as ABG, HAST should be performed, particularly if there is a history of hypoxic event in a previous air trip [14].
- SpO_2 <92% - Needed prescription for in-flight supplemental oxygen, without further work up [37,38].

Peripheral pulse oxygenation of about 90% correspond to a PaO2 of approximately 60 mmhg. Current air travel statements recommend supplemental oxygen when PaO_2 is expected to fall below 6.6 or 7.3 kPa (50 or 55 mmHg) [14,39].

Exercise test

It has been shown that both exercises induced desaturation [26,34,40] and aerobic capacity [24,25] correlate significantly with in-flight PaO_2. The 6-minute walk test (6MWT) is a simple and practical field test, not requiring any sophisticated equipment [41]. An algorithm has been proposed [36] using a combination of SpO_2 at rest and at sea level (baseline) and exercise induced desaturation during 6MWT. Categories for baseline SpO_2 were >95%, 92-95% and <92%, the cut-off value for SpO_2 during 6MWT was calculated as 84%.

- Individuals with baseline SpO_2 >95% combined with SpO_2 during 6MWT ≥ 84% may travel by air without further assessment.
- In-flight supplemental oxygen is recommended if baseline SpO_2 92-95% combined with SpO_2 during 6MWT <84% or if baseline SpO_2 <92%.
- Otherwise, HAST should be performed.

The UK Flight Outcomes Study has shown that, even in specialist centres, only 10% of patients undergo a walk test as part of a fitness to fly assessment [5]. The British Thoracic Society has, therefore, removed the earlier reference to walk tests from its recommendations [14]. Stroller has removed ABG, from the list of required tests [37].

Lung function

The most widely available tool to quantify the severity of COPD is lung function. Some authors have found that the forced expiratory volume at 1 second (FEV_1) as an additional parameter might improve predictive yield for estimating in-flight PaO_2 [42]. It has been reported that individuals with COPD and reduced carbon monoxide diffusion capacity (DL_{CO}) are likely to experience the greatest altitude associated desaturations [43]. Another study concluded that vital capacity and SaO_2 at rest and after exercise could predict hypoxemia during HAST in individuals with respiratory diseases (including COPD) [44]. It is important to remind that in individuals with COPD exertional dyspnoea is not correlated with severity of airway obstruction [45].

A tentative flow chart of simple pre-flight evaluations of fitness to fly is described in Figure 2.

Prescription of in-flight supplemental oxygen

The answer to the straightforward question, in MEDIF (Medical Information for Fitness to Travel or Special Assistance) [7], "*Does the patient need supplementary oxygen in-flight?*" needs details: self -arranged or carrier -supplied, which phase (s) of flight, continuous or pulse flow, which flow rate?

- If the whole trip involves multiple airlines, all of them must be contacted because policies and procedures may differ.
- The airline(s) should be notified If the passenger prefers to use his/her own Portable Oxygen Concentrator (POC), and allowance must be obtained in advance.

Official regulatory documents and guidelines

The airlines have the right to refuse passengers, unfit to fly for medical reasons [46]. However, the fitness for air travel has become a growing issue [47]. Fit to fly? Whose decision is final? the attending physician or the airline?

IATA's regulations regarding medical clearance

The IATA's Medical Manual has made it clear that the medical clearance (permission to board the plane) is entire discretion of the carrier airline (which has the right to impose conditions of

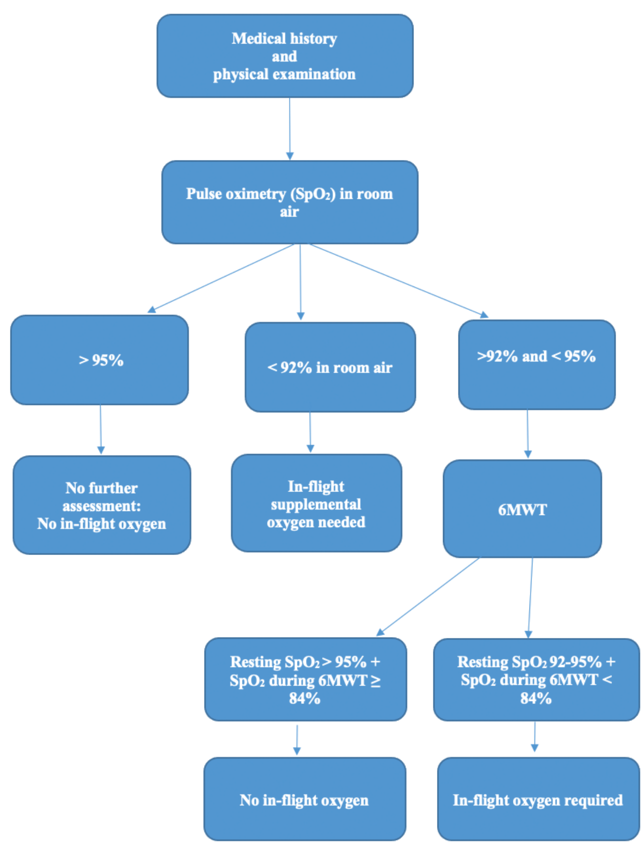

Figure 2. Flow chart of evaluation of fitness to fly.

