

# Review: Flight times > 8 hours and the presence of risk factors for VTE increase travel-related VTE

Philbrick JT, Shumate R, Siadaty MS, Becker DM. Air travel and venous thromboembolism: a systematic review. *J Gen Intern Med.* 2007;22:107-14.

**Clinical impact ratings:** GIM/FP/GP ★★★★★☆ Hematol/Thrombo ★★★★★☆ Trop & Travel Med ★★★★★☆☆

## QUESTIONS

What are the risk factors for travel-related venous thromboembolism (VTE)? Which preventive treatments are effective?

## METHODS

**Data sources:** MEDLINE (1966 to December 2005), Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects, and bibliographies of relevant studies.

**Study selection and assessment:** Case-control or cohort studies and randomized controlled trials (RCTs) that evaluated any form of travel as a risk factor for VTE or preventive measures for travel-related VTE. Case reports, abstracts, and subgroup analyses of previously published studies were excluded. 25 studies met the selection criteria: 6 case-control studies ( $n = 207$  to 988), 10 cohort studies ( $n = 320$  to > 135 million), and 9 RCTs ( $n = 186$  to 833); most studies evaluated air travel. The interventions evaluated in the 9 RCTs were low-molecular-weight heparin, aspirin, graduated compression stockings (12 to 30 mm Hg at the ankle), and herbal remedies with putative anti-thrombotic properties. Quality assessment of individual studies was based on 8 methodological criteria, which included adequate description of patient selection criteria, diagnosis, and treatment; equally matched com-

parison groups; and follow-up. 21 of 25 studies met  $\geq 4$  methodological criteria.

**Outcomes:** Incidence of VTE (pulmonary embolism, deep venous thrombosis [DVT], or both) after travel; associations between travel duration, clinical VTE risk, and travel-related VTE.

## MAIN RESULTS

In RCTs and cohort studies evaluating air travel, the risk for asymptomatic VTE ranged from 0% to 12% and risk for symptomatic VTE was 27 per 1 million travelers. Multivariate logistic regression analysis showed that mean duration of air travel > 8 hours and high clinical risk for VTE ( $\geq 1$  of previous DVT, prothrombotic blood disorder, body weight > 90 kg, limited mobility, cancer, or large varicose veins) increased risk

for air-travel-related VTE (Table). In 9 studies (126 patients with VTE), additional risk factors were age > 40 years and use of female hormones. In 6 RCTs ( $n = 2482$ ) evaluating air travel, use of compression stockings conferred a lower incidence of DVT than did no intervention (0.2% vs 3.7%,  $P < 0.001$ ).

## CONCLUSIONS

Mean duration of air travel > 8 hours and higher clinical venous thromboembolism risk increase risk for air-travel-related VTE. Graduated compression stockings are effective for preventing air-travel-related VTE.

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*For correspondence:* Dr. J.T. Philbrick, University of Virginia Health Sciences Center, Charlottesville, VA, USA. E-mail [jtp9b@virginia.edu](mailto:jtp9b@virginia.edu). ■

### Risk factors for travel-related venous thromboembolism (VTE)\*

Risk factors	Odds ratio (95% CI)
Mean duration of air travel < 6 h	0.01 (0.002 to 0.11)
Mean duration of air travel 6 to 8 h	1.0
Mean duration of air travel > 8 h	2.3 (1.4 to 3.6)
Low clinical VTE risk†	1.0
High clinical VTE risk‡	3.6 (2.2 to 5.8)

\*CI defined in Glossary. A multivariate logistic regression model was used.

†No known risk factors for VTE.

‡Previous deep venous thrombosis, prothrombotic blood disorder, body weight > 90 kg, limited mobility, cancer, or large varicose veins.

## COMMENTARY

VTE occurring in association with air travel was first described as the “economy class syndrome” (1). Although highly publicized, the clinical importance of this association remains unclear. In the systematic review by Philbrick and colleagues, strengths and weaknesses of available studies addressing this issue are comprehensively evaluated and summarized.

In brief, overall risk for symptomatic VTE following air travel appears to be very low—approximately 27 VTEs per 1 million travelers. This is lower than commonly reported estimates of VTE in the general population (2). Philbrick and colleagues appropriately conclude that persons without risk factors for VTE do not warrant prophylaxis even with extended travel (> 8 h).

Perhaps a more clinically important question is whether persons with risk factors for VTE are at significantly increased risk for air-travel-related VTE. Unfortunately, such data on these persons are even more limited. Philbrick and colleagues identified 5 RCTs (all by the same investigative group) evaluating preventive measures in participants with risk factors for VTE ( $n = \sim 1700$ ). In these studies, the risk for asymptomatic DVT detected by venous ultrasonography in participants who did not receive any preventive interventions was approximately 4.5%.

However, as in other settings, the clinical significance of asymptomatic DVT is controversial. Interestingly, no episodes of symptomatic VTE occurred in either the intervention or control groups of these studies. As such, the need for DVT prophylaxis during air travel, even in persons with VTE risk factors, is far from established.

Given the very low incidence of symptomatic VTE overall, physicians may consider VTE prevention measures (compression stockings or low-dose low-molecular-weight heparin) only for persons at highest risk for VTE, such as those with prior VTE, cancer, or recent lower-extremity fracture. For these and other travelers, sensible recommendations to minimize risk for VTE include ensuring adequate hydration and leg exercises and ambulation to prevent venous stasis. Future studies evaluating air-travel-related VTE and its prevention should focus on these high-risk groups and use symptomatic VTE as the primary endpoint.

Frederick A. Spencer, MD  
McMaster University  
Hamilton, Ontario, Canada

## References

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