

LITERATURE REVIEW

Respiratory Travel Medicine

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ARTICLE INFO	ABSTRACT
<p><i>Article history:</i> Received 21 April 2022 Received in revised form 23 September 2022 Accepted 29 September 2022 Available online 30 September 2022</p> <hr/> <p><i>Keywords:</i> Pre-flight assessment Public health, Respiratory, Travel medicine.</p>	<p>International tourist arrivals continue to increase over time due to global economic growth, increasing middle class in developing countries, technological advances, innovative business concepts, cost-effective travel, and facilitation of visas. The increase in tourist visits has resulted in health problems due to the trips. Respiratory tract infections are the main reason tourists seek medical care. Respiratory infections occur in 20% of all tourists, almost the same as the incidence of diarrhea. The majority of international inbound tourism involved air travel. Though physiological changes happen in everyone while air travel, people with lung disease are at high risk for significant complications and necessitate a specific risk assessment strategy. A pre-flight evaluation is conducted if there is any uncertainty regarding the patient's fitness for flight and the effect of eligibility to fly. This literature review summarized the important aspect of travel medicine from the respiratory medicine point of view.</p>

INTRODUCTION

Global economic growth, an increasing number of middle-class people in developing countries, technological developments, innovative business concepts, affordable travel costs, and visa facilitation have led to an increase in international tourist arrivals. Based on the World Tourism Organization (WTO), in 2019, international tourist arrivals were around 1.426 billion, and domestic tourists were around 4.611 billion. Traveling can pose various risks to health, such as experiencing changing height, humidity, and temperature, as well as being exposed to various infectious infections that might cause illness. Serious health conditions can occur in areas with insufficient accommodation, inadequate hygiene, poorly developed medical services, and unavailability of clean water. The Coronavirus disease 2019 (COVID-19) pandemic has been a catastrophe for society and the economy. The economies of both developed and developing countries

have been impacted. Compared to 2020, global tourism increased by 4% in 2021 (415 million vs 400 million). According to the preliminary United Nations World Tourism Organization (UNWTO) figures, foreign tourist arrivals (overnight visitors) were still 72% lower than in the pre-pandemic year of 2019. 2020 was the worst year for tourism, with overseas arrivals falling by 73%. Increased immunization rates and better coordination are required for recovery.¹

Travel medicine has developed rapidly as more and more people travel to unusual and remote places. It has also gotten more complicated due to dynamic developments in the global epidemiology of infectious diseases, change in drug resistance patterns, and a rise in the number of travelers suffering from chronic illnesses. Nearly one billion tourists cross international borders every year. Nevertheless, previous studies showed that few travelers sought health advice before traveling (pre-travel). Many got pre-travel advice from less competent practitioners to provide current and accurate information.²

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Everyone planning a trip must know the health risks that can occur and how to protect themselves, therefore they can minimize the risk of contracting the disease. Travelers who plan to visit a destination are strongly advised to consult a health professional before traveling. Consultation is conducted at least 4-8 weeks before the trip. It includes information about possible health risks, vaccinations, and medications that the tourists may need.¹

Respiratory tract infections are the main reason tourists seek medical care. Respiratory infections occur in 20% of all tourists, almost the same as the incidence of diarrhea. Upper respiratory tract infections occur more often than lower respiratory tract infections. Anamnesis about travel history is necessary to evaluate patients with respiratory infections.³ This literature review discussed respiratory travel medicine before the COVID-19 pandemic.

DISCUSSION

Risk Factors for Health Problems in Travelers

Some factors used to determine the risks that can occur to tourists are the type of transportation used, tourist destinations, duration and season of travel,

accommodation standards, sanitation, and tourist health status. The mode of transportation and length of travel are crucial factors in determining the risk of infectious disease exposure and the requirement for particular immunizations. The duration of the trip also determines the possibility of tourists experiencing disturbances caused by altitude, temperature, and humidity.⁴

Direct physical interaction, droplet dispersion, and minuscule suspended particles are all possible pathways for transmission. The congregation of huge groups of people at airports, cruise ships, and hotels can also help spread respiratory diseases. Inflammation of the respiratory tract, exacerbations of asthma and chronic obstructive pulmonary disease (COPD), bronchitis, and pneumonia are all linked to poor air quality at destinations and exposure to SO₂, NO₂, CO, and ozone. Children, the elderly, and travelers with comorbidities such as asthma and COPD are at a higher risk of contracting respiratory tract infections.³

