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Review

Care pathways for patients with cancer-associated thrombosis: From diagnosis to long-term follow-up

Marie-Antoinette Sevestre[a,l,*], Yoann Gaboreau[b], Eric Douriez[c], Virginie Bichon[d], Coralie Bozec[e], Pascale Gendron[f], Didier Mayeur[g], Florian Scotté[h], Isabelle Mahé[i,j,l,1], Olivier Sanchez[j,k,l,1], for the INNOVTE CAT Working Group[2]

[a] *Service de médecine vasculaire, EA Chimère 7516, CHU Amiens, 80054 Amiens, France*
[b] *Département de médecine générale, faculté de médecine, université Grenoble-Alpes, université de Grenoble, techniques de l'ingénierie médicale et de la complexité (TIMC), Grenoble, France*
[c] *Pharmacie de la Mairie, 94320 Thiais, France*
[d] *Service d'oncologie, hôpital européen Georges-Pompidou, AP–HP, Paris, France*
[e] *AFIC, IPA onco-hématologie, centre Eugène-Marquis, centre hospitalier de Dinan, Rennes, France*
[f] *ONCORIF, dispositif spécifique régional de cancérologie Île-de-France, Paris, France*
[g] *Département d'ocologie médicale, centre Georges-François-Leclerc, Dijon, France*
[h] *Département interdisciplinaire d'organisation des parcours patients (DIOPP), institut Gustave-Roussy, Villejuif, France*
[i] *Service de médecine interne, hôpital Louis-Mourier, AP–HP, Colombes, France*
[j] *Université Paris Cité, Inserm UMR S1140, innovations thérapeutiques en hémostase, Paris, France*
[k] *Service de pneumologie et de soins intensifs, hôpital européen Georges-Pompidou, AP–HP, Paris, France*
[l] *F-CRIN INNOVTE network, Saint-Etienne, France*

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ABSTRACT

Venous thromboembolism (VTE) in patients with cancer is associated with a high risk of bleeding complications and hospitalisation, as well as with increased mortality. Good practice recommendations for diagnosis and treatment of VTE in patients with cancer have been developed by a number of professional bodies. Although these guidelines provide consistent recommendations on what treatment should be offered to patients presenting with cancer-associated thromboembolism (CAT), many questions remain unanswered, in particular about the modalities of management (Who? When? Where?) and, for this reason, we have developed a consensus proposal for an appropriate multidisciplinary care pathway for patients with CAT, which is presented in this article. The proposal was informed by the recent scientific literature retrieved through a systematic literature review. This proposal is centred on the development of a shared care plan individualised to each patient's needs and expectations, patient information and shared decision-making to promote adherence, involvement of all relevant hospital- and community- based healthcare providers in the development and implementation of the care plan, and regular re-evaluation of the treatment strategy.

1. Abbreviations

alloTC	allo-thrombose-cancer
CAT	cancer-associated thromboembolism
DDI	drug-drug interaction
DVT	deep vein thrombosis
DXI	direct oral factor Xa inhibitor
ECPC	European Cancer Patient Coalition
GP	general practitioner
LMWH	low-molecular weight heparin
MCT	Multidisciplinary Care Team
OR	odds ratio
PACC	Prevention in the Ambulatory Cancer Clinic
PACT-Q	Perception Anticoagulant Treatment Questionnaire
PE	pulmonary embolism
PELICAN	Patient Experience of LIving with CANcer
QoL	Quality of Life

* Corresponding author.
E-mail address: sevestre.marie-antoinette@chu-amiens.fr (M.-A. Sevestre).

[1] These two authors contributed equally to the role of last author for this manuscript.

[2] A full list of the INNOVTE CAT Working Group can be found at the end of the article, in Appendix A. INNOVTE CAT Reviewers are listed in Appendix B.

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RIETE Registro Informatizado de Enfermedad TromboEmbólica
VKA vitamin K Antagonist
VTE venous thromboembolism

2. Introduction

Venous thromboembolism (VTE) in patients with cancer is associated with a high risk of bleeding complications and hospitalisation, as well as with increased mortality [1]. For these reasons, good practice recommendations for diagnosis and treatment of VTE have been developed by a number of professional bodies. In 2020, the American Society for Clinical Oncology, published guidelines recommending that anticoagulants should generally be used in patients with cancer-associated thrombosis (CAT) for as long as the cancer is active [2]. In practice, this means that patients should receive anticoagulants for at least the first six months, but could be for lifetime use if the patient remains at risk for VTE recurrence and hospitalisation due to the persistence of active cancer. In 2021, French good practice recommendations for management of CAT were published, endorsed by several national scientific societies [3]. In 2021, an update dedicated to CAT completed the document [4]. These guidelines specify that oral or injectable anticoagulant treatment should be given to all patients experiencing a CAT for at least six months. Nevertheless, many questions remain unanswered and, for this reason, we have now developed a consensus proposal for an appropriate multidisciplinary care pathway for patients with CAT. This proposal was based on a review of the relevant published literature over the last ten years, performed in February 2023 (Search strategy for the literature review in 'Literature Searches').

3. How good is the management of cancer-associated thrombosis and adherence to guidelines?

Several cohort studies have evaluated treatment adherence over time in both inpatients and outpatients. These show that overall compliance with treatment recommendations was good in the short-term (during the first weeks after diagnosis), but declined during follow up (Table 1). It should be noted that these studies were generally performed before the introduction of oral direct Factor Xa inhibitors (DXIs) for the treatment of CAT.

Several factors have been implicated in the failure of patients to maintain long-term anticoagulation therapy [5]. For example, a post hoc analysis of the Hokusai-VTE Cancer Study highlighted the role of low ECOG performance status as a risk factor for discontinuation of long-term anticoagulation therapy with dalteparin or edoxaban, for any reason apart from death [6]. Changes to medical treatment, aggravation or complications may also change the risk profile of the patient and consequently lead to changes to the anticoagulant treatment prescribed [7].

The failure to follow anticoagulant treatment guidelines is all the more regrettable given the high morbidity and mortality associated with CAT, which, apart from cancer itself, is the most frequent cause of death in patients with cancer [8,9]. The available data from randomised clinical trials demonstrate that long-term anticoagulant treatment provides a clear benefit in terms of preventing recurrence of VTE in patients with CAT, best documented over the first six months [1], and it is these findings that underlie current practice guidelines [2,4]. Nonetheless, the impact of long-term anticoagulant therapy on quality of life (QoL) remains poorly documented [10], and there is little evidence for a clear benefit in terms of QoL [11]. For this reason, the absence of a readily perceptible treatment effect may discourage patients with CAT from pursuing long-term anticoagulation. There are thus multiple challenges to overcome to ensure that all patients who have experienced CAT receive the optimal standard of care [5]. This requires that an integrated care pathway is identified and implemented by a multidisciplinary care team (MCT) from the time when the diagnosis of CAT is made and for at least six months of anticoagulation [12]. Healthcare professionals in the community who will be managing the patient over the long term will frequently not be experts in anticoagulation, and it is important that they have access to the resources and knowledge to manage treatment and its possible complications appropriately [5]. The attitude of the patients is also critical, and patient perceptions and expectations, need to be taken into account in order to provide a personalised treatment approach [1].

4. Who is involved in the care of patients with cancer-associated thrombosis?

Many types of healthcare professional are involved with the care of patients with CAT, and with their family and carers, who intervene at several levels (Fig. 1). The principal levels of intervention are the management of cancer, the management of thrombosis and community care. Healthcare professionals operating at different levels do not necessarily interact, but communication between them is essential to achieve optimal care.

