

Development and Validation of a Stakeholder-Informed Requirements Framework for a Thrombosis and Anticoagulation Clinical Decision Support System

Abstract

Aims: To derive and validate a stakeholder-informed set of requirements for a clinical decision support system (CDSS) designed to support thrombosis and anticoagulant management.

Methods: A sequential mixed-methods design was conducted comprising a targeted literature review, semi-structured interviews, iterative questionnaire development, content validation, and quantitative analysis. Seven experts participated in the qualitative phase, and 35 cardiologists and clinical pharmacists completed the final 48-item questionnaire. Content validity was assessed using the content validity ratio (CVR) and item-level content validity index (I-CVI), internal consistency using Cronbach's alpha, and group and age-related differences using nonparametric tests.

Findings: The literature review included 55 studies and indicated that existing CDSSs commonly address venous thromboembolism risk assessment, thromboprophylaxis, anticoagulant prescribing, or atrial fibrillation-related management. Interviews identified six requirement domains and 42 subthemes. All retained items had a CVR of 1.00, with an overall mean I-CVI of 0.996. Domain-level mean scores ranged from 4.42 to 4.67 on a five-point scale, and overall Cronbach's alpha was 0.973. No significant differences were found between cardiologists and clinical pharmacists. Age was positively associated with the Clinical Information Requirements domain ($p=0.372$, $p=0.033$).

Conclusion: The validated framework encompasses clinical functionality, information requirements, workflow fit, perceived usefulness, usability, and trust. These findings provide stakeholder-informed requirements for specifying and evaluating thrombosis-focused CDSSs while supporting individualized anticoagulation decisions and preserving clinician oversight.

Keywords: Thrombosis; Anticoagulants; Decision Support Systems, Clinical; Surveys and Questionnaires; Medical Informatics

MeSH URLs:

Thrombosis: <https://meshb.nlm.nih.gov/record/ui?ui=D013927>

Anticoagulants: <https://meshb.nlm.nih.gov/record/ui?ui=D000925>

Decision Support Systems, Clinical: <https://meshb.nlm.nih.gov/record/ui?ui=D020000>

Surveys and Questionnaires: <https://meshb.nlm.nih.gov/record/ui?ui=D011795>

Medical Informatics: <https://meshb.nlm.nih.gov/record/ui?ui=D008490>

1. Introduction

Thrombotic disease creates a substantial clinical burden, while anticoagulant therapy introduces a second layer of risk because treatment decisions must balance prevention of thrombosis against bleeding. Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a major component of this burden, and anticoagulants are also central to the management of atrial fibrillation and other thromboembolic conditions [1–5].

Anticoagulation decisions are rarely determined by a single clinical variable. Dose selection and treatment duration may depend on renal and hepatic function, age, interacting medicines, pregnancy, bleeding risk, thrombophilia, platelet count, procedural plans, and the indication for therapy.

Consequently, clinicians must combine patient-specific information with recommendations that are periodically revised [2,5,6].

CDSSs are designed to make such information actionable at the point of care. Conventional systems can provide reminders, alerts, risk calculations, prescribing support, and guideline-linked recommendations, while newer approaches incorporate artificial intelligence and machine learning [7–10]. Evidence from thrombosis-related applications suggests benefits in areas such as VTE risk assessment, prophylaxis, and medication management; however, many systems remain limited to a particular decision or patient group [11–13].

User requirements are therefore a central design issue rather than a secondary usability consideration. A technically accurate recommendation can have limited clinical value if required data are unavailable, the system interrupts workflow, explanations are inadequate, or clinicians do not trust the output. The Technology Acceptance Model emphasizes perceived usefulness and ease of use, whereas Task-Technology Fit focuses on the match between system capabilities and clinical tasks [15,16]. User-centered CDSS research likewise supports involving clinicians in development and implementation [9,14].

Despite substantial work on thrombosis-related CDSSs, the available literature provides limited guidance on the broader combination of functions, information, workflow characteristics, usability, and trust requirements that should be considered before development of a comprehensive thrombosis-focused system. The present study addressed this gap by integrating evidence from the literature with stakeholder interviews and questionnaire validation.

The objective was to develop and quantitatively validate a stakeholder-informed requirements framework for a CDSS supporting thrombosis and anticoagulant management. The study specifically examined content validity, internal consistency, perceived importance of requirement domains, professional-group differences, and the association between age and domain scores.

