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## Clinical Practice Guidelines for Primary Care Providers' Evaluation of Patient Fitness to Fly

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CLINICAL PRACTICE GUIDELINES FOR PRIMARY CARE PROVIDERS'  
EVALUATION OF PATIENT FITNESS TO FLY

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## THE GRADUATE COLLEGE

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## ABSTRACT

Commercial air travel is amongst the safest forms of transportation yet the environment within the aircraft cabin to which the passenger is exposed may have adverse physiological and psychological effects on passengers, especially for those with pre-existing medical issues. A comprehensive, systematic review and analysis of current literature was performed to develop evidenced-based guidelines for evaluation of passenger fitness to fly for integration into primary care practice. Recommendations from the most current fitness to fly guidelines and disease-specific published research related to in-flight medical issues were evaluated and the Grades of Recommendation Assessment, Development and Evaluation (GRADE) method was utilized to assess the quality of available evidence and the strength of guideline recommendations.

The clinical practice guideline provides an overview of the major health systems affected by air travel and conditions that warrant healthcare provider review for clearance to fly. The need exists for randomized trials and large group research to further identify and evaluate health conditions that are impacted or affected by commercial air travel. True incidence of health related issues and further guidance for research would benefit from the establishment of a universal health related incidence reporting method or repository to collect data of in-flight health events. The guidelines developed as a result of this capstone report will change practice and contribute to the development of evidence-based guidance to primary care providers and clinicians who are required to provide fitness to fly clearance exams for commercial airline passengers.

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## CHAPTER 1

### Introduction

Commercial passenger air travel has increased exponentially over recent years as a result of economic growth, increased affordability of air travel as a mode of transportation and appreciably larger long-range aircraft. Every day over 1.7 million passengers travel by air within the U.S. and annually approximately 2 billion people travel in commercial aircraft (Kim & Lee, 2007; Silverman & Gendreau, 2009). Current research of population and travel demographics estimate that the number of passengers traveling by commercial aircraft will double in the next 20 years (Patel & Simon, 2010). Increased globalization and improved medical care combined with an rapidly expanding number of aging and overweight population pose risks to air travelers who may not have previously considered air as a mode of travel (Budd et al., 2011; Valani, Cornacchia, & Kube, 2010).

By 2030, current estimates predict that at least half of all airline passengers will be over the age of 50 years (Sand, Bechara, Sand, & Mann, 2009). The mean age of passengers who suffer from in-flight medical events is 44 years for men and 49 years for women. Passengers older than 70 years have the highest rate of in-flight health related events (Silverman & Gendreau, 2009). The increasing number of elderly and more infirmed airline passengers in conjunction with the improved commercial airline ability to accommodate disabilities escalates the potential risk for more in-flight medical events (Valani et al., 2010).

Although air travel is amongst the safest forms of transportation, the environment within the aircraft cabin to which the passenger is exposed may have adverse physiological and psychological effects on passengers, especially for those passengers with pre-existing medical issues. Air travel, especially over long distances, exposes passengers to multiplicity risk factors that can result in adverse effects on at-risk passenger's general health and welfare (Budd, Warren, & Bell, 2011). Passengers with pre-existing health conditions are at greater risk and should consult their primary care provider, specialist, or a travel medicine clinic before embarking on commercial airplanes (Silverman & Gendreau, 2009; Patel & Simon, 2010).

Commercial aircraft passenger's failure to disclose pertinent health information as well as failure of primary care providers to understand the risk of air travel and provide preventive health education to their patients can result increased incidence of preventable in-flight medical emergencies. A study by Burnett (2006) found that greater than 95% of persons with preexisting health conditions who travel by air stated that they would like to receive more medical advice from their healthcare provider. Routine medical histories and screening procedures rarely, if ever, involve questions related to travel or mode of travel (Price et al., 2011). Primary care providers concerned for passengers with pre-existing health problems need to be educated on the effect of air travel on these pre-existing health conditions to incorporate pre-travel precautions in their preventive health education in order to minimize risks to their patients (Silverman & Gendreau, 2009).

The ubiquity of commercial air travel as a dominant mode of transportation and ignorance of the potential health threats imposed upon passengers by the aircraft cabin environment can lead to emergency health issues and disrupted flight plans. Aviation



medicine has long been the domain of the military and aircraft industry. The majority of aviation research on the effects of flight physiology and fitness to fly focused on the pilot and crewmembers who are routinely subject to health screening for employment and by virtue of the health-related occupational requirements are in better health than the average traveling passenger. Travel by air may not only exacerbate pre-existing medical conditions but may result in new onset of medical conditions that occur as a result of altitude and the cabin environment. Medical emergencies can occur in-flight if traveling passengers do not disclose pertinent health information or their healthcare providers do not understand the potential health threats imposed on a passenger by the commercial passenger cabin environment and air travel (Valani et al., 2010; Archard & Nicholson, 2007). Aviation medicine is not typically addressed in primary care provider education and there is a general lack of awareness of the health effects of flying amongst primary care providers (Wise, 2008).

Ultimately the commercial air carrier is responsible for making the determination whether or not a passenger is capable to fly on their airline (Patel & Simon, 2010). Most airlines do not have medical personnel on staff to perform this function and there is no lone universally established clearance process or screening methodology utilized by the airlines for their passengers. The air carrier possesses the right to request that a passenger obtain a fitness to fly certificate or other documentation related to the passenger's health condition and their needs associated with air travel if the airline has reason to believe that a passenger's health may be at risk during flight or may impact the flight plans. In instances where pre-authorization fitness to fly is requested, the airline will rely on the documentation provided by the passenger's health care provider to make their decision

related to risks associated with travel by air (Patel & Simon, 2010). Regardless of whether or not a travelling passenger requests documentation from their primary care provider for fitness to fly, it is a responsibility of the primary care provider to include travel related preventive health counseling to patients, especially for those patients with pre-existing health conditions that can be adversely affected by air travel.

At present there are neither universal reporting methods nor a central registry for health related air travel incidents (Rushkin, 2009). Each airline tracks its own diversions and medical events and has its own method of classifying the cause of the event. As a result, accurate epidemiologic data related to the incidence and severity of air travel related medical emergencies does not exist (Sand et al., 2009). Flight diversions due to medical emergencies cause significant financial and legal costs to airlines and can place a passenger at risk for suboptimal care due to the lack of appropriate emergency medications, equipment and skilled personnel onboard at the time of the incident as well as at the end destination (Valani et al., 2010).

It has estimated that the frequency of in-flight medical incidents ranges from 1 per 10,000 to 1 per 40,000 passengers with approximately 1 in 150,000 of these incidents resulting in the use of in-flight medical equipment or medications (Gallagher, Marienau, Illig, & Kozarsky, 2012). Flight crew receive minimal training related to the use of medical equipment and medication and rely on available healthcare personnel flying as passengers or, when available, on air-to-ground medical advice services. Vasovagal syncope, gastrointestinal events, respiratory events, cardiac events and neurologic events are the most commonly encountered in-flight medical events (Gallagher et al., 2012). Although fourth most common in incidence, cardiac events account for approximately

two-thirds of the estimated 0.3 per 1 million passenger deaths aboard commercial flights (Gallagher et al., 2012).

There is no standard regulation and considerable variability exists amongst the contents of the onboard emergency medical kit (Rushkin, 2009). Airline policies regarding the contents of medical equipment, crew training and treatment of passengers are at the discretion of each airline's host country and vary by airline (ASMA, 2003). Typically cabin crew are trained in first aid, resuscitation procedures and how to recognize medical conditions that may cause an emergency as well as how to appropriately act upon and manage such emergencies in flight (World Health Organization (WHO, 2005). Regulations related to the presence of a medical kit onboard of a commercial aircraft outside of the U.S. vary and may be limited, especially on economy airlines (Rushkin, 2009).

Appendix A provides the most recent recommendations for the contents of the emergency medical kit by the Aerospace Medical Association (IATA, 2011). Most commercial airlines operating today also carry automated external defibrillator and many use on-ground telemedical assistance to provide medical advice and support for passengers suffering from in-flight medical issues (Silverman & Gendreau, 2009). In the United States, the Federal Aviation Administration (FAA) requires U.S. airlines carrying 30 or more passengers to have medical kits onboard but does not regulate the contents of the kits carried.

Flight diversions and incidences of in-flight medical events could be reduced through pre-travel medical evaluation and screening. The Aerospace Medical Association found that 62% of in-flight medical emergencies were associated with pre-

existing passenger medical conditions (Valani et al., 2010). Unfortunately, while the number of passengers seeking medical clearance is increasing, so is the rate of diversions per million revenue-passenger miles flown. Valani et al. (2010), posit that this may indicate that more passengers are flying with more severe medical conditions and support further research correlating pre-screening with passenger-related diversion.

Primary care health providers are confronted today with a limited amount of time to assess and manage patients and regulations related to reimbursement associated with the practice of evidenced based medicine. Many of the chronic health conditions which place commercial airline passengers at risk are managed by primary care providers who can be called upon by an airline to make a determination of whether or not a passenger is safe to travel. Health risks associated with air travel can be minimized if the passenger receives pre-travel preventive health education as well as advice for planning for travel-related disruption or emergencies that may adversely affect the passenger's health (Silverman & Gendreau, 2009). An evidenced-based resource for primary care providers to utilize in assessing the physiologic and environmental stressors associated with commercial air travel and making the determination for a passenger's fitness to fly is needed and could be used by primary care providers to guide both screening and healthcare decision-making.

### **Fitness to Fly**

Fitness to fly is the clearance by medical personnel which authorizes a passenger to travel and identifies any specific air travel-related needs in order to minimize the passenger's health risks. The IATA (2011) recommends that airlines request medical certificates for clearance to fly from a passenger's personal healthcare provider. Health

care professionals who are not familiar with the environmental and physiologic challenges of air travel may unknowingly place themselves and their patients at risk by completing requested fitness to fly medical clearances.

The IATA (2011) identifies the following instances when medical clearance is required prior to air travel if the passenger:

- a. suffers from any active contagious or communicable disease (Appendix B)
- b. may be at risk or cause discomfort to other passengers because of a physical or behavioral condition:
- c. may pose a potential safety hazard or affect the punctuality of a flight including the possibility of flight diversion or an unscheduled landing;
- d. requires special assistance and is incapable of caring for themselves:
- e. has an underlying medical condition that may be adversely affected by air travel or the aircraft environment.

Passengers who do not meet any of the medical clearance criteria noted above do not routinely require medical clearance but those with pre-existing medical conditions may still be at risk and routine screening and preventive guidance should be included in primary care practice. The recommendations provided by the IATA are developed by a working group of twelve aviation medical experts and the publication notes that there is “very limited amount of research data on this material and most of the guidelines are based on practical experience (IATA, 2011, p. 52).” Airline personnel have the right to request a medical clearance for passengers who pose a concern to passenger or aircraft safety because of observed behaviors or symptoms of illness that occur prior to, during, or after air travel. Each airline has the right to design its own procedure related to

documentation and wording requirements for medical clearance to fly and airlines may deny boarding to passengers who appear to have communicable diseases or health problems (IATA, 2011; WHO, n.d.).

The British Medical Association (2004) suggested the following considerations that should be taken into account when assessing a patient's fitness to fly:

- The effect of mild hypoxia and decreased cabin air pressure.
- The effect of decreased range of motion and/or immobility
- The ability in the event of an emergency landing to perform the bracing position.
- The timing of prescribed medications for long distance travel.
- The psychological and physiological effects and the patient's ability to cope with travel to and through the airport including embarkation and disembarkation.
- The potential for a patient's medical condition to adversely affect aircraft operation and/or the comfort or safety of other passengers.
- Travel health insurance, or financial resources, of the patient to deal with potential healthcare costs in case of problems that develop from travel.

Effective travel health consultation relies not only on an understanding of the physiologic and psychological effects of flight on health conditions but also on appropriate risk assessment and risk management (Simons & Wong, 2011). Risk assessment should include traveler specific risks as well as travel itinerary, medical facilities and resources at the planned destination and planned travel-related activities that may pose specific risks. Identification of potential travel-related hazards and the relative

risk that they pose on an individual's health and able the healthcare provider and traveler to plan appropriately for preventive measures as well as to develop a plan for travel related emergencies and post travel evaluation.

The patient's primary care provider is often called upon to provide a passenger clearance to fly and in order to do so needs to have a thorough understanding of the physiologic effects of air travel on a patient's health and well-being. The most appropriate time to address fitness to fly for passengers is well in advance of travel. As part of a preventive education plan, the healthcare provider can review with the patient concerns related to the effects of travel on their medical condition, timing of medication, immunizations and hygiene measures to reduce exposure to infectious disease and contagions and the need for any additional special assistance or devices in order to promote safe travel. Cardiovascular disease, deep venous thrombosis, respiratory disease, surgical conditions, neurologic disorders, mental illness, pregnancy and chronic medical issues such as diabetes should trigger a discussion of pre-travel preventive medical education between a healthcare provider and their patient. Healthcare providers who have questions or concerns related to their patient's fitness to fly should contact the passenger's airline medical department or consider referral of the patient to a travel medicine specialist for fitness to fly medical certification.

### **Purpose of the Study**

This capstone project set out to develop clinical practice guidelines (CPG) for primary care providers to utilize in establishing commercial passenger fitness to fly. The specific aims of the capstone project were

- 1) to identify the physiologic and environmental hazards associated with air travel that place a commercial airline passenger at risk,
- 2) to review current guidelines on common health issues associated with commercial air travel,
- 3) to analyze and synthesize current research findings in the identified health areas
- 4) to compile all data from the specific aims in an evidenced-based clinical practice guideline for dissemination via publication and use by primary care providers in determining passenger fitness to fly.

### **Policy Implications**

The development of a CPG will change practice and provide evidence-based guidance to primary care providers and clinicians who are required to provide fitness to fly clearance exams for commercial airline passengers. Publication by a peer-reviewed professional nurse practitioner journal will provide an avenue for dissemination of the CPG amongst the primary care provider community and support future CPG development by nurse practitioners.



## CHAPTER 2

### Review of Literature

The aircraft cabin environment places several different environmental and physiologic challenges upon passengers that do not routinely occur in other modes of public transportation. During normal operation scientific evidence has not shown that the standard aircraft cabin environment poses any risks to healthy passengers (IATA, 2011). However, the unique aspects of the aircraft cabin environment may pose problems for passengers who may be traveling in less than optimum health or for those who may have underlying health conditions that can be affected by the physiologic challenges associated with commercial flight. More passengers are traveling, including more elderly persons and patients with pre-existing medical issues that are at-risk for the adverse effects that the aircraft travel conditions may present. An understanding of the aircraft cabin environment under normal operating circumstances is essential for healthcare providers who are making decisions related to a potential passenger's fitness to fly.

### Hypobaric Hypoxia

Modern commercial aircraft are pressurized to maintain a fairly constant air pressure. The primary difference between travel by air and by ground transportation is the difference in pressurization which is not equivalent to ground level barometric pressure (IATA, 2011). Boyle's law states that with altitude, the volume of a gas expands and so has a lower pressure. As the aircraft ascends, cabin pressure decreases and resulting in gas volume expansions up to 30% (Patel & Simon, 2010). While most commercial aircraft cruise at an altitude between 35,000 and 40,000 feet, cabin air pressure varies between the external environmental pressure at the altitude of the airport when the plane

is not in flight up to what is the airline industry accepted maximum air pressure equal to 8,000 feet altitude.

Aircraft are pressurized by bleeding air from the engines. The pressurization system draws air from different stages of the engines (which act as compressors) before it enters the combustion chamber and redirects it to the internal aircraft environment (IATA, 2011). The assistance of an outflow valve allows the pressure to be raised and maintained to a predetermined desirable level. The maximum desired pressurization level of 8000 feet was selected based upon studies demonstrating that at that level the average healthy aircraft passenger hemoglobin oxygen saturation normally remains above ninety percent. The 8,000 foot level is not an international aviation requirement but rather an industry-related practice that is meant to provide a concession between an acceptable level of mild hypoxia, a comfortable environment for traveling passengers, acceptable pressurization upon the aircraft, minimal structural weight penalty and economical fuel usage (Aerospace Medical Association, 2008). The recommendation was put in place decades ago before the changing demographics of traveling passengers and questions exist as to whether or not the recommended maximum equivalent pressure is still valid in today's environment where passengers may be older and suffering from acute or chronic health conditions (IATA, 2011).

In the United States, Federal Aviation Regulations require that an aircraft be capable of maintaining no greater than 8,000-ft cabin altitude at the maximum operating altitude but there is variability in aircraft cabin pressure with altitude and one in-flight study demonstrated cabin altitudes as high as 8915 feet (Aerospace Medical Association, 2008). Cabin air pressure is not maintained at a constant level during long-haul

commercial flight and decreases as aircraft cruise at higher altitudes in the latter part of longer flight sectors (Kelly, Seccombe, Rogers, & Peters, 2007). Fitness to fly evaluations related to concerns for hypobaric hypoxia and related complications can be confounded by studies that have demonstrated cabin pressure simulation tests expose subjects to more hypoxic conditions than will be experienced during flight on a Boeing 747 (Kelly et al., 2007). Despite the possibility that cabin simulation studies may pose the potential for more hypoxia than a passenger may encounter in a true flight environment, it would be prudent to evaluate a potential passenger at risk during hypoxia at a lower standard to account for the variability in cabin environment, potential inability of an airline to support supplemental in-flight oxygen and the passenger's inability to control for altitude during flight. Passengers at risk for hypoxia at other high altitude environments will likely suffer from hypoxia in a cabin environment that is pressurized to 8,000 feet.

Aircraft flying at higher altitudes are more fuel-efficient and avoid turbulence for passengers comfort and for that reason it is estimated that many aircraft do exceed the 8,000 feet pressurization limit at some time during a flight pattern. Prediction of cabin altitude for any flight is difficult because the actual cabin altitude experienced is dependent upon variables such as aircraft model, weather patterns, and air traffic control (Kelly et al., 2009). At cruising altitude there is a significant reduction of barometric pressure compared to the barometric metric pressure found at sea level which results in a concomitant decrease in the partial pressure of alveolar oxygen ( $\text{PaO}_2$ ) resulting in passenger hypoxemia (Patel & Simon, 2010; Aerospace Medical Association, 2008).  $\text{PaO}_2$  levels typically decrease from 103 mmHg at sea level to around 70 mm Hg while in

flight. The end result is a drop in oxygen saturation levels by 3% when travelling at 3,000 feet and at the highest cabin altitude of 8000 feet equates to an oxygen saturation of 85 to 9% (Patel & Simon, 2010; Johnston, 2009).

Dozing passengers have been found to have oxygen saturation levels around 80% (Hinninghofen & Enck, 2006). The normal maximum cabin pressure is 750 hPa which is approximately equal to the pressure when breathing 15% oxygen at a typical sea level pressure of 1016 hPa (Kelly, Seccombe, Rogers, & Peters, 2007). Most healthy passengers experience an average pulse oximetry of 92% in-flight and can compensate for the decreased oxygen saturation (Kelly et al., 2007). The resultant decrease in oxygen saturation can exacerbate pre-existing conditions for some passengers bringing them to the steep part of the oxyhemoglobin dissociation curve resulting in very low oxygen saturation and may pose a health risk to coronary, pulmonary, cerebrovascular, ocular or hemodynamically challenged passengers as well as others suffering from acute medical issues (IATA, 2011; Bayer, Mutlu, Akay, & Bayraktar, 2008; ASMA, 2003).

In the United States there is no requirement for all passengers to be provided with supplemental oxygen until the internal cabin pressure altitude exceeds 15,000 feet (Aerospace Medical Association, 2008). Passengers over the age of 40 experience a steady decrease in oxygen saturation that is estimated at a decrease of 5 mmHg per 10 years. Elderly passengers as a result of decline in respiratory condition associated with aging, have even lower daily oxygen saturation levels. When elderly passengers combine lower daily oxygen saturation levels with a decrease due to increased altitudes and cabin air pressure they may experience hypobaric hypoxia. Hypoxia can have multiple effects on the circulatory system including: local vasodilatation of coronary and cerebral

vascular beds, increased heart rate, increased systemic blood pressure, increased myocardial contractility, increase in cardiac output and an increase in pulmonary artery pressure (Smith et al., 2010). The issue of hypobaric hypoxia can be further compounded in passengers who consume alcohol due to the resultant increased hypoxic effect of alcohol on the brain (Girasek & Olsen, 2009).

Hyperbaric Chamber (HC) exposure to flight simulated hypoxia and hypoxia-altitude simulation test (HAST) are amongst the standard tests utilized to replicate the hypoxia of air travel at 8,000 feet, these tests may not be readily available and may be cost-prohibitive for pre-flight evaluation of commercial air passengers (Figure 6). A recent randomized cross-over study of oxygen titration during a HAST and in a HC was performed in which the data suggested that titration of supplemental oxygen via a nasal cannula during a HAST may provide falsely high  $\text{PaO}_2$  values as a result of oxygen accumulation in the facemask and therefore the HAST results may not be utilized with confidence due to individual variability (Akerö et al., 2011). Additional concerns resulting from the Akerö et al. study (2011) include the results of their evaluation of various type of oxygen equipment in the HC and their findings that the use of a portable oxygen concentrator (POC) resulted in lower  $\text{PaO}_2$  values. The POC at a pulse setting of two gave a  $\text{PaO}_2 \geq 5.7\text{kPa}$  (50mm Hg) and was needed to reach an  $\text{SpO}_2 \geq 90\%$  in most of the patients evaluated. Physical activity, including walking, in flight resulted in a drop of  $\text{SpO}_2$  requiring even higher doses of supplemental oxygen. Akerö et al. (2011) recommend that based upon the findings of their study patients traveling with POC should increase their oxygen flow compared with supplemental oxygen given with compressed gaseous oxygen systems.

Pulse oximetry can be utilized pre-flight and in-flight to monitor and titrate oxygen levels. A small study (n=14) of oxygenation response to air travel in subjects without obstructive lung disease and not receiving supplemental oxygenation demonstrated that air travel resulted in desaturation including further declines associated with walking during the flight (Kelly et al., 2009). Although in the Kelly et al. (2009) study there was significant desaturation in subjects, reported symptoms of respiratory distress were minimal leading to even further concerns of a flying patient with a compromised pre-travel oxygen status to be able to effectively evaluate their symptoms during flight. The Kelly et al. (2009) study found that baseline SpO<sub>2</sub> was a better predictor of in-flight desaturation than HCT. Ultimately it is imperative that clinicians understand the individual characteristics of the patient's oxygen control, need for supplemental oxygen in daily life, and the pre-flight health condition of the patient, flight duration, and altitude in order to make a determination of whether or not supplemental oxygen may be needed.

Passengers with chronic obstructive pulmonary disease (COPD) have a limited capability of increasing minute ventilation in response to hypoxia and the presence of an alteration in the perfusion/ventilation ratio can make it hard to compensate during air travel (Tzani, Pisi, Aiello, Olivieri, & Chetta, 2010). Passengers with hemoglobin levels less than 7.5 g/dl or in sickle cell crisis have an increased need for supplemental oxygen and may experience problems associated with decreased PaO<sub>2</sub> levels (Aerospace Medical Association, Aviation Safety Committee, Civil Aviation Subcommittee, 2008).

The decrease in cabin air pressure as the aircraft climbs in altitude causes gas to

expand increasing in volume by nearly 30% which can create problems when gasses become trapped in the body (WHO, 2011; Aerospace Medical Association, Aviation Safety Committee, Civil Aviation Subcommittee, 2008). At 8,000 feet above sea level, the volume of a gas increases by a factor of 1.4. The main areas affected by gas expansion in passengers are the middle ear, the sinuses, the stomach, pleural cavities, the skull and the bowels (IATA, 2011; Hinninghofen & Enck, 2006). Aircraft descent causes a reduction in the trapped air which creates a vacuum in closed spaces such as the ear and sinuses. Trapped gas leads to passenger discomfort and the potential for medical complications in passengers with pneumothorax, recent thoracic, abdominal or ocular surgery. Gas expansion when trapped in the ears can cause minor to severe discomfort and possible perforation especially in infants and young children (Bagshaw, 2007). Divers and other passengers who have been exposed to hypobaric conditions prior to flight should wait at least 12 hours from their last dive or hypobaric incident, or 24 hours from multiple dives before flying to prevent decompression illness (WHO, 2011).