Pre-Travel Assessment

Patient evaluation before travel includes fitness assessment or travel contraindications (such as pre-existing disease, fit to fly), evaluation of travel itinerary or risk assessment (such as previous activities, travel to

Table 1. Passengers with the following conditions must be evaluated before traveling:⁹

No.	Condition	Special Condition
1	Patients with respiratory conditions that are potential to worsen acutely, resulting in disability and/or requiring medical assistance.	Severe (FEV1 less than 50% predicted) or uncontrolled obstructive airways disease characterized by symptoms, oxygen demand, and exacerbations that are severe and/or frequent Restrictive pulmonary disease with symptoms or chest wall abnormalities or a history of weakened respiratory muscle leading to shortness of breath and exercise limitation Pulmonary hypertension Comorbid conditions that worsen due to hypoxemia (cerebrovascular or cardiac disease) Hospitalization due to respiratory conditions within <6 weeks Continuous positive airway pressure (CPAP) or ventilatory support requirements such as non-invasive ventilator Pulmonary involvement due to active cancer Long-term oxygen therapy (LTOT) or other oxygen requirements
2	History of pneumothorax within <6 weeks	-
3	History of pulmonary embolism or deep vein thrombosis or higher risk of venous thromboembolism (VTE) within < 6 weeks	-
4	People with a history of experiencing substantial symptoms following a previous flight or whose doctor is concerned about their condition	-

rural or urban areas), relevant medical history (such as vaccination history, allergies, chronic illness, mental health history, and medication), good mental health screening, and ability to deal with stress in a hostile environment.²

Travelers who have plans to visit developing countries are advised to consult a medical professional before traveling. Consultation should be conducted at least 4-8 weeks before the trip and preferably can be completed sooner if traveling for a long period. The consultation includes information about possible health risks, determining the need for vaccinations, and other medical items that may be needed during the trip. All travelers are strongly advised to seek adequate travel insurance.⁴

Medical emergencies occur in 1 in 604 flights and

1 in 30,000 passengers.^{5,6} Respiratory diseases accounted for about 12% of in-flight problems. Other conditions include syncope (37.4%), symptoms of heart disease (7.7%), stroke (2%), and cardiac arrest (0.3%). At altitudes above 3,048 m (10,000 ft), hypoxemia becomes more evident, and oxygen saturation drops to 89% in healthy people.^{7,8} Another possible risks of air travel include low relative humidity and gas expansion due to altitude in enclosed lung parenchymal spaces according to Boyle's law. At an altitude of 2,438 (8,000 ft), a 38% expansion of the humidified gas occurs.⁹

A pre-flight assessment is conducted if there is any doubt about the patient's medical condition for air travel and the effect of comorbidities on the patient's health condition. Patients should generally be stable and have been cured from exacerbations before traveling.⁹

Table 2. The conditions listed below are classified as contraindications for air travel:⁹

No.	Condition
1	Ventilatory failure that has not been treated
2	Pneumothorax that has not been treated
3	Respiratory infections that can pose a threat to others, such as tuberculosis, severe acute respiratory syndrome, middle east respiratory syndrome, COVID-19
4	Bronchogenic cyst. Cerebral air embolism has been reported in airplane passengers due to the rupture of a bronchogenic cyst.
5	The highest fixed flow rate typically accessible on commercial airplanes is 4 L/min, therefore severe hypoxemia patients who need >4L/min oxygen while flying are traditionally urged not to fly. This limit is no longer applicable due to the presence of POCs that have been approved for a flight that supply a variety of flow rates that are continuous and intermittent. The highest flow rate is limited by the technology present during in-flight oxygen delivery. Pulse-dose delivery devices, on the other hand, can make determining the flow provided more difficult and might not be properly accepted. Breathing through the mouth, talking, snoring, and/or sleeping should all be considered. On commercial airplanes, high-flow nasal oxygen (HFNO) could not be provided.

