

# Cancer patients' experiences of living with venous thromboembolism: A systematic review and qualitative thematic synthesis

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## Abstract

**Background:** Cancer-associated thrombosis is common. Recommended treatment is daily injected low-molecular-weight heparin for 6 months. Most studies focus on prophylaxis and treatment; few have explored the patients' experience.

**Aims:** To identify and synthesise the available literature concerning patients' experience of cancer-associated thrombosis.

**Design:** Systematic literature review and qualitative thematic synthesis.

**Data source:** MEDLINE, Embase, CINAHL, PsycINFO (until 10/2016; limited to English) were searched. Eligible papers were qualitative studies of adult patients' experience of cancer-associated thrombosis. Two researchers screened titles/abstracts/papers against inclusion criteria with recourse to a third for disagreements. Critical Appraisal Skills Programme qualitative checklist tool was used for quality appraisal.

**Results:** A total of 1397 articles were identified. Five qualitative studies (total  $n = 92$ ; age range 32–84 years) met the inclusion criteria. Participants had various cancer types. Most had advanced disease and were receiving palliative care. Four major themes emerged from the data: knowledge deficit (patients and clinicians), effects of cancer-associated thrombosis (physical and psychological), effects of anticoagulation and coping strategies.

**Conclusion:** The cancer journey is difficult in itself, but thrombosis was an additional, frightening and unexpected burden. Although the association between cancer and thromboembolism is well-known, cancer patients are not routinely educated about the risk or warning symptoms/signs of thromboembolism which may otherwise be misattributed to the cancer by patient and clinician alike. This systematic review highlights the impact of cancer-associated thrombosis on the lives of cancer patients, and calls for education for patients and clinicians to be part of routine care and further work to address this patient priority.

## Keywords

Venous thromboembolism, qualitative, patient experience, cancer-associated thrombosis

### What is already known about the topic?

- Cancer-associated thrombosis is a common complication related to cancer itself as well as to cancer treatments that affects nearly 50% of cancer patients.
- The optimal treatment of cancer-associated thrombosis requires long-term anticoagulation that associated in many cases with high risk of bleeding, reoccurrences of thrombosis and low survival rate.

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**What is not known about the issue?**

- The patients' experiences of living with cancer and thrombosis.

**What this paper adds?**

- This systematic review highlights the impact of cancer-associated thrombosis on cancer patients' lives.

**Implications for practice, theory or policy**

- This article calls for education for patients and clinicians to be part of routine care and further work to address this patient priority equal to that of other cancer complications such as spinal cord compression or neutropenic sepsis.

## Introduction

Venous thromboembolism is a life-changing diagnosis. Comprising deep vein thrombosis and pulmonary embolus, it is a common phenomenon worldwide. It affects one in 1000 patients – 6.5 million people globally each year.<sup>1,2</sup> The risk of venous thromboembolism increases by six folds to sevenfold in patients with cancer compared with non-cancer patients.<sup>3,4</sup> Approximately, 20% of all newly diagnosed cases of venous thromboembolism are cancer patients,<sup>5</sup> and post-mortem studies have demonstrated rates of venous thromboembolism in patients with cancer to be as high as 50%.<sup>6</sup> Up to 20% of patients with malignancy will develop cancer-associated thrombosis.<sup>5</sup>

Although the risk increases with late-stage and during chemotherapy, over 50% of venous thromboembolism occurs during the first 3 months from diagnosis<sup>3</sup> and interferes with cancer management.<sup>6</sup>

International guidelines for the treatment of cancer-associated thrombosis recommend anticoagulation with weight-adjusted low-molecular-weight heparin for 3–6 months.<sup>7–9</sup> However, even with an optimal anticoagulation, cancer-associated thrombosis is associated with a higher recurrence rate than non-cancer venous thrombosis and a poorer prognosis than cancer patients without thrombosis.<sup>10–12</sup>

Apart from conferring a worse prognosis, the diagnosis of venous thromboembolism is a physically and emotionally distressing phenomenon that affects patients' experience and quality of life.<sup>13,14</sup>

Systematic reviews and meta-analysis on cancer-associated thrombosis are limited to biomolecular markers associated with cancer-associated thrombosis<sup>15,16</sup> risk assessment of venous thromboembolism in cancer patients<sup>17,18</sup> or both,<sup>19</sup> clinical outcome, thromboprophylaxis,<sup>20</sup> management<sup>21–23</sup> and risk stratification.<sup>24</sup>

In order to improve our understanding and raise awareness of cancer-associated thrombosis and to stimulate improvements in the supportive care of cancer patients, we undertook a systematic literature review to answer the following question, 'what is the experience of people living with cancer-associated thrombosis?'

