

ORIGINAL ARTICLE

Venous thromboembolism prevention in cancer care: implementation strategies to address underuse

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Abstract

Background: Evidenced-based interventions have been developed to prevent venous thromboembolism (VTE) in ambulatory patients with cancer, including VTE-risk assessment for all patients and targeted primary thromboprophylaxis for high-risk patients. Despite supportive evidence and recommendations, oncologists rarely assess VTE risk or provide primary prophylaxis. Our previous work identified barriers and facilitators to using VTE prevention interventions in oncology practice.

Objectives: To identify potential strategies that address the identified barriers and leverage facilitators to achieve successful implementation of evidence-based interventions for VTE prevention in oncology practice.

Methods: We used the Implementation Research Logic Model, an implementation science framework, to map the relationships among barriers and facilitators, feasible and effective implementation strategies, and implementation and clinical outcomes that will be used to evaluate the implementation strategies.

Results: We identified 12 discrete implementation strategies (eg, conducting clinician education and training and staged implementation scale-up) that address barriers and leverage facilitators through their mechanisms of action (eg, increased clinician awareness of evidence and targeting the highest effectiveness). We identified key implementation (eg, penetration, adoption, acceptability, fidelity, appropriateness, and sustainability), system (eg, integration of VTE-risk assessment into clinical workflow), and clinical (eg, lower VTE rates) outcomes targeted by the selected strategies.

Conclusion: Using the Implementation Research Logic Model framework and building on our knowledge of barriers and facilitators, we identified implementation strategies and important outcomes to evaluate these strategies. We will use these results to test and measure the strategies to improve the uptake of evidence-based recommendations for VTE prevention in oncology practice.

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KEYWORDS

evidence-based practice, implementation science, neoplasms, risk assessment, venous thromboembolism

Essentials

- Interventions to prevent venous thromboembolism are underused in oncology practice.
- We used implementation research to address barriers and facilitators contributing to underuse.
- We identified implementation strategies and important outcomes to evaluate these strategies.
- This knowledge helps inform the broader implementation of venous thromboembolism prevention in oncology practice.

1 | INTRODUCTION

Venous thromboembolism (VTE), including pulmonary embolism and deep vein thrombosis, is a common complication for patients with cancer. Of an estimated 900,000 VTE diagnosed annually in the US, approximately 20% occur in patients with cancer. Cancer-associated VTE causes increased morbidity and mortality [1,2]. Evidenced-based interventions, including VTE risk assessment with validated clinical scoring systems (such as the Khorana Score [3]) and targeted primary thromboprophylaxis for high-risk patients [4,5], have been developed to prevent cancer-associated thrombosis. Expert guidelines, including those from the American Society of Clinical Oncology, the National Comprehensive Cancer Network, the International Initiative on Thrombosis and Cancer, and the American Society of Hematology, endorse these interventions for VTE prevention in ambulatory oncology patients [6–9].

However, despite evidence and guidelines that have existed for years, oncologists do not regularly use VTE risk assessment or primary prophylaxis. Our prior study showed that at a tertiary National Cancer Institute-designated Cancer Center, 90% of responding oncology clinicians never or rarely used VTE risk assessment, and among patients with cancer at high risk of VTE, none received primary prophylaxis [10–12]. We also used qualitative methods to identify clinician, patient, and system barriers to and potential facilitators of following evidence-based interventions for VTE prevention in clinical oncology practices in a tertiary care center and community-based practices [13]. We found that both clinicians and patients placed value on preventing VTE, and clinicians wanted to increase the use of evidence-based recommendations to facilitate VTE prevention. Barriers included a lack of knowledge and limited familiarity with evidence and recommendations to support VTE prevention, resource limitations, and relative priority compared with active cancer treatment [13]. In addition, stakeholder participants in the qualitative study offered initial suggestions (eg, presentation of VTE information early on in the course of illness, but not at the first visit, and creation of decision support tools and patient education handouts) that may assist in integrating VTE prevention into clinical practice.

In this study, in order to bridge the gap between guideline recommendations for VTE prevention interventions and their use in

oncology practice, we used implementation science frameworks to select strategies to systematically address the barriers and leverage facilitators previously identified by stakeholder participants [14]. Implementation science provides methodology designed to facilitate broader and consistent uptake of evidence-based interventions found to be effective in clinical studies. The field was designed in response to findings that clinical practice guidelines alone have little impact in changing physician behavior or increasing adherence to evidence-based practice. An important part of implementation science is guiding the identification of relevant strategies chosen to address identified barriers and build on existing facilitators that are appropriate to the clinical setting. Studies have shown that the use of implementation frameworks, both at the planning and implementation stages, ensures that essential implementation strategies are included to improve the outcomes of the study and enhance the interpretability and generalizability of study findings [15].

