Original Article

Current Indications for Thrombophilia Testing – A Modified Delphi Consensus Study in Switzerland

Alessandra Bosch[1], Cosima Suter[2], Lukas Graf[3]‡, Sabine Ruosch-Girsberger[4]‡

Affiliation addresses are listed at the end of the article.

ABSTRACT

Background Thrombophilia is a hereditary or acquired condition associated with an increased risk of venous thromboembolism (VTE) and VTE recurrence. Existing recommendations on patient selection vary across guidelines, resulting in variability of testing practices. This heterogeneity reflects persistent uncertainty regarding appropriate testing strategies in routine care.

This modified Delphi survey was conducted to establish expert consensus on clinical indications for thrombophilia testing in Switzerland.

Methods A modified Delphi study was performed with clinical experts managing patients with VTE in Switzerland. A steering committee developed clinical scenarios and statements on thrombophilia testing. These were distributed to the expert panel who rated their agreement and provided written feedback in two rounds. Consensus was defined as ≥70% of experts rating a statement ≥5 on a 7-point Likert scale.

Results Forty-two clinical experts completed the survey. Consensus was reached after two rounds on 32 statements addressing indications for thrombophilia testing in various clinical scenarios, including unprovoked VTE, provoked VTE (including hormone-associated events), unusual site VTE, pediatric VTE, and patients without VTE. For example, consensus supported thrombophilia testing in patients aged <60 years with unprovoked VTE or unusual site VTE, and in women with hormone-associated VTE.

Conclusion In this modified Delphi process, an expert panel achieved consensus on 32 statements regarding indications for thrombophilia testing in various clinical scenarios. These statements reflect current expert opinion, may help inform clinical decision-making, support consistent testing practices in routine care, and may inform the future development of evidence-based recommendations.

Keywords thrombophilia, venous thrombosis, laboratory screening, Delphi consensus, clinical decision-making

received February 24, 2026 | **accepted after revision** April 15, 2026 | **article published online** 2026

Bibliography Hämostaseologie **DOI** 10.1055/a-2858-0105 **Art ID** HAMO-26-02-0046

‡ These authors contributed equally to this work.

Correspondence Dr. Alessandra Bosch, Universitäts- Kinderspital Zürich – Eleonorenstiftung, Department of Haematology, Lenggstr 30, 8008 Zürich, Switzerland, Email: alessandra.bosch@kispi.uzh.ch

Introduction

Thrombophilia is a hereditary or acquired condition associated with an increased risk of venous thromboembolism (VTE).[1] The most frequent thrombophilias included in thrombophilia testing panels are inherited deficiencies of antithrombin, protein C, protein S, and the gain-of-function gene variants factor V Leiden (FVL) and prothrombin G20210A mutation (PGM).[1,2] Antiphospholipid syndrome (APS) is a clinically relevant acquired thrombophilia and is defined by persistent antiphospholipid antibodies in combination with thrombotic or pregnancy complications.[1,3]

Thrombophilia testing is commonly performed in patients with VTE, especially in young patients, in unprovoked or recurrent events, thrombosis at unusual sites, or in patients with a positive family history of VTE or thrombophilia.[1,2,4–9] Typical laboratory panels include assays for hereditary thrombophilias and tests for antiphospholipid antibodies.[1,2] However, interpretation of test results is complex: levels of coagulation factors and physiological anticoagulants vary with acute thrombosis, liver disease, pregnancy, and anticoagulant therapy, and some results reflect acquired temporary rather than genetic abnormalities.[2] The risk of thrombosis varies considerably among different thrombophilias: Low-risk thrombophilias (i.e., heterozygosity for the FVL and PGM mutation) have only a modest impact on the occurrence of a first or recurrent event, whereas high-risk thrombophilias (deficiencies of AT, Protein C, and Protein S) increase the risk to a greater extent.[1,10]

Despite its widespread use, the clinical utility of thrombophilia testing remains uncertain, particularly for low-risk hereditary

thrombophilias. The evidence is limited, that test results may meaningfully guide management. In contrast, identification of high-risk hereditary thrombophilia or APS more frequently impacts clinical management decisions, such as duration and intensity of anticoagulation, choice of anticoagulant, as well as thromboprophylaxis in selected high-risk situations (e.g., pregnancy). Therefore, thrombophilia testing should be reserved for well-defined clinical scenarios only. However, international guidelines differ in their recommendations regarding indications for testing.[4,5,10] These discrepancies partly reflect differing objectives, with some guidelines focusing on individual patient management, whereas others also incorporate considerations related to family screening and cascade testing. This heterogeneity has contributed to ongoing debates and considerable variability in clinical practice across regions and institutions.

Broad thrombophilia panels are often performed without fully considering the individual clinical context, reflecting ongoing uncertainty, divergent interpretations of guidelines, potential financial incentives, and medico-legal or patient-driven motivations. In Switzerland, there is currently no national consensus defining appropriate indications for thrombophilia testing.

To address this gap, a modified Delphi study among Swiss experts in thrombosis and hemostasis was conducted to establish expert consensus and identify areas of uncertainty regarding indications for thrombophilia testing in Switzerland.

Methods

The Delphi consensus method is a process for collecting knowledge from experts in the field anonymously, by distributing questionnaires with statements or recommendations, and for obtaining possible structured feedback on all items, with the aim of reaching consensus in several rounds.[11–13] The Delphi consensus method was used due to the existing uncertainty and the lack of knowledge on this topic and because traditional research methods are not satisfactory for the generation of evidence-based medicine.[11]

A steering committee consisting of one adult hematologist (S.R.G.), one adult hematologist and laboratory medicine specialist (L.G.), and one pediatric hematologist (A.B.) generated the statements included in this Delphi survey. They did not participate in the Delphi process.