carriage). The role of personal doctor is just advisory, limiting to filling the MEDIF which has two parts: Part A (Information Sheet for Passengers Requiring Special Assistance, to be completed by the passenger or his/her representative) and Part B (Information Sheet for Passengers requiring medical clearance, to be completed by the treating physician). In addition to the complete physical examination, in the present scenario (stable COPD, non-hypoxemic at rest and at sea level), the attending physician must follow the protocol designed by the airlines, for chronic pulmonary conditions. It is of note that even after giving green signal to fly, the airline requires to be notified immediately of any change in health status or requirements of the intending traveller PRIOR to travel. Furthermore, the intending traveller whose condition has deteriorated later on or has not been accurately described in the MEDIF may be refused boarding in line with flight safety considerations [7].

Official regulations regarding disabilities

Although the vast majority of potential air travellers are people who either are healthy or have no reason to believe they are not, the Fifth Report of House of Lords Science and Technology Committee titled "Air Travel and Health" [2] emphasizes the importance of fitness to fly and the need for intending travellers to satisfy themselves that they are generally fit to fly - not only for their own health but also for the health others. [2]. The European Union Parliament [8] and The Air Carrier Access Act (ACAA) of the United States, enforced through the Department of Transportation [9], state unequivocally that airlines cannot discriminate against passengers because of their disability. However, the concerns of operating carriers have legal issues that must be addressed. Chronic obstructive pulmonary disease may be associated with comorbidities and disabilities, raising concerns about flight safety and comfort.

Official regulations regarding availability and usage of in-flight oxygen

Delivery of supplemental oxygen, on board, is a complex issue. Airlines are not required to provide oxygen service, and many do not [11]. If they do, they have their own policies with specific price structure. Stroller's suggestion to the intending travellers to "shop around" for an appropriate airline is a very well-rewarding advice [37].

Typically, oxygen is not permitted during taxing, take-off, or landing. Prior approval is required if oxygen is required throughout the flight. Some airlines have a policy of not providing in-flight oxygen if the flight time is less than six hours. Furthermore, airlines are not responsible for managing oxygen supplementation during stopovers. If the traveller requires oxygen in transit or if the journey involves multiple airlines, separate arrangements must be made in advance [7]. The attending physician should advise the traveller based on his or her knowledge of the in-flight oxygen delivery system.

According to FAA, the carriage of passenger's own oxygen containers (containing liquid or compressed gas), on board is banned [11]. The FAA and the Department of Transportation's Final Rule titled "Oxygen and portable oxygen concentrators for medical use by passengers" allows passengers to use POC if it meets certain acceptance criteria and bears a label indicating conformance with the acceptance criteria [10]. Some airlines, however, prohibit carrying personal POC on board and require passengers to purchase oxygen from them [48,49].

Although in-seat power is available, some airlines refuse to provide it to needy passengers [EFA]. The FAA recommends that the POC users never rely on available onboard aircraft electrical power during a flight and instead bring their battery-powered POCs, which must have at least 1.5 times life as the flight duration, including a contingency supply for anticipated delays [50].

Although the POC batteries can be recharged during layovers, access to electrical outlets is not always guaranteed. To avoid impending emergency egress [51], the passenger operating a POC may be prohibited from occupying an exit seat in the airplane [12]. Portable oxygen bottles (POB) provided by the carrier are a reliable and officially approved option, but the passenger must pay for them. The payment structure is determined by the airline as well as the segment(s) of the trip.

Clinical practice points

Because being non-hypoxic at rest and at sea level does not guarantee that an individual with COPD declared fit to travel without supplemental oxygen will remain symptom free during air travel, he/she should be advised to bring a Pocket Pulse Oximeter as a convenient and reliable self-monitoring device. The safe oxygenation threshold is to maintain $SpO_2 \geq 85\%$ during the flight. If any symptom appears, the crew should be notified. The immediate response will be to administer oxygen through the POBs at a rate of 2-4 L/min while monitoring SpO_2 to reverse the hypoxemia [52].