In addition, it is advised for a diver to avoid flying for at least 12 hours following the diver's last dive because the decreased cabin pressure might trigger decompression sickness. After multiple dives, this interval should be prolonged to 24 hours. Tourists should consult with a specialist medical team from a diving school.⁴

Travel-related health concerns are greater for specific types of travelers, including newborns and young kids, expectant mothers, the elderly, people with disabilities, and travelers with compromised immune systems and pre-existing health problems.⁴

Age

Air travel is not recommended for newborns <48 hours due to variations in cabin air pressure, which can cause discomfort. The elderly are not always contraindication for a trip; if they are generally healthy, it is advisable to consult a medical professional before traveling.⁴ Infants and younger children are at a higher risk of experiencing hypoxia during air travel due to various factors, including a shift in the oxygen dissociation curve to the left (because fetal hemoglobin

is present), narrower airway, lesser alveoli, a more flexible rib cage, and an increase in the tendency of bronchoconstriction and pulmonary vasoconstriction, resulting in a mismatch of ventilation-perfusion due to hypoxia.⁹

Pregnancy

Commercial flights are relatively safe in uncomplicated pregnancies at >36 weeks and >32 weeks in multiple pregnancies. Pregnant women should check the airline's requirements when booking flights. After 28 weeks, most airlines require a medical certificate confirming the estimated delivery date and no complications.³ Traveling during the second trimester is the safest option for pregnant women. It is not advised to travel to remote areas when pregnant.⁴

Disability

If the traveler is generally healthy, physical disability is usually not a contraindication. Airlines have policies regarding passengers with disabilities who require support from someone that can provide comprehensive assistance to passengers.⁴

Pre-Existing Disease

Travelers suffering from chronic diseases must consult a doctor before preparing for a trip. The following conditions that can raise the risks of health while traveling are cardiovascular disease, chronic hepatitis, chronic inflammatory bowel disease (IBD), chronic kidney disease (CKD) requiring dialysis, chronic respiratory disease, diabetes mellitus, epilepsy, drug-induced immunosuppression or human immunodeficiency virus (HIV) infection, a history of thromboembolic disease, severe anemia, impaired severe mental illness, transplantation, oncological conditions, and chronic hematological conditions.⁴

Mental Status

Travel is often a stressful experience. Tourists face a new place, a different culture and language, and are unfamiliar with local health facilities. For people with a predisposition to mental disorders, the disorder may appear for the first time during a trip. Although stressful events are unpredictable, taking precautions can reduce travel-related stress. Travelers should collect appropriate information before traveling, such as the type of accommodation, duration of the trip, the purpose, and the difficulties that may be encountered. With this preparation, it will be possible to maintain the tourists' confidence.⁴

Management of Respiratory Disease Patients Planning Air Travel

Although all people experience physiological changes during flight, people with lung disease are at a higher risk of significant complications and require a specific risk assessment strategy. Respiratory complaints are the second most common medical issue while flying after syncope or presyncope.¹⁰

Without cabin pressure, passengers can be exposed to hypoxic conditions because the partial pressure of oxygen at an altitude of over 45,000 feet is about 1/3 the pressure at sea level. The aircraft cabin is pressurized at an altitude of 8,000 feet, corresponding to about 15.1% oxygen at sea level.¹⁰ Partial arterial pressure of oxygen (PaO₂) at an altitude of 8,000 feet (2,438 m) in healthy passengers is affected by age and minute ventilation but decreases to 60-75 mmHg and

oxygen saturation (SpO₂) 88-94%, which is measured by pulse oximetry. This situation does not cause symptoms in healthy people. Altitude exposure can worsen hypoxemia in passengers with lung disease. The physiological compensation for acute hypoxemia is triggering peripheral chemo-receptors in carotid bodies that stimulate mild to moderate hyperventilation with increased tidal volume, which is influenced by increasing minute ventilation to maximize alveolar oxygen pressure (PAO₂) and PaO₂. There was a decrease in carbon dioxide artery pressure (PaCO₂) due to hyperventilation, but hypoxia neutralized the effects of cerebral vasoconstriction and maintained oxygen transport to the brain. Tachycardia causes an increase in cardiac output, which helps to maintain blood flow and oxygen transport.¹¹

Pulmonary disease patients who will travel should have their primary doctor/pulmonologist/specialist evaluate them before flying, pack medication and therapeutic devices in carry-on baggage with extra supplies (batteries, infusion pumps/tubing, and many more), and notify the airline in advance if special accommodations are required. Advice for more specific requests differs based on the disease. Table 1 lists the patient factors that need to be evaluated further to determine if supplementary oxygen is required.¹²

FEV₁ and SpO₂ are important markers for severity. However, in patients with pulmonary diseases, this marker cannot accurately predict the occurrence of hypoxemia or complications during or after the flight.¹³ It is recommended that doctors must evaluate preceding flight information, flight duration and destination, and also the time of last exacerbation in patients with the risk of hypoxemia or other problems due to air travel. Patient care routines, such as bronchodilators, must be optimized before traveling.¹¹

Patients with medical needs that often air travel can obtain a Frequent Traveler's Medical Card (FREMEC) that records essential medical details and replace the forms required for each flight. After being registered, medical support may be provided whenever the patient travels. FREMEC is issued by various airlines. If a patient travels on a different airline, they must verify the validity with the new airline.¹¹ The patient factors that need to be evaluated further to determine if supplementary oxygen is required according to various health organization are described in Table 3.