An invite email to participate as a clinical expert in this Delphi survey was sent out to all members of the Swiss Society of Haematology and the Swiss Society of Paediatric Haematology and Oncology. Interested clinical experts registered their email addresses to receive the survey on SurveyMonkey®.[14]

In the Delphi survey, participants rated their level of agreement with respect to the statements on a 7-point Likert scale and were invited to give qualitative feedback concerning their ranking anonymously. The clinical experts had the option of abstention, where they felt they did not hold sufficient expertise. The 7-point Likert scale is given in **Fig. 1**.

The steering committee determined a priori how responses would be managed. Statements with at least 70% of the clinical experts rating their agreement as 5 or higher would be retained in the final consensus statements, and this is based on the published Delphi methodology literature, which has suggested that this level of agreement is sufficient to establish consensus.[11,13] Statements with less than 50% of clinical experts rating their agreement as 5 or higher would be discarded from the final consensus statements. Statements with 50-69% of the clinical experts rating their agreement as 5 or higher would be revised based on the provided qualitative feedback and redistributed to the expert panel in a subsequent round.[11,12,15] For statements where no consensus was reached, individual free-text comments from the expert panel were collected, summarized, and grouped thematically to capture the reasons underlying the lack of agreement.

For the first round, the clinical experts received the list of statements via SurveyMonkey® and had two weeks' time to complete the survey, with a reminder email sent after one week. The steering committee evaluated all the responses. The statements with 50–69% of the expert panel rating their agreement as 5 or higher were revised based on the qualitative feedback provided. For the second Delphi consensus round, the revised statements were sent to the clinical experts who had already participated in the first round.[15] The panelists again had two weeks' time to provide their level of agreement and qualitative feedback, with a reminder email sent after one week (**Fig. 2**).

The definition of thrombophilia testing was based on previously defined thrombophilia definitions and distributed to all participating clinical experts in the form of a cheat sheet for both rounds (**Supplementary Fig. 1**). Thrombophilia was defined as follows: low-risk hereditary thrombophilia (mutations factor V Leiden (FVL) and prothrombin G20210A gene mutation (PGM)), high-risk hereditary thrombophilia (deficiencies of antithrombin, protein C, or protein S, homozygous/compound heterozygous FVL/PGM), acquired thrombophilia (antiphospholipid antibodies (1 or more of Lupus anticoagulant, anticardiolipin antibodies, and anti–β2-glycoprotein 1 antibodies).[1–3,16] MTHFR polymorphisms and FVIII, FIX, FXI, and PAI-1 polymorphisms were not considered as clinically relevant thrombophilias due to missing or conflicting data.[1] Additionally, a positive family history for

Fig. 1 Seven-point Likert scale used to assess expert agreement. Levels of agreement range from 1 (strongly disagree) to 7 (strongly agree).

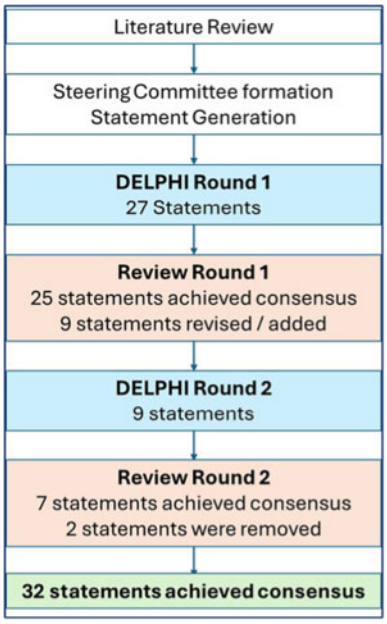

Fig. 2 Overview of the modified Delphi consensus study. Statements with at least 70% of clinical experts rating their agreement as Likert-5 or higher were retained in the final consensus; statements with 50–69% agreement of Likert-5 or higher were revised based on the provided qualitative feedback and redistributed to the expert panel in a second round; statements with less than 50% of agreement of Likert-5 or higher were removed.

VTE was defined as having a first- or second-degree relative with VTE at a young age (<50 years old).[17–19] Congruently, the definition for a positive family history for thrombophilia was having a first- or second-degree relative with thrombophilia.

In the survey statements, transient risk factors were referred to as "major" and "minor," with illustrative examples provided. This terminology is consistent with previously published definitions.[20]

For statistical analysis, all data gathered from both Delphi survey rounds were transferred from SurveyMonkey® to a Microsoft Excel spreadsheet and subsequently evaluated in the statistics program "R".[14,21] Findings were summarized with descriptive statistics including median, interquartile ranges (IQR), and frequencies (%). Only the statements that reached the a priori criteria were included in the final list of consensus statements.

Results

Sixty-nine experts provided their email addresses in response to the Delphi survey invitation, 46 completed the first round, and 42 clinical experts completed both rounds of the survey, with a response rate of 67% in round 1 and 91% in round 2. The panel comprised clinical experts from nine medical specialties, with the majority holding specialty certificates in more than one field. Their median time in clinical practice was 14 years (IQR 10–20 years). Participant characteristics for both rounds are shown in **Table 1**.

In the first round, 27 statements were distributed, of which 25 met the a priori consensus agreement (**Table 2** – green) and were retained as final consensus (**Fig. 3**). These statements addressed indications for thrombophilia testing in the following clinical scenarios: unprovoked VTE, unusual site VTE, provoked VTE with minor and major risk factors, hormone- or pregnancy-associated VTE, individuals without VTE but with a positive family history of VTE and/or thrombophilia, and pediatric VTE.

Median Likert scores among consensus statements ranged from 5.5 to 7, reflecting overall agreement across the evaluated statements (**Table 2**). The remaining two statements received 50–69% of the Likert score ≥5 and were therefore revised based on the qualitative feedback received from the expert panel (**Table 2** – orange).