If this is not the case, the crew will act quickly, according to IATA's Airline Medical Event Response Programs [7], making an announcement "*is there any doctor on board?",* and contacting the earth station for advice from ground-based support companies [53].

To optimize health outcomes, communication must take place between the traveller, family physician, and airline carrier when there is any doubt about fitness for air travel. Travelers should carry current medications in their original containers and a list of their medical conditions and allergies; they should adjust timing of medications as needed based on time zone changes. Trapped gases that expand at high altitude can cause problems for travellers with recent surgery; casting; ear, nose, and throat issues; or dental issues. Insulin requirements may change based on duration and direction of travel. Travelers can minimize risk for deep venous thrombosis by adequately hydrating, avoiding alcohol, and performing seated isometric exercises. Wearing compression stockings can prevent asymptomatic deep venous thrombosis and superficial venous thrombosis for flights five hours or longer in duration. Physicians and travellers can review relevant pretravel health information, including required and recommended immunizations, health concerns, and other travel resources appropriate for any destination worldwide on the Centres for Disease Control and Prevention travel website.

People with COPD should follow instructions regarding their medical examination and follow up until they board the plane, as well as be aware of do's and don'ts before and during travel. Before their request for special assistance can be processed, they must sign the following undertaking: *"I am prepared at my own risk to bear any consequences which carriage by air may have for my state of health and I release the carrier, its employee's servants and agents from any liability for such consequences. I agree to* *reimburse the carrier upon demand for any special expenditures or costs in connection with my carriage” [7].*

Conclusions

In summary, people affected by COPD with stable and mild disease should not be routinely checked before flying. All the others with late intensification of disease, new changes in medications, recent acute exacerbation/ hospitalization or anticipated emotional and physical stress during the proposed air travel should be carefully evaluated by the caring family or specialist physician. The official regulatory documents and guidelines are freely accessible. They are clear, specific, easy to comprehend and practicable both for the intending traveller and the attending physician. The latest IATA regulations make it clear that it is entire discretion of the airline(s) whom, and on what conditions, to carry on board. They have enforced a strict procedure of medical clearance for those in need of special assistance which should be taken seriously by the intending traveller. This in order to provide the best comfort and safety of all passengers but also caring for those more fragile including COPD patients.