Medical devices such as pneumatic splints, feeding tubes, urinary catheters and cuffed endotracheal or tracheostomy tubes are affected by gas expansion and the instillation of water rather than air can eliminate air-travel related adverse events (Silverman & Gendreau, 2009). Gas expansion also may cause a multitude of problems for post-operative patients especially if gas has been introduced as a result of recent surgery such as abdominal or ophthalmologic procedures. Passengers who are in the post-operative phase after a major or minor surgical procedure have a need for increased oxygen due to surgical trauma, rising adrenergic outflow, and possible sepsis (Aerospace Medical Association, Aviation Safety Committee, Civil Aviation Subcommittee, 2008).

It is not contraindicated for pregnant women less than 36 weeks gestation, to fly on commercial airlines however, the expansion of gas in the abdomen may cause some discomfort (Bagshaw, 2007). Women over 28 weeks gestation may need additional documentation from their OB/GYN prior to travel (Archard & Nicholson, 2007).

### **Aircraft Ventilation**

Ventilation of the pressurized cabin is required to provide for passenger comfort as well as to reduce air contaminants. Aircraft cabins are supported by two types of ventilation systems, one which provides 100% fresh air continuously. Air that is brought in from the engines is passed through air conditioning units to cool the air before it enters the aircraft cabin. The cooled air is passed through the outflow valve and is replaced by fresh air coming from the outside as well as the air conditioning system (IATA, 2011). A second ventilation system provides a combination of fresh air and recirculated cabin air. Recirculated cabin air is passed through a High Efficiency Particulate (HEPA) filter which traps particulates but have no effect on gases. HEPA filters vary in their level of efficiency and there are no federal or international regulations that require a minimum level of efficiency in aircraft cabins (IATA, 2011). The ration of fresh air to recirculated air in commercial planes is typically 50:50 with the entire cabin air being exchanged approximately every 3-4 minutes (IATA, 2011). While passenger concerns may exist related to the recirculation of air on planes, the aircraft ventilation systems are similar to those found in commercial buildings.

One primary difference that exists between commercial building and aircraft space is the density of population per area. Recently the transmission of disease by biologic contaminants has gained media attention due to concerns related to cases



involving tuberculosis and influenza transmission. The HEPA filters when installed as part of the ventilation system are a means of trapping dust, bacteria, fungi and viruses which may circulate within the cabin environment (Figure 9). No research to date has supported a significant risk of disease transmission when the aircraft ventilation systems are functioning adequately (IATA, 2011). While the proximity of passengers to a potentially contagious person can increase transmission, the ventilation system within an aircraft has not been shown to be a factor in disease transmission. The risk of transmission of disease is greatest when the aircraft is on the ground and an auxiliary power unit provides ventilation. Auxiliary ventilation is utilized before the main engines are started, but may not always be operated due to environmental noise or technical reasons (WHO, n.d.). Transmission of infection may occur between passengers who are seated in the same area through direct contact with other passengers, aircraft cabin parts, furnishings or through respiratory droplet spread during coughing or sneezing. The risk associated with disease transmission in these circumstances is not different than the risk posed in any other public situation where individuals are in close contact. (WHO, n.d.).

Most commercial aircraft have a laminar air flow system which moves the air from top to bottom and not from front to back or back to front. In cases of suspect disease transmission the laminar airflow system limits risk of transmission to only those passengers within the immediate vicinity of a contagious passenger and not to all passengers travelling on the plane (WHO, n.d.).

### **Relative Humidity**

Studies have shown that air travel does not result in a change in osmolality therefore cannot be linked to travel dehydration (Johnston, 2009). However, inside an

aircraft cabin the humidity levels are fairly low, around 10-20%, compared to the 40 to 50% found in a standard commercial building. Flight distance exacerbates the problem of low relative humidity and at the end of a long distance flight the humidity can be as low as 2-3% (Hinninghofen & Enck, 2006). Low cabin humidity results from air being drawn into the cabin from the outside air in which moisture is absent at high altitudes (Patel & Simon, 2010). Aircraft traveling at an altitude of 35,000 feet draw in air that is atmospherically less dense, colder and drier than air conditions found at ground level (Budd, Bell, & Warren, 2011). Superficial dehydration results from the decreased levels of humidity can cause dry, itchy or irritated eyes, nasal congestion and dried mucous membranes of the nose, throat and skin (IATA, 2011; Patel & Simon, 2010; Johnston, 2008). Flight related dehydration can be compounded by the diuretic effects of medications, alcohol and caffeine (Hinninghofen & Enck, 2006). The effect of the low relative humidity and superficial dehydration, while temporarily uncomfortable to the passenger, does not pose any long term effects to passenger health or well-being (IATA, 2011).

### **Passenger Space and Comfort**

Long-haul aircraft today are capable of flying non-stop for 20 hours which makes passenger seat spacing and comfort important for both passenger health and well-being. Seat comfort includes seat pitch, seat width, leg room, upholstery quality and angle of recline (Silverman & Gendreau, 2009; Hinninghofen & Enck, 2006). The minimum dimensions between aircraft cabin seats are regulated by the aircraft standards of the country of aircraft origin (Figure 10).

The airline seat pitch is an indication of the available legroom and refers to the space between a point on one seat and the same point on the seat in front of it. Seat pitch is usually expressed in inches and ranges from 28 inches in low-cost carrier economy class to up to 100 inches in some long-haul carrier first class sections (Hinninghofen & Enck, 2006). More seat pitch can mean more legroom, but it is also affected by the thickness of the seat back. Airlines have claimed that a reduction of seat pitch can be compensated for by a thinner seat-back design. Close seat pitch is associated restricted degree of seat tilt and the reduction in size correlates with poor passenger comfort (Brundrett, 2001).

Seat width is measured by the distance from armrest to armrest and ranges averages between 16-18 inches in economy class to 21-36 inches in first class. Narrow seat widths can impede normal circulation and combined with prolonged sitting can increase the risk of deep vein thrombosis and edema (Brundrett, 2001). Cramped passenger seating affects not only passenger comfort but can also make it difficult for passengers to leave the seat for exercise and has been associated with disturbed respiration, restricted gastrointestinal mobility and blood circulation and may result in edema and ischemia of the lower extremities (Hinninghofen & Enck, 2006).

Long-range air travel greater than 4 hours combined with decreased liquid consumption, increased inactivity and low humidity levels can place travelers at risk for traveler's thrombosis. Venous blood flow to the lower extremities is decreased by 2/3 when people are in the sitting position. Each hour people remain in the sitting position there is further reduced venous blood flow and increased hematocrit levels combined

with rises in plasma protein creating venous pooling “inducing hemoconcentration and depressed fibrinolytic activity contributing to hypercoagulability” put many passengers at risk for deep vein thrombosis (DVT) (Sandor, 2008; Brenner, 2006).

### **Disrupted Circadian Rhythm**

The body’s natural cycle extends over a 24 hour period and is referred to as the circadian rhythm. Jet lag is a result of the interruption or desynchronization of the circadian rhythm. Jet lag is well tolerated by healthy individuals however with the loss or addition of time in the rhythm cycle there may be a need for an adjustment in some passenger medication dosages (Johnston, 2009; Aerospace Medical Association, Aviation Safety Committee, Civil Aviation Subcommittee, 2008). East-west and west-east flights involving rapid transit through several time zones can upset the balance between extrinsic time and physiological time and result in indigestion, bowel disturbance, fatigue, malaise, daytime sedation, insomnia and reduced physical and mental performance and disorientation (WHO, 2011; Budd, Bell, & Warren, 2011). Passengers travelling east bound lose time in their day and for those traveling west bound add time to their day. Typically westbound flights are more easily tolerated than eastbound flights. Other factors that may affect jetlagged include the number of time zones crossed, sleep deprivation, and environmental stimulation associated with the activities of the internal cabin (Patel & Simon, 2010).

Insulin dependent diabetics may need to adjust regular or long-acting insulin dosages to account for the time change (Johnston, 2008; Bagshaw et al., 2002). Jet lag combined with a time change can promote problems for passengers with cardiovascular disease as well. Passengers often are confused as to when they should take their

medications at the new or previous time zone and alterations in daily routine often result in forgetting medications all together. People travelling with stable heart failure, angina or arrhythmia it is very important that they maintain the regularity of their medication (Smith et al., 2010).

## **Stress**

All passengers are subject to travel related stress regardless of the duration of their flight (ASMA, 2003). In addition to the physiologic stress associated with pre-existing health conditions, additional stressors that may occur as a result of traveling include walking long distances, carrying heavy baggage, and prolonged sitting in confined spaces. Psychological stressors can impact a passengers health during travel and can manifest as new onset or exacerbations of existing psychiatric illnesses particularly in vulnerable individuals (Al-Zurba, Saab, & Musharrafieh, 2007; Hinninghofen & Enck, 2006). For the average traveler potential psychological stressors include concern and anxiety related to preparation to travel, transportation to and from airport's, frustration associated with check-in and security procedures, and worry related to flight delay as well as fear of flying (Patel & Simon, 2010). Business travelers have been shown to have high to very high levels of travel stress and cited social and emotional concerns such as isolation and the impact of travel on family as the greatest contributor to their stress level followed by health concerns (Burkholder, Joines, Cunningham-Hill, & Xu, 2010). Cabin noise, vibration, turbulence, varying temperatures, and uncomfortable seating room can pose additional stressors in-flight (ASMA, 2003). Alcohol, often consumed by anxious passengers pretravel and in-flight, can exacerbate psychological symptoms as well as pre-existing disorders.

## **Evidence Based Practice**

In healthcare there are variations in practice making it both an art and a science. The Institute of Medicine (IOM) (2008) issued a report emphasizing the need for evidenced based practice (EBP) as a means of promoting quality care and improving practice outcomes. Evidence-based practice requires clinicians to incorporate current scientific research with their clinical experience while balancing the individual characteristics and diverse needs of each patient (Turner, Misso, Harris, & Green, 2008). Inconsistent, absent, or inaccurate use of medical research can be a source of practice variation and ultimately lead to increased healthcare costs without improvement in outcomes (Shiffman et al., 2009). Health care delivery and decision-making should be rooted in the use of evidenced-based current best practice with the ultimate goal of a standardized guideline development and implementation process which will result in improved clinical practice and outcomes (IOM, 2008; Harrison, Legare, Graham, & Fervers, 2010; Turner et al., 2008).

## **Clinical Practice Guidelines**

Clinical practice guidelines are statements that contain recommendations designed to support clinical decision-making by healthcare professionals and patients in specific situations (IOM, 2008; Shiffman et al., 2009). CPGs should be reflective of current scientific research and involve a systematic review and appraisal of the literature and available evidence (Poolman, Verheyen, Kerkhoffs, Bhandari, & Shunemann, 2009; Turner et al., 2008). The goal of CPG development is to summarize the most current evidenced-based best practice (Shiffman et al., 2009).

CPGs are being developed by teams of experts at local, regional and national levels and may be subject to bias and development deficiencies depending upon the source of the guideline development, political or economic incentives for implementation and the priorities of the health care system in which they are being implemented (Bondmass, 2008; Clutter, 2009; Turner et al., 2008). Shiffman et. al. (2009) identify problems in guideline quality, language, knowledge synthesis implementation, uptake and formulization that can impede the applicability of guidelines. The IOM Report Brief (2008) notes that many current guidelines have been developed without the necessary scientific rigor and their reliability may be in question due to their lack of method transparency and failure to comprehensively and systematically assess all available clinical evidence.

### **The Guideline Development Process**

The CPG development process includes a formal definition of a problem for study, review of the evidence, development of a consensus, formulation of the guideline, dissemination of the information with the goal of translation and implantation of the recommendations into clinical practice (Papadopoulos, 2003). A comprehensive systematic review of the literature will provide information related to the problem being examined as well as current knowledge related to the effectiveness of healthcare interventions (IOM, 2008). The development of a CPG involves not only the systematic review of the literature but the integration of the findings of the review into recommendations for care (IOM, 2008). A panel of experts who have access to current evidence and an understanding of the clinical problem should be involved in the

development of the CPG as there may be inherent gaps in available research to support clinical recommendations (IOM, 2008).

The process of CPG development should include the incorporation of two grading systems: one system to address the quality of available evidence and another to address the strength of study recommendation (IOM, 2008). The quality of evidence grade represents the level of confidence that if the recommendations are followed appropriate outcomes will occur. The grade given to the strength of the recommendation is a balance of the risk/benefit ratio associated with the recommended interventions and the expert panel's interpretation of the importance associated with following guideline recommendations (IOM, 2008).

An important determinant in the strength of the recommendation is the type of research evaluated in the CPG review. Peer-reviewed, published controlled clinical trials are considered to provide the best information regarding the effectiveness of a therapeutic approach (Embree, 2000). Peer-reviewed, published epidemiologic studies provide the next best level of evidence in support or against a therapy (Embree, 2000). The lowest strength rating is assigned to published case report recommendations and opinions based upon personal clinical experience of the expert panel (Embree, 2000). The IOM (2008) recommends that the CPG development process be scientifically rigorous, document standards utilized, and take efforts to protect from bias so that the final published guidelines are effective.

### **GRADE Method**

There are several systems available for evaluating and grading clinical evidence in the development of CPGs. The Grades of Recommendation Assessment, Development



and Evaluation (GRADE) method was introduced in 2004 after the GRADE developmental working group compared six existing systems and found that they lacked consistency in agreement amongst the systems (Kavanagh, 2009). GRADE has been accepted and adopted by national and international medical organizations, government and healthcare regulatory agencies (Kavanagh, 2009). One advantage of the GRADE method in comparison to other grading modalities is that it allows for CPG reviewers to interpret, pass judgment and classify the quality of evidence classifying evidence as high, moderate, low and very low (Gugiu & Gugiu, 2010; Jaeschke et al., 2008). The GRADE framework allows for definition of evidence quality based upon the guideline panel's level of confidence related to the research validity and the benefit/risk ratio for implementation of a given recommendation (Ansari, Tsertsvadze, & Moher, 2009).

The factors that influence the strength of a recommendation in the GRADE framework include not only assessment of the quality of evidence but also the balance between risk/benefit effects, values, preferences and cost of recommendation implementation (Jaeschke et al., 2008). Strengths of the GRADE system include transparency related to the judgments and opinions regarding the evidence and recommendations and the fact that while weight is provided to the study design it is not a singular factor in judging the evidence quality (Brozek et al., 2009). Expert opinion, when applied in the GRADE system, is not a quality of evidence but serves as an interpretation of existing evidence. The GRADE system of review recognizes the necessity of expert opinion for the translation and integration of clinical evidence into the final recommendation (Brozek et al., 2009). The application of the GRADE system includes systematic literature review of all available diagnostic and management

approaches and the summary of evidence into tables that are succinct, transparent and informative related to the quality of the evidence, the effects of application on patient care outcomes, and the means for determining the evidence rating (Guyatt et al., 2011).

### **Cardiovascular Disease**

In-flight medical incidents related to cardiovascular disease are amongst the top five recorded incidents and account for two-thirds of all in-flight passenger mortalities. As previously discussed, the lack of an international aviation registry for passenger related medical incidents makes it difficult to statistically quantify the number of incidents that occur annually. Classification of in-flight related events which may be cardiac related may also be recorded under different medical categories such as syncope or respiratory distress (Shurlock, 2011). Recognizing the need for clear advice to guide general practitioners, a working group of the British Cardiovascular Society was established to develop guidelines for evaluation of fitness to fly in cardiovascular patients (Smith et al., 2010). The guidelines presented by the group in 2010 were focused on conditions of the heart and great vessels alone and, in the absence of randomized controlled trials and clinical studies of passengers with existing cardiovascular disease the recommendations, were based on the physics and physiology of the aircraft cabin environment along with expert opinion of the Cardiologists serving on the working group (Shurlock, 2011).

While most patients with cardiac conditions can travel safely by air, travel medicine experts suggest that the contraindications to commercial airline travel for patients with cardiovascular disease are included in along with GRADE evaluation of the quality and strength of supporting evidence presented. Patients with cardiovascular

disease may be negatively affected by the decrease in oxygen saturation during flight which results in hypoxia that leads to increased heart rate and subsequent cardiac demand (ASMA, 2003). As a result in-flight oxygen is indicated for patients with the following cardiovascular conditions:

- require oxygen at their home baseline altitude
- congestive heart failure class III-IV
- baseline PaO<sub>2</sub> less than 70 mm Hg
- class III-IV angina
- cyanotic congenital heart disease
- primary pulmonary hypertension
- other cardiovascular disorders associated with baseline hypoxia.

Passengers with pacemakers and implantable cardiac defibrillators are not restricted from flying once stable. It is important to inform passengers with pacemakers and implantable defibrillators that they need to identify themselves in advance to the security screening personnel as they need to be screened by alternate devices other than the standard x-ray equipment.

It is important for patients to understand that the airlines do not provide oxygen supply for their needs during flight and that it is the patient's responsibility to make arrangements in advance for portable oxygen that is approved for use in commercial airline travel as well as an adequate supply of oxygen tanks to meet their needs.

Unanticipated delays related to weather, missed connections or aircraft equipment malfunction often results in extended travel time over that which is initially planned.

Therefore, patients should carry an excess supply of oxygen and rechargeable tanks for use in the event of delayed travel.

Available studies evaluating the effect of flight upon cardiopulmonary physiology principally evolve from studies of subjects living on land at high altitude or by studying the effects of normobaric hypoxia in a laboratory setting (Smith et al., 2010). While some characteristics of these environments can simulate the effects of traveling by commercial aircraft the environments are not equivocal and therefore any application of such research would have to be considered to be speculative.

No direct studies of the effect of hypoxia during commercial air travel upon patients with cardiovascular ischemia were located and after applying the results of the evaluated studies to the physiology of ischemia the authors concluded that there would be little to no effect in precipitating ischemia on commercial airline passengers. A retrospective analysis of 213 patients who were transported via commercial airlines after acute myocardial infarction controlled hypoxia with supplemental oxygen and therefore was unable to identify whether or not untreated hypoxic situations may have resulted in further cardiac ischemia or events (Thomas et al., 2006).

The ability for patients with clinically stable pulmonary hypertension to tolerate air travel was evaluated in an anonymous survey (Thamm et al., 2011). Patients with pulmonary hypertension were identified with inclusion criteria including a confirmed diagnosis of pulmonary arterial hypertension that were stable as identified as having no specific therapeutic changes three months prior to travel. Patients with severe lung diseases, left ventricular diseases and other concurrent chronic diseases were excluded from the capstone project. A total of 720 questionnaires were distributed with 430

returned (60% response rate). Not all of the 430 respondents had flown since their diagnosis which resulted in only 179 diagnosed patients who had flown at least once since their diagnosis. Of those flyers, 20 (11%) reported having had one or more adverse events during or directly after at least one of their flights. Adverse events reported included dyspnea (3.4%), peripheral edema (3.4%), exhaustion (1.7%), heart palpitations (1.1%), chest pain (1.1%), headache (1.1%), worsening of general condition (1.1%) and fear of flying (0.6%).

Thamm et al. (2011) acknowledge in their publication the potential for selection bias in their review. An additional noted limitation was that the hemodynamic status of the respondents was not known prior to air travel and therefore the classification of disease severity into WHO classes was limited to patient self-report. While the authors suggest that air travel can be safe and well-tolerated by patients with stable pulmonary hypertension, their final consensus was that physician evaluation is required prior to travel for every patient. The Thamm et al. (2011) study size was small and the biases involved bring into question the generalizability of the statement of safety. At present, there are no data from controlled trials examining the safety of air travel for patients with pulmonary hypertension (Thamm et al., 2011).

### **Respiratory Disease**

Healthy passengers without underlying respiratory disease will experience a significant desaturation during commercial air travel as a result of hypobaric hypoxia but typically do not experience dyspnea (Kelly et al., 2008). Due to the lack of a universal method for reporting air travel related illness and it's cause there are no exact numbers of passengers with respiratory conditions that are affected by air travel. What is known is

that respiratory symptoms are the third most frequent cause of flight diversion related to a medical issue (Ahmedzai et al., 2011). In an effort to ease decision-making for fitness to fly in respiratory patients Tzani (2010) offered an algorithm to provide some direction for healthcare providers to evaluate respiratory patients and estimate the potential need for supplemental oxygen or further evaluation prior to air travel (Figure 11).

The majority of in-flight oxygen requests and pre-flight oxygen clearances are for passengers with chronic respiratory diseases (Patel & Simon, 2010). Overall recommendations for medical advice related to fitness to fly clearance should depend upon the type, reversibility and functional severity of the underlying respiratory condition and the healthcare provider's assessment of the passenger's ability to tolerate the commercial aircraft cabin environment and hypobaric hypoxia in flight (Patel & Simon, 2010; UK Civil Aviation Authority, 2007). Passengers who may be subject to worsening conditions associated with hypoxia in-flight can be cleared for travel with the assistance of an airline approved therapeutic oxygen device.

A cross-sectional study of 391 COPD passengers and 184 non-COPD passengers were evaluated for lung function, blood gas values, exercise capacity, air travel habits and in-flight symptoms to determine the prevalence of in-flight symptoms in patients with COPD (Edwardsen et al., 2011). The Edwardsen et al. (2011) study was the first known flight outcome study comparing COPD patients with non-COPD subjects and the data from the study showed a 3-fold increase in hypoxia related symptoms and near 7-fold increase in dyspnea and air hunger amongst COPD patients compared to non-COPD patients. No significant difference was noted in other air travel related symptoms such as ear pressure, sinus pressure or edema between the groups. After adjustments were made

for smoking status, age and gender, the odds ratio for COPD passengers to experience dyspnea or air hunger was 6.6 (95% CI 2.5-17.3,  $p < 0.001$ ) compared to non-COPD subjects. Pre-flight scores on the Medical Research Council (MRC) Dyspnea scale were strongly associated with in-flight dyspnea ( $p < 0.001$ ) and while the possibility of recall bias may have been a result of the design the strong association of the MRC Dyspnea score with the observed results offers an interesting avenue for further investigation of alternate means of evaluating respiratory patients pre-flight.

Several prior studies support Edvardsen et al. (2011) findings of increased incidence of dyspnea in patients with COPD. The UK Flight Outcomes Study (Coker, Shiner, & Partridge, 2007) was a prospective multicenter observational study examining the outcomes of commercial air travel in patients with respiratory disease. Of the patients evaluated, 243 (39%) had a diagnosis of COPD with disease severity ranging from mild (2%), moderate (29%), severe (43%) to very severe (26%). During flight, 18% of the patients in the UK Flight Outcomes Study reported respiratory distress manifested as dyspnea. Similarly, a retrospective study of 391 patients with COPD resulted in 25% reporting experienced hypoxia-related symptoms during air travel with increased symptom frequency in passengers with more severe baseline dyspnea (Dillard, Beninati, & Berg, 1991).

The British Thoracic Society has recently issued new recommendations for managing air passengers with stable respiratory disease (Ahmedzai et al., 2011). The decision by the British Thoracic Society (BTS) to revise the recommendations for passengers with respiratory disease traveling by air was based upon studies which confirmed that neither resting sea level oxygen saturations nor forced expiratory volume

in 1 second (FEV<sub>1</sub>) are reliable predictors of hypoxemia or complications associated with air travel in patients with respiratory disease. Ahmedzai et al. (2011) determined that as a result of the failure to predict response that there is no reliable threshold that can accurately determine the safety of air travel or the need for in-flight oxygen in an individual traveler with respiratory disease.

The 2011 recommendations by the BTS included review of guidelines currently available from British, American, Canadian and European fitness to fly recommendations and acknowledged that there were not consistent, practical nor comprehensive coverage of recommendations for providers caring for patients with respiratory disease. As was the case with their cardiology colleague's recommendation for fitness to fly, Ahmedzai et al. (2011) developed consensus recommendations rather than clinical practice guidelines. The goals of the recommendations were to provide advice for respiratory specialists and other health care providers who are involved in determination of passenger fitness to fly.