Additionally, new statements were generated based on the written feedback, resulting in a total of nine statements involved in the second round. Of these, seven reached the a priori established consensus criteria (**Table 2** – green) and were added to the final consensus statements (**Fig. 3**). These scenarios included unprovoked VTE with additional persisting clinical risk factors (e.g., obesity, other chronic inflammatory conditions), VTE provoked by minor risk factors, and patients without VTE but with a positive family history for VTE and/or thrombophilia. The remaining two statements of round 2 achieved agreement levels below 50% (Likert score ≥5) and were thus discarded as defined a priori (**Table 2** – red).

These two statements (29 and 30) proposed not performing hereditary thrombophilia testing in patients with unprovoked VTE and with an additional persisting clinical risk factor (e.g., obesity or chronic inflammatory conditions, excluding malignancy) in patients ≤40 and 40–60 years of age, respectively. Agreement was low for both age groups (24% and 46% for patients ≤40 and 40–60 years, respectively). Comments provided in the free-text responses were summarized to describe the reasons for the lack of consensus (see **Supplementary Table 1**). **Fig. 3** summarizes the consensus on indications for thrombophilia testing in various clinical scenarios based on the findings from this modified Delphi process.

Discussion

Expert consensus was obtained through this modified Delphi survey based on a harmonized thrombophilia testing approach within Switzerland to be directly applied to the clinical care of patients. Two rounds with 42 clinical experts were conducted to reach consensus on 32 clinical scenarios and thrombophilia testing.

When considering whether it is appropriate to test for thrombophilia, it is important to be aware of the multiple objectives that the testing may serve. These include guiding management of an individual patient's VTE treatment,[4] identifying potential underlying causes of a thromboembolic event, assessing the risk of thrombosis recurrence in affected patients, or estimating the risk of a first thrombotic event in asymptomatic family members with potential implications for primary prevention.[1,2,4,10] The American Society of Haematology (ASH) guidelines primarily

Table 1 Characteristics of Delphi survey participants for each round.

Details of Delphi survey participants	Round 1 *N* = 46[1]	Round 2 *N* = 42[1]
I am a physician and I hold a specialty certificate in...*		
Hematology	30/46 (65%)	27/42 (64%)
Internal Medicine	22/46 (48%)	22/42 (52%)
Pediatric Hematology	10/46 (22%)	10/42 (24%)
Laboratory medicine	6/46 (13%)	6/42 (14%)
Pediatrics	4/46 (9%)	4/42 (10%)
Medical oncology	1/46 (2%)	1/42 (2%)
Angiology	1/46 (2%)	1/42 (2%)
Transfusion medicine	1/46 (2%)	1/42 (2%)
Palliative care	1/46 (2%)	–
In training (Hematology)	1/46 (2%)	–
My clinical practice is...*		
Hospital based	41/46 (89%)	37/42 (88%)
Private practice	6/46 (13%)	6/42 (14%)
Consultant	1/46 (2%)	1/42 (2%)
My clinical practice is...		
Mainly hemostaseology (2/3 of patients)	13/46 (28%)	13/42 (31%)
General hematology with hemostaseology >50% of patients	7/46 (15%)	7/42 (17%)
General hematology with hemostaseology <50% of patients	25/46 (54%)	21/42 (50%)
Other	1/46 (2%)	1/42 (2%)
Thrombophilia testing is executed at...*		
Own laboratory (Practice)	7/46 (15%)	7/42 (18%)
Laboratory affiliated to hospital	33/46 (72%)	27/42 (68%)
Third-party laboratory	11/46 (24%)	8/42 (20%)
Years of clinical experience since specialization	14 (10, 20)	14 (10, 20)
How many thrombophilia referrals per week do you see/supervise (total number)?	3 (2, 5)	3 (2, 5)
How many thrombophilia diagnostics per week do you conduct/supervise (total number)?	2 (1, 5)	3 (1, 5)

[1] *n*/*N* (%); Median (Q1, Q3);
*more than one answer possible.

focus on whether the thrombophilia test results would impact management or treatment of the individual patient.[4] In contrast, the British Society of Haematology (BSH) guidelines place less emphasis on therapy impact and instead highlight targeted testing in clearly defined clinical scenarios, while also noting that testing should only be performed when the clinical utility is clear.[5] Due to a lack of strong clinical evidence, the majority of recommendations in the published guidelines are conditional, based on weak evidence or on expert opinions.

Through this Delphi survey, we have established the current consensus practice with regard to thrombophilia testing in Switzerland; these consensus statements do not fully align with the ASH or BSH guidelines (**Supplementary Table 2**). The results of this survey are not intended to serve as formal guidelines for thrombophilia testing. However, they may aid clinicians in decision-making around thrombophilia testing in daily clinical practice and support more consistent testing practices in routine care.

Key consensus findings in this survey were identified across several clinical scenarios. *Age-related testing:* Patients aged >60 years with VTE (unprovoked, provoked, unusual site) are not to be tested for hereditary thrombophilia. The age categories used in the Delphi process (<40, 40–60, and >60 years) were predefined as pragmatic clinical strata and capture the clinical concept that hereditary thrombophilia is more likely to occur in younger patients. The age threshold of 60 years was derived from the Delphi process itself: statements addressing age-dependent testing were initially voted upon across the three age groups, and where responses were identical for the two younger groups, these were combined. This yielded a consensus-suggested age cutoff at 60 years. This threshold is higher than the 45–50 years given by some previous publications, but it reflects expert consensus and aligns with epidemiological data showing a marked increase in VTE incidence after age 60.[1,22] *VTE provoked by major risk factors:* In patients with VTE provoked by surgery, a nonsurgical major transient risk factor, or malignancy,

Table 2 Delphi consensus statements, voting results, and consensus classification across all rounds.

