Appendix 1: Testing for heritable thrombophilia in acute venous thromboembolism

Heritable thrombophilias are inherited disorders that increase the risk of thrombosis. The following five thrombophilic disorders are commonly included in a panel of heritable thrombophilia testing.

Thrombophilic disorder	**Estimated population prevalence**	**Risk of VTE recurrence (HR with 95% CI*)**	**Mechanism of regulation of coagulation**
Factor V Leiden	In white Europeans: 1 in 20 heterozygous, 1 in 5,000 homozygous	1.3 (0.8-2.1)	Mutation in factor V protein confers resistance to inactivation by activated protein C (activated protein C resistance)
Prothrombin gene mutation (PG20210A)	In white Europeans: 1 in 50 heterozygous	0.7 (0.3–2.0)	Mutation in prothrombin (Factor II) that leads to hyperprothrombinemia (mechanism unknown)
Protein C deficiency	1 in 250	1.8 (0.9–3.8)**	Protein C is a natural anticoagulant that inhibits factors V and VIII
Protein S deficiency	1 in 2,000	1.8 (0.9–3.8)**	Protein S is an essential co-factor for protein C
Antithrombin deficiency	1 in 2,000–5,000	1.8 (0.9–3.8)**	Antithrombin is a natural anticoagulant that primarily inhibits thrombin

Note: CI = confidence interval, HR = hazard ratio, VTE = venous thromboembolism.

*HR with 95% confidence intervals, relative to those without the abnormality and adjusted for age, sex, and anticoagulation.[1]

**HRs for the three natural anticoagulant deficiencies were pooled into one risk estimate for recurrent VTE. The presence of any sole thrombophilic abnormality did not substantively increase the risk of VTE recurrence compared with other clinical factors.[1]

References:

1. Christiansen SC, Cannegieter SC, Koster T, et al. Thrombophilia, clinical factors, and recurrent venous thromobotic events. *JAMA* 2005;293:2352-61.

Appendix to: Tseng E, Selby R. Testing for heritable thrombophilia in acute venous thromboembolism. *CMAJ* 2017. doi: 10.1503/cmaj.160062.