Table 3. The patient factors that need to be evaluated further in order to determine if supplementary oxygen is required^{11,12,14,15}

Organizations	Factors
British Thoracic Society (BTS)	SpO ₂ 92-95% and one of the following: <ul style="list-style-type: none"> • Hypercapnia • Predicted FEV₁ <30% • Lung carcinoma • Restrictive lung disease • Ventilator support • Disease of Cerebrovascular or cardiac • Exacerbation of chronic lung or heart disease within 6 weeks of flight
American Thoracic Society (ATS) European Respiratory Society (ERS)	One or more of the following: <ul style="list-style-type: none"> • COPD accompanied by comorbidities • Previous experience with in-flight symptoms • Exacerbation of pulmonary disease recently • Administration of oxygen due to hypoventilation
Aerospace Medical Association (AsMA) Canadian Thoracic Society (CTS) Department of Veterans Affairs	PaO ₂ <70 mmHg at sea level COPD accompanied by severe or mild hypoxia (SpO ₂ <90%)

Table 4. 6MWT interpretation¹²

6MWT SpO ₂	Resting SpO ₂		
	<92%	92-95%	>95%
<84%	In-flight O ₂	In-flight O ₂	Continued to HCT
≥84%	In-flight O ₂	Continued to HCT	No O ₂ required

Pre-Flight Assessment

Pulse oximetry is the first and easiest screening test. Previously, it was thought that people with oxygen saturation >95% at rest at sea level did not need oxygen while flying.⁹ Patients with a resting saturation of <92% on room air should take supplementary oxygen in flight because of a significant risk of hypoxemia at high altitudes. Saturation between 92 and 95% should be investigated further, especially if there are established risk factors for hypoxemia during flying by airplane^{9,10} Table 4 shows a comparison between pulse oximetry at rest and other assessment methods of hypoxemia while flying by airplane.

Spirometry is usually recommended in people with acute or chronic pulmonary or pulmonary disease symptoms. However, parameters of lung function in most cases are difficult to predict hypoxemia or complications.⁹ There are several procedures used to assess a person's eligibility to fly, namely (1) walk tests, (2) hypoxemia prediction from equations, and (3) hypoxic challenge test.¹¹

Walk Tests

People who can walk 50 meters or climb 10-12 stairs without shortness of breath are believed to have adequate cardiopulmonary reserves for flight. The capacity to enhance minute ventilation and cardiac output

during exercise is an excellent test for assessing cardiopulmonary reserve. However, recent data shows that the 50 m walk test is not sensitive for assessing fitness to fly, although it is sometimes still used as a reference by airlines and aviation authorities. A pulmonologist has experience with other walking tests, for example, the 6- or 12-minute walk test (6MWT or 12MWT) and the shuttle walk test (SWT). Baseline walk test values (6MWT and SWT) could not predict in-flight hypoxemia under various respiratory conditions but changes in SpO₂ at 6MWT and SWT are correlated with hypoxic challenge testing (HCT) outcomes in ILD, COPD, and chest wall deformities. The walk test could not estimate in-flight oxygen demand but can tell which person requires further testing.^{9,11} A walk test may determine whether or not HCT is necessary. HCT and in-flight oxygen should not be required for persons with COPD who undertake SWT or 6MWT, and the saturation did not fall below 84%.⁹ A study by Edvardsen, *et al.* implied that it is fair to prescribe oxygen at 2 L/min during flight without proceeding to HCT if SpO₂ is between 92 and 95% at rest and falls below 84% but has no signs of CO₂ retention. HCT will be needed to estimate the flow rate of oxygen if there are issues with CO₂ retention.^{9,16} 6MWT interpretation is described in Table 4.

