Designing comprehensive and impactful implementation strategies for cancer-associated thrombosis prevention

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ABSTRACT

Despite strong evidence and professional society recommendations for interventions to reduce cancer-associated thrombosis, uptake in clinical practice remains low. Implementation science offers structured approaches to close this evidence-to-practice gap. Frameworks such as the Implementation Research Logic Model and Consolidated Framework for Implementation Research guide identification of barriers, selection of strategies to address the barriers, and evaluation of clinical and implementation outcomes. Herein, the application of implementation science to close the gap between evidence for cancer-associated thrombosis prevention and use in clinical practice is discussed. Multi-level strategies, including clinician and patient education and electronic health record decision support, are essential to improve adoption. Clinical programs such as the Vermont Model demonstrate feasibility but highlight challenges in sustainability and scale-up. Integrating recommended cancer-associated prevention interventions into routine oncology care through tailored implementation strategies can reduce preventable morbidity and mortality, improving outcomes for patients with cancer.

Key words: cancer-associated thrombosis; venous thromboembolism; prevention, implementation science.

Introduction

Cancer associated thrombosis (CAT) is a major, yet largely preventable, cause of morbidity and mortality among people with cancer. Venous thromboembolism (VTE) occurs in up to 25% of people with cancer during the course of their disease, and CAT is a leading cause of cancer-related death.[1] As the risk of VTE varies by patient and cancer characteristics, risk assessment models were developed to identify those mostly likely to benefit from prophylaxis. One of the earliest (developed in 2008) and most widely cited risk scores is the Khorana Score, which stratifies CAT risk based on five clinical variables: white blood cell count, hemoglobin, platelet cell count, body mass index and cancer type.[2] Subsequently, numerous risk scores have been developed and validated in various populations.[3] Early randomized trials of primary thromboprophylaxis in unselected ambulatory patients with cancer starting systemic therapy demonstrated modest benefit, limiting widespread adoption. However, subsequent randomized controlled trials targeting those at highest CAT risk showed an approximately 40-55% reduction in VTE risk with prophylactic anticoagulation, translating to a number-needed to treat of 17, compared to a number needed to harm of >300.[4-7] These findings informed professional society recommendations to conduct risk assessment using validated scores and provide VTE education to all patients with cancer starting systemic cancer-directed therapy, and to consider thromboprophylaxis for intermediate and high VTE risk patients.[8-11]

Evidence to practice gap

Despite the longstanding awareness of CAT risk, randomized trial data supportive of thromboprophylaxis, and professional society recommendations for VTE prevention interventions in ambulatory oncology, uptake into routine clinical practice remains strikingly low. In a 2003 survey, only 5% of medical oncologists reported routinely using thromboprophylaxis in ambulatory cancer patients.[12] Over ten years later, at an NCI-designated tertiary cancer center in the Midwest, out of 181 high risk Khorana patients, none had an anticoagulation prescription for thrombopro-

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phylaxis.[13] Similarly, an academic New England health system reported the use of VTE risk assessment for all patients and prophylaxis for high risk patients occurred in <5% of patients.[14] In a survey from Association of Community Cancer Centers in 2016, 29% of survey respondents indicated that <10% of very high-risk solid tumors receive VTE prophylaxis and an additional 10% reported <30% receive prophylaxis.[15] In another study that surveyed 34 academic oncologists, 67% reported unfamiliarity with the Khorana Score or guideline recommendations regarding risk-based VTE prophylaxis, and 90% "never" or "rarely" used VTE risk assessment.[13] These data highlight the persistent gap between guideline recommendations for VTE prevention strategies and their widespread implementation into clinical practice.

Why does the gap exist?

Evidence alone is insufficient; meaningful implementation requires dedicated study to identify effective strategies to implement evidence-based practices. Implementation science, which is the study of methods and strategies to promote the systematic uptake of evidence-based practices into routine clinical practice and policy, can help address this challenge. Implementation science emphasizes understanding the factors ("determinants") that impair or facilitate the translation of research and guidelines into clinical practice across organizational, individual, and contextual levels. Importantly, the goal of implementation science is to develop generalizable strategies by comprehensively studying contextual barriers in various settings and from different perspectives. From there, strategies are selected to address the determinants, based on their mechanism of action, and outcomes are selected to evaluate both implementation and clinical success. This process of mapping determinants, linking strategies through their mechanism of action, and defining outcomes is illustrated by the Implementation Research Logic Model (IRLM; Figure 1),[16] which can be applied to CAT prevention.

Following the IRLM, to close the gap between CAT prevention interventions and their use in clinical practice, it is necessary to understand barriers and facilitators to guide targeted strategy selection. One widely used framework for this purpose that is incorporated into the IRLM is the Consolidated Framework for Implementation Research (CFIR).[17] CFIR guides the comprehensive evaluation of contextual factors organized into 5 domains: intervention characteristics, inner setting, outer setting, individual characteristics (both intervention deliverers and intervention recipients), and implementation process.

In one study, using CFIR-informed interview guides, investigators interviewed academic and community-practice clinicians and patients with cancer within a health system in which no dedicated CAT prevention program existed. Identified barriers to uptake of CAT prevention interventions included lack of knowledge of Khorana Score and phase III studies of primary thromboprophylaxis, lack of familiarity with professional society recommendations, perception of overwhelmed patients at cancer diagnosis who may not be able to absorb information about VTE risk, and resource barriers such as limited clinician time and relative priority of cancer management discussions relative to VTE prevention. Clinicians additionally raised several clinical factors as barriers, including generalizability of risk-assessment scores to certain cancer subtypes (e.g., indolent lymphomas or post-surgical ovarian cancer) and concerns with bleeding risk. Facilitators identified by clinicians were a desire for change and willingness to perform dedicated VTE prevention strategies and a belief that patients would appreciate proactively addressing VTE prevention. Patients reported a desire to learn about CAT prevention, despite their cancer diagnosis, and a willingness to hear about CAT prevention from any health care team member.[18]

