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## More on 'universal' versus 'selected' screening for thrombophilia: the hidden costs of false-positive diagnosis – response to Favaloro and Keeling

We thank Dr Favaloro and Dr Keeling (Keeling, 2006) for their correspondence.

Dr Favaloro referred to the accuracy of diagnosis of thrombophilia, in particular inherited deficiencies in protein C and protein S. The uncertainty about normality and deficiency for these physiological anticoagulants has been long recognised (Greaves & Baglin, 2000) and was addressed in our study.

Our decision model took into account the following patient pathways: (i) test positives (true positives) – patients with thrombophilia and accurately tested positive; (ii) false positives – patients with thrombophilia, but inaccurately tested negative; (iii) false negatives – patients without thrombophilia, but inaccurately tested positive; and (iv) test negatives (true negatives) – patients without thrombophilia and accurately tested negative. Therefore, the false-positive diagnosis was represented by patient pathway (iii). As in clinical practice, following a positive-test result, the model assumed that these patients would be given prophylaxis; however, the probability of subsequent venous thromboembolic events in these patients would be lower than those with a true-positive result.

The test sensitivity and specificity for individual tests for thrombophilia is unclear. Based on the limited existing data in the literature (Preston *et al*, 2003) we assumed the overall sensitivity and specificity of the thrombophilia screening tests to be 80% in the main analysis. As Dr Favaloro has highlighted, this may be an overestimate in testing for protein C and protein S. Therefore, this was tested in the sensitivity analysis, in which we varied the test sensitivity and specificity between 50% and 100%. This resulted in substantial changes in the incremental cost-effectiveness ratios, but did not alter the overall results.

Cost-effectiveness analysis is based on the fundamental assumption that the comparisons apply to where the decision maker is already faced with a budget and mutually exclusive options. Incremental cost-effectiveness ratios are ranked with the least cost per unit of health effect being the most desirable. Our study showed that when comparing the high-risk patient groups, screening prior to prescribing hormone replacement therapy was the most cost-effective strategy (incremental cost-effectiveness ratio £6824). However, when comparing universal

screening with selective screening, selective screening was more cost-effective in all groups.

Dr Keeling referred to scenarios where purchasers express a willingness to pay £15 000 or £80 000 to achieve a unit of outcome (Keeling, 2006). We disagree that this would mean that universal screening for some groups would therefore be preferred to selective screening. The option with the lowest cost per unit of outcome in a comparison (such as selective compared with universal screening) would always be chosen, as this would free resources to be available for other cost-effective uses. We believe that cost-effectiveness acceptability thresholds should be used to compare different healthcare programmes. Our study was not designed to evaluate the relative cost-effectiveness of screening compared with other uses of scarce NHS resources. In order to evaluate this, alternative forms of economic evaluation, which allow comparisons between diverse healthcare programmes, such as cost-benefit or cost-utility analysis (Drummond *et al*, 1987), are required.

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