Concept analysis has been used to develop an integrative conceptual framework for patient-centred care pathways, which proposed 28 subcategories grouped into seven attributes [13]. Attention to these attributes in designing a care pathway could be a key success factor. In this way, the patient could avoid unnecessary delays, unnecessary examinations and poor-quality information provision. A key component of successful care pathways is the identification of a specific health professional who coordinates care for the patient; this professional is not only a link between all the specialists involved, but also with family, with the healthcare administration and funding. The exact nature of the integrated care pathway will depend, however, on local needs and resources and the capacity for healthcare provision.

5. Organisation of care delivery

Multidisciplinary care teams (MCTs) are recommended when treating patients with cancer [14] in order to provide patients with individualised treatment, to optimise clinical decision-making and to improve outcomes in the short and long term. They also provide multiple channels to take into account the perceptions and wishes of the patient. According to the 2003 Cancer Plan of the French Ministry of Health [14], such MCTs should involve at least three types of healthcare professionals. In hospital settings, MCTs have been shown to improve clinical decision-making, not only in the context of CAT, but also in VTE management outside the cancer setting when clinical decision-making is challenging [15].

Cancer-associated thrombosis is generally diagnosed by a radiologist, a vascular physician, a chest physician, a cardiologist or an oncologist. These specialists are initially involved in initiating anticoagulant treatment and in giving the relevant information to the patient to ensure adherence, and are also responsible for ensuring that the MCT is alerted and informed. The MCT will generally involve hospital and community physicians, including a haemostasis specialist and a member of the oncology team, specialised VTE practice nurses and, potentially pharmacists and physiotherapists. However, the precise structure of the MCT may differ between countries due to the differences in the structure of the healthcare service. The MCT will be responsible for the initiation and implementation of a structured management plan covering the anticipated treatment period [1,5,12,14]. An example of a structured care pathway for the management of CAT is proposed in Fig. 2.

Table 1
Adherence to treatment guidelines in patients with cancer-associated thrombosis.

Year	Population	Study design	Adherence to treatment guidelines
Kahn et al., 2012 [45]	868 outpatients with acute symptomatic VTE (DVT: 67.2%; PE: 30.2%; 2.6%: unusual sites) Idiosyncratic VTE: 46%; CAT: 8.5%; transient risk factors: 37.7%; 7.8%: hormonal treatment Treated with VKA or LMWH	Prospective observational study (RECOVERY) in 12 centres in Canada Evaluated at baseline and at 6 months follow-up Objective: to document VTE management and adherence by clinicians to treatment guidelines	CAT patients 59.5% prescribed LMWH at least once 43.2% received LMWH for > 3 months
Belhadj Chaidi et al., 2013 [30]	145 patients with cancer and VTE (PE and DVT)	Retrospective, single centre survey Objective: to evaluate adherence to guidelines in hospitalised patients in France	57.2% prescribed LMWH and 22.7% VKA for > 10 days At 6 months, 19.3% still received LMWH and 18.6% received VKA
Rahme et al., 2013 [46]	2,070 patients with CAT 29.5% taking warfarin at index date 60.1% taking LMWH at index date 10.4% taking warfarin + LMWH at index date	Retrospective insurance claims database study in Canada Objective: to study characteristics of patients with CAT and describe patterns of anticoagulant use	60% of patients still taking anticoagulant treatment at 6 months
Kaatz et al., 2014 [47]	2002 anticoagulant-naïve patients starting VTE treatment Including 329 patients with CAT	Retrospective insurance claims database study in USA Objective: to evaluate anticoagulant treatment duration	Mean treatment duration: Overall: 294 ± 261 days CAT: 297 ± 217 days Treatment duration < 6 mo: 43.4% (overall)
Sevestre et al., 2014 [48]	500 patients with CAT hospitalised at the time of the study	National cross-sectional observational study in 47 centres Objective: to evaluate adherence to guidelines in hospitalised patients in France	98% compliance with initial treatment 62% compliance at six months
Mahé et al., 2016 [49]	48,481 consecutive patients included in the RIETE registry (41,625 analysed) Including 6345 patients with CAT 4210 prescribed LMWH alone 2135 prescribed a VKA	Retrospective analysis of patients experiencing a VTE entered into the multinational European RIETE registry between 2001 and 2013. Objective: to evaluate anticoagulant practices for VTE treatment and identify variables associated with guideline-adherent use	66.4% received long-term LMWH in accordance with guidelines Age > 70 years (OR: 1.39), chronic heart disease (OR: 1.50), chronic lung disease (OR: 1.36) and initial PE (1.15) independently predicted poor adherence to guidelines The presence of metastases (OR: 3.22), anaemia (OR: 1.83) and recent immobility (OR: 1.51) independently predicted long-term use of LMWH therapy
Mahé et al., 2016 [50]	240 patients hospitalised with CAT	Retrospective cohort study using data from the national hospital claims database concerning three hospitals in the Paris region (France) Objective: to assess adherence to VTE treatment guidelines in routine hospital practice	Overall, 52% of patients adhered to guidelines Adherence was highest in patients with PE (60%), catheter-related thrombosis (62%), class III/IV advanced cancer (58.0%) and metastatic malignancies (60.3%). Only 40% of patients with DVT received a treatment consistent with guidelines
Mahé et al., 2016 [51]	> 10,000 patients	Systematic review of prospective or retrospective studies and surveys of CAT (14 studies evaluated) Objective: to study the gap between guidelines and practice	25 to 68% of cancer patients with VTE received adequate treatment depending on patient profile and comorbidities
Van der Wall et al., 2017 [52]	472 patients with CAT prescribed LMWH	Prospective cohort study in everyday clinical practice in Spain and the Netherlands.	51% of patients discontinued treatment within six months, and 21%of these discontinuations were due to side effects

CAT: cancer-associated thrombosis; DVT: deep vein thrombosis; LMWH: low-molecular weight heparin; OR: odds ratio; PE: pulmonary embolism; RIETE: Registro Informatizado de Enfermedad TromboEmbólica; VKA: vitamin K antagonist. VTE: venous thromboembolism.

During the first week, when the diagnosis of CAT has been confirmed, a choice for the initial anticoagulant treatment needs to be made jointly by the MCT and the patient and, following this decision. At this stage, if LMWH is prescribed, self-injection training (if relevant) should be initiated. Within the first month, therapeutic education should be initiated for the patient and eventually the patient's entourage, and a structured management plan for the following months should be established jointly by the MCT and the patient. The patient's clinical status with respect to cancer progression and biological status (for example, renal function) should be evaluated and taken into account in the structured management plan. At quarterly intervals thereafter, the tolerability of treatment and the patient's adherence should be assessed, and treatment modified if necessary. The clinical status of the patient should be re-evaluated and the management plan revised in light of the findings if necessary. The therapeutic education programme may need to be adapted or, alternatively, could be stopped. After six months, a decision will need to be taken jointly by the MCT and the patient on whether to stop or continue anticoagulant treatment. If a decision to stop treatment is taken, then imaging should be performed to identify any sequelae of VTE and the patient should be informed of warning signs for recurrence of VTE (see cf. Section 6 below).

When comparing decisions taken with or without MCT involvement, unresolved questions about the duration of treatment are less frequent with MCT [15]. Although adherence to guidelines

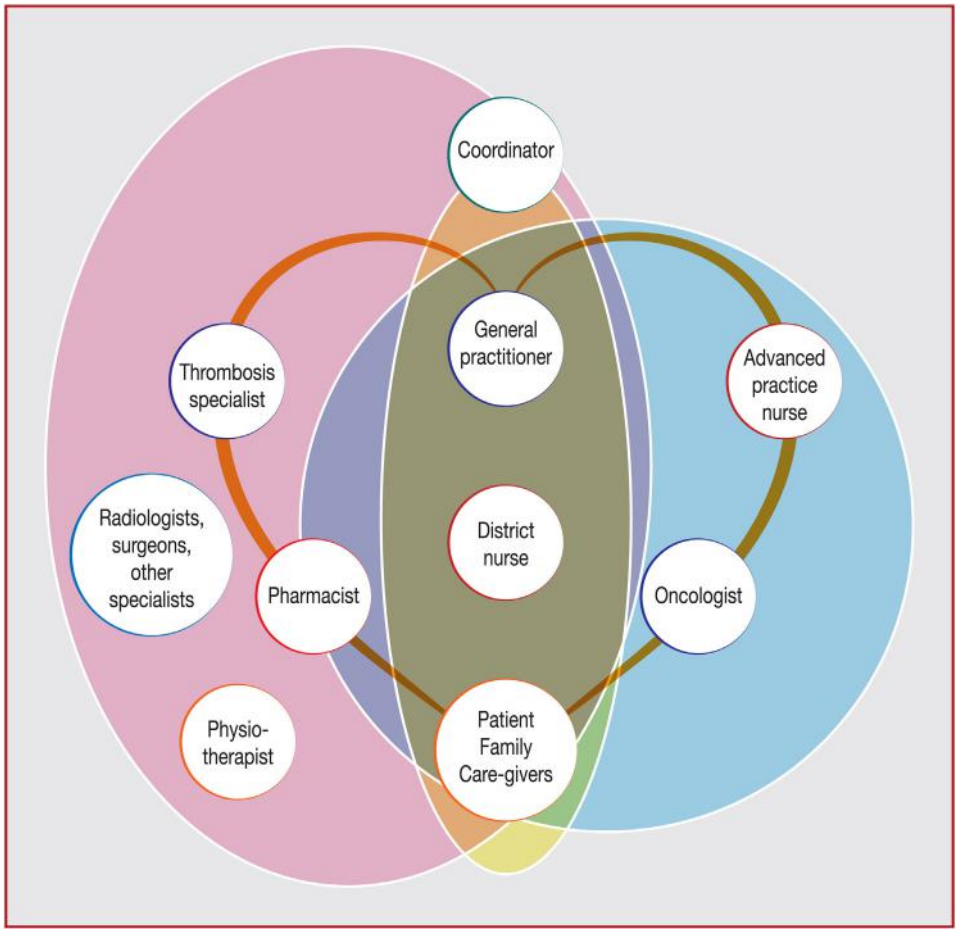


Fig. 1. Healthcare providers involved with the care of patients with cancer-associated thrombosis. Pink circle: healthcare professionals involved in thrombosis care; blue circle: healthcare professionals in cancer care; yellow area: everyday community care.

improves with MCT and physicians' familiarity with guidelines and confidence are increased with MCT [16], whether it provides a significant improvement in the overall health of the patient with CAT is still unknown (Table 2). Even though it is difficult to evaluate correctly the benefit of MCT in terms of health improvement, preliminary data suggest that the involvement of an MCT may be associated with improved survival. For example, in a registry study of 3999 patients with cancer, involvement of an MCT was demonstrated to be associated with a reduction in mortality [17]. In a multivariate Cox analysis taking into account other known predictors of survival, the hazard ratio for death for patients not managed by a an MCT compared to patients without MCT involvement was 2.8 [95% CI: 2.4–3.4] ($P < 0.001$) [17].

A cross-specialty team dedicated to CAT management has been implemented within a regional cancer centre in Wales [18] in order to improve patient management following an audit which highlighted important unmet medical needs with routine CAT management. The system was established by an MCT including oncologists, thrombosis specialists, primary care and palliative care physicians. The care programme comprised four components, namely a shared care agreement for community prescribing of LMWH, patient information leaflets, an explicit patient referral pathway and a dedicated outpatient clinic for CAT. A survey of 457 patients sequentially referred to the CAT service over an 18-month period and their referring oncologists indicated a high level of satisfaction. Compared to the previous audit, the level of adherence to LMWH treatment guidelines was increased by 88%. Patients reported a better understanding of their disease and felt better equipped for discussing treatment decisions with their physicians. Physicians reported that the existence of a dedicated CAT expert service provided them with reassurance that their patients were receiving the optimal treatment (Table 2).

Education of healthcare professionals participating in MCT is crucial to change behaviours and improve the quality of patient management. Smartphone applications are currently being developed to provide E-learning solutions for physician education on VTE risk assessment, VTE prophylaxis or awareness of guidelines. However, the superiority of digital methods has not yet been rigorously evaluated and further studies are needed to define the place of such applications to overcome the challenges of ensuring physical attendance at conventional teaching sessions.

As recently emphasised by Lammila-Escalera et al., implementation of such integrated CAT management programmes is highly dependent on the organisation and funding of healthcare in each country, especially with respect to the role of primary care, and, for this reason, effective programmes in one country may not be easily transposable to another and specific multidisciplinary management programmes will need to be developed in each country [19]. Some examples of cross-disciplinary CAT management programmes are listed in Table 2. Evaluation of actions aimed at improving VTE management.

Who participates in the MCT and how it functions will depend on how care provision is organised on a national and local level. For example, in the United States context, Kapoor et al. initiated a care and education programme for patients with VTE involving a visit by a clinical pharmacist, information on medications, and subsequent telephone consultations with an anticoagulation expert [20]. Satis-

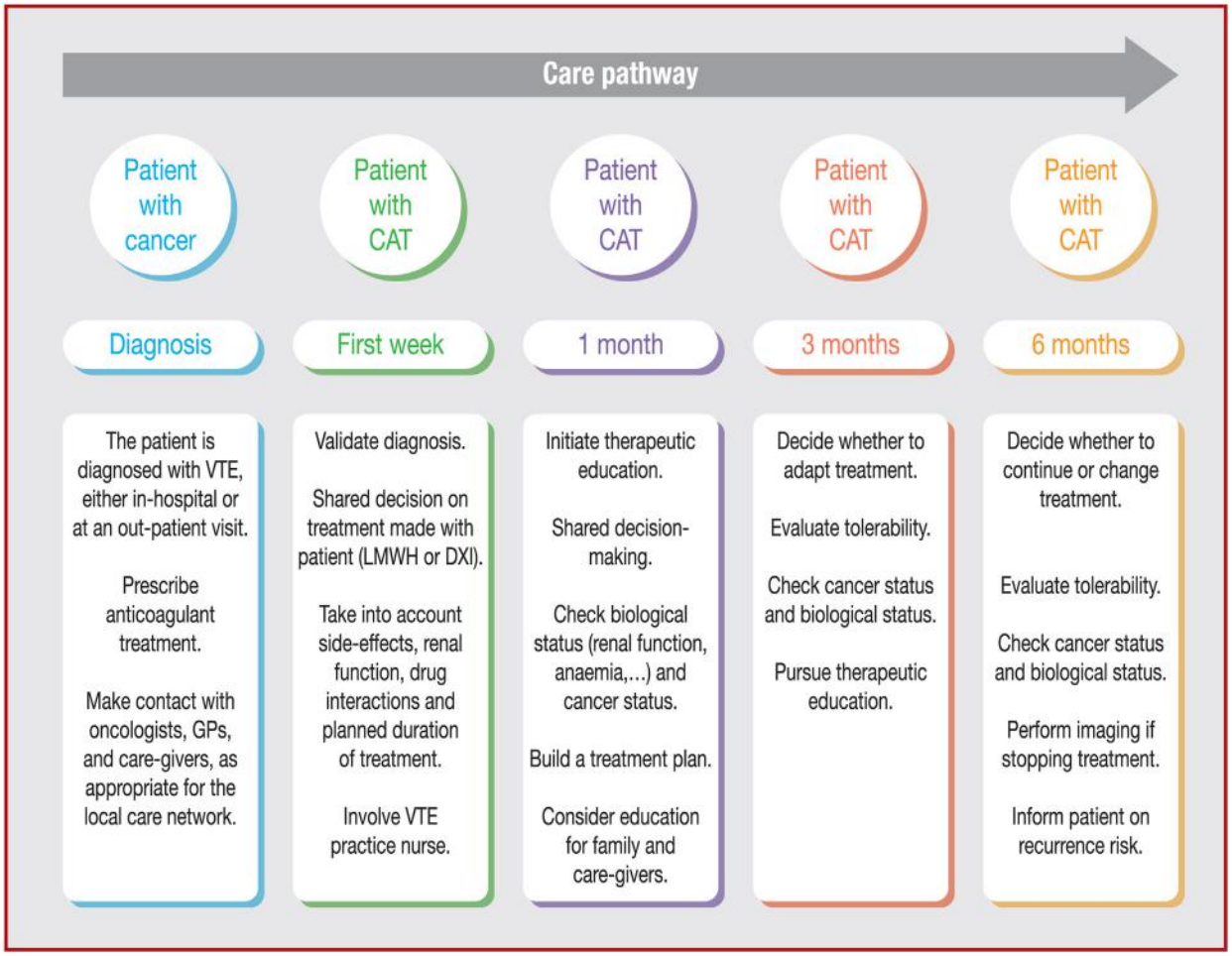


Fig. 2. Timeline of the care pathway of patients with cancer-associated thrombosis. CAT: cancer-associated thrombosis; DXI: direct oral Factor Xa inhibitor; GP; general practitioner; LMWH; Low molecular weight heparin; VTE: venous thromboembolism.

faction with the programme was high, although patient knowledge and adherence did not seem to be improved.

A CAT management programme involving community pharmacists has been implemented in the Canadian province of Alberta (ClotAssist) in order to limit the pressure on overcrowded emergency departments and to assuage anxiety associated with the risk of VTE in patients with a stabilised tumour pathology [21]. After diagnosis of VTE and information from the oncologist, the pharmacist received the patient's data and information on the location of the clot and the anticipated low molecular weight heparin (LMWH) treatment protocol. The roles of the pharmacist included calculating the dose, weighing the patient, organising the laboratory tests necessary for the prescription, initiating the prescription, educating the patient about self-injection, and possibly injecting LMWH for the first 14 days, if necessary. Patient satisfaction with the programme was high, as was confidence in the quality of their VTE management. Treatment proved to be safe and effective and no events of bleeding or VTE recurrence were reported for the 55 patients included. In addition, the cost of the programme to the health system was reduced. The success of the ClotAssist programme has been such that it will be rolled out to other Canadian cities and to other VTE risk population such as pregnant women or postoperative patients.

In the VTE PACC programme in the USA [22], a specialist oncology nurse was the privileged contact of the patient during follow-up. This programme aimed to provide individualised treatment based on the risk level of each patient, assessed by a specialist nurse using a standardised electronic health record. The nurse also provided educational material on VTE signs and symptoms to all patients. Follow-up was individualised and referral to a thrombosis specialist, oncologist or pharmacist was available. Participation in the VTE PACC programme improved VTE risk assessment and education and facilitated individualised care delivery.

Telephone follow-up is a simple, cheap and potentially useful way to ensure adherence to guidelines. The available evidence indicates that adherence to practice guidelines improves when patients receive dedicated telephone follow-up, compared to standard care. For example, the alloTC MCP programme implemented in France includes an individualised care plan, regular follow-ups, telephone counselling, and a patient education programme [23]. In an observational study comparing 50 patients enrolled in the alloTC programme with 50 historical controls receiving standard care, adherence to clinical practice guidelines at six months was 68% in the alloTC group compared to 16% in the control group.

A structured patient education programme for patients has been implemented in France which involves three modules of interventions including self-injection training and therapeutic education. The utility of this programme was evaluated after a six-year period in a retrospective survey of 182 patients [24]. Despite a significant improvement in quality of life, few patients participated in the survey and only a few participants had completed all planned training sessions. To improve participation, the authors suggested implementing the programme using smartphone applications, such as that developed by the International Initiative on Thrombosis and

Table 2
Evaluation of actions aimed at improving VTE management.

Study	Patients	Intervention	Outcome
Mauger et al., 2020 [15]	142 patients including 49 CAT cases evaluated for treating decisions	Multidisciplinary care team	Significant changes in choice of anticoagulation regimen and duration
Majeed et al., 2022 [16]	96 patients with intervention 46 parallel controls 98 historical controls	Electronic clinical decision tool	Improved familiarity with guidelines and enhanced confidence of prescribers
Noble et al., 2016 [18]	457 consecutive patients participating in a dedicated CAT management service referred over an 18-month period.	Cross-specialty teams with dedicated referral pathway and access to medication	88% increase in adherence to LMWH prescription guidelines Improved access to specialist advice and information Better patient understanding and empowerment Satisfaction of patients and caregivers
Easaw et al., 2019 [21]	55 patients with CAT	"ClotAssist" programme (pilot study) Community pharmacy based follow-up: prescribing pharmacists trained in LMWH treatment provided treatment, education, and initial follow-up	73% of patients very satisfied with the programme 80% felt well-educated about their VTE diagnosis 69% confident in their ability to self-inject 94% cost savings to the health service
Holmes et al., 2020 [22]	Cohort of 918 patients with cancer followed for 2 years	"VTE PACC" programme Computer-assisted risk assessment for VTE Multidisciplinary care team Patient education	VTE risk assessment and patient education rates increased from 5 to 94.7% after implementation of the programme
Kapoor et al., 2020 [20]	162 patients with VTE (without cancer)	Clinical pharmacist visit Educational material Telephone follow-up with a coagulation expert	Increased patient satisfaction but no change in patient knowledge or quality of care transition
Sebuhyan et al., 2021 [24]	182 patients included over six years	Patient education programme including self-injection training and therapeutic education	Satisfaction of patients More patients self-injecting Better treatment adherence Improved quality of life
Benzidia et al., 2022 [23]	100 patients 50 alloTC participants and 50 historical controls	"alloTC" programme Individualised care plan, regular follow-up, telephone counselling, patient education programme	16 to 68% adherence to guidelines

alloTC: Allo-Thrombose-Cancer; CAT: cancer-associated thrombosis; LMWH: low molecular-weight heparin; PACC: Prevention in the Ambulatory Cancer Clinic; VTE: venous thromboembolism.

Cancer, rather than requiring the patient to come to the clinic in person [25].

6. The point of view of the patient

In CAT, as in many other areas of medicine, the point of view of the patient, together with patient understanding of the disease and its complications, are crucial to the success of CAT management. It is important to take into account the way the patients understand their disease, their goals and their preferences, and it is not appropriate to deliver the same information to all patients, who may vary considerably with respect to their degree of anxiety, family support and health priorities [26]. In addition, cultural differences between countries may exist with regard to patient expectations and involvement in their disease management [26].

The Patient Experience of LIving with CANcer-associated thrombosis (PELICAN) programme was a series of qualitative studies aimed at exploring the patient experience of living with CAT. The original study was performed in Wales in 2013–2014 [27], and has since been replicated in France [26], Canada [28] and Spain [29]. All these studies have indicated that patients with cancer have limited awareness of the risk of VTE, and that the support and information that they receive is perceived as inadequate. The diagnosis of CAT was found to be highly distressing to the patient in the Welsh and Spanish surveys, but not in the French one, which may be due to the fact that the French patients were not informed about the implications of this diagnosis. In contrast, the French patients found the need for injections and requiring the support of a community nurse inconvenient. The Spanish survey highlighted the impact of CAT on the patient's family and the importance of family support.

6.1. Patient knowledge

Most patients are not aware of the thrombotic risk associated with cancer, or that CAT may be associated with VTE recurrence and bleeding despite treatment [25,27,29–31]. In the general population, and even in cancer patients, awareness of CAT is low as shown in the Roadmap-CAT study in Greece [32]. The Roadmap-CAT study also indicated that physicians frequently did not get involved in discussing the risk of VTE in their patients with cancer [32]. The European Cancer Patient Coalition (ECPC) also performed a survey of the level of awareness of CAT in 1365 patients in six European countries [33]. In this survey, 72% of participants were unaware of the elevated risk of VTE in cancer patients and 26% heard about CAT for the first time when they experienced a blood clot. On the basis of this survey, the ECPC recommended that appropriate educational material on the risk of CAT and how to manage it should be provided to all patients who receive a diagnosis of cancer all along the continuum of cancer care. Examples of such material include the ECPC's 'Be Clot conscious' toolbox (https://ecpc.org/tool-box/cancer-associated-thrombosis-cat/) and educational material developed by Thrombosis UK (https://thrombosisuk.org/).

6.2. Patient expectations

In an ancillary study of the TROPIQUE trial (a prospective observational study of tinzaparin in CAT in France), patient perceptions of CAT management were explored using the Perception Anticoagulant Treatment Questionnaire (PACT-Q) [34]. There was no comparator group in this study. The principal expectations of the 409 participating patients related to prevention of VTE recurrence, symptom relief and ease of use. Overall, 69.1% of patients were sat-

isfied or very satisfied with their LMWH treatment, and considered it convenient. These findings would suggest that, overall, patients prioritise treatment efficacy over comfort.

6.3. Patient preference

Anticoagulant therapies approved for the treatment of CAT include DXIs and injectable LMWHs, such as dalteparin, enoxaparin or tinzaparin. The choice of treatment proposed may be restricted due to the tumour site or certain characteristics of the patient such as renal insufficiency [7].

Most importantly, the choice of anticoagulant therapy must take into account the patient's choice. Patient participation in the decision-making process is crucial in order to obtain adherence to long-term (several months) anticoagulation therapy. Without dialogue and trust, patient experience and preferences, and how they may change over time, are often difficult to predict. Qualitative studies examining the experiences of patients with CAT have reported that certain anticoagulant therapies prescribed may contribute further to an already burdensome patient experience with cancer [27,29,31].

Qualitative studies have suggested that LWHM injections are an "acceptable" intervention for management of CAT. Notably, patients appreciate that this class of anticoagulant interferes minimally with antineoplastic drugs, reduces the risk of VTE recurrence and carries a low risk of major bleeding events [31,35]. A survey of treatment attributes important to patients with CAT has been performed in Germany and the United Kingdom [35]. A discrete choice experiment was carried out to rank patient preferences among seven attributes selected from patient interviews. The most important attributes identified were 'Little interference with cancer therapy' (relative importance: 39%), 'Low risk of VTE recurrence rate' (24%), 'Low risk of major bleeding' (19%) and 'Oral administration over injection' (13%) [35].

Nonetheless, recent studies have shown that patient preferences may be moving towards anticoagulants with an oral route of administration. The COSIMO study, an ancillary study of the SELECT-D trial, confirmed that patients who switched from LMWH to rivaroxaban declared that the treatment burden was reduced. For 65.5% of them, switching to rivaroxaban was the patient's choice [36,37]. Recent randomised clinical trials have provided further support for this notion. In the CONKO-011 trial, patients expressed a preference for rivaroxaban over LMWH, and more patients on LMWH requested to discontinue the study treatment preterm (19.4 vs. 11.1%) [38]. The trend toward better quality of life with DXIs was confirmed in the ADAM-VTE trial, which evaluated quality of life as a secondary endpoint [39]. In the SELECT-D trial, more patients discontinued dalteparin during the six-month follow-up compared to those who discontinued rivaroxaban [40]. A few patients from SELECT-D were interviewed about their experience with anticoagulant administration. Most of them were able to practice self-injection and perceived a gain in autonomy over home nursing care. Nonetheless, these patients still confirmed a preference for oral over subcutaneous administration [31]. However, it should be emphasised that these findings from clinical trials may not be confirmed in real life settings [41].

6.4. Drug interactions

The management of thrombosis in cancer patients is challenging due to a number of patient and cancer-related characteristics, including drug-drug interactions (DDIs). Drug interactions due to anticoagulant treatment may have an impact on the efficacy and safety of cancer treatment [42]. In addition, clinically relevant drug interactions may lead to poor observance by the patient or a decision to interrupt anticoagulant treatment. A detailed description of DDIs involving anticoagulants is provided in [7].

A recent literature review has evaluated 1799 proposed DDIs between antineoplastic agents and supportive care drugs on the one hand and anticoagulants (three DXIs, warfarin and two LMWHs) on the other [43]. For apixaban and rivaroxaban, 85% of DDIs were not considered to be clinically significant, and 10% represented listed contraindications or were considered clinically relevant. The proportion representing contraindications or clinically relevant DDIs was highest for warfarin (26%) and lowest for LMWHs (8%).

As there are many possible DDIs between anticoagulant drugs and antineoplastic and supportive care drugs, paying greater attention to them will reduce the risks to the patient, and many websites are available which document these interactions [7]. In addition, caution should be exercised with certain over-the-counter medications, foodstuffs and herbal remedies. Peppermint, liquorice, eucalyptus, garlic, orange, grapefruit, grape juice are the best-known herbs and foodstuffs that inhibit CYP3A4. Ginkgo biloba, curcumin berberine, green tea and grape juice are also inhibitors of P-gp but no direct evidence of any relevant clinical interactions with anticoagulants has been reported for these substances [44].

7. Proposals of the expert group

7.1. Patient information and shared decision-making

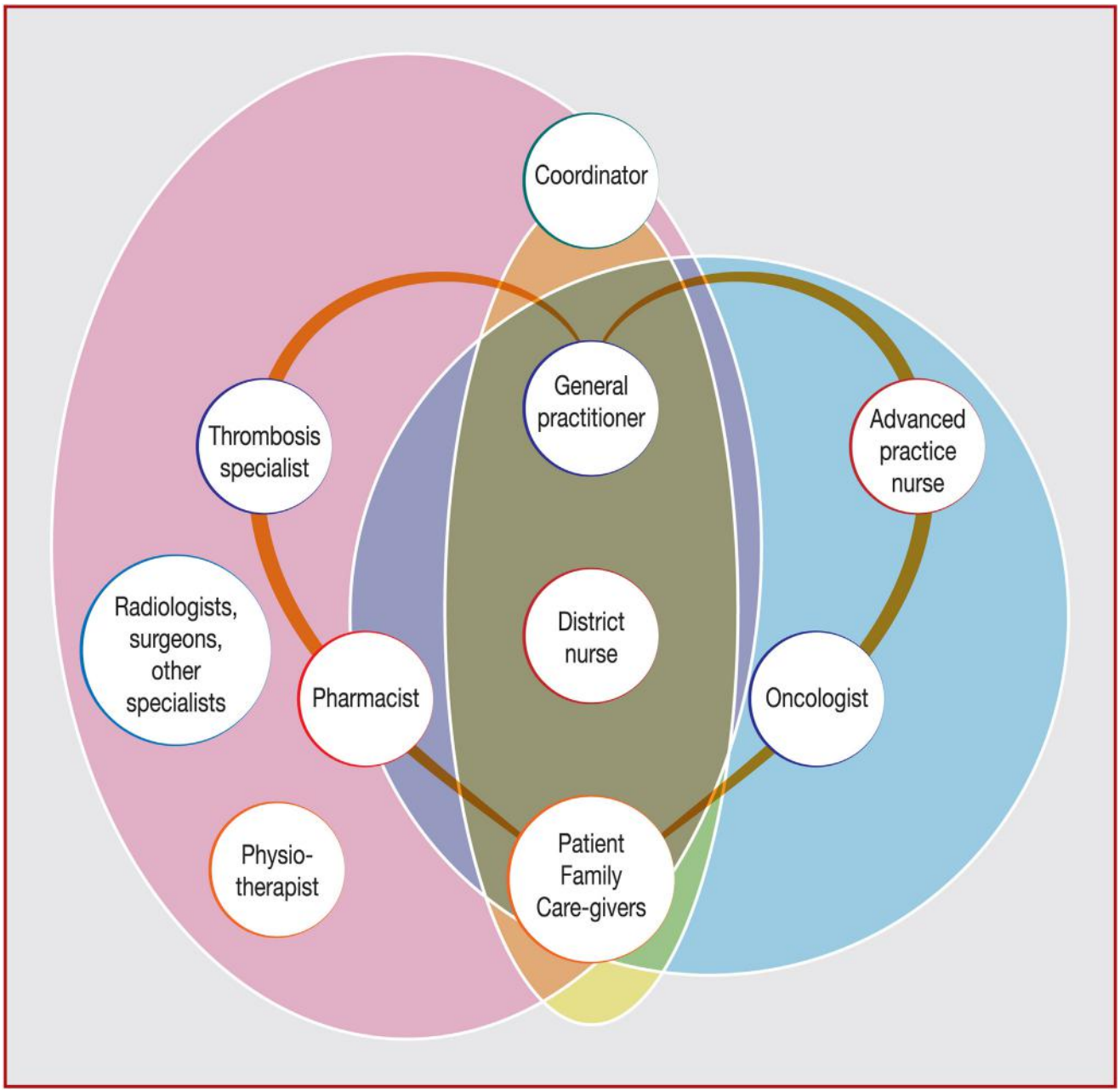
Patient information and shared decision-making:

- we suggest informing all patients with cancer of the risk of thrombosis and their potential complications at a dedicated time as soon as the patient is considered receptive. Expert panel ranking: 3.86 out of 4.00;
- we recommend announcing the occurrence of VTE to patients who develop CAT during a face-to-face visit. Expert panel ranking: 3.90 out of 4.00;
- we recommend presenting the potential benefits and harms of the different available treatment regimens to the patient and coming to a shared medical decision with the objective of promoting patient adherence. Expert panel ranking: 3.90 out of 4.00;
- we suggest reassessing the initial treatment decision and management strategy within three days and at 14 days if the patient is treated at home, and then for all patients, at 1, 3 and 6 months, and at least annually thereafter for the entire duration of anticoagulant therapy (Fig. 2). Expert panel ranking: 3.69 out of 4.00.

7.2. Multidisciplinary thrombosis teams

Multidisciplinary thrombosis teams:

- we suggest setting up a multidisciplinary thrombosis team with the following missions:
  - to ensure diffusion of guidelines to all healthcare providers,
  - to ensure care provision according to guidelines,
  - to implement a shared care plan individualised to each patient's needs and expectations in order to take into account the preferences and quality of life of the patient,
  - Expert panel ranking: 3.86 out of 4.00;
- we suggest building a shared care plan to define the responsibilities of all involved healthcare providers over the long-term. Expert panel ranking: 3.79 out of 4.00;
- we suggest involvihis plan all relevant healthcare providers, including, but not limited to, the GP, the pharmacist, the oncologist, advanced practice nurses and home care providers (Fig. 1). Expert panel ranking: 3.79 out of 4.00 (Central Illustration).



Central Illustration. Healthcare providers involved with the care of patients with cancer-associated thrombosis. Pink circle: healthcare professionals involved in thrombosis care; blue circle: healthcare professionals in cancer care; yellow area: everyday community care.

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Appendix A. INNOVTE CAT Working Group

Ygal BENHAMOU, CHU Charles-Nicolle, Rouen, 0000-0001-8890-7341; Asmahane BENMAZIANE, Hôpital Foch, Suresnes, 0000-0001-7387-7338; Laurent BERTOLETTI, CHU de Saint-Étienne, 0000-0001-8214-3010; Virginie BICHON, Hôpital européen Georges-Pompidou, Paris; Coralie BOZEC, Centre hospitalier de Dinan, Rennes; Ariel COHEN, Assistance publique–Hôpitaux de Paris, Paris; Francis COUTURAUD, CHU de Brest, 0000-0002-1855-8032; Philippe DEBOURDEAU, Hôpital Joseph-Imbert, Arles, 0000-0003-3761-9264; Pascale DIELENSEGER, Institut Gustave-Roussy, Villejuif; Éric DOURIEZ, Union régionale des professionnels de santé pharmaciens Île-de-France, Paris; Antoine ELIAS, Centre hospitalier intercommunal Toulon La Seyne-sur-Mer, Toulon, 0000-0002-1337-1826; Olivier ESPITIA, CHU, Nantes, 0000-0003-0821-9990; Corinne FRERE, Assistance publique–Hôpitaux de Paris, Paris, 0000-0001-6303-4732; Yoann GABOREAU, Université Grenoble-Alpes, Grenoble, 0000-0002-8198-099X; Pascale GENDRON, ONCORIF, Paris; Philippe GIRARD, Institut du thorax Curie Montsouris, Paris, 0000-0002-1559-8055; Olivier HANON, Hôpital Broca, AP–HP, Paris, 0000-0002-4697-122X; Ahmed IDBAIH, institut du cerveau, Paris, 0000-0001-5290-1204; Silvy LAPORTE, CHU de Saint-Étienne, 0000-0001-6197-8668; Isabelle MAHÉ, Université Paris Cité, Paris, 0000-0003-1760-7880; Didier MAYEUR, Centre Georges-François-Leclerc, Dijon, 0000-0003-4724-7871; Patrick

MISMETTI, CHU de Saint-Étienne, 0000-0003-1511-0555; Farès MOUSTAFA, Hôpital de Clermont-Ferrand, 0000-0003-0949-1558; Gilles PERNOD, CHU de Grenoble-Alpes, Grenoble, 0000-0001-6494-5984; Pierre-Marie ROY, Centre hospitalier universitaire, Angers, 0000-0003-4811-6793; Marie-Eve ROUGE BUGAT, Université Paul-Sabatier Toulouse III, 0000-0002-3562-5815; Olivier SANCHEZ, Hôpital européen Georges-Pompidou, Paris, 0000-0003-1633-8391; Jeannot SCHMIDT, CHU de Clermont-Ferrand, 0000-0003-3424-337X; Florian SCOTTE, Institut Gustave-Roussy, Villejuif; Marie-Antoinette SEVESTRE, CHU d'Amiens-Picardie, Amiens, 0000-0002-1779-6936.

