



VENOUS THROMBOEMBOLISM (VTE) IN CANCER PATIENTS: CANCER, CHEMOTHERAPY AND CLOTS

CANCER SURVEY RESULTS 2016 - 2019

MARCH 2020

CONTENTS

Chair's Foreword: Lyn Brown MP	3
Summary of Findings	4
Aims and Objectives	5
Results	7
Discussion and Observations	14
Conclusions and APPTG Recommendations	16
References	17
Contact Details	17

Anticoagulation UK pays Four Health to act as the group's secretariat from grants received from the BMS-Pfizer Alliance and Bayer.





ABOUT VTE

Venous thromboembolism (VTE) is a condition in which a thrombus – a blood clot – forms in a vein. Usually, this occurs in the deep veins of the legs and pelvis and is known as deep vein thrombosis (DVT). After that, the clot can break free and travel through the circulatory system towards the lungs. This is known as a pulmonary embolism (PE). VTE is a collective term for both DVT and PE.

With an estimated incidence rate of 1-2 per 1,000 of the population, VTE is a significant cause of mortality and disability in England, with thousands of deaths directly attributed to it each year. One in twenty people will have VTE during their lifetime and more than half of those events are likely to be associated with prior hospitalisation. At least two thirds of cases of hospital-associated thrombosis are preventable through VTE risk assessment and the administration of appropriate thromboprophylaxis.

Both DVT and PE may also occur in patients with cancer, especially those undergoing treatment such as surgery, chemotherapy or radiotherapy. Around one in ten cancer patients will have an episode of VTE during the course of their illness; however, awareness of this is very low. This is referred to as cancer-associated thrombosis (CAT), and is a condition which has been increasingly recognised by physicians that deal with venous thromboembolism (VTE) and oncologists as important.

CHAIR'S FOREWORD



Dear Colleague,

As the Chair of the All-Party Parliamentary Thrombosis Group (APPTG), I am delighted to launch the latest edition of our research into the risks of VTE in cancer patients.

Since the APPTG started its work back in 2006, we have produced reports to support best practice in VTE prevention. It's so important to continually take stock of how our NHS is doing in tackling this deadly condition, and to draw on evidence gathered by surveys, local case studies and official national statistics in doing so.

The APPTG has been concerned about the specific risk of VTE for cancer patients, especially as awareness of this issue appears to be low within the NHS. Our two previous 'VTE in Cancer Patients: Cancer, Chemotherapy and Clots' reports, in 2015 and 2016, found that an average of 4,000 deaths per year in England and Wales may be caused by preventable blood clots. Unfortunately, much more needs to be done to reduce the risk for these patients.

This year's report shows that potentially avoidable deaths from VTE are still occurring in hospitals, however we have been affected by a low response rate for this part of the survey. This suggests that patient data about this neglected area of VTE isn't being captured. If we are going to shed greater light on the current situation, that needs to change.

We are also concerned that cancer and VTE diagnoses rates have continued to slip year-on-year, a trend that has been evident since the previous edition of this report was released in 2016. This could suggest that diagnoses are being missed on a large scale, particularly as cancer rates have increased massively over the same period.

Likewise, the VTE risk assessment rates for ambulatory cancer remain low at 27.6%. More needs to be done to help these patients receive the best care possible. It is heart breaking that a patient can successfully battle cancer thanks to the wonderful care available within our NHS, only to die because a clot that could have been easily diagnosed and treated is missed. By raising awareness of these crucial issues, we can work together to support patient safety and save lives.

**Lyn Brown MP,
Chair, All-Party Parliamentary Thrombosis Group**

SUMMARY OF FINDINGS

Cancer and VTE Diagnosis

The incidence rates for patients diagnosed with cancer and VTE has declined steadily from 1.6% in 2016 to 1.4% in 2018, continuing a trend from 2012-2014, where the incidence rate was 2.4%.

Incidence and Variation

The region with the largest proportion of patients diagnosed with cancer and VTE was the South West, with a 2.5% incidence rate in 2018. The lowest was shared between the North West and Midlands who each had a 0.7% incidence rate.

Mortality

Of the trusts that responded to this portion of the FOI request, the total number of patients where cancer of any type was listed as the primary cause of death over a cumulative three-year period declined from 11,891 in 2016 to 10,911 in 2018.