	Statement	Median Likert (IQR)	Agreement for Likert ≥ 5 *n*/*N* (%)
	DELPHI ROUND 1		
	Unprovoked VTE		
1	40 y.o. or younger patient with unprovoked VTE i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	7 (6, 7)	44/46 (96%)
2	40 to 60 y.o. patient with unprovoked VTE i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	6 (5, 6)	39/43 (91%)
3	>60 y.o. patient with unprovoked VTE i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	6 (5, 7)	36/43 (84%)
4*	Patient with unprovoked VTE, and additional persisting clinical risk factor (e.g., obesity) i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	5 (3, 6)	24/45 (53%)
5	Patient with thrombophlebitis in varicose vein (superficial, <10 cm) i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest NOT to do acquired thrombophilia testing	7 (6, 7)	43/45 (96%)
	Provoked VTE		
6	Patient with VTE and surgical transient risk factor (e.g., spinal surgery with immobilization) i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest NOT to do acquired thrombophilia testing	6.5 (6, 7)	42/46 (91%)
7	Patient with VTE and nonsurgical major transient risk factor (e.g., confined to bed in hospital for at least 3 days with an acute illness, leg fracture, etc.) i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest NOT to do acquired thrombophilia testing	6 (6, 7)	39/46 (85%)
8	Patient with VTE and malignancy i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest NOT to do acquired thrombophilia testing	6 (6, 7)	41/46 (89%)
9	40 y.o. or younger patient with VTE and non-surgical minor transient risk factor (e.g., Long-distance travel ± dehydration) i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	6 (6, 7)	40/46 (87%)
10	40–60 y.o. patient with VTE and nonsurgical minor transient risk factor (e.g., long-distance travel ± dehydration) i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	5.5 (5, 6)	37/44 (84%)
11*	>60 y.o. patient with VTE and nonsurgical minor transient risk factor (e.g., long-distance travel ± dehydration) i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest NOT to do acquired thrombophilia testing	6 (5, 6.5)	36/43 (84%)
	Provoked VTE – women, hormonal		
12	Female patient, pregnant, presents with VTE, no other provoking factors, no family history of VTE i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	6 (6, 7)	37/45 (82%)
13	Female patient, taking estrogen containing contraceptive, presents with VTE, no other provoking factors i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	6 (5, 7)	36/45 (80%)
	Unusual site VTE		
14	40 y.o. or younger patient with CSVT (cerebral sino-venous thrombosis) or splanchnic vein thrombosis, no provoking VTE factors. Normal CBC – normal WBC, normal Hb, normal platelets, normal indices i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing iii. Consider to do further diagnostics (tests for paroxysmal nocturnal hemoglobinuria (PNH), myeloproliferative neoplasm (MPN) – incl. JAK2 mutation)	7 (6, 7)	46/46 (100%)

(*Continued*)

Table 2 (*Continued*)

	Statement	Median Likert (IQR)	Agreement for Likert ≥ 5 *n*/*N* (%)
15	40 to 60 y.o. patient with CSVT or splanchnic vein thrombosis, no provoking VTE factors. Normal CBC – normal WBC, normal Hb, normal platelets, normal indices i. Suggest to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing iii. Consider to do further diagnostics (tests for PNH, MPN – incl. JAK2 mutation)	6.5 (6, 7)	44/44 (100%)
16	>60 y.o. patient with CSVT or splanchnic vein thrombosis, no provoking VTE factors. Normal CBC – normal WBC, normal Hb, normal platelets, normal indices i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing iii. Consider to do further diagnostics (tests for PNH, MPN – incl. JAK2 mutation)	6 (5, 7)	38/44 (86%)
	No VTE in patient		
17*	<60 y.o. patient, no VTE in patient. Positive family history for VTE AND familial thrombophilia i. High-risk thrombophilia: suggest to do targeted thrombophilia testing (i.e., selectively test for the known familial thrombophilia) ii. Low-risk thrombophilia: suggest NOT to do targeted thrombophilia testing	6 (4.25, 6)	34/46 (74%)
18	No VTE in patient, first-degree relative with VTE, unknown familial thrombophilia status. i. Suggest NOT to do hereditary thrombophilia testing	6 (5, 7)	36/46 (78%)
19	No VTE in patient, no family history of VTE, but positive family history for low-risk thrombophilia i. Suggest NOT to do thrombophilia testing	6 (5, 7)	38/46 (83%)
	No VTE in patient – women, hormonal		
20	Female patient planning pregnancy or before starting estrogen containing contraceptive. No VTE in patient, positive family history for VTE AND for familial thrombophilia i. High-risk thrombophilia: suggest to do targeted thrombophilia testing (i.e., selectively test for the known familial thrombophilia) ii. Low-risk thrombophilia: suggest to do targeted thrombophilia testing (i.e., selectively test for the known familial thrombophilia)	6 (6, 7)	42/46 (91%)
21*	Female patient, No VTE in patient, positive family history for VTE, unknown familial thrombophilia status. Thrombophilia testing before planning pregnancy or start estrogen containing contraceptive? i. Suggest NOT to do hereditary thrombophilia testing	5.5 (2.25, 6)	27/46 (59%)
22	Female patient considering hormone replacement therapy (HRT), no VTE in patient, positive family history for VTE, known familial thrombophilia i. High-risk thrombophilia: suggest to do targeted thrombophilia testing (i.e., selectively test for the known familial thrombophilia) ii. Low-risk thrombophilia: suggest NOT to do thrombophilia testing	6 (5, 6)	37/45 (82%)
23	Female patient with history of pregnancy complications (e.g., recurrent miscarriages, preeclampsia), No VTE in patient i. Suggest NOT to do hereditary thrombophilia testing ii. Suggest to do acquired thrombophilia testing	6 (6, 7)	40/44 (91%)
24	Female patient, no VTE, no family history of VTE, no family history of thrombophilia. Considering estrogen containing contraception i. Suggest NOT to do thrombophilia testing	7 (7, 7)	46/46 (100%)
	Pediatric VTE		
25	Newborn with purpura fulminans or other severe unprovoked VTE (e.g., extensive CSVT) i. Suggest to do high-risk thrombophilia testing immediately	7 (6, 7)	35/37 (95%)
26	Asymptomatic otherwise healthy child, with positive family history of VTE, positive family history of thrombophilia i. High-risk thrombophilia: suggest to do targeted thrombophilia testing after first year of life ii. Low-risk thrombophilia: suggest NOT to do thrombophilia testing. Counseling later in adolescence – according to adult thrombophilia practices	6 (5, 6)	28/36 (78%)
27	Child with provoked VTE (e.g., central venous line), no family history for VTE, no family history for thrombophilia i. suggest NOT to do thrombophilia testing	6 (6, 7)	34/36 (94%)

(*Continued*)

Table 2 (*Continued*)

	Statement	Median Likert (IQR)	Agreement for Likert ≥ 5 *n*/*N* (%)
	DELPHI ROUND 2		
28	Patient with unprovoked VTE, and additional persisting clinical risk factor (e.g., obesity, other chronic inflammatory conditions, not malignancy) (a) Suggest to do acquired thrombophilia testing (independent of patient's age)	6 (5, 6)	34/42 (81%)
29	Patient with unprovoked VTE, and additional persisting clinical risk factor (e.g., obesity, other chronic inflammatory conditions, not malignancy) (b) 40 y.o. or younger: suggest NOT to do hereditary thrombophilia testing	2 (2, 4)	10/41 (24%)
30	Patient with unprovoked VTE, and additional persisting clinical risk factor (e.g., obesity, other chronic inflammatory conditions, not malignancy) (c) 40–60 y.o.: suggest NOT to do hereditary thrombophilia testing	4 (3, 5.5)	18/39 (46%)
31	Patient with unprovoked VTE, and additional persisting clinical risk factor (e.g., obesity, other chronic inflammatory conditions, not malignancy) (d) >60 y.o.: suggest NOT to do hereditary thrombophilia testing	6 (6, 7)	34/39 (87%)
32	>60 y.o. patient with VTE and nonsurgical minor transient risk factor (e.g., Long-distance travel ± dehydration) (a) Suggest NOT to do hereditary thrombophilia testing	6 (6, 7)	35/39 (90%)
33	>60 y.o. patient with VTE and nonsurgical minor transient risk factor (e.g., Long-distance travel ± dehydration) (b) Suggest to do acquired thrombophilia testing	6 (3.5, 6)	28/38 (74%)
34	<60 y.o. male patient, no VTE in patient. Positive family history for VTE AND positive history for familial thrombophilia (a) High-risk thrombophilia: suggest to do targeted thrombophilia testing (i.e., selectively test for the known familial thrombophilia)	6 (6, 7)	38/42 (90%)
35	<60 y.o. male patient, no VTE in patient. Positive family history for VTE AND positive history for familial thrombophilia (b) Low-risk thrombophilia: suggest NOT to do targeted thrombophilia testing	6 (5, 6)	35/42 (83%)
36	Female patient, No VTE in patient, positive family history for VTE, familial thrombophilia status not possible to determine. Thrombophilia testing before planning pregnancy or start estrogen containing contraceptive? (i) Suggest NOT to do hereditary thrombophilia testing: The complete VTE risk assessment in this patient is not possible without knowing the thrombophilia status of the index patient, i.e., a negative hereditary thrombophilia test result in this patient could give false reassurance of the actual risk	6 (4, 6)	30/42 (71%)

Statements were rated on a 7-point Likert scale. Statements with at least 70% of clinical experts rating their agreement as 5 or higher were retained in the final consensus (green); statements with 50–69% agreement of Likert-5 or higher in round 1 were revised based on the provided qualitative feedback and redistributed to the expert panel in round 2 (orange); statements with less than 50% of agreement of Likert-5 or higher were removed (red).
*: Statements which were revised based on qualitative feedback.
Abbreviations: CBC (complete blood count), CSVT (cerebral sinovenous thrombosis), Hb (hemoglobin), IQR (interquartile range), VTE (venous thromboembolism), WBC (white blood count), y.o. (years old).

no thrombophilia testing is required. *Thrombophlebitis in varicose veins:* no thrombophilia testing is required. Of note, this statement applies specifically to superficial thrombophlebitis in varicose veins of limited extent (<10 cm), intended to represent a predominantly local, varicose-triggered event. More extensive or clinically higher-risk superficial vein thrombosis such as close proximity to the deep venous system or not confined to varicose veins were not addressed in this survey and warrant individualized clinical assessment regarding thrombophilia testing.[23,24] *Pregnancy-related complications (not VTE)*: testing should focus on acquired thrombophilia (antiphospholipid antibodies) testing only; hereditary thrombophilia testing is not required in this scenario. *Family history of thrombophilia:* for families with known high-risk thrombophilia, targeted testing is to be offered to first- and second-degree relatives. In families with known low-risk thrombophilia, targeted testing is not offered to children or male members but is offered to women considering estrogen-containing contraceptives or pregnancy, as these may affect the type of contraceptive or post-partum thromboprophylaxis. This statement specifically refers to the fact that estrogen-containing contraceptives/combined oral contraception (COC) and progestin-only contraceptives, except for depot medroxyprogesterone acetate, are not associated with a significant increase in thromboembolic risk and can generally be used safely in women at risk of VTE.[4,25] *Pediatrics*: in children with severe unprovoked VTE (e.g., purpura fulminans, extensive DVT), thrombophilia testing should be done immediately to offer optimal treatment (e.g., protein C replacement in protein C

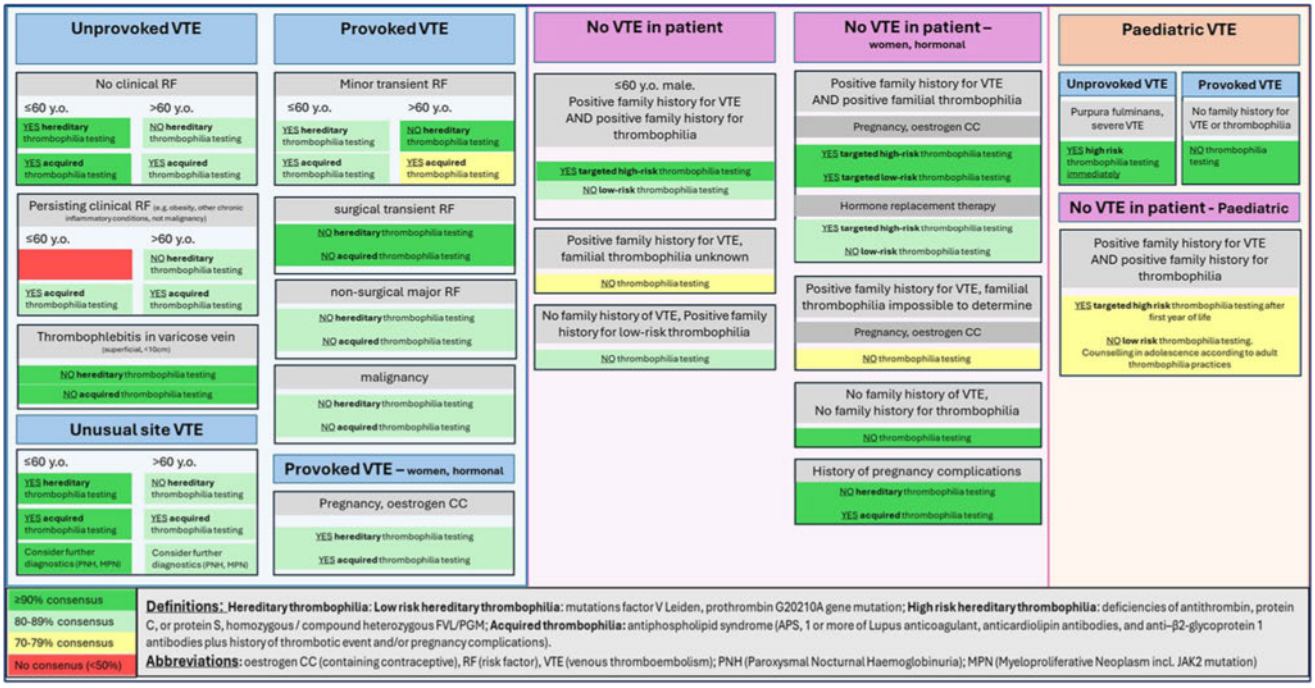

Fig. 3 **Consensus-based indications for thrombophilia testing across clinical scenarios. Clinical scenarios are presented for patients with VTE (blue), for patients without VTE (purple), and for children (orange). Level of consensus is shown: dark green (≥90% consensus), light green (80–89% consensus), yellow (70–79% consensus), red (<50% consensus).**

deficiency); children with provoked VTE (e.g., central venous line) do not require thrombophilia testing.

There were strong opinions among the experts regarding families with a positive family history for VTE and unknown thrombophilia status. The overall input was that the index patients with VTE should be identified first and they should undergo thrombophilia testing according to the consensus practices outlined in this survey; only then should family testing be considered according to the consensus practices developed for relatives. The identification of hereditary thrombophilia in an index patient has important downstream consequences beyond the individual, including implications for relatives and the potential for cascade testing. Genetic counseling is an integral part of this process, ensuring that patients and their relatives are adequately informed about the implications, limitations, and potential consequences of testing, including psychological burden and possible implications for insurance, in line with national legal requirements (e.g., the Federal Act on Human Genetic Testing in Switzerland).[26]

Notably, the only scenarios without consensus were Statements 29 and 30, which suggested not performing hereditary thrombophilia testing in patients aged <60 years with unprovoked VTE and an additional persisting clinical risk factor (e.g., obesity or other chronic inflammatory conditions, excluding malignancy). Expert comments highlighted several sources of disagreement: patient age, ambiguity in defining truly unprovoked VTE, implications for long-term anticoagulation dosing, and the potential relevance for family counseling. These findings emphasize that decisions may depend on context-dependent weighting of risk factors and the intended purpose of testing, reflecting a genuinely uncertain scenario, which is not addressed in current ASH or BSH guidelines either and warrants further studies.[4,5]

Importantly, the timing of thrombophilia testing in relation to an acute clinical event was not within the scope of this Delphi survey. Nonetheless, several preanalytical factors are crucial when performing and interpreting thrombophilia tests, as results may be significantly influenced by the clinical context. Thrombophilia testing should generally be deferred until at least 3 months after an acute event, since protein C, protein S, and antithrombin levels can be transiently reduced due to consumption, potentially leading to misleading results.[1,10] In addition, ongoing anticoagulant therapy itself can interfere with testing: vitamin K antagonists decrease protein C and S levels, while direct oral anticoagulants interfere with clot-based assays, chromogenic antithrombin activity assays, and lupus anticoagulant testing, in particular.[1,3] Physiological changes during pregnancy, such as reduced protein S levels and acquired APC resistance, require cautious interpretation and, if needed, confirmation postpartum.[27] Although these factors were not explicitly addressed in the Delphi statements, they remain important to ensure reliable thrombophilia test results in clinical practice.