Accordingly, this study addressed the following research questions:

RQ1: What clinical, information, workflow, usability, usefulness, and trust requirements should be considered when developing a thrombosis and anticoagulation CDSS?

RQ2: Do the identified questionnaire items demonstrate acceptable content validity and internal consistency for measuring these requirements?

RQ3: How do clinicians rate the importance of the identified requirement domains?

RQ4: Do the perceived importance of the requirement domains differ between cardiologists and clinical pharmacists or across levels of professional experience?

RQ5: Is clinician age associated with the perceived importance of the identified requirement domains?

2. Materials and Methods

2.1 Study Design and Overall Procedure

This study employed a sequential mixed-methods design to identify, operationalise, and quantitatively evaluate stakeholder-informed requirements for a clinical decision support system (CDSS) for thrombosis and anticoagulation management [17]. The study comprised five sequential phases: (1) a literature review to identify reported CDSS functions, requirements, and limitations; (2) stakeholder interviews and qualitative analysis to elicit user-informed requirements; (3) questionnaire development through integration of interview-derived requirements and literature-derived evidence; (4) expert review and content validation of the candidate questionnaire; and (5) quantitative administration of the final questionnaire to assess the perceived importance and internal consistency of the identified requirements. The overall methodological process is presented in Figure 1.

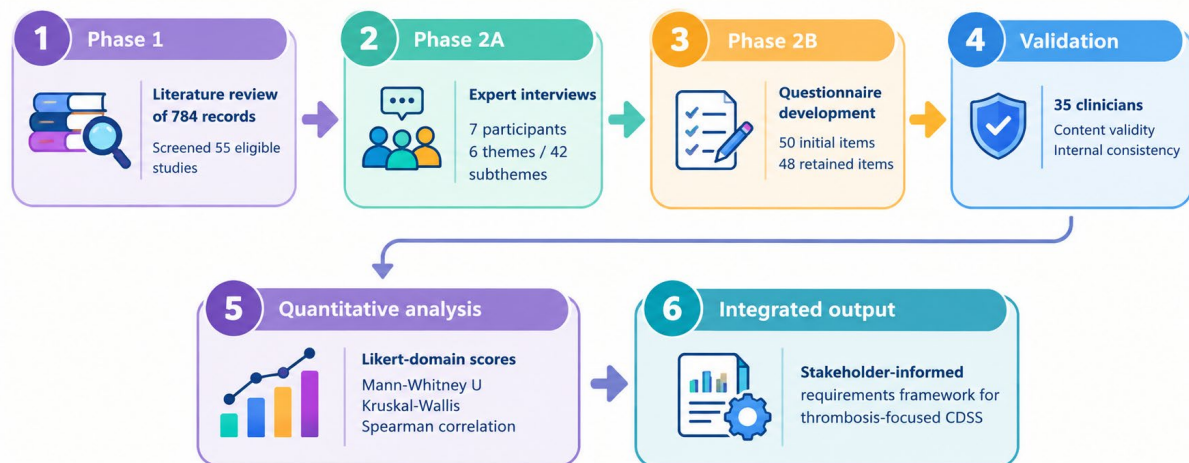


Figure 1. Integrated study workflow

2.2 Phase 1: Literature Review

A targeted literature review was conducted to identify existing CDSS applications for thrombosis and anticoagulation management and to identify recurring functions, requirements, and limitations relevant to questionnaire development. Searches were conducted in PubMed, Scopus, Web of Science, and Embase for studies published between January 2020 and March 2026. The search strategy incorporated terms related to clinical decision support systems, computerized provider order entry, artificial intelligence, thrombosis, venous thromboembolism, deep vein thrombosis, pulmonary embolism, anticoagulants, direct oral anticoagulants, dosing, and drug interactions.

A total of 784 records were identified. Following deduplication and screening, 55 studies were retained for detailed analysis. The review focused on identifying reported CDSS capabilities, application domains, outcomes, advantages, and gaps or limitations relevant to thrombosis and anticoagulation management. The literature findings were used as an evidence-mapping input for questionnaire development rather than as a separate systematic-review outcome. Detailed characteristics of the included studies and the identified requirements and limitations are provided in Supplementary Material 1.