## Methods

### Search strategy

Two independent researchers conducted the search (N.B.B. and M.W.I.). MeSH terms and text words for cancer, venous thromboembolism and quality of life (see Supplementary Table 1) were combined. The following electronic databases were searched: Embase, MEDLINE, CINAHL and PsycINFO, until October 2016 and limited to English language, according to a pre-constructed protocol. In addition, an online search was performed for the following journals: *Journal of Thrombosis Haemostasis* (ISTH/JTH) and *Thrombosis Research and Haematologica*. Bibliographies from relevant articles were examined for further related studies.

### Inclusion criteria

Studies of adult cancer patients with venous thromboembolism with or without treatment for the venous thromboembolism were included. The review included qualitative studies that assessed the quality of life or experience of this group of patients.

### Study selection

The titles, abstracts and full studies were screened by two independent researchers (N.B.B. and M.W.I.) against the inclusion criteria. Disagreement was resolved by discussion with access to a third opinion (M.J.J.). Studies that matched the selection criteria were retrieved and their full text version analysed.

### Data extraction

Data were extracted by N.B.B.; demographics of the included papers (author, year, design, population, question, main findings) and the primary quotations presented in the results.

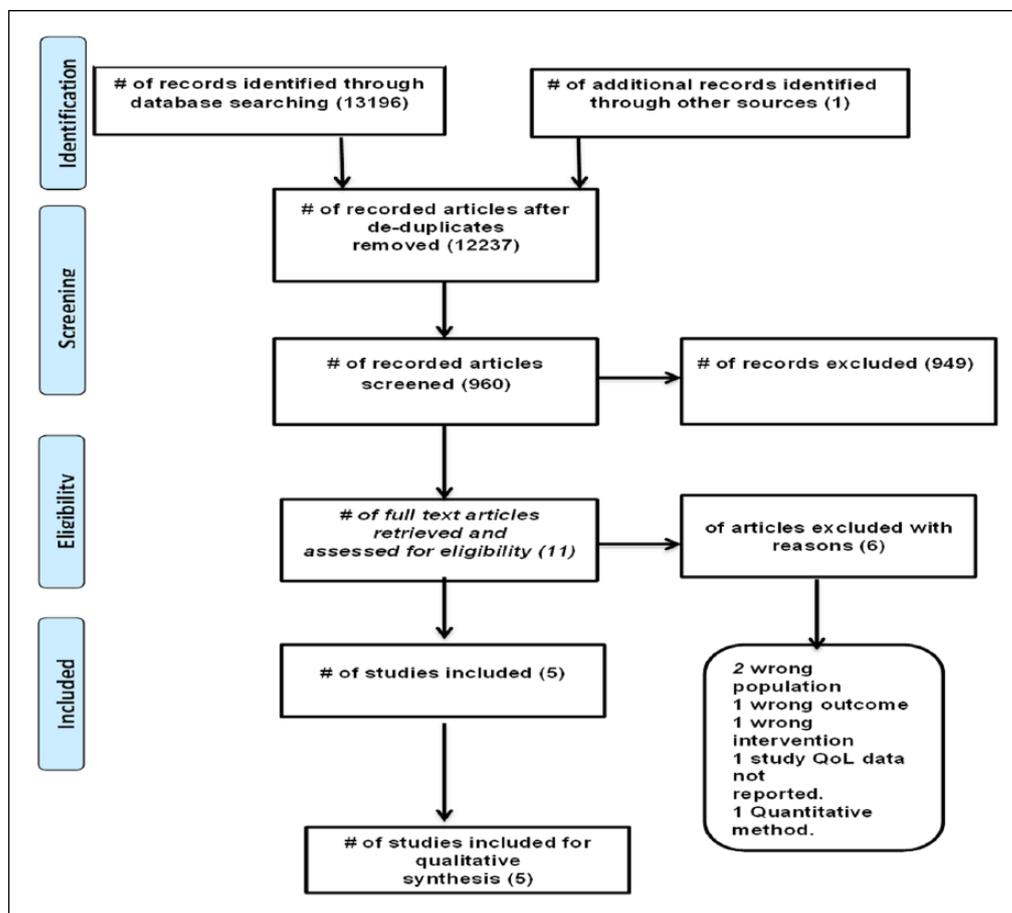


Figure 1. PRISMA flow diagram.

### Quality appraisal

All articles were assessed against the Critical Appraisal Skills Programme checklist tool for qualitative studies by N.B.B. and M.W.I. independently.<sup>25</sup> Studies were not excluded on the basis of quality, but the assessment of quality was taken into account during analysis.

### Analysis

The primary quotation data were synthesised by N.B.B. using thematic synthesis<sup>26</sup> and the principles of thematic analysis used to explore the understanding of long-term effects of venous thromboembolism on cancer patient's life quality.<sup>27</sup> This allows the context of each study to be taken into account while aiming to produce a generalisable synthesis.<sup>28</sup> Direct quotes from patients and the researcher comments under the headings 'results, findings, or discussion' from each study were extracted for coding.

Thematic synthesis involved the following: line-by-line coding of the findings of primary articles after reading and rereading of the papers to get familiarised with the data included, then the codes were discussed with M.J.J. and a coding framework formed which was used to code all

papers followed by development of descriptive and analytical themes from the codes, in discussion with M.J.J. and J.D.S.<sup>29</sup> Both inductive (allowing themes to arise from the specific observations) and deductive (working within existing knowledge about the effect of venous thromboembolism on people without cancer, looking specifically within our data for similarities and differences) processes were involved.

## Results

### Overview of articles

The search identified a total 13,197 articles: Embase (11,632), MEDLINE (1272), CINAHL (254) and PsycINFO (38) articles. One additional article was identified through searches of relevant bibliographies. A total of 11 full articles were retrieved and assessed for eligibility; 6 articles were excluded following review. This is summarised in the PRISMA flow diagram (Figure 1).