Appendix B. INNOVTE CAT Reviewers

Rebecca AIM, Nice; Nadine AJZENBERG, Paris; Caroline DEHAIS, Paris; Audrey ECHE GASS, Toulouse; Ronan FLIPPOT, Villejuif; Alexandre GODON, Grenoble; Joseph GLIGOROV, Paris; Thibaut KUBIACK, Paris; Emilie LE RHUN, Lille; David MALKA, Paris; Alexandre MANSOUR, Rennes; Nicolas MENEVEAU, Besançon; Jean-Philippe METGES, Brest; Stéphane MOULY, Paris; Elena PAILLAUD, Paris; Marie-Eve ROUGE BUGAT, Toulouse; Arnaud SCHERPEREEL, Lille; Emeline TABOURET, Marseille; Charles-Ambroise TACQUARD, Strasbourg; Stéphanie TRÄGER, Paris.

Appendix C. Supplementary material

Supplementary material associated with this article can be found in the online version available at https://doi.org/10.1016/j.acvd.2023.11.005.

Disclosure of interest

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References

[1] Khorana AA, Mackman N, Falanga A, Pabinger I, Noble S, Ageno W, et al. Cancer-associated venous thromboembolism. Nat Rev Dis Primers 2022;8:11.
[2] Key NS, Khorana AA, Kuderer NM, Bohlke K, Lee AYY, Arcelus JI, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO Clinical practice guideline update. J Clin Oncol 2020;38:496–520.
[3] Sanchez O, Benhamou Y, Bertoletti L, Constant J, Couturaud F, Delluc A, et al. Recommendations of good practice for the management of thromboembolic venous disease in adults. Short version. Rev Mal Respir 2019;36:249–83.
[4] Mahé I, Meyer G, Girard P, Bertoletti L, Laporte S, Couturaud F, et al. French guidelines for the treatment of cancer-associated venous thromboembolism – 2023 update. Respir Med Res 2023;84:101056.
[5] Ades S, Holmes CE. Implementing guidelines to prevent cancer associated thrombosis: how can we do better? Res Pract Thromb Haemost 2023;7:100038.
[6] Farmakis IT, Barco S, Mavromanoli AC, Konstantinides SV, Valerio L. Performance status and long-term outcomes in cancer-associated pulmonary embolism: insights from the Hokusai-VTE cancer study. JACC CardioOncol 2022;4:507–18.
[7] Mahé I, Mayeur D, Couturaud F, Scotté F, Benhamou Y, Benmaziane A, et al. Anticoagulant treatment of cancer-associated thromboembolism. Arch Cardiovasc Dis 2024;117, http://dx.doi.org/10.1016/j.acvd.2023.11.010.
[8] Ikushima S, Ono R, Fukuda K, Sakayori M, Awano N, Kondo K. Trousseau's syndrome: cancer-associated thrombosis. Jpn J Clin Oncol 2016;46:204–8.
[9] Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. J Thromb Haemost 2007;5:632–4.
[10] Kahale LA, Hakoum MB, Tsolakian IG, Matar CF, Terrenato I, Sperati F, et al. Anticoagulation for the long-term treatment of venous thromboembolism in people with cancer. Cochrane Database Syst Rev 2018;6:CD006650.
[11] Napolitano M, Mansueto MF, Raso S, Siragusa S. Quality of life in patients with cancer under prolonged anticoagulation for high-risk deep vein thrombosis: a long-term follow-up. Clin Appl Thromb Hemost 2020;26 [1076029620918290].
[12] Zalunardo B, Panzavolta C, Bigolin P, Visonà A. Multidisciplinary care for the prevention and treatment of venous Thromboembolism in patients with cancer-associated thrombosis (CAT): impact of educational interventions on CAT-related events and on patients' and clinicians' awareness. Life (Basel) 2022;12:1594.
[13] Gartner J-B, Abasse KS, Bergeron F, Landa P, Lemaire C, Côté A. Definition and conceptualization of the patient-centered care pathway, a proposed integrative framework for consensus: a Concept analysis and systematic review. BMC Health Serv Res 2022;22:558.
[14] Jullian O, Cvetojevic D. Third French Cancer Plan: six years at the service of the French people. Bull Cancer 2021;108:117–24.
[15] Mauger C, Gouin I, Gueret P, Gac FN, Baillerie A, Lefeuvre C, et al. Impact of multidisciplinary team meetings on the management of venous thromboembolism. A clinical study of 142 cases. J Med Vasc 2020;45:192–7.
[16] Majeed J, Turner BS, Kelly D, Poon C, Thompson JA, Barrett J, et al. Implementing a clinical decision tool to improve oncologic venous thromboembolism management. J Adv Pract Oncol 2022;13:382–91.
[17] Rollet Q, Bouvier V, Moutel G, Launay L, Bignon A-L, Bouhier-Leporrier K, et al. Multidisciplinary team meetings: are all patients presented and does it impact quality of care and survival – a registry-based study. BMC Health Serv Res 2021;21:1032.
[18] Noble S, Pease N, Sui J, Davies J, Lewis S, Malik U, et al. Impact of a dedicated cancer-associated thrombosis service on clinical outcomes: a mixed-methods evaluation of a clinical improvement exercise. BMJ Open 2016;6:e013321.
[19] Lammila-Escalera E, Greenfield G, Barber S, Nicholls D, Majeed A, Hayhoe BWJ. A systematic review of interventions that use multidisciplinary team meetings to manage multimorbidity in primary care. Int J Integr Care 2022;22:6.
[20] Kapoor A, Landyn V, Wagner J, Burgwinkle P, Huang W, Gore J, et al. Supplying pharmacist home visit and anticoagulation professional consultation during transition of care for patients with venous thromboembolism. J Patient Saf 2020;16:e367–75.
[21] Easaw JC, McCall S, Azim A. ClotAssist: a program to treat cancer-associated thrombosis in an outpatient pharmacy setting. J Oncol Pharm Pract 2019;25:818–23.
[22] Holmes CE, Ades S, Gilchrist S, Douce D, Libby K, Rogala B, et al. Successful model for guideline implementation to prevent cancer-associated thrombosis: venous thromboembolism prevention in the ambulatory cancer clinic. JCO Oncol Pract 2020;16:e868–74.
[23] Benzidia I, Crichi B, Montlahuc C, Rafii H, N'Dour A, Sebuhyan M, et al. Effectiveness of a multidisciplinary care program for the management of venous thromboembolism in cancer patients: a pilot study. J Thromb Thrombolysis 2022;53:417–24.
[24] Sebuhyan M, Crichi B, Deville L, Le Maignan C, Bonnet C, Marjanovic Z, et al. Patient education program at the forefront of cancer-associated thrombosis care. J Med Vasc 2021;46:215–23.
[25] Potere N, Barco S, Mahé I, Cesarman-Maus G, Angchaisuksiri P, Leader A, et al. Awareness of venous thromboembolism among patients with cancer: preliminary findings from a global initiative for World Thrombosis Day. J Thromb Haemost 2022;20:2964–71.
[26] Mahé I, Chidiac J, Pinson M, Pinson M, Swarnkar P, Nelson A, et al. Patients experience of living with cancer associated thrombosis in France (Le PELICAN). Thromb Res 2020;194:66–71.
[27] Noble S, Prout H, Nelson A. Patients' experiences of living with cancer-associated thrombosis: the PELICAN study. Patient Prefer Adherence 2015;9:337–45.
[28] Noble S, Nelson A, Scott J, Berger A, Schmidt K, Swarnkar P, et al. Patient experience of living with cancer-associated thrombosis in Canada (PELICANADA). Res Pract Thromb Haemost 2020;4:154–60.
[29] Font C, Nelson A, Garcia-Fernandez T, Prout H, Gee P, Noble S. Patients' experience of living with cancer-associated thrombosis in Spain (PELICANOS). Supportive Care Cancer 2018;26:3233–9.