Predictive Equations

For predicting which patients may require oxygen supplementation while flying, a number of predictive

models have been presented. These equations have the advantage of being simple and easy to employ during an office visit.¹⁰ Predictive equations might be a less expensive and time-consuming alternative to an HCT, especially in primary care, but they substantially underestimate the requirement of in-flight O₂ in the vast majority of patients.¹⁷

PaO₂ is calculated using the following equations (Alt)¹⁷

- (1) PaO₂ (Alt) (mmHg) = 0.410 x PaO₂ (ground) (mmHg) + 1.7652
- (2) PaO₂ (Alt) (mmHg) = 0.519 x PaO₂ (ground) (mmHg) + 11.855 FEV₁ (l) – 1.760
- (3) PaO₂ (Alt) (mmHg) = 0.453 x PaO₂ (ground) (mmHg) + 0.386 x (FEV₁%) + 2.44

$$(4) \text{ PaO}_2 (\text{Alt}) (\text{mmHg}) = 22.8 - (2.74 \times \text{altitude in thousands of feet}) + 0.68 \times \text{PaO}_2 (\text{ground}) (\text{mmHg})$$

Hypoxic Challenge Testing (HCT)

Hypoxic challenge testing/HCT (sometimes referred to as High Altitude Simulation Test or HAST) is conducted using a 15% oxygen-enriched inspired gas mixture, which produces an approximation comparable to inspired oxygen pressure (PO₂) as inhaling air at the highest cabin pressure allowed (2,438m or 8,000 ft). HCT is commonly conducted in a specialized respiratory physiology unit.^{9,10} Pre-flight evaluation of individuals with chronic airflow obstruction and restrictive respiratory disease using HCT is described in Figures 1 and 2.

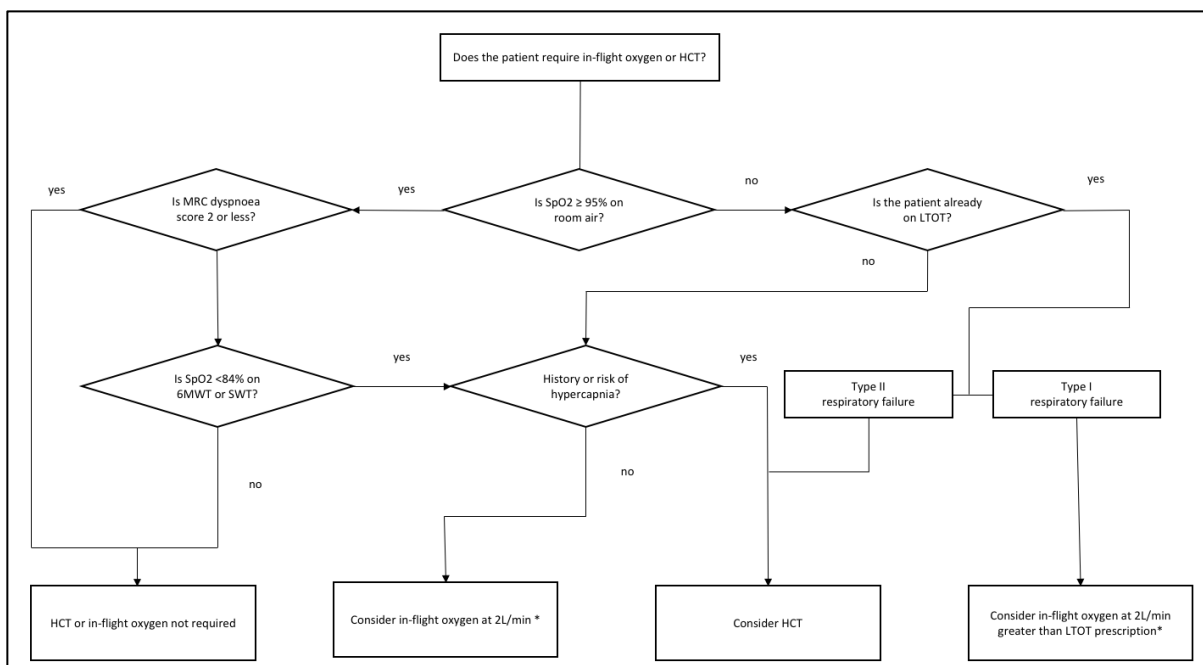


Figure 1. Pre-flight evaluation of individuals with chronic airflow obstruction. HCT, hypoxic challenge test; LTOT, long-term oxygen therapy; 6MWT, 6-minute walk test; SWT, shuttle walk test (incremental); *, flight oxygen is commonly pulsed delivery which may not be suitable for some patients. If in doubt, HCT should be considered.⁹

