

**Exploring the Basis of Practice Variation Among Experts in a Medical  
Specialty: A Mixed-methods Study**

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THESIS

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I would like to dedicate my thesis project to current and future thrombosis fellows who have completed their fellowships and still do not know what the right answer is.

Medicine is the science of uncertainty and the art of probability – *William Osler*

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## **LIST OF ABBREVIATIONS**

**ASA:** Aspirin

**BMI:** Body mass index

**DOAC:** Direct oral anticoagulant

**DVT:** Deep vein thrombosis

**ET:** Essential thrombocythemia

**GI:** Gastrointestinal

**Hb:** Hemoglobin

**LMWH:** Low-molecular-weight heparin

**NSAIDs:** Non-steroidal anti-inflammatories

**PE:** Pulmonary embolism

**PVT:** Portal vein thrombosis

**SCT:** Script concordance test

**SVT:** Superficial vein thrombosis

**TFA:** Tolerance for ambiguity

**WBC:** White blood cell count

**VKA:** Vitamin K antagonist

**VTE:** Venous thromboembolism



## SUMMARY

**Background:** How physicians navigate the uncertainty of diagnosis and management of medical conditions with limited evidence is largely unknown. One lens to look at uncertainty in medicine is through evaluating practice variation among physicians, or their differences in their clinical management among cases where a single, acceptable answer is not known in the general medical community. The purpose of this thesis study is to (1) determine the quantity and type of practice variation that exists among thrombosis experts, (2) determine the level of acceptability of practice variation among thrombosis experts, and (3) identify any guiding principles that specialists used when making decisions in areas of clinical uncertainty. **Methods:** Five challenging clinical vignettes were presented to thrombosis experts in Ottawa, Canada in semi-structured interviews. The same case vignettes and all management options chosen in the interviews were included in an anonymous survey to the same experts, to delineate the acceptability of other experts' answers. **Results:** Ten (100%) thrombosis specialists completed interviews and eight completed the follow-up survey. Complete consensus where all specialists recommended a management option was reached in only three (3.4%) items. Despite wide practice variation, there was a high level of acceptability of the different management options among experts. Analysis of interview data identified how experts managed clinical uncertainty, which included: (1) knowing the latest evidence or relying on colleagues' expertise, (2) using past experiences, (3) using clinical gestalt and common sense, (4) weighing the benefits against the risks, and (5) improving the patient experience. **Conclusions:** By better defining the nature and acceptability of practice variation in medical specialties, insights into how to improve the instruction and assessment of learners in situations when uncertainty exists may be possible.

## 1. INTRODUCTION

In medicine “only uncertainty is a sure thing. Certainty is an illusion”<sup>1</sup>. How physicians navigate the uncertainty of diagnosis and management of medical conditions with limited evidence is largely unknown. Physicians, the public and policymakers place value on finding ‘the right answer’ through evidence-based medicine, and translate and disseminate medical knowledge using clinical practice guidelines and standardized protocols. While this approach has led to significant advances in healthcare, how physicians make sense of the “grey-scale space” is needed, for individualizing both patient care and the instruction and assessment of learners<sup>1</sup>. Precision medicine is a personalized and “emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment and lifestyle for each person” according to the National Institutes of Health (NIH)<sup>2</sup>. Extrapolating population-based data to treatment of an individual patient adds inherent complexity and treatment uncertainty, with physicians expected to “bridge the rift” to make treatment decisions and help patients navigate ambiguity<sup>3</sup>. Furthermore, how does clinical uncertainty affect the instruction or assessment of learners? In competency-based medical education residents are routinely judged against uniform competencies, but what happens to the validity of an assessment system when there is inherent uncertainty and physician subjectivity<sup>4</sup>?

Uncertainty in the diagnosis or management of a patient (termed clinical uncertainty) is often because a single, acceptable answer is not known in the general medical community for a given clinical scenario. A common reason that clinical uncertainty exists is the lack of direct evidence or scientific research in certain clinical scenarios. When clinical uncertainty arises, physicians may have different approaches to diagnosis or management (termed practice variation) because

of their different experiences or interpretation of existing evidence. One lens to look at *clinical uncertainty* in medicine is through evaluating the *practice variation* among physicians, i.e., their differences in diagnosis or clinical management. For this study, the definition of practice variation is limited to the variation that exists because a single, acceptable answer is lacking in the general medical community. By learning more about practice variation among physicians, we can better learn how physicians navigate and understand clinical uncertainty.

Practice variation among physicians has been explored in the context of procedural variation in surgery, where types of variation have been analyzed (defined using a *Principles* versus *Preferences* framework, see Section 1.1) and considered in terms of how such types of variation may influence learner instruction and assessment<sup>5-7</sup>. How these results relate to less procedure-focused and more medical management-focused specialties is unknown. While practice variation has been documented in medical specialties through practice-pattern surveys, such as in thrombosis medicine, it is often in the context of planning future clinical trials with little information available on what that practice variation means for the practicing physician, patients, or learners<sup>8-10</sup>. By better understanding the nature and acceptability of practice variation in a medical specialty, we can gain insight into how to best navigate personalized health care and the instruction and assessment of learners in situations when ambiguity exists.

Using the medical subspecialty of thrombosis medicine, the aims of this study are to (1) document the quantity and type of variation among experts' responses in challenging clinical vignettes, (2) determine the level of acceptability of practice variation among experts, and (3) identify guiding principles used by experts to navigate clinical uncertainty. By exploring and

understanding the factors that contribute to experts' practice variations and beliefs about acceptability of variation, further research can be directed towards optimizing patient care and the instruction and assessment of learners in areas of clinical uncertainty. This study will also contribute to research on the development of expertise and clinical decision-making in challenging situations.

### **1.1 Conceptual frameworks**

Two theoretical frameworks informed this thesis project. Apramian et al. described how surgical variations were influenced by social and cultural norms, identifying three social processes that influence practice variation among surgeons at academic centres: (1) *Seeking improvement*: Surgeons used practice variation to solve problems in everyday practice, and also sought out variation based on their professional goals; (2) *Orienting self and others to variations*: Surgeons took stock of variation, shared stories, and then placed trust in those stories and others when adapting practice variation; (3) *Acting under cultural and material conditions*: Participants assessed the risk and benefit of variations and made a decision about their practice “based on the kind of image he or she is working to cultivate”<sup>11</sup>. Surgeons were wary of both innovations and best practices, and focused on showing the logic and underlying rationale for a change<sup>11</sup>. While certain processes described in this framework are specific to procedural variations, how physicians in a medical specialty assess other physicians' management plans, including why they choose to adopt those plans or not, should be considered in a larger sociocultural context.

Apramian et al. developed a second theoretical framework that describes practice variation in the context of postgraduate surgical education. Two types of practice variation were derived from observation of 45 cases and 14 surgeons in the operating room: unwritten rules or *Principles*

where there is considered one acceptable answer and *Preferences* where there may be multiple acceptable answers<sup>5</sup>. Each surgeon had a different “threshold” on what procedural decisions were *Preferences* (perceived unimportant variation) or *Principles* (perceived important variation)<sup>5</sup>. Through observations, Apramian et al. found that surgeons’ thresholds were opaque: what procedural variations were important or unimportant was not explicitly discussed with learners, leaving learners to navigate these variations on their own in the operating room<sup>5</sup>. Do physicians in a medical specialty also perceive practice variation through this framework of *Principles* or *Preferences*? What variation in a management plan is acceptable (or unacceptable) to other physicians? To explore these questions, the present study will be grounded in the framework of *Principles* and *Preferences*.

## **1.2. Review of the relevant literature**

### **1.2.1. Practice variation literature**

Practice variation, the differences in the diagnosis or management of patients among physicians, exists in a variety of clinical situations: in the diagnosis of dermatological or pathological specimens by experts<sup>12–14</sup>, pre-operative medical consultation<sup>15</sup>, pre-surgical planning<sup>16,17</sup>, and types and techniques of surgery<sup>5,18,19</sup>. Practice variation in different medical specialties has been best captured in the scientific literature through surveys of experts on either uncommon or challenging clinical scenarios, also known as practice-pattern surveys<sup>9,10,20–22</sup>.

Data from hospital databases have provided insight into the determinants of practice variation. A large portion of variation seen is because of regional variation or patient-specific factors, such as medical co-morbidities<sup>15,18,19,23,24</sup>. Other factors that contribute to variation among individual

physicians are less well-defined due to the nature of database research and how the data was collected<sup>19,25</sup>.

In a qualitative content-analysis of 33 practice-pattern surveys in thrombosis medicine, practice variation was described in all studies ranging from minor variation present to descriptions of clinical equipoise<sup>10</sup>. Authors of practice-pattern surveys frequently valued external sources such as evidence-based medicine, specific and clear guidelines, and the opinion of experts. In contrast, participants' responses were often based on individual clinical judgments, including use of past training and experience, the specific context and evaluation of the risks versus benefits for a particular treatment decision<sup>10</sup>. Contextual factors included patients' clinical factors, drug cost, logistical difficulty of treatment, physicians' comfort with a specific drug profile (e.g. reversibility of an anticoagulant), patients' comfort or preference, and medico-legal liability. System-level factors such as cost-effectiveness, institution or country-specific practice, and involvement of multiple different specialists (e.g. hematology and vascular surgery treating the same disease) also affected management decisions<sup>10</sup>. Only 2 of the 33 studies acknowledged that multiple "right" solutions may exist, whereas 12 (36%) studies recommended development of some form of "standardized, evidence-based" guidelines to help achieve consensus<sup>10</sup>.

Consistent with the notion that there is some acceptance of practice variation among physicians, some educators and scholars have begun to design clinical reasoning assessments to deliberately sample clinical situations that do not lend themselves to a single correct answer. The script concordance test (SCT) is one method of assessing learners' clinical reasoning in scenarios when medical experts disagree, in which learners may receive partial credit according to how many

experts agree with their responses<sup>26,27</sup>. While there are serious threats to the validity with which SCTs reflects clinical reasoning ability<sup>28–30</sup>, the existence of the method highlights the perceived acceptability of experts' practice variation in the medical education community.

### **1.2.2. Clinical practice guideline literature**

In the era of evidence-based medicine there are a large number of clinical practice guidelines available where groups of experts distill evidence into a single recommendation. The goal of consensus-based clinical practice guidelines is to decrease unwanted clinical variation and improving quality patient care and clinical outcomes<sup>13,31</sup>. Physician adherence to practice guidelines is a complex phenomenon where multiple factors can affect adherence through knowledge, attitudes and behaviors<sup>32</sup>. Mercuri and colleagues discovered that physician experts deviated from clinical practice guidelines more than novice physicians, especially when a patient's context was described in the case vignette<sup>33</sup>. Furthermore, clinical outcomes improved when physicians individualized care based on a patient-specific factors<sup>34</sup>.

Given the challenges of applying or extrapolating results of randomized controlled trials (assuming results are available) for any given patient, clinical reasoning and individual decision-making is paramount when developing and interpreting guidelines<sup>35</sup>. There are clinical practice guidelines that include statements of patient preferences and values and they acknowledge the importance of shared decision-making<sup>36</sup>. Other guidelines explicitly list different experts' answers to a given patient problem, or highlight that a recommendation could not be made because of expert disagreement<sup>37</sup>.

### **1.2.3. Clinical reasoning literature**

While expert clinicians may primarily use experience-based pattern recognition (intuition) in clinical decision-making, they may use analytical thought-processes during clinical reasoning of difficult or uncommon scenarios, either on a continuum or as parallel dual processes<sup>38-41</sup>. More research is needed on how and when expert clinicians use analytical-processing when making clinical decisions for patient management. There are several rationalizations of decision making in patient care described by Kennedy and colleagues in a qualitative study evaluating family medicine residents<sup>42</sup>. Justifications in clinical decision making included level of certainty, sense of urgency, relationship with patients and colleagues, patient agenda, clinician's knowledge and personal style, and system barriers<sup>42</sup>. Further data is needed to better understand the rationale for decision-making among thrombosis experts.

### **1.3. Summary**

Practice variations in areas of clinical uncertainty have been studied in a variety of ways, with methodologies that include database research, surveys of practicing physicians, and interview-based studies. Broad categories of factors that influence decision-making, and may partially explain the practice variation seen between physicians, may include patient contextual factors, sociocultural and system-level influences, and physician qualities such as tolerance of uncertainty or ambiguity. By better characterizing and understanding these different factors, as well as understanding physicians' beliefs about the variations seen in other physicians' practice patterns, we can get a richer understanding of practice variation. This will help us develop instruction and assessments for learning that may better guide learners, as well as understand how best to communicate with, and navigate clinical uncertainty with patients.



## 2. METHODS

### **2.1. Study Objectives**

Using challenging clinical vignettes, the objectives of the study were to:

#### **2.1.1. Primary Objectives**

- 1) Determine the quantity and type of practice variation among thrombosis experts.
- 2) Determine what practice variation is acceptable among thrombosis experts, with reference to what a reasonable standard of care for thrombosis medicine would be.

#### **2.1.2. Secondary Objectives**

- 3) Identify guiding principles among thrombosis experts that provide a basis for decision-making in areas of clinical uncertainty.
- 4) Understand the relationship between the personality trait of ‘tolerance for ambiguity’ and level of acceptability to other thrombosis experts’ responses.

### **2.2. Study Methods**

The study was comprised of two parts: (1) an initial interview to document experts’ preferred management strategies in five challenging clinical vignettes that have standardized uncertainty (Appendix A), and (2) an anonymous questionnaire to determine each expert’s beliefs about the acceptability for each of the management strategies identified in the initial interviews (Appendix B); a 16-item Tolerance for Ambiguity (TFA) scale was also included in the questionnaire (Appendix C). Both the interview and questionnaire incorporated the conceptual framework of *Principles and Preferences*. This study was approved by the Ottawa Health Science Network Research Ethics Board and the University of Illinois at Chicago Institutional Review Board.

While the semi-structured interviews and the follow-up questionnaire are described separately below, the two methods are related. Participants' responses in the interview were used to inform the questions and items in the follow-up questionnaire. Participants outlined their management strategies to five standardized challenging clinical vignettes in the interview. Then, the management strategies described by all participants were included as a list of different management options in the follow-up questionnaire to the two questions: (1) what would you recommend for the following management strategy, and (2) how approach is the following management strategy. Further details for both the interview and follow-up questionnaire are listed in Section 2.2.1 and 2.2.2.

### **2.2.1. Part 1: Interviews**

All thrombosis medicine experts (hematologists or general internal medicine specialists with a clinical focus in thrombosis medicine) in Ottawa were approached to participate in a 60-minute semi-structured interview. The interviewer (L.S.) presented five challenging clinical vignettes from topics that have documented practice variation and no clear answer in the literature. The purpose of the initial interview was to document the experts' preferred management strategy, with probing questions to explore the details and rationale for why they chose that strategy. The clinical vignettes were pilot-tested with an informant who has expertise in thrombosis and medical education (C.G.). Scenarios were presented in paper format and read aloud to the participants during the interview. The different cases were chosen to highlight different factors that may contribute to practice variation. Appendix A includes each case vignette and interview guide.

**Case 1: Management of a pregnant patient with pulmonary embolism (PE):** Subtle differences in treatment (dosing, anti-Xa lab monitoring), to question the role of *Principles*

versus *Preferences* (acceptability/unacceptability) in a high-risk scenario; use of clinical practice guidelines.

**Case 2: Management of symptomatic superficial vein thrombosis (SVT):** Competing contextual factors: symptoms and quality of life versus drug cost and risk of bleeding; use of experience, existing evidence and clinical practice guidelines.

**Case 3: Management of a portal vein thrombosis (PVT) in a patient with cirrhosis and thrombocytopenia (low platelet count):** Competing contextual factors: patient characteristics and the risk of thrombosis versus bleeding; use of experience.

**Case 4: Management of recurrent pregnancy loss in a patient with positive antiphospholipid antibodies:** Patient preferences and values in a high-stakes decision; use of clinical gestalt/experience, guidelines and conflicting evidence.

**Case 5: Management of a patient with possible Essential Thrombocythemia (ET) with a deep vein thrombosis (DVT):** No evidence for this uncommon scenario; use of extrapolated evidence.

### **2.2.2. Part 2: Questionnaire**

After all interviews were complete, a 15-minute online questionnaire was distributed to the same participants that were interviewed (thrombosis experts in Ottawa). The questionnaire included questions about demographic information such as sex, years in practice, number of thrombosis medicine clinics per month, and percentage of time dedicated to thrombosis research. The case vignettes from the interviews were included in the questionnaire, as long as more than one management strategy was discussed for a case. In three of the clinical vignettes, the clinical stem varied (e.g. how close the SVT was to the deep vein junction; what the platelet count was for a

patient with a PVT, and the number of pregnancy losses and antibody type for a patient with possible antiphospholipid syndrome).

All possible management strategies discussed in the interviews were listed in the questionnaire, and thrombosis experts were asked two questions for each strategy: (1) how likely or unlikely you would be to recommend each management strategy to a patient, and (2) regardless of how likely or unlikely you are to recommend or use each management strategy, how appropriate is each management strategy, taking into account what a reasonable standard of care for thrombosis medicine is. See Appendix B for the questionnaire items, with responses listed below:

**(1) What would you recommend for the following management strategy?**

Strongly recommend against; Recommend against; Neither recommend for nor against; Recommend for; Strongly recommend for.

**(2) How appropriate is the following management strategy (with reference to what a reasonable standard of care for thrombosis medicine would be)?**

This strategy is very inappropriate; this strategy is somewhat inappropriate; This strategy is somewhat appropriate; This strategy is very appropriate; I do not know.

In addition to including the options chosen from the interviews, options were also included from published clinical practice guidelines<sup>43</sup>. At least one clearly unacceptable option was included in the questionnaire. A TFA scale was included at the end of the questionnaire, and is considered a measure of *intolerance* to ambiguity (i.e., higher scores reflect less tolerance). It includes three subcomponents: novelty (intolerant of new or unfamiliar information), complexity (intolerant of

distinctive or unrelated information), and insolubility (intolerant to problems that are difficult to solve) (Appendix C).

## **2.3. Data analysis**

### **2.3.1. Qualitative analysis**

Interview data were audio recorded and transcribed. Themes were developed (L.S.) through open coding with constant comparative analysis<sup>44</sup>. Themes were also developed using analytic, focused coding, based on themes identified using the conceptual framework *Principles and Preferences*. One thrombosis expert (C.G.) and one non-thrombosis expert (L.H.) reviewed the developed themes. After the survey and interviews were complete, a summary of the themes was presented to the thrombosis experts who were interviewed to solicit additional comments. Data was analysed using NVivo 12 software (QSR International, Inc., Doncaster, Australia).

### **2.3.2. Quantitative analysis**

Questionnaire data was analysed with descriptive statistics, with means, standard deviations (SD), and ranges for continuous variables, and frequencies with percentages for dichotomous variables. The TFA scale was reported among participants, with the total TFA score correlated to the number of acceptable answers chosen using Pearson's correlation coefficient. Two subgroup analyses were conducted between the number of acceptable answers chosen and years in practice or percent time for dedicated research, with  $p$  values  $< 0.05$  considered significant.