Ahmedzai et al. (2011) provided a thorough guide for managing patients with stable respiratory disease planning air travel based upon the BTS recommendations. Key points and recommendations from the guide for healthcare providers evaluating patients with respiratory disease for fitness to fly include:

- Cabin altitude may worsen hypoxemia in pulmonary disease and the physiologic compensation for acute hypoxia is mild to moderate hyperventilation and moderate tachycardia
- FEV<sub>1</sub> and SpO<sub>2</sub> are useful markers of clinical severity in patients with respiratory disease however, neither resting sea level SpO<sub>2</sub> nor FEV<sub>1</sub> appear to predict hypoxemia or complications of respiratory disease associated with air travel.



- Healthcare providers evaluating a patient with respiratory disease for fitness to fly should consider the patient's prior flight experience, flight duration, destination and time since last exacerbation of their respiratory condition.
- Hypoxic challenge test (HCT) is not a test to determine fitness to fly but is utilized to aid in the decision-making of whether a patient will require in-flight oxygen
- Patients with complex respiratory disease can be referred for hypobaric chamber testing
- The patient needs to take responsibility for the decision to fly and needs to understand that the airline can refuse travel if the passenger's health or safety is in doubt at the time of presentation for travel.

BTS recommendations also include the statement that Respiratory physicians or pediatricians should be the central referral point for consideration of safety to fly in all cases. While this recommendation may be appropriate in the UK, the availability of specialists for decision-making may not be practical in the U.S. and guidelines could be evaluated by primary care providers with knowledge of flight physiology and patient disease history.

### **Deep Vein Thrombosis**

Venous stasis as a result of immobility in hospitalized patients has been documented as a risk factor for the development of Deep vein thrombosis (DVT). Passengers traveling for long distances who remained immobile have also been thought to be at increased risk for DVT development and amongst all health conditions associated with air travel is one with the most available studies (Scurr, Ahmad, Thavaraian, &

Fisher, 2010). IATA (2011) fitness to fly guidelines for passengers with deep vein thrombosis recommend evaluation by a health care professional for patients with active DVT and clearance to fly for DVT patients who are asymptomatic.

DVTs result when there is a partial or complete blockage of the deep venous system of the body by a blood clot, typically in the legs. Symptoms of DVT develop gradually and diagnosis can be difficult. The signs and symptoms attributed to DVT may include lower leg redness, a swollen or painful calf or thigh, increased skin temperature in a change in coloration of skin over the affected area. Untreated DVT's place a patient at risk for developing pulmonary embolism which can result in death. Two longitudinal cohort studies of ambulatory populations estimated 11% rate of 28-day mortality amongst first episode venous thromboembolism (VTE) subjects (Chandra, Parisini, & Mozaffarian, 2009).

In 1954, a 54-year-old doctor who had completed a 14 hour flight was the first documented report of a DVT which developed as a result of venous thrombosis related to air travel (Clarke, Hopewell, Juszczak, Eising, & Kjeldstrom, 2006). In 1977, the term 'economy class syndrome' was coined to describe DVTs which were thought to occur as a result of prolonged sitting in the confined conditions associated with air travel (Clarke et al., 2006). Several systematic reviews have been undertaken over the past decade to attempt to definitively clarify the relationship between air travel and risk for venous thromboembolism (MacCallum et al., 2011).

A 2002 systematic review of observational studies failed to conclude that there was definitive evidence that air travel increase the risk of deep vein thrombosis (Clarke et al., 2006). In 2007, another systemic review of 25 studies (6 case-control studies, 10

cohort studies and 9 randomized controlled trials) was published with the end objective to measure the methodological strength of the literature, estimate the risk of thrombosis related to air travel, evaluate the efficacy of preventive treatments and develop evidence-based recommendations for practice (Philbrick, Shumate, Siadat, & Becker, 2007). The systematic review was once again unable to determine the risk of travel-related venous thromboembolism because of three main weaknesses noted. The largest of the cohort studies did not include routine screening for DVT but instead identified cases through a retrospective medical record review. The authors found that retrospective studies tended to report higher case counts attributable to the lack of limits on time or setting (Philbrick et al., 2007). Routine screening in other case studies identified more cases, mostly of asymptomatic DVTs, which would have erroneously been reported in a retrospective study as related to travel.

There has been evidence suggesting that flights of eight hours or more may increase the risk of deep vein thrombosis if a passenger has additional risk factors (Clarke et al., 2006). Air travel-related risk factors for DVT include prolonged immobilization and narrow economy class seats with limited legroom, dehydration, insufficient fluid intake, and low humidity (Clarke et al., 2006). Additional risk factors related to passenger's personal health included hereditary or acquired clotting disorders, prior history of DVT, older age, recent surgery or trauma, cancer, smoking, pregnancy, chronic heart disease and obesity (Clarke et al., 2006).

A systematic review and meta-analysis of studies of travel and the risk for VTE was published by Chandra, Parasini and Mozaffarian in 2009. The authors followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines

throughout the design, implementation and reporting of the meta-analysis. The study selection identified 1560 abstracts via searches of MEDLINE, EMBASE, BIOSIS, CINAHL, the Cochrane library, grey literature sources and a hand-search of the studies identified in the reference lists of the selected abstracts. Of the 1560 abstracts identified, 1518 were excluded because they were commentaries, general reviews or case reports. The remaining 42 studies were further examined and an additional 28 studies were excluded because of study design issues such as lacking a non-traveling comparison group, preventive measures for travel-related VTE and failure to meet the criteria for VTE diagnosis.

The 14 selected studies in the meta-analysis included one prospective cohort study (Schwarz et al., 2003), one retrospective cohort study (Kuipers et al., 2007), one case-crossover study (Kelman et al., 2003), and eleven case-control studies (Chandra et al., 2009). Pooled risk estimates for risk for VTE with travel were obtained by using random-effects models with inverse-variance weighting. The authors noted in their analysis that due to the uncommon outcome of travel-related VTE they pooled together the odds ratios from case-control studies approximate risk ratios or relative risks from cohort studies to generate one common relative risk.

The pooled relative risk for VTE among air travelers across the studies was 2.0 (95% CI, 1.5 to 2.7;  $p < 0.001$ ) compared with non-travelers (Chandra et al., 2009). Significant heterogeneity ( $P$  for  $Q$  statistic  $< 0.001$ ) was noted and determined to occur in the selection criteria for control participants in the case-control studies ( $P = 0.008$ ). When the authors classified the 14 included studies by use of referred control participants, a case crossover design or a cohort they identified a statistically significant

association between travel and VTE with an overall pooled estimate of 2.8 (CI, 2.2 to 3.7) as shown in Figure 14 (Chandra et al., 2009).

The pooled risk estimate for travel by air (RR, 2.2 (CI, 1.4 to 3.2)) was noted to be higher but not statistically significant ( $P$  for heterogeneity = 0.140) than for travel by surface means (RR, 1.14 (CI, 1.0 to 2.1)) (Chandra et al., 2009).

The meta-analysis of more than 4000 cases of VTE identified a 2-fold higher risk for travelers compared to non-travelers. In case-control studies using individuals referred for VTE evaluation as control participants there was no association found. The results of the meta-analysis indicated that in non-referred control case studies, cohort or case-only studies there was nearly a 3-fold higher risk for VTE in travelers leading the authors to a conclusion that there was a higher risk for VTE associated with travel (Chandra et al., 2009).

A dose-response relationship between duration of travel and risk of VTE was identified by evaluation of 4 of the studies included in the meta-analysis where the data was available for assessment (Figure 15). The authors observed an 18% higher risk for VTE for each 2-hour increase in travel duration (Chandra et al., 2009).

Of the 14 original studies included in the meta-analysis, only 4 studies contained the available data to assess risk associated with duration of travel and the resultant confidence limits of the effect estimate are wide (4% to 33% higher risk) (Chandra et al., 2009). Chandra et al. (2009) posit that the dose-response relationship appeared stronger (26% higher risk/2 travel hours) amongst passengers traveling by air but had insufficient data to compare direct pooled dose-response estimates for passengers travelling by air versus surface travel modes. Regardless of the modality of travel, the dose-response

analysis highlights the importance of preventive measures for VTE as duration of travel increase.

The association between cumulative flight duration and risk of VTE was evaluated further in a British community-based case-control study (MacCallum et al., 2011). The authors sought to reduce bias by designing the selection of controls to include subjects registered within the same general practice, same gender and closest in age to the matched case in the practice register. As illustrated in Figure 16, cases were excluded if the index events occurred outside of the pre-determined study entry, were not matched to controls or did not have objectively confirmed VTE (MacCallum et al., 2011). Table 4 illustrates the characteristics of case and controls along with the univariate analysis of risk factors. The MacCallum et al. (2011) results indicate that a cumulative flying time of greater than 12 hours is associated with a similar risk of VTE within four weeks as long-haul air travel in which one or more flights is longer than 4 hours in duration.

An increased risk of VTE was associated with previous VTE, increased weight and increased height (MacCallum et al., 2011). These findings were consistent with other studies evaluating the risk factors associated with VTE (MacCallum et al., 2011). Recent surgery was a significantly greater risk factor for VTE than air travel (MacCallum et al., 2011). The risks associated with minor surgery were a similar order of magnitude to those associated with long-haul air travel while the risk associated with major surgery was one or two orders of magnitude greater than the risk associated with long-haul travel (MacCallum et al., 2011).

A 2010 Cochrane review exists for evaluation of compression stockings for preventing deep vein thrombosis in airline passengers (Clarke, Hopewell, Juszczak, Eising, & Kjeldstrom, 2006). The authors of the Cochrane review acknowledged the lack of correlative evidence between air travel and DVT but posited that due to the low incidence of deep vein thrombosis in the general population it is unlikely that studies with adequate sample sizes to detect slight increases in risk will ever be conducted (Clarke et al., 2006). The Cochrane review focused not on determining the correlation between air travel and DVT development but rather the effectiveness of wearing compression stockings in the prevention of DVT in passengers traveling for long distances. Randomized trials that compared passengers wearing compression stockings against passengers not wearing them during long-haul flights were included in the analysis. The primary outcome evaluated was the diagnosis of symptomatic or symptomless DVT (diagnosed by ultrasound, venogram or isotope). Secondary outcome measures evaluated included diagnosis of pulmonary embolism, death, superficial venous thrombosis, edema, and adverse effects as a result of the use of compression stockings.

A 2012 executive summary published by the American College of Chest Physicians (ACCP) reviewed the current recommendations associated with prevention of thrombosis in traveling patients in an effort to establish an evidence-based clinical practice guideline for antithrombotic therapy and thrombosis prevention (Guyatt, Akl, Crowther, Gutterman, & Schunemann, 2012). The ACCP reviewed available literature and graded the current recommendations for long-distance travelers at risk of VTE. At risk travelers were identified in the guideline as those who had previous VTE, recent surgery or trauma, active malignancy, pregnancy, estrogen use, advanced age, limited

mobility, severe obesity or known thrombophilic disorders (Kahn et al., 2012). The result of their evidence-based review included the following recommendations for prevention of VTE in non-surgical patients traveling long-distance:

- frequent ambulation, calf muscle exercises or sitting in an aisle seat if feasible
- during travel the use of properly fitted, below-knee graduated compression stockings (GCS) which provide 15-30 mm HG of pressure at the ankle

In addition to the recommendations above, the guidelines advice against the use of GCS by long-distance travelers not meeting the conditions listed as at increased risk of VTE and avoidance of the use of aspirin or other anticoagulants to prevent VTE in long-distance travelers (Kahn et al., 2012).

The recommendations by the ACCP in their 2012 supplement were analyzed using GRADE criteria. Each of the recommendations received a Grade 2C rating identifying the recommendation as having a questionable benefit/risk and having been derived from a low quality of evidence (Guyatt et al., 2006). The 2012 ACCP recommendations include a further downgrading from the 8<sup>th</sup> edition of ACCP clinical practice guidelines which listed calf muscle contraction as an ACCP grade 1C recommendation and aspirin therapy as an ACCP grade 1B recommendation (Gerts et al., 2008). The ACCP published a disclaimer to their 2012 guidelines related to their recommendations requesting that caution be exercised in performance measure development and public reporting of guideline recommendations graded in the 1C, 2 A, 2B and 2C category according to the ACCP Grading System (Guyatt et al., 2012). The ACCP recommendations could be subject to future revision based upon the findings of



the World Health Organization Research into Global Hazards of Travel (WRIGHT) Project's phase 2 publication (WHO, 2007).

### **Blood Disorders**

The recommendations associated with assessment of fitness to fly for passengers with anemic disorders are based upon the principles of the effect of flight physiology on the hematologic system. No recent research studies were found evaluating the parameters of fitness to fly and current guideline recommendations appear to be based upon experience and recommendations of the sponsoring organizations.

The ASMA (2002) recommendations establishing hemoglobin levels for concern at less than 8.0 gm/dl are due to potential for passenger lightheadedness or potential for loss of consciousness during flight especially when associated with ambulation to the bathroom or physical activity during flight (ASMA, 2003). Recommendation for oxygen in patients experiencing sickle cell crisis was made to avoid potential life-threatening sequela that may be induced as a result of the combination of sickle cell crisis and the hypobaric hypoxic environment induced with flight. Per the ASMA (2002), sickle cell trait has not been associated with health problems at cruising altitude. Recommendations for travel without use of supplemental oxygen in-flight ranged from 7.5 g/dl to the IATA recommendation of 9.5 g/dl (UK Civil Aviation Authority, 2007; Patel & Simon, 2010; DeHart, 2003; International Civil Aviation Organization and International Air Transport Association [ICAO & IATA], 2005) by publication regarding the absolute hemoglobin level. While the recommendations appear to be prudent, no record of basis for determination of hemoglobin levels by evidence-based guidelines could be located in any of the available research.

## Central Nervous System Disorders

The recommendations associated with assessment of fitness to fly for passengers with central nervous system disorders are based upon the principles of the effect of flight physiology on the central nervous system. No recent research studies were found evaluating the parameters of fitness to fly and current guideline recommendations appear to be based upon experience and recommendations of the sponsoring organizations. General recommendations found by literature search, while lacking in reference source information, were consistent with the IATA (2011) recommendations are included in ASMA (2003) guidelines caution patients with epilepsy to refrain from consuming alcohol before or during air travel and note that epileptic patients should be informed of the potential seizure threshold-lowering effects of fatigue, delayed meals, hypoxia and circadian rhythm disruption associated with long-distance travel.

Seth, Mir, Dhir, Cheeseman & Singh (2009) addressed evaluation of fitness to fly post craniotomy. The authors found sparse and contradictory data related to intercranial pressure changes (ICP) associated with cabin altitude and noted that there are no well-conducted studies available that demonstrate the effect of long distance air travel on post craniotomy patients (Seth, Mir, Dhir, Cheeseman, & Singh, 2009).

Sirven et al. (2002) evaluated a total of 2,042 medical incidents that were reported to the Mayo Clinic Department of Emergency Medicine and Medical Transportation Service that resulted in 312 flight diversions. Neurologic symptoms were the largest category of medical incidents (31%) resulting in 626 air-to-ground medical calls to the clinics (Sirven et al., 2002). Dizziness/vertigo was the most common report neurologic symptom (Table 8) followed by seizures, headaches, pain, and cerebrovascular

symptoms yet the most common cause for flight diversion were seizures. It was hypothesized that the increased incidence of diversion was likely due to the “dramatic presentations” which led to an immediate call for crew attention (Sirven et al., 2002, p. 3).

A prospective analysis of patients with neurologic symptoms referred from the Madrid-Barajas International Airport to the emergency department at the Hospital Universitario Ramon y Cajal for neurologic consultation resulted in the evaluation of 77 patients over a 21 month period from May 2008 to January 2010 (Alonso-Canovas et al., 2011). Of the 77 cases identified, seizures were the cause for consultation for 39 (50.6%), Stroke 18 (23.4%) and the remaining 20 (26%) were attributed to other causes. Twenty-five (61%) of the seizure patients identified had no prior history of seizure. Classification of causes of identified seizures included idiopathic (20/48/8%), acute symptomatic or provoked as a result of missed doses of antiepileptic medication or drugs/alcohol contributed to 39% of the remaining subjects. Recreational drug use ( $p=0.0008$ ) and past history of seizures ( $p=0.0007$ ) were significantly associated with referral for seizure activity in flight (Alonso-Canovas et al., 2011). Eighteen patients referred for stroke (23.4%) of which 14 reported vascular risk factors including hypertension, tobacco use, cardiopathy, hypercholesterolemia and diabetes mellitus. Vascular risk factors were significantly associated with stroke ( $p=0.0017$ ). Alonso-Canovas et al. (2011) suggested that air travel may be a factor for induction of neurologic problems while noting that the study was limited by a lack of information related to the flight diversion or treatment applied in-flight. Additionally, in patients diagnosed as

having a stroke, 1/3 were noted in post diagnostic evaluation to have carotid stenosis (over 50% occlusion) which likely was a significant contributor to stroke etiology.

Airplane headache has been reported as a new type of headache with specific symptoms temporarily related to air travel (Alonso-Canovas et al., 2011; Berilgen & Mungen, 2011). The characteristics of airplane headache are a headache that starts suddenly during aircraft ascent and/or descent. The headache associated with air travel is typically severe, stabbing, unilateral, most often localized to the periorbital region and has a mean duration of 20 minutes subsiding shortly after landing (Berilgen & Mungen, 2011; Evans, Purdy, & Goodman, 2007; Berilgen & Mungen, 2006). Thirty-three cases (28 male, 5 female) of suspected headache associated with air travel were identified Berilgen and Mungen (2011). The case study headaches were not associated with other migraine history or symptoms and of those 33 cases, 22 were evaluated by a neurologist and found to be normal. Berilgen and Mungen (2011) analyzed the cases and hypothesize that the headache associated with air trauma is likely due to temporary sinus barotraumas or local inflammation in the sinus area as a result of hypoxia or reduced cabin humidity. Of note is that of the patients evaluated, 95% of the identified cases did not have recurrent headache symptoms in subsequent flights when premedicated one hour before take off with 550mg of naproxen sodium. A separate self-reported case study of what was considered to be airplane headache also responded positively to premedication with naproxen (Marchioretto, Mainardi, & Zanchin, 2008).

### **Eye, Ear, Nose and Throat**

The recommendations associated with assessment of fitness to fly for passengers with ear, nose and throat (ENT) disorders are based upon the principles of the effect of

flight physiology on the ENT system. The recommendations associated with assessment of fitness to fly for passengers with ophthalmologic disorders are based upon the principles of the effect of flight physiology on the ophthalmologic system. In-flight evaluation of intraocular pressure (IOP) change in healthy subjects during air travel was examined by Bayer et al., 2008. Twenty-five healthy volunteers underwent evaluation of IOP for change from ground level measurement, at cabin pressures of 8000 feet and post landing in an attempt to determine the effect of air travel on the IOP of healthy subjects (Bayer et al., 2008). Total flight duration was 2 hours and 55 minutes and repeated ANOVA test was used for IOP value comparison between the consecutive measurements with p values of 0.05 considered to be significant. A significant decrease in IOP was noted on the second hour of flight (13.4%,  $p = 0.005$ ) and after landing (15.7%,  $p = 0.001$ ). Bayer et al. (2008) were unable to determine the length of time post landing that the decrease in IOP persisted as no further measurements post landing were performed. Conclusions were drawn from hypobaric chamber studies which demonstrated a return to normal of IOP 2-5 hours after exposure to high altitude simulation (Bayer et al., 2008). The Bayer et al. (2008) study offers initial information related to the effects of air travel on IOP, the study is limited by the small sample size and does not offer information related to the effects of long-haul travel or the duration of IOP decrease post landing. The statistical significance of the study would support further investigation.

Exposure to allergens in flight is of particular concern for patients who have severe allergic reactions such as anaphylaxis or exacerbation of asthma after exposure to irritants. The consequences of a severe allergic reaction mid-flight without appropriate medical assistance can be life-threatening. One in ten individuals is known to have

allergies to animals but few consider the potential for exposure that may occur in animals brought onboard the aircraft by other passengers. Exposure to dander cannot be avoided by restricting seating away from animals within the cabin because of capacity filled flights as well as the persistence of dander even after a passenger with a pet has deplaned. Stanbrook, Kovesi and Hebert (2010) reported that one study found clinically significant cat dander concentrations have been noted on 100% of sampled domestic airline seats and 16% of seats on international flights. As of 2010, the Canadian Transportation Agency began examining pet policies on commercial aircraft carriers to evaluate whether the admission of animals within aircraft cabins could pose a threat to the health and well-being of some passengers (Kondro, 2010).

Several airlines have ceased to serve peanuts following reported anaphylactic reactions in passengers who inhaled peanut dust (Stanbrook, Kovesi, & Hebert, 2010). While the removal of peanut, nut and seed products by airlines reduces the risk of exposure to passengers, the ability and commonplace occurrence of other passengers on an aircraft bringing food sources or items with peanut, nut or seed dust on them cannot be regulated by the airlines. To assist at-risk passengers, the IATA (2011) recommends that passengers with severe allergies plan ahead by contacting their physician, discussing travel related risks and obtaining the prescription of an epinephrine auto-injector or other allergy medicine to be carried onboard for use as needed.

## **Trauma**

The recommendations associated with assessment of fitness to fly for passengers with trauma are based upon the principles disease management as well as the effect of flight physiology. Key flight physiologic considerations for the healthcare provider to

consider when evaluating a post-surgical or post-trauma passenger for fitness to fly include:

- Passengers in this category are at risk for increased oxygen consumption as a result of trauma or surgery. Supplemental oxygen may be considered if the patient is anemic, volume depleted or known to have concomitant cardiopulmonary disease which may be further compromised by the hypoxic conditions of flight (ASMA, 2003).
- Intestinal gas will expand 25% by volume at a cabin altitude of 8000 feet and patients who are post-abdominal surgery may be at risk for bleeding, perforation or tearing at suture sites as a result of increased pressure, stretching gastric or intestinal mucosa (ASMA, 2003).
- Patients with bowel obstruction as well as post colonoscopy may not be able to accommodate the additional gastrointestinal gas expansion during flight (ASMA, 2003).
- Neurosurgical and passengers post ophthalmologic surgery may be subject to trapped gas which will cause increased pressure in flight (ASMA, 2003).

No recent research studies were found evaluating the parameters of fitness to fly and current guideline recommendations appear to be based upon experience and recommendations of the sponsoring organizations.

### **Pregnancy**

There are various air travel restrictions placed upon pregnant passengers by both domestic and international airlines which vary by airline. Yet, there is no clinical practice guideline nor formal clinical evidence exists that provides an absolute

contraindication to travel for pregnant women (Hezelgrave, Whitty, Shennan, & Chappell, 2011). The decision upon whether to provide fitness to fly for a pregnant traveler is made on an individual basis by the passenger's healthcare provider and is dependent upon gestational age, the degree of clinical compromise and the presence of pre-existing comorbid conditions (Hezelgrave et al., 2011). The basis of concern for most airlines to restrict air travel for pregnant women is to avoid the undesirable consequence of flight diversion or delivery in flight where they may be a lack of appropriate facilities or care providers to manage labor and pregnancy complications (Royal College of Obstetricians and Gynaecologists [RCOG], 2008; UK Civil Aviation Authority, 2007). The American College of Obstetricians and Gynecologists issued a committee opinion on obstetric practice in 2009 in which they posited that in the absence of medical or obstetrical complications that air travel is safe for pregnant women (American College of Obstetricians and Gynecologists [ACOG], 2009).

Not surprisingly, there is a paucity of research available on air travel during pregnancy and recommendations by obstetric sources are made based upon the scientific knowledge related to the physiology of flight and the physiologic changes of pregnancy. Hezelgrave, Whitty, Shennan and Chappell (2011) note that while most pregnant women are low risk pregnancy and can be expected to travel without any complications, there are additional risks that should be considered during each trimester which can be further complicated by comorbid medical conditions.

A search of the literature resulted in two research studies which directly addressed the issue of passenger air travel and pregnancy outcomes. A retrospective analysis of 992 healthy pregnant women with single pregnancies of gestational ages of 20 weeks or



greater admitted for delivery over a 12-month period between May 2003 and May 2004 was performed to analyze whether there was an elevated risk of adverse pregnancy outcomes associated with air travel (Chibber, Al-Sibai, & Qahtani, 2006). The study was performed in the antenatal clinics of a Saudi Arabian university teaching hospital designated as tertiary care centers. The study group consisted of pregnant women who had travelled by air at least once during their pregnancy and the control group were those who did not travel. Study group members were asked to provide gestational age, destination, length of flight and any complications during travel. Chart review by an investigator blinded to the travel status of the participants was performed to obtain medical history, obstetric complications and pregnancy outcome information.

