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Cancer patients' experiences of living with venous thromboembolism: A Systematic review and qualitative Thematic synthesis

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1 **Abstract**

2

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

6 **Aims**

7 To identify and synthesise the available literature concerning patients' experience of cancer
8 associated thrombosis.

9

10 **Design**

11 Systematic literature review and qualitative thematic synthesis.

12 **Methods**

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

18

19 **Results**

20 1397 articles were identified. Five qualitative studies (total n=92; age range 32 to 84 years) met the
21 inclusion criteria. Participants had various cancer types. Most had advanced disease and were
22 receiving palliative care. Four major themes emerged from the data: knowledge deficit (patients and
23 clinicians); effects of cancer associated thrombosis (physical and psychological); effects of
24 anticoagulation; coping strategies.

25

26 **Conclusion**

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

34

1 **Key words:** Venous thromboembolism, qualitative, patient experience, cancer-associated-

2 thrombosis

3

1 INTRODUCTION

2 Venous thromboembolism is a life changing diagnosis. Comprising deep vein thrombosis and
3 pulmonary embolus it is a common phenomenon worldwide. It affects one in 1,000 patients; 6.5
4 million people globally each year(1, 2). The risk of venous thromboembolism increases by 6-7 folds in
5 patients with cancer compared with non-cancer patients (3, 4). Approximately 20% of all newly
6 diagnosed cases of venous thromboembolism are cancer patients (5), and post-mortem studies have
7 demonstrated rates of venous thromboembolism in patients with cancer to be as high as 50%(6)
8 Up to 20% of patients with malignancy will develop cancer-associated thrombosis (5)
9 Although the risk increases with late-stage and during chemotherapy, over 50% of occurs during the
10 first three months from diagnosis(3) and interferes with cancer management(6).

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

16 Apart from conferring a worse prognosis, the diagnosis of venous thromboembolism is a physically
17 and emotionally distressing phenomenon that affects patients' experience and quality of life (13, 14).
18 However, data available on how cancer associated thrombosis and its treatment affect the cancer
19 patients' experience is scarce compared with that in relation to treatment or prevention.

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

24

1 In order to improve our understanding and raise awareness of cancer associated thrombosis and to
2 stimulate improvements in the supportive care of cancer patients, we undertook a systematic
3 literature review to answer the following question, “ what is the experience of people living with
4 cancer associated thrombosis?
5

6 **METHODS**

7 **Search strategy**

8 Two independent researchers conducted the search (NB, WI). MeSH terms and text words for
9 cancer, venous thromboembolism and quality of life (see supplementary Table 1) were combined.
10 The following electronic databases were searched: Embase, MEDLINE, CINAHL, and PsychINFO, until
11 October 2016 and limited to English language, according to a pre-constructed protocol. In addition
12 an online search was performed for the following journals: Journal of Thrombosis Hemostasis
13 (ISTH/JTH), Thrombosis Research and Hematologica. Bibliographies from relevant articles were
14 examined for further related studies.

15 **Inclusion criteria**

16

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

20 **Study selection**

21

22 The titles, abstracts and full studies were screened by two independent researchers (NB, WI) against
23 the inclusion criteria. Disagreement was resolved by discussion with access to a third opinion (MJ).
24 Studies that matched the selection criteria were retrieved and their full text version analysed.
25

1 **Data extraction**

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

4 **Quality Appraisal**

5 All articles were assessed against the Critical Appraisal Skills Programme (CASP) checklist tool for
6 qualitative studies by NB and WI independently (25). Studies were not excluded on the basis of
7 quality, but the assessment of quality was taken into account during analysis.

8 **Analysis**

9 The primary quotation data were synthesised by NB using thematic synthesis (26) and the principles
10 of thematic analysis to explore the understanding of long term effects of venous thromboembolism
11 on cancer patient's life quality(27). This allows the context of each study to be taken into account
12 whilst aiming to produce a generalizable synthesis(28). Direct quotes from patients and the
13 researcher comments under the headings "results, findings, or discussion" from each study were
14 extracted for coding.

15 Thematic synthesis involved: line by line coding of the findings of primary articles after reading and
16 rereading of the papers to get familiarised with the data included, then the codes were discussed
17 with MJ, and a coding framework formed which was used to code all papers followed by
18 development of descriptive and analytical themes from the codes, in discussion with MJ and JS (29).
19 Both inductive (allowing themes to arise from the specific observations) and deductive (working
20 within existing knowledge about the effect of venous thromboembolism on people without cancer,
21 looking specifically within our data for similarities and differences) processes were involved.

22 **RESULTS**

23 **Overview of articles**

24 The search identified a total 13197 articles, Embase (11632); MEDLINE (1272); CINAHL (254); and
25 PsycINFO (38) articles. One additional article was identified through searches of relevant

1 bibliographies. Eleven full articles were retrieved and assessed for eligibility; six articles were
2 excluded following review. This is summarised in the PRISMA flow diagram (Figure 1).

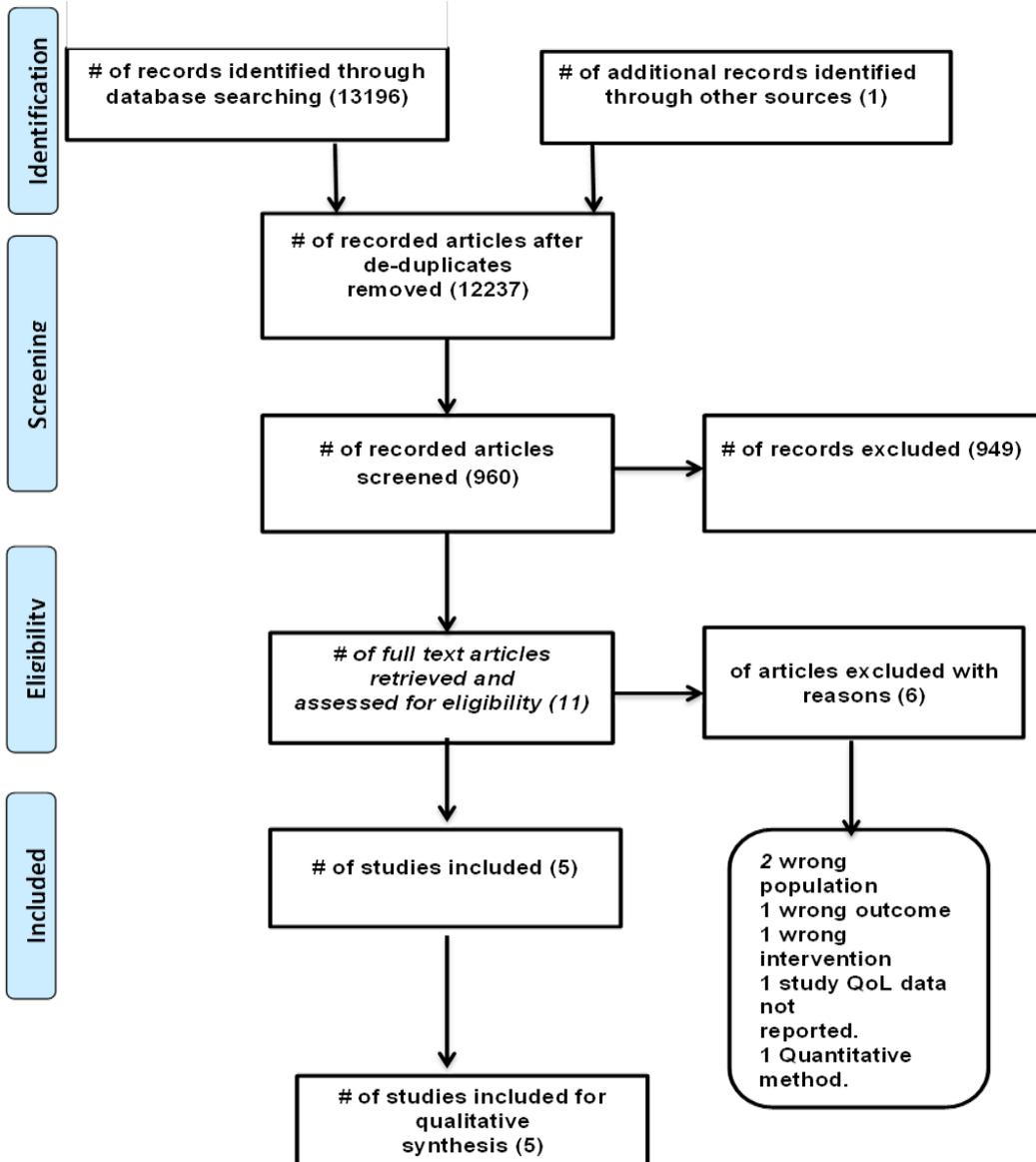
3 Five qualitative studies published between 2005 and 2015, met the inclusion criteria. Four of them
4 were conducted in the UK. The key characteristics of the studies are summarised in Table 1.

5 **Study populations**

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

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3 Figure 1: (PRISMA) Flow diagram

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1 **Themes**

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

5 **Knowledge deficit**

6 Two studies investigated the patients' knowledge about cancer associated thrombosis in the context
7 of cancer journey(13, 30)

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

12 *"During my cancer treatments, I was never told that there was a risk of getting a blood clot. I didn't
13 know about it... I was pretty shaken up"(30)*

14 *"I have never heard of venous thromboembolism, so that's why I was so shocked"(30)*

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

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

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

1 On other hand participants with prior knowledge about venous thromboembolism respond in calm
2 and seek medical help immediately.

3 *"I was out of breath and I said to my partner, 'I think we are going to hospital' without panic because*
4 *I knew that it was something that could be rectified effectively)(30)*

5 There was also evidence of limited awareness about venous thromboembolism and cancer amongst
6 health care professionals (13) . This is consistent with patient reports of delayed diagnosis of the
7 venous thromboembolism; on many occasions alternative causes were considered first.

8 *"It just got bigger and bigger and bigger, over months really [...] then they doubled them (diuretics),*
9 *and then they trebled them". [RG05].(13)*

10

11 **Effects of cancer associated thrombosis**

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

14 **Effects of diagnosis process**

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

20 *"Having the cancer and then the thrombosis on top of it, not knowing how bad it was"(13)*

21 *"The fact that there were clots meant we couldn't operate on my leg. Not being able to operate my*
22 *leg pushed back my radiation and chemotherapy. So everything was shifted in time"(30)*

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1 **Psychological effects**

2

3 Four studies reported that the diagnosis of cancer associated thrombosis was distressing, especially
4 in those without prior knowledge of the symptoms, had a major impact on patients' lives and was
5 perceived as life threatening (13, 30-32)

6 *"PE is not cancer but it's dangerous too, because with both you are playing with your life"(30)*

7 *"I felt I was having a heart attack....that stress made (the symptoms) worse"(30).*

8 *"[...] having the cancer and then the thrombosis on top of it, erm, not knowing how bad it was when I
9 went in, I know I was in terrific pain with my chest and that erm, it was frightening to be honest.*

10 *[VCC01]"(13)*

11 *"It frightened the life out of me, I was more scared of that than the cancer. You know blood clots can
12 kill you like that (clicks fingers), cancer you've got a little bit of chance, you know. [PT13]"(31)*

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

15 *"Knowing [that it is a PE] reassures you a little, nevertheless. . . I knew I need to go to the hospital as
16 fast as possible"(30)*

17 *"Would er the main thing that did it was erm apprehension basically about er the clot and if a clot
18 does occur it hits you like that bang" (Interview NC5)(32)*

19

20 **Physical Effects**

21

22 The acute and chronic symptoms of cancer associated thrombosis were profound and negatively
23 affected patients' lives. *Mockler 2012* and *Seaman 2014* described the negative impact of symptoms
24 that interfered with patients' daily living(30, 31).

25 In particular participants with PE described that being short of breath prevented them from

1 completing even small tasks at home. Symptoms from cancer associated thrombosis prevented them
2 from returning to normal life and activities; unable to do daily activities around the house or to
3 mobilize unaided.

4 *"I cannot do anything...will I always continue heading in this regression"(30)*

5 *"The lack of energy and being out of breath....it's just so frustrating ...Frustration of not being able to*
6 *be where I should be, in my mind"(30)*

7 *"I couldn't breathe; I literally couldn't breathe and couldn't talk. [PT6]"(31)*

8 *"I was very breathless, even bending down to the washing machine to put a wash in I was gasping for*
9 *air. [PT11](31)*

10

11 **Effects of venous thromboembolism treatments**

12

13 This theme captured patients' experience of anticoagulation treatment (self-injected weight-
14 adjusted Low molecular weight heparin, warfarin and direct oral anticoagulants). Four studies
15 assessed patients' responses to anticoagulation focusing on the acceptability of Low molecular
16 weight heparin (30-33) It was clear that the treatment had a positive effect on patients' life,
17 especially, for those who had experienced distressing symptoms.

18 Most participants were started on Low molecular weight heparin and others had been on warfarin
19 but changed to Low molecular weight heparin due to absorption difficulties, uncontrolled INR and/or
20 venous thromboembolism recurrence. There was a general agreement by patients that Low
21 molecular weight heparin was acceptable treatment and better than warfarin where comparison was
22 possible. Self-injected Low molecular weight heparin allowed more self-control over their life and
23 more freedom. However, this benefit was not without compromise, as side effects of bruising and
24 injection-site lumps were common.

25 *"The heparin is so much simpler than all the ****ing about with warfarin' (22CS)" (33)*

1 *"I really don't feel like pricking myself, but if it's that or dying well I'd rather prick myself"(30).*

2

1 *"I used to spend my life travelling to hospital for a warfarin check ... sat in the car ... sat in the waiting*
2 *room ... not much of a life really" (19CS) (33)*

3 *"With the warfarin, what was kind of crappy was that I had to do blood tests every two weeks. But*
4 *with Low molecular weight heparin no need for draws" (30)*

5 *"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*
6 *stomach gets really hard and then you've got to really force them in". [PT8](31)*

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

10 *"I know I'm going to die. I know that the doctors don't have any more chemo to give ... you don't like*
11 *feeling that you've been put on the scrap heap ... the injection isn't stopping the cancer but it is*
12 *stopping the blood clots" (14CS)(33)*

13 *"It is important to know that people are still doing something"(15C) (33)*

14 Some patients wish to take Low molecular weight heparin for longer than 6 months as long because
15 of the continued risk and the peace of mind they felt with ongoing anticoagulation. This is expressed
16 clearly by a patient in ALICAT study where views were sought on being randomised to continuation
17 or cessation.

18 *"The thing that bothered me at that time was that I'd already had two episodes of of a blood clot and*
19 *I thought if I was in the group that didn't have the medication um there was a good chance that I'd*
20 *I'd have another one and it could could have a lot more serious repercussions than if I just continued*
21 *to take this medication". (Interview NC3)(32)*

22 *"Um I thought no I think I'll carry on rather than, you know, spending another day in hospital being*
23 *prodded and probed like I was last time". (Inerview NC2)(32)*

24 *However; some patients wanted to stop Low molecular weight heparin injection after 6 months*
25 *because of the side effects of the injections and others wanted to restore their normal life without*
26 *injections.*

27 *" I was just happy to get off of it to be honest with you, um it was more or less the same time every*

1 *night, um and the pain as I said eh to me was terrible, horrific and a lot of bruising and things”*
2 *(Interview NC1)(32)*

3 *“And so I was very keen I have to say, I was predisposed I don’t want any further injections once the*
4 *treatments finished I just want to try to get back to as much normality as I can”. (Interview NC8)(32)*

5

6 **Employment of coping mechanisms**

7

8 It was clear that the response to the dual diagnosis of cancer and cancer associated thrombosis was
9 very individual, with some regarding it as a greater shock than their cancer, particularly among
10 patients who considered cancer associated thrombosis as a setback on the road to cancer recovery,
11 and others viewing it as less significant in comparison with their cancer (30).

12 *“I never broke down when I was told about the cancer [...] I had the operation, went on the chemo,*
13 *everything. The only time I broke down was when I went back in hospital when they told me I had*
14 *blood clots [...] the cancer to a point they can treat, hold it back – blood clots they go so quick and*
15 *that frightened me, it was the only time I broke down”. [PT13](31)*

16 *“During chemotherapy, I didn’t have any great nausea, and brachytherapy went well too. So I told*
17 *myself, “Well, I’m going to overcome the cancer but No! Then I started to go down again”.(30)*

18 The employment of coping mechanisms theme illustrated ways that patients developed to move on
19 with their lives. The treatment of venous thromboembolism brings with it symptomatic relief,
20 reassuring patients that their condition is improving. This reduces distress and allows patients, over
21 time, to get back to ‘some sort of normality’(13). Participants described the development of strict
22 routines and rituals to ensure Low molecular weight heparin was administered on time and without
23 fail.(31)

24 *“I usually take them between 8 and half past 8. And then I know it’s done, and I don’t forget for the*
25 *day, then, because someone I was talking to, he was saying “You don’t do it in the night, do you?”*
26 *and I said, “No, I get up, have my cup of tea then 8, half past 8 do it.” [PT13](31)*

1 “[...] is a ritual now”. [VCC10](13)

2 **DISCUSSION**

3 The cancer journey is difficult in itself, but thrombosis was an additional, frightening and unexpected
4 burden. The association between cancer and venous thromboembolism was first reported in the
5 19th century(34). However, cancer patients are still not routinely educated about the risk or warning
6 symptoms/signs of venous thromboembolism which may otherwise be misattributed to the cancer
7 by patient and clinician alike.

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

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

17

18 **Lack of knowledge of cancer associated thrombosis**

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

1 Eventhough the cancer associated thrombosis is not a new phenomenon, a lack of clinician
2 awareness of cancer associated thrombosis appears to compound the lack of patient knowledge (36,
3 37). In a study of 18 patients who had had venous thromboembolism, (not cancer-related),
4 misdiagnosis and diagnostic delay made patients feel angry and distrustful of their medical team.(38)
5 However, similar to *Mockler's* study of people with cancer associated thrombosis, patients with a
6 previous history of venous thromboembolism were less distressed, having recognised the symptoms
7 and sought medical help more quickly (30).

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

12 Inadequate information-giving is not new (41). However, people with venous thromboembolism
13 appear clear about the degree of information they need including understanding their diagnosis,
14 what they should do/ do not from diagnosis and with treatment (42). Information needs are
15 individual and vary by gender, age and stage of disease; some wishing for full details; others want
16 basic information only (43).

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19 **Psychological burden**

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

1

2 **Effects of cancer associated thrombosis treatment**

3 *Seaman et al* found that efficacy of treatment was paramount despite the hypothetical preference of
4 a tablet over an injection(31). This finding was also highlighted in the study by *Noble et al(46)*, where
5 patients were concerned about safety, efficacy, and lack of interference with anticancer therapies
6 ahead of method of administration. Patients in this review included those with advanced disease,
7 but despite previously stated concerns about patient burden with Low molecular weight heparin
8 (47), the use of Low molecular weight heparin was acceptable. The daily injections of precalculated
9 dose of Low molecular weight heparin giving more control than the blood tests and dose alterations
10 of warfarin.

11

12 **Employment of coping mechanisms**

13 Patients tried to maintain a sort of normality in everyday life consistent with previous findings that
14 cancer patients find ways to minimize the impact of the side effects of cancer in their new life
15 situation. (45)

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

20 **Uncertainty and information**

21 The varying responses to the threat of cancer associated thrombosis and its treatment seem to be
22 related to uncertainty as to whether the cancer associated thrombosis will recur, whether it will
23 resolve, whether the treatment will be effective and/or harmful. Uncertainty management
24 theory(50, 51) is one theoretical framework to help the understanding of how patients encounter,

1 appraise levels of danger, seek information, respond to and cope with health-related threats. The
2 differing needs for information, ways of seeking it and success in receiving it are seen within these
3 data presented. Likewise, some patients appraised the cancer associated thrombosis as very
4 dangerous, whereas others (often those with previous experience and better information) were able
5 to appraise it as less dangerous because they knew what to look for and how to act. Whilst the
6 relationship between uncertainty and danger appraisal is complex, tailored and accessible
7 information seems to play a key part in reducing anxiety even if absolute reassurances cannot be
8 given(52, 53). As Brashers states, uncertainty occurs when, “information is unavailable or
9 inconsistent; and when people feel insecure in their own state of knowledge or the state of
10 knowledge in general” (50).

11 **Strengths and limitations**

12 As with any systematic review it is possible to miss relevant studies. The included studies were
13 qualitative research which is designed to give insights from the patients involved rather than to be
14 generalizable. However through synthesis more generalizable findings can be derived(26). Only one
15 included study came from outside the UK, however, they were from different centres, but still
16 indicated similar concerns.

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

19

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

21 Raised clinical awareness and the provision of basic information for patients about the risk of cancer
22 associated thrombosis is a policy priority in the UK.(54) Information about cancer associated
23 thrombosis, both written and verbal, should be provided routinely for patients at diagnosis. cancer
24 associated thrombosis should be part of standard training and education for all clinicians caring for
25 people with cancer, including those in primary and palliative care. Recent initiatives such as the

1 International Initiative on Thrombosis and Cancer(55) should help raise awareness and help with
2 high quality training. Streamlined clinical services for diagnosis and treatment of cancer associated
3 thrombosis aiming to minimise time in hospital awaiting tests, especially for those with advanced
4 disease, should improve clinical decision making.(37, 56, 57)

5

6 **Conclusion**

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

11

12 **Declarations.**

13 **Authorship;** NB, MJ and AM conceived the research question, NB, MJ developed the search strategy,
14 NB, MJ, JS and AH contributed to design. NB, WI screened titles and abstracts with recourse to MJ;
15 NB extracted data and wrote the first draft; All authors interpreted the data and contributed to
16 drafts and approved the final manuscript

17 **Funding,** This work was conducted as part of a self-funded PhD (NB)

18 **Conflicts of interest:** Authors have the following interests to declare: AH, AM and MJ received
19 funding to complete a qualitative substudy of anticoagulation patient experience funded by BAYER,
20 JD, WI and NB have nothing to declare.

21 **Ethics and consent:** This was not required for this published anonymised evidence synthesis.

22 **Data sharing:** Data are available from the published papers in this review

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Table 1. Overview of the articles included

Study	Study design	Methods & Setting	Aim	Participants characteristics	Analysis	Principal findings
Noble.S, et al. 2015.(13) PELICAN	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) Age: 53-81 years Different primary cancers receiving Low molecular weight heparin for (2-20 months)	Framework analysis	Diagnosis and treatment of cancer associated thrombosis : <ul style="list-style-type: none"> • 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 : <ul style="list-style-type: none"> • Treatment helps get over the initial shock, i getting on with life, ritualization of new routines

Mockler, A, et al. 2012(30)	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	<p>N = 10 (4 women and 6 men) aged 35-78 years</p> <p>Various cancer types diagnosed 2-18 months prior to the interview</p> <p>Various stages from early with active treatment to advanced stage</p>	Thematic analysis	<p>Coping with venous thromboembolism:</p> <ul style="list-style-type: none"> • 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. <p>Attitudes about venous thromboembolism treatments:</p> <ul style="list-style-type: none"> • 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, S et al. 2014(31)	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	<p>N =14 (8women and 6 men) Age 52-84 years</p> <p>Receiving Low molecular weight heparin for confirmed venous thromboembolism (PE n=8/ DVT n=6),</p> <p>8 patients were on Warfarin then changed to Low molecular weight heparin</p>	Thematic analysis	<p>Impact of venous thromboembolism:</p> <ul style="list-style-type: none"> • Symptom burden of cancer associated thrombosis , • cancer associated thrombosis in context of cancer, • Impact on activities of daily living. <p>Acceptability of Low molecular weight heparin :</p> <ul style="list-style-type: none"> • Necessary inconvenience, • Systematic approach to injection. <p>Hypothetical views on New Oral Anticoagulants:</p> <ul style="list-style-type: none"> • Efficacy paramount, • Willing to engage in clinical trials.

Noble.S, et al. 2015.(32) ALICAT	Embedded Qualitative study within a RCT	<p>Focus groups with clinicians.</p> <p>Semistructured interviews with patients and their relatives</p>	<p>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.</p> <p>●Patients' perception of cancer associated thrombosis and Anticoagulation</p>	<p>N of clinician= 3-11/ group (3 focus group)</p> <p>Oncology, Heamatology and Primary care.</p> <p>N of patients=8 (4 femals)</p> <p>Locally advanced or metastatic cancer. Receiving Low molecular weight heparin for cancer associated thrombosis .</p>	Framework analysis	<ul style="list-style-type: none"> ● 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 a symptomatic ●Patients with experience of symptomatic cancer associated thrombosis were willing and keen to continue on Low molecular weight heparin injection as long s 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
Noble. S and Finlay. I.G. 2005(33)	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	<p>N = 40 (18 male and 22 female)</p> <p>Age 32-76 years</p> <p>Advanced cancer, receiving Low molecular weight heparin for confirmed cancer associated thrombosis .</p> <p>33 patients had initially received Warfarin then changed to Low molecular weight heparin due to poor control.</p>	Thematic analysis	<ul style="list-style-type: none"> ● 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: 11 patients described bruising as a negative aspect of Low molecular weight heparin .