## **2.4. Reflexivity statement**

Reflexivity is the process of examining and reflecting on oneself as a researcher, and the research relationship. The researcher L.S. created the interview guides, interviewed participants and analysed the qualitative and quantitative data. During her internal medicine residency (5 years

before this thesis project), L.S. completed and published a practice-pattern survey to document practice variation for clinical research purposes. During this thesis project, L.S. was completing a two-year thrombosis medicine subspecialty fellowship where she frequently faced clinical uncertainty, and had to navigate how and why different thrombosis experts (her supervisors) made different management decisions. As an “insider” during the interviews, L.S. carried a unique perspective and could understand the nuances of the cases and experts’ answers. However, as an insider, she was aware that interpretation of the participants’ answers may include her own management biases or assumptions. These limitations were mitigated during interviews by asking standardized and open-ended questions, and by including the follow-up questionnaire.

### 3. RESULTS

#### **3.1. Demographic Data**

At the time of the study there were eleven thrombosis experts in Ottawa, and one (C.G.) was excluded from participating in the study. The remaining ten (100%) thrombosis experts in Ottawa completed interviews, and eight (80%) thrombosis experts completed the follow-up online questionnaire. Among the thrombosis experts there were six men and four women. The mean number of thrombosis clinics per month was 7.5 (5-12, SD 2.8). Most thrombosis experts who completed the questionnaire had practiced for more than 10 years (75%). There was a wide range of percentage of time dedicated per week to thrombosis research across participants (Table I). Participants answered every question in the questionnaire, so there were no missing data.

**TABLE I. QUESTIONNAIRE DEMOGRAPHIC DATA**

<b>Sex, n (%) (N=8)</b>	
Male	6 (75)
Female	2 (25)
<b>Specialty, n (%)</b>	
Hematology	5 (62.5)
General internal medicine	3 (37.5)
<b>Years in practice, n (%)</b>	
<5 years	1 (12.5)
5-10 years	1 (12.5)
11-20 years	4 (50)
>20 years	2 (25.0)
<b>Thrombosis clinics per month, mean (range, SD)</b>	7.5 (5-12, SD 2.8)
<b>Time for thrombosis research per week, n (%)</b>	
0%	3 (37.5)
1-25%	1 (12.5)
26-50%	0 (0)
51-75%	2 (25.0)
>75%	2 (25.0)

Abbreviations: SD: standard deviation

### **3.2. Objective 1: Assessing the quantity and type of practice variation**

#### **3.2.1. Quantitative Data**

There was practice variation identified across all five vignettes. The mean number of recommended options chosen per question in a vignette was 4.3 and ranged from 1 to 10 (Table II). For example, for management of a pregnant patient with a new pulmonary embolism (PE), there was variation across participants in the management of anticoagulation within the first 30 days (4 recommended options chosen among 8 participants), management of anticoagulation after 30 days (5 recommended options among 8 participants), and whether to recommend induction of labor or to test for an underlying inherited thrombophilia. There were also different management options selected in the vignettes that had multiple versions of the same question stem (e.g. varying proximity of a superficial vein thrombosis to the deep vein junction) (Table II).

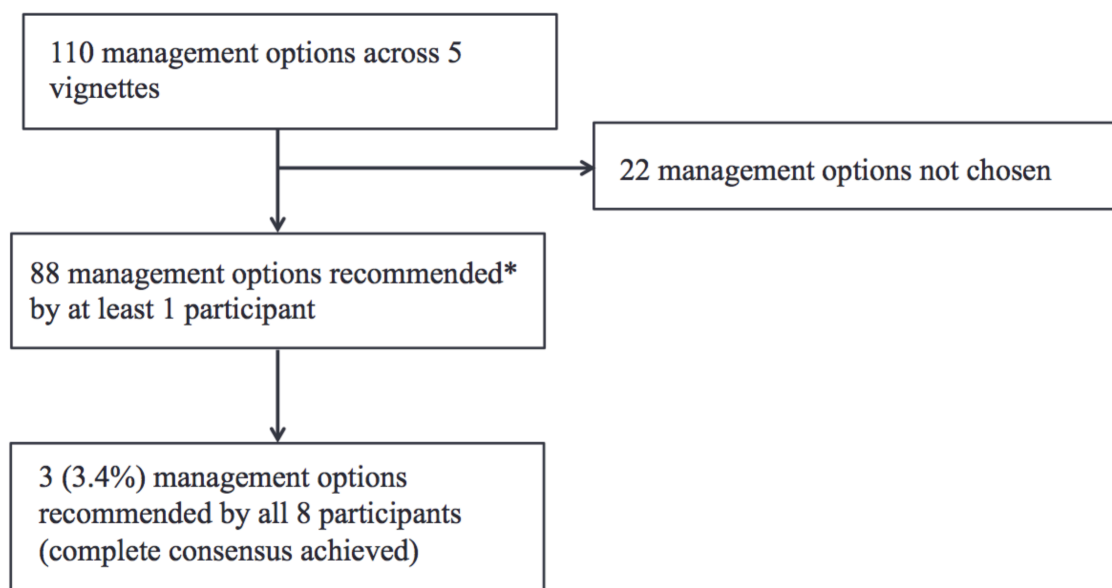


**TABLE II. OPTIONS RECOMMENDED BY AT LEAST ONE PARTICIPANT IN THE QUESTIONNAIRE**

<b>Vignette Number</b>	<b>Possible options listed in the questionnaire</b>	<b>Options recommended by at least one participant in the questionnaire</b>
<b>Vignette 1: PE in Pregnancy</b>		
Dosing in the first month	5	4
Dosing after the first month	5	5
Labor management	2	2
Thrombophilia testing	2	2
<b>Vignette 2: Superficial vein thrombosis</b>		
4 cm from deep vein system	8	7
1 cm from deep vein system	8	6
<b>Vignette 3: Portal vein thrombosis</b>		
Asx PVT, cirrhosis, plt 43	10	6
Sx PVT, cirrhosis, plt 43	10	9
Asx PVT, cirrhosis, plt >50	10	7
Asx PVT, cirrhosis, plt <30	10	2
Asx PVT, no cirrhosis, plt N	10	10
<b>Vignette 4: Pregnancy loss and antiphospholipid antibodies</b>		
2 early losses, low-titre B2GP1	3	3
3 early losses, low-titre B2GP1	3	3
1 late loss, low-titre B2GP1	3	3
2 early losses, high-titre B2GP1	3	3
2 early losses, high-titre ACA	3	3
<b>5: DVT in a patient with Essential Thrombocythemia</b>		
Anticoagulation type	4	4
Long-term anticoagulation	2	1
Prophylaxis in future pregnancy	4	4
<b>Mean number of options in all vignettes (range)</b>	<b>5.5 (2-10)</b>	<b>4.3 (1-10)</b>

Abbreviations: PE: Pulmonary embolism; Asx: Asymptomatic; Sx: Symptomatic; plt: Platelet count; B2GP1: Beta-2 glycoprotein 1 antibodies; ACA; Anticardiolipin antibodies; DVT: Deep vein thrombosis

There were 110 total management options presented to the participants from the five clinical vignettes. Of these 110 management options, there were 22 options that were not recommended by any participant, leaving 88 management options chosen by at least one participant. A detailed list of what the different options were for each of the vignette questions are listed in Appendix B. Among the 88 management options chosen by at least one participant, only three (3.4%) management options were recommended by all 8 participants (Figure 1). The three management options that achieved complete consensus (100% of participants) among the group were: (1) Use of a 100% weight-based low-molecular-weight heparin dose in the first 30 days for a pregnant patient with a pulmonary embolism; (2) Do not anticoagulate a patient with cirrhosis and an asymptomatic portal vein thrombosis with a platelet count  $< 30 \times 10^9/L$ ; and (3) Continue long-term anticoagulation in a patient with essential thrombocythemia and a deep vein thrombosis. Consensus, defined as  $>50\%$  of participants recommending or strongly recommending a management option, was achieved in 23 (26%) of the management options, which further highlights the practice variation present. In summary, there was both a wide range of management strategies chosen by thrombosis experts.

**Figure 1.** Flow diagram of number of recommended options chosen by participants

\*Included 'recommended for' or 'strongly recommended for' answers

### **3.2.2. Qualitative Data**

When participants were interviewed about how they managed theoretical cases, they also reflected on similar challenges they face in real-life practice. Experts acknowledged the clinical uncertainty that exists in thrombosis medicine, and the nuances in clinical practice:

"I think the standard cookie cutter thrombosis you can have a fellowship for a month with DVT/PE. But that's only, I think, representative of 20% of what I see in clinic, and all the other stuff is largely nuances and unknowns" [Participant 02]

"No, this is evidence-free medicine." [06]

"A lot of these cases, they're hard to put in a cookie cutter." [06]

"And the problem is these portal vein clots are so variable. A non-occlusive branch clot of the right portal vein completely occlusive main portal vein extending back into the mesenteric vein with risk of bowel infarction, completely different animals, right?.. So, even if you're going to make an RCT to try and deal with the clinical equipoise, I am not sure you can answer the question, because there is too much clinical variability in this" [02]

In the interviews that focused on the management of challenging clinical vignettes, the participants explicitly acknowledged practice variation that exists within the group for these challenging cases:

“And you can tell just when we talk about these cases in our little group, right, the variation is tremendous.” [02]

“I’m sure you’re getting ten answers from ten people.” [10]

When participants explained their management decisions (based on a theoretical case), they often described their practice in terms of how it differed from the rest of their colleagues:

“No, I never re-image these people, ever, as opposed to everybody else.” [05]

“So, are you going to tell me what Dr. Y said?” [03]

Participants were aware of variation in others’ practices, and often predicted others’ practice patterns and responses:

“.. I know Dr. X is like, why are you treating any of this, right?.... “I don’t care what Dr. X says. But he may be right. He may be very right.” [02]

Not only did participants acknowledge the practice variation exists between colleagues, but they also identified variation within their own practice:

“ It’s one of those things that I’m sure if you were to audit my practice, you’d see a huge variation.” [09]

“... And it might depend on the day of the week. Some days I might feel like using a DOAC and others I ... It’s really that random truly, I mean, no one knows.” [05]

In addition to practice variation on a day-to-day basis, participants also described a change to their practice over time that was largely guided by experience:

“And that [practice] has morphed over the years. I think initially when I started I was much more aggressive.... And I realized over the years I was torturing patients making them do the [twice daily injections] and I never changed therapy based on an anti-Xa level I think unless something was crazy. And they never really were that crazy. So, I stopped anti-Xas...I have streamlined my pregnancy practice and I do once a day actual weight-based treatment and that’s all I do.” [02]

In summary, participants acknowledged the practice variation that exists among the group and within their own practice in challenging cases, and could often predict what that variation would be.

### **3.3. Objective 2: Determine what practice variation is acceptable among thrombosis experts**

#### **3.3.1. Qualitative data**

Participants describe different management strategies that they have used in the past, to highlight the acceptability of different management options for a particular case.

“I think I would still use an oral agent. I’ve done low-molecular-weight heparin to warfarin in these cases, and I’ve done DOACs in these cases so I think I would be okay doing both.” [04]

“I’ve managed...DVT and PE [in patients with myeloproliferative disorders] with low-molecular-weight heparin and warfarin and been satisfied with the results.” [06]

When talking about practice variation, participants described the concept that some types of thrombotic presentations have good outcomes “no matter what you do”, which leads to more acceptability of the practice variation seen:

“I’ve had no bad experiences doing different things in pregnant women, they all seem to have done fine, so I don’t have any anecdotal, like, wow, I did this and something bad happened and therefore I’m practicing this way. There hasn’t been that kind of thing so I can’t say my past experience with pregnant women have colored the way I do it, or maybe it has because they’ve done well no matter happens, so maybe it has colored it.” [05]

“Yeah, because most of my patients have done well with what I’ve done in the year, so anecdotally most of my patients do well, at least tend to get better almost no matter what you do.. So, I obviously think the clinical equipoise in these type of cases is fine because most of the patients are just going to do fine.” [02]

However, there were also some scenarios where a management strategy led to a bad outcome where participants viewed that management option as less acceptable:

“At postpartum I’ve been burned...One was a lady with a mechanical valve actually, and I was super aggressive postpartum. She bled like crazy and she went off anticoagulation for 10 days because of the

bleed. I think you're putting people at way more risk if you cause postpartum bleeding than if you just take a more conservative approach." [02]

"I had a young lady with breast cancer in her 30s that I looked after and she had a portal vein thrombosis. She failed. I think it was on prophylactic dose [LMWH] and died. It was awful...Many people have told me over the years that this is a pretty benign condition and that was a rude awakening to it not being a benign condition." [06]

To summarize, there were some case examples where participants described some level of acceptability of different management strategies. However, there were other cases where a participant identified that a management strategy was not acceptable. Quantitative data helps to tease out these differences by identifying when thrombosis experts thought certain strategies were acceptable or not.

### **3.3.2. Quantitative data**

Participants were asked how appropriate management strategies were for each case vignettes, with reference to what a reasonable standard of care for thrombosis medicine would be, regardless of if they would have recommended that management option. Participants chose more 'appropriate' management options than they chose 'recommended' management options (Table III).

**TABLE III. NUMBER OF RECOMMENDED AND APPROPRIATE RESPONSES PER PARTICIPANT PER VIGNETTE**

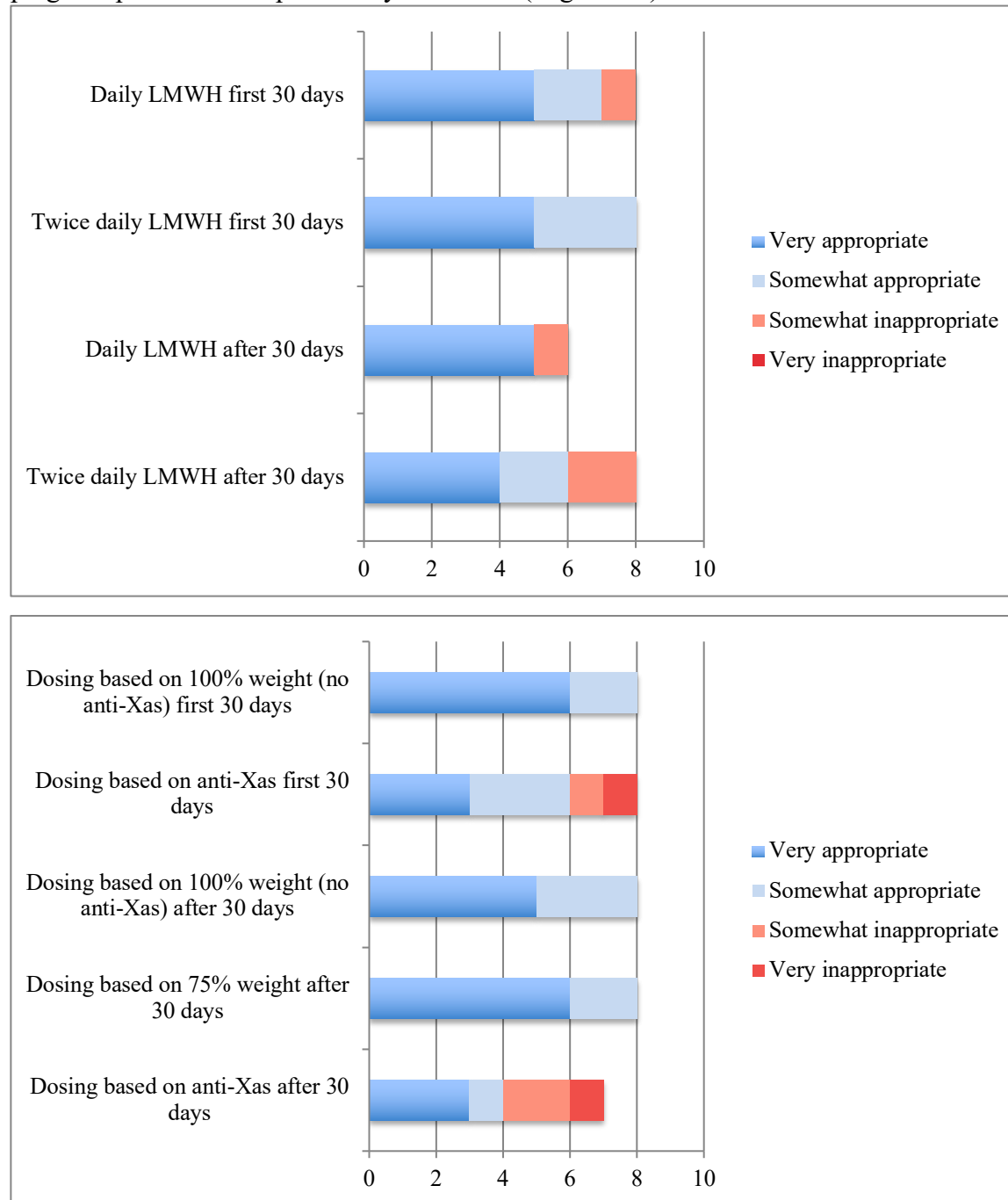
<b>Vignette</b>	<b>Number of recommended responses per participant mean (range, SD)</b>	<b>Number of appropriate responses per participant mean (range, SD)</b>
1 (13 items)	6.3 (5-8, 1.0)	10.0 (8-12, 1.3)
2 (22 items)	8.5 (7-10, 1.1)	16.3 (12-22, 4.0)
3 (50 items)	12.6 (5-25, 6.8)	23.4 (8-42, 11.2)
4 (15 items)	6.9 (4-15, 3.7)	11.9 (7-15, 3.0)
5 (10 items)	4.5 (3-7, 1.4)	8.0 (4-10, 1.9)

Recommended includes 'recommended for' or 'strongly recommended for'  
Appropriate includes 'somewhat appropriate' or 'very appropriate'

There were many acceptable management options for each vignette, which is shown in Figures 2-6. For example, in a patient with a moderately symptomatic superficial vein thrombosis, there were 7 chosen management options that were deemed very appropriate or somewhat appropriate by participants. While there were many acceptable options chosen, there were also a small number of answers that were deemed inappropriate (Figures 2-6). This acceptability was somewhat context specific, with more unacceptable answers chosen based on the level of risk, such as a higher thrombotic risk with a SVT that was closer to the deep vein system, or a higher bleeding risk with worsening thrombocytopenia in a patient with cirrhosis and a PVT.

There were also some management options that were found to be both appropriate and inappropriate by different participants in each of the case vignettes (Figures 2-6). For example, in a patient with an asymptomatic PVT without cirrhosis and a normal platelet, half of participants thought it was very appropriate or somewhat appropriate to withhold anticoagulation, and half of participants thought it was very inappropriate or somewhat inappropriate to withhold anticoagulation (Figure 4E). Individual response details are available in Appendix 4.