Women with any pre-pregnancy medical complications, vaginal bleeding, history of tocolysis administration for preterm labor, fetal anomalies, neonatal structural anomalies or chromosomal anomalies were excluded from the study. The study group consisted of 546 women who travelled at least once during their pregnancy of which 312 (57%) were primiparous, and 234 (43%) multiparous. The study group flew for the first time during pregnancy at a gestation age of 11.2 +/- weeks with average flight times lasting 7.8 +/- 1.2 hours and a median of 7 flights (range 1-18). There was a statistically significant incidence of expatriates among the travel group over Saudi nationals (see Table 15). The control group consisted of 447 pregnant women of which 241(54%) were primiparous and 206 (46%) were multiparous.

Amongst primiparous passengers, air travel during pregnancy was associated with an increased risk of preterm birth at <37 and > 34 week gestation (OR 1.5; 95% CI 1.2, 1.8, see Table 16). Regression analysis demonstrated a relationship between gestational

age at delivery and gestational age at first air travel ( $r = 0.002$ ,  $P = 0.01$ ) and total hours of flight ( $r = 0.012$ ,  $P = 0.01$ ) of which the risk factor associated for preterm delivery persisted when evaluated on the whole group analysis of data . When adjustments were made for age, socioeconomic status there was a decrease in magnitude of the association between travel and preterm primiparous delivery but the association remained statistically significant (Chibber et al., 2006). While the birthweights of the preterm infants were lower than controls, no statistically significant increased risk of admission to the neonatal intensive care unit was noted suggesting that these infants were not at any greater risk than the controls for respiratory distress or intraventricular hemorrhage associated with preterm delivery.

Several confounding variables existed in the study which may have contributed to bias in the results. There was a significant racial difference amongst the women who travelled and those who did not which Chibber et al. (2006) acknowledge correlates with cultural and lifestyle choices of foreigners in Saudi Arabia who may be more likely to travel during months of greater heat or who may choose to travel because they are challenged by the local customs and find the lifestyle and dress codes restrictive. The failure of the authors to assess tobacco use and alcohol consumption was another potentially significant confounding variable in the study as both substances are known to be associated with preterm delivery and lower birth weight. In the absence of this data, the results, despite appropriate statistical analysis of the data, may be biased.

A strength of the Chibber et al. (2006) study was the ability to accurately assess gestational age of the women studied. Additionally, the study had a larger sample size than prior research evaluating the effect of air travel and pregnancy outcomes.

A whole group analysis was performed and it was determined from the findings that air travel during pregnancy was associated with an increased risk of preterm births at  $< 37$  and  $> 34$  weeks gestation (Chibber et al., 2006). Gestational age at delivery correlated with lower birthweight among the women. No differences or risk elevations were found between pregnant air travelers and non-air travelers in the rates of other evaluated sequel.

The second study located by literature search was a 6-month questionnaire of women admitted to Georgetown University Medical Center in Washington D.C. with impending delivery while at least one of the author's of the study was on call (Freeman et al., 2004). The study population accounted for 13% of the deliveries in the facility during the study period.

Exclusion criteria included fetal anomalies, neonatal structural or chromosomal anomalies ( $n= 3$ ). Medical history obstetric complications and pregnancy outcomes were obtained by a chart review blinded to air travel status. Variables collected on the study population included maternal age and race, parity, history of adverse pregnancy outcome, presence of pre-pregnancy complications, medications during pregnancy, initial hematocrit at first prenatal visit and hematocrit at the time of delivery (Freeman et al., 2004). Adverse pregnancy outcomes were evaluated using a composite analysis of stillbirth, Apgar score at 5-minutes, preterm delivery  $<37$  weeks, preeclampsia and birth weight and the between group prevalence (Table 19). Logistic regression analysis was performed to account for the significant differences in racial distribution between the groups.

Limitations of the Freeman et al. (2004) study included the sample size as well as the convenience sampling criteria associated with investigator availability. Power analysis performed by the Freeman et al. (2004) found that a sample size of 2,803 women per group would be needed in order to demonstrate that air travel has a protective effect against adverse pregnancy outcome ( $\alpha = 0.05$ ,  $\beta = 0.80$ ). The sample studied was substantially smaller and to date there are no studies performed with sample sizes of pregnant travelers that large.

Another potential for bias and study limitation was that the questionnaire was administered by the authors and it is therefore subject to recall reliability and failure to disclose information may have impacted the results as well as selection bias. The authors note that women admitted in preterm labor or experiencing pregnancy complications generally manifest a over-recall rather than an under-recall of potential causative factors (Freeman et al., 2004). The bias related to recall may still exist in this study as it was a convenience sample that included both women presenting to deliver without complications as well as those who may be delivering preterm or with complications.

Racial differences, as noted previously, was another potential confounding variable in the study and the authors noted in the study that the higher rate of Caucasian women who traveled may reflect a sociodemographic difference between the two groups and may also be reflective of the higher hematocrit in air travelers since they were predominantly Caucasian which is a race known to normally have higher hematocrit levels than other races (Freeman et al., 2004). No significant association between air travel and composite adverse pregnancy outcomes were found when a logistic regression

analysis was performed taking into account race as well as other demographic variables (Freeman et al., 2004).

A literature search was published in 2010 which aimed at evaluating the relationship of air travel and spontaneous abortion, intrauterine fetal demise (IUFD), low birth weight (<10<sup>th</sup> percentile), preterm delivery and neonatal intensive care unit admissions (Magann et al., 2010). The literature search identified 128 publications of which 9 abstracts evaluated air travel and pregnancy outcomes. The Chibber et al. (2009) and Freeman et al. (2004) studies addressed previously was the only two studies of the nine which specifically evaluated the outcomes in traveling passengers and not flight attendants and/or aviators. Flight attendants and aviators were excluded from our review based upon the concept that their health, risk factors, flight times and number of flights differ significantly from the average travelling passenger. Regardless, with the inclusion of the flight attendants and aviators in their review, Magann et al. (2010) were unable to identify an increased risk of neonatal intensive care unit admissions (OR: 1.19, 95% CI: 0.74, 1.82), low birth weight (OR: 1.25, 95% CI: 0.62, 2.48) or pre-eclampsia (OR: 0.86, 95% CI: 0.58, 1.27) when subjects were compared to controls. The risk of pregnancy loss (spontaneous abortion or IUFD) was greater in flight attendants than controls (OR: 1.62, 95% confidence interval: 1.29, 2.04) but none of these studies evaluated pregnant passengers versus controls so a generalization may not be valid given the increased risk factors of flight time exposure amongst flight attendants (Magann et al., 2010). No similar increased risk of pregnancy loss was found in either the Chibber et al. (2009) or the Freeman et al. (2004). Results of the Chibber et al. (2009) study indicating an associated increased risk of preterm birth (<37 weeks) was reported by the authors.

Magann et al. (2010) noted that the correlation between air travel on pregnancy outcomes has been poorly studied and the inadequacy and lack of data on air travel an pregnancy outcomes makes an evidence-based recommendation impossible to provide.

### **Psychological Disorders**

It is estimated that fear of flying affects 10-40% of the commercial air traveling population (Van Gerwen, Spinhoven, & Van Dyck, 2006). Symptoms associated with flight related anxiety range from mild anxiety to pathological fear. Air rage is described as disruptive behavior associated with air travel and is thought to be associated with travel related stress and exacerbated by alcohol ([WHO], 2011).

Matsumoto and Goebert (2001) retrospectively reviewed 1375 physician consultation calls in 1997 to a 24 hours medical consultation service that provided coverage to 9 commercial domestic and international airlines and found that 3.5% of all medical in-flight emergencies fell under the category of mental disorders. Of the consultations provided in the Matsumoto and Goebert study, 90% were had anxiety as their primary symptom and 4% psychosis. Avoidance behavior, behavior and cognitive therapy and anxiolytic medications may be means by which transient anxiety and stress associated with air travel can be controlled and therefore fear of flying is not considered to be a condition that would warrant a fitness to fly examination (Bogaerde & De Raedt, 2008; Van Gerwen, Spinhoven, & Van Dyck, 2006; Waterhouse, Reilly, & Edwards, 2004).

Concern exists that the stress associated with traveling to and within a busy airport terminal as well as the physiologic changes of flight and environmental conditions within the aircraft cabin may lead to exacerbation on underlying psychiatric conditions or decompensation of previously stable conditions (DeHart, 2003). Jet lag and disruption of

the circadian rhythm is also thought to be a contributory factor for the potential exacerbation of psychotic conditions (Katz, 2011). While conditions leading to exacerbations of psychiatric disorders are temporary and not likely to lead to long-term problems with the passenger's health, concern for the ability of the crew to safely conduct a flight may require prior medical clearance for passengers exhibiting psychiatric symptoms of concern to air or ground crew. Passengers who are aggressive, unpredictable, disruptive, disorganized or unsafe may trigger airline personnel to request further evaluation which prohibits the passenger from flying (ASMA, 2003). Most guideline recommendations for fitness to fly related to psychotic patients recommend that travel be accompanied by a trained medical escort or other individual who can ensure psychiatric medication management and assist with control of the affected passenger when needed (Patel & Simon, 2010; UK Civil Aviation Authority, 2007).

## **Diabetes**

Evaluation of the effects of air travel on patients with diabetes is an emerging area of comorbidity that has only recently begun to be evaluated in terms of flight related physiology. A study of the effects of atmospheric pressure on insulin pump delivery during flight identified unintended insulin delivery in pumps by bubble formation and expansion of bubbles (King, Goss, Paterson, Crock, & Anderson, 2011). King, et al. (2011) evaluated the effect of ambient pressure during simulated flight in hypobaric chambers mimicking ascent, descent and catastrophic depressurization on insulin pump delivery, bubble formation, bubble size and cartridge plunger movement in ten insulin pumps connected to capillary tubes. A Student *t* test of the results found that excess insulin delivery of 0.623% of the cartridge volume occurred ( $p < 0.001$ ) in both types of

pumps evaluated (Animas and Medtronic). No statistical difference was noted between pump types when abnormal insulin delivery was evaluated as a percentage of insulin volume (King et al., 2011). While this study was not performed on diabetic patients with insulin pumps in place, it does raise the question of whether or not there may be unintentional hypoglycemia that results during air travel for passengers with insulin pumps. Unintentional hypoglycemia in combination with travel fatigue, jet lag, limited food availability in flight can result in serious consequences if not monitored (Waterhouse, Kao, Edwards, Atkinson, & Reilly, 2006).

### **Miscellaneous Conditions**

The recommendations associated with assessment of fitness to fly for passengers with communicable disease, terminal illness and decompression syndrome are based upon the principles disease management as well as the effect of flight physiology. Despite concerns associated with spread of infection in aircraft cabins, there is very little risk of infectious disease transmission on board of commercial aircraft (WHO, 2011). Transmission of infection may occur between passengers in close contact related to seating areas but the aircraft ventilation system utilized in commercial aircraft is similar to that found in hospital surgical suites and intensive care units. HEPA filter systems help reduce transmission of particles, bacteria, fungi and viruses during recirculation exchange and the rate of disease transmission onboard an aircraft is no more likely than that which would occur for the same passenger in a commercial building (WHO, 2011). Recommendations to avoid travel until passengers with infectious disease are beyond the period of contagion are the same as would be offered for the patient avoidance of public areas to reduce the spread of disease.



## CHAPTER 3

### Conceptual Framework

The ACE Star Model of Knowledge Transformation (ACE) is the conceptual framework chosen for this capstone project as it is a model which allows for the transformation of knowledge and integration it into evidence based practice (EBP) (Kirchhoff, 2008). The ACE model is based upon a five point star (Appendix C) that depicts the stages of knowledge transformation (Stevens, 2004). The model stages include discovery, summary, translation, integration and evaluation. In the ACE model evidence translation is developed as each stage of transformation is a building block for the previous stage resulting in newly discovered knowledge being implemented into practice (Kirchhoff, 2008).

Discovery is the first star point of the ACE model (Stevens, 2004). The discovery stage involves knowledge generated through the conduction of quantitative and qualitative primary research studies. The evidence generated from these primary studies is utilized to develop clinical decisions (Stevens, 2004).

Evidence summary, the second star point, generates knowledge through the development of a summary of available research into statements to guide practice. A systemic approach is utilized to reduce bias and provide for reliability of the evidence (Stevens, 2004). Systematic reviews, evidence summaries, review of the literature and meta-analyses are examples of evidence summaries (Stevens, 2004).

The third star point, translation, involves the summary of evidence into standards of practice or clinical practice guidelines (CPG). CPGs provide a means for healthcare

providers, patients and organizations to make informed clinical decisions and provide for standardization of clinical practice (Stevens, 2004).

Integration, the fourth star point, is the stage at which CPGs are implemented into practice. Practice integration of evidence occurs at individual and/or organizational levels with the goal of the stage being the adoption of recommendations into routine practice (Stevens, 2004; Kirchhoff, 2008).

Evaluation is the fifth star point of the ACE process. The assessment of the effect of the utilization of the CPG on patient outcomes, patient satisfaction ratings, system efficiency, and cost analysis are methods by which the evaluation stage leads to continued improvement in clinical practice (Stevens, 2004).

The proposed capstone project will focus on the development of a CPG for primary care providers to be able to utilize in their daily practice. The capstone project will focus predominantly on the evaluation and integration stages of the ACE Star Model. The CPG developed will provide an evidenced-based guideline for integration into primary care practice.

## CHAPTER 4

### Methodology

#### Evidence-based Project Plan

The intent of the capstone project was to perform an evidence-based systematic review and synthesis for the purpose of the development of a clinical practice guideline (CPG). Literature from was obtained by internet and electronic database searches of published evidence via Medline, PubMed, the Cochrane Library CINAHL (EBSCOHost), and other electronic sources for admissible evidence or studies published between February 2001 and February 2012. Search terms included air, plane, aircraft, travel, airline, fitness to fly, commercial air, hypoxia, hypoxemia, pre-flight, post-flight, cardiovascular, circulatory, blood, hematology, anemia, pulmonary, COPD, respiratory, asthma, restrictive lung, non-restrictive lung, neurologic, neurology, central nervous system, gastrointestinal, abdomen, ear, nose, throat, psychiatric, anxiety, psychosis, eye, ophthalmologic, pregnancy, children, pediatric, orthopedic, surgical, surgery, trauma, disease, infection, pain, and prevention. Identified studies were limited to those written in English or with available English translations. Expert opinion and guidelines developed by other sources were included in the guideline development and all efforts were be made to correlate opinion and published guidelines to primary sources of research.

Patient outcomes of interest were identified and the GRADE approach (Appendix D) was utilized to assess the magnitude of effect of recommendations and quality of evidence. Categories of evaluation for the capstone project followed the areas of the IATA medical group recommendations related to passenger fitness for air travel:

cardiovascular disease, blood disorders, pulmonary disorders, central nervous system disorders, gastrointestinal disorders, ear/nose/throat disorders, psychiatric illness, ophthalmologic disorders, pregnancy, trauma and miscellaneous conditions.

### **Resources Required**

No funding was required for completion of the capstone project. The primary resource requirement was the investigator's time to perform the search for studies, grade the reviews and synthesize the data into an evidenced-based practice guideline. There was no cost associated with the review of the guideline by the clinical content professionals. Minimal costs were associated with printing necessary for project completion and were covered by the project author.

### **IRB Approval**

The project was submitted to the University of Nevada Las Vegas Office of Research Integrity for IRB approval for exempted research consideration based upon the criteria as being a collection or study of publicly available data that does not involve human subjects or individual subject identifiers. On October 18, 2011 the protocol was reviewed by the University of Nevada Las Vegas Office of Research Integrity – Human Subjects and was deemed excluded from IRB review (Appendix E).

## CHAPTER 5

### Results

A comprehensive systematic review of the literature was performed and current knowledge in the form of expert opinion and published guidelines was incorporated into the final clinical practice guideline. The CPG developed graded the applicable data according to both the quality of available evidence and the strength of the recommendations. The CPG was developed in the format accepted by the Agency for Healthcare Research and Quality and is included in this paper as Appendix G.

## CHAPTER 6

### **Summary, Conclusions and Recommendations**

After an exhaustive review of the literature it became evident that although published research existed on fitness to fly guidelines for a variety of health related issues, there were few direct clinical evidence studies of the pathophysiologic effects of commercial airline travel on passengers with pre-existing diseases. The majority of published research and fitness to fly guidelines were developed by applying the principles of the effects of flight on physiologic systems, based upon research conducted in hypoxic simulated laboratory environments, developed from studies performed on subjects adapting to altitude on land, or formulated as opinion by expert individuals or working groups. Attempts to apply the grade approach to the research resulted in downgrading of evidence recommendations in the developed guidelines due to the small sample sizes, lack of study randomization and blinding, failure to control for bias and other design-related issues that affected the research reliability. The majority of the available research anecdotal clinical case studies and expert opinion and therefore fell under the category of very low quality of strength of recommendation.

Shurlock (2010) acknowledged the lack of clinical data available to make appropriate guidelines for fitness to fly. Instead of focusing on diseases, per se, the Working Group of the British Cardiovascular Society (Smith et al., 2010) focused on the cabin environment and stratifications of levels of risk. The final published report of the Working Group acknowledges that there are few direct clinical studies of the pathophysiological effects of air travel on patients with existing diseases and therefore their guideline advice was based on the physics and physiology of the aircraft cabin

environment and its potential impact on patients with pre-existing conditions.

Ultimately, the British Cardiovascular Society working group gave their recommendations based upon their expert knowledge because of the lack of randomized controlled trials available to meet the criteria of a clinical practice guideline. The aim of the guidelines, according to Smith et al. (2010), was not to be restrictive but to allow passengers to fly. Smith et al. (2010) also acknowledged that the lack of randomized controlled trials, meta-analysis and registries regarding the effect or risks of air travel upon patients with cardiovascular disease prevented them from developing clinical practice guidelines. As a result, the working group chose to review available evidence and then apply clinical professional judgment in conjunction with present knowledge of the physiological effects of the aircraft environment on the pathophysiology of cardiovascular disease as had other expert panels addressing the issues associated with fitness to fly.

The currently available clinical guidelines for establishing fitness to fly produced by disease-specific specialty group sources such as ASMA (2003), IATA (2011), the UK Civil Aviation Authority (2009), the British Thoracic Society (Ahmedzai et al., 2011), the British Cardiovascular Society (Smith et al., 2010) and ACOG (2009) provide similar recommendations related to passenger disease or pre-existing condition and the need for evaluation prior to travel. Their recommendations are also based predominantly on case study reports, expert opinion, simulated environment research studies and small studies with limitations in quality outcome measures. A review of the updated BTS fitness to fly guidelines suggested that based on the “lack of clarity” in the available advice, inadequate data for classification of in-flight events and “anachronistic advice that did not

consider levels of risk” it would be best to not develop fitness to fly guidelines but rather to determine which patient should be cleared to fly on the basis of the risk of a spontaneous event in an aircraft cabin environment with limited available emergency treatment (Shurlock, 2011, p. 1045).

There is validity associated with concerns related to guidelines that are not supported by evidence-based research and it can be argued that no evidence-based clinical practice guideline could be developed for commercial airline passenger fitness to fly due to the lack of quality clinical research findings. Few of the available published studies evaluated for this capstone project exceeded the GRADE guideline for low quality research because of the lack of the reliance on case reports, consensus opinion and contradictory small studies with limitations lowering the strength of the results. Regardless, evidence-based analysis can be applied and the guideline presented as a result of this capstone project can be implemented as a resource to guide primary care professional screening, decision-making and preventive care based upon currently available information.

The field of travel medicine is a new and emergency specialty area and recommendations for further evaluation include improving undergraduate and postgraduate travel medicine education, adding travel history to initial health history forms, development of instruction sheets for dissemination to primary care providers, airlines and the traveling public as well as performing larger, higher quality research studies to clinically evaluate travel related health issues (Talbot, Chen, Sanford, McCarthy, & Leder, 2010; Ruis, Van Rijckevorsel, Van den Hoek, Koeman, & Sonder, 2009; Van De Winkel, Van den Daele, Van Gompel, & Van den Ende, 2007). The



research, expert opinion and published guidelines identified in this study focused on individual issues or health problems and the paucity of studies in each of the IATA identified areas warrants further investigation to validate recommendations. Several areas of future research and opportunity were identified during the review of the evidence.

One means of improving the reliability of information and data gathering would be for the implementation of an international registry to document in-flight medical emergencies. Accuracy of data collected related to in-flight medical events would be improved significantly if standardized reporting requirements and terminology were implemented as part of the registry process. Data collected from an international database with standardized categories could be used to identify actual incidences of health related occurrences and provide direction for further epidemiologic research. International flight related medical occurrence data could be utilized to adapt and standardize the contents of the onboard medical kits to meet the actual identified needs of in-flight health issues. Extrapolated epidemiologic data could also be utilized to develop preventive health information and improved pre-flight screening strategies for healthcare providers. Future recommendations and research should include patients with comorbid conditions to evaluate the potential for cumulative negative effects.

Hypobaric hypoxia is one of the physiologic changes that occur during flight as a result of the cabin pressurization. Hypoxia can have effect the circulation by causing local coronary and cerebral vasodilatation, increase in heart rate, hyperventilation, increase in blood pressure, increased myocardial contractility, increase in cardiac pressure, increase in cardiac output and increase in pulmonary artery pressure (Bartsch &

Gibbs, 2007). In addition to the effect of altitude and cabin pressurization on oxygen partial pressure in healthy adults, there is an age related decrease in oxygen partial pressure that occurs above the age of 40 years which is approximated to be a loss of 5 mm Hg per decade of age (Smith et al., 2010).

Patients who present to their primary care provider requesting a medical certificate of fitness to fly, approval for use of portable oxygen concentrators for air travel, a pregnancy information form, or a medical information form (MEDIF) for air travel should trigger preventive screening for the status of current health conditions that may be affected by the stressors of travel and the aircraft environment. Primary care providers completing these supporting documents need to have an understanding of the impact of air travel on medical issues and use available information and prudent judgment before establishing a patient's approval to fly in order to prevent patient adverse health events as well as the potential liability issues that can occur with negative outcomes. Recommendations from the British Medical Association (BMA) advise health care providers to carefully word statements on an individual's fitness to fly indicating the information on which the healthcare provider's advice is based rather than providing a positive certification of a person's fitness to fly (UK Civil Aviation Authority, 2007).

BMA recommendations include the use of statements on MEDIF forms such as:

- I know of no obvious reason why this person should not fly or
- There is nothing available in the medical record to indicate that flying may place this patient at a health risk

These types of statements do not provide a guarantee of a patient being able to travel without incident but rather indicate that evidence available to the healthcare provider

does not indicate that air travel will place their patient at a greater risk than other traveling passengers.

The proposed next step of translation of the capstone project findings will be to submit the capstone guidelines recommendations, once approved by the capstone committee and successfully defended, for a review and recommendation of approval by subject matter experts at the International Society of Travel Medicine. Capstone recommendations will be summarized for an invited podium presentation at the American Academy of Nurse Practitioner 2012 National Conference. The summarized clinical practice guidelines will be submitted to the Journal of the American Academy of Nurse Practitioners for publication consideration. Publication in a peer-reviewed primary care journal is preferential so that the information can reach the intended audience of primary care professionals who may benefit from integrating the capstone project findings into practice.

The Aerospace Medical Association (2009) estimates that 62% of in-flight emergencies occur in passengers with pre-existing medical conditions. Preparation and thorough screening of passengers with known medical conditions would prevent most in-flight medical emergencies (Valani et al., 2010). Further examination and research related to air travel health issues for passengers with comorbid conditions is needed especially in light of the fact that the air travel population is aging and therefore more likely to have one or more comorbid conditions that could be adversely affected by air travel. Traveling passengers may be reluctant to disclose pre-existing medical information to airline personnel that could prohibit them from a planned flight, especially when such a delay may cause the passenger to incur additional fees and financial

consequences associated with disrupted travel plans. Preventive evaluation, identification and proactive management of conditions by healthcare providers who are knowledgeable regarding the risks associated with air travel can reduce air travel related adverse health events. Health care providers who have an understanding of the physiologic changes that occur in flight can provide individual plans of prevention tailored to meet the specific conditions of at-risk patients.

## APPENDIX A: AERSOPACE MEDICAL ASSOCIATION RECOMMENDATIONS FOR ONBOARD EMERGENCY MEDICAL KIT

Medication	Equipment
Epinephrine 1:1000	Stethoscope
Antihistaminic Injectable	Sphygmomanometer (electronic preferred)
Dextrose 50% inj. 50 ml (or equivalent)	Airways, oropharyngeal (appropriate range of sizes)
Nitroglycerin tab. or spray	Syringes (appropriate range of sizes)
Major analgesic, inj. Or oral	Needles (appropriate range of sizes)
Sedative anticonvulsant inj.	Intravenous catheters (appropriate range of sizes)
Antiemetic inj.	Antiseptic wipes
Bronchial dilator inhaler	Gloves (disposable)
Atropine inj.	Sharps disposal box
Adrenocortical steroid inj.	Urinary catheter
Diuretic inj.	System for delivering intravenous fluids
Medication for postpartum bleeding	Venous tourniquet
Sodium chloride 0.9% (minimum 250 ml)	Sponge gauze
Acetyl Salicylic Acid (aspirin) for oral use	Tape Adhesive
Oral beta blocker	Surgical mask
A list of medications (Generic names with trade names if and as it appears on the item)	Emergency tracheal catheter (or large gauge intravenous cannula)
	Umbilical cord clamp
	Thermometer
If a cardiac monitor is available (with or without an AED) add to the above list:	
Epinephrine 1:10000 (can be a dilution of epinephrine 1:1000)	Basic Life Support and Advanced Life Support cards
	Bag-valve mask
	Flashlight and batteries (Operator may decide to have one per aircraft in an easily accessible location)
	A list of equipments

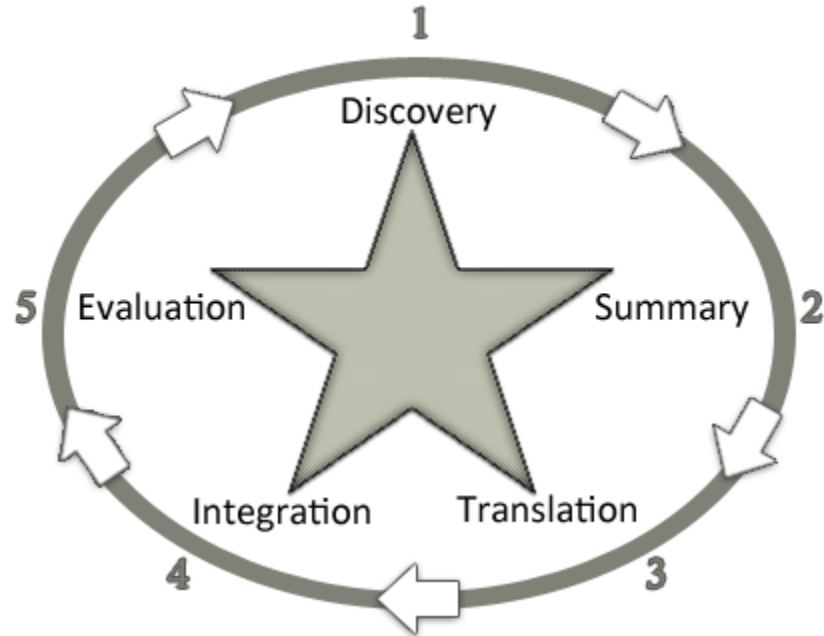
## APPENDIX B: INCUBATION AND INFECTIVITY COMMUNICABLE DISEASE

INCUBATION PERIODS OF IMPORTANT INFECTIONS		
INFECTION	INCUBATION PERIOD	
	Maximum Range	Usual Range
Anthrax	2-5 days	
Amoebiasis	14-28 days	21 days
Bacillary Dysentery	1-7 days	
Brucellosis	7-21 days	
Chicken Pox	14-21 days	* Infectious 5 days before rash – 6 days after last lesion
Cholera	Hours – days	2-3 hours
Diphtheria	2-5 days	* Infectious 2-3 weeks, shorter with antibiotic therapy
Filariasis	3+ months	
Gonorrhea	2-5 days	
Hepatitis A	2-6 weeks	4 weeks
Hepatitis B	6wks – 16 mos	12 weeks
Leishmaniasis (cutaneous)	1 wk – months	
Leishmaniasis (visceral)	2 weeks – 12 years	2-4 months
Leprosy	Months – years	
Malaria	10-14 days	
Measles	7-14 days	* Infectious from onset of prodromal symptoms until 4 days after onset of rash
Meningococcemia	2-10 days	3-4 days
Mumps	12-21 days	* Infectious days before salivary swelling – 7 days after
Pertussis	7-10 days	* Infectious 7 days after exposure to 3 weeks after onset of rash, shortened to 7 days by antibiotics
Poliomyelitis	3-21 days	7-10 days
Psittacosis	4-14 days	10 days
Rabies	Variable	2-8 weeks
Rubella	14-21 days	* Infectious 7 days before onset of rash – 4 days after
Scarlet Fever	1-3 days	* Infectious 10-21 days after onset of rash, shortened to 1 day by antibiotics
Smallpox	7-17 days	11 days
Trypanosoma (rhodesiense)	14-21 days	
Trypanosoma (gambiense)	weeks - years	
Typhoid fever	7-21 days	
Typhus fever	7-14 days	12 days

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## APPENDIX C: ACE STAR MODEL OF KNOWLEDGE TRANSFORMATION

### ACE Star Model of Knowledge Transformation



Retrieved from: <http://www.acestar.uthscsa.edu/acestar-model.asp>

## APPENDIX D: GRADE SYSTEM TABLE

### THE GRADE APPROACH TO ASSESSMENT OF EVIDENCE

Table 1: Ranking the Quality of Evidence

Quality of evidence (summary score)	Study design	Lower if *	Higher if *
<b>High (4)</b>	Randomized trial or valid accuracy study for diagnostic tests	<b>Study quality:</b> -1 Serious limitations -2 Very serious limitations	<b>Strong association:</b> +1 Strong, no plausible confounders, consistent and direct evidence
<b>Moderate (3)</b>		-1 Important inconsistency	
<b>Low (2)</b>	Observational study or indirect accuracy studies for diagnostic tests	<b>Directness:</b> -1 Some uncertainty -2 Major uncertainty	+2 Very strong, no major threats to validity and direct evidence
<b>Very low (1)</b>		-1 Sparse or imprecise data  -1 High probability of reporting bias	+1 Evidence of a dose response gradient

\* 1 = move up or down one grade (for example from high to intermediate)

2 = move up or down two grades (for example from high to low)

⊕⊕⊕⊕ High = Further research is very unlikely to change our confidence in the estimate of effect.

⊕⊕⊕○ Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

⊕⊕○○ Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

⊕○○○ Very low = Any estimate of effect is very uncertain.

**Limitations** = include problems in study design, such as for RCTs, lack of blinding or allocation concealment, incomplete reporting, selective outcome reporting, or use of unvalidated outcomes measures.

**Inconsistency** = Differences exist in the direction and size of the effect across the studies.

**Uncertainty** = Indirect comparisons or indirect populations have been considered across the studies, and there may be compelling reasons to expect important differences in the size of the effect.

**Validity** = Patients participating in RCTs are assessed to have same risk and/or mortality as non enrolled patients in whom the intervention is expected to be required.

Retrieved from <http://www.ichrc.org/evaluate.html>



APPENDIX E: UNLV BIOMEDICAL IRB NOTICE OF EXCLUDED ACTIVITY



**Biomedical IRB  
Notice of Excluded Activity**

**DATE:** October 18, 2011

**TO:** **Dr. Mary Bondmass**, Physiological Nursing

**FROM:** Office of Research Integrity – Human Subjects

**RE:** Notification of review by /Cindy Lee-Tataseo/Cindy Lee-Tataseo, BS, CIP, CIM  
Protocol Title: **Clinical Practice Guidelines for Primary Care Providers' Evaluation of Patient Fitness to Fly**  
Protocol# 1110-3942M

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This memorandum is notification that the project referenced above has been reviewed as indicated in Federal regulatory statutes 45CFR46.

The protocol has been reviewed and deemed excluded from IRB review. It is not in need of further review or approval by the IRB.

Any changes to the excluded activity may cause this project to require a different level of IRB review. Should any changes need to be made, please submit a Modification Form.

If you have questions or require any assistance, please contact the Office of Research Integrity – Human Subjects at [IRB@unlv.edu](mailto:IRB@unlv.edu) or call 895-2794.

## APPENDIX F: SUMMARY OF EVIDENCE TABLES

Evidence Table: Cardiovascular Disorders

Author/Year	Study Design	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
Ingle, 2011	Cross-sectional Survey	<p>Purpose: Evaluate air travel experiences of stable chronic heart failure (CHF) patients</p> <p>Sample Size: 464/1293 (39% response rate) cohort of patients from UK community heart failure clinic</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcome: Location of health problems: to airport, to flight-gate, through security, during flight, disembarkation, to destination, at destination</p> <p>Type of health problems: breathlessness, dizziness, ankle edema, headache, chest pain, fatigue, labored walking, palpitations, angina or defibrillator firing.</p>	<ul style="list-style-type: none"> <li>65 % (165/252) no health-related problems</li> <li>35% (46/262) problem at one location, 6% (16/252) at two locations, 5% (12/252) at three locations and 5% at more than three locations</li> <li>9% (8/89) problem with security at airport due to pacemaker/ICD</li> <li>9% (8/89) in-flight dyspnea, dizziness, edema, headache and chest pain</li> <li>3/8 experiencing dyspnea required O<sub>2</sub> supplementation</li> <li>25% (22/89) had health-related cardiovascular problems at final destination</li> <li>2/22 had defibrillator firing</li> <li>27% (125/464) would not fly in future due to difficulty (32%), health concerns (23%)</li> </ul>	●●○○ Low
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	<p>Purpose: Establish a guide to the timeframe that should elapse between a medical event and commercial air travel</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Patients are cleared to fly without restriction who have the following cardiovascular conditions:</p> <p>Angina – no restriction if controlled at rest</p> <p>MI (uncomplicated): after ≥ 10 days</p> <p>Cardiac Failure: controlled (able to walk 50 meters or climb one flight of stairs on room air at a normal pace without breathlessness) and condition is stable. In-flight oxygen needs to be considered</p> <p>Pulmonary Edema: resolved and any precipitating condition May need to comply with MI rules</p> <p>Cardiac Surgery: after ≥ 10 days</p>	●○○○ Very low

			<p>Angiography: after <math>\geq 24</math> hours if original condition stable</p> <p>Angioplasty: after <math>\geq 3</math> days if asymptomatic</p> <p>Pulmonary embolism: <math>\geq 5</math> days if anticoagulation stable and PaO<sub>2</sub> normal on room air</p> <p>All other conditions require "assessment by a doctor with aviation medicine experience" (IATA, 2011 p. 53).</p>	
Smith, 2010	Review of clinical studies and development of expert consensus statement by British Cardiovascular Society	<p>Purpose: establish guidance for general practitioners and passengers to determine the risks of travel by commercial air for patients with cardiovascular disorders.</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Travel post acute MI:</p> <ul style="list-style-type: none"> <li>Low risk passengers (age &lt;65 years, first event, successful reperfusion, EF &gt; 45%, no complications and no planned interventions) post acute coronary syndrome may safely fly as early as 3 days after event.</li> <li>Medium risk (EF &gt; 40%, no symptoms of heart failure, no evidence of inducible ischemia or arrhythmia and no further interventions planned) may fly 10 days after</li> <li>High risk (EF &lt; 40% with signs and symptoms of heart failure, those pending further investigation and possible revascularization or device therapy) defer until stable</li> </ul> <p>Chronic Heart failure:</p> <ul style="list-style-type: none"> <li>Stable without recent changes in symptoms or medication clear to fly.</li> <li>NYHA class IV symptoms may require in-flight O<sub>2</sub></li> </ul> <p>Arrhythmia:</p> <ul style="list-style-type: none"> <li>symptomatically stable with low frequency of events, no restriction</li> <li>permanent or persistent atrial fibrillation, should be stable with rate control and</li> </ul>	<p>●○○○ Very low</p>

			<p>anticoagulation before flying</p> <ul style="list-style-type: none"> <li>• uncontrolled hemodynamically significant ventricular arrhythmia should not travel on commercial aircraft</li> </ul> <p>Cyanotic congenital heart disease: (Eisenmenger syndrome) – no restriction but O<sub>2</sub> in-flight may be needed</p> <p>Cardiac catheterization: delay flight for one day post uneventful procedure</p> <p>Elective PCI: uncomplicated delay flying for 2 days</p> <p>Pacemaker insertion: in absence of post-insertion pneumothorax or other complications, delay flight 1-2 days after implantation</p> <p>Ablation: delay until stable anticoagulation</p> <p>Open heart surgery: including coronary artery bypass grafting and valve replacement - without complications delay 10 days for travel. 10days – 6 wks postop may require ground assistance</p> <p>Pacemakers and ICDS: stable, may travel without restriction</p>	
Ross, 2004	Executive summary of Canadian Cardiovascular Society based on expert opinion	Purpose: establish recommendations for fitness of passengers with cardiovascular disease to fly on commercial airlines. Fitness to fly recommendations based on New York Heart Association (NYHA) functional class	<p>Angina Pectoris: I &amp; II - no restriction III - supplemental O<sub>2</sub> IV only if medically necessary and accompanied by physician with attached ECG/defibrillator, O<sub>2</sub> and appropriate medications</p> <p>Post MI: I delay travel one to two weeks if uncomplicated II to IV – only if medically necessary and accompanied by physician with attached ECG/defibrillator, O<sub>2</sub> and appropriate medications</p> <p>Heart failure: I &amp; II – unrestricted</p>	●●○○ Low

			<p>III - supplemental O<sub>2</sub> required</p> <p>Valvular disease: I &amp; II – unrestricted, supplemental O<sub>2</sub> if pulmonary hypertension III - supplemental O<sub>2</sub> required IV – only if medically necessary and accompanied by physician with attached ECG/defibrillator, O<sub>2</sub> and appropriate medications</p> <p>Congenital disease: I &amp; II – unrestricted, supplemental O<sub>2</sub> if PaO<sub>2</sub> &lt; 70mmHg III - supplemental O<sub>2</sub> required IV – only if medically necessary and accompanied by physician with attached ECG/defibrillator, O<sub>2</sub> and appropriate medications</p> <p>Post-CABG/valve surgery: I-II- 4 days postop if hemoglobin ≥ 90g/L if flight &lt; 2 hours or 7 days postop if hemoglobin ≥ 90g/L if flight ≥ 2 hours</p> <p>Therapeutic intervention- PCI/ASD closure: I-II – 1 day postprocedure. If PCI following MI, follow post-MI guidelines</p> <p>Arrhythmia/post arrhythmia procedure: I-II – unrestricted if well-controlled supraventricular arrhythmia, 2 days post procedure for ventricular arrhythmias II-IV – restrict flying by commercial aircraft if uncontrolled hemodynamically significant ventricular arrhythmia</p> <p>Post-pacemaker/ICD/loop recorder implant: I-II – delay flight 1 day postimplant if no pneumothorax and device functions normally and is programmed appropriately</p> <p>ICD patients: I-II – delay travel 1 month following last intervention from device associated with severe presyncope /syncope</p>	
Roby, 2002	Randomized, single-blind, controlled trial	<p>Purpose:</p> <p>1) Examine the safety of</p>	<p>2% (1/38) Myocardial ischemia diagnosed by Holter monitor</p>	<p>●●●○ Moderate</p>

		<p>patients traveling by commercial air 2 weeks after myocardial infarction (MI)</p> <p>2) Determine if supplemental oxygen was associated with reduced risk of in-flight adverse events</p> <p>3) Determine the need for a medical escort</p> <p>Sample : 38 patient with mean of 15-16 days post acute Myocardial Infarction</p> <p>Intervention: travel by commercial aircraft Oxygen</p> <p>Outcomes: Major endpoint:</p> <ul style="list-style-type: none"> <li>Myocardial ischemia detected by Holter monitoring</li> </ul> <p>Minor endpoints:</p> <ul style="list-style-type: none"> <li>Chest pain</li> <li>Dyspnea</li> <li>O<sub>2</sub> saturation &lt;90%</li> </ul>	<p>13% (5/38) decreased O<sub>2</sub> saturation</p> <p>2 % (1/38) evidence of S-T depression</p> <p>5% (2/38) chest pain</p> <p>13% (5/38) ventricular ectopy or tachycardia</p> <p>No difference in minor endpoints between O<sub>2</sub> (5/13) and non-O<sub>2</sub> (6/15) groups (p=0.93)</p>	
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	<p>Purpose: establish recommendations for fitness of passengers with cardiovascular and other medical diseases to fly on commercial airlines</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Uncomplicated acute MI: Delay travel 2-3 weeks after resumption of usual daily activities</p> <p>Old MI: no contraindication unless significant angina or left ventricular dysfunction</p> <p>Severe decompensated CHF: flying contraindicated</p> <p>CABG and other chest surgeries: no risk after fully recovered without complications. Recommend 10-14 day delay post surgery to prevent risk associated with barotraumas</p> <p>PCI: uncomplicated: no risk after fully recovered without complications.</p> <p>PCI: complicated: delay travel 1-2 weeks</p> <p>Symptomatic valvular heart disease – flying contraindicated</p> <p>Hypertension: no contraindication if controlled</p> <p>Pacemakers/ICD: no contraindication if controlled</p>	<p>●○○○ Very Low</p>

			<p>Cardiovascular contraindications to commercial airline flight:</p> <ol style="list-style-type: none"> <li>1. Uncomplicated MI within 2-3 weeks</li> <li>2. Complicated MI within 6 weeks</li> <li>3. Unstable angina</li> <li>4. Congestive heart failure, severe, decompensated</li> <li>5. Uncontrolled hypertension</li> <li>6. CABG within 10-14 days</li> <li>7. CVA within 2 weeks</li> <li>8. Uncontrolled ventricular or supraventricular tachycardia</li> <li>9. Eisenmenger syndrome</li> <li>10. Severe symptomatic valvular heart disease</li> </ol>	
Zahger, 2000	Longitudinal Study	<p>Purpose: evaluate patients returning by commercial air after acute coronary syndrome, effect of timing and short-term complications</p> <p>Sample: 21 tourists admitted to an Israeli coronary care unit with acute coronary syndrome between May 1996 – May 1999.</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcomes:</p> <ul style="list-style-type: none"> <li>- flight duration</li> <li>- symptoms during flight</li> <li>- recurrent angina requiring hospitalization</li> </ul>	<p>Days from acute event to flight home <math>18.2 \pm 11</math> days</p> <p>Flight duration <math>12.5 \pm 3</math> hours</p> <p>0 - Cardiac symptoms in flight 90% - 19/21 remained symptom free at follow up 21 days <math>\pm 13</math></p>	<p>●○○○ Very Low</p>

Evidence Table: Respiratory Disorders

Author/Year	Study Design Level of Evidence	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
Akero, 2011	Randomized crossover trial	<p>Purpose: evaluate efficacy of pre-flight testing of COPD patient's to predict oxygen needs at 8,000 ft altitude</p> <p>Sample: 16 patients with COPD from two Norwegian outpatient pulmonary clinics</p> <p>Interventions: Hypoxia induced by a hypoxia-altitude simulation test (HAST) and in a hypobaric chamber (HC) Oxygen</p> <p>Outcome: Pao<sub>2</sub> with and without supplemental oxygen</p> <p>Secondary outcome – comparison of effect of Pao<sub>2</sub> on various types of oxygen equipment in the HC</p>	<p>Without supplemental O<sub>2</sub>, PaO<sub>2</sub> was lower during the HAST than in the HC (p=0.005)</p> <p>56% (9/16) patients reported dyspnea during exposure to hypoxia.</p> <p>Continuous oxygen at 2L/min or an oxygen conserving device at pulse setting 2 is needed to reach an Spo<sub>2</sub> of 90% (p&lt;.001)</p> <p>In-flight physical activity resulted in a drop in Spo<sub>2</sub> and increased supplemental oxygen.</p> <p>In a HC simulating altitude of 8,000ft, compressed gaseous O<sub>2</sub> with continuous flow or with an oxygen-conserving device resulted in the same Pao<sub>2</sub>. Portable Oxygen Concentrator (POC) showed significantly lower Pao<sub>2</sub> values than continuous flow or oxygen conserving devices (p=.003)</p>	●●●○ Moderate
Tam, 2011	Cross-sectional survey	<p>Purpose: evaluate the safety of air travel after percutaneous transthoracic needle biopsy (PTNB)</p> <p>Study population: 179 patients who underwent PTNB followed by air travel within 14 days of the procedure. 36% (65/179) patients experienced a post-biopsy pneumothorax prior to travel.</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcomes: In-flight medial event requiring attention or diversion</p> <p>Worsening of existing respiratory symptoms or new onset of respiratory symptoms</p>	<p>81% of all patients and 77% of patients with post-biopsy pneumothorax traveled within 4 days of the final post-biopsy chest radiograph.</p> <p>No patient reported in-flight medical events</p> <p>8% (14/179) experienced worsening of existing respiratory symptoms or new onset of symptoms during or after the flight.</p>	●●○○ Low



Bossley, 2011	Case Control Study	<p>Perform fitness to fly tests using a body plethysmograph in ex-preterm babies without bronchopulmonary dysplasia (BPD) and compare them with normal term babies to determine whether routine preflight testing should be recommended in ex-preterm babies without BPD.</p> <p>41 term infants and 30 ex-preterm infants recruited from neonatal units and postnatal wards in Australia</p> <p>Intervention: Hypoxia induced environment in sealed body plethysmograph</p> <p>Outcomes: Changes in SpO<sub>2</sub>, pulse and FiO<sub>2</sub></p>	<p>All subjects experienced a significant desaturation (median drop of 6%) when breathing FiO<sub>2</sub> 0.15.</p> <p>No difference was noted between the healthy term and ex-preterm babies at 3 or 6 months corrected gestational age during testing. Feeding at FiO<sub>2</sub> 0.15 resulted in a significant drop in SpO<sub>2</sub> for both groups (P&lt;0.0001) without any significant difference among groups. The fall in SpO<sub>2</sub> occurred at the initiation of feeding and was transient.</p>	<p>●●○○○ Low</p>
Edvardsen, 2011	Case Control Study	<p>Purpose: determine the prevalence of in-flight symptoms in COPD patients and non-COPD subjects and to evaluate associations between symptoms and pre-flight variables</p> <p>Subjects: 391 COPD patients and 184 non-COPD subjects were recruited from hospital and specialist practices in Norway. Of the recruited patients, 54% (211/391) with COPD and 86.4% (159/184) flew during the previous 2 years</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcomes: lung function, blood gas values, Medical Research Council (MRC) dyspnea scale, 6-minute walk test, air travel habits (frequency &amp; duration of travel, pre-flight medical consultation) and in-flight symptoms (dyspnea, dizziness, headache, chest pain, air hunger, cough, fainting, palpitations)</p>	<p>One or more hypoxia related symptoms were reported by 24.6% (52/211) of the COPD group and by 8.8% (14/159) of the non-COPD group (OR = 3.4, 95% CI, 1.8-5.4, p &lt; 0.001).</p> <p>COPD patients experienced significantly more frequent hypoxia-related symptoms of dyspnea and air hunger during air travel than non-COPD subjects (P&lt;0.001).</p> <p>Odds ratio for COPD patients to experience dyspnea or air hunger was 6.6 (95% CI, 2.5-17.3, p&lt;0.001) after adjusting for smoking status, age and gender compared to non-COPD subjects.</p> <p>In-flight dyspnea correlated with pre-flight sea-level MRC dyspnea scores.</p>	<p>●●●○○ Moderate</p>
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	<p>Purpose: establish a guide to the timeframe that should elapse between a medical event and commercial air travel</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Patients are cleared to fly without restriction who have the following respiratory conditions:</p> <p>Pneumothorax – 7 days after full inflation</p> <p>Chest surgery ≥ 11 days with uncomplicated recovery</p>	<p>●○○○○ Very low</p>

			<p>Pneumonia – fully resolved or symptom free with X-ray signs persistent</p> <p>COPD – exercise tolerance &gt;50 meters without dyspnea and stable condition. Full recovery if recent exacerbation.</p> <p>All conditions not meeting above requirements for clearance should have “assessment by a doctor with aviation medicine experience” (IATA, 2011 p. 54).</p>	
Thamm, 2011	Cross-sectional survey	<p>Purpose: determine the proportion of patients with pulmonary hypertension (PH) who had travelled by air contrary to medical advice</p> <p>Subjects: 430 patients completed the survey sent to 720 patients (60% response rate). 42% (179/430) had flown since PH diagnoses.</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcomes: Worsening of respiratory and new onset of other health symptoms</p>	<p>89% (159/179) had no adverse events during or directly after their air travel</p> <p>11% (20/179) reported one or more events associated with travel – 3.4 % ( 6) dyspnea 3.4% (6), peripheral edema, 3 (1.7%) exhaustion, 2 (1.1%) heart palpitations, chest pain, headache or worsening of general condition.</p>	<p>●●○○ Low</p>
Ahmedzai, 2011	Review of clinical studies and development of expert consensus statement by British Thoracic Society	<p>Purpose: establish guidance for general practitioners and passengers to determine the risks of travel by commercial air for patients with respiratory disorders.</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Summary of potential risks posed by air travel by condition:</p> <p>Asthma &amp; COPD: acute bronchospasm, hypoxemia or infective exacerbation</p> <p>Bronchiectasis: hypoxemia, infective exacerbation</p> <p>Lung cancer: hypoxemia, overall deterioration or sepsis</p> <p>Cardiac comorbidity: myocardial ischemia, hypoxemia, arrhythmia, peripheral edema, venous thromboembolism, worsening of heart failure</p> <p>Hyperventilation or dysfunctional breathing: acute</p>	<p>●○○○ Very low</p>

			<p>exacerbation</p> <p>Airborne infections: hypoxia, transmission to other passengers</p> <p>HIV infection: exacerbation of pre-existing opportunistic infection</p> <p>Interstitial lung disease: hypoxemia, infective exacerbation</p> <p>Neuromuscular disease and kyphoscoliosis: hypoxemia</p> <p>Obstructive sleep apnea syndrome (OSAS): worsening hypoxemia when asleep, exacerbation of jet lag with potential adverse effect on driving</p> <p>Obesity: hypoxemia, VTE</p> <p>Pneumothorax: 38% expansion of residual air at 8000ft; possible recurrence within at least 1 year unless pleurodesis has been performed via thoracotomy</p> <p>Pulmonary arteriovenous malformations (PAVM): hypoxemia, stroke, VTE and PAVM hemorrhage</p> <p>Sinus and middle ear disease: barotraumas</p> <p>Thoracic surgery: 38% expansion of residual air at 8000 ft</p> <p>At risk of VTE: increased risk of VTE on all flights especially those &gt;8 hour or following multiple shorter journeys over a short period.</p>	
Tiemensma, 2010	Case study report	Patient being treated for pulmonary tuberculosis with a medical history which included drainage of pneumothoraces and pleural effusions	<p>Patient experienced shortness of breath and chest pain shortly after take-off and subsequently died from pneumothorax.</p> <p>Patients with</p>	<p>●○○○</p> <p>Very Low</p>

			pulmonary diseases need pre-flight evaluation and possible supplemental oxygen in –flight to prevent complications.	
Lapostolle, 2009	Case study report	Two, 26 year old, female patients traveling long-distance (17,000km and 20:45h) suffered sudden asystolic cardiac arrest upon arrival	Embolectomy and clot examination revealed that both pulmonary emboli were newly formed.  The most likely risk factor for pulmonary embolism was long distance air travel	●○○○ Very Low
Kelly, 2009	Longitudinal cohort	Purpose: quantify the hypoxemic response to air travel and to identify baseline correlates to predict the response in passengers with non-obstructive lung disease.  Subjects: 14 volunteers (7 female/7 male)  Intervention: Hypoxemic challenge test Travel by commercial aircraft  Outcomes: respiratory function testing, in-flight SpO <sub>2</sub> , cabin pressure and dyspnea and post flight hematocrit level	13/14 subjects experienced in-flight significant hypoxia (SpO <sub>2</sub> <89%)  Respiratory function did not predict in-flight desaturation.  Pre-flight SpO <sub>2</sub> measures had strongest correlation ( $r=0.91$ , $p<0.001$ ) with in-flight SpO <sub>2</sub> .  Respiratory function testing showed no correlation with in-flight measurements or the Hct response.  In-flight desaturation did not correlate with increased symptoms of respiratory distress.	●○○○ Very Low
Lehmann, 2009	Cross-sectional survey	Purpose: evaluate the incidence of travel-associated pulmonary embolism (PE)  Subjects: 257 patients with PE as primary diagnosis at discharge  Outcome: Prognosis post event	18% (45/257) patients were identified to have PE associated with air travel, only patients with idiopathic PE (32%, $n=83$ ) and thrombophilia (30%, $n=78$ ) occurred with more frequency.  Intrahospital mortality was not statistically significant between both groups (4.3% overall)  3-month mortality rate in both groups was similar ( $p>0.999$ ).  Low incidence of flight-associated PD (0.2 cases per 1 million passengers arriving at Frankfurt airport)	●●○○ Low

			compared with other trial estimates	
Taveira-DaSilva, 2009	Cross-sectional study	<p>Purpose: determine the prevalence of pneumothorax associated with air travel in patients with lymphangioleiomyomatosis (LAM), idiopathic pulmonary fibrosis (IPF) and sarcoidosis</p> <p>Subjects: 281 subjects with LAM, 76 with IPF and 92 with sarcoidosis admitted to NIH Clinical Research Center.</p> <p>Intervention: travel by commercial air</p> <p>Outcome: new onset pneumothorax</p>	<p>2% (7/281) LAM patients had evidence of a new pneumothorax.</p> <p>Pneumothorax patients did not experience symptoms of dyspnea or chest pain during travel</p> <p>Prior history of pneumothorax correlated 100% to new onset pneumothorax diagnosis in LAM patients.</p> <p>None of the patients with IPF or sarcoidosis presented with pneumothorax.</p>	●●○○ Low
Martin, 2008	Case-control study	<p>Purpose: investigate how well the pre-flight hypoxia test cutoff values of 85% and 90% discriminated between health children and those with neonatal chronic lung disease (nCLD).</p> <p>Subjects: 34 healthy children and 35 children with a history of nCLD.</p> <p>Intervention: Hypoxia challenge test</p> <p>Outcomes: SpO<sub>2</sub> and heart rate</p>	<p>90% cutoff value did not discriminate between the two groups. 12/24 healthy and 14/23 nCLD failed the hypoxia test (p=0.56)</p> <p>85% was more discriminatory test. 1/24 healthy and 6/23 nCLD failed hypoxia test (p=0.048)</p> <p>In both groups children &gt; 2 years passed the hypoxia test at 90%.</p> <p>Children with nCLD who were &lt;2 years had an increased risk of failing the hypoxia test at 85% cutoff (p = 0.039) and a correlation was noted with failure and neonatal supplemental oxygen use</p>	●●○○ Low
Kelly, 2008	Longitudinal cohort	<p>Purpose: assess the predictive capability of the hypoxia inhalation test (HIT) in passengers with COPD</p> <p>Subjects: 13 volunteers with COPD (7 female)</p> <p>Intervention: Hypoxia inhalation test Travel by commercial aircraft 6-minute walk test</p>	<p>Air travel caused significant desaturation preflight (95 ± 1%); mean in-flight (86 ± 4%) which was worsened by activity (78 ± 6%).</p> <p>HIT resulted in desaturation comparable to that of air travel (84 ± 4%).</p>	●●○○ Low

		<p>Outcomes: respiratory function, pulse oximetry, cabin pressure and dyspnea</p>	<p>Mean in-flight partial pressure of inspired oxygen (<math>P_iO_2</math>) was higher than the HIT <math>P_iO_2</math> (<math>113 \pm 3</math> mm HG vs. <math>107 \pm 1</math> mm HG, <math>p &lt; 0.001</math>)</p> <p>The strongest correlation was found between the HIT <math>SpO_2</math> and in-flight <math>SpO_2</math> (<math>r = 0.84</math>; <math>p &lt; 0.001</math>)</p>	
Jones, 2008	Quasi-experimental	<p>Purpose: evaluate the role of ventilation-perfusion ratio (<math>V_A/Q</math>) and pulmonary shunt on <math>SpO_2</math> of patients with pulmonary dysfunction when exposed to air/nitrogen mixtures as cabin pressure (<math>P_iO_2</math>) falls.</p> <p>Subjects: 18 patients with chronic lung disease</p> <p>Intervention: airline equivalent hypoxia delivered by nitrogen mixtures of 17kPa (equivalent to 5000 ft altitude) and 15kPa (equivalent to 8000 ft altitude)</p> <p>Outcomes: <math>P_iO_2</math> vs. <math>SpO_2</math> along the <math>PO_2</math> axis and <math>V_A/Q</math> shunt (change of shape and downward shift of the same curve)</p>	<p>During hypoxia, the lowest <math>SpO_2</math> was correlated with reduced <math>V_A/Q</math> (<math>R^2=0.89</math>).</p> <p>9/10 patients with <math>V_A/Q \leq 0.69</math> developed profound hypoxia. 5/9 hypoxic had ground level <math>SpO_2 \geq 92\%</math>.</p> <p>Patients with <math>V_A/Q &gt; 0.70</math> maintained <math>SpO_2 \geq 84\%</math>.</p> <p>Reduced <math>V_A/Q</math> predisposed to a greater degree of hypoxemia than increased shunt at 15kPa <math>P_iO_2</math>.</p> <p>Measurement of <math>V_A/Q</math> and shunt during hypoxic hypoxia improves prediction of patient need for supplemental <math>O_2</math> during air travel</p>	<p>●●○○ Low</p>
Broberg, 2007	Cross-sectional survey	<p>Purpose: analyze experience and determine incidence of adverse events in patients with Eisenmenger syndrome who travel by air compared to controls with known congenital heart disease (CHD)</p> <p>Subjects: 53 adult patients with Eisenmenger syndrome, 48 acyanotic patients with known CHD</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcomes: Major adverse events requiring hospitalization: stroke, ischemic chest pain, syncope or heart failure Minor adverse events: headache, edema, supplemental oxygen</p>	<p>No difference was found between groups for use of supplemental oxygen during flight (1 of each group)</p> <p>Nonsignificant incidence in report of headache during flight (6/40, 9%) Eisenmenger and (4/48, 9%) control subjects)</p>	<p>●●○○ Low</p>

		required during flight		
Currie, 2007	Case Report	<p>Evaluation of two adult patients with history of chronic pneumothorax requesting fitness to fly exams</p> <p>Subject : 36 year old male smoker and 31 year old female smoker both with history of stable pneumothorax for &gt; 1 year</p> <p>Evaluation: review of history, clinical assessment, computed tomographic imaging, hypoxic challenge test and exposure to hypoxic hypobaric environment in a decompression chamber</p>	<p>Both patients sustained oxygen saturations &gt;90% during testing and were asymptomatic.</p> <p>Both patients successfully traveled by air without adverse events.</p> <p>Patients with closed chronic pneumothorax can fly without adverse consequences. Risk determination should be made through assessment, CT of chest, a hypoxic challenge test and simulation of flying at altitude in a decompression chamber with close monitoring of symptoms and oxygen saturation.</p>	●○○○ Very Low
Udomittipong, 2006	Cross-sectional retrospective review	<p>Purpose: identify clinical factors predictive of an in-flight oxygen requirement from a review of hypoxia challenge tests in infants referred for fitness to fly assessment</p> <p>Subjects: 47 infants with a history of neonatal lung disease not receiving O<sub>2</sub> at the time of hypoxia testing</p> <p>Intervention: Hypoxic challenge test</p> <p>Outcome: SpO<sub>2</sub>, pulse rate and activity state</p>	<p>81% of children studied exhibited desaturation below 85% during hypoxic testing despite all infants having normal room air SpO<sub>2</sub> ≥ 95%.</p> <p>Age at the time of hypoxia test significantly predicted the outcome of the hypoxia test (OR 0.82; 95% CI 0.62-0.95; p = 0.005).</p> <p>Children passing the hypoxia test were significantly older (12 months vs. 37 weeks) than those requiring in-flight oxygen (p&lt;0.0001).</p>	●●○○ Low
Kelly, 2006	Quasi-experimental	<p>Purpose: quantify the degree of desaturation in healthy subjects during a normobaric hypoxia inhalation test (NHIT) and air travel and to assess the validity of the NHIT when compared with actual in-flight responses</p> <p>Subjects: 15 health adults (age 23-57 years: 10 women) volunteers</p> <p>Intervention: NHIT (inspired oxygen 15%), cruising altitude in commercial aircraft</p>	<p>Significant desaturation was noted during NHIT (pre: 98 ± 2%; post 92 ± 2%) and at cruising altitude (pre: 97 ± 1%; post 92 ± 2%)</p> <p>No difference was found between the final NHIT SpO<sub>2</sub> and the mean in-flight SpO<sub>2</sub>.</p> <p>Significant difference</p>	●●○○ Low

		Outcomes: lung function, arterial blood gas, pulse oximetry. In-flight oxygenation was compared with preflight NHIT.	was noted between the lowest in-flight SpO <sub>2</sub> (88 ± 2%) versus the lowest NHIT SpO <sub>2</sub> (90 ± 2%)	
Almeida, 2006	Case study	71 year-old male experiencing right-sided chest discomfort shortly after take-off of a commercial flight, followed by headache and sudden loss of consciousness  48-72 hours patient admitted to prior treating facility was noted that CT scan performed prior imaging studies revealed a right pulmonary cyst	Authors posit that pre-existing intrapulmonary cyst expansion led to leakage of air into the surrounding vessels followed by brain gas emboli.	●○○○ Very Low
Humphreys, 2005	Prospective cohort study	Purpose: determine the degree of hypoxemia during short haul and long haul air travel  Subjects: 84 passengers (55 long haul > 2 hr duration and 29 short haul < 2 hr duration) aged 1-78 years. Subjects were anesthetists and their traveling companions; each passenger was their own control).  Intervention: travel by commercial air  Outcomes: SpO <sub>2</sub>	Statistically significant reduction in SpO <sub>2</sub> in all passengers traveling regardless of flight duration (p<0.05).  Mean ground level SpO <sub>2</sub> was 97% (93-100; 1.33) and at cruising altitude was 93% (85-98; 2.33)  54% of healthy passengers had SpO <sub>2</sub> ≤ 94% at cruising altitudes	●●○○ Low
Closon, 2004	Case Report	43 year-old male asthmatic smoker experiencing sudden loss of consciousness followed by dyspnea and agitation 20 minutes after take-off of a commercial flight.  Flight diverted and patient was admitted to ICU, CT scan demonstrated right lower lobe bulla.	Diagnosis of air embolism involving the brain and heart was made based on the presence of the pulmonary cyst.	●○○○ Very Low
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	Establish recommendations for fitness of passengers with pulmonary and other medical diseases to fly on commercial airlines  Studies utilized to establish recommendation were not identified in the report.	Ground level PaO <sub>2</sub> of >70 mm Hg does not require restriction.  PaO <sub>2</sub> of <70 mm Hg may be effectively managed with in-flight medical oxygen therapy.  Hypercapnea (elevated Pco <sub>2</sub> = poor pulmonary reserve and indicates potential risk at altitude, even with oxygen therapy.  Fitness to fly testing: Most practical: 50 yard walk without severe dyspnea	●○○○ Very Low



			<p>More sophisticated testing: hypoxia altitude simulation test or HAST. If <math>P_{aO_2}</math> is low during testing (<math>&lt;55</math> mm HG), medical oxygen must be considered.</p> <p>Asthma – air travel contraindicated if asthma is labile, severe or passenger has had recent hospitalization.</p> <p>COPD – preflight evaluation by <math>P_{aO_2}</math>, HAST or ability to walk &amp; climb stairs is extremely important</p> <p>Bronchiectasis and cystic fibrosis – no restriction if lung infection controlled and secretions are loose and clear</p> <p>Pneumothorax – travel contraindicated for 2-3 weeks after successful draining.</p> <p>Pleural effusion – delay travel for 14 days post drainage and clearance by CXR prior to travel</p> <p>Pulmonary vascular disease – medical oxygen, anticoagulation and restriction from exercise during flight to reduce risk of hypoxia-induced pulmonary vasoconstriction.</p>	
Lee, 2002	Prospective cohort study	<p>Purpose: determine the degree of oxygen saturation decline occurring in children during long-haul commercial air travel</p> <p>Subjects: 80 healthy children (43 boys) ages 6 mos – 14 years flying between Honolulu Hawaii and Taipei, Taiwan.</p> <p>Intervention: travel by commercial aircraft</p> <p>Outcomes: <math>SpO_2</math> and heart rate preflight at sea level compared to 3 hours and 7 hours in flight.</p>	<p>Mean <math>SpO_2</math> declined from mean sea-level <math>SpO_2</math> of 98.5 to 95.7% after 3 hours and 94.4% after 7 hours (<math>p&lt;0.001</math>).</p> <p>Mean heart rate (BPM) increased from sea level of 100 BPM to 105BPM after 3 hours and 108BPM after 7 hours of flight (<math>p&lt;0.001</math> and <math>p=0.01</math>)</p>	<p>●●○○ Low</p>

Evidence Table: Venous Thromboembolism(VTE)

Author/Year	Study Design Level of Evidence	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
MacCallum, 2011	Case-control study	Purpose: quantify the risks of VTE associated with both long-haul air travel and cumulative flying time.  Subjects: 550 VTE cases identified from practice records. 1971 controls.  Intervention: travel by commercial air  Outcomes: VTE, duration of travel	Patients flying >12 hours within 4 weeks before VTE had a threefold increase in the risk of VTE (OR 2.75, 95% CI, 1.44-5.28)  Patients flying >4 hours within 4 weeks before VTE had a two-fold increase risk of VTE (OR 2.2, 95% CI, 1.29-3.73)  No association between flying time and VTE was noted more than 12 weeks prior to VTE diagnosis.	●●●○ Moderate
Schreijer, 2010	Quasi-experimental	Purpose: determine if hypoxia, stress, inflammation or viral infection are contributors to the prothrombotic state in air travelers.  Subjects: 71 healthy adult volunteers  Interventions: 8 hour flight 8 hour movie marathon 8 hours of regular activities  Outcomes: Plasminogen activator inhibitor-1 (PAI-1), stress, plasma factor (F) VIII coagulant activity (FVIIIc), soluble P-selectine (sP-selectine), interleukin-8 (IL-8) and neutrophil elastase.	PAI-1 increased by 4.2ng mL <sup>-1</sup> (CI95:-49.5 to 6.5) in volunteers with an activated clotting system and decreased in those without (-20.0ng mL <sup>-1</sup> , CI95:-33.2 to -14.0). FVIIIc levels rose more in individuals with clotting activation (18.0%, CI 95:-1.0to 33.0) than in those without (2.0%, CI95: -2.0 to 5.0). The increases in FVIIIc were not associated with stress, which was found to be unrelated to clotting activation. sP-selectin increased in those with clotting activation (3.5 µg L <sup>-1</sup> , CI95:-3.0to 10.0) and decreased in those without (-0.5 µg L <sup>-1</sup> , CI95:-2.0to 2.0) No difference was found in change in level of neutrophil elastase or IL-8 between subject groups.  Results of the study do not support the hypotheses that stress, infection, or air pollution are involved in prothrombotic state development in air travelers.  The authors posited that after long haul air travel, patients with risk factors may have a more pronounced state which may be caused by hypoxia, triggering systemic inflammation and platelet activation resulting in coagulation induction and degranulation of platelets.	●●○○ Low
Chandra, 2009	Meta-analysis	Purpose: estimate the risk for VTE in travelers, determine whether a dose-response relationship exists and identify reasons for contradictory results in previous studies	Compared with non-travelers, the overall pooled relative risk for VTE in travelers was 2.0 (95%CI, 1.5-2.7).  Excluding studies that used referred control participants	●●●○ Moderate

		Data Synthesis: 1560 abstracts were identified of which 14 studies (11 case-control, 2 cohort and 1 case-crossover) met inclusion criteria including 4055 cases of VTE	<p>resulted in an increased pooled relative risk for VTE in travelers to 2.8 (95% CI, 2.2-3.7).</p> <p>A dose-response relationship was identified with an 18% higher risk for VTE for each 2-hour increase in duration of travel by any mode (<math>p = 0.010</math>) and a 26% higher risk for every 2 hours of air travel (<math>p = 0.005</math>).</p>	
Kuipers, 2007	Systematic review of the literature	<p>Purpose: quantify the risk of VTE after long-distance travel.</p> <p>Data Synthesis: 528 Abstracts were reviewed and screened to 10 case-control studies, 20 observational follow-up studies, 11 intervention studies and 14 pathophysiological studies.</p>	<p>Long distance travel increased the risk of VTE two to fourfold. The absolute risk of VTE within 4 weeks of flights longer than 4 hours is 1/4600 flights. The risk of severe pulmonary embolism (PE) occurring immediately after air travel increases with duration of travel from 0 in flights shorter than 3 hours up to 4.8 per million in flights lasting longer than 12 hours. The risk of fatal PE immediately after arrival is estimated at &lt;0.6 per million passengers in flights longer than 3 hours. The risk of VTE is not increased after travel shorter than 3-4 hours. The risk of asymptomatic VTE after long-haul flights ranged up to 12%.</p>	●●●○ Moderate
Schreijer, 2008	Case-control study	<p>Purpose: Evaluate the effect of flight-related behavior on the risk of VTE after air travel</p> <p>Subjects: 80 patients and 108 control subjects who had travelled more than 4 hours by plane within 8 weeks of the data collection.</p> <p>Intervention: travel by commercial air</p> <p>Outcomes: Venous thrombosis, anxiety, sleep, seat assignment, exercise, alcoholic beverage consumption</p>	<p>The risk of VTE was slightly lower in passengers who flew business class compared to economy class (OR 0.7; 95% CI: 0.2-1.8). Passengers seated in a window seat had a more than twofold increased risk of VTE than passengers who were seated at an aisle seat (OR 2.2; 95% CI: 1.1-4.4). Risk increased with obesity (BMI &gt; 39 kg/m<sup>2</sup>, OR 6.1; 95% CI: 0.5-76.2 after adjustment for age and gender) and was also increased in overweight participants (BMI 25-30 kg/m<sup>2</sup>, OR 2.6; 95% CI: 0.7-9.3).</p> <p>No increased risk was noted in passengers who were seated in the middle seat. The use of alcohol did not increase the risk of VTE. Drinking one glass of alcohol appeared to have a protective affect compared to non-alcohol drinkers (OR 0.5; 95% CI: 0.2-1.2).</p> <p>With every hour of sleep, the risk of VTE after air travel increased by 10% (OR 1.10; 95% CI: 0.2-1.2). Passengers who slept during the flight had a 1.5-fold increased risk of VTE compared to passengers who did not sleep during flight.</p> <p>Subjects who noted anxiety during travel had an increased relative risk of thrombosis of</p>	●●○○ Low

			2.5 (OR 2.5; 95%CI: 0.9-7.0).  Preventive measures of drinking non-alcoholic beverages, exercising during flight or wearing compression stockings did not have a protective effect.	
Kuipers, 2007	Cohort Study	Purpose: to assess the absolute risk of venous thrombosis after air travel  Subjects: 8,755 employees exposed to long-haul flight  Outcome: VTE	Incidence rate of 3.2/1000 PY compared to 1.0/000 PY in individuals not traveling by air (IRR 3.2, 95%CI: 1.8-5.6). The rate was equivalent to a risk of one VTE per 4,656 long-haul flights. Risk increased with exposure to more flights within a short time frame and with increasing flight duration. Higher risks were noted in travelers less than 30 years, women using oral contraceptives and individuals who were overweight, short or tall.	●●○○ Low
WHO, 2007	Meta-analysis	Purpose: confirm the risk of VTE is increased by air travel and determine the magnitude of risk, the effect of other factors on the risk and to study the effect of preventive measures on risk	Two-fold increased risk of VTE after long-haul flight of > 4 hours. Increased risk applied to other forms of travel (car, bus or train) where travelers were exposed to prolonged seated immobility. Risk increases with the duration of travel and with multiple flights over a short period. Obesity, height extremes, use of oral contraceptives and the presence of prothrombotic blood abnormalities were found to contribute to increased risk of travel-related VTE. The absolute risk of VTE per more than 4 hours flight in a cohort of healthy passengers was 1 in 6,000.	●●●○ Moderate
Philbrick, 2006	Systematic Review	Purpose: To review the methodologic strength of the literature, estimate the risk of travel-related VTE, evaluate the efficacy of preventive treatments and develop evidence-based recommendations for practice.  Study selection: all clinical studies reporting primary data concerning travel as a risk factor for VTE or testing preventive measures for travel-related VTE were included  Data Synthesis: 25 studies met inclusion criteria – 6 case control studies, 10 cohort studies and 9 randomized controlled trials.	Method of screening for VTE (ultrasound versus clinical assessment, OR 390), outcome measure (all VTE compared to PE only, OR 21), duration of travel (<6 hours compared to 6-8 hours, OR 0.011) and clinical risk (higher compared to lower OR 3.5) were significantly related to VTE rate.  Graduated compression stockings prevented travel-related VTE (p<0.05 in 4 of 6 studies). Aspirin and low-molecular-weight heparin failed to demonstrate significant protective benefits in any of the studies.	●●●○ Moderate
Aryal, 2006	Literature Review	Purpose: to quantify the risk of VTE following air travel and assess methods of prevention  Study Selection: 43 studies were found relevant to the study variables, 18 of which met the inclusion	An association of VTE with air travel was found to have a pooled odds ration 1.59 (CI 1.04-2.43) from three case control studies and a relative risk of 2.93 (CI 1.5-5.58) in two cohort studies.	●●○○ Low

		<p>criteria – 5 case control studies, 2 controlled cohort and 8 randomized controlled trials.</p> <p>Outcome: VTE with air travel</p>	<p>The incidence of pulmonary embolism increases when the distance travelled is more than 5,000 miles (1.5 PE per million passengers) or the flight time is more than 8 hours in duration (2.57 PE/1 million passengers).</p> <p>The quantitative risk of lower limb VTE after long haul flights in high risk-subjects was 5% per flight and 1.6% per flight in low risk subjects.</p>	
Schwarz, 2003	Prospective, controlled cohort study	<p>Purpose: To assess the incidence of venous thrombosis with long-haul flights</p> <p>Subjects: 964 passengers with flight durations <math>\geq</math> hours and 1213 non-traveling control subjects.</p> <p>Intervention: travel by commercial air</p> <p>Outcome: Venous thrombosis diagnosed by ultrasound Symptomatic pulmonary embolism and death</p>	<p>The risk of venous thrombosis after air travel of <math>\geq</math> 8 hours duration was double for isolated calf muscle venous thrombosis when compared to non-traveling controls (RR 2.83, 95% CI, 1.46-5.49)</p> <p>Symptomatic pulmonary embolism occurred in only 1 passenger (p=.44)</p>	<p>●●○○ Low</p>
Jacobson, 2003	Prospective study	<p>Purpose: To determine the incidence of DVT in low and intermediate-risk passengers comparing passengers travelling in business and economy class.</p> <p>Subjects: 434 subjects</p> <p>Outcomes: DVT as diagnosed by ultrasound, D-dimer levels</p>	<p>No passengers developed VTE by ultrasound.</p> <p>10% of passengers travelling by air had elevated D-dimer levels upon arrival at destination regardless of class travelled by air (OR 0.61, p=0.038).</p>	<p>●●○○ Low</p>

Evidence Table: Blood Disorders

Author/Year	Study Design Level of Evidence	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	Establish a guide to the timeframe that should elapse between a medical event and commercial air travel  Studies utilized to establish recommendation were not identified in the report.	Patients with hemoglobin levels <9.5 g/dl should defer travel until hemodynamically stable. If acutely anemic, Hgb level should be assessed more than 24 hrs after last  Sickle Cell Disease- travel is not recommended within 9 days of sickling crises. Travel clearance can be provided after 10 days. Oxygen supplementation is always needed.  All conditions not meeting above requirements for clearance should have "assessment by a doctor with aviation medicine experience" (IATA, 2011 p. 54-55).	●○○○ Very Low
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	Establish recommendations for fitness of passengers with pulmonary and other medical diseases to fly on commercial airlines  Studies utilized to establish recommendation were not identified in the report.	Special consideration should be given to anyone with a hemoglobin below 8.5 g /dl due to increased risk of lightheadedness or loss of consciousness during flight, particularly with physical exertion during flight.  Sickle cell disease, may be exacerbated by reduced oxygen Pressures during flight. Because such a crisis could be life-threatening, sickle cell patients should be advised not to travel by air without medical oxygen.	●○○○ Very Low

Evidence Table: Neurologic Disorders

Author/Year	Study Design  Level of Evidence	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
Berilgen, 2011	Retrospective Case Reviews	<p>Purpose: To determine if there are specific characteristics of headaches associated with air travel</p> <p>Subjects: 22 cases of headache referred to an outpatient Neurology clinic</p> <p>Outcome: ENT examination, Neurologic examination, Brain MRI &amp; MRA, CT of paranasal sinus, description of headache by timing, location, quality, intensity, duration, accompanying symptoms, pre-existing diseases and other primary headache history</p>	<p>Airplane headache characterized as starting suddenly during ascent and/or descent of the aircraft, mean duration 20 minutes, usually unilaterally and commonly localized to the periorbital region. Described as severe, stabbing or jabbing, and generally subsides in a short time period.</p> <p>Authors proposed that headache associated with airplane travel results from the temporary local inflammation caused by hypoxia or dryness in the sinus mucosa or sinus barotraumas.</p> <p>All 22 subjects reported headache during flight. Headache associated with airplane travel did not occur in 95% of the patients in subsequent flights when they received naproxen sodium (550mg) 1 hour prior to take off.</p>	●○○○ Very Low
Arnaiz, 2011	Case report	52 year old woman who experienced sudden episode of dyspnea and a 5-minute generalized tonic-clonic seizure followed by loss of consciousness. The patient had experienced two similar episodes on prior flights and had no non-flight related seizure activity.	CT of head revealed small corticosubortical gas emboli and subsequent thoracic CT demonstrated a large bronchogenic cysts on the right lung.	●○○○ Very low
Alonso-Canovas, 2011	Prospective analysis of registry of referred patients	<p>Purpose: To study neurological problems associated with air travel</p> <p>Subjects: 77 patients with neurologic problems associated with air travel</p> <p>Outcomes: Seizures, stroke, alternative diagnosis</p>	<p>53.2% (41/77) presented with seizures of which 61% (25) had no prior seizure history. Long flight duration was noted in 53.6% of the cases. 56.6% (19) subjects had a history of regular or recent use of drugs , especially alcohol (14; 34.1%). 51.2 % (21) had a single seizure, 31.7% (13) multiple and 17.1% (7) had status epilepticus. Of the 13 patients with known epilepsy, 10 had missed doses of antiepileptics in prior days, 4 had sleep deprivation and 3 had used recreational drugs</p>	●●○○ Low

			<p>Stroke 23.4% (18/77) had diagnoses of stroke. Of those affected hypertension was noted in 10, tobacco use in 4, cardiopathy with high embolic risk in 4, hypercholesterolemia in 3 and diabetes mellitus in 1. 10.4% (8 patients) had an ischemic stroke and 10.4% (8 patients) patients had an intracranial hemorrhage.</p> <p>26% (20/77) cases had an alternative diagnosis: drug toxicity (4), non-organic symptoms (4), syncope (2), peripheral neuropathy (2), delirium (2), neoplasms of the CNS (2), viral meningoencephalitis (1), chronic stroke (1), migraine with aura (1) and transient global amnesia (1)</p>	
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	<p>Establish a guide to the timeframe that should elapse between a medical event and commercial air travel</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Patients are cleared to fly without restriction who have the following respiratory conditions:</p> <p>Transient Ischemic Attack – 2 days after evaluation</p> <p>CVA 5-14 days if stable or improving with a nurse escort. Supplemental oxygen is recommended the first 2 weeks after stroke</p> <p>Grand mal fit <math>\geq</math> 24 hours if generally well controlled</p> <p>Cranial surgery <math>\geq</math> 10 days, cranium free of air and adequate general condition.</p> <p>All conditions not meeting above requirements for clearance should have “assessment by a doctor with aviation medicine experience” (IATA, 2011 p. 54).</p>	●○○○ Very Low
Parees, 2010	Case Report	44 year old woman with an acute anterior circulation stroke after a transatlantic flight.	CT and MRA revealed a single pulmonary arteriovenous malformation in the lower right lung lobe.	●○○○ Very low
Ipekda, 2010	Case Report	Three cases of airplane headache were reported on in children ages 12, 13, & 14	Barotrauma due to nasal mucosal inflammation, adenoidal and tonsillar hypertrophy and sinusitis were found to be the causative factors for the airplane headache.	●○○○ Very low
Domitrz, 2010	Case Report	Case report of a “young man” with airplane headache	Author posits that pathophysiology of airplane headache is unclear and secondary causes must be ruled out.	●○○○ Very low



Seth, 2009	Case Report	51-year-old male post craniotomy for a glioblastoma multiforme and the determination of fitness to fly	The authors noted concerns for post-surgical pneumocephalus based upon literature review encountering only case reports and posited that the absence of any intracranial air is the best indicator of fitness to fly.	●○○○ Very low
Almeida, 2007	Case Report	62-year-old female who became unresponsive and rigid 20 minutes into a commercial flight from Denver to Omaha	Bilateral acute infarcts associated with cerebral edema secondary to air emboli were noted on CT of the head. CT of the chest with contrast revealed a large thin-walled cystic lesion with a small air-fluid level consistent with the diagnosis of congenital cystic adenomatoid malformation.	●○○○ Very low
Mainardi, 2007	Case Report	A case of airplane headache was reported in Italy	First Italian reported case of a headache consistent with the characteristics of airplane headache.	●○○○ Very low
Aquilina, 2006	Case Reports	Two case reports of air travelers – an 81-year-old male and a 74-year old female who experienced cognitive impairment precipitated by travel	Both cases had an association between air travel and a sudden decline in cognitive function which presented initially as delirium. The only diagnostic changes found on examination were cerebral ischemia and partial improvement occurred in both cases after several months.	●○○○ Very low
Berilgen, 2006	Case Reports	Six case reports of headache associated with airplane travel	All patients were male, suffering from severe, short lasting, unilateral, periocular localized cluster-like headaches. None of the patients had a prior history of cluster headache. Attacks lasted between 15-20 minutes and resolved spontaneously.  The authors posit that barotraumas caused by changes in cabin pressure during take-off and landing could affect the ethmoidal nerves and/or nociceptors in the ethmoidal arteries activating the trigeminovascular system resulting in headache.	●○○○ Very low
Trevorrow, 2006	Prospective survey	Purpose: determine if air travel increases seizure activity both during and after flying, and to identify flight characteristics that promote increased seizure activity  Subjects: 37 patients with known seizure diagnosis  Intervention: travel by commercial aircraft	Seizures were significantly more common after flying ( $p=.02$ ).  No in-flight seizure activity was noted by participants  Participants experiencing an increase in seizure frequency had: a higher baseline seizure frequency ( $p = .004$ ), were more likely to have experienced increased seizure activity after flying ( $p= .001$ ), were more worried about having a seizure while flying	●●○○ Low

		Outcomes: Self-monitored seizure activity	(p=.001) and were more likely to avoid air travel (p=.02). There was no significant correlation between distance traveled, time zones crossed, duration of flight or direction of flight with increased seizure activity.	
Belvis, 2005	Case Report	36-year-old female with no significant medical or family history had onset of dyspnea followed 20 minutes later by depressed level of consciousness, right hemiparesis and global aphasia after an 11.35 hour flight from Peru to Spain.	A pulmonary scintigraphy demonstrated a pulmonary thromboembolism and a cranial MRI revealed ischemic infarct in the left middle cerebral artery.  The authors posit that the appearance of a stroke following long-haul travel was suggestive of paradoxical embolism through a patent foramen ovale.	●○○○ Very low
Kakkos, 2003	Case Report and literature review	49-year-old male who collapsed two days after traveling by air for 19 hours from Alaska to London.	The authors located 12 similar cases of stroke occurring in close approximation to long-haul flight travel. Venous thromboembolism was present in 58% and patent foramen ovale was diagnosed in all but one case.	●○○○ Very low
Foerch, 2003	Case Reports	Report of three long-distance air passengers (ages 21, 63 & 64 years) with first-time neurological deficits that occurred during long-haul flights	Embolitic cerebral ischemia with persistent foramen ovale was found by MRI in all three cases. No venous thrombosis was found on scans of the patient's legs.	●○○○ Very low
Lapostolle, 2003	Case Reports	Four cases of stroke associated with pulmonary embolism and deep venous thrombosis associated with long-haul travel	Patent foramen ovale was found to be the mechanism for ischemic stroke in all four cases.	●○○○ Very low
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	Establish recommendations for fitness of passengers with neurologic and other medical diseases to fly on commercial airlines  Studies utilized to establish recommendation were not identified in the report.	Patients with epilepsy can fly safely but should be made aware of the potential seizure threshold-lowering effects of fatigue, delayed meals, hypoxia and disturbed circadian rhythm if passing through multiple time zones.  Patients who have had a recent cerebral infarction or other acute neurological event should not travel until neurological condition is stable.	●○○○ Very Low
Sirven, 2002	Retrospective review of medical incidents that led to flight diversions	Purpose: analyze the frequency of neurologic events during commercial airline flights and to assess whether onboard emergency medical kits were adequate for in-flight	Neurologic symptoms were the most frequent source of emergency calls and the fourth most likely cause for flight diversion.  Incidence of symptoms: Dizziness/vertigo (354) Seizures (131)	●●○○ Low

		<p>neurologic emergencies.</p> <p>Subjects: 2,042 medical incidents leading to 312 diversions between 1995-2000 reported to the Mayo clinic air-to-ground medical service</p> <p>Outcomes: Neurologic symptoms reported in-flight</p>	<p>Headache (37) Loss of consciousness/syncope (34) Pain (no organ system) (25) CVA (21) Confusion (6) Numbness (6) Tremor (2)</p> <p>The authors posited that pressurization of the cabin, turbulence and hypoxemia may be causative factors for neurologic symptoms in-flight</p>	
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Evidence Table: Ophthalmology, Otolaryngology & Allergy

Author/Year	Study Design  Level of Evidence	Study Purpose/ Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	Establish a guide to the timeframe that should elapse between a medical event and commercial air travel  Studies utilized to establish recommendation were not identified in the report.	Patients are cleared to fly without restriction who have the following conditions:  Otitis Media & Sinusitis – if able to clear ears and not acutely ill  Middle ear surgery $\geq 10$ days post operatively with medical certificate from treating ENT  Tonsillectomy $\geq 4$ days  Wired Jaw – if escorted with cutters or self quick release wiring  Penetrating eye injury $\geq 7$ days after injury  Intra-ocular surgery $\geq 7$ days post operative  Cataract surgery $\geq 24$ hour  Corneal laser surgery $\geq 24$ hour  All conditions not meeting above requirements for clearance should have “assessment by a doctor with aviation medicine experience” (IATA, 2011 p. 54-55).	●○○○ Very Low
Bayer, 2008	Longitudinal cohort	Purpose: to investigate the effect of air flight on intraocular pressure (IOP)  Subjects: 25 healthy volunteers  Intervention: Cruising cabin pressure of 8,000ft  Outcomes: Change in IOP	Baseline IOP $14.2 \pm 2.7$ mmHg. Non-significant reduction at reaching cruising altitude $-0.2 \pm 2.7$ mmHg (-1.4%).  Significant IOP reduction $12.3 \pm 2.5$ mmHg (-13.4%) on the second hour of flight ( $p=0.005$ ) and after landing $12.0 \pm 1.7$ mmHg (-15.8%) ( $p=0.001$ ).	●●○○ Low
Comstock, 2008	Cross-sectional survey	Purpose: Characterize reactions to foods experienced by passengers on commercial planes  Subjects: 41 respondents with known nut and seed allergy  Outcome:	9% (41/471) respondent's self-reported nut and seed allergy associated with air travel. 10% (4/41) had experienced more than one reaction on an airplane.  Mode of exposure: 58% (n=26) inhalation, 9% (n=4) contact, 33% (n=33%) ingestion.	●○○○ Very Low

		Self-report of allergic symptoms and severity or reaction by symptoms of pruritus, urticaria, flushing, angioedema, nasal congestion, sneezing, nausea vomiting, throat tightness or throat pruritus, diarrhea, hoarseness, wheezing, cyanosis, mild hypotension or light-headedness, respiratory arrest, severe hypotension or loss of consciousness	<p>63% reported carrying epinephrine although 80% had been given a prescription.</p> <p>Peanuts were the primary cause of reaction (73%) followed by tree nuts (18%), sesame seeds (4.5%) and mixed nuts (4.5%).</p> <p>80% of reactions during flight caused moderate-to-severe symptoms by self-report</p> <p>29% (12/41) individuals reported the reaction to a flight attendant</p> <p>32% (11/34) experiencing moderate to severe reactions reported the reaction a flight attendant.</p>	
Mahmood, 2003	Cross-sectional survey	<p>Purpose: to determine current professional advice to patient related to air travel following zygomatic fractures</p> <p>Subjects: 184 oral and maxillofacial surgeons (OMFS) in the United Kingdom. 71% response rate 184/261 questionnaires sent.</p> <p>Outcomes: Length of time to refrain from travelling by air</p>	<p>No restrictions were advised by OMFS for:</p> <p>40% open reduction and internal fixation</p> <p>42% closed reduction</p> <p>47% non-operative management</p> <p>30% advised delay of travel for 8-14 days</p> <p>15% advised delay of travel for 3-8 weeks</p>	●●○○ Low
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	<p>Purpose: establish recommendations for fitness of passengers with medical diseases and conditions to fly on commercial airlines</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	Post-op facial plastic surgical procedures, tonsillectomy & adenoidectomy, palatoplasty, nasal or facial fractures can fly once postoperative bleeding risk has passed after clearance by their surgeon (usually 1-2 weeks).	●○○○ Very Low
Monaghan, 2002	Case Report	<p>Report of orbital emphysema caused by pressure changes during air travel</p> <p>Subject: 21 year old male</p>	<p>Subject hit his face on a curb resulting in laceration repair and routine radiological examination after injury. Subject flew 2 days post-injury and developed intense pain in the affected eye and edema of the periorbital tissues with residual double vision and eye pain.</p> <p>Post-flight CT revealed an orbital floor fracture with large quantities of intraorbital air with proptosis of the</p>	●○○○ Very Low

			globe	
Jassar, 2001	Controlled cohort study	<p>Purpose: evaluate whether air travel affects graft take rates after myringoplasty</p> <p>Subjects: 37 adult and pediatric post-myringoplasty subjects who traveled by air within a week of surgery compared with 37 matched non-traveling post-myringoplasty</p> <p>Intervention: 45-60 minute flight duration</p> <p>Outcome: Graft status at first follow-up</p>	<p>No difference in take rates between study and control groups (<math>p=0.32</math>)</p> <p>95% CI of difference in take rates were -9% (flying group 9% worse) to 27% (flying group 27% better).</p>	<p>●○○○ Very Low</p>
Mills, 2001	Nonrandomized comparative trial	<p>Purpose: To investigate the safety of air flight for patients with small volumes of residual postoperative intraocular gas</p> <p>Subjects: 17 eye (9 gas filled (7 with 10-15% gas volume and 2 with 20% gas volume) and 8 control eyes) of nine eye patients and one eye of one control subject</p> <p>Outcome: absolute and percentage change in IOP with varied cabin pressure</p>	<p>Results of 10-15% gas volume group: IOP increased an average of 109% from baseline during ascent to an average cabin altitude of 7429 ft. IOP decreased to 30% above baseline during cruise altitude and further decreased to an average of 38% below baseline on return to baseline altitude.</p> <p>Results for 20% gas volume group: IOP raised an average of 84% from baseline during ascent and dropped to an average of 42% below baseline on return to baseline altitude.</p> <p>IOP in the contralateral control eyes did not vary with altitude changes.</p>	<p>●●○○ Low</p>

## Evidence Table: Pregnancy

Author/Year	Study Design  Level of Evidence	Study Purpose/ Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	Establish a guide to the timeframe that should elapse between a medical event and commercial air travel  Studies utilized to establish recommendation were not identified in the report.	Clearance not required before 36 weeks for single, uncomplicated pregnancy or before 32 weeks for multiple, uncomplicated pregnancy but doctors certificate needed after 28 weeks.  Assessment by a doctor with aviation medicine experience is recommended beyond the end of the 32 <sup>nd</sup> week for multiple uncomplicated, beyond the end of the 36 <sup>th</sup> week of Gestation. For single, uncomplicated pregnancy, and for miscarriage (threatened or complete) with active bleeding.	●○○○ Very Low
Magann, 2010	Literature review	Purpose: Examine current information available on air travel and pregnancy outcomes for the frequent air traveler, flight attendant and female aviator.  Sample: 128 abstracts evaluated, 9 of which evaluated air travel and pregnancy outcomes  Outcomes: spontaneous pregnancy loss (SAB), intrauterine fetal demise (IUFD), low birth weight (<10 <sup>th</sup> percentile), preterm delivery and neonatal intensive care unit admissions.	Risk of pregnancy loss (SAB or IUFD) was greater in flight attendants than controls (OR 1.52, 95% CI; 1.29, 2.04). Meta-analysis of data on SAB alone did not reveal significant differences in flight attendants when compared to controls  Risk of preterm birth <37 weeks greater in passengers than controls (OR 1.44, 95% CI; 1.07, 1.93)  No increased risk noted for preeclampsia, neonatal intensive care unit admissions, or low birth weight noted among groups.	●●○○ Low
ACOG, 2009	Advisory Committee Opinion	Purpose: Consensus statement on risk of air travel during pregnancy  Studies utilized to establish recommendation were not identified in the report.	In the absence of obstetric or medical complications occasional air travel is safe for pregnant women.	●○○○ Very Low
RCOG, 2008	Advisory Committee Opinion	Purpose: Consensus statement on risk of air travel during pregnancy  Studies utilized to establish recommendation were not identified in the	There is no specific risk to pregnancy associated with air travel.  For women with uncomplicated pregnancy and no medical or obstetric risk factors for complications that would contraindicate air travel, there is no indication	●○○○ Very Low

		report.	to advice against commercial air travel.	
Chibber, 2006	Case-control survey	<p>Purpose: Assess whether air travel increases the risk of adverse pregnancy outcomes</p> <p>Subjects: 992 women admitted for delivery at a Saudi Arabian hospital within a 12 month period. 55% (546) traveled at least once during pregnancy, 45% (447) controls who did not travel</p> <p>Outcomes: pre-eclampsia, vaginal bleeding, birth &lt;34 weeks, birth &gt;34 weeks &lt;37 weeks, birth weight &lt;10 centile, cesarean section, admission to NICU, stillbirth, and neonatal death</p>	<p>Among primagravidae women who traveled by air there was an increased risk of preterm birth &gt;34 weeks &lt;37 weeks when compared to controls (OR 1.5; 95% CI, 1.2, 1.8).</p> <p>Preterm birth was noted to be more frequent among expatriate women traveling long distances and frequent flights during pregnancy.</p> <p>No other outcomes had significant increased risk between groups</p>	●●○○ Low
Freeman, 2004	Retrospective analysis	<p>Purpose: To evaluate if air travel affects pregnancy outcome</p> <p>Subjects: 222 women admitted for delivery at a gestational age &gt;20 weeks over a 6-month period. 53% (n=118) traveled at least once during pregnancy</p> <p>Outcomes: gestational age at delivery, neonatal birthweight, vaginal bleeding, preterm delivery &lt; 37 weeks, preeclampsia, neonatal intensive care unit admission or cumulative adverse obstetric outcome</p>	There were no statistical differences in pregnancy outcomes between traveling and non-traveling women	●●○○ Low
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	<p>Establish recommendations for fitness of pregnant passengers with and those with other medical diseases to fly on commercial airlines</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	No increased risk from commercial aircraft environment to normal pregnancy.	●○○○ Very Low