Five qualitative studies published between 2005 and 2015 met the inclusion criteria. Four of them were conducted in the United Kingdom. The key characteristics of the studies are summarised in Table 1.

**Table 1.** Overview of the articles included.

Study	Study design	Methods and settings	Aim	Participants' characteristics	Analysis	Principal findings
Noble and Finlay <sup>20</sup>	Qualitative	Semi-structured interview; palliative care patients, both in the community and in-patient units – Cardiff, UK.	Assessing the appropriateness of low-molecular-weight heparin in palliative care patients and the extent of daily injection burden.	N = 40 (18 male and 22 female); Aged 32–76 years; Advanced cancer, receiving low-molecular-weight heparin for confirmed cancer-associated thrombosis; In total, 33 patients had initially received warfarin then changed to low-molecular-weight heparin due to poor control. N = 10 (4 women and 6 men); Aged 35–78 years; Various cancer types diagnosed 2–18 months prior to the interview; Various stages from early with active treatment to advanced stage.	Thematic analysis	Acceptability – all patients understood why they are on low-molecular-weight heparin and considered it acceptable. Simplicity – the majority found that daily injection of low-molecular-weight heparin simpler than the frequent INR needed for warfarin. Freedom – many patients expressed a feeling of freedom from hospitals, from being restricted to their home. Optimism – the feeling that something active being done. Bruising – a total of 11 patients described bruising as a negative aspect of low-molecular-weight heparin.
Mockler et al. <sup>31</sup>	Qualitative	Semi-structured interview; inpatients and outpatients of a large urban university-affiliated hospital – Montreal, Canada.	Exploring the experiences of patients with cancer who developed venous thromboembolism.		Thematic analysis	Coping with venous thromboembolism: Prior knowledge of cancer-associated thrombosis risk and symptoms (or lack of knowledge) determined reaction to cancer-associated thrombosis symptoms. For some, cancer-related concerns overshadowed those due to cancer-associated thrombosis. Cancer-associated thrombosis as a setback in cancer care: Cancer-associated thrombosis symptoms preventing a return to normal life after cancer treatment; Cancer-associated thrombosis treatment interfering with their cancer care; Attitudes about venous thromboembolism treatments: Positive for some participants however associated with a sense of obligation; Many show acceptance of self-injection of low-molecular-weight heparin especially among those with previous experience with warfarin.
Seaman et al. <sup>32</sup>	Qualitative	Semi-structured interview; palliative care and cancer-associated thrombosis unit – Cardiff, UK.	Exploring the acceptability of long-term low-molecular-weight heparin for the treatment of cancer-associated thrombosis in the contexts of living with cancer and quality of life.	N = 14 (8 women and 6 men) Aged 52–84 years Receiving low-molecular-weight heparin for confirmed venous thromboembolism (pulmonary embolism = 8/deep vein thrombosis = 6); A total of eight patients were on warfarin then changed to low-molecular-weight heparin.	Thematic analysis	Impact of venous thromboembolism: Symptom burden of cancer-associated thrombosis; Cancer-associated thrombosis (CAT) in context of cancer; Impact on activities of daily living. Acceptability of low-molecular-weight heparin: Necessary inconvenience; Systematic approach to injection. Hypothetical views on new oral anticoagulants: Efficacy paramount; Willing to engage in clinical trials.