2.3 Phase 2: Stakeholder Interviews and Qualitative Analysis

2.3.1 Participant Selection and Interviews

Stakeholder interviews were conducted to elicit user-informed requirements for a thrombosis and anticoagulation CDSS. Purposive sampling was used to recruit seven participants with relevant clinical or technical expertise, comprising two cardiologists, three clinical pharmacists, and two bioinformatics experts. Interviews were conducted using a semi-structured interview guide developed based on the literature findings and informed by the Technology Acceptance Model (TAM) and Task-Technology Fit (TTF) frameworks [15,16].

TAM and TTF were used to inform the areas explored during the interviews, particularly aspects related to perceived usefulness, ease of use, acceptance, and the fit between clinical tasks and technology [15,16]. However, the final requirement domains and subthemes were not predetermined by these frameworks. Instead, they were derived from the empirical interview data.

2.3.2 Qualitative Analysis

The interview data were analysed using thematic analysis [19,20]. Coding focused on participants' perspectives regarding CDSS functions, clinical and informational requirements, workflow integration, usefulness, usability, acceptance, and trust.

Two researchers independently coded the interview data. The coding outputs were subsequently reviewed and synthesised by a third researcher. Through this process, the final qualitative structure comprised six overarching domains and 42 subthemes. The six domains were Clinical Functional Requirements, Clinical Information Requirements, Technology & Workflow Fit, Perceived Usefulness, Ease of Use/Attitude/Behavioral Intention, and Trust in CDSS.

The identified domains and subthemes were then used to formulate stakeholder-informed questionnaire requirements. Representative quotations supporting the identified themes and subthemes are provided in Supplementary Material 2. Thus, the qualitative phase provided the empirical basis for the final requirement structure, while TAM and TTF served as theoretical frameworks for informing the interview guide rather than as predefined coding categories.

2.4 Phase 3: Questionnaire Development and Item Generation

Questionnaire items were developed by integrating two complementary sources of evidence: (1) requirements and concepts emerging from the stakeholder interviews and (2) requirements, gaps, and limitations identified through the literature review.

The six domains and 42 subthemes generated through the qualitative analysis provided the primary structure for mapping stakeholder-informed requirements. Literature-derived requirements were subsequently incorporated where the reviewed evidence identified additional clinically or technologically relevant requirements. An item-level traceability matrix was developed to link each questionnaire item to its underlying qualitative theme/subtheme and to relevant literature-derived requirements and references. Accordingly, individual items could be informed by the interview findings, the literature, or both sources. The detailed item-level traceability matrix is provided in Supplementary Material 3.

This integration resulted in an initial pool of 50 questionnaire items. The items were designed to represent the requirements identified across the six empirically derived domains while incorporating additional requirements identified through the literature review.

2.5 Phase 4: Expert Review and Content Validation

The initial 50-item questionnaire was reviewed by five experts comprising two cardiologists and three clinical pharmacists. Expert review was undertaken to assess the relevance and appropriateness of the candidate items and to identify overlapping items and issues related to wording and clarity. In addition to providing quantitative content-validity assessments, experts were able to provide comments on individual items, including their wording and clarity.

Following expert review, two overlapping items were removed, resulting in a 48-item questionnaire. Content validity was subsequently assessed using the content validity ratio (CVR) and item-level content validity index (I-CVI) [21–23]. With five experts, a CVR threshold of 0.99 was used as the retention criterion, while an I-CVI greater than 0.78 was considered acceptable [21–23].

All 48 retained items demonstrated a CVR of 1.00, while I-CVI values ranged from 0.93 to 1.00. The final questionnaire therefore comprised 48 items distributed across the six empirically derived requirement domains.

2.6 Phase 5: Quantitative Survey and Reliability Assessment

The final 48-item questionnaire was administered electronically using Google Forms to assess clinicians' perceptions of the importance of the identified CDSS requirements. Eligible participants were cardiologists and clinical pharmacists with at least one year of professional experience and direct involvement in thrombosis or anticoagulation-related clinical decision-making.

Each item was rated using a five-point Likert scale. The quantitative phase assessed the perceived importance of the identified requirement domains and examined whether domain-level ratings differed according to professional group or level of professional experience. The association between participant age and domain-level ratings was also examined.

Internal consistency reliability was assessed using Cronbach's alpha for each requirement domain and for the questionnaire as a whole [26].