[30] Belhadj Chaidi R, Thollot C, Ferru A, Roblot P, Landron C. Adherence to guidelines for the treatment of venous thromboembolism in cancer patients: a retrospective analysis of 145 cases. J Mal Vasc 2013;38:185–92.
[31] Hutchinson A, Rees S, Young A, Maraveyas A, Date K, Johnson MJ. Oral anticoagulation is preferable to injected, but only if it is safe and effective: an interview study of patient and carer experience of oral and injected anticoagulant therapy for cancer-associated thrombosis in the select-d trial. Palliat Med 2019;33:510–7.
[32] Souliotis K, Golna C, Nikolaidi S, Dreden PV, Vatheia G, Gerotziafas GT. Public awareness on cancer-associated thrombosis among the greek population: first findings from the ROADMAP-CAT awareness study. TH Open 2022;6:e89–95.
[33] Falanga A, Girvalaki C, Monreal M, Easaw JC, Young A. How well do European patients understand cancer-associated thrombosis? A patient survey. Cancer Treat Res Commun 2022;31:100557.
[34] Cajfinger F, Debourdeau P, Lamblin A, Benatar V, Falvo N, Benhamou Y, et al. Low-molecular-weight heparins for cancer-associated thrombosis: adherence to clinical practice guidelines and patient perception in TROPIQUE, a 409-patient prospective observational study. Thromb Res 2016;144:85–92.
[35] Noble S, Matzdorff A, Maraveyas A, Holm MV, Pisa G. Assessing patients' anticoagulation preferences for the treatment of cancer-associated thrombosis using conjoint methodology. Haematologica 2015;100:1486–92.
[36] Picker N, Lee AY, Cohen AT, Maraveyas A, Beyer-Westendorf J, Mantovani LG, et al. Anticoagulation treatment in cancer-associated venous thromboembolism: assessment of patient preferences using a discrete choice experiment (COSIMO Study). Thromb Haemost 2021;121:206–15.
[37] Cohen AT, Maraveyas A, Beyer-Westendorf J, Lee AYY, Mantovani LG, Bach M, et al. COSIMO – patients with active cancer changing to rivaroxaban for the treatment and prevention of recurrent venous thromboembolism: a non-interventional study. Thromb J 2018;16:21.
[38] Riess H, Sinn M, Kreher S, für den Arbeitskreis Hämostaseologie der Deutschen Gesellschaft für Hämatologie und Medizinische O. CONKO-011: evaluation of patient satisfaction with the treatment of acute venous thromboembolism with rivaroxaban or low molecular weight heparin in cancer patients. A randomized phase III study. Dtsch Med Wochenschr 2015;140(Suppl. 1):S22–3.
[39] McBane 2nd RD, Wysokinski WE, Le-Rademacher JG, Zemla T, Ashrani A, Tafur A, et al. Apixaban and dalteparin in active malignancy-associated venous thromboembolism: the ADAM VTE trial. J Thromb Haemost 2020;18:411–21.
[40] Young AM, Marshall A, Thirlwall J, Chapman O, Lokare A, Hill C, et al. Comparison of an oral factor xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized trial (SELECT-D). J Clin Oncol 2018;36:2017–23.
[41] Scotte F, Leroy P, Chastenet M, Aumont L, Benatar V, Elalamy I. Treatment and prevention of cancer-associated thrombosis in frail patients: tailored management. Cancers (Basel) 2019;11:48.
[42] Wang TF. Drug-drug interactions: implications for anticoagulation, with focus in patients with cancer. Thromb Res 2022;213(Suppl. 1):S66–71.
[43] Peixoto de Miranda EJF, Takahashi T, Iwamoto F, Yamashiro S, Samano E, Macedo AVS, et al. Drug-drug interactions of 257 antineoplastic and supportive care agents with 7 anticoagulants: a comprehensive review of interactions and mechanisms. Clin Appl Thromb Hemost 2020;26 [1076029620936325].
[44] Di Minno A, Frigerio B, Spadarella G, Ravani A, Sansaro D, Amato M, et al. Old and new oral anticoagulants: food, herbal medicines and drug interactions. Blood Rev 2017;31:193–203.
[45] Kahn SR, Springmann V, Schulman S, Martineau J, Stewart JA, Komari N, et al. Management and adherence to VTE treatment guidelines in a national prospective cohort study in the Canadian outpatient setting. The Recovery Study. Thromb Haemost 2012;108:493–8.
[46] Rahme E, Feugère G, Sirois C, Weicker S, Ramos E. Anticoagulant use in patients with cancer associated venous thromboembolism: a retrospective cohort study. Thromb Res 2013;131:210–7.
[47] Kaatz S, Fu A-C, AbuDagga A, LaMori J, Bookhart BK, Damaraju CV, et al. Association between anticoagulant treatment duration and risk of venous thromboembolism recurrence and bleeding in clinical practice. Thromb Res 2014;134:807–13.
[48] Sevestre MA, Belizna C, Durant C, Bosson JL, Vedrine L, Cajfinger F, et al. Compliance with recommendations of clinical practice in the management of venous thromboembolism in cancer: the CARMEN study. J Mal Vasc 2014;39:161–8.
[49] Mahé I, Sterpu R, Bertoletti L, López-Jiménez L, Mellado Joan M, Trujillo-Santos J, et al. Long-term anticoagulant therapy of patients with venous thromboembolism. What are the practices? PLoS One 2015;10:e0128741.
[50] Mahé I, Puget H, Buzzi JC, Lamuraglia M, Chidiac J, Strukov A, et al. Adherence to treatment guidelines for cancer-associated thrombosis: a French hospital-based cohort study. Supportive Care in Cancer 2016;24:3369–77.
[51] Mahé I, Chidiac J, Helfer H, Noble S. Factors influencing adherence to clinical guidelines in the management of cancer-associated thrombosis. J Thromb Haemost 2016;14:2107–13.
[52] van der Wall SJ, Klok FA, den Exter PL, Barrios D, Morillo R, Cannegieter SC, et al. Continuation of low-molecular-weight heparin treatment for cancer-related venous thromboembolism: a prospective cohort study in daily clinical practice. J Thromb Haemost 2017;15:74–9.