Air travel as a risk factor for venous thromboembolism (VTE) and the effectiveness of preventative measures

Authors' objectives
To assess whether air flight is a risk factor for the future development of venous thromboembolic disease (VTE), and to examine strategies for the prevention of VTE with air travel. This abstract focuses upon interventions for the prevention of VTE.

Searching
MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews, the Cochrane Controlled Trials Register and the National Research Register were searched without any language restrictions; the search terms and dates were reported. In addition, the internet sites of several health organisations were searched, references in identified studies and reviews were handsearched, and experts in the field were contacted.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared any prophylactic interventions for VTE with no intervention, placebo, or any other forms of comparative intervention, were eligible for inclusion. Studies were excluded if they were experimental simulations of flight conditions. The specific interventions assessed were compression stockings, low molecular weight heparin (LMWH) and aspirin. The duration of flight time ranged from 12.5 to 24 hours across the included studies (where reported).

Participants included in the review
Studies that included any individual who had travelled by air, regardless of gender, age or risk status, were eligible for inclusion. The participants included in the review ranged in age from 20 to 80 years (where reported).

Outcomes assessed in the review
Studies that reported the rates of asymptomatic or symptomatic VTE confirmed by clinical or diagnostic methods, pulmonary embolism, or related mortality up to one month after exposure, were eligible for inclusion. The primary outcome assessed in the included studies was the rate of deep vein thrombosis (DVT). In one study, the secondary outcome was the rate of superficial thrombosis.

How were decisions on the relevance of primary studies made?
Two independent reviewers assessed studies for inclusion in the review.

Assessment of study quality
The quality of the included studies was assessed according to: the methods of randomisation; allocation concealment; reporting of the baseline characteristics; specification of eligibility criteria; blinding of the outcome assessors; equal treatment of the intervention groups; the reporting of losses to follow-up; analysis by intention-to-treat; and whether the unit of analysis was appropriate. Study quality was assessed. However, the authors did not state how many reviewers were involved in this process.

Data extraction
One reviewer extracted the data, while a second reviewer checked their accuracy. The outcomes for both the
intervention and control groups were extracted and expressed as an absolute risk reduction (ARR), relative risk reduction (RRR) and number-needed-to-treat (NNT), along with the 95% confidence intervals (95% CIs).

**Methods of synthesis**

*How were the studies combined?*

Data for each study were tabulated and combined in a narrative. Where appropriate, the results were combined in a meta-analysis using a fixed-effect model.

*How were differences between studies investigated?*

Differences between the studies were discussed in relation to differences between the participant populations (high risk versus low risk) and the different interventions.

**Results of the review**

Three RCTs (total n=1,364) were included.

The three RCTs were of moderate quality, with one scoring 6 out of 10 on the quality assessment checklist, and two scoring 5 out of 10.

**Below-knee stockings versus no stockings (2 RCTs).**

The first RCT (n=231) included only participants who were at low risk of DVT. The results showed that significantly more participants in the control group sustained symptomless DVT at 48 hours after flight travel than those who were assigned to wear stockings (RRR 100%, 95% CI: 96, 100). The ARR was 10% and the NNT was 10 (95% CI: 6, 17). However, significantly more participants in the intervention group experienced superficial thrombophlebitis comparison with the control group, with an absolute risk increase of 3.5% observed. This corresponded to a number-needed-to-harm of 29 (95% CI: 12, 493). The second RCT (n=833) that assessed below-knee stockings included only participants who were at high risk for the development of DVT. The results showed that within 24 hours of flight travel, significantly more of the control group had experienced DVT than those in the intervention group (RRR 95%, 95% CI: 89, 97). The corresponding ARR was 4.26% and the NNT was 24 (95% CI: 15, 41). The overall pooled effect of stockings was an odds ratio of 0.04 (95% CI: 0.01, 0.23).

**Prophylactic aspirin versus LMWH versus no treatment (1 RCT).**

This RCT (n=300) included only participants at high risk for the development of DVT. The results showed that treatment with LMWH significantly reduced the risk of experiencing DVT, with 4.82% of the control group experiencing DVT compared with 3.6% of the aspirin-treated participants and 0% of the LMWH-treated group. The corresponding RRR, ARR and NNT in the aspirin and LMWH treatment groups were, 25% and 100%, 1.22% and 4.82%, and 81 benefit (18 harm to 12 benefit) and 21 (95% CI: 9, 476), respectively, compared with no treatment. Treatment with aspirin and heparin was found to be associated with adverse side-effects.

**Authors' conclusions**

There was little or no evidence of increased risk for the development of DVT with air travel in otherwise healthy individuals. The authors also concluded that, given the lack of evidence about effective interventions, it cannot be recommended that any additional clinical review or interventions for high-risk individuals are given prior to air travel.

**CRD commentary**

The review question was clearly defined in terms of the participants, interventions, outcome measures and study designs. Several sources were searched for relevant studies, and efforts were made to minimise both language and publication bias. Reviewer bias and errors were minimised in the study selection and data extraction processes. The quality of the included studies was adequately assessed, but it was not reported how many reviewers performed the quality assessment.
Given the different interventions assessed, the studies were appropriately combined in a narrative, with a meta-analysis only being undertaken on a subgroup of studies. Differences between the studies were also briefly explored in relation to differences between the participant groups and the interventions. Overall, the authors' conclusions are cautious and appropriately reflect the paucity of the evidence base reviewed.

**Implications of the review for practice and research**

Practice: The authors did not recommend any additional clinical review or interventions for high-risk individuals prior to air flight.

Research: The authors stated that the need to precisely quantify the additional risk of flight in high-risk individuals remains, particularly for the outcome of pulmonary embolism. However, rather than further case-control studies being undertaken, further research should focus on the combination of prospective controlled and epidemiological modelling studies. Careful consideration needs to be given to the power of any future research.

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**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.