Table 1. (Continued)

Study	Study design	Methods and settings	Aim	Participants' characteristics	Analysis	Principal findings
Noble et al. <sup>13</sup> PELICAN (Patients' Experiences of Living with CANcer-associated thrombosis)	Qualitative	Semi-structured interview; cancer-associated thrombosis clinic within regional cancer centre and district general hospital – Cardiff, UK.	Exploring the patients experiences of cancer-associated thrombosis within the context of cancer journey.	N = 20 patients (10 women and 10 men); Aged 53–81 years; Different primary cancers receiving low-molecular-weight heparin for (2–20 months).	Framework analysis	Diagnosis and treatment of cancer-associated thrombosis: Lack of knowledge of venous thromboembolism in the context of cancer, patients unaware of risks of thrombosis or symptoms to look out for; Limited awareness among health professionals; Symptoms of cancer-associated thrombosis attributed to cancer or chemotherapy and therefore delayed presentation to hospital; Initial reaction is shock, little information. Living with cancer-associated thrombosis: Treatment helps get over the initial shock, getting on with life, ritualisation of new routines.
Noble et al. <sup>23</sup> ALICAT	Embedded qualitative study within a RCT	Focus groups with clinicians; semi-structured interviews with patients and their relatives.	Explore clinicians' attitudes/patients' and their relatives' experiences towards the RCT of ongoing low-molecular-weight heparin treatment for cancer-associated thrombosis versus cessation at 6 months in patients with locally advanced or metastatic cancer; patients' perception of cancer-associated thrombosis and anticoagulation.	N of clinician = 3–11/group (three focus group); Oncology, haematology and primary care; N of patients = 8 (4 females); Locally advanced or metastatic cancer. Receiving low-molecular-weight heparin for cancer-associated thrombosis.	Framework analysis	The study adds further information on cancer patients' decisions to continue or stop low-molecular-weight heparin treatment is highly influenced by their experience of symptomatic venous thromboembolism versus asymptomatic; Patients with experience of symptomatic cancer-associated thrombosis were willing and keen to continue on low-molecular-weight heparin injection as long as it takes; Patients who had a symptomatic cancer-associated thrombosis were keen to stop low-molecular-weight heparin injection as soon as possible aiming to have some normality back.

RCT: randomised control therapy; ALICAT: Anticoagulation with Low-molecular-weight heparin In the treatment of Cancer-Associated Thrombosis, PELICAN: Patients' Experiences of Living with CANcer-associated thrombosis.

## Study populations

A total of 92 cancer patients with venous thromboembolism were included in these studies. All were adult patients of mixed gender with mean age of 58 years (range 32–84). Participants represent a wide variety of cancer types and stage. The most cancers were breast, colorectal, ovary, lung, prostate, pancreas and renal.