2.7 Statistical Analysis and Ethical Considerations

Statistical analyses were performed using IBM SPSS Statistics version 27. The distribution of quantitative data was assessed using the Shapiro–Wilk test [27]. Because the data did not meet the assumptions for parametric analysis, nonparametric statistical tests were used.

The Mann–Whitney U test was used to compare domain-level ratings between cardiologists and clinical pharmacists. The Kruskal–Wallis test was used to examine differences across professional-experience groups. Spearman's rank correlation was used to assess associations between participant age and domain-level ratings. Statistical significance was set at $p < 0.05$.

The study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.TIPS.REC.1403.140). Interview participants provided verbal informed consent. Participation in the quantitative questionnaire was anonymous and voluntary.

3. Findings

3.1 Evidence and stakeholder requirements

The literature search yielded 784 records, of which 55 met the study criteria after duplicate and relevance screening. The reviewed systems most often addressed VTE risk assessment, thromboprophylaxis, anticoagulant prescribing, or atrial-fibrillation-related anticoagulation. Recurrent limitations included narrow clinical scope, insufficient support for complex anticoagulation decisions, incomplete handling of drug interactions and special populations, alert burden, limited explainability, and inadequate prospective validation.

Table 1. Consolidated findings from the literature review.

Characteristic	Condensed finding
Main clinical applications	VTE risk assessment; thromboprophylaxis; anticoagulant prescribing; atrial-fibrillation-related anticoagulation
Technology approaches	Rule-based systems; EHR-integrated tools; alerts; risk calculators; AI/ML-supported systems
Recurring limitations	Narrow scope; incomplete complex-case support; interaction and special-population gaps; alert fatigue; limited explainability/validation
Workflow issues	Integration with clinical work; usability; response time; excessive alerts; clinician acceptance
Underrepresented needs	Pregnancy-associated thrombosis; thrombophilia; thrombocytopenia; unusual-site thrombosis; peri-procedural management
Design gap	Limited comprehensive, stakeholder-informed specification covering clinical, information, workflow, usability, and trust requirements

3.2 Questionnaire structure and measurement properties

Seven interviews produced six overarching domains and 42 subthemes. Clinical Functional Requirements represented the largest theme with 15 subthemes, followed by Technology and Workflow Fit with 11. The final questionnaire contained 48 items. All retained items had a CVR of 1.00, while I-CVI values ranged from 0.93 to 1.00 and the overall mean I-CVI was 0.996.

Internal consistency was high across all domains. Cronbach's alpha ranged from 0.814 for Trust in CDSS to 0.956 for Clinical Functional Requirements; the coefficient for the complete 48-item instrument was 0.973. Domain scores were also consistently high, with mean values between 4.42 and 4.67. The most highly rated individual requirements concerned guideline updating, system stability, avoidance of workflow delay, renal/hepatic dose adjustment, and drug-interaction management.

Table 2. Integrated questionnaire structure, reliability, and domain-level findings.

Domain	Items	Cronbach α	Mean $\pm$ SD	Examples / highest-rated requirements
Clinical Functional Requirements	15	0.956	4.53 $\pm$ 0.55	Guideline updating; renal/hepatic dose adjustment; clinical judgment support
Clinical Information Requirements	6	0.944	4.63 $\pm$ 0.46	Drug/laboratory information; patient-specific data; interaction information

Technology & Workflow Fit	11	0.879	4.63±0.37	System stability; no workflow delay; clear recommendations
Perceived Usefulness	6	0.903	4.42±0.61	Evidence-based assistance; practical decision support
Ease of Use, Attitude & Behavioral Intention	6	0.894	4.43±0.56	Ease of interaction; acceptable clinical use
Trust in CDSS	4	0.814	4.67±0.39	Guideline basis; transparency; scientific references

3.3 Participants and inferential analysis

Thirty-five healthcare professionals completed the questionnaire: 19 clinical pharmacists (54.3%) and 16 cardiologists (45.7%). Nineteen participants were women and 16 were men; mean age was 34.0±5.92 years. Most respondents had 1–5 years of professional experience (n=23), and 10 participants reported previous CDSS experience.

No statistically significant difference was identified between clinical pharmacists and cardiologists for any domain. Effect sizes were negligible to small ($r=0.036$ – 0.171). The Kruskal–Wallis test also showed no significant difference across the four experience groups ($H=1.162$, $p=0.762$). Age was positively associated with Clinical Information Requirements ($\rho=0.372$, $p=0.033$); correlations with the other domains were not statistically significant.