References

1. International Civil Aviation Organization [Internet]. The world of air transport in 2019. Accessed February 22, 2021. Available from: https://www.icao.int/annual-report-2019/Pages/the-world-of-air-transport-in-2019.aspx
2. House of Lords, UK Parliament [Internet]. Science and Technology- Fifth Report. Accessed February 22, 2021. Available from: https://publications.parliament.uk/pa/ld199900/ldselect/ldsctech/121/12101.htm
3. Bagshaw M, Illig P. 47 - The Aircraft Cabin Environment. In: JS Keystone, P. Kozarsky, BA Connor, HD Nothdurft, M Mendelson, K Leder, Editors. Travel Medicine. Elsevier: Amsterdam; 2019. p. 429-36.
4. Martin-Gill C, Doyle TJ, Yealy DM. In-flight medical emergencies: A review. JAMA 2018;320:2580-90.
5. Coker RK, Shiner LRJ, Partridge MR. Is air travel safe for those with lung disease? Eur Respir J 2007;30:1057-63.
6. Global Initiative for Chronic Obstructive Lung Disease – GOLD [Internet]. 2022 GOLD Reports. Global strategy for prevention, diagnosis, and management of COPD. Accessed February 22, 2021. Available from: https://goldcopd.org/2022-gold-reports/
7. International Air Transport Association - IATA [Internet]. Medical Manual. 2020, 12th Edition. Geneva.
8. European Parliament. Regulation (EC) No 1107/2006 of the European Parliament and of the Council of 5 July 2006 concerning the rights of disabled persons and persons with reduced mobility when travelling by air (Text with EEA relevance). Accessed February 22, 2021. Available from: https://www.legislation.gov.uk/eur/2006/1107
9. US Department of Transportation. Passengers with Disabilities. Accessed February 22, 2021. Available from: https://www.transportation.gov/airconsumer/passengers-disabilities
10. Federal Aviation Administration – FAA [Internet]. Acceptance Criteria for Portable Oxygen Concentrators. Accessed February 22, 2021. Available from: https://www.faa.gov/about/initiatives/cabin_safety/portable_oxygen/
11. Federal Aviation Administration – FAA [Internet]. Oxygen Equipment Use in General Aviation Operations. Accessed February 22, 2021. Available from: https://www.faa.gov/pilots/safety/pilotsafetybrochures/media/oxygen_equipment.pdf
12. Legal Information Institute Cornell Law School [Internet]. Oxygen and portable oxygen concentrators for medical use by passengers. Accessed February 22, 2021. Available from: https://www.law.cornell.edu/cfr/text/14/121.574
13. National Research Council. The Airline Cabin Environment and the Health of Passengers and Crew-Consensus Study Report. Washington DC: The National Academics Press; 2002.
14. Ahmedzai S, Balfour-Lynn IM, Bewick T, et al. Managing passengers with stable respiratory disease planning air travel: British Thoracic Society recommendations. Thorax 2011;66: i1-i30.
15. ATS/ERS Task Force for COPD Research. An official American Thoracic Society/ European Respiratory Society statement: research questions in COPD. Eur Respir J 2015;45:879-905.
16. International Civil Aviation Organization [Internet]. Manual of Civil Aviation Medicine – Doc 8984 AN /895 -International Civil Aviation Authority 3rd Edition 2012. Available from: https://www.icao.int/publications/documents/8984_cons_en.pdf
17. Federal Aviation Administration – FAA [Internet]. Introduction to Aviation Physiology - Civil Aerospace Medical Institute Aeromedical Education Division, Oklahoma City; 2016.
18. Roach RC, Lawley JS, Hackett PH. Mountain Medicine Part 1 - High-Altitude Physiology. Accessed February 22, 2021. Available from: https://eu-ireland-custom-media-prod.s3-eu-west-1.amazonaws.com/UKMEAEU/eSample/9780323359429-sample-chapter.pdf
19. US National Research Council. Committee on Air Quality in Passenger Cabins of Commercial Aircraft. The airliner cabin environment and the health of passengers and crew. Washington DC: National Academies Press; 2002.
20. Morris A, Kanner RE, Crapo R, et al. Clinical Pulmonary Function Testing. A Manual of Uniform Laboratory Procedures. Intermountain Thoracic Society: Salt Lake City; 1984.
21. Sutton JR, Reeves JT, Wagner PD, et al. Operation Everest II: oxygen transport during exercise at extreme simulated altitude. J Appl Physiol 1988;64:1309-21.
22. National Air Transportation Center of Excellence for Research in the Intermodal Transport Environment (RITE). Health effects of aircraft cabin pressure in older and vulnerable passengers. Airliner Cabin Environment Research (ACER) Program-November 2011 Final Report No. RITE-ACER-CoE2011. Accessed February 22, 2021. Available from: https://www.faa.gov/data_research/research/med_humanfacs/cer/media/HealthEffectsVulnerablePassengers.pdf
23. Carvalho AM, Poirier V. So you think you can fly? Determining if your emergency department patient is fit for air travel. Can Fam Physician 2009;55:992-5.
24. Christensen CC, Ryg M, Refvem OK, Skjønsberg OH. Development of severe hypoxaemia in chronic obstructive pulmonary disease patients at 2,438 m (8,000 ft) altitude. Eur Respir J 2000;15:635-9.
25. Akerø A, Christensen CC, Edvardsen A, Skjønsberg OH. Hypoxaemia in chronic obstructive pulmonary disease patients during a commercial flight. Eur Respir J 2005;25:725-30.
26. Seccombe LM, Kelly PT, Wong CK, et al. Effect of simulated commercial flight on oxygenation in patients with interstitial lung disease and COPD. Thorax 2004;59:966-70.
27. Higgins C. Oxygen saturation – better measured than calculated. Accessed February 22, 2021. Available from: https://acute-

