BLEEDING, THROMBOSIS AND VASCULAR BIOLOGY
Editor-in-Chief: Giovanni de Gaetano, Italy | eISSN: 2785-5309
The Official Journal of the Italian Society for the Study of Hemostasis and Thrombosis
SISET
Società Italiana per lo Studio dell'Emostasi e Trombosi

SUPPLEMENTARY MATERIAL

Expanding the genetic landscape of hereditary thrombophilia: classical defects, novel variants, and genomic perspectives. A narrative review

Chiara Simion,[1,2] Elena Campello,[1,2] Walter Ageno,[1,3] Paolo Simioni[1,2]

[1]Department of Medicine, University of Padua; [2]First Division of Internal Medicine, Hospital University of Padua; [3]Emergency Medicine Unit, University Hospital of Padua, Italy

Corresponding author: Chiara Simion, Department of Medicine, University of Padua, Via Giustiniani 2, 35128 Padova, Italy. Email: chiara.simion@unipd.it

Bleeding, Thrombosis and Vascular Biology 2026; 5:427
doi:10.4081/btvb.2026.427

Supplementary Table 1. Incidence and risk of venous thromboembolism associated with inherited thrombophilic defects. Prevalence and risk estimates are derived from heterogeneous observational and family cohort studies and should be interpreted as approximate ranges. Absolute risk estimates are mainly available from family studies and vary according to age, concomitant acquired risk factors, and study design. For rare gain-of-function variants, quantitative risk estimates are not available and clinical relevance is inferred from reported familial clustering and recurrence patterns. Adapted from Middeldorp et al.(175), Makris et al.(176), Philippe et al.(177), and Khider et al.(178), with additional data for rare gain-of-function variants derived from individual reports(101,102,104,115,116). Abbreviations**:** AT, antithrombin; PC, protein C; PS, protein S; FVL, factor V Leiden; PTM, prothrombin G20210A mutation; FVIII, factor VIII; FIX, factor IX; FXI, factor XI; VTE, venous thromboembolism.

Thrombophilic defect	Prevalence in general population	Relative risk of first VTE	Estimated absolute risk of first VTE
AT deficiency	0.02–0.2%	~5–15-fold	~1.5–2.0% per year (family studies)
PC deficiency	0.2–0.4%	~4–7-fold	~1.0–1.5% per year (family studies)
PS deficiency	0.03–0.13%	~1–10-fold	~0.5–1.5% per year (family studies)
FVL (heterozygous)	3–7%	~3–5-fold	~0.3–0.6% per year
FVL(homozygous)	~0.02%	~10–80-fold	~1.5–2.0% per year
PTM (heterozygous)	0.7–4%	~2–3-fold	~0.3–0.5% per year
PTM (homozygous)	Very rare	Higher than heterozygous	Not reliably quantifiable
Non-O blood group	~60%	~1.5–2.5-fold	Low; acts as a risk modifier
Elevated FVIII levels	~10–15%	~3–5-fold	Not reliably quantifiable
Elevated FIX levels	~10%	~2–3-fold	Not reliably quantifiable
Elevated FXI levels	~10%	~2-fold	Not reliably quantifiable
FVIII Padua	Extremely rare	Not quantifiable	Not quantifiable
FVIII Aurora	Extremely rare	Not quantifiable	Not quantifiable
FIX Padua	Extremely rare	Not quantifiable	Not quantifiable
Prothrombin Arg596 variants (AT resistance)	Extremely rare	Not quantifiable	Not quantifiable