Table 3. Consolidated inferential analysis of professional group, experience, and age.

Analysis	Domain comparison /	Statistic	p value	Effect interpretation /
Mann–Whitney U	Clinical Functional Requirements	U=171.0	0.533	$r=0.106$; small
Mann–Whitney U	Clinical Information Requirements	U=159.0	0.816	$r=0.039$; negligible
Mann–Whitney U	Technology & Workflow Fit	U=182.5	0.312	$r=0.171$; small
Mann–Whitney U	Perceived Usefulness	U=144.0	0.797	$r=0.045$; negligible
Mann–Whitney U	Ease of Use / Attitude / Intention	U=158.5	0.839	$r=0.036$; negligible
Mann–Whitney U	Trust in CDSS	U=144.0	0.791	$r=0.045$; negligible
Kruskal–Wallis	Four experience groups	$H=1.162$	0.762	No significant difference
Spearman	Age vs Clinical Information Requirements	$\rho=0.372$	0.033	Weak positive association
Spearman	Age vs remaining domains	$\rho=0.105$ – 0.245	0.169–0.560	No significant associations

4. Discussion

The principal result of this study is a validated requirements framework that combines clinical functionality with information availability, workflow fit, usefulness, usability, and trust. Rather than treating thrombosis CDSS design as a problem of algorithm selection alone, the findings show that

clinicians expect a system to support a broad set of anticoagulation decisions while remaining compatible with routine clinical work.

The literature review provides context for this result. Existing thrombosis-related CDSSs frequently address discrete tasks such as VTE risk assessment, prophylaxis, prescribing, or atrial-fibrillation management [11–13,29]. Such systems can improve selected process measures, but the reviewed evidence also showed gaps in complex and less common clinical situations. The stakeholder findings extend this observation by identifying the specific functions clinicians would expect from a broader system, including individualized dose adjustment, drug-interaction assessment, bleeding management, pregnancy-related decisions, thrombophilia, thrombocytopenia, and peri-procedural anticoagulation.

Clinical functionality was the largest qualitative domain, containing 15 subthemes. This pattern is compatible with the nature of anticoagulant prescribing, where the same medication may require different decisions according to indication, organ function, interacting therapies, and patient characteristics. The high ratings for renal/hepatic dose adjustment and interaction management therefore reinforce the need for patient-specific rather than generic recommendations. These requirements also provide a practical specification for later rule-engine or knowledge-base development.

Trust was the highest-rated quantitative domain (4.67 ± 0.39). Participants particularly valued guideline-based recommendations, scientific references, transparency, and retention of clinician judgment. This result is relevant to both conventional and AI-enabled CDSSs. Explainability and accountability have been identified as important issues in clinical AI, particularly when recommendations may influence clinical decision-making [10]. The present findings suggest that a thrombosis CDSS should expose the evidentiary basis of recommendations and function as an aid to professional judgment rather than as an autonomous decision-maker.

Technology and Workflow Fit also received a high score (4.63 ± 0.37). System stability, absence of workflow delay, and clarity of recommendations were among the highest-rated individual requirements. This is consistent with evidence that CDSS effectiveness can be undermined when alerts disrupt clinical work or when system design does not adequately fit users' needs [7–9,30]. For thrombosis care, the practical implication is that integration with the electronic health record, rapid retrieval of relevant clinical variables, and concise presentation of recommendations should be treated as core functional requirements.

The absence of significant differences between cardiologists and clinical pharmacists suggests substantial agreement across the two professional groups represented in this study. This convergence is useful for initial requirements engineering because it indicates that the identified domains are not restricted to one professional perspective. Nevertheless, the sample was small and purposively selected; therefore, the results should be interpreted as stakeholder evidence for specification rather than as population estimates. In addition, the study was conducted within a single national healthcare context; therefore, differences in clinical workflows, healthcare organisation, prescribing practices, and digital maturity across countries may influence the applicability of the identified requirements in other settings.

The positive association between age and Clinical Information Requirements was statistically significant, although weak. Participants who were older tended to place greater importance on information-related support. Because several associations were tested and the sample was limited, this result should be considered exploratory. It may indicate that information integration becomes particularly salient when clinicians manage more complex cases, but this interpretation requires confirmation in larger samples.