caretesting.org/en/articles/oxygen-saturation-better-measured-than-calculated
28. Ergan B, Arikan H, Akgün M. Are pulmonologists well aware of planning safe air? The SAFCOP study. Int J COPD 2019;14: 1895-900.
29. Josephs LK, Coker RK, Thomas M, et al. Managing patients with stable respiratory disease planning air travel: a primary care summary of the British Thoracic Society recommendations. Prim Care Respir J 2013;22:234-48.
30. Mortazavi M, Eisenberg MJ, Langleben D, et al. Altitude-related hypoxia: risk assessment and management for passengers on commercial aircraft. Aviat Space Environ Med 2003;74:922-7.
31. Silverman D, Gendreau M. Medical issues associated with commercial flights. Lancet 2009;373:2067-77.
32. Bradi AC, Faughnan ME, Stanbrook MB, et al. Predicting the need for supplemental oxygen during airline flight in patients with chronic pulmonary disease: a comparison of predictive equations and altitude simulation. Can Respir J 2009;16:119-24.
33. Robson AG, Lenney J, Innes JA. Using laboratory measurements to predict in-flight desaturation in respiratory patients: are current guidelines appropriate? Respir Med 2008;102:1592-7.
34. Gong H Jr, Tashkin DP, Lee EY, Simmons MS. Hypoxia-altitude simulation test. Evaluation of patients with chronic airway obstruction. Am Rev Respir Dis 1984;130:980-6.
35. Tzani P, Pisi G, Aiello M, et al. Flying with respiratory disease. Respiration 2010;80:161-70.
36. Dine CJ, Kreider ME. Hypoxia altitude simulation test. Chest 2008;133:1002-5.
37. Edvardsen A, AkerøA, Christensen CC, et al. Air travel and chronic obstructive pulmonary disease: a new algorithm for pre-flight evaluation. Thorax 2012;67:964-9.
38. Stroller JK. Evaluation of patients for supplemental oxygen during air travel. Accessed February 22, 2021. Available from: https://www.uptodate.com/contents/evaluation-of-patients-for-supplemental-oxygen-during-air-travel?search=evaluation-of-patients-for-supplemental-oxygen-during-air%20travel&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
39. Pilcher J, Ploen L, McKinstry S, et al. A multicentre prospective observational study comparing arterial blood gas values to those obtained by pulse oximeters used in adult patients attending Australian and New Zealand hospitals. BMC Pulm Med 2020;20:7.
40. Aerospace Medical Association Medical Guidelines Task Force. Medical Guidelines for Airline Travel. Aviat Space Environ Med 2003;74:A1-19.
41. Chetta A, Zanini A, Pisi G, et al. Reference values for the 6-min walk test in healthy subjects 20-50 years old. Respir Med 2006;100:1573-8.
42. Giannitsi S, Bougiakli M, Bechlioulis A, et al. 6-minute walking test: a useful tool in the management of heart failure patients. Ther Adv Cardiovasc Dis 2019;13:1753944719870084.
43. Dillard TA, Rajagopal KR, Slivka WA, et al. Lung function during moderate hypobaric hypoxia in normal subjects and patients with chronic obstructive pulmonary disease. Aviat Space Environ Med 1998;69:979-85.
44. Kelly PT, Swanney MP, Stanton JD, et al. Resting and exercise response to altitude in patients with chronic obstructive pulmonary disease. Aviat Space Environ Med 2009;80:102-7.
45. Ling IT, Singh B, James AL, Hillman DR. Vital capacity and oxygen saturation at rest and after exercise predict hypoxaemia during hypoxic inhalation test in patients with respiratory disease. Respirology 2013;18:507-13.
46. O'Donnell DE, Gebke KB. Activity restriction in mild COPD: a challenging clinical problem. Int J Chron Obstruct Pulmon Dis 2014;9:577-88.
47. Jorge A, Pombal R, Peixoto H, Lima M. Preflight medical clearance of ill and incapacitated passengers: 3-year retrospective study of experience with a European airline. J Travel Med 2005;12:306-11.
48. Silverman D, Gendreau M. Medical issues associated with commercial flights. Lancet 2008;373:2067-77.
49. European Federation of Allergy and Airways Diseases – EFA. Enabling air travel with oxygen in Europe: An EFA booklet for patients with chronic respiratory disease. Accessed February 22, 2021. Available from: https://www.efanet.org/images/2013/09/Enabling-Air-Travel-with-Oxygen-in-Europe-An-EFA-Booklet-for-Patients-with-Chronic-Respiratory-Disease.pdf
50. US Department of Transportation, Federal Aviation Administration. Portable Oxygen Concentrators - Advisory Circular dated May 24, 2016 AC No: 120-95A. Accessed February 22, 2021. Available from: https://cdn.shopify.com/s/files/1/0127/9646/1114/files/FAA-POC.pdf?6728652040129714599
51. Keystone JS, Kozarsky PE, Connor BA, et al. Travel Medicine. Amsterdam: Elsevier; 2019.
52. Tsiligianni IG, van der Molen T, et al. Air travel for patients with chronic obstructive pulmonary disease: a case report. Br J Gen Pract 2012;62:107-8.
53. Kodama D, Yanagawa B, Chung J, Fryatt K, Ackery AD. "Is there a doctor on board?": Practical recommendations for managing in-flight medical emergencies. CMAJ 2018;190:E217-22.