



## Objective:

To summarize the available literature on the risk of venous thromboembolism (VTE) related to air travel and provide recommendations for preventative measures while traveling long distances.

## Background:

Long-distance travelling by plane increases the risk of VTE, which includes deep vein thrombosis (DVT) or pulmonary embolism (PE); however, the absolute VTE risk from travel is small.

The etiology of travel-related thrombosis likely arises from a combination of immobility (blood stasis in the leg veins), hypobaric environment, vessel damage, and dehydration. Known risk factors for travel-associated VTE include advanced age (>40 years), height (>185 cm or <165 cm), obesity (BMI >30), hormonal therapy, thrombophilia, pregnancy (including the postpartum period), active cancer, recent major surgery, or a prior history of VTE. Window seating compared to aisle seating has been associated with greater risk and the effect is most pronounced in passengers with BMI >30.

Long distance travelers have a 3-fold increase in VTE risk compared to the general population (3.2 per 1000 patient-years within 8 weeks of a long distance (>4 hours) flight, compared with 1.0 per 1000 patient-years with no travel exposure). The incidence of symptomatic VTE after flights of greater than 4 hours is 1 in 4,656. The risk of symptomatic PE immediately after air travel was 0.39 cases per 1 million travelers, with an increased risk for flight durations greater than 8 hours (1.65 cases per 1 million travelers) versus flights that are 6-8 hours in duration (0.25 cases per 1 million travelers). Individuals who develop a fatal PE while traveling or symptomatic PE in the weeks following air travel are not included in these estimates.

To put it in perspective, this risk is lower than that with other minor provoking risk factors, such as knee arthroscopy or immobilization with a below-knee cast. The risk of DVT is highest in the first 2 weeks after long distance travel, after which it gradually decreases back to baseline by 8 weeks. Airplane pilots do not appear to be at increased risk of travel-related VTE.

## Preventative of travel-related VTE:

### General preventative measures:

General preventative measures aim to minimize the impact of environmental factors that predispose to travel-related VTE. While there have been no studies evaluating the efficacy of general preventative measures, accepted recommendations include:

- Getting up and walking every 1-2 hours
- Exercising and stretching legs regularly

- Wearing loose fitting clothing
- Minimizing baggage in the space under the seat
- Staying hydrated and avoiding alcohol while traveling

### **Compression stockings**

Compression stockings reduce the symptoms of leg swelling and may help prevent DVT while traveling. In a systematic review of 9 randomized trials in which half the passengers wore compression stockings and half the passengers did not, the risk of asymptomatic DVT was reduced by 90% in the group that wore compression stockings. Four of the trials used graduated compression stockings of 20-30 mmHg, and five of the trials used graduated compression stockings of 10-20 mmHg. The small numbers of asymptomatic DVTs diagnosed in these studies were detected on screening leg ultrasound examinations of passengers shortly after their flight. Passengers who had additional risk factors for VTE benefited the most from compression stockings. The clinical significance of the small number of asymptomatic DVTs that were found and prevented is unknown.

### **Use of aspirin or anticoagulants**

The effectiveness of taking a short course of aspirin or anticoagulants to prevent travel-related VTE is unknown and is not routinely recommended. There are no studies evaluating the use of direct oral anticoagulants for short-term prophylaxis to prevent travel-related VTE. One small randomized trial evaluated the effect of preventing travel-related asymptomatic DVTs using a single injection of low-molecular-weight heparin (LMWH) (enoxaparin 1 mg/kg) given to high-risk individuals 2-4 hours prior to flying, compared to 3 days of daily aspirin starting 12 hours prior to flying, or no therapy. When participants completed leg ultrasound screening after a long (10-15 hour) flight, there were fewer asymptomatic DVTs in the LMWH arm (0/82, 0%), compared to the aspirin arm (3/84, 3.6%) or no therapy arm (4/83, 4.82%). Similar to the studies evaluating compression stockings, the clinical significance of the small, asymptomatic DVTs that were found and prevented is unknown.

For individuals who have additional risk factors for VTE, there is little data to guide management. The recommendations below are all based on low quality evidence, and an individualized management plan that takes into account both the risks and benefits of treatment is needed.

### **Recommendations:**

For travelers who are already on preventative or treatment doses of anticoagulants for any indication, no additional action is required to prevent travel-related VTE. For all long-distance (>4hr) travelers, general preventative measures are recommended to prevent travel-related VTE, including frequent ambulation, exercising and stretching legs regularly, avoiding constrictive clothing, and keeping hydrated.

#### **Travels not already on an anticoagulant:**

For long-distance travelers who are not at increased risk of VTE, the use of compression stockings is not routinely recommended to prevent travel-related VTE.

For long-distance travelers who are not at increased risk of VTE, the use of short-term prophylaxis with an anticoagulant or antiplatelet is not routinely recommended to prevent travel-related VTE.

For long-distance travelers who are at increased risk of VTE (previous unprovoked or travel-related VTE, active cancer, recent surgery or trauma,  $\geq 2$  risk factors including combinations of the above with obesity,

limited mobility, advanced age, known thrombophilia, pregnancy, or estrogen use) the use of graduated compression stockings is recommended to prevent travel-related VTE, at a stocking strength of 20-30 mmHg.

A short course of prophylactic-dose anticoagulation may be considered in select patients who are at very high risk of VTE, based on an individualized decision that weighs the risks and benefits of therapy and takes into account patient values and preferences. Given peak anticoagulant effects of 2-4 hours with LMWH and direct oral anticoagulants (DOACs), a single **prophylactic** dose can be taken shortly before the journey starts. The optimal number of doses around travel is unknown. DOACs should not be used in pregnant or breastfeeding women.

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