## Themes

Four major themes were identified: knowledge deficit, the effects of cancer-associated thrombosis (physical and psychological effects), the effects of cancer-associated thrombosis treatments and coping strategies.

## Knowledge deficit

Two studies investigated the patients' knowledge about cancer-associated thrombosis in the context of cancer journey.<sup>13,31</sup>

Despite the fact that cancer-associated thrombosis may develop as early as the first few months of diagnosis of cancer and that the risk is increased with cancer treatments (chemotherapy, surgery and hospitalisation), disease progression participants were often not aware of their increased risk or of the warning symptoms of cancer-associated thrombosis:

During my cancer treatments, I was never told that there was a risk of getting a blood clot. I didn't know about it... I was pretty shaken up.<sup>31</sup>

I have never heard of venous thromboembolism, so that's why I was so shocked.<sup>31</sup>

[...] but they don't tell you you're gonna get clots after chemo, that's the one thing they haven't, they never said but we, we just put it down to, it's just my breathing [...] just that one item of information that we weren't aware of. (VCC07)<sup>13</sup>

Moreover, patients on chemotherapy usually experienced different side effects, when they develop a venous thromboembolism, they associate it with chemotherapy and do not recognise that their symptoms are symptoms of a venous thromboembolism:

[...] but um this time again first set of chemo, she felt terrible and the thing is, when we went back to hospital really desperate, the only problem we thought was that it was the chemotherapy that was causing it. (RG02)<sup>13</sup>

However, participants with prior knowledge about venous thromboembolism respond in calm and seek medical help immediately:

I was out of breath and I said to my partner, 'I think we are going to hospital, without panic because I knew that it was something that could be rectified effectively.'<sup>31</sup>

There was also evidence of limited awareness about venous thromboembolism and cancer among healthcare professionals.<sup>13</sup> This is consistent with patient reports of delayed diagnosis of the venous thromboembolism; on many occasions, alternative causes were considered first:

It just got bigger and bigger and bigger, over months really [...] then they doubled them (diuretics), and then they trebled them. (RG05)<sup>13</sup>

## Effects of cancer-associated thrombosis

The effects of cancer-associated thrombosis theme include three subthemes (responses to venous thromboembolism diagnosis, psychological and physical effects).

## Effects of diagnosis process

Patients' perspective on cancer-associated thrombosis diagnosis varied. Some participants reacted to the diagnosis of cancer-associated thrombosis as an entity distinct to the cancer, while others considered cancer-associated thrombosis as a complication of their cancer. However, in both cases, the diagnosis of cancer-associated thrombosis had a negative impact; it led to delays in cancer treatment and added more burden to their health:

Having the cancer and then the thrombosis on top of it, not knowing how bad it was.<sup>13</sup>

The fact that there were clots meant we couldn't operate on my leg. Not being able to operate my leg pushed back my radiation and chemotherapy. So everything was shifted in time.<sup>31</sup>

## Psychological effects

Four studies reported that the diagnosis of cancer-associated thrombosis was distressing, especially in those without prior knowledge of the symptoms had a major impact on patients' lives and was perceived as life threatening.<sup>13,31–33</sup>

PE is not cancer but it's dangerous too, because with both you are playing with your life.<sup>31</sup>

I felt I was having a heart attack...that stress made (the symptoms) worse.<sup>31</sup>

[...] having the cancer and then the thrombosis on top of it, erm, not knowing how bad it was when I went in, I know I was in terrific pain with my chest and that erm, it was frightening to be honest. (VCC01)<sup>13</sup>

It frightened the life out of me, I was more scared of that than the cancer. You know blood clots can kill you like that (clicks fingers), cancer you've got a little bit of chance, you know. (PT13)<sup>32</sup>

The response to the diagnosis was less stressful among participants with previous experience of venous thromboembolism who reported being calm and not shocked:

Knowing [that it is a PE] reassures you a little, nevertheless ... I knew I need to go to the hospital as fast as possible.<sup>31</sup>

Wouldn't be the main thing that did it was to calm apprehension basically about the clot and if a clot does occur it hits you like that bang. (Interview NC5)<sup>33</sup>

### Physical effects

The acute and chronic symptoms of cancer-associated thrombosis were profound and negatively affected patients' lives. Mockler et al.<sup>31</sup> and Seaman et al.<sup>32</sup> described the negative impact of symptoms that interfered with patients' daily living.