The high alpha coefficients demonstrate strong internal consistency, but the overall value of 0.973 should not be interpreted as proof of construct validity. Very high internal consistency can also occur when items overlap conceptually. The present study established content validity and internal consistency; factor structure was not tested. Future studies should therefore examine the dimensionality of the instrument using exploratory and confirmatory factor analysis in larger, more diverse samples.

Taken together, the findings support a user-centered specification strategy for thrombosis CDSS development. A subsequent system should incorporate continuously maintained clinical knowledge, patient-specific data, transparent recommendations, workflow-compatible interaction, and mechanisms for clinician oversight. These requirements can also serve as measurable criteria for usability and clinical evaluation of a future prototype.

4.1 Implications for CDSS specification

The combined quantitative and qualitative results can be translated into a practical specification for a future thrombosis CDSS. First, the clinical layer should accommodate more than prophylaxis or risk scoring. The requirement set indicates a need for decision support that can move from indication identification to anticoagulant selection, patient-specific dose adjustment, interaction assessment, bleeding-related considerations, and management of special populations. This broader scope is important because anticoagulation decisions often involve several linked judgments rather than a single prescribing action.

Second, the information layer should make relevant patient data readily available. The Clinical Information Requirements domain received a mean score of 4.63 ± 0.46 , and age was significantly associated with this domain. The findings therefore support integration of laboratory results, renal and hepatic function, relevant risk scores, medication lists, and other clinical variables into the decision process. Such integration could reduce the need to search for information across multiple sources, provided that the displayed information remains concise and clinically relevant.

Third, the knowledge layer should support guideline maintenance. The highest-rated individual requirement was the ability to update guidelines (4.89 ± 0.32). This result is particularly relevant in anticoagulation because recommendations and evidence can change over time. A maintainable knowledge base should therefore allow updates to recommendations while preserving traceability to the supporting evidence. The related emphasis on scientific references and transparency indicates that clinicians should be able to identify the basis of an important recommendation rather than receiving an unexplained output.

Finally, the interaction layer should be designed around workflow. System stability, lack of workflow delay, and recommendation clarity were among the most highly rated requirements. These findings suggest that a future prototype should be evaluated not only for technical accuracy but also for response time, information presentation, navigation, alert burden, and compatibility with existing clinical processes. These characteristics should be treated as measurable design requirements during prototype testing rather than as subjective preferences assessed only after implementation.

4.2 Methodological contribution

The study also provides a methodological contribution by linking three evidence sources during requirements engineering. The literature review established what had already been implemented and where limitations remained; interviews captured requirements that may not be apparent from published system descriptions; and the questionnaire quantified the perceived importance of the resulting domains. The traceability process further connected individual questionnaire items to literature gaps or stakeholder-derived requirements. This sequence reduces the risk that the final instrument represents only the researchers' assumptions about what a thrombosis CDSS should contain.

The use of both CVR and I-CVI provided complementary evidence for content validity. CVR addressed whether an item was considered necessary, whereas I-CVI assessed item relevance. The unanimous CVR of 1.00 and overall I-CVI of 0.996 indicate strong agreement among the five content experts. At the same time, these indices should be interpreted in relation to the small expert panel. Very high agreement in a small group can demonstrate strong content agreement without establishing that the questionnaire has the same structure in a larger population.

The reliability findings should similarly be interpreted with appropriate caution. All six domains exceeded the conventional threshold for internal consistency, but the overall alpha of 0.973 is very high. High alpha can reflect coherent measurement, but it can also arise when multiple items capture closely related aspects of the same construct. The present study therefore supports reliability for the current application but does not justify removing or retaining individual items solely on the basis of alpha. Item-level analysis and factor-analytic testing in a larger sample would be appropriate next steps.

The nonparametric analysis was selected to match the distributional characteristics and small sample. The absence of statistically significant professional-group differences should not be interpreted as evidence that the groups are identical; rather, the observed data did not demonstrate a statistically detectable difference. Likewise, the significant age association was modest and should be regarded as an exploratory finding. A larger, multicenter validation study involving clinicians from diverse geographical regions and practice settings could provide more precise estimates and assess the reproducibility and generalisability of the framework across different healthcare contexts. Such