The Implementation Research Logic Model (IRLM) can be used to guide the design and evaluation of the implementation of evidence-based intervention by mapping the interconnections between the barriers and facilitators to the intervention to strategies that can address the barriers and facilitators through their mechanisms of action, and implementation and effectiveness outcomes [16]. It combines several commonly used implementation research frameworks, including (1) the Consolidated Framework for Implementation Research (CFIR) to guide the identification of barriers and facilitators that influence the implementation of an evidence-based intervention (Supplementary Table) [17] and (2) Proctor and colleagues' [18] taxonomy of implementation outcomes, which measure the success of the strategies in getting the evidence-based intervention into clinical practice and outcomes at the system and patient levels.

In the current study, our objective was to identify potential strategies to implement guideline-recommended evidence-based interventions for VTE prevention in clinical oncology practice. We used the IRLM as an organizing framework that allowed us to identify implementation strategies based on our previously identified barriers and facilitators, as well as to link the strategies to targeted clinical and implementation outcomes that will evaluate the success of the implementation strategies.

2 | METHODS

Guided by the IRLM framework, we mapped and interpreted data [19]. First, we defined the evidence-based intervention as VTE risk assessment for all patients with cancer starting systemic therapy and targeted primary prophylaxis for high-risk patients. Next, we performed a secondary analysis of previously collected qualitative data identifying barriers and facilitators to using evidence-based interventions for VTE prevention in oncology practice [13]. More detailed methods of the qualitative study, which was approved by the Institutional Review Board of Northwestern University, have been published previously [13]. Briefly, we conducted focus groups and semistructured interviews of 18 oncology clinicians (including 9 academic physicians, 6 oncologists at community-based affiliate practices, and 3 advanced practice providers [nurse practitioners and physician assistants]) and 11 oncology patients with a VTE diagnosis. Clinician and patient participants were from a single health care system and signed informed consent. Interviews were transcribed and analyzed independently by 2 study team members (K.A.M. and M.J.L.) who assigned codes (ie, words or short phrases to represent ideas/topics identified in the transcripts) to the transcripts. For this secondary analysis, we mapped these previously identified codes to the CFIR (version 1.0) domains of actors (ie, oncology clinicians and patients), intervention characteristics (VTE risk assessment and targeted primary prophylaxis), inner setting (clinic), and outer setting [17]. After organizing the codes into CFIR domains, we reviewed the quotes

associated with each code to ensure that they were accurately mapped to the designated CFIR domains. Mapping results were presented to the larger research team for feedback, critique, and final domain mapping. The research team was composed of a hematologist (K.A.M.), a qualitative analyst (M.J.L.), a communication science and qualitative methods expert (K.A.C.), 2 internists who have expertise in behavioral interventions (J.A.L. and M.J.O.), and a physician implementation scientist (L.R.H.). Next, using a compilation of effective strategies developed by expert implementation scientists, we mapped barriers to strategies identified as effective in addressing the specific barriers [20]. Finally, we identified implementation outcomes that would evaluate the success of the selected implementation strategies from a published taxonomy of implementation outcomes from Proctor et al. [18]. We followed the Standards for Reporting Implementation Studies in our reporting of this study [21].

3 | RESULTS

3.1 | Barriers and facilitators grouped to Consolidated Framework for Implementation Research domains

We grouped the previously identified transcript codes, representing barriers and facilitators, into 4 CFIR domains (Figure B). In the individual actors (both clinicians and patients) domain, clinicians' lack of

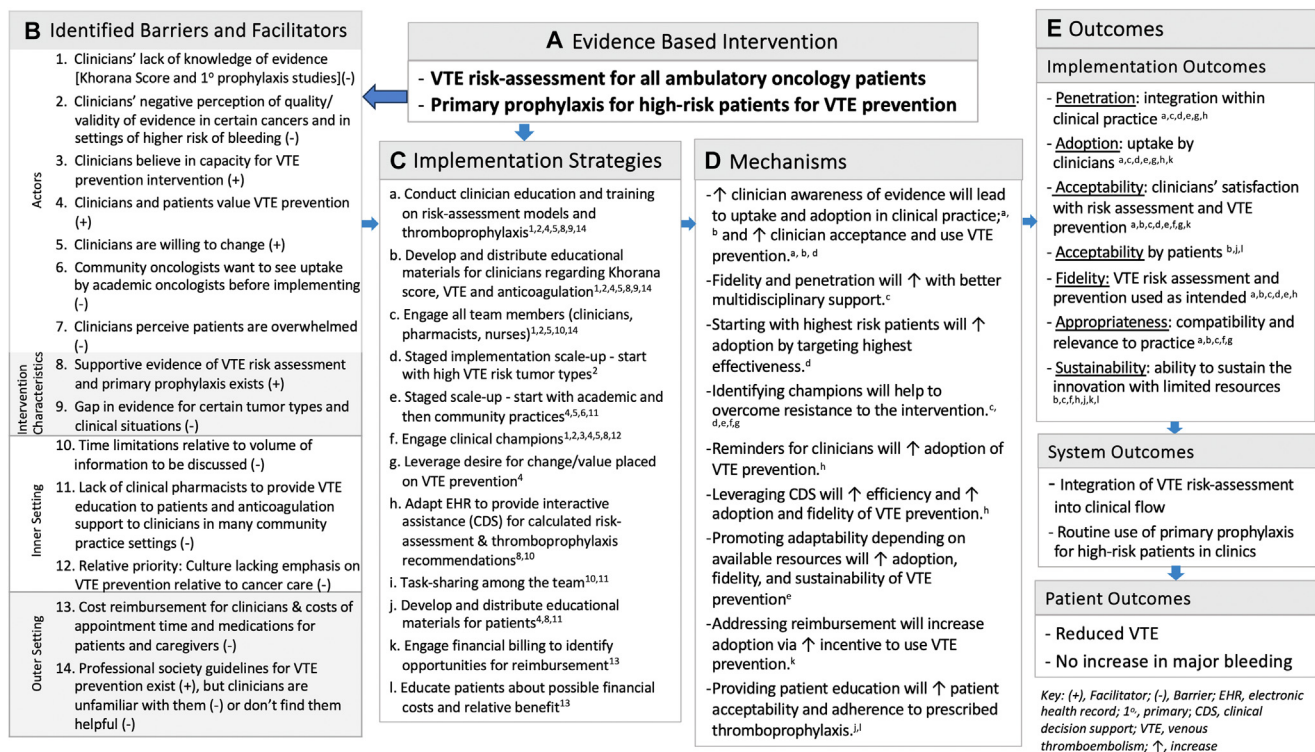


FIGURE Implementation Research Logic Model (IRLM) applied to evidence-based interventions for venous thromboembolism (VTE) prevention in ambulatory oncology practice. The framework identifies selected strategies to address contextual factors and facilitates targeted outcomes.

knowledge and familiarity with the data behind the evidence-based intervention were prominent barrier. Furthermore, some clinicians had a negative perception of the quality of the evidence for patients with certain cancers (specifically, lymphoma and nonovarian gynecologic malignancy) and thought they might have different VTE risks than the risk assessment tool indicates. Clinicians also perceived that using primary prophylaxis could be challenging and risky for patients with a higher risk of bleeding. Community clinicians noted the desire to see the uptake of the intervention by academic practices prior to implementing it in their clinics. An important facilitator identified was that clinicians endorsed high self-efficacy in performing both risk assessment and prescribing anticoagulation prophylaxis. Both patients and clinicians placed a high value on VTE prevention, with patients placing value on learning about VTE risk with cancer, although clinicians perceived that patients are overwhelmed with cancer-related information and may not have the capacity to hear about VTE risk as well.

Regarding *intervention characteristics*, a facilitator identified the existence of supportive evidence of both components of VTE-risk assessment and primary prophylaxis. An identified barrier was the gap in evidence regarding the safety of thromboprophylaxis in clinical situations associated with an increased risk of bleeding, such as with certain tumor types or thrombocytopenia induced by chemotherapy.

In the *inner setting* domain, barriers identified included time limitations relative to the volume of information to be delivered to patients in the clinic, the lack of pharmacists to carry out parts of the evidence-based intervention in certain practice settings, and the lack of priority placed on VTE prevention relative to cancer and cancer-management.

Finally, in the *outer setting* domain, a barrier identified included costs, both related to clinician reimbursement for performing the evidence-based intervention and costs to patients for medications and appointment time. Professional society guidelines supporting the evidence-based intervention were considered a facilitator in the outer setting; however, this was tempered by the barriers noted earlier that clinicians were unfamiliar with the guidelines.

3.2 | Relevant strategy components, mechanisms, and outcomes

Following the IRLM approach, 12 discrete implementation strategies were selected to address the identified barriers and facilitators through distinct mechanisms of action (Table 1 and Figure C, D). Notably, a given strategy may address more than one barrier and/or facilitator. For example, the strategy of “Conduct clinician education and training on risk assessment models and anticoagulation thromboprophylaxis” addresses barriers of the lack of knowledge of the evidence and negative perception of the validity for certain tumor types while simultaneously leveraging the facilitator of professional society guidelines that support the evidence-based intervention. The strategy of “Engaging all team members” leverages clinicians’ willingness to change and the importance placed on the intervention while

addressing the lack of knowledge of the evidence and time limitations for oncology clinicians. Notably, strategies target both patients and clinicians. Education and distribution of educational materials target both patients (education about VTE) and clinicians (education about data/evidence for the evidence-based intervention). Educating patients about costs and relative benefit addresses concerns related to patient costs, whereas engaging financial billing to identify opportunities for clinician reimbursement addresses clinician concerns about reimbursement and time costs.

We also described the distinct mechanisms of action through which the strategies work to change the context or behavior and influence the desired outcomes (Figure D). For example, the strategy of “conducting clinician education and training” works by (1) increasing clinician awareness of evidence and data behind the intervention, leading to an uptake in penetration and adoption of the evidence-based interventions in clinical practice, and (2) increasing clinician acceptance and use of the innovation. “Engaging clinical champions” helps to overcome resistance to evidence-based intervention. “Conducting patient education” works by increasing the acceptability of the intervention to patients and increasing adherence to prescribed thromboprophylaxis.

The implementation outcomes identified as necessary to evaluate the work to increase uptake of the VTE prevention intervention through strategies were as follows: (1) *penetration* (number of targeted clinic settings that are reached by the intervention), (2) *adoption* (uptake and use of the intervention by clinicians), (3) *acceptability* (satisfaction of clinicians and patients), (4) *fidelity* (intervention is used as intended), (5) *appropriateness* (compatibility and relevance to ambulatory oncology practice), and (6) *sustainability* (use of the intervention is maintained in ambulatory oncology practice) (Table 2 [18] and Figure E). We also identified selected metrics and measures of implementation outcomes, as shown in Table 2. In addition to implementation outcomes, we identified system-based outcomes, including integration of VTE-risk assessment into the clinical flow and routine use of primary prophylaxis for high-risk patients in clinics, as important to evaluate the success of the chosen implementation strategies to increase sustainability through integration and use. Finally, lower VTE rates were identified as the critical patient outcome to measure the implementation of VTE prevention for patients with cancer without an increase in major bleeding.

4 | DISCUSSION

Using an implementation science framework to guide the next step from identifying barriers and facilitators to action, we identified targeted strategies to increase the use of evidence-based interventions for VTE prevention in ambulatory oncology practice. Guided by the IRLM, we built on barriers and facilitators directly identified by stakeholders (namely, oncology clinicians and patients) to identify potential implementation strategies that address these factors through distinct mechanisms. The framework also supported the identification of outcomes beyond the effectiveness of VTE

TABLE 1 Identified strategies for implementing evidence-based interventions for venous thromboembolism prevention in oncology practice.

| Selected barriers/facilitators addressed | Identified strategy |
|--|--|
| <ul style="list-style-type: none"> - Clinicians' lack of knowledge of evidence (Khorana Score) and primary prophylaxis studies (-) - Clinicians' negative perception of quality and validity of evidence in certain cancers and in settings of higher risk of bleeding (-) - Clinicians are willing to change (+) - Supportive evidence of VTE risk assessment and primary prophylaxis (+) | <ul style="list-style-type: none"> - Conduct clinician education and training on risk assessment models and anticoagulation thromboprophylaxis |
| <ul style="list-style-type: none"> - Clinicians' lack of knowledge of evidence (Khorana Score) and primary prophylaxis studies (-) - Professional society guidelines for VTE prevention exist (+) but clinicians are unfamiliar with them (-) or don't find them helpful (-) | <ul style="list-style-type: none"> - Develop and distribute educational materials for clinicians regarding the Khorana score, VTE, and anticoagulation |
| <ul style="list-style-type: none"> - Clinicians are willing to change (+) - Supportive evidence of VTE risk assessment and primary prophylaxis (+) - Time limitations relative to the volume of information to be discussed | <ul style="list-style-type: none"> - Engage all team members (clinicians, pharmacists, nurses, etc.) |
| <ul style="list-style-type: none"> - Clinicians have a negative perception of the quality and validity of evidence in certain cancers or in settings of higher risk of bleeding (-) | <ul style="list-style-type: none"> - Staged implementation scale-up: start with high VTE-risk tumor types |
| <ul style="list-style-type: none"> - Community oncologists want to see uptake by academic oncologists before implementing in their setting (-) | <ul style="list-style-type: none"> - Staged implementation scale-up: start with academic and then community practices |
| <ul style="list-style-type: none"> - Clinicians are willing to change (+) - Clinicians believe in their capabilities to perform the VTE prevention intervention (+) - Clinicians place importance on preventing VTE (+) | <ul style="list-style-type: none"> - Engage clinical champions |
| <ul style="list-style-type: none"> - Clinicians and patients place importance on preventing VTE (+) | <ul style="list-style-type: none"> - Leverage the desire for change/value placed on VTE prevention |
| <ul style="list-style-type: none"> - Time limitations relative to the volume of information to be discussed (-) | <ul style="list-style-type: none"> - Adapt EHR to provide interactive assistance (such as clinician-decision support) for calculated risk assessment and thromboprophylaxis recommendations |
| <ul style="list-style-type: none"> - Time limitations relative to the volume of information to be discussed (-) | <ul style="list-style-type: none"> - Task sharing among the team |
| <ul style="list-style-type: none"> - Patients place importance on preventing VTE (+) | <ul style="list-style-type: none"> - Develop and distribute educational materials for patients |
| <ul style="list-style-type: none"> - Cost reimbursement for clinicians (-) | <ul style="list-style-type: none"> - Engage financial billing to identify opportunities for reimbursement |
| <ul style="list-style-type: none"> - Costs, including the expense of appointment time and medications, and for patients and caregivers (-) | <ul style="list-style-type: none"> - Educate patients about possible financial costs and relative benefit |

(-), barrier; (+), facilitator; EHR, electronic health record; VTE, venous thromboembolism.

prevention to include implementation and system outcomes achievable through the use of the strategies. Given the known challenges in moving evidence-based recommendations into clinical practice [23,24] and those emerging from dedicated work specifically in this area [13,14], intentional, directed development of comprehensive implementation strategies is essential to closing this gap. Using this implementation framework, we show multilevel strategies that are critical to addressing the contextual barriers to using evidence-based

interventions for VTE prevention in the oncology setting. This process demonstrates important insights into using implementation research to generate generalizable knowledge to inform the broader, context-adapted implementation of VTE prevention in oncology practice.

Currently, few studies have addressed the gap between guideline recommendations and the lack of evidence-based interventions used for VTE prevention in oncology practice [14]. The University of Vermont implemented a successful quality-improvement initiative to

TABLE 2 Targeted implementation outcomes for venous thromboembolism prevention interventions in oncology practice.^a

| Implementation outcome | Selected metrics | Selected measures |
|------------------------|--|---|
| Penetration | Is the implementation strategy integrated within the practice setting? | <ul style="list-style-type: none"> Percentage of new patients who were screened using the implementation strategies, eg, percentage of new patients for whom the Khorana Score is calculated |
| Adoption | Did clinicians use/deliver the intervention? Did patients get VTE education? | <ul style="list-style-type: none"> Percentage of clinicians who document discussion of VTE risk Percentage of high-risk patients for whom prophylaxis is prescribed Patient knowledge of VTE |
| Acceptability | Are the delivery and content satisfactory to both clinicians and patients? Are patients willing to accept prescribed prophylaxis? | <ul style="list-style-type: none"> Acceptability of intervention measures [22] |
| Fidelity | Were the strategies implemented as planned and used appropriately? Did patients appropriately get thromboprophylaxis? | <ul style="list-style-type: none"> Percentage of patients with appropriate prophylaxis, eg, anticoagulation prescribed for high-risk and not prescribed for low-risk patients |
| Appropriateness | Are the implementation strategies a good fit to deliver the evidence-based intervention? | <ul style="list-style-type: none"> Intervention appropriateness measures [22] |
| Sustainability | Did the implementation strategy become a stable and enduring part of clinical practice? | <ul style="list-style-type: none"> Percentage of clinicians using the intervention over time Percentage of high-risk patients started on thromboprophylaxis who continue to receive prescriptions at 6 mo |

VTE, venous thromboembolism.