In this Delphi survey, the statements were generated to portray typical clinical scenarios. We do acknowledge, that in clinical practice each patient has to be considered individually. Nuances could not be captured for all possible scenarios in this survey, but the consensus statements may aid as a foundation or orientation in clinical decision-making. In addition, also terms such as

"major" or "minor" transient risk factors were used in the survey statements with illustrative examples; no exhaustive or formal definitions were provided to participants and individual interpretations may therefore have varied. The Delphi survey was also not designed to achieve consensus on genetic thrombophilia screening panels ordered by some professionals. Furthermore, no additional prerequisites beyond society membership were required to participate as an expert, and the expert panel was not formally matched to the demographic structure of the Swiss hematological societies. The practice setting and associated laboratory access may influence testing preferences and thresholds: The majority of respondents were hospital-based with mostly in-house thrombophilia laboratory testing. This distribution reflects the structure of hematology practice in Switzerland, where the vast majority of hematologists are hospital-based and only a limited proportion practice in outpatient settings. While practice-based clinicians may also have access to thrombophilia testing through affiliated laboratories, differences in access and testing logistics may nevertheless have influenced responses. This potential source of bias should be considered when interpreting the consensus statements.

Limitations

While the Delphi method provides a structured approach to consensus-building, several limitations should be considered when interpreting the findings of this consensus survey. First, the expert panel was composed primarily of clinicians with experience in thrombosis and hemostasis, which may limit the generalizability of the results to broader clinical settings or to specialties less familiar with thrombophilia testing. Although efforts were made to ensure diversity in specialty and practice environments, the panel may not fully represent all relevant stakeholders, including primary care providers and patient representatives. Additionally, the absence of high-certainty outcome data and reliance on expert opinion mean that consensus statements are conditional and may change as new evidence emerges. The lack of consensus on specific scenarios, such as unprovoked VTE with persisting minor risk factors, further underscores the need for ongoing research and harmonization of practice.

Outlook

The consensus identified in this Delphi process reflects current expert opinion and practice regarding thrombophilia testing in Switzerland. It may serve as a resource to inform clinicians on current consensus practices for specific clinical scenarios. These statements should not be regarded as formal guidance or guidelines. In the future, integration of the results of this survey with emerging evidence may contribute to the development of formal guidance or guidelines for thrombophilia testing.

Although these consensus statements were developed within the Swiss context, the findings are likely applicable to other Central European healthcare settings with comparable clinical practice patterns. A recently published Delphi consensus from Germany addressing thrombophilia testing in women reached largely similar recommendations supporting the broader relevance of our findings.[28] However, differences in healthcare systems, laboratory access, reimbursement structures, and genetic counseling requirements may influence thrombophilia testing practices across countries. Local adaptation of these statements may therefore be warranted.

Conclusion

The consensus process in this Delphi study engaged an expert panel to develop harmonized statements for thrombophilia testing across various clinical scenarios. Through iterative rounds, the panel achieved agreement on targeted testing strategies, emphasizing individualized risk assessment and the importance of clinical context.

These consensus statements reflect current expert opinion and practice and may serve as a resource to support more consistent testing practices and inform clinical decision-making. Dissemination of these statements to front-line clinicians and laboratories may facilitate knowledge translation and ongoing education. Further research and integration with emerging evidence are essential to refine testing practices and address remaining uncertainties in the field.

Author Affiliations

1 Haematology, University Children's Hospital Zürich, Zurich, ZH, Switzerland
2 Medical Oncology and Haematology, University Hospital Zurich, Zürich, ZH, Switzerland
3 Eastern Switzerland Haemophilia and Haemostasis Centre, Sankt Gallen Centre for Laboratory Medicine, St. Gallen, SG, Switzerland
4 Haematology, Cantonal Hospital of Lucerne, Lucerne, Switzerland

Statements and Additional Information

Conflict of Interest The authors have no conflicts of interests to declare related to this study. Alessandra Bosch is supported by research grants from the "Claus Cramer Foundation," "Filling the gap program," and "Walter and Gertraud Siegenthaler Foundation" from the University of Zurich, Switzerland.

Acknowledgements *This is a project of the WPH (Working Party Haemostasis) of the SSH (Swiss Society of Haematology).* We thank all clinical experts from the Swiss Society of Haematology and the Swiss Society of Paediatric Haematology and Oncology who participated in this Delphi survey for their valuable contributions and discussion points. We also thank Lars Asmis who helped with the conceptualization of this study, and Lorenzo Alberio for his expert advice on the interpretation of findings and refining of the manuscript.

Contributors' Statement A.B.: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Visualization, Writing—original draft, Writing—review & editing. C.S.: Project administration, Validation, Visualization, Writing—review & editing. L.G.: Conceptualization, Formal analysis, Project administration, Supervision, Validation, Writing—review & editing. S.R.-G.: Conceptualization, Formal analysis, Project administration, Supervision, Validation, Writing—review & editing.

Supplementary Material is available online at https://doi.org/10.1055/a-2858-0105

References

1 Connors JM. Thrombophilia testing and venous thrombosis. Longo DL, editor. N Engl J Med 2017;377(12):1177–1187. 10.1056/NEJMra1700365
2 Laer CV, Vanrenterghem M, Jacquemin M, et al. Genotype vs laboratory phenotype correlation of defects in natural anticoagulants in patients with

venous thromboembolism. J Thromb Haemost 2025;23(09):2873–2882. 10.1016/j.jtha.2025.05.016 PubMed PMID: 40436275

3 Devreese KMJ, de Groot PG, de Laat B, et al. Guidance from the scientific and standardization committee for lupus anticoagulant/antiphospholipid antibodies of the international society on thrombosis and Haemostasis. J Thromb Haemost 2020;18(11):2828–2839. 10.1111/jth.15047