**Figure 2.** The level of appropriateness of the chosen management options for treatment of a pregnant patient with a pulmonary embolism (Vignette 1)

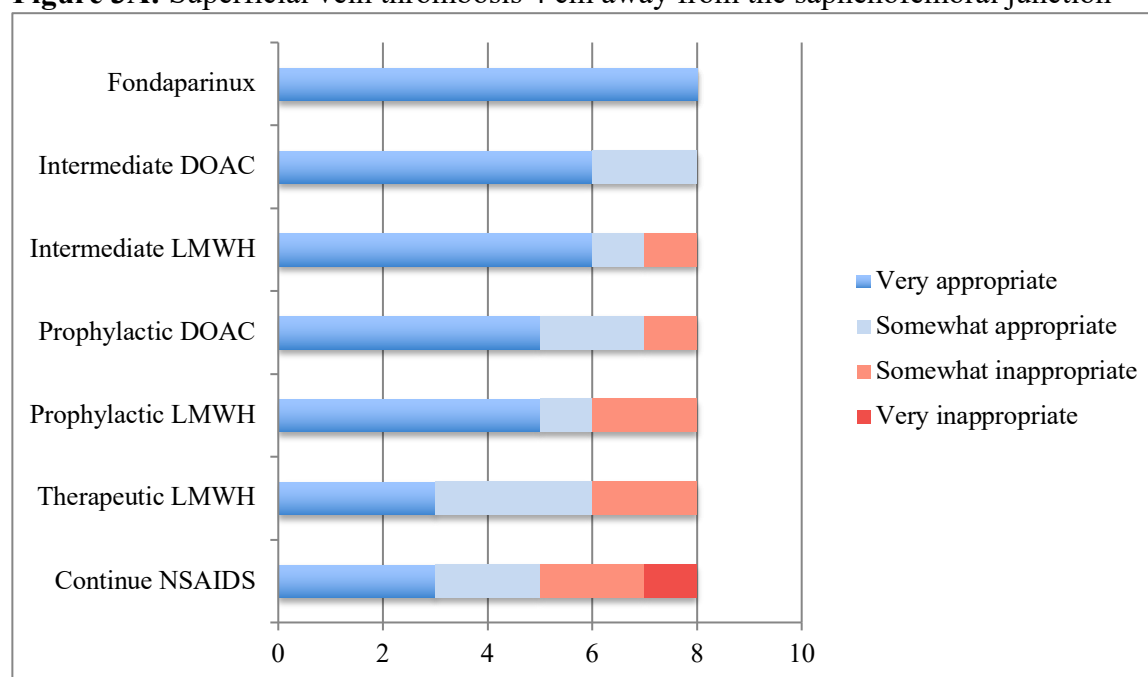


Abbreviations: LMWH: Low-molecular-weight heparin

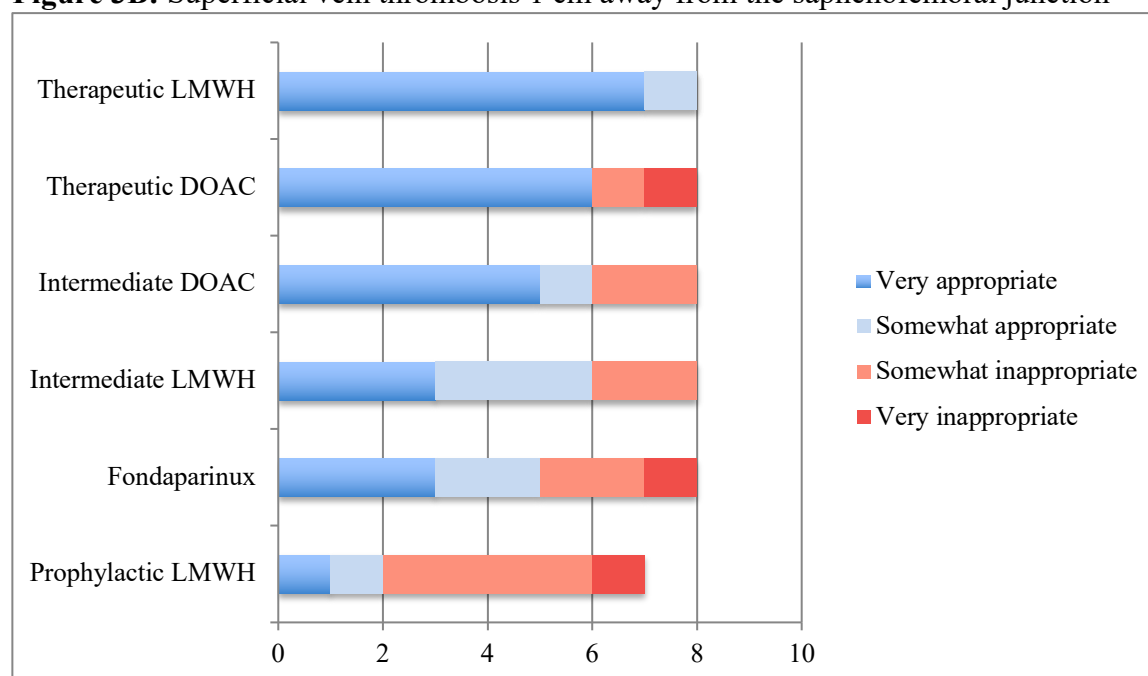


**Figure 3.** The level of appropriateness of the chosen management options for treatment of a patient with a superficial vein thrombosis 4 cm and 1 cm away from the deep vein system (Vignette 2)

**Figure 3A:** Superficial vein thrombosis 4 cm away from the saphenofemoral junction



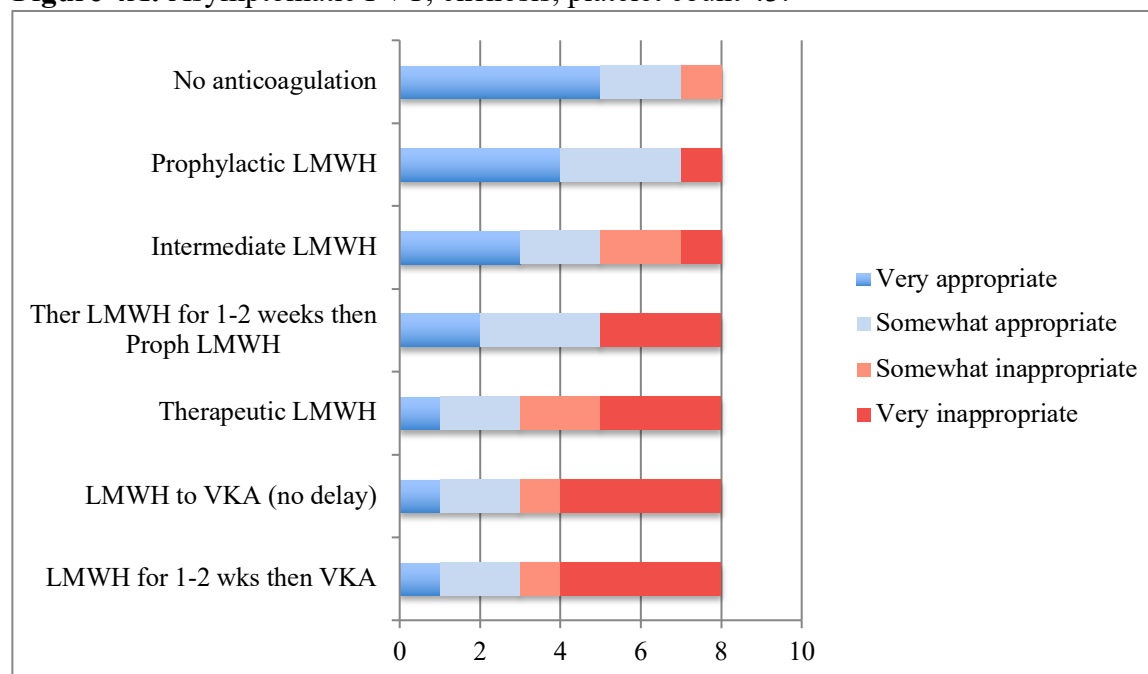
**Figure 3B:** Superficial vein thrombosis 1 cm away from the saphenofemoral junction



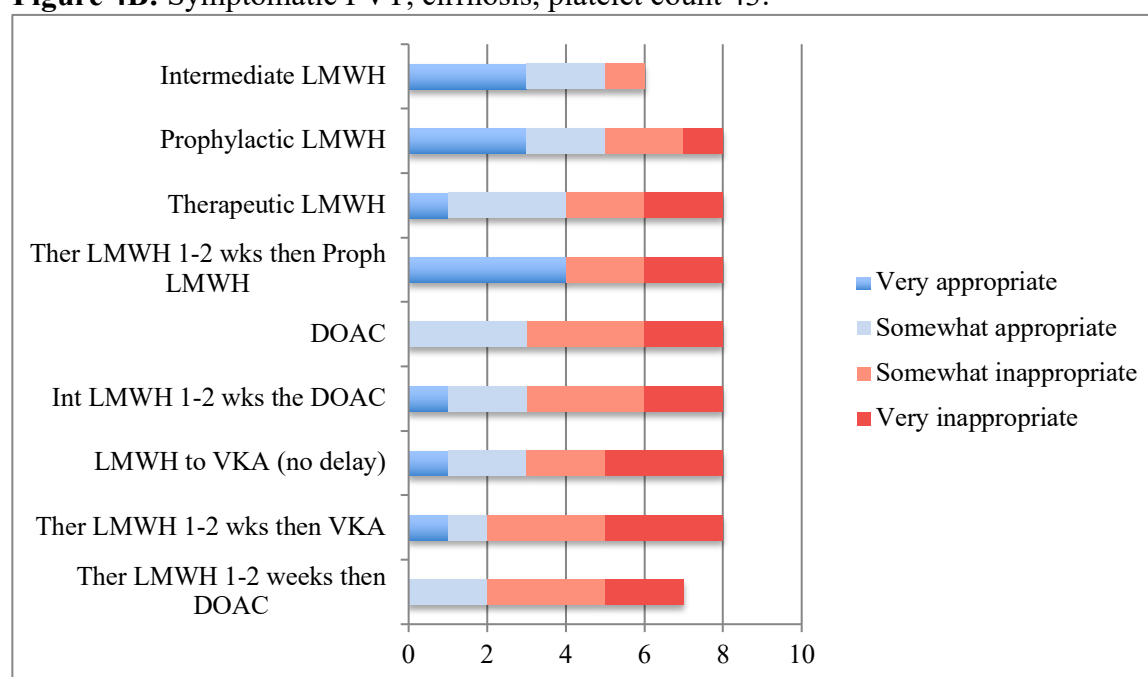
Abbreviations: DOAC: Direct oral anticoagulants; LMWH: Low-molecular-weight heparin; NSAIDS: non-steroidal anti-inflammatories

**Figure 4.** The level of appropriateness of the chosen management options for treatment of a patient with an asymptomatic portal vein thrombosis in a patient with cirrhosis and thrombocytopenia (Vignette 3)

**Figure 4A:** Asymptomatic PVT, cirrhosis, platelet count 43:



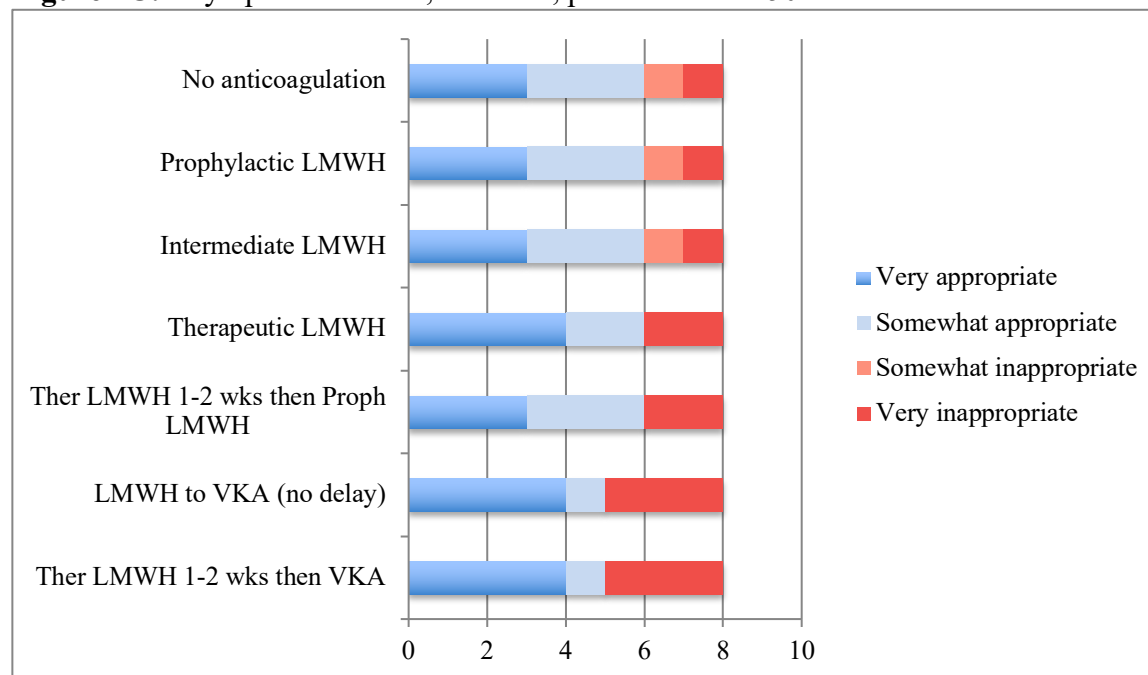
**Figure 4B:** Symptomatic PVT, cirrhosis, platelet count 43:



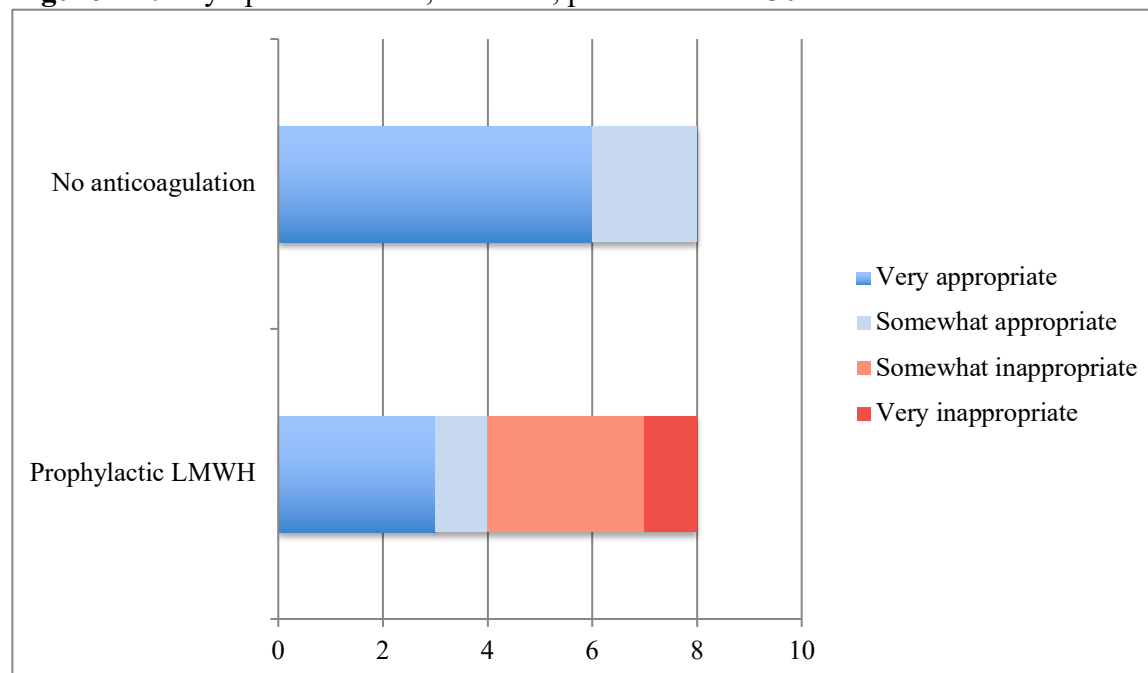
Abbreviations: LMWH: Low-molecular-weight heparin; Ther: Therapeutic; Proph: Prophylactic; DOAC: Direct oral anticoagulant; VKA: vitamin K antagonist

**Figure 4.** The level of appropriateness of the chosen management options for treatment of a patient with an asymptomatic portal vein thrombosis in a patient with cirrhosis and thrombocytopenia (Vignette 3) (continued)

**Figure 4C:** Asymptomatic PVT, cirrhosis, platelet count >50



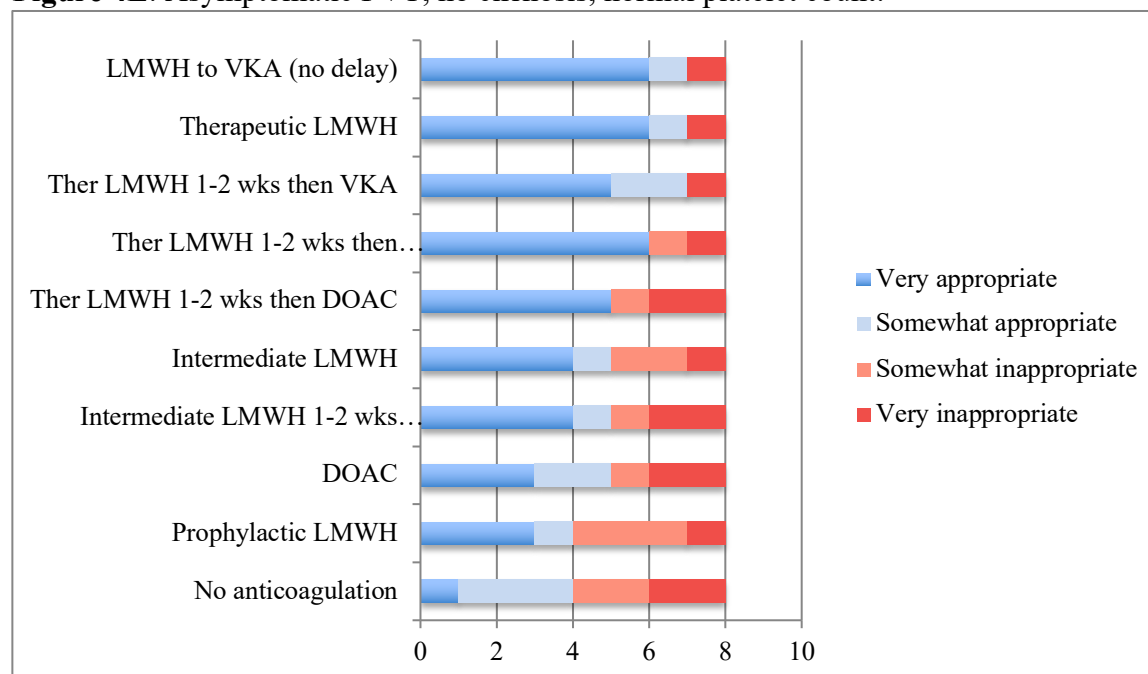
**Figure 4D:** Asymptomatic PVT, cirrhosis, platelet count <30:



Abbreviations: LMWH: Low-molecular-weight heparin; Ther: Therapeutic; Proph: Prophylactic; DOAC: Direct oral anticoagulant; VKA: vitamin K antagonist

**Figure 4.** The level of appropriateness of the chosen management options for treatment of a patient with an asymptomatic portal vein thrombosis in a patient with cirrhosis and thrombocytopenia (Vignette 3) (continued)