Evidence Table: Psychological Disorders

Author/Year	Study Design Level of Evidence	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
IATA, 2011	Executive summary of the International Air Transport Association of travel restrictions based on expert opinion	Establish a guide to the timeframe that should elapse between a medical event and commercial air travel  Studies utilized to establish recommendation were not identified in the report.	Patients are cleared to fly without restriction who have the following psychiatric conditions:  Chronic psychiatric disorders – properly controlled by medication and stable  Acute psychosis and unstable chronic psychiatric disorders should be assessed by a doctor with aviation medicine experience	●○○○ Very low
Bor, 2003	Retrospective study	Evaluation of 487 incidences of physical violence on board British aircraft. 48%; (236/487) involved passengers.	Use of alcohol 45% and illegal smoking in the aircraft toilet 36% were the two main factors  Disruptive passenger profiles were consistent over the four year reporting period: 74-78% male 75% between ages 30-49 years 5% business or first class passengers  On average 22 passengers/year required physical restraint	●○○○ Very low
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	Establish recommendations for fitness of passengers with medical diseases to fly on commercial airlines  Studies utilized to establish recommendation were not identified in the report.	Persons with psychiatric disorders whose behavior is unpredictable, aggressive, disorganized, disruptive or unsafe should not travel by air. Patients with psychotic disorders who are stabilized on medication and are accompanied by a knowledgeable companion may be able to fly. (ASMA, 2003, p. A13)	●○○○ Very low
Smart, 2003	Case Reports	Analysis of 29 air rage cases reported to Canadian Press from 1998-2000	Use of excessive alcohol and tobacco smoking were most important precipitating factors.	●○○○ Very low
Matsumoto, 2001	Retrospective study	Purpose: Ascertain the incidence of in-flight psychiatric emergencies, their associated factors and outcomes.	3.5% (48/1375) calls were categorized as psychiatric emergencies.  Mean age of affected	●○○○ Very low

		<p>Subjects: 1375 in-flight calls for physician consultation of company providing consult to 24% of the flights within the U.S. during the time of the events.</p> <p>Outcomes: events categorized as psychiatric/psychological emergencies</p>	<p>passenger was 39.6 yr, median 35 yr</p> <p>73% of calls (35/48) were for female passengers</p> <p>90% (43/48) were for anxiety 4% (2/48) psychosis 4% (2/48) non-psychotic disruptive passenger 2% (1/48) conversion disorder No incidences of air rage or other aggressive behaviors were reported.</p>	
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Evidence Table: Diabetes

Author/Year	Study Design Level of Evidence	Study Purpose/Study Sample Study Intervention Study Outcome	Results	GRADE Quality of Evidence
King, 2011	Quasi-experimental	<p>Purpose: study the effects of atmospheric pressure during airplane flight on insulin pump delivery</p> <p>Subjects: 10 insulin pumps(5 Animas 2020 and 5 Medtronic Paradigm)</p> <p>Intervention:</p> <p>Outcome: insulin delivery</p>	<p>During ascent both pumps delivered excess insulin (Animas 1.37 units (u) and Medtronic 1.01 u) (P&lt;.001)</p> <p>During descent both pumps delivered a deficit of insulin (Animas 0.87 u and Medtronic 0.58 u) (P&lt;0.01)</p> <p>Unintended insulin delivery was determined to be due to air coming out of the solution and forming bubbles when the pressure decreased. Bubbles displace insulin in the pump causing excess delivery. During descent, increase in air pressure leads to the bubbles redissolving which stops insulin delivery until the deficit is replaced. Mechanical function was not affected by changes in ambient pressure.</p>	●●●○ Moderate
Hinninghofen, 2006	Two by two repeated measurement design  Simulated in hypobaric chamber	<p>Purpose: To evaluate the effects of altitude and diet on gastric emptying cardiovascular function and bodily complaints</p> <p>Subjects:16 healthy volunteer adults</p> <p>Intervention: Hypobaric chamber simulated flight altitude of equivalent to 8200 ft</p> <p>Outcomes: Heart rate, gastrointestinal symptoms of distension, bloating, belching and gastric emptying assessed by 13C-octanoic acid breath test.</p>	<p>Heart rate increased throughout the simulation independent of the dietary condition. (p=0.011)</p> <p>At 8200 ft altitude gastric emptying was significantly delayed when a high-fiber meal was given (<math>146.3 \pm 48.4</math> min low fiber vs. <math>193.9 \pm 54.3</math> m high fiber; p= 0.039).</p> <p>The symptom score for gastric distention (<math>1.33 \pm 0.3</math> vs. mean <math>1.07 \pm 0.15</math>; p = 0.022) and bloating (<math>1.82 \pm 0.47</math> vs. mean <math>1.34 \pm 0.35</math>; p=0.015) were also significantly increased at 8200 ft altitude for the high-fiber meal compared with the low-fiber meal.</p>	●●●○ Moderate
Burnett, 2006	Census study self-administered questionnaire	<p>Purpose: To determine types of problems experienced by people with diabetes mellitus while traveling by air</p> <p>Subjects: 493 (37.1% response rate) patients using insulin from a clinic in Aberdeen UK over a</p>	<p>94% denied experiencing problems related to air travel. Those with difficulty noted difficulty in obtaining diabetic meals ordered or low blood sugar due to delay in meal delivery.</p> <p>91% carried food with</p>	●●●○ Low

		<p>period of 3 months</p> <p>Outcomes: hypoglycemia</p>	<p>them for the journey. More men than women did not take additional food (<math>\chi^2 = 5.54</math>, <math>p = 0.019</math>).</p> <p>15% of insulin users did not inform any airline personnel of their diabetes. 8 patients (<math>\chi^2 = 4.84</math>, <math>p = 0.028</math>) did not carry identification of their disease on their person.</p> <p>20.1% of long-haul travelers and 32.1% of short-haul travelers experienced delays. 10% of delayed travelers experienced difficulties due to late meals as a result of the delay.</p> <p>10.2% of both long and short haul travelers experienced hypoglycemia while traveling abroad and for the first 24 hours after arrival. Hypoglycemia was more likely to be delayed until the first 8 hours after arrival at the destination in the long-haul group and was less likely to be severe. 31% of those experiencing hypoglycemic symptoms described them as severe and requiring help.</p> <p>Hyperglycemia while traveling was more likely to occur in long-haul travelers than short-haul travelers (<math>\chi^2 = 10.1</math>, <math>p=0.00</math>)</p> <p>50% of long-haul and 41.6% of short-haul travelers sought advice about managing their diabetes while traveling</p>	
ASMA, 2003	Recommendations based on expert opinion for primary care and specialist physicians to advise patients with medical conditions	<p>Establish recommendations for fitness of passengers with medical diseases and conditions to fly on commercial airlines</p> <p>Studies utilized to establish recommendation were not identified in the report.</p>	<p>Diabetic travelers under reasonable control can fly anywhere safely if they plan in advance and discuss the proposed journey with their healthcare provider.</p> <p>Travel crossing several time zones and depending on the direction traveled may shorten or lengthen the 24 hour day which may require adjustments in insulin regimens.</p> <p>The use of short-acting soluble insulin or fast-</p>	<p>●○○○ Very low</p>

			<p>acting insulin analogues during long flights is recommended.</p> <p>Traveling east the day is shortened by 2 hours and there may be the need to take fewer units of intermediate or long acting insulin. Conversely traveling west may require supplemental injections or increased dosing of insulin.</p> <p>On the first morning of eastbound travel at the end destination 2/3 dose of the usual morning dose of insulin should be taken to account for the decreased hours since the previous morning's injection. When traveling westbound, no adjustments in daily dosing need to be made.</p> <p>Type 1 diabetics should carry additional carbohydrate to cover meal delayed meals, should consider alerting flight crew to their condition and should have accessible identification on their person.</p>	
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## APPENDIX G: CLINICAL PRACTICE GUIDELINE

### Guideline Title

Guideline for Passenger Fitness to Fly Evaluation in Primary Care

### Bibliographic Source

Pending acceptance by peer-reviewed journal

### Guideline Status

This is the current recommendation report pending review by expert panel prior to dissemination.

### FDA Warning/Regulatory Alert

Not applicable as no drugs or devices are recommended in this guideline

### Scope

#### Disease/Condition(s)

- Cardiovascular disease (CVD)
- Pulmonary disease
- Deep Vein Thrombosis/Venous Thromboembolism
- Neurologic disease
- Ear, eye, nose and throat disease
- Pregnancy
- Psychiatric disorders
- Diabetes mellitus

#### Guideline Category

Counseling  
Evaluation  
Management  
Prevention  
Risk Assessment  
Screening

#### Clinical Specialty

Family Practice  
Internal Medicine  
Obstetrics  
Pediatrics

Preventive Medicine  
Travel Medicine

**Intended Users**

Advanced Practice Nurses  
Health Care Providers  
Physician Assistants  
Physicians

**Guideline Objective**

- To identify medical conditions that may be affected by the physiologic and pathologic effects of commercial air travel
- To assist the primary care provider in making fitness to fly decisions to improve practice

**Target Population**

Any patient planning commercial air travel particularly those with pre-existing medical conditions

**Interventions and Practices Considered**

1. Screening for pre-existing medical conditions that may be adversely affected by commercial air travel
2. Assessment of fitness to fly

**Management/Prevention**

1. Management of specific patient populations
  - Patients with cardiovascular conditions
  - Patients with respiratory conditions
  - Patients with risk for venous thromboembolism
  - Patients with neurologic conditions
  - Patients with eye, ear, nose and throat conditions
  - Patients who are pregnant
  - Patients with psychiatric conditions

**Major Outcomes Considered**

- Morbidity and Mortality associated with commercial air travel
- Quality of life
- Adherence to lifestyle modifications

**Methodology**

**Methods Used to Collect/Select the Evidence**

Searches of Electronic Databases

**Description of Methods Used to Collect/Select the Evidence**

Medline, PubMed, the Cochrane Library CINAHL (EBSCOHost), and other electronic sources for admissible evidence or studies published between February 2001 and February 2012. Search terms included air, plane, aircraft, travel, airline, fitness to fly, commercial air, hypoxia, hypoxemia, pre-flight, post-flight, cardiovascular, circulatory, blood, hematology, anemia, pulmonary, COPD, respiratory, asthma, restrictive lung, non-restrictive lung, neurologic, neurology, central nervous system, gastrointestinal, abdomen, ear, nose, throat, psychiatric, anxiety, psychosis, eye, ophthalmologic, pregnancy, children, pediatric, orthopedic, surgical, surgery, trauma, disease, infection, pain, and prevention. Identified studies were limited to those written in English or with available English translations. Expert opinion and guidelines developed by other sources were included in the guideline development and all efforts were made to correlate opinion and published guidelines to primary sources of research.

### Number of Source Documents

72 articles were included in the evidence review.

### Methods Used to Assess the Quality and Strength of the Evidence

Weighting according to the Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

Level of evidence	Qualifying Studies
<b>High (4)</b> ●●●●	High-quality, multi-centered or single-centered, randomized controlled trial with adequate power; or a systematic review of these studies
<b>Moderate (3)</b> ●●●○	Lesser-quality, randomized controlled trial; prospective cohort study; or a systematic review of these studies
<b>Low (2)</b> ●●○○	Retrospective comparative study, case-control study or a systematic review of these studies
<b>Very Low (1)</b> ●○○○	Case reports, expert opinion or evidence based on physiology

\*Evidence level can be increased or decreased based upon study quality directness and strength of association.

### Methods Used to Analyze the Evidence

Systematic Review

### Description of the Methods Used to Analyze the Evidence

The supporting literature was critically appraised for study quality according to criteria referenced in key publications on evidence-based practice. Depending on the study design and quality, each reference was assigned a corresponding level of evidence (High-Low) and the evidence was synthesized into practice



recommendations.

### Methods Used to Formulate Recommendations

Expert Consensus (pending)

### Description of Methods Used to Formulate Recommendations

Systematic Review

### Rating Scheme for the Strength of the Recommendations

Grade	Descriptor	Qualifying Evidence	Implications for practice
A	Strong Recommendation	Level 4 evidence or consistent findings from multiple studies of levels 3, 2 or 1	Primary care providers should follow a strong recommendation unless a clear and compelling rationale for alternative approach is present
B	Recommendation	Levels 3, 2 or 1 evidence and findings are generally consistent	Primary care providers should follow a recommendation but should monitor new information and be sensitive to patient preference.
C	Option	Levels 3, 2 or 1 evidence and findings are inconsistent	Primary care providers hold be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
D	Option	Little or no systematic empirical evidence	Primary care providers should consider all options in their decision-making and monitor for new published evidence that clarifies the risk versus benefit; patient preference should have a substantial influencing role.

### Cost Analysis

A cost analysis was not performed and published cost analyses were not reviewed.

### Method of Guideline Validation

Comparison with guidelines from other groups  
 External peer review  
 Internal peer review

## Description of Method of Guideline Validation

The guideline will be submitted for approval by the International Society of Travel Medicine.

## Recommendations

### Major Recommendations

Definitions for the levels of evidence (1-4) and the grades of the recommendations (A-D) are provided at the end of the “Major Recommendations” field (Appendix G).

Recommendations	Supporting Evidence	Grade
<b>Cardiovascular Conditions/Disorders</b>		
<ul style="list-style-type: none"> <li>• Patients with hemodynamically stable, asymptomatic cardiac conditions without recent changes in symptoms or medications should not be restricted from travel by commercial air</li> <li>• Chronic Heart Failure – clear to fly if able to climb one flight of stairs or walk 50 meters at normal pace without breathlessness. Flying contraindicated for severe, decompensated conditions. Consider supplemental O<sub>2</sub> for NYHA class IV or those with comorbid conditions which may impact oxygenation.</li> <li>• Cardiac Surgery – travel should be delayed for at least 10 days post operatively without complications. Additional ground support may be needed to meet the travel to/within/from the airport.</li> <li>• Angiography – cleared to fly <math>\geq 24</math> hours after procedure if condition is stable</li> <li>• Angioplasty - cleared to fly <math>\geq 3</math> days after procedure if asymptomatic</li> <li>• Eisenmenger Syndrome – consider O<sub>2</sub> in flight</li> <li>• Cardiac conditions or procedures requiring anticoagulation – delay travel until stable anticoagulation levels achieved</li> <li>• Pacemakers and ICDs – delay travel one days post placement if asymptomatic and no pneumothorax</li> </ul> <p>** Supplemental and in-flight oxygen should be considered to meet the additional physical demands of travel to/within/from the airport to destination as well as for potential hypoxemia associated with hypobaric aircraft cabin conditions for any patient with labile health condition or with comorbidity that may affect oxygenation.</p>	<p>Ingle et al., 2011; IATA, 2011; Smith et al., 2010; ASMA, 2003; Roby, Lee, &amp; Hopkins, 2002; Zahger, Leibowitz, Tabb &amp; Weiss, 2000</p>	C

Recommendations	Supporting Evidence	Grade
<b>Respiratory Conditions/Disorders</b>		
<ul style="list-style-type: none"> <li>• Patients with stable, asymptomatic respiratory conditions with full recovery from any exacerbation and an exercise tolerance of &gt;50 meters without dyspnea can be cleared to fly without restrictions</li> <li>• Pneumothorax and pleural effusion- delay travel for at least 7 days after full inflation</li> <li>• Chest surgery – clear to travel once free from residual air.</li> <li>• Pulmonary arteriovenous malformation (PAVM) and pulmonary cysts – advise significant caution against travel by air due to high risk for venous thromboembolism (VTE), stroke and sudden death.</li> <li>• Any condition where pre-flight SpO<sub>2</sub> &lt;89% of PaO<sub>2</sub> &lt;70 mmHg, in-flight oxygen should be considered</li> </ul> <p>** Supplemental and in-flight oxygen should be considered to meet the additional physical demands of travel to/within/from the airport to destination as well as for potential hypoxemia associated with hypobaric aircraft cabin conditions for any patient with labile health condition or with comorbidity that may affect oxygenation.</p>	<p>Akero et al., 2011; Tam et al., 2011; Bossley et al., 2011; Edvardsen et al., 2011; IATA, 2011; Thamm et al., 2011; Ahmedzai et al., 2011; Tiemensma, Buys &amp; Wade, 2010; Lapostolle et al., 2009; Kelly et al., 2009; Lehmann et al., 2009; Taveira-DaSilva et al., 2009; Martin et al., 2008; Kelly et al., 2008; Jones et al., 2008; Broberg et al., 2007; Currie, Kennedy, Paterson, &amp; Watt, 2007; Udomittipong et al., 2006; Kelly et al., 2006; Almeida et al., 2006; Humphreys et al., 2005; Clososn et al., 2004; ASMA, 2003; Lee, Yamamoto, &amp; Relles, 2002</p>	C

Recommendations	Supporting Evidence	Grade
<b>Venous Thromboembolism Risk</b>		
<ul style="list-style-type: none"> <li>• Prior history of Cerebral emboli, PE, VTE or DVT should have ultrasound screening before clearance to fly to rule out presence of asymptomatic thrombus</li> <li>• Patients on anticoagulation therapy should be stable at therapeutic level before clearance to fly</li> <li>• Flight times or multiple short leg air travel &gt;4 hours within 4 weeks increases risk of VTE 2-4 fold</li> </ul>	<p>MacCallum et al., 2011; Schreijer, et al., 2010; Chandra et al., 2009; Schreijer et al., 2008; Kuipers et al., 2007; WHO, 2007; Philbrick et al., 2006; Aryal et al., 2006; Schwarz et al., 2003; Jacobson et al., 2003</p>	B

<b>Anemia and Bleeding disorders</b>		
<ul style="list-style-type: none"> <li>• Caution should be advised to patients with hemoglobin levels below 8.5 g /dl due to increased risk of lightheadedness or loss of consciousness during flight, particularly with physical exertion during flight.</li> <li>• Patients with Sickle cell disease need to be made aware that their condition can be exacerbated by reduced oxygen pressures during flight. Because such a crisis could be life-threatening, sickle cell patients should be advised not to travel by air without medical oxygen.</li> </ul>	<p>IATA, 2011 &amp; ASMA, 2003</p>	D

Neurologic Disorders		
<ul style="list-style-type: none"> <li>Stable CNS disorders without recent exacerbation or prior history of event associated with air travel do not require restrictions.</li> <li>History of CNS changes in prior air travel should be a contraindication for travel until complete cardiopulmonary and CNS examination has been performed</li> <li>CVA – delay travel at least two weeks post event unless medically escorted with supplemental O<sub>2</sub></li> <li>Seizure Disorder/Epilepsy – clear to fly if stable on medications and no recent change in dosage. Caution patient regarding seizure-threshold lowering effects of ETOH, fatigue, delayed meals, hypoxia and disturbed circadian rhythm. Advise patient to carry identification and medication on person during travel.</li> <li>Headache (in absence of migraine history or other CNS disorder) associated with ascent/descent may respond to Naproxen 550 mg po one hour before take-off</li> </ul>	MacCallum et al., 2011; Schreijer, et al, 2010; Chandra et al., 2009; Schreijer et al., 2008; Kuipers et al., 2007; WHO, 2007; Philbrick et al., 2006; Aryal et al., 2006; Schwarz et al., 2003; Jacobson et al., 2003	C

Ophthalmology, Otolaryngology & Allergy		
<ul style="list-style-type: none"> <li>Cataract or corneal laser surgery – delay travel for 24 hours after procedure</li> <li>Intra-ocular surgery or penetrating eye injury – delay travel for 7 days after injury or procedure</li> <li>Ophthalmologic conditions negatively affected by changes in intra-ocular pressure should avoid travel</li> <li>Orbital, zygomatic or sinus surgery – delay travel until bleeding risk controlled and cleared by surgeon</li> <li>Tonsillectomy delay travel for at least 4 days after surgery or control of active bleeding</li> <li>Patients with known significant allergy-sensitive conditions should travel with antihistamines and epinephrine as medically indicated.</li> <li>Passengers with pet allergies should be aware of the possible contact or inhalation of pet dander from cabin-traveling animals.</li> <li>Passengers with peanut, nut or seed allergies can avoid potential inhalation exposure by requesting information in advance from the airline. Note, as many passengers are now carrying food on planes, the likelihood of inhalation exposure can still exist.</li> </ul>	IATA, 2011; Bayer et al., 2008; Comstock et al., 2008; Mahmood et al., 2003; ASMA, 2003; Monaghan et al., 2002; Jassar et al., 2001; Mills et al., 2001	D

Pregnancy		
<ul style="list-style-type: none"> <li>Pregnancy is not a contraindication for air travel</li> </ul> <p>*Airlines may require clearance to fly for pregnant women &gt;28 week gestation.</p> <p>**The availability of OB/GYN services at the travel destinations should be weighted into passenger's decision to travel by air.</p>	IATA, 2011; Magann et al., 2010; ACOG, 2009; RCOG, 2008; Chibber et al., 2006; Freeman et al., 2004, ASMA, 2003	B

Psychiatric Disorders		
<ul style="list-style-type: none"> <li>A stable, controlled, psychiatric condition is not a contraindication to air travel. Acute psychosis and unstable chronic psychiatric disorders should be assessed by a doctor with aviation medicine experience</li> </ul>	IATA, 2011; Bor et al, 2003; ASMA, 2003; Smart et al., 2003; Matsumoto et al., 2001	D

Diabetes Mellitus		
<ul style="list-style-type: none"> <li>Patients with diabetes controlled by insulin pump should monitor blood sugars closely during travel by air</li> <li>Diabetics should carry medical condition identification, medications and on person</li> </ul>	<ul style="list-style-type: none"> <li>King et al., 2011; Hinninghofen et al, 2006; Burnett et al., 2006; ASMA, 2003</li> </ul>	D

### **Definitions:**

### **Evidence Rating Scale for Studies Reviewed**

Level of evidence	Qualifying Studies
<b>High (4)</b> ●●●●	High-quality, multi-centered or single-centered, randomized controlled trial with adequate power; or a systematic review of these studies
<b>Moderate (3)</b> ●●●○	Lesser-quality, randomized controlled trial; prospective cohort study; or a systematic review of these studies
<b>Low (2)</b> ●●○○	Retrospective comparative study, case-control study or a systematic review of these studies
<b>Very Low (1)</b> ●○○○	Case reports, expert opinion or evidence based on physiology

### **Scale for Grading Recommendations**

Grade	Descriptor	Qualifying Evidence	Implications for practice
A	Strong Recommendation	Level 4 evidence or consistent findings from multiple studies of levels 3, 2 or 1	Primary care providers should follow a strong recommendation unless a clear and compelling rationale for alternative approach is present
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D	Option	Little or no systematic empirical evidence	Primary care providers should consider all options in their decision-making and monitor for new published evidence that clarifies the risk versus benefit; patient preference should have a substantial influencing role.

### **Clinical Algorithm(s)**

None provided

### **Evidence Supporting the Recommendations**

### **References Supporting the Recommendations**

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### **Types of Evidence Supporting the Recommendations**

The type of supporting evidence is identified and graded for each recommendation (see “Major Recommendations”).

#### **Benefits/Harms of Implementing the Guideline Recommendations**

##### **Potential Benefits**

These guidelines will assist primary care providers in the screening and clinical decision-making regarding clearance to fly for their patients with pre-existing medical conditions that may be adversely affected by commercial air travel.

##### **Potential Harms**

Risks inherent in commercial air travel, which can be minimized through appropriate patient screening and adherence to recommended practices.

#### **Qualifying Statement**

The recommendations are provided only as assistance to primary care providers making clinical decisions regarding the care of their patients by providing a

framework for screening and assessment. It is not intended to replace or substitute for individual provider judgment made in each clinical situation.

The recommendations reflect the best understanding of the science of medicine available at the time of publication. Guideline implementation should be used with the clear understanding that continued research may result in new knowledge and recommendations.

This guideline has several limitations, largely due to the paucity of clinical research in the areas and limitations in the available evidence base. Further research is needed to establish more accurate incidence of morbidity and mortality as well as improved methods of screening for fitness to fly.

### **Implementation of the Guideline**

An implementation strategy is pending peer review.

### **Institute of Medicine (IOM) National Healthcare Quality Report Categories**

#### **IOM Care Need**

Living with Illness

Staying Healthy

#### **IOM Domain**

Effectiveness

Patient-centeredness

### **Identifying Information and Availability**

Pending peer review and approval of guidelines

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