4 Middeldorp S, Nieuwlaat R, Baumann Kreuziger L, et al. American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. Blood Adv 2023;7(22):7101–7138. 10.1182/bloodadvances.2023010177 PubMed PMID: 37195076; PubMed Central PMCID: PMC10709681

5 Arachchillage DJ, Mackillop L, Chandratheva A, Motawani J, MacCallum P, Laffan M. Thrombophilia testing: a British Society for Haematology guideline. Br J Haematol 2022;198(03):443–458. 10.1111/bjh.18239 PubMed PMID: 35645034; PubMed Central PMCID: PMC9542828

6 Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv 2020;4(19):4693–4738. 10.1182/bloodadvances.2020001830

7 Cohn DM, Vansenne F, de Borgie CA, Middeldorp S. Thrombophilia testing for prevention of recurrent venous thromboembolism. Cochrane Database Syst Rev 2012;12(12):CD007069. 10.1002/14651858.CD007069.pub3 PubMed PMID: 23235639; PubMed Central PMCID: PMC7389374

8 Schünemann HJ, Cushman M, Burnett AE, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. Blood Adv 2018;2(22):3198–3225. 10.1182/bloodadvances.2018022954

9 Di Nisio M, Valeriani E, Riva N, Schulman S, Beyer-Westendorf J, Ageno W. Anticoagulant therapy for splanchnic vein thrombosis. J Thromb Haemost 2020;18(07):1562–1568. 10.1111/jth.14836

10 Stevens SM, Woller SC, Bauer KA, et al. Guidance for the evaluation and treatment of hereditary and acquired thrombophilia. J Thromb Thrombolysis 2016;41(01):154–164. 10.1007/s11239-015-1316-1 PubMed PMID: 26780744; PubMed Central PMCID: PMC4715840

11 Hohmann E, Cote MP, Brand JC. Research pearls: expert consensus based evidence using the Delphi method. Arthroscopy: J Arthrosco Relat Surg 2018;34(12):3278–3282. 10.1016/j.arthro.2018.10.004

12 McPherson S, Reese C, Wendler MC. Methodology update: Delphi studies. Nurs Res 2018;67(05):404–410. 10.1097/NNR.0000000000000297 PubMed PMID: 30052591

13 Naveed K, Goldberg N, Shore E, et al. Defining ferritin clinical decision limits to improve diagnosis and treatment of iron deficiency: a modified Delphi study. Int J Lab Hematol 2023;45(03):377–386. 10.1111/ijlh.14016 PubMed PMID: 36602151

14 SurveyMonkey: The World's Most Popular Survey Platform [Internet]. [cited 2026 Feb 14]. Available from: https://www.surveymonkey.com/

15 Boel A, Navarro-Compán V, Landewé R, van der Heijde D. Two different invitation approaches for consecutive rounds of a Delphi survey led to comparable final outcome. J Clin Epidemiol 2021;129:31–39. 10.1016/j.jclinepi.2020.09.034 PubMed PMID: 32991995

16 Mannucci PM, Franchini M. Classic thrombophilic gene variants. Thromb Haemost 2015;114(05):885–889. 10.1160/TH15-02-0141 PubMed PMID: 26018405

17 Couturaud F, Leroyer C, Tromeur C, et al. Factors that predict thrombosis in relatives of patients with venous thromboembolism. Blood 2014;124(13):2124–2130. 10.1182/blood-2014-03-559757 PubMed PMID: 25049279; PubMed Central PMCID: PMC4186541

18 Zöller B, Li X, Ohlsson H, Ji J, Sundquist J, Sundquist K. Family history of venous thromboembolism as a risk factor and genetic research tool. Thromb Haemost 2015;114(11):890–900. 10.1160/TH15-04-0306

19 Bezemer ID, van der Meer FJM, Eikenboom JCJ, Rosendaal FR, Doggen CJM. The value of family history as a risk indicator for venous thrombosis. Arch Intern Med 2009;169(06):610–615. 10.1001/archinternmed.2008.589

20 Kearon C, Ageno W, Cannegieter SC, et al. Categorization of patients as having provoked or unprovoked venous thromboembolism: guidance from the SSC of ISTH. J Thromb Haemost 2016;14(07):1480–1483. 10.1111/jth.13336

21 R: The R Project for Statistical Computing [Internet]. [cited 2026 Feb 14]. Available from: https://www.r-project.org/

22 Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. Arch Intern Med 1998;158(06):585–593. 10.1001/archinte.158.6.585

23 Piazza G, Krishnathasan D, Hamade N, et al. Superficial vein thrombosis: a review. JAMA 2025;334(22):2020–2030. 10.1001/jama.2025.15222

24 Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest 2021;160(06):e545–e608. 10.1016/j.chest.2021.07.055 PubMed PMID: 34352278

25 Tepper NK, Nguyen AT, Whiteman MK, Curtis KM. Progestin-only contraception and thrombosis: an updated systematic review. Contraception 2025:110978. 10.1016/j.contraception.2025.110978 PubMed PMID: 40451566; PubMed Central PMCID: PMC12381897

26 Fedlex [Internet]. [cited 2026 Mar 29]. SR 810.12 - Bundesgesetz vom 15. Juni 2018 über genetisch... Available from: https://www.fedlex.admin.ch/eli/cc/2022/537/de

27 American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics. ACOG practice bulletin no. 197: inherited Thrombophilias in pregnancy. Obstet Gynecol 2018;132(01):e18–e34. 10.1097/AOG.0000000000002703 PubMed PMID: 29939939

28 Linnemann B, Bauersachs R, Bergmann F, et al. Thrombophilia testing in women and adolescent girls—position paper from the standing committee on women's health issues of the Society for Thrombosis and Haemostasis Research (GTH). Hamostaseologie 2026. 10.1055/a-2780-3709