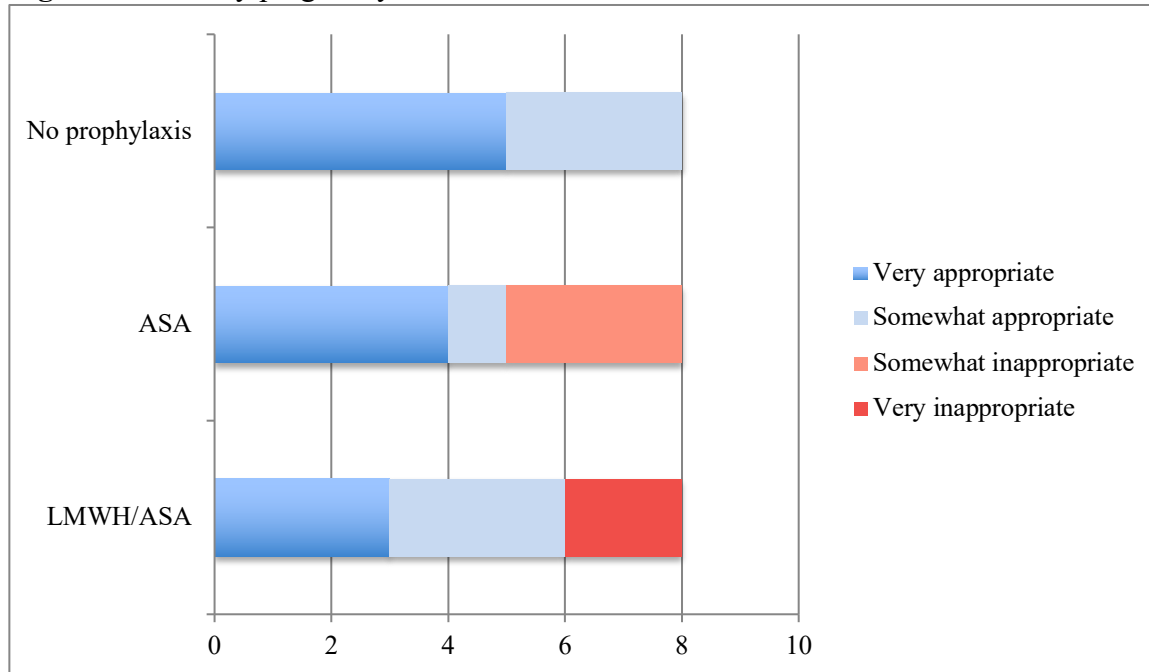
**Figure 4E:** Asymptomatic PVT, no cirrhosis, normal platelet count:



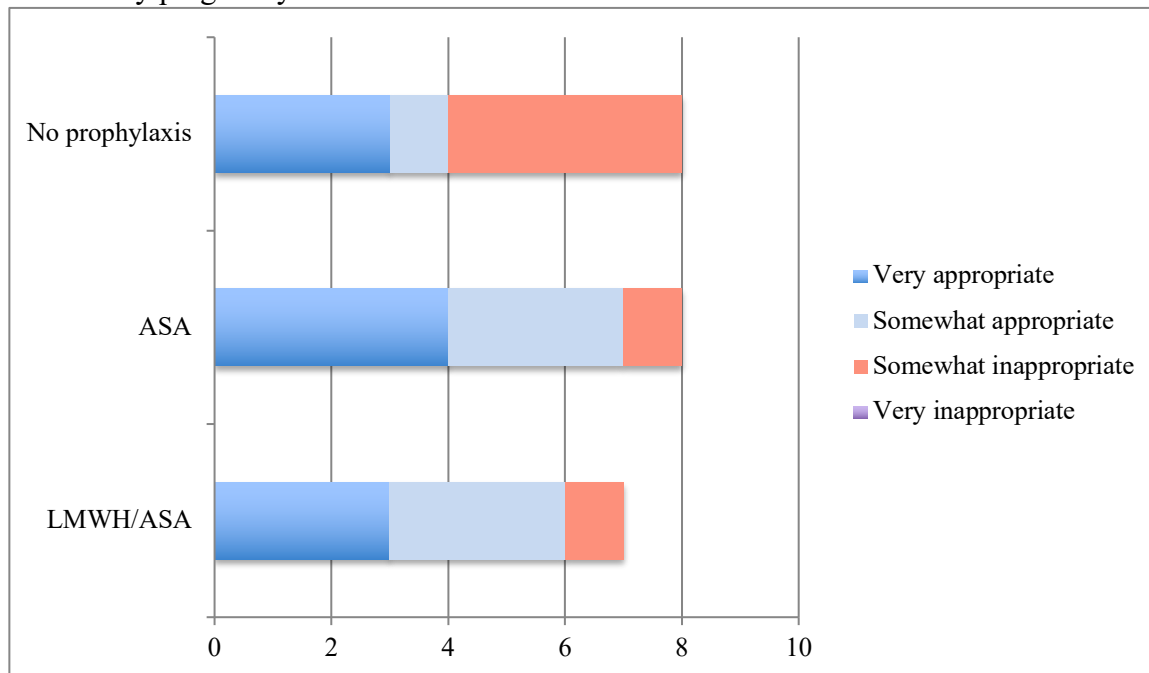
Abbreviations: LMWH: Low-molecular-weight heparin; Ther: Therapeutic; Proph: Prophylactic; DOAC: Direct oral anticoagulant; VKA: vitamin K antagonist

**Figure 5.** The level of appropriateness of the chosen management options for future treatment during pregnancy in a patient with prior pregnancy losses and positive antiphospholipid antibodies (Vignette 4)

**Figure 5A:** 2 early pregnancy losses and low-titre anti-B2GP1:



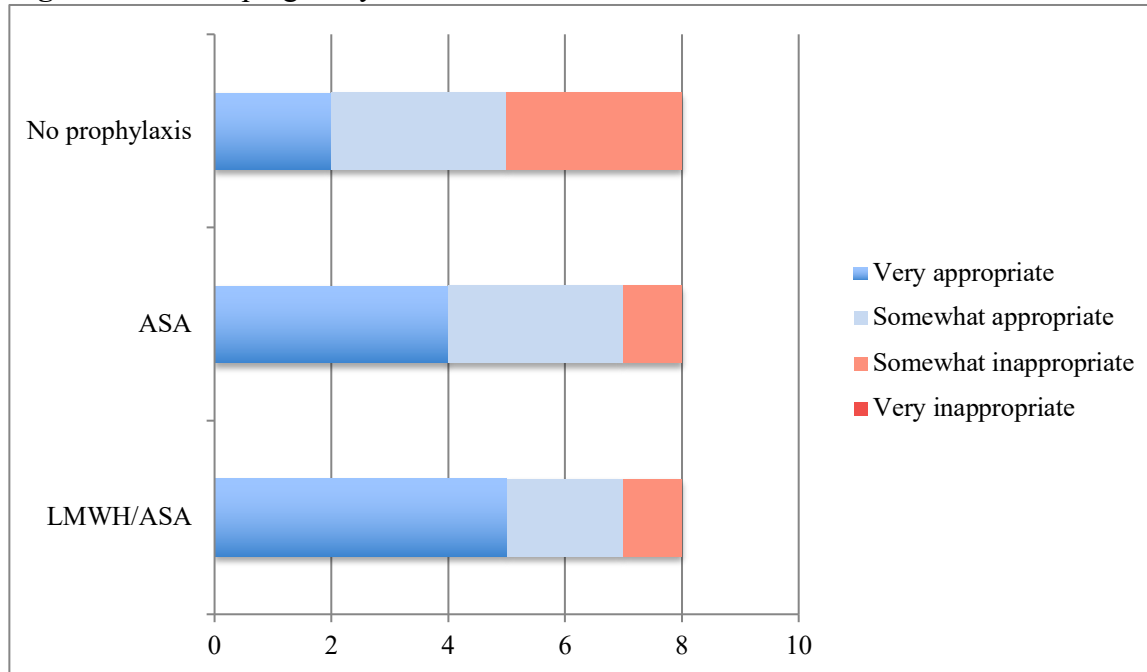
**5B:** 3 early pregnancy losses and low-titre anti-B2GP1:



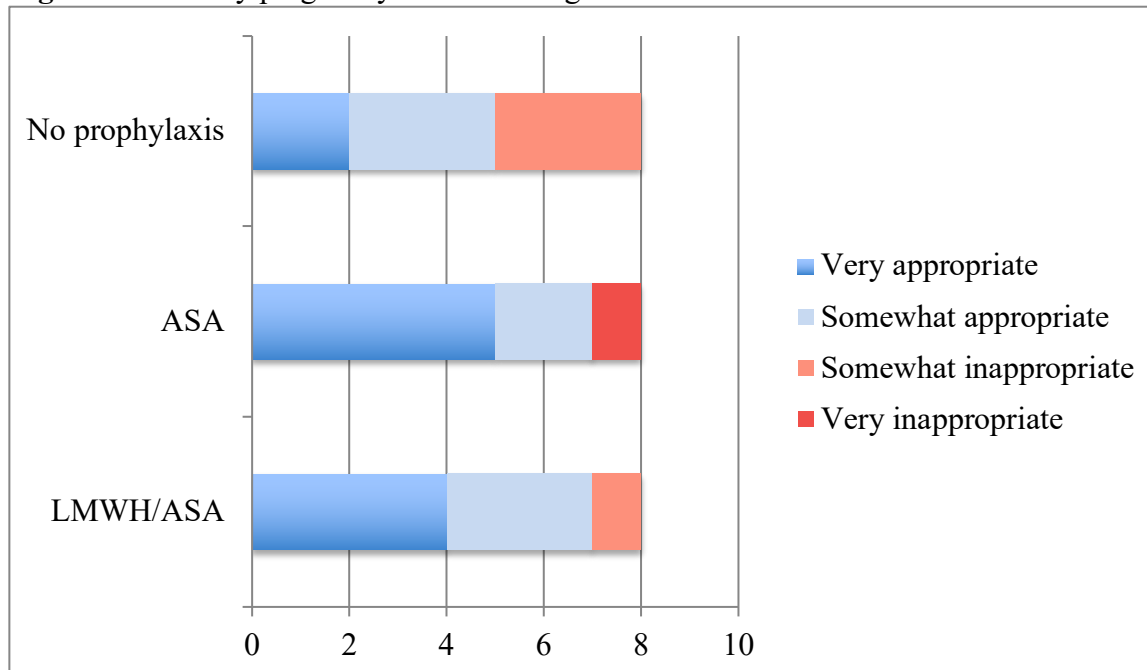
Abbreviations: ASA: Aspirin; LMWH: Low-molecular-weight heparin

**Figure 5.** The level of appropriateness of the chosen management options for future treatment during pregnancy in a patient with prior pregnancy losses and positive antiphospholipid antibodies (Vignette 4) (continued)

**Figure 5C:** 1 late pregnancy loss and low-titre anti-B2GP1:



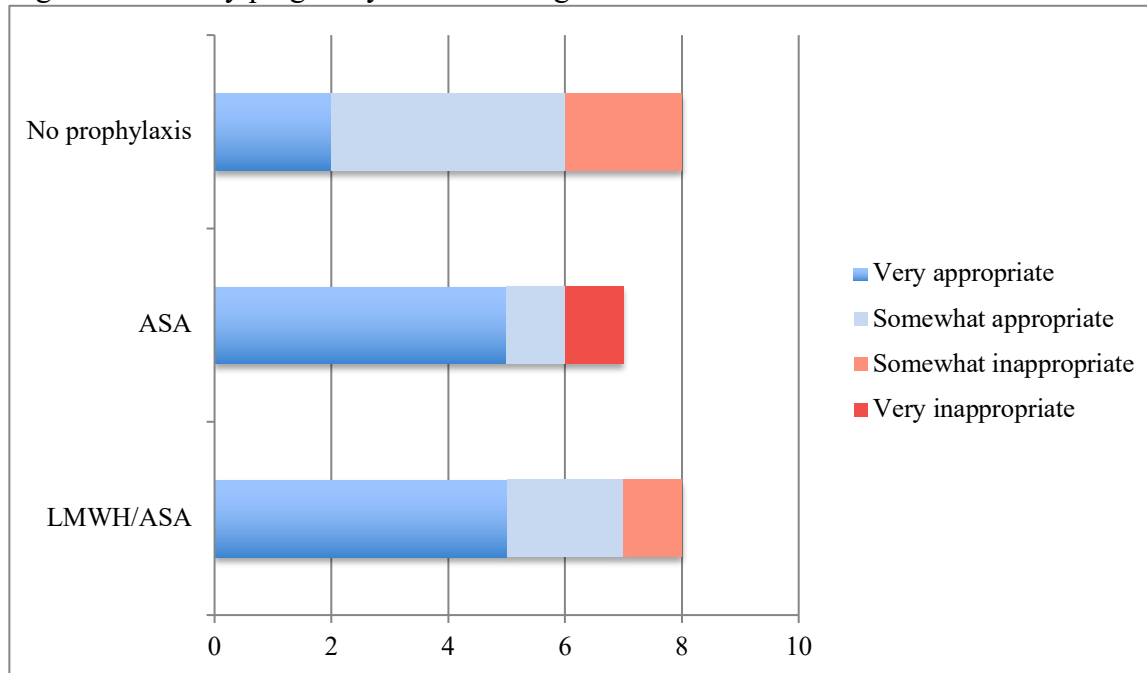
**Figure 5D:** 2 early pregnancy losses and high-titre anti-B2PG1:



Abbreviations: ASA: Aspirin; LMWH: Low-molecular-weight heparin

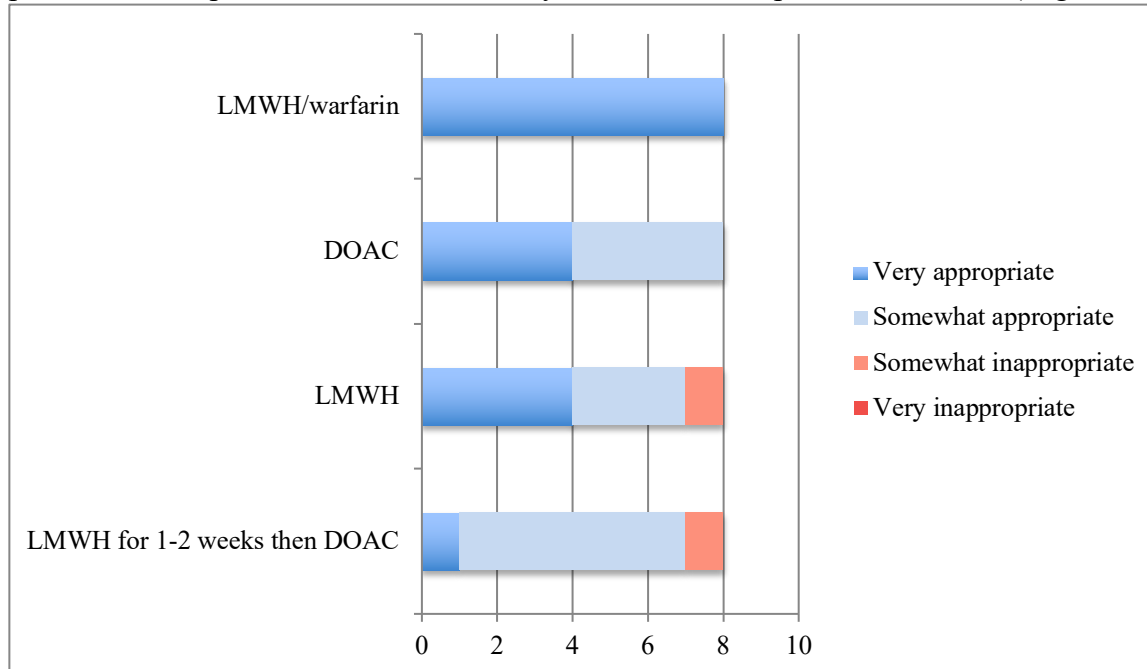
**Figure 5.** The level of appropriateness of the chosen management options for future treatment during pregnancy in a patient with prior pregnancy losses and positive antiphospholipid antibodies (Vignette 4) (continued)

Figure 5E: 2 early pregnancy losses and high-titre ACA:



Abbreviations: ASA: Aspirin; LMWH: Low-molecular-weight heparin

**Figure 6.** The level of appropriateness of the chosen management options for treatment of a patient with suspected essential thrombocythemia and a deep vein thrombosis (Vignette 5)



Abbreviations: LMWH: Low-molecular-weight heparin; DOAC: Direct oral anticoagulant

To summarize the data presented in Figures 2-6, there was a high level of acceptability among participants for the different management options chosen by other participants. However, there were also some chosen management strategies that were deemed somewhat or very inappropriate by participants. Importantly, there was disagreement between participants about which of these strategies were appropriate or inappropriate.

A subgroup analysis was performed to identify if the number of acceptable answers chosen differed according to protected research time ( $\leq 50\%$  versus  $>50\%$ ) or years in practice ( $\leq 10$  years versus  $>10$  years). The mean number of acceptable answers chosen across vignettes did not differ in a statistically discernible way according to protected research time ( $\leq 50\%$  time for research: 59.8 versus  $>50\%$  time for research: 79.3,  $p=0.08$ ). Similarly, there was no statistically



discernible difference in the mean number of acceptable answers chosen across vignettes based on years in practice ( $\leq 10$  years 75.5 versus  $>10$  years: 67.5,  $p=0.58$ ).

### **3.4. Objective 3: Identify guiding principles among thrombosis experts that provide a basis for decision-making in areas of clinical uncertainty**

#### **3.4.1. Qualitative data**

Participants described several strategies to help manage clinical uncertainty in practice: (1) Knowing the latest evidence or relying on colleagues' expertise; (2) Using experience; (3) Using clinical gestalt and common sense; (4) Weighing the benefits against the risks; and (5) Improving the patient experience. Participants identified similar management strategies when they were explicitly asked at the end of the interview for any "guiding principles" they follow, with no new themes identified.

#### **Knowing the latest evidence or relying on the expertise of colleagues**

Participants described grounding their decisions in the "evidence" and latest literature:

"Certainly, when there is evidence, I try to stick to it for sure." [07]

"Evidence, none. I'd like to say it would influence my decision." [02]

When discussing clinical vignettes, participants often quoted evidence to support their decision.

In one vignette, two participants quoted different studies to support the different decisions they made. Participants often relied on the knowledge of colleagues', who were felt to be up-to-date in the literature in different areas within thrombosis medicine:

"If I'm an expert in an area, I really should know the nuances, the literature in that area when managing difficult cases. If I don't, then I might rely on guidelines and my colleagues that do know the nuances in the management of those areas. I'm not a big fan of dogmatism, of this is how we do it." [06]

"I haven't gone back and done a review of all literature recently, but in this environment, I think I would have heard about changes in management." [01]

“I think that Dr. A and Dr. B looked at the data recently, and we had a discussion.” [03]

“And I’m impressed I have to say in our group with how much people know. I’m blown away everyday by people in our group and how up-to-date they are, how up-to-date on the literature they are. I actually really am.” [02]

### *The role of clinical practice guidelines varies*

Clinical practice guidelines were another way that experts managed patient scenarios when they were less familiar with the literature, or wanted reassurance in their approach:

“Because, people that write guidelines are people like me, that read the literature and then do their best to make a decision about what they think is best. But, I can appreciate that people that are not experts in the field, that don’t spend a whole lot of time reviewing the minutia would turn to guidelines to help them manage volume of information to make decisions and rely on others that have given it lots of thought.” [06]

“Well, this is an area that I don’t spend a whole lot of my life reading the minutia, so I do actually rely on my colleagues who write guidelines a bit more.” [06]

“Evidence is poor, but the American Association for the Study of Liver Diseases support not treating chronic portal vein thrombosis, but it does give me some reassurance. So, I think my experience and my concerns with bleeding are justified, or I get reassurance that experts in the field would agree with that approach.” [09]

However, not all participants perceived the utility of guidelines the same way, where some participants focused on the “raw data” or used guidelines to identify the latest evidence rather than the actual recommendation:

“So, I would say I don’t trust the guidelines more than I trust the raw data, right? And they are so heterogeneous. There are mostly opinions from the panels. It’s one of the areas where I don’t feel mandated or I don’t feel committed to follow the guidelines.” [07]

“[In this case] I tend to read the [the guidelines] more, just because I’m less familiar with the scarce literature. So, I tend to read them from time to time.” [07]

“There’s really very little in pregnancy, as you know very well, it’s all just case theories, small cohorts, there’s insufficient information to make real, proper decisions in pregnant patients. And experts make decisions much the way we’re doing it, they’re interpretation of the literature, which is all subject to their own biases.” [05]

Not only did participants turn to their colleagues for knowledge, but also for their experience in challenging areas:

“We all have our special interest, and if he would have a different opinion, then he’s way more into this type of data than I am. So, even if the data is not strong...well, that’s his own practice too so I’d feel much more comfortable following his advice than clinical practice guidelines, given his great experience.” [03]

### *Interacting with colleagues*

How participants interacted with colleagues varied, but was largely for reassurance that their management plans were reasonable:

“I think it’s more to make sure that what you’re doing is within range of what’s felt appropriate by others, right? Not too distant.” [07]

“I’m generally completed unembarrassed about running things by colleagues. We should do that, right? And we do that all the time. I’m lucky... We always run cases by each other...Sometimes it’s just for reassurance I think more than anything else. You kind of have a plan and, okay, this is what I’m thinking of doing, what do you think of that. Well, yeah, that sounds reasonable.” [02]

Participants described having a set management plan, and were open to changing their plan only if there was new information or a compelling reason presented:

“If it’s just more their own anecdotal experience on something that I see or feel reasonably confident with, I probably would not change my practice. But if they saw something or read something that made a difference, then maybe I would.” [03]

“Yeah, I think it depends on their reason... So, if it’s something that I missed... then sure, but if it’s something where I don’t necessarily feel strongly, I might say thank you. I appreciate the input, but I’ll do [something different] and see what happens.” [04]

“I think a lot of the conversations we have in clinic are to bounce ideas off of each other for reassurance, to make sure you’re not completely out in left field. Maybe this is where Dr. X will say, no, what are you talking about? There was that cohort in Turkey in 2006.” [02]

Proximity to other experts mattered. “Bouncing ideas off of each other” when participants were in clinic was easy to do, rather than seeking out colleagues from a distance:

“I might run it by. Say I was in clinic with Dr. J and Dr. C, I’m probably pretty sure I would do it. But I’d say, hey guys, an ET clot, have you guys used a DOAC yet?...Dr. C will go, sure, yeah. I know how the conversation would go.” [02]

“I wouldn’t page somebody to ask for an opinion, but if they’re there, I might say hey, what would you do?” [04]

While many participants valued discussing challenging cases with colleagues, others did not:

“I like to make my own mistakes” [03]

But why would you...if it’s opinion-based? If it’s something you don’t know, if it’s something you forget, so, let’s say a fact that might weigh my decision. But if it’s opinion-based, if I went in a room, just like you’re going to find when you’re doing your [interviews], you’re going to get a different opinion from every person so how is that going to help you? It’s only going to confuse you, create conflict in your own mind about the decision you made, change the way interact now with the patient, you’re going to have less confidence with the patient. I’m a rationale, logical-based, pragmatic person, so I don’t want these things that are going to interfere with my thought processes, because they do. ... Some colleagues who are as

opinionated as me will say exactly the opposite thing. How can that not affect me when I go and see them when they say the exact opposite thing? Now I'm going to have doubt. [05]

“I think you can say there's not much point in seeking advice from a colleague for something where it basically comes down to opinion. You have your own opinion, and you ask someone else and they have a different opinion, what are you going to do?” [05]

### **Using experience to guide practice**

Participants describe how their past experiences shapes their practice and gave them reassurance in their management decisions:

“Experience influences your decision all the time...I don't think I've seen a whole lot of extension ...so that's why I feel comfortable with careful watching.” [03]

“I'm extremely reassured by 15 years of practice of serial imaging for [superficial] vein clots. I haven't gotten burned doing that, with any nasty complications.” [06]

“Like I said, this is anecdotal, right, so I've been doing this long enough that I have seen a very similar situation and I'll know that they've responded to let's say the proph doses of rivaroxaban.” [08]

### ***Experience with different management strategies supports acceptability of practice variation***

Participants describe different management strategies that they have used in the past for similar case presentations, to highlight the acceptability of different management options. They also talked about certain types of clinical scenarios that have good outcomes “no matter what you do”, which supports the clinical equipoise seen. This data been further expanded upon with examples in Section 3.3.1, the qualitative analysis section of Objective 2. While there was acceptability of different management options for certain scenarios, participants also described their bad experiences and “getting burned” that influenced their future practice:

“So, in cancer patients, I got burned, right?” [07]

“I looked after a woman that had crescendo TIAs at term and we delivered her at full dose IV heparin. She almost bled to death. So, I'll never forget her. I walked in the room and she was white as a sheet. It was awful.” [06]

## Using clinical gestalt and common sense

In addition to experience, clinical gestalt and participants' gut reactions played a role in decision-making:

"I don't always practice evidence-based on this one. This one is my gestalt, more my experience." [04]

"Yeah. I mean I think probably reflecting on what the [guideline] recommendations are in general, understanding that those are recommendations and that anecdotal experience and some gestalt will influence how I manage the same diagnosis in different situations." [08]

During the clinical vignettes, participants often talked through their reactions to components of the case:

"These numbers are pretty low, and my gut feeling says that they're not high enough, even if she did have three miscarriages, to say that this is the cause, you know what I mean? I guess if she did have three miscarriages and you had these numbers and this hospital [laboratory] calls this as 99 percentile, then I guess I would almost be forced to classify her as that. But in the back of my mind, I would think that it's not really relevant." [01]

"So, the cirrhosis doesn't excite me too much... The platelet count does excite me. And the varices concern me." [06]

"I just worry that..." [09]; "So I've convinced myself.." [09]

"The bleeding risk is so low, people do well, so I wouldn't be too fussed" [05]

One participant highlighted the concept of using common sense and logic to guide practice:

"The common guiding principle, yeah, there's a common guiding principle in all medicine and what do you think I'm going to say that is? Common sense. [05]

"If you have 10 siblings and one has had a clot, it's probably not a potent thrombophilia, I mean, that's just logical." [05]

## Weighing the benefits against the risks

One management principle that arose in many of the vignettes was the concept that the benefits of a treatment should outweigh the risks:

"You're always looking at the complications of what you're going to be doing. You don't want to cause complications. I need to be kind of be sure that what you're treating is actually something new and acute and warrants anticoagulation. And to do it for that reason, as opposed to doing anticoagulant because the ultrasound says non-occlusive popliteal DVT, and then say that's a DVT, and I'm just going to anticoagulate based on that because I have to. You really have to figure out is this actually a new DVT? Is it symptomatic? Is it incidental? You have to dig a little deeper than that." [01]

There was a constant balancing act between the risk of recurrent thrombosis off of an anticoagulant and bleeding from an anticoagulant:

“So, my gestalt risk of bleeding assessment versus the benefits of anticoagulation, based on experience, push me away from anticoagulation in cirrhotic patients.” [09]

“..it’s always balancing what’s the risk of recurrence with what’s the risk of your intervention, and try to aim for what’s the best ratio. So, holding anticoagulation if you don’t think it’s worth it or pushing for anticoagulation assuming a risk of bleeding if you think it’s warranted.” [03]

“So, I think for all of them, it’s the usual stuff that we look at in terms of bleeding risk, and clotting risk, and trying to balance those...Whenever you’re going to consider anticoagulating a patient, is it safe to do that? And then if you’re going to consider anticoagulating a patient, do you have to do that? Are there other options?” [04]

## **Improving the patient experience**

Different patient characteristics and case details helped to shape decision-making:

“I have to say my treatment of superficial thrombosis is very non guideline based, only because I’m looking at symptoms, size, location, risk factors. It’s very case-based, so not strict.” [08]

Well, if the clot is right at the saphenofemoral junction, then we’re all a little more nervous about that case” [05]

“The platelet count, also, by then may have evolved one direction or another. That might also force my hand.” [06]

When there were different possible management options in a case, decisions were often focused on minimizing patient symptoms and side effects of treatment:

“.. if you give the choice to a patient for a parenteral drug for six weeks versus oral anticoagulation for six weeks..the choice is pretty easy.” [03]

“Yeah, for me, maybe an injection might end up being a little bit better than a DOAC, I don’t know, not enough that it’s worth it to worry about, so it’s certainly not like life and death. And maybe if it prevents a 1 or 2% risk of extension, I still don’t think that’s worth it because it hasn’t been proven to be statistically different or statistically compelling in the studies that I’ve looked at.” [05]

## ***Patient values and preferences matter***

A focus on patient values and preferences was at the forefront of many management decisions.

“It’s addressing the patient’s needs, not your own. In every scenario, I try and see how is the patient doing with respect to side effects, with respect to cost, with respect to their mental status, and that’s different in every single person. What are their preferences and their things in life that make them comfortable? I think you always have to address those when there’s no evidence.” [05]

“I guess that’s the balance of it. So, I’d settle on reassurance that there’s no right answer, and combining more patient perspective, quality of life, her preference with choices, I think that’s reasonable.” [09]

Patient engagement and shared decision-making was highlighted as important when there was clinical uncertainty, in order to help guide management:

“I always try to make sure that that’s congruent with whatever the patients want or need or feel, or making sure they are in line with what we do. Making sure that they’ve heard the various options...I usually try to make sure they get the variety of the options we can do when there is no strong evidence and that we find a common decision...The less evidence there is, much more it’s important to make sure that everybody agrees to the plan” [07]

“Yeah, so I don’t know what to do. That’s one of the cases where really I tend to propose them the wide panel of what we can do, right? [07]

“So, I think when there’s not a clear answer from the evidence, like clearly this is something you should do, you should treat DVTs, then trying to find a way of explaining the evidence and leaving the patients to be more involved in the decision. Because that’s when the patient’s values come into play.” [09]

### ***This is the art of medicine***

In summary, decision making in areas of clinical uncertainty are “the art of medicine” – when faced with a clinical problem with little evidence to guide practice, a clinician must learn about and incorporate a patient’s values and preferences into the decision, while balancing the risks and benefits of treatment:

“..it’s kind of like the art of medicine, you have to get to know, as best you can, your patient, have an understanding of where they’re coming from. What is their willingness to take risk?...Are they medication averse? ...Do they favor medication? You have to go through all those issues with the patient and it’s a difficult thing because this is the first time you’ve ever met the person, probably, so you don’t have any relationship, or you haven’t developed any trust with the person yet so it’s a tricky thing but that’s what you try and do.” [05]

### **3.4.2. Quantitative data**

We were unable to identify strategies or guiding principles from quantitative data alone, however, trends in the questionnaire quantitative data supports the qualitative themes. The qualitative theme “Weighing the benefits against the risks” was indirectly supported by a higher proportion of very or somewhat inappropriate responses when anticoagulating a patient with an

asymptomatic PVT and a high bleeding risk (cirrhosis, platelet count <30 or 43), when compared to the lower risk scenario of a patient without cirrhosis and a normal platelet (Vignette 3, Figure 4).

The theme of “Improving the patient experience” by involving patients in decision-making was indirectly supported by the questionnaire responses. In case vignette 2, where participants frequently described involving patients in the decision in the interviews, 7 of the 8 participants chose more than one management option per question. However, this may not have been the only explanation for choosing more than one management option because fewer participants (3 out of 8) chose multiple management options per question for vignette 4, which was also designed to focused on patient values and preferences and where participants described involving patients in the decision-making process during interviews. There are also major differences in these cases, including available evidence for multiple options in vignette 2 and not 4, and a component of clinical judgment for vignette 4 for how important or causative the antiphospholipid antibodies were in the case.

### **3.5. Objective 4: Understand the relationship between the personality trait of ‘tolerance for ambiguity’ and level of acceptability to other thrombosis experts’ responses**

#### **3.5.1. Qualitative data**

One participant identified that there may be different “comfort levels” in the group for certain treatments that lack of direct evidence, which contributed to practice variation:

“I reflect this back on comfort level. It’s a continuum level in terms of people’s comfort level... When the DOACs first came out, some people were very strict on their use. Whereas some people in our group would be using them for...portal vein thrombosis, cerebral vein thrombosis. As options for treatment evolve, you’ll see a bit more of a comfort level and then practice patterns may evolve over time” [08]



This concept of having different levels of comfort or tolerance to uncertainty is further explored using the TFA scale, as described below.

### **3.5.2. Quantitative data**

All participants completed all questions of the TFA scale. The mean TFA score was 49.3 (36-58, SD 7.7), with a total possible score of 112 where the higher the TFA score, the more *intolerant* to ambiguity someone is. The mean scores for the novelty, complexity and insolubility subcomponent questions are listed in Table V. There was no statistically discernible correlation with the number of acceptable answers chosen and the total TFA score or any of the subscores (Table VI and Figure 7).

**TABLE IV. MEAN TOLERANCE FOR AMBIGUITY (TFA) SCORE AND CORRELATION TO THE NUMBER OF APPROPRIATE ANSWERS CHOSEN**

<b>TFA Score</b>	<b>Mean (Range, SD)</b>
Total Score (total score 112)	49.3 (36-58, 7.70)
Novelty subscore* (total score 28)	17 (13-25, 4.14)
Complexity subscore** (total score 63)	26.4 (19-32, 4.96)
Insolubility subscore*** (total score 21)	5.9 (3-10, 2.36)

\* Novelty indicates the extent to which a participant is intolerant of new, unfamiliar information or situations<sup>54</sup>

\*\*Complexity score indicates the extent to which a participant is intolerant of multiple, distinctive or unrelated information<sup>54</sup>

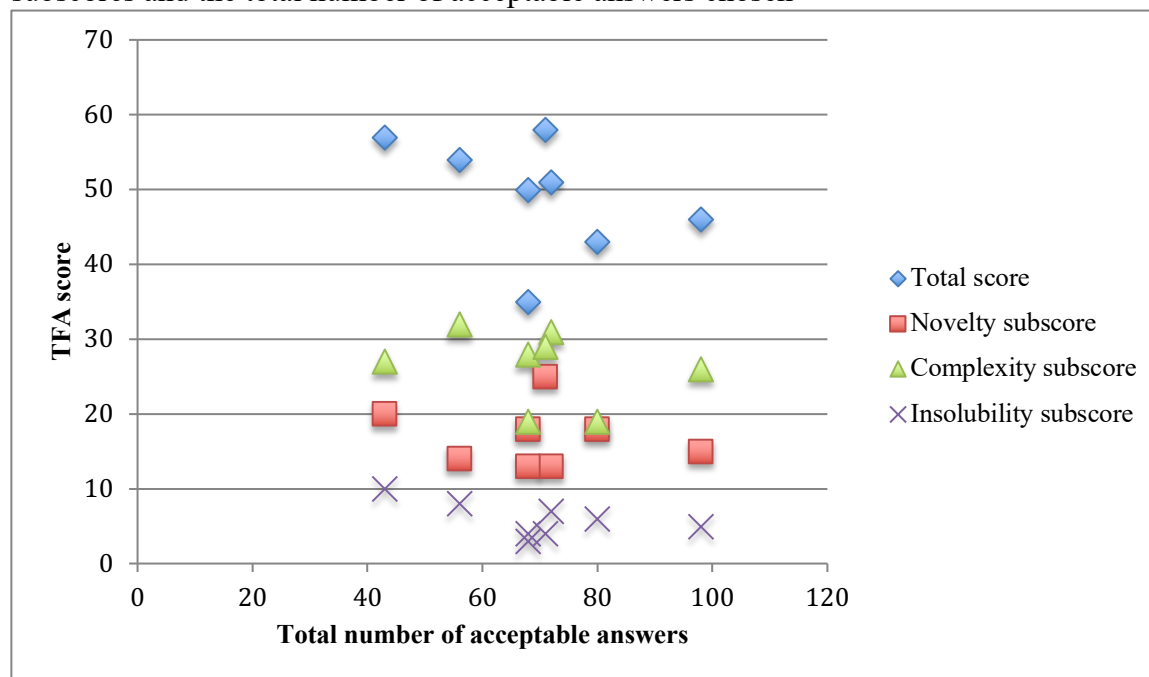
\*\*\*Insolubility indicates the extent to which is a participant is intolerant of problems that are very difficult to solve because, for example, alternative solutions are not evident, information is not available, or the problem components seem unrelated to each other<sup>54</sup>

**TABLE V. TOTAL TOLERANCE FOR AMBIGUITY (TFA) SCORE CORRELATED TO THE NUMBER OF ACCEPTABLE ANSWERS CHOSEN PER CLINICAL VIGNETTE**

Vignette	Pearson correlation with total TFA score* (Pearson co-efficient r)	P-value
Vignette 1	0.198	0.64
Vignette 2	0.312	0.45
Vignette 3	-0.593	0.12
Vignette 4	-0.388	0.34
Vignette 5	-0.501	0.21
All vignettes	-0.448	0.27

\*The higher the TFA score, the more *intolerant* to ambiguity someone is.

**Figure 7.** Scatterplot of the association between Tolerance for Ambiguity (TFA) score and subscores and the total number of acceptable answers chosen



In summary, while hypothesis generating, there was no statistically discernable association between the TFA scores and number of acceptable answers chosen.

## 4. DISCUSSION

### **4.1. Summary of results and methods used**

Not surprisingly, we found that practice variation exists among ten Ottawa thrombosis experts in five challenging case vignettes. We found that the practice variation seen within a small group of experts was extensive, and that most of the thrombosis experts identified the existing practice variation as somewhat or very acceptable, with respect to what a reasonable standard of care in thrombosis medicine would be. There were a smaller proportion of cases where experts disagreed in the chosen management options, i.e. at least one participant chose a management option that was deemed unacceptable by another participant. Qualitative data from the semi-structured interviews identified several management strategies that thrombosis experts used when making decisions in areas of clinical uncertainty, and included looking to the available evidence or colleagues who knew the evidence, using past experience, using clinical gestalt and common sense weighing the benefits against the risks, and improving the patient experience.

Several factors were evaluated to identify sources that could have influenced the amount of acceptability in management seen among participants, such as time dedicated to thrombosis research, time in practice and the personality trait of a tolerance for ambiguity. Our hypothesis was that if an expert was more familiar with the research (or lack of research), or had seen changes in practice over time, then they would have more acceptability of other participants' chosen options. In our subgroup analyses, there were no statistically discernible associations; however, given the small numbers of participants these subgroup analyses these analyses were largely exploratory. The concepts of keeping up to date and knowing the latest evidence, changes

in practice patterns over a career, and differing comfort levels with lack of data were identified in the qualitative interviews as playing a role in decision making, and deserve further study.

A major strength to our study was the mixed-methods design. Each of the thrombosis experts were interviewed to identify and understand their individual practice patterns, and then this data was used to inform different management options in a follow-up questionnaire, which aimed at understanding what management strategies were deemed appropriate by other thrombosis experts. Both qualitative and quantitative data contributed to answering each of the study objectives. To date, the majority of research has been in the area of diagnostic decision-making and not management reasoning<sup>45-47</sup>. Researching management decisions in cases is challenging, as there is often not a single known right answer or a “gold standard” to compare to, each case may have multiple decision points, and other contextual factors including patient preferences and values need to be considered<sup>45-47</sup>. Our study methodology helped to systematically describe practice variation and its acceptability in management areas, so has the possibility to be applied to medical specialties outside of thrombosis medicine. Downsides to our methodology is that it requires a considerable amount of buy-in from participants and it is time intensive, especially if several decision points are evaluated per case.

#### **4.2. How our findings relate to the existing literature**

The script concordance test (SCT) is an assessment method to assess learners in areas where clinical uncertainty exists, with the goal to assess how well an examinee interprets key findings to support or refuse a hypothesis<sup>27</sup>. A unique aspect of SCTs is that expert variation is built into the scoring key where answers may be given full or partial credit depending on how many

experts agree<sup>27</sup>. Lineberry and colleagues used SCTs as a tool to evaluate the concept of acceptability of practice variation. Ten gastroenterologists from Argentina who initially participated on an SCT panel as experts were asked follow-up questions that included their reactions to other experts' perspectives<sup>48</sup>. Based on a Likert rating scale, experts found other experts' responses to be moderately compelling, and switched their own answers 20% of the time (which was, in part, case dependent)<sup>48</sup>. Experts reflected that there were “multiple partially correct actions” that often depended on what local resources were available. In a second research study that evaluated adding written “think aloud” answers to a standard SCT, researchers acknowledged that additional “right” answers were justified based on clinical reasoning, in addition to the possible diagnostic or management options proposed by an expert panel<sup>49</sup>. Fourteen surgeons' practice patterns were observed in the operating room, which gave rise to the *Principles and Preferences* framework (see Section 1.1 and Section 4.3). In follow-up interviews of the same group of surgeons, when talking about procedural variation they rarely criticized the variations of other surgeons<sup>7</sup>. Not only was procedural variation seen as acceptable, it was also seen as beneficial. Participants believed that procedural variation was advantageous to learners in order for learners to develop and synthesize a “broad catalog of procedural approaches”<sup>7</sup>. While procedural variation is different than variation seen in medical management of a medical specialty, the acceptance of variation among experts was similar.

“To act with confidence while simultaneously remaining uncertain is a paradox that epitomizes expert practice”<sup>45</sup>. Ilgen and colleagues recently completed a critical review of the literature to define and elaborate on the concept of “comfort with uncertainty”. They defined *certainty* as “the confidence in the interpretation of a clinical situation” and *comfort* as “the confidence in one's

ability to act”<sup>45</sup>. How do experts navigate and have “comfort with uncertainty”? Ilgen et al. identified a framework using a cognitive psychology lens that included experience-based and theory-based mechanisms: (1) physicians’ prompts about comfort with uncertainty are drawn from their lived experiences (experience-based cue) and (2) their theories about their own situation, and that they believe in their own mastery (theory-based cue). The perception of fluency may be based on both past experiences as well as staying attentive, or “monitoring”, during the automaticity of problem solving<sup>45</sup>. In our study, thrombosis experts drew on their past experiences to make decisions about cases, which helped with the confidence of their decisions (e.g. “experience influences your decision all the time...I don’t think I’ve seen a whole lot of extension...so that’s why I feel comfortable with careful watching”). Theory-based cues include an experts’ belief that they have sufficient amount of past experience of all the possible scenarios they could face, as well as the ability to control the situation through planning<sup>45</sup>. Improving comfort with uncertainty includes identifying multiple management plans and outcomes, and identifying possible resources that can be used in the future. The concept of forward planning was identified in our study as participants acknowledged the risks and benefits of different treatment options, and walked through many decisions within a given scenario without prompting (i.e. management of a VTE from early pregnancy to labor and delivery to postpartum management). A limitation to a cognitive psychology lens used by Ilgen and colleagues is the lack of socio-cultural perspective in describing why experts may have “comfort in uncertainty”<sup>45</sup>. In our study, local culture contributes to the acceptability of practice variation and comfort with uncertainty, such as the ability to ask colleagues for advice (see Section 4.5 for further details).

### **4.3. How our findings relate to the conceptual framework chosen**

The conceptual framework of *Principles* and *Preferences* was used to help design and interpret this study<sup>5</sup>. This framework was developed in reference to surgical procedural variation, where some procedural variation was found to be a preference with an interchangeable acceptable option, and some procedural variation was a principle without an acceptable alternative. In our study, there were similarities to the framework because there were multiple alternative management options. Similar to Apramian et al's study, what was deemed acceptable (somewhat or very appropriate) or unacceptable (somewhat or very inappropriate) differed between thrombosis experts.

However, there were also important differences to the conceptual framework chosen. More so than with a surgical technique, the context of the clinical scenario mattered. For example, there were many acceptable management options for a patient with a SVT 4 cm away from the deep vein system (lower perceived risk), however, there was less tolerability of alternative options when the SVT was 1 cm away from the deep vein system (higher perceived risk). Similarly, when the perceived risk of bleeding increased, there were fewer acceptable options in a patient with cirrhosis with an asymptomatic PVT. This dynamic assessment of weighing the risks and benefits of treatment was also identified from qualitative data. Context specificity mattered. The acceptability of a newer anticoagulant was different if the patient had a PVT or had suspected ET, even though both areas lacked evidence for use of these newer medications. Alternative factors were also considered such as risk of progressive thrombosis, risk of bleeding and medication safety. Further research is needed into the interaction between the clinician, and the details of the clinical scenario.

#### **4.5. Interpretation of study results using a sociocultural lens**

The results of our study were shaped by local cultural norms. Some, but not all, participants describe sharing their management plans with others to seek advice and check that what they had planned was an acceptable option. The participants frequently commented on what he or she thought other participants would have done in that scenario – so had awareness of others’ practice patterns as they made decisions. In the interviews, participants often talked about their colleagues in a positive light. One participant commented on how “blown away every day by people in our group and how up-to-date they are”, highlighting the importance of local group dynamics.

Because this study was conducted in one specialty at one centre, we are unable to directly study how the socioculture norms of thrombosis medicine in Ottawa can be applied to the other thrombosis medicine centres or areas of medicine. Apramian et al. interviewed surgeons to understand the social processes that shape how surgeons interpret and enact procedural variations<sup>11</sup>. Similar to what we found in our study, surgeons informally “shared stories” about procedural variation on a day-to-day basis, and “placed trust” in those stories based on reputation, credibility, positions of leadership, and having relationships where the participants could rely on others for support<sup>11</sup>. Part of the culture in surgery were participants “being wary” of innovation and “showing the logic” of a procedural variation; they often related variations to available scientific evidence<sup>11</sup>. This cultural focus on “evidence based medicine” and analytic principles was also seen among physicians in emergency medicine, general medicine and family medicine in an interview study about clinical decision making; physicians valued evidence-based medicine principles that were often at odds with their experience and intuition<sup>40</sup>. Thrombosis



experts in our study focused on the evidence and logic (i.e. balancing the risks and benefits of treatment), but also relied on their own experiences and the experiences of colleagues they trust.

#### **4.6. Implications for medical education**

“Training for uncertainty” is not a new concept in medical education, as Renee Fox described in detail in 1957<sup>50</sup>. Fox outlined the importance of medical students’ acknowledging and recognizing clinical uncertainty, and learning to “come to terms” with uncertainty as their competence and experience grew<sup>50</sup>. Understanding and managing clinical uncertainty in the current era of competency-based medical education is needed, where summative decisions about a learner’s competence are based on assessment of a series of diagnostic and management decisions in real life cases. Our study identified that there may be multiple acceptable or “right” answers in challenging scenarios, but that some thrombosis experts also identified (and disagreed upon) what answers were unacceptable. Further research is needed on how to reconcile differences between examiners, especially around fundamental concepts about what a reasonable standard of care is for a given specialty. Shifting away from specific milestones to gestalt-based entrustment decisions or focusing on underlying clinical reasoning may be more accurate. Alternatively, collecting data from different raters who hold differing perspectives could enrich the assessment process by providing a broader view of competence (and expertise)<sup>51</sup>. While the five case vignettes were particularly challenging and may be more appropriate for the level of a sub-specialty fellow, real life cases may be equally challenging or complex<sup>52</sup>.

This study also highlighted the context specificity of decision-making, and so understanding how specific contexts (including level of risk in a scenario) affect competency-based entrustment

decisions is needed. Additional instruction and assessment of learners that focus on contextual factors, including patient preferences and values, may help to improve training and assessment in these challenging areas. Individual management decisions are not made in isolation.

Understanding how learners navigate clinical uncertainty and associated practice variation with supervisors and patients in a medical specialty is needed.

#### **4.7. Implications for patient care**

One strategy that helped participants' makes management decisions was involving patients in the decision, and focusing on patients' values and preferences. Participants identified that when clinical uncertainty exists, the more important it was to involve patients in decision-making. More research is needed in how thrombosis experts engage patients in making these decisions, including how much information to present (and how they decide this), and how they guide patients in decision-making in these challenging areas.

#### **4.8. Study limitations**

Interviews offer a source of rich, detailed data on the area of practice variation. For feasibility reasons, the interviews were conducted at one institution only. There were differences in practice between each of these ten thrombosis experts; however, this sample likely did not represent the maximum variation seen among thrombosis experts across Canada or internationally. Similarly, this study only assessed the acceptability of practice variation seen among experts in areas of uncertainty, and so was not in an area where a single correct management plan was more established, nor was it exploring clinical uncertainty among general practitioners. There are sociocultural influences to consider; a member of a small thrombosis group may be more tolerant of another member's management strategies if they are in the same group, either in real life or in a questionnaire, compared to another thrombosis expert at a different centre or a general

practitioner. It is possible that participants may be categorizing, identifying and comparing themselves (“experts”) to outsiders, a process described by social identity theory<sup>53</sup>. To minimize this possible effect and study limitation, we also included a broader range of management options from clinical practice guidelines and options that are inappropriate based on the product monograph. Further research is needed to understand the acceptability of options across centres and across specialties, and among topics with more well-established answers based on high-quality evidence.

Another limitation was that case vignettes were used instead of observing real life cases, which is not reflective of real life. Vignettes and interview questions were used to help standardize the cases seen. Participants may interpret findings differently on paper, and the cases may not represent all of the clinical information used to make decisions in real life. Multiple management options were chosen in the questionnaire, which would not have happened in real life. This may be reflective of what participants would have presented to patients, or may it have been their interpretation of the questions. The mean number of chosen answers was lower than the mean number of appropriate/acceptable answers chosen, which do suggest that they interpreted these questions differently. Correlating the accuracy of questionnaire data with real life direct observations would be helpful to corroborate the questionnaire results, however, was not possible for practical reasons. Instead, qualitative data from interviews helped to support our quantitative findings.

#### **4.9. Future research directions**

Learners in medical specialties often have to navigate practice variations among experts, particularly in challenging clinical scenarios where there is little evidence to guide practice. How

best to instruct learners when there is clinical uncertainty and practice variation among experts is largely unknown. The next steps in my research agenda is to understand how residents and subspecialty thrombosis fellows navigate supervisors' practice variations and manage uncertainty in complex scenarios. Specific research questions include (1) How accurate or knowledgeable are residents and thrombosis fellows in their prediction of expert practice variation using the same challenging cases? and (2) Can residents and thrombosis fellows 'learn the controversy' by outlining multiple acceptable management strategies, and if so, what is a learner's rationale in choosing their own preferred management strategy? Additionally, understanding how thrombosis experts navigate and discuss clinical uncertainty (and other experts' practice variation) with learners is needed.

Shared decision making with patients is particularly important in the 'grey spaces' of medicine. Learning how thrombosis experts decide when and how to engage patients in decision-making, and incorporate patient preferences and values into their decisions, is still needed. Interviewing patients about their experiences in areas with practice variation and clinical uncertainty may help to guide physicians and optimize patient encounters.

## 5. CONCLUSIONS

In this study we explored the practice variation present among thrombosis experts, and the concept of *acceptability* of practice variation among experts. In a mixed-methods study design, we used a combination of semi-structured interviews and a follow-up questionnaire of thrombosis experts. We identified that a large amount of practice variation present was acceptable, but that there was also disagreement between experts about what was or was not acceptable, with reference to what a reasonable standard of care in thrombosis medicine was. We also identified ways for how experts managed clinical uncertainty, including (1) Knowing the latest evidence or relying on colleagues' expertise; (2) Using past experiences; (3) Using clinical gestalt and common sense; (4) Weighing the benefits against the risks and (5) Improving the patient experience. These results help to inform future research in how experts navigate clinical uncertainty, which have implications in the instruction and assessment of learners, as well as patient care.

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## 7. APPENDICES

### **APPENDIX A. Case Vignettes and Interview Guide**

**Case 1.** You are referred a 24-year-old woman who is pregnant G1P0 at 20 weeks gestation, who has a new diagnosis of pulmonary embolism. She initially presented to the Emergency Department with new shortness of breath, and was diagnosed with a PE based on a high-probability ventilation perfusion (V/Q) scan with large mismatched defects in the left lower lobe. She has no chest pain, hemoptysis or any leg symptoms. She was observed in hospital for 24 hours because of an elevated heart rate of 118, with normal blood pressure and oxygen saturation. She was discharged to see you in clinic the following day, on full-dose low-molecular-weight heparin for her weight (Fragmin 15,000 units sc daily for weight 75 kg). Her pregnancy has otherwise been unremarkable; she has no other past medical history. Her only other medication is a prenatal vitamin.

She has a family history of unprovoked DVT in her sister and father.

Examination: BP 119/72, p102, oxygen saturation 97% on room air. Chest clear to auscultation, no crackles or wheeze. No evidence of DVT on examination.

Investigations: WBC 8.0, Hb 108, Platelet count 250, Creatinine 40

- (1) Based on the information provided, how would you manage the patient in this scenario?
  - a. Walk me through how you came to your decisions
    - i. Treatment? Dose of anticoagulant and monitoring over pregnancy (first month, and after)?
    - ii. Management around delivery?
    - iii. Thrombophilia testing?
    - iv. Management after 6 weeks postpartum? Future birth control?
  - b. What factors did you consider when making your decision about management?
  - c. What factor or factors did you think were most important or did you weigh the most when deciding on your management strategy?
  - d. What other information would you seek in real patient care – if any – to help make your decision?
  - e. What if?
    - i. PE was diagnosed earlier in pregnancy?
    - ii. PE was diagnosed later in pregnancy, close to delivery?
    - iii. She had a DVT and PE, instead of a PE alone?
    - iv. She did not require admission for monitoring?
    - v. She did not have a family history of DVT/PE
  - f. How did evidence or guidelines influence your decision, if at all?
  - g. How did your past experiences influence your decision, if at all?
  - h. Have you, or would you discuss or seek advice from a colleague about a similar case?
    - i. If so, what would you do with the information if a colleague offered management advice that differed from your initial impression or plan?

**Case 2.** A 32-year-old woman is referred to your clinic for management of a moderately symptomatic superficial vein thrombosis of the left leg involving the greater saphenous vein. Her symptoms started 5 days ago and have persisted. On the advice of her family physician she tried

ibuprofen 400mg 3-4 times a day for the last 3 days with little relief. She has no shortness of breath, chest pain or hemoptysis.

She has no other past medical history. Her only medication is the oral contraceptive pill, which she has been on for the last 10 years. She has never been pregnant and is not planning any future pregnancies. She has no family history of SVT, DVT or PE.

Examination: 70kg. She has a 6-cm palpable cord with erythema and pain on her inner thigh, she has no leg edema. She has no evidence of varicose veins.

Investigations: WBC 6.0, Hb 138, Platelet count 215, Creatinine 57.

Ultrasound: Non-compressible left greater saphenous vein, 4cm from the saphenofemoral junction.

(2) Based on the information provided, how would you manage the patient in this scenario?

- a. Walk me through how you came to your decision
  - i. Treatment? Choice of anticoagulant? Duration?
  - ii. Stop OCP? Thrombophilia testing?
- b. What factors did you consider when making your decision about management?
- c. What factor or factors did you think were most important or did you weight the most when deciding on your management strategy?
- d. What other information would you seek in real patient care – if any – to help make your decision?
- e. What if?
  - i. Her thrombus was <3 cm from the saphenofemoral junction
    1. Treatment? Choice of anticoagulant? Duration?
  - ii. She was less or more symptomatic
  - iii. She was not on an oral contraceptive pill
    1. Advice for future oral contraceptive pill use or pregnancy?
- f. How did evidence or guidelines influence your decision, if at all?
- g. How did your past experiences influence your decision, if at all?
- h. Have you, or would you discuss or seek advice from a colleague about a similar case?
  - i. If so, what would you do with the information if a colleague offered management advice that differed from your initial impression or plan?

**Case 3:** A 63-year-old man is referred to your clinic for management of an asymptomatic portal vein thrombosis picked up incidentally on an abdominal ultrasound that was completed for cancer screening. He has no abdominal pain. The ultrasound showed thrombus of the main portal vein and the left and right branch of the portal vein, with no evidence of malignancy. Prior ultrasound Doppler imaging 2 years ago showed no evidence of a portal vein thrombus.

He has a history of cirrhosis secondary to non-alcoholic steatohepatitis (NASH). He has never had a gastrointestinal bleed. He had a screening endoscopy 1 year ago with small-moderate sized esophageal varices for which he is on Nadolol. He also has Type 2 DM on metformin.

Exam: Weight 90kg. He has no abdominal pain or ascites on examination.

Investigations: WBC 5.0, Hemoglobin 110, Platelet count: 43, INR 1.1, PTT 26, creatinine 62, albumin 35, bilirubin 12, AST 82, ALT 140, ALP 40, GGT 150.

(3) Based on the information provided, how would you manage the patient in this scenario?

- a. Walk me through how you came to your decision
  - i. Treatment? Choice of anticoagulant? Duration?
- b. What factors did you consider when making your decision about management?
- c. What factor or factors did you think were most important or did you weight the most when deciding on your management strategy?
- d. What other information would you seek in real patient care – if any – to help make your decision?
- e. What if:
  - i. He was symptomatic
  - ii. His platelet count was  $<30$
  - iii. His platelet count was  $>50$
  - iv. His INR was elevated (if so, what is your cutoff?)
  - v. He had a history of GI bleeding in the last year from a treated gastric ulcer
  - vi. He had a history of GI bleeding in the last year from a cause that was not easily fixed (ie. portal hypertensive gastropathy)
  - vii. He did not have cirrhosis, with normal platelet count
- f. How did evidence or guidelines influence your decision, if at all?
- g. How did your past experiences influence your decision, if at all?
- h. Have you, or would you discuss or seek advice from a colleague about a similar case?
  - i. If so, what would you do with the information if a colleague offered management advice that differed from your initial impression or plan?

**Case 4:** A 30-year-old woman is referred to you after 2 consecutive, early pregnancy losses. She has never had a successful pregnancy, with pregnancy losses at 7 weeks gestation and 9 weeks gestation. She saw an obstetrician and there were no other identifiable cause of her miscarriages found. Her obstetrician completed blood work to check for antiphospholipid syndrome, and she was found to have elevated anti-beta-2 glycoprotein-1 antibodies on repeated testing 3 months apart. She has never had a past DVT/PE, and she is otherwise healthy with no other medical comorbidities. She has no family history of DVT/PE. She wants to get pregnant again, and would like your advice about management during a future pregnancy.

Investigations:

WBC 4.6, Hb 110, platelet count 321, Creatinine 45

B2glycoprotein-1 IgG: 14 GU, repeat 3 months later was 17 GU ( $>99\%$ , upper limit of normal is 13)

B2glycoprotein-1 IgM: 6 MU, repeat 3 months later was 5 MU

Anticardiolipin Ab IgG: 5 GU, repeat 3 months later was 4 GU

Anticardiolipin Ab IgM: 6 MU, repeat 3 months later was 5 MU

Lupus anticoagulant: negative

- (4) Based on the information provided, how would you manage the patient in this scenario?
  - a. Walk me through how you came to your decision
    - i. Treatment? Type and dose of antiplatelet and/or anticoagulant? During pregnancy? Postpartum?

- b. What factors did you consider when making your decision about management?
- c. What factor or factors did you think were most important or did you weight the most when deciding on your management strategy?
- d. What other information would you seek in real patient care – if any – to help make your decision?
- e. What if?
  - i. 3 or more early pregnancy losses
  - ii. Late pregnancy loss >10 weeks gestation
  - iii. Stillbirth loss >20 weeks gestation
  - iv. Age, younger or older?
  - v. Requiring fertility treatments?
  - vi. Antibodies were different
    - 1. Anticardiolipin antibodies
    - 2. Lupus anticoagulant
  - vii. If participant initially said no treatment: What if Obstetrician recommended treatment? Or patient wanted treatment?
- f. How did evidence or guidelines influence your decision, if at all?
- g. How did your past experiences influence your decision, if at all?
- h. Have you, or would you discuss or seek advice from a colleague about a similar case?
  - i. If so, what would you do with the information if a colleague offered management advice that differed from your initial impression or plan?

**Case 5:** A 28-year-old female presents with a left leg swelling and a popliteal DVT detected on ultrasound imaging. She has left leg pain and swelling, but has no chest pain, shortness of breath, or any bleeding symptoms.

She has no other past medical history, on no medications including not on the oral contraceptive pill.

Her routine blood work showed a platelet count of 950, confirmed on repeat tested. With a suspected diagnosis of Essential Thrombocythemia, a myeloproliferative neoplasm. JAK-2 testing has been sent off and is pending.

She has no family history of DVT/PE or abnormal blood counts.

Examination: Weight 70kg, BMI 27. Erythema and edema of her left leg.

Investigations: WBC 7.7, Hb 140, Platelet count 950, creatinine 67

Ultrasound: left occlusive popliteal vein thrombus

- (5) Based on the information provided, how would you manage the patient in this scenario?
  - a. Walk me through how you came to your decision
    - i. Treatment? Type of anticoagulant? Duration?
    - ii. What if:
      - 1. ET is confirmed with JAK2+: Type of anticoagulant?
      - 2. In the future, her platelet count is well controlled with medication like hydroxyurea. Duration of anticoagulation?
      - 3. Pregnancy plans?
  - b. What factors did you consider when making your decision about management?

- c. What factor or factors did you think were most important or did you weight the most when deciding on your management strategy?
- d. What other information would you seek in real patient care – if any – to help make your decision?
- e. How did evidence or guidelines influence your decision, if at all?
- f. How did your past experiences influence your decision, if at all?
- g. Have you, or would you discuss or seek advice from a colleague about a similar case?
  - i. If so, what would you do with the information if a colleague offered management advice that differed from your initial impression or plan?

Closing question: We have talked about 5 different clinical scenarios. What are some common guiding principles that you may have used when deciding on these management strategies, if any?

## **APPENDIX B: Questionnaire**

### **Part A. Demographic questions**

- 1) What is your area of specialty?
  - ☐ General Internal Medicine
  - ☐ Hematology
  - ☐ Other: \_\_\_\_\_
- 2) What is your sex?
  - ☐ Female
  - ☐ Male
- 3) How many years have you been in practice?
  - ☐ Less than 5 years
  - ☐ 5-10 years
  - ☐ 11-20 years
  - ☐ 21 or more years
- 4) On average, how many half-day thrombosis clinics do you have **per month**  
 \_\_\_\_\_ (Will be drop down window ranging from 0-20 clinics per month)
- 5) What percentage of your time do you allocate to **thrombosis research** per week?
  - ☐ 0%
  - ☐ 1-25%
  - ☐ 26-50%
  - ☐ 51-75%
  - ☐ 76-100%

**Part B. Below are the cases that were presented in your interview, with questions about each case.**

**There were several management strategies identified. For each strategy you will be asked:**

- (1) How likely or unlikely you would be to recommend each management strategy to a patient, and
- (2) Regardless of how likely or unlikely you are to recommend or use each management strategy, how appropriate is each management strategy, taking into account what is a reasonable standard of care for thrombosis medicine

### **Case 1: Management of a pregnant patient with pulmonary embolism (PE)**

For each management option two questions were asked:

- a) Very unlikely to recommend this management strategy
  - b) Somewhat unlikely to recommend this management strategy
  - c) Neutral, would not recommend for or against this management strategy
  - d) Somewhat likely to recommend this management strategy
  - e) Very likely to recommend this management strategy
- 
- a) This management strategy is very inappropriate
  - b) This management strategy is somewhat inappropriate
  - c) This management strategy is somewhat appropriate
  - d) This management strategy is very appropriate

#### **Treatment in the first 30 days:**

- 1) Daily LMWH
- 2) Twice daily LMWH
- 3) Anticoagulant dosing based on anti-Xa levels
- 4) 100% weight-based LMWH dose (no anti-Xa levels)
- 5) 75% weight-based LMWH dose (no anti-Xa levels) *inappropriate option*

#### **Treatment after 30 days**

- 1) Daily LMWH
- 2) Twice daily LMWH
- 3) Anticoagulant dosing based on anti-Xa levels
- 4) 100% weight-based LMWH dose (no anti-Xa levels)
- 5) 75% weight-based LMWH dose (no anti-Xa levels)

#### **Delivery management**

- 1) Induction of labor
- 2) Spontaneous labor

#### **Thrombophilia testing**

- 1) Offer thrombophilia testing

### **Case 2: Management of symptomatic superficial vein thrombosis (SVT):**

#### **Treatment of symptomatic SVT (4 cm away from the saphenofemoral junction):**

- 1) Continue management with regular anti-inflammatories with follow-up
  - 2) Prophylactic-dose LMWH daily
  - 3) Intermediate-dose LMWH daily (50-75% weight-based dose)
  - 4) Therapeutic-dose LMWH daily (100% weight-based dose)
  - 5) Fondaparinux 2.5 mg daily
  - 6) Prophylactic-dose DOAC
- Examples: Rivaroxaban 10 mg orally daily, or Apixaban 2.5 mg orally twice daily*



## 7) Intermediate-dose DOAC

*Examples: Rivoraxaban 20 mg orally daily, or Apixaban 5 mg orally twice daily*

## 8) Therapeutic-dose DOAC

*Examples: Rivoraxaban 15 mg orally twice daily for 3 weeks and then 20 mg daily;  
Apixaban 10 mg orally twice daily and then 5 mg orally twice daily*

**Treatment of symptomatic SVT (1 cm away from the saphenofemoral junction):**

## 1) Continue management with regular anti-inflammatories with follow-up

## 2) Prophylactic-dose LMWH daily

## 3) Intermediate-dose LMWH daily (50-75% weight-based dose)

## 4) Therapeutic-dose LMWH daily (100% weight-based dose)

## 5) Fondaparinux 2.5 mg daily

## 6) Prophylactic-dose DOAC

*Examples: Rivoroxaban 10 mg orally daily, or Apixaban 2.5 mg orally twice daily*

## 7) Intermediate-dose DOAC

*Examples: Rivoraxaban 20 mg orally daily, or Apixaban 5 mg orally twice daily*

## 8) Therapeutic-dose DOAC

*Examples: Rivoraxaban 15 mg orally twice daily for 3 weeks and then 20 mg daily;  
Apixaban 10 mg orally twice daily and then 5 mg orally twice daily*

**Case 3: Management of a portal vein thrombosis in a patient with cirrhosis and thrombocytopenia (low platelet count):****Asymptomatic PVT in a patient with cirrhosis and a platelet count of 43:**

## 1) No anticoagulation

## 2) Prophylactic-dose LMWH

## 3) Intermediate-dose LMWH (50-75% weight-based dose)

## 4) Therapeutic LMWH (100% weight-based dose)

## 5) Therapeutic LMWH for 1-2 weeks then prophylactic-dose LMWH

## 6) LMWH transition to VKA (no delay)

## 7) Therapeutic LMWH for 1-2 weeks then DOAC

## 8) DOAC

**Symptomatic PVT in a patient with cirrhosis and a platelet count of 43:**

## 1) No anticoagulation

## 2) Prophylactic-dose LMWH

## 3) Intermediate-dose LMWH (50-75% weight-based dose)

## 4) Therapeutic LMWH (100% weight-based dose)

## 5) Therapeutic LMWH for 1-2 weeks then prophylactic-dose LMWH

## 6) LMWH transition to VKA (no delay)

## 7) Therapeutic LMWH for 1-2 weeks then DOAC

## 8) Intermediate LMWH for 1-2 weeks then DOAC

## 9) DOAC

**Asymptomatic PVT in a patient with cirrhosis and a platelet count of >50:**

- 1) No anticoagulation
- 2) Prophylactic-dose LMWH
- 3) Intermediate-dose LMWH (50-75% weight-based dose)
- 4) Therapeutic LMWH (100% weight-based dose)
- 5) Therapeutic LMWH for 1-2 weeks then prophylactic-dose LMWH
- 6) LMWH transition to VKA (no delay)
- 7) Therapeutic LMWH for 1-2 weeks then DOAC
- 8) Intermediate LMWH for 1-2 weeks then DOAC
- 9) DOAC

**Asymptomatic PVT in a patient with cirrhosis and a platelet count of <30:**

- 1) No anticoagulation
- 2) Prophylactic-dose LMWH
- 3) Intermediate-dose LMWH (50-75% weight-based dose)
- 4) Therapeutic LMWH (100% weight-based dose)
- 5) Therapeutic LMWH for 1-2 weeks then prophylactic-dose LMWH
- 6) LMWH transition to VKA (no delay)
- 7) Therapeutic LMWH for 1-2 weeks then DOAC
- 8) Intermediate LMWH for 1-2 weeks then DOAC
- 9) DOAC

**Asymptomatic PVT in a patient without cirrhosis and a normal platelet count:**

- 1) No anticoagulation
- 2) Prophylactic-dose LMWH
- 3) Intermediate-dose LMWH (50-75% weight-based dose)
- 4) Therapeutic LMWH (100% weight-based dose)
- 5) Therapeutic LMWH for 1-2 weeks then prophylactic-dose LMWH
- 6) LMWH transition to VKA (no delay)
- 7) Therapeutic LMWH for 1-2 weeks then DOAC
- 8) Intermediate LMWH for 1-2 weeks then DOAC
- 9) DOAC

**Case 4: Management of recurrent pregnancy loss in a patient with positive antiphospholipid antibodies:**

**2 early pregnancy losses and low-titre anti-B2 glycoprotein 1 antibodies (anti-B2GP1)**

- 1) No treatment
- 2) ASA
- 3) LMWH/ASA

**3 early pregnancy losses and low-titre anti-B2GP1**

- 1) No treatment
- 2) ASA
- 3) LMWH/ASA

**1 late loss and low-titre anti-B2GP1**

- 1) No treatment
- 2) ASA
- 3) LMWH/ASA

**2 early losses and high-titre anti-B2GP1**

- 1) No treatment
- 2) ASA
- 3) LMWH/ASA

**2 early losses and high-titre anticardiolipin antibodies (ACA)**

- 1) No treatment
- 2) ASA
- 3) LMWH/ASA

**Case 5: Management of a patient with possible Essential Thrombocythemia (ET) with a deep vein thrombosis (DVT):****DVT treatment in a patient with ET**

- 1) Therapeutic-dose LMWH
- 2) Therapeutic-dose LMWH transition to VKA (no delay)
- 3) Therapeutic-dose LMWH for 1-2 weeks then a DOAC
- 4) DOAC

**Long-term anticoagulation**

- 1) Continue anticoagulation

**Secondary prevention of VTE in a future pregnancy**

- 1) Prophylactic-dose LMWH
- 2) Prophylactic-dose LMWH until 20 weeks gestation then twice daily dosing
- 3) Intermediate-dose LMWH (50-75% weight-based dose)
- 4) Therapeutic-dose LMWH (100% weight-based dose)

## **APPENDIX C. Tolerance for Ambiguity Scale**

Source: Budner, 1962<sup>54</sup>

Please respond to the following statements by indicating the extent to which you agree or disagree with them. Fill in the blanks with the number from the rating scale that best represents your evaluation of the item.

### Rating Scale

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Neither agree nor disagree
- 5 Slightly agree
- 6 Moderately agree
- 7 Strongly agree

1. \_\_\_\_ An expert who doesn't come up with a definite answer probably doesn't know much
2. \_\_\_\_ I would like to live in a foreign country for a while
3. \_\_\_\_ There is really no such thing as a problem that can't be solved.
4. \_\_\_\_ People who fit their lives to a schedule probably miss most of the joy of living
5. \_\_\_\_ A good job is one where what is to be done and how it is to be done are always clear
6. \_\_\_\_ It is more fun to tackle a complicated problem than to solve a simple one
7. \_\_\_\_ In the long run it is possible to get more done by tackling small, simple problems rather than large and complicated ones
8. \_\_\_\_ Often the most interesting and stimulating people are those who don't mind being different and original
9. \_\_\_\_ What we are used to is always preferable to what is unfamiliar.
10. \_\_\_\_ People who insist upon a yes or no answer just don't know how complicated things really are.
11. \_\_\_\_ A person who leads an even, regular life in which few surprises or unexpected happenings arise really has a lot to be grateful for.
12. \_\_\_\_ Many of our most important decisions are based upon insufficient information.
13. \_\_\_\_ I like parties where I know most of the people more than ones where all or most of the people are complete strangers.
14. \_\_\_\_ Teachers and supervisors who hand out vague assignments give one a chance to show initiative and originality
15. \_\_\_\_ The sooner we all acquire similar values and ideals the better
16. \_\_\_\_ A good teacher is one who makes you wonder about your way of looking at things

### Scoring Key

Having intolerance for ambiguity means that an individual tends to perceive situations as threatening rather than promising. Lack of information or uncertainty, for example, would make

such a person uncomfortable. Ambiguity arises from three main sources: novelty, complexity and insolubility. These three subscales exist within this instrument.

High scores indicate a greater INTOLERANCE of ambiguity. To score the instrument, the even numbered items must be reverse-scored. That is, the 7s become 1s; 6s become 2s etc. After reversing the even-numbered items, sum the scores for all 16 items to get your total score.

The 3 subscales also can be computed to reveal the major source of intolerance of ambiguity. Here are the items associated with each subscale.

Item	Subscale	Item	Subscale	Item	Subscale	Item	Subscale
1	I	5	C	9	N	13	N
2	N	6	C	10	C	14	C
3	I	7	C	11	N	15	C
4	C	8	C	12	I	16	C

(N) Novelty Score (2,9,11,13) \_\_\_\_\_

(C) Complexity Score (4,5,6,7,8,10,14,15,16) \_\_\_\_\_

(I) Insolubility Score (1, 3, 12) \_\_\_\_\_

TOTAL SCORE \_\_\_\_\_

Novelty indicates the extent to which you are (in)tolerant of new, unfamiliar information or situations.

Complexity score indicates the extent to which you are (in)tolerant of multiple, distinctive or unrelated information.

Insolubility indicates the extent to which you are in(tolerant) of problems that are very difficult to solve because, for example, alternative solutions are not evident, information is not available, or the problem components seem unrelated to each other.

Remember, the higher the score(s) the more intolerant of ambiguity you scored.

**APPENDIX D. List of all acceptable options for management options chosen by participants for each clinical vignette**

**Table 1.** Level of appropriateness per participant for each chosen recommendation in Vignette 1

	Participant number								Number of appropriate (+ or ++), n	Number of inappropriate (- or - -), n
	1	2	3	4	5	6	7	8		
Treatment first 30 days <sup>a</sup>										
Daily LMWH	++	++	++	++	+	++	+	-	7	1
Twice daily LMWH	+	++	++	+	++	+	++	++	8	0
Dosing based on anti-Xa levels	+	++	++	--	++	-	+	+	6	2
100% weight-based dose (no anti-Xa levels)	++	++	++	++	+	++	++	+	8	0
Treatment after 30 days										
Daily LMWH	++	++	++	?	++	++	-	-	5	2
Twice daily LMWH	-	+	++	+	++	-	++	++	6	2
Dosing based on anti-Xa levels	-	+	++	--	++	-	?	++	4	3
100% weight-based dose (no anti-Xa levels)	+	++	++	+	++	++	+	++	8	0
75% weight-based dose (no anti-Xa levels)	++	+	++	++	++	+	++	++	8	0
Delivery management										
Induction of labor	+	++	++	++	++	++	++	++	8	0
Spontaneous labor	+	+	++	-	-	--	-	+	4	4
Thrombophilia testing										
Offer testing	-	++	-	++	++	+	+	+	6	2

Legend: ++ very appropriate; + somewhat appropriate; - somewhat inappropriate; - - very inappropriate; ? I do not know  
LMWH: Low-molecular-weight heparin

**Table 2.** Level of appropriateness per participant for each chosen recommendation in Vignette 2

	Participant number								Number of appropriate (+ or ++), n	Number of inappropriate (- or - -), n
	1	2	3	4	5	6	7	8		
Treatment of symptomatic SVT (4 cm away from the SFJ)										
Continue NSAIDS	-	--	++	-	+	++	+	++	5	3
Prophylactic LMWH	-	++	++	-	++	++	+	++	6	2
Intermediate LMWH	++	++	++	++	++	++	-	+	7	1
Therapeutic LMWH	+	+	++	++	++	-	-	+	6	2
Fondaparinux 2.5 mg	++	++	++	++	++	++	++	++	8	0
Prophylactic DOAC	-	++	++	+	+	++	++	++	7	1
Intermediate DOAC	++	++	++	++	+	++	++	+	8	0
Treatment of symptomatic SVT (1 cm away from the SFJ)										
Prophylactic LMWH	-	-	-	--	++	--	-	+	2	6
Intermediate LMWH	++	+	-	+	++	-	+	++	6	2
Therapeutic LMWH	+	++	++	++	++	++	++	++	8	0
Fondaparinux 2.5 mg	++	-	-	++	++	--	+	+	5	3
Intermediate DOAC	++	+	-	++	++	-	++	++	6	2
Therapeutic DOAC	-	++	++	--	++	++	++	++	6	2

Legend: ++ very appropriate; + somewhat appropriate; - somewhat inappropriate; - - very inappropriate; ? I do not know  
SVT: Superficial venous thrombosis; SFJ: Saphenofemoral junction; NSAIDS: Non-steroidal anti-inflammatories; LMWH: Low-molecular-weight heparin; DOAC: Direct oral anticoagulants. Please see questionnaire details for anticoagulant dosing

**Table 3.** Level of appropriateness per participant for each chosen recommendation in Vignette 3

[illegible]



No anticoagulation	++	+	++	+	+	-	--	++	6	2
Prophylactic LMWH	--	++	+	+	++	+	-	++	6	2
Intermediate LMWH	--	+	++	+	++	++	+	-	6	2
Therapeutic LMWH	--	+	++	+	++	++	++	--	6	2
Therap LMWH for 1-2 weeks then Proph LMWH	--	+	++	+	++	++	+	--	6	2
LMWH transition to VKA (no delay)	--	+	++	--	++	++	++	--	5	3
LMWH for 1-2 weeks then transition to VKA	--	+	++	--	++	++	++	--	5	3
<b>Asymptomatic PVT in a patient with cirrhosis and a platelet count &lt;30</b>										
No anticoagulation	++	++	++	+	+	++	++	++	8	0
Prophylactic LMWH	--	-	++	+	++	++	-	-	4	4
<b>Asymptomatic PVT in a patient without cirrhosis and a normal platelet count<sup>c</sup></b>										
No anticoagulation	++	--	-	+	+	-	--	+	4	4
Prophylactic LMWH	--	-	+	++	++	-	-	++	4	4
Intermediate LMWH	--	-	++	++	++	+	-	++	5	3
Therapeutic LMWH	--	++	++	++	++	++	+	++	7	1
Therap LMWH for 1-2 wks then Proph LMWH	--	++	++	++	++	++	-	++	6	2
LMWH transition to VKA (no delay)	--	++	++	+	++	++	++	++	7	1
LMWH for 1-2 wks then transition to VKA	--	++	++	+	++	++	+	++	7	1
Therap LMWH for 1-2 weeks then DOAC	--	-	++	++	++	++	--	++	5	3
Intermediate LMWH for 1-2 wks then DOAC	--	-	++	++	++	+	--	++	5	3
DOAC	--	-	++	++	+	+	--	++	5	3

Legend: ++ very appropriate; + somewhat appropriate; - somewhat inappropriate; -- very inappropriate; ? I do not know  
PVT: Portal vein thrombosis; LMWH: Low-molecular-weight heparin; Proph: Prophylactic-dose; Therap: Therapeutic-dose;  
Wks: Weeks; VKA: Vitamin K antagonist; DOAC: Direct oral anticoagulant

**Table 4.** Level of appropriateness per participant for each chosen recommendation in Vignette 4

	Participant number								Number of appropriate (+ or ++), n	Number of inappropriate (- or - -), n
	1	2	3	4	5	6	7	8		
2 early losses and low-titre anti-B2GP1										
No treatment	++	++	+	++	++	+	++	+	8	0
ASA	-	++	++	-	++	+	-	++	5	3
LMWH/ASA	--	+	++	+	++	+	--	++	6	2
3 early losses and low-titre anti-B2GP1										
No treatment	-	++	-	++	++	+	-	-	4	4
ASA	+	++	++	-	++	+	+	++	7	1
LMWH/ASA	+	+	++	+	++	+	-	++	7	1
1 late loss and low-titre anti-B2GP1										
No treatment	-	++	+	+	++	-	-	+	5	3
ASA	+	++	++	-	++	+	+	++	7	1
LMWH/ASA	+	+	++	++	++	++	-	++	7	1
2 early losses and high-titre anti-B2GP1										
No treatment	+	++	+	+	++	-	-	-	5	3
ASA	+	++	++	--	++	+	++	++	7	1
LMWH/ASA	-	+	++	+	++	++	+	++	7	1
2 early losses and high-titre ACA										
No treatment	+	++	+	+	++	-	-	+	6	2
ASA	+	++	++	--	++	+	++	++	7	1
LMWH/ASA	-	+	++	++	++	++	+	++	7	1

Legend: ++ very appropriate; + somewhat appropriate; - somewhat inappropriate; - - very inappropriate; ? I do not know

Losses: Pregnancy losses, early defined as <10 weeks gestation; anti-B2GP1: Anti-beta-2 glycoprotein 1 antibody; ASA: Aspirin;

LMWH/ASA: Prophylactic-dose low-molecular-weight heparin and aspirin; ACA: anti-cardiolipin antibody

**Table 5.** Level of appropriateness per participant for each chosen recommendation in Vignette 5

	Participant number								Number of appropriate (+ or ++), n	Number of inappropriate (- or - -), n
	1	2	3	4	5	6	7	8		
DVT treatment in a patient with ET										
Therapeutic LMWH	-	++	++	+	+	++	+	++	7	1
LMWH transition to VKA	++	++	++	++	++	++	++	++	8	0
LMWH for 1-2 wks then a DOAC	-	+	+	+	+	+	+	++	7	1
DOAC	++	+	+	++	+	+	++	++	8	0
Long-term anticoagulation <sup>a</sup>										
Continue anticoagulation	++	+	++	+	++	++	++	++	8	0
Secondary VTE prevention in a future pregnancy										
Prophylactic LMWH	-	-	++	++	-	+	+	++	5	3
Prophylactic LMWH until 20 wks then BID	++	++	++	+	++	++	++	++	8	0
Intermediate LMWH	-	++	++	-	++	++	+	++	6	2
Therapeutic LMWH	-	+	++	-	++	+	- -	++	5	3

Legend: ++ very appropriate; + somewhat appropriate; - somewhat inappropriate; -- very inappropriate; ? I do not know

DVT: Deep vein thrombosis; ET: Essential thrombocythemia; VTE: Venous thromboembolism; wks: Weeks gestation; BID: twice daily

## 8. VITA

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### EDUCATION:

**Bachelor of Science Honors with Distinction, Life Sciences**  
Queen's University, Kingston, Ontario, Canada; 2003-2007

**Doctor of Medicine**  
University of Calgary, Calgary, Alberta, Canada; 2007-2010

**Internal Medicine Residency**  
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**Hematology Residency**  
University of Calgary, Calgary, Alberta, Canada; 2013-2015

**Thrombosis Medicine Fellowship**  
University of Ottawa, Ottawa, Ontario, Canada; 2015-2017

**Master of Health Professions Education**  
University of Illinois at Chicago (UIC) Chicago, Illinois, USA; 2015-Present

**Clinical Assistant Professor**  
University of Calgary; Calgary, Alberta, Canada; 2018-Present

### TEACHING:

Clinical core preceptor, Hematology undergraduate course; 2018-Present

Small group preceptor, Hematology undergraduate course, 2018-Present

### INVITED PRESENTATIONS:

**Understanding practice variation in areas of clinical uncertainty:  
Lessons learned from Ottawa thrombosis specialists**  
Hematology Grand Rounds, Ottawa Blood Disease Centre  
University of Ottawa, Ottawa, Ontario; February 2019

**Venous thromboembolism, anticoagulation and its reversal**  
Highlights of American Society of Hematology  
Chicago, IL and San Francisco, CA; February 2019

**Management of high-risk acquired thrombophilias**

American Society of Hematology Education Program,  
San Diego, CA; December 2018

**A clinical trial in obstetrical antiphospholipid syndrome:****Understanding the patient perspective**

CanVECTOR Research Conference  
Montreal, Quebec; October 2018

**Women's Health and Thrombosis**

Facilitator, Round Table session, Thrombosis Canada Conference  
Montreal, Quebec; October 2018

**Thrombophilia and pregnancy complications: What is the role of low-molecular-weight heparin?**

International VTE Conference  
Dublin, Ireland; September 2018

**Diagnosis and treatment of PE in pregnancy**

Master Class, International Society of Thrombosis and Hemostasis  
Dublin, Ireland; July 2018

**Diagnosing PE in Pregnancy: Consensus and Controversies**

Emergency Medicine Hodsman Lecture series  
University of Calgary, Calgary, Alberta, Canada; May 2018

**CanVECTOR mentorship program and research training curriculum**

CanVECTOR Research Conference  
Ottawa, Canada; February 2017

**Exploring the concept of a minimal clinically important difference among women with antiphospholipid syndrome: Introduction to a mixed-methods study**

Foundation of Women and Girls with Blood Disorders Conference  
Columbus, Ohio; September 2016

**Antiphospholipid syndrome and pregnancy complications**

World Thrombosis Day Conference  
Ottawa, Canada; October 2016

**AWARDS:****2016**

**American Society of Hematology Abstract Achievement Award**  
American Society of Hematology

<b>2016</b>	<b>Phil Wells Research Trainee Award</b> Division of Hematology, University of Ottawa
<b>2015</b>	<b>Helios Scholarship Award</b> Postgraduate Medical Education, University of Calgary
<b>2015-2017</b>	<b>Thrombosis Canada CanVECTOR Research Fellowship Award</b> Thrombosis Canada and CanVECTOR Research Network
<b>2015-2017</b>	<b>Postgraduate Fellowship Award</b> Department of Medicine, University of Ottawa
<b>2014</b>	<b>American Society of Hematology Abstract Achievement Award</b> American Society of Hematology
<b>2014</b>	<b>Hematology Course Bronze Teaching Award</b> Undergraduate Hematology Course, University of Calgary
<b>2013</b>	<b>Mannucci Prize: Young Investigator Award</b> Journal of Thrombosis & Haemostasis
<b>2013</b>	<b>The Dr. Aneez Mohamed &amp; Ms. Channele Morgan Chief Resident Award</b> Internal Medicine Residency Training Program, Western University
<b>2013</b>	<b>The David Meltzer Postgraduate Award in Hematology</b> Division of Hematology, Western University
<b>2012</b>	<b>Program Director Award of Merit</b> Internal Medicine Residency Training Program, Western University
<b>2012</b>	<b>Resident Research Day Award</b> Department of Medicine, Western University
<b>2011</b>	<b>American Society of Hematology Abstract Achievement Award</b> American Society of Hematology
<b>2011</b>	<b>Canadian Hematology Society Abstract Award</b> Canadian Hematology Society
<b>2009</b>	<b>Charles E. Frosst Research Award</b> Department of Medicine, University of Calgary

## HONORS:

- 2016**      **DIME Medical Education Fellowship**  
 Department of Innovation in Medical Education, University of Ottawa
- 2016**      **Top Abstract in Women's Health Issues in Thrombosis and Haemostasis**  
 ISTH's Scientific and Standardization Committee (SSC) Conference

## PROFESSIONAL MEMBERSHIPS:

Alberta Medical Association  
 Royal College of Physicians and Surgeons of Canada  
 International Society on Thrombosis and Haemostasis  
 American Society of Hematology  
 Thrombosis Canada  
 Canadian Hematology Society  
 Hemostasis and Thrombosis Research Society  
 CanVECTOR Thrombosis Research Network  
 Foundation for Women and Girls with Blood Disorders  
 Libin Cardiovascular Institute  
 O'Brien Institute of Public Health

## ABSTRACTS:

**Peer-Reviewed Oral Abstracts**

**Skeith L**, Ridinger H, Srinivasan S, Givi B, Youssef N, Harris I. Exploring the thesis experience of Master of Health Professions Education students: A qualitative study. *2017 UIC MHPE Summer Conference, Chicago, Illinois*

Gauthier K, **Skeith L**, Noghani P, Forster A, Rodger MA. Venous thromboembolism prophylaxis in the postpartum period, a before and after study. *2016 Department of Medicine Research Day, University of Ottawa, Ottawa.*

**Skeith L**, Carrier M, Kaaja R, Martinelli I, Petroff D, Schleussner E, Laskin CA, Rodger MA. A meta-analysis of low-molecular-weight heparin to prevent pregnancy loss in women with thrombophilia. *SSC 2016 International Society on Thrombosis and Haemostasis, Montpellier, France*

**Skeith L**, Taylor J, Lazo-Langner A, Kovacs MJ. Conservative peri-procedural anticoagulation management in patients with venous thromboembolic disease results in a low proportion of thrombosis and bleeding. *2011 American Society of Hematology Conference, San Diego, CA (Oral)*

## Peer-Reviewed Poster Abstracts

**Skeith L**, Taylor TS, Bates SM, Duffett L, Silver RM, Rodger MA. Engaging patients in clinical trial planning: Exploring the concept of a minimal clinically important difference among patients with obstetrical antiphospholipid syndrome. *2018 American Society of Hematology, San Diego, CA.*

**Skeith L**, Rodger MA, Bates SM, Gonsalves G, Taylor TS. “Part of the ritual”: A qualitative study of patient and physician perspectives on the use of anticoagulation for improving pregnancy outcomes in obstetrical antiphospholipid syndrome. *2018 American Society of Hematology, San Diego, CA.*

**Skeith L**, Rodger MA, Bates SM, Gonsalves G, Taylor TS. “Part of the ritual”: A qualitative study of patient and physician perspectives on the use of anticoagulation for improving pregnancy outcomes in obstetrical antiphospholipid syndrome. *2018 CanVECTOR Research Conference, Montreal, Quebec*

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**Skeith L**, Carrier M, Le Gal G, Shivakumar S, Langlois N, Harris I, Gonsalves C. Development of a national research training program in Thrombosis Medicine: A targeted needs assessment to guide curriculum development. *2017 International Conference on Residency Education, Quebec City, QC*

**Skeith L**, Ridinger H, Srinivasan S, Givi B, Youssef N, Harris I. Exploring the thesis experience of Master of Health Professions Education students: A qualitative study. *2017 International Conference on Residency Education, Quebec City, QC*

**Skeith L**, Gonsalves C. A window into the factors influencing practice variation in Thrombosis Medicine: A qualitative content analysis of published practice-pattern surveys. *2017 UIC MHPE Summer Conference, Chicago, Illinois*

**Skeith L**. Does clinical practice variation among experts threaten validity of learner assessments in specialty training programs? *2017 UIC MHPE Summer Conference, Chicago, Illinois*

Hews-Girard J, **Skeith L**, Rydz N. Management of a pregnant patient with antithrombin deficiency and acute venous thromboembolism. *2017 International Society on Thrombosis and Haemostasis. Berlin, Germany*

**Skeith L**, Taylor TS, Bates SM, Silver RM, Rodger MA. Planning the APPLE (AntiPhosPholipid syndrome Low-molecular-weight heparin pregnancy loss Evaluation) clinical



trial: An international survey of physicians. *2017 Women's Health Issues in Thrombosis and Haemostasis, Barcelona, Spain*

**Skeith L**, Carrier M, Robinson S, Aliman Samah, Rodger MA. The risk of venous thromboembolism in pregnant women with essential thrombocythemia: A systematic review and meta-analysis. *2016 American Society of Hematology, San Diego, CA*

**Skeith L**, Carrier M, Kaaja R, Martinelli I, Petroff D, Schleussner E, Laskin CA, Rodger MA. A meta-analysis of low-molecular-weight heparin to prevent pregnancy loss in women with thrombophilia. *SSC 2016 International Society on Thrombosis and Haemostasis, Montpellier, France*

**Skeith L**, Rydz N, Goodyear D, O'Beirne M, Poon M-C. A single-centre pilot study investigating the rate of pregnancy loss in women with von Willebrand disease. *2014 American Society of Hematology, San Francisco, CA*

**Skeith L**, Goodyear D, Rydz N, O'Beirne M, Poon M-C. Epidural analgesia use in women with von Willebrand disease: A cross-sectional single-centre study. *2014 American Society of Hematology, San Francisco, CA*

**Skeith L**, Lazo-Langner A, Kovacs MJ. The equipoise of perioperative anticoagulation management: a Canadian cross-sectional survey. *2013 Department of Medicine Resident Research Day, London, ON*

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**Skeith, L**, Taylor J, Lazo-Langner A, Kovacs MJ. Conservative perioperative anticoagulation management results in a low proportion of thrombosis and bleeding. *2012 Department of Medicine Resident Research Day, London, ON*

**Skeith L**, Jackson SC, Brooks J, Poon M-C. A Retrospective evaluation of baseline joint hypermobility as a risk factor for arthropathy in moderate and severe hemophilia. *2009 First Annual University of Calgary Leaders in Medicine Research Symposium, Calgary, AB*

**Skeith L**, Jackson SC, Brooks J, Poon M-C. Hypermobility and arthropathy in hemophilia: A retrospective evaluation of joint hypermobility as a risk factor for arthropathy in severe and moderate hemophilia. *2009 XXII Congress of the International Society on Thrombosis and Haemostasis (ISTH), Boston, MA.*

**Skeith L**, Lomax AE. Undergraduate thesis: Using a novel *in vivo* technique to examine neural regulation of submucosal arterioles in a model of inflammatory bowel disease. *2007 Queen's University Life Sciences symposium, Kingston, ON*

## PUBLICATIONS:

**Skeith L.** Anticoagulating patients with high-risk acquired thrombophilias. *Blood* 2018;132:2219-2229.

**Skeith L.** Anticoagulating patients with high-risk acquired thrombophilias. *Hematology Am Soc Hematol Educ Program* 2018;1:439-449.

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**Skeith L, Ridinger H, Srinivasan S, Givi B, Youssef N, Harris I.** Exploring the thesis experience of Master of health professions education graduates: A qualitative study. *Int J Med Educ* 2018; 9:113-121.

**Skeith L, Abou-Nassar, KE, Walker M, Ramsay T, Booth R, Wu Wen S, Smith GN, Rodger MA.** Are anti- $\beta$ 2 glycoprotein 1 antibodies associated with placenta-mediated pregnancy complications? A nested case-control study. *Am J Perinatol* 2018;35:1093-1099.

**Skeith L, Carrier M, Shivakumar S, Langlois N, Le Gal G, Harris I, Gonsalves C.** Guiding curriculum development of a national research training program in thrombosis medicine: A needs assessment involving faculty and trainees. *Thromb Res* 2018;162:79-86.

Bannow BTS, **Skeith L.** Diagnosis and management of postpartum ovarian vein thrombosis. *Hematology Am Soc Hematol Educ Program* 2017;2017:168-171.

**Skeith L.** Preventing venous thromboembolism during pregnancy and postpartum: crossing the threshold. *Hematology Am Soc Hematol Educ Program* 2017;2017:160-167.

**Skeith L, Mohamed M, Karovitch A, Liddy C, Afkham A, Archibald D, Keely E.** The use of eConsults to improve access to specialty care in thrombosis medicine. *Thromb Res* 2017;160:105-108.

**Skeith L, Gonsalves C.** Identifying the factors influencing practice variation in thrombosis medicine: A qualitative content analysis of published practice-pattern surveys. *Thromb Res* 2017;159:52-57.

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**Skeith L, Rodger MA.** Pulmonary complications of pregnancy: Venous thromboembolism.

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