Hypobaric hypoxia results from an inverse correlation between the partial pressure of oxygen and altitude, which cause a drop in alveolar partial oxygen pressure (PaO₂) during ascent and lower arterial blood oxygenation. Euphoria, headache, tiredness, lassitude, and dizziness are all symptoms of hypobaric hypoxia, which, if left untreated, can cause unconsciousness and even death.¹⁸

Increased minute ventilation, heart rate, and cardiac output compensate in healthy individuals; therefore, most people experience no physiological

influence at typical cabin altitudes. People with a history of pulmonary disease, particularly hypoxemia at sea level, might be unable to adapt to the lower PO₂ at altitude by utilizing these processes, resulting in hypoxia of the alveolar and tissue.¹⁹ Lung mechanics may be harmed by changes in breathing patterns, which may be exacerbated by gas expansion, vital capacity reduction, and increased residual volume.⁹

HCT determines whether or not travelers with respiratory conditions require oxygen during flying and at what flow rate. It does not determine fitness for flight,

despite the name "fitness to fly" examination.⁹ In otherwise healthy people, HAST testing can also predict in-flight hypoxemia rather accurately.¹⁰ The results of the HCT do not predict respiratory problems when flying. Such symptoms appear to be caused by bad respiratory mechanics and a diminished respiratory reserve affecting the response to hypoxemia rather than hypoxemia itself. Those who have more severe dyspnea at sea level are more prone to develop symptoms. By using in-flight oxygen, individuals whose oxygen saturation falls during HCT and who have a history of respiratory symptoms while air travel can prevent this. Anxiety related to flying might also cause symptoms.⁹

HCT procedure is as follows: for 20 minutes, patients sit at rest and inhale a 15% oxygen gas mix through a Douglas bag with a non-rebreathe valve and mouthpiece or a nitrogen-driven gas combination through a 40% venturi mask. SaO₂ level is monitored during the test, which will be called off if it goes below 86%. Before and after the test, arterial blood gas tensions are measured.²⁰

BTS recommendations for the results of HCT are:⁹

- In-flight oxygen is not required if PaO₂ is ≥ 6.6 kPa (≥ 50 mm Hg) or SpO₂ is $\geq 85\%$
- In-flight oxygen is required if PaO₂ is < 6.6 kPa (< 50 mm Hg) or SpO₂ is $< 85\%$
- Oxygen titration is conducted to maintain PaO₂ ≥ 6.6 kPa or SpO₂ $\geq 85\%$ in adults and SpO₂ 90% in children aged more than one year, as needed
- If there is a history of hypercapnia, keep an eye on pH and pCO₂

- When PaO₂ is kept at ≥ 6.6 kPa and SpO₂ is $\geq 85\%$, consider recommending against air travel if pH drops to < 7.35 and PCO₂ rises by more than 1 kPa (7.5 mm Hg) from baseline

Flowchart of patient selection for HCT to evaluate individuals with chronic airflow obstruction (Figure 1) and restrictive respiratory disease (Figure 2).

Emergency Response during Flight

When a passenger has a respiratory problem on a flight, intervention choices are limited. The following actions should be followed in the first assessment and management of passengers who experience difficulty breathing or increased work of breathing:¹²

- Examine vital signs and give oxygen supplementation if necessary
- Check for breath sounds and evaluate for deviation of the trachea
- If necessary, request that the pilot descend to a lower altitude and consult a ground medical consultant if one is available

Patients with dyspnea need to be managed more specifically, which will be determined by their overall clinical picture.¹²

Post-Travel Evaluation

A medical examination is usually unnecessary upon returning home after a routine trip for short periods. Except for particular populations like refugees and foreign adoptees, the Centers for Disease Control and Prevention (CDC) has no established recommendations for screening international travelers who do not display any disease symptoms.³

