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Activation of coagulation system during air travel - Reply

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Citation

Schreijer, A. J. M., Cannegieter, S. C., Buller, H. R., & Rosendaal, F. R. (2006). Activation of coagulation system during air travel - Reply. *Lancet*, 368, 26-26. Retrieved from <https://hdl.handle.net/1887/5007>

Version: Not Applicable (or Unknown)

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Note: To cite this publication please use the final published version (if applicable).

Schreijer and colleagues only vaguely refer to “disease affecting coagulation”, without specifying whether efforts were made to screen for other potential risk factors—eg, methylene tetrahydrofolate reductase deficiency, antithrombin III levels, protein C and S functionality, antiphospholipid antibodies including lupus anticoagulant, and high serum homocysteine that could have affected the results.

We declare that we have no conflict of interest.

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Authors’ reply

The first issue raised by Gabriele Bertoni and Vincenzo Rampoldi concerns possible interference by lifestyle variables. Smoking is a relevant concern since it is known to influence coagulation variables.¹ However, smoking will not have affected our findings since the proportion of smokers was similar among the high responders (9% [1/11]) and the non-responders (15% [9/60]). Furthermore, smoking was not allowed on any of the study days, so any acute effects of smoking² were prevented. Other recreational or medicinal drug use, with the exception of oral contraceptive use, was an exclusion criterion.

Haematological variables were not a key subject of this paper and will be reported separately. Other coagulation variables are currently

being analysed to further unravel the pathophysiology of air-travel-related thrombosis.

We did not do radiological investigations for asymptomatic clots since our study was aimed at clarifying the effect of air travel on thrombin generation. Besides, in a trial with a study size like ours only very few, if any, asymptomatic events could be expected, since these are estimated to occur in only about 3% of air travellers.³ The use of a thromboelastograph, although an interesting idea, was not feasible during our somewhat challenging study conditions.

Other studies have shown conflicting results of the effects of hypobaric hypoxia on markers of clotting activation. Most of these studies did not take circadian variation into account, nor did they disentangle the effects of immobilisation and hypoxic hypobaria. Also, analyses were done at a group level, so individual effects might have been missed. Furthermore, these studies generally included healthy individuals, whereas the risk of travel-related thrombosis is increased mainly in those with risk factors such as factor V Leiden and hormone use.^{4,5} That is why we included individuals with either or both of these risk factors, and saw hyper-responsive effects predominantly in those with the combination of risk factors. Other thrombophilic defects are rare and unlikely to have been present in a group of 71 volunteers. By “diseases affecting coagulation”, we did not refer to thrombophilia, but to clinical conditions such as a history of cancer or liver disease.

We declare that we have no conflict of interest.

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Inhaled insulin

Your Editorial on inhaled insulin (April 29, p 1372)¹ claims that the decision to prescribe inhaled insulin “should be left to the individual physicians in discussion with their patients”. Patients’ choice is, of course, one of the cornerstones of medical practice, but it isn’t open-ended. No equitable health-care system should give cost-ineffective treatments to some patients at the expense of denying cost-effective ones to others. Patients’ choice has to be from a menu.

The UK National Health Service cares for millions of patients each year and all deserve access to the highest affordable standards of care. But resources are finite, and the National Institute for Health and Clinical Excellence (NICE) is required to advise both on the clinical effectiveness and the cost-effectiveness of the health technologies it considers. The Institute’s decisions are reached only after inordinate care. Clinical experts, as well as patients and carers, are invited to present their views to our independent advisory committee before a provisional conclusion is reached.

Those with an interest in the appraisal of inhaled insulin have had the opportunity to comment on these provisional conclusions and all their responses have been scrutinised carefully ahead of the final guidance’s publication in October. Patients’ choice is necessary but not over-riding.