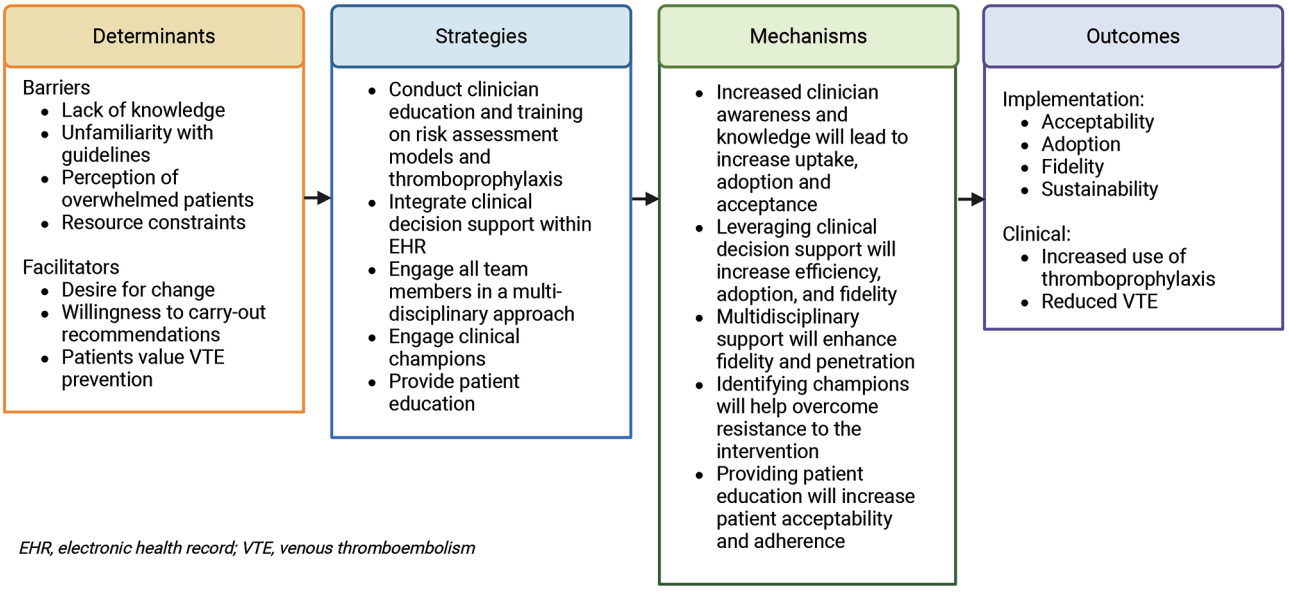

Figure 1. Simplified implementation research logic model applied to cancer-associated thrombosis prevention. Acknowledgments: Figure was created in BioRender, Martin K. (2026) https://BioRender.com/de8ydqt

Strategies to address the practice gap

Implementation science frameworks, such as the IRLM framework, provide a structured approach to help identify potential strategies to address the determinants and facilitate intervention uptake. Based on the identified barriers and facilitators, 12 discrete implementation strategies to increase uptake of CAT prevention interventions were identified, each linked to their mechanisms of action and associated outcomes (Figure 1): conduct education and training; develop and distribute educational materials for clinicians and patients; engage all team members; staged scale-up; staged implementation scale-up; leverage desire for change; adapt electronic health record to provide interactive assistance; task-sharing amongst the team; engage financial billing; and educate patients on relative benefits.

For one such strategy, adapt electronic health record to provide interactive assistance, the feasibility of incorporating risk-assessment scores into the electronic health record has been shown in several unique healthcare systems.[19,20] Another program has developed an entire clinical program, called the Vermont Model, to incorporate CAT prevention interventions. The Vermont Model uses a multidisciplinary approach. First, for patients starting systemic anti-cancer therapy, oncology nurses conduct VTE and bleeding risk-assessment using flowsheets embedded in the EHR, which calculate a Khorana and Protecht Score, as well as a bleeding risk score. If patients are identified as high VTE risk, a referral is placed to thrombosis specialist, who then discusses with the patient the risks and benefits of primary thromboprophylaxis. The thrombosis specialist makes a recommendation regarding thromboprophylaxis to the treating oncologist; if the recommendation is for thromboprophylaxis, the oncologist is then responsible for prescribing and managing prophylactic anticoagulation.[14] Recently, this model showed feasibility in a Portuguese center, suggesting adaptability across clinical settings.[21] However, when implemented in rural and community-based settings in New England without thrombosis specialists, the Vermont Model maintained high rates of risk-assessment, but achieved lower rates of VTE prophylaxis for high-risk patients.[22,23] A subsequent evaluation of the existing Vermont Model using the CFIR framework aimed to understand factors supporting its success, as well as existing challenges needing to be addressed in order to adapt the Vermont Model to a fully oncology-delivered model. Factors supporting success included a strong culture valuing VTE prevention and presence of a local champion. Identified challenges to successfully implementing a fully oncology-delivered model included lapses in intervention education/training, communication gaps amongst health care team, and relative priority with existing workload (*data unpublished*).

Implications

Professional society recommendations alone are insufficient to ensure widespread uptake of CAT prevention strategies in ambulatory cancer care. Closing this gap requires application of implementation science methods to identify barriers, leverage facilitators, and design strategies that integrate evidence-based interventions into routine workflows. Implementation science frameworks, such as the IRLM and CFIR, provide structured approaches to map determinants, select strategies based on their mechanisms of action to address the determinants, and evaluate both implementation and clinical outcomes.

Specifically for CAT prevention, enhancing uptake will require moving beyond merely disseminating guidelines toward multi-level, tailored implementation strategies that incorporate education about evidence and guidelines, workflow integration, and clinical decision support. By systematically applying implementation science methods, we can enhance adoption and sustainability. Ultimately, embedding CAT prevention into standard oncology practice will reduce preventable morbidity and mortality to improve outcomes for patients with cancer.

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