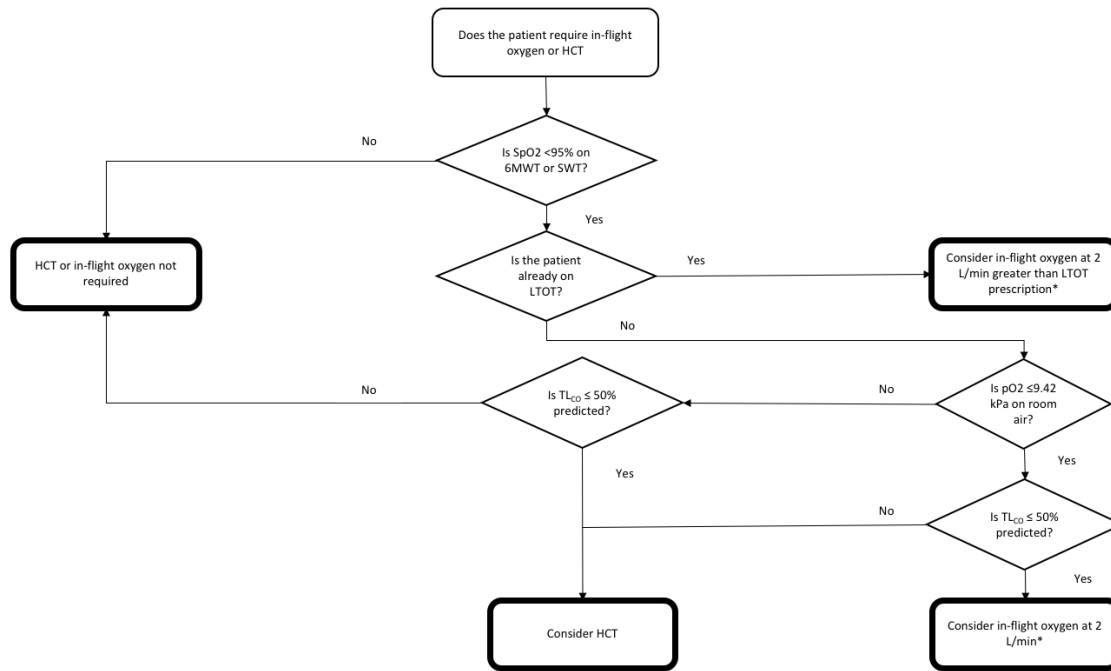


Figure 2. Pre-flight evaluation of individuals with restrictive respiratory disease. HCT, hypoxic challenge test; LTOT, long-term oxygen therapy; 6MWT, 6-minute walk test; SWT, shuttle walk test (incremental); *, data is limited in this group and pulsed delivery oxygen may not be suitable for some patients, therefore they should be assessed on case-by-case basis. If in doubt, HCT should be considered.⁹

Travelers should seek a medical evaluation when they return if:⁴

- Returning from a country where malaria is or might be found with a fever, to rule out malaria as the source of their ailment
- If they have a chronic disease like cardiovascular disease, diabetes mellitus, chronic respiratory disease, or have been on anticoagulants
- In the weeks after they return home, they may become ill, especially if they have a fever, chronic diarrhea, vomiting, jaundice, urinary abnormalities, skin disease, or genital infection
- They were treated for malaria while on the trip
- While traveling, they could have been exposed to a deadly infectious disease
- Have stayed in a developing country for more than three months

Returning tourists frequently experience respiratory problems, which are usually caused by common respiratory viruses. The most prevalent vaccine-preventable disease linked to overseas travel is influenza. The majority of post-travel diseases can be treated as outpatients, but certain patients, particularly those with systemic febrile disorders, may require hospitalization.³

SUMMARY

Everyone planning a trip must know the health risks that can occur and how to protect themselves, therefore they can minimize the risk of contracting the disease. Patient evaluation before travel includes fitness assessment or travel contraindications, evaluation of travel itinerary or risk assessment, relevant medical history, good mental health screening, and ability to deal with stress in a hostile environment. A pre-flight assessment is conducted if there is any hesitation about the patient's medical condition to fly and if comorbidities affect the patient's health.

Patients with a resting saturation of <92% on room air should take supplementary oxygen in flight due to a significant risk of hypoxemia at high altitudes. Saturation between 92 and 95% should be investigated further, especially if there are established risk factors for hypoxemia during a flight. There are several procedures used to assess a person's eligibility to fly, namely (1) walk tests, (2) hypoxemia prediction from equations, and (3) HCT.

When a respiratory emergency happens during a flight, intervention options are limited. A medical

examination is usually not necessary when returning home after routine travel for short periods. Except for particular populations like refugees and foreign adoptees, the CDC has no established recommendations for screening international travelers who do not display any disease symptoms.

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Conflict of Interest

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Author's Contributions

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