^aAdapted from Proctor et al. [18].

increase VTE prevention interventions in ambulatory oncology; the cornerstones of the program were an electronic health record-based risk assessment tool, patient education on VTE, and referrals to thrombosis specialists for anticoagulation discussion [12]. Our study confirms that similar support strategies for clinicians in assessing a patient's VTE risk and patient education are critical to closing the gap between evidence-based recommendations and clinical practice. In our study, by using the IRLM, we advanced understanding to show that additional, multilevel strategies are likely also necessary to overcome barriers, including staged scale-up and engagement of financial billing specialists to encourage clinician buy-in, conducting oncology clinician education on supporting evidence for the intervention, and distributing educational materials to both clinicians and patients, among others. Notably, in our study, oncology clinicians reported high self-efficacy in performing the intervention themselves, without the need to routinely involve hematology/thrombosis specialists, which offers an alternative strategy and may facilitate the sustainability of the intervention broadly given the widespread shortage of thrombosis specialists. Perhaps critically, leveraging patients' and clinicians' desire for change to increase awareness of and prevention of VTE and clinicians' self-efficacy in performing the interventions were identified as key strategies and are also likely essential to the sustainability of the intervention in clinical practice. Furthermore, in addition to naming important clinical and systems outcomes targeted by the strategies, using the IRLM framework allowed us to identify *implementation* outcomes critical to evaluate the success and sustainability of the innovation and provided a roadmap to test these strategies.

Understanding the implementation needs of different clinical settings will also be crucial to close the practice gap. We included stakeholders from different practice settings to elucidate more comprehensive barriers and facilitators, although, within a single health care setting, we found many strategies to be similar for community-based and academic-based oncology clinics. In addition, the barriers and facilitators experienced in our health system are similar to those reported by the University of Vermont [14]. However, the community-based oncologists in our study wanted to follow academics' uptake rather than leading, which led to the implementation strategy of staged scale-up, first implemented in academic settings and then in community-based settings. Furthermore, while the strategies that address the common barriers/facilitators are expected to also apply to other similar health care settings, they would need to be formally studied outside of the US, particularly in settings with more limited resources.

Given the paucity of data, specifically in the medical oncology setting, we compared our findings with studies that have evaluated strategies to improve adherence to recommendations for extended prophylaxis following cancer surgery. One study used local consensus discussions, clinician education, and resources to improve adherence to extended VTE prophylaxis following abdominopelvic cancer surgery [25]. Another used targeted clinician education to improve adherence to extended thromboprophylaxis following colorectal cancer surgery and used audit and feedback to increase success [26]. Although our identified strategies for the ambulatory medical oncology population align with these prior findings, using the implementation framework to systematically guide the evaluation allowed us to identify additional

strategies that more comprehensively address the identified barriers, which should help to achieve success more rapidly and sustainably.

Strengths of the study include using the implementation science IRLM framework, which enabled simultaneously addressing the planning and mapping of the execution and evaluation of a practice change initiative to facilitate implementation success. This process may be generalizable to oncology practices with similar barriers to using evidence-based interventions for VTE prevention. One limitation of the study is that the interview guide was not created based on CFIR, so the fact that we did not identify aspects to address in each CFIR domain may be due to not probing all of the domains in the interviews. In addition, we have not yet tested the identified strategies, although we plan to do so in future work: informed by findings from the current study, we are developing multilevel implementation strategies, including electronic health record-based clinical decision support to aid in risk assessment and guidance for primary prophylaxis, clinician education about the evidence behind the recommendations, and patient education resources.

5 | CONCLUSION

Using the IRLM framework, we drew from existing qualitative insights on contextual factors to identify comprehensive implementation strategies that facilitate the uptake of evidence-based interventions to prevent VTE in ambulatory oncology practice. The next step in this work is to test the identified strategies, with the ultimate goal of reducing morbidity and mortality associated with VTE in patients with cancer.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the concept and design of the study, or acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be submitted.

RELATIONSHIP DISCLOSURE

There are no competing interests to disclose.

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SUPPLEMENTARY MATERIAL

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