In particular participants with pulmonary embolism described that being short of breath prevented them from completing even small tasks at home. Symptoms from cancer-associated thrombosis prevented them from returning to normal life and activities – unable to do daily activities around the house or to mobilise unaided:

I cannot do anything...will I always continue heading in this regression.<sup>31</sup>

The lack of energy and being out of breath...it's just so frustrating ... Frustration of not being able to be where I should be, in my mind.<sup>31</sup>

I couldn't breathe; I literally couldn't breathe and couldn't talk. (PT6)<sup>32</sup>

I was very breathless, even bending down to the washing machine to put a wash in I was gasping for air. (PT11)<sup>32</sup>

### Effects of treatments of venous thromboembolism

This theme captured patients' experience of anticoagulation treatment (self-injected weight-adjusted low-molecular-weight heparin, warfarin and direct oral anticoagulants). Four studies assessed patients' responses to anticoagulation focusing on the acceptability of low-molecular-weight heparin.<sup>31–33</sup> It was clear that the treatment had a positive effect on patients' life, especially, for those who had experienced distressing symptoms.

Most participants were started on low-molecular-weight heparin, and others had been on warfarin but changed to low-molecular-weight heparin due to absorption difficulties, uncontrolled INR (the international

normalized ratio) and/or venous thromboembolism recurrence. There was a general agreement by patients that low-molecular-weight heparin was acceptable treatment and better than warfarin where comparison was possible. Self-injected low-molecular-weight heparin allowed more self-control over their life and more freedom. However, this benefit was not without compromise, as side effects of bruising and injection-site lumps were common:

The heparin is so much simpler than all the \*\*\*\*ing about with warfarin'. (22CS)<sup>30</sup>

I really don't feel like pricking myself, but if it's that or dying well I'd rather prick myself.<sup>31</sup>

I used to spend my life travelling to hospital for a warfarin check ... sat in the car ... sat in the waiting room ... not much of a life really. (19CS)<sup>30</sup>

With the warfarin, what was kind of crappy was that I had to do blood tests every two weeks. But with Low Molecular Weight Heparin no need for draws.<sup>31</sup>

I'm using the tops of my legs now so it isn't as painful. I was using my stomach but after a while your stomach gets really hard and then you've got to really force them in. (PT8)<sup>32</sup>

Those with advanced disease felt that treatment of their cancer-associated thrombosis with optimal anticoagulation meant that their doctors did not give up on them, influencing their optimism and expectation of their doctors:

I know I'm going to die. I know that the doctors don't have any more chemo to give ... you don't like feeling that you've been put on the scrap heap ... the injection isn't stopping the cancer but it is stopping the blood clots. (14CS)<sup>30</sup>

It is important to know that people are still doing something. (15C)<sup>30</sup>

Some patients wish to take low-molecular-weight heparin for longer than 6 months as long because of the continued risk and the peace of mind they felt with ongoing anticoagulation. This is expressed clearly by a patient in the Anticoagulation with Low-molecular-weight heparin in the treatment of Cancer-Associated Thrombosis (ALICAT) study where views were sought on being randomised to continuation or cessation:

The thing that bothered me at that time was that I'd already had two episodes of a blood clot and I thought if I was in the group that didn't have the medication um there was a good chance that I'd have another one and it could have a lot more serious repercussions than if I just continued to take this medication. (Interview NC3)<sup>33</sup>

Um I thought no I think I'll carry on rather than, you know, spending another day in hospital being prodded and probed like I was last time. (Interview NC2)<sup>33</sup>

However, some patients wanted to stop low-molecular-weight heparin injection after 6 months because of the side effects of the injections and others wanted to restore their normal life without injections:

I was just happy to get off of it to be honest with you, um it was more or less the same time every night, um and the pain as I said eh to me was terrible, horrific and a lot of bruising and things. (Interview NC1)<sup>33</sup>

And so I was very keen I have to say, I was predisposed I don't want any further injections once the treatments finished I just want to try to get back to as much normality as I can. (Interview NC8)<sup>33</sup>

### *Employment of coping mechanisms*

It was clear that the response to the dual diagnosis of cancer and cancer-associated thrombosis was very individual, with some regarding it as a greater shock than their cancer, particularly among patients who considered cancer-associated thrombosis as a setback on the road to cancer recovery and others viewing it as less significant in comparison with their cancer:<sup>31</sup>

I never broke down when I was told about the cancer [...] I had the operation, went on the chemo, everything. The only time I broke down was when I went back in hospital when they told me I had blood clots [...] the cancer to a point they can treat, hold it back – blood clots they go so quick and that frightened me, it was the only time I broke down. (PT13)<sup>32</sup>

During chemotherapy, I didn't have any great nausea, and brachytherapy went well too. So I told myself, 'Well, I'm going to overcome the cancer but No! Then I started to go down again'.<sup>31</sup>

The employment of coping mechanisms theme illustrated ways that patients developed to move on with their lives. The treatment of venous thromboembolism brings with it symptomatic relief, reassuring patients that their condition is improving. This reduces distress and allows patients, over time, to get back to 'some sort of normality'.<sup>13</sup> Participants described the development of strict routines and rituals to ensure low-molecular-weight heparin was administered on time and without fail:<sup>32</sup>

I usually take them between 8 and half past 8. And then I know it's done, and I don't forget for the day, then, because someone I was talking to, he was saying 'You don't do it in the night, do you?' and I said, 'No, I get up, have my cup of tea then 8, half past 8 do it'. (PT13)<sup>32</sup>

[...] is a ritual now. (VCC10)<sup>13</sup>

## **Discussion**

The cancer journey is difficult in itself, but thrombosis was an additional, frightening and unexpected burden. The association between cancer and venous thromboembolism was first reported in the 19th century.<sup>34</sup>

However, cancer patients are still not routinely educated about the risk or warning symptoms/signs of venous thromboembolism which may otherwise be misattributed to the cancer by patient and clinician alike.

This systematic review highlights the impact of cancer-associated thrombosis on the lives of cancer patients, and calls for education for patients and clinicians to be part of routine care and further work to address this patient priority.

The four themes from this synthesis of primary qualitative studies (knowledge deficit, effects of cancer-associated thrombosis, effects of anticoagulation and employment of coping mechanisms) illustrate the ways in which cancer-associated thrombosis affects quality of life. Thrombosis with its complex presentation, diagnosis and treatment was seen by many patients as a significant additional, frightening and unexpected burden affecting cancer treatment and which impose psychosocial and functional limitations.

### *Lack of knowledge of cancer-associated thrombosis*

A survey of cancer patients found a better level of knowledge of cancer-associated thrombosis risk than those in this review, but still half (53%) of participants were unaware of the increased risk of cancer-associated thrombosis although three quarters knew that venous thromboembolism can be prevented.<sup>35</sup>

Even though the cancer-associated thrombosis is not a new phenomenon, a lack of clinician awareness of cancer-associated thrombosis appears to compound the lack of patient knowledge.<sup>36,37</sup> In a study of 18 patients who had had venous thromboembolism (not cancer-related), misdiagnosis and diagnostic delay made patients feel angry and distrustful of their medical team.<sup>38</sup> However, similar to Mockler et al.'s<sup>26</sup> study of people with cancer-associated thrombosis, patients with a previous history of venous thromboembolism were less distressed, having recognised the symptoms and sought medical help more quickly.<sup>31</sup>

This lack of routine information-giving is in contrast to other cancer-related complications such as malignant spinal cord compression and post-chemotherapy neutropenia, where guidelines are systematically applied for patients and their family, and carers. Education includes the symptoms and signs to look for, when to seek medical help and who to contact.<sup>39,40</sup>

Inadequate information-giving is not new.<sup>41</sup> However, people with venous thromboembolism appear clear about

the degree of information they need including understanding their diagnosis, what they should do/not to do from diagnosis and with treatment.<sup>42</sup> Information needs are individual and vary by gender, age and stage of disease; some wishing for full details, others want basic information only.<sup>43</sup>

### *Psychological burden*

The long-term outcomes following acute venous thromboembolism extend beyond the physical burden<sup>44,45</sup> and the experience of symptomatic pulmonary embolism is a life-changing, distressing and frightening event.<sup>42</sup> Similar psychological effects were seen in this review, but in addition, cancer patients have to process this event in the context of the underlying cancer. For some, the potential of cancer-associated thrombosis as a sudden killer came as a great shock, especially those who had viewed their cancer as a chronic illness.

### *Effects of treatments of cancer-associated thrombosis*

Seaman et al.<sup>32</sup> found that efficacy of treatment was paramount despite the hypothetical preference of a tablet over an injection. This finding was also highlighted in the study by Noble et al,<sup>46</sup> where patients were concerned about safety, efficacy and lack of interference with anticancer therapies ahead of method of administration. Patients in this review included those with advanced disease, but despite previously stated concerns about patient burden with low-molecular-weight heparin,<sup>47</sup> the use of low-molecular-weight heparin was acceptable. The daily injections of precalculated dose of low-molecular-weight heparin give more control than the blood tests and dose alterations of warfarin.

### *Employment of coping mechanisms*

Patients tried to maintain a sort of normality in everyday life consistent with previous findings that cancer patients find ways to minimise the impact of the side effects of cancer in their new life situation.<sup>44</sup>

Education and support is important with regard to coping. One of the earliest reported educational group programmes for people with cancer was the 'I Can Cope' programme.<sup>48</sup> This has been well evaluated showing reduced anxiety, improved disease-related knowledge and sense of meaning.<sup>49</sup>

### *Uncertainty and information*

The varying responses to the threat of cancer-associated thrombosis and its treatment seem to be related to uncertainty as to whether the cancer-associated thrombosis will

recur, whether it will resolve, whether the treatment will be effective and/or harmful. Uncertainty management theory<sup>50,51</sup> is one theoretical framework to help the understanding of how patients encounter, appraise levels of danger, seek information, respond to and cope with health-related threats. The differing needs for information, ways of seeking it and success in receiving it are seen within these data presented. Likewise, some patients appraised the cancer-associated thrombosis as very dangerous, whereas others (often those with previous experience and better information) were able to appraise it as less dangerous because they knew what to look for and how to act. While the relationship between uncertainty and danger appraisal is complex, tailored and accessible information seems to play a key part in reducing anxiety even if absolute reassurances cannot be given.<sup>52,53</sup> As Brashers<sup>50</sup> states, uncertainty occurs when, 'information is unavailable or inconsistent; and when people feel insecure in their own state of knowledge or the state of knowledge in general'.

### *Strengths and limitations*

As with any systematic review, it is possible to miss relevant studies. The included studies were qualitative research which is designed to give insights from the patients involved rather than to be generalisable. However, through synthesis, more generalisable findings can be derived.<sup>26</sup> Only one included study came from outside the United Kingdom, however, they were from different centres, but still indicated similar concerns.

Only limited papers were found, illustrating that this area has been under-researched. The serious concerns highlighted by this review show that further work is needed.

### *Implications for clinical practice and policy makers*

Raised clinical awareness and the provision of basic information for patients about the risk of cancer-associated thrombosis is a policy priority in the United Kingdom.<sup>54</sup> Information about cancer-associated thrombosis, both written and verbal, should be provided routinely for patients at diagnosis.

Cancer-associated thrombosis should be part of standard training and education for all clinicians caring for people with cancer, including those in primary and palliative care.

Recent initiatives such as the International Initiative on Thrombosis and Cancer<sup>55</sup> should help raise awareness and help with high-quality training. Streamlined clinical services for diagnosis and treatment of cancer-associated thrombosis aiming to minimise time in hospital awaiting tests, especially for those with advanced disease, should improve clinical decision-making.<sup>37,56,57</sup>

## Conclusion

This systematic review highlights the impact of cancer-associated thrombosis on the lives of cancer patients, and calls for education for patients and clinicians to be part of routine care and further work to address this patient priority equal to that of other cancer complications such as spinal cord compression or neutropenic sepsis.

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## Data sharing

Data are available from the published papers in this review.

## Declaration of conflicting interests

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