High Risk Cancers

In nine out of ten comorbidities, the number of deaths decreased between 2016 and 2018; with only kidney cancer seeing a slight increase.

Risk Assessment

Of the trusts that responded, only 35.7% of ambulatory cancer patients who are receiving chemotherapy are routinely risk assessed for their risk of developing CAT /VTE, with 54.7% not receiving this assessment.

Treatment

Just under 50% of patients are offered low-molecular-weight heparin (LMWH), the highest % of any treatment option. Direct oral anticoagulants (DOACs) are used as treatment in 28% of patients, compared to 10% for aspirin and 5% for Warfarin. 6% of patients were not given any of these treatments.

AIMS AND OBJECTIVES

This report seeks to further establish the known links between the treatment of cancer patients and the risk of VTE. It aims to build on previous APPTG data published in 2015 and 2016 through analysis of newly available information, and to evaluate the current state of VTE and cancer treatment.

Background

The links between VTE and patients with cancer is well-established in the healthcare community, representing a major cause of morbidity and mortality. However, amongst patients the link between the two conditions is less well known, and although VTE is associated with high rates of mortality and morbidity in cancer patients, its severity is still underestimated by many oncologists.ⁱ

Cancer is known to increase the risk of VTE and about 20% of all cases are associated with cancer. Patients with cancer have a four to seven times increased risk of developing VTE.ⁱⁱ Furthermore, VTE is the second most common cause of death in patients with the diseaseⁱⁱⁱ, however prevention and treatment remains inadequate for those with cancer. For example, many show an elevated risk for VTE, bleeding or both, and there are significant gaps in the provision of prophylaxis.^{iv}

The incidence of VTE varies not only according to the type of cancer, but also within cancer type, including brain, lung, uterus, bladder, pancreas, stomach and kidney. In these indications, the rate of VTE is between four and thirteen times higher among patients with metastatic disease compared to those with localised disease. In addition, while receiving chemotherapy, cancer patients have a six-fold risk of developing VTE compared to other patients without the disease^v.

The National Institute for Health and Care Excellence (NICE) recommends that patients with active cancer and confirmed proximal DVT or PE are offered low-molecular-weight heparin (LMWH) and take the treatment for six months. At six months, an assessment regarding the risks and benefits of continuing anticoagulation is suggested^{vi}. Although these approaches can be very effective for many patients, cancer patients have a substantial risk of recurrent VTE^{vii}.

The last edition of the VTE in Cancer Patients report was published in October 2016. The report's key findings were:

- The number of patients diagnosed with both cancer and VTE averaged 2.4% across England.
 - On average, 4,047 patients who die of cancer in England and Wales each year also have VTE listed on their death certificate as a cause of death.
 - Across all regions, just under half of trusts are providing patients with both written and verbal information about the risk of developing VTE during chemotherapy, symptoms to look out for and what action they should take if they suspect a DVT or PE.
 - Only 35% of trusts have a dedicated policy or pathway for the management of suspected VTE in patients receiving chemotherapy.
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RESULTS

We grouped the responses received according to the 7 NHS England regions: North East and Yorkshire, North West, East of England, London, Midlands, South East and South West. The map opposite from NHS England's regional teams' web pages show the area boundaries.

North East and Yorkshire

- 1 Cumbria and the North East
- 2 West Yorkshire and Harrogate
- 3 Humber, Coast and Vale
- 4 South Yorkshire and Bassetlaw

North West

- 5 Lancashire and South Cumbria
- 6 Greater Manchester
- 7 Cheshire and Merseyside

Midlands

- 8 Staffordshire and Stoke on Trent
- 9 Shropshire, Telford and Wrekin
- 10 Derbyshire
- 11 Lincolnshire
- 12 Nottinghamshire
- 13 Leicester, Leicestershire and Rutland
- 14 The Black Country
- 15 Birmingham & Solihull
- 16 Coventry and Warwickshire
- 17 Herefordshire and Worcestershire
- 18 Northamptonshire

East of England

- 19 Cambridgeshire and Peterborough
- 20 Norfolk and Waveney
- 21 Suffolk and North East Essex
- 22 Bedfordshire, Luton and Milton Keynes
- 23 Hertfordshire and West Essex
- 24 Mid and South Essex

London

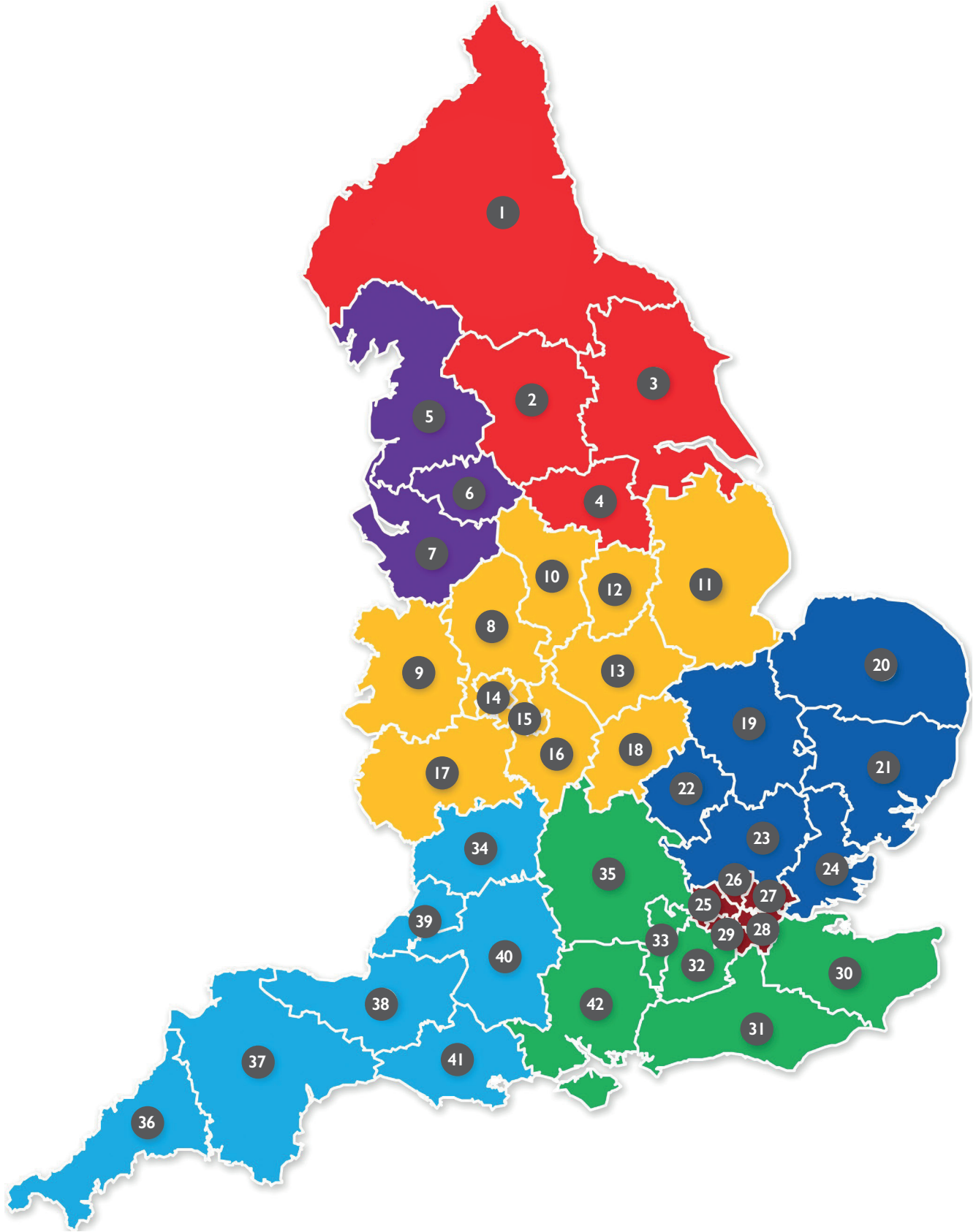
- 25 North West London
- 26 Central London
- 27 East London
- 28 South East London
- 29 South West London

South East

- 30 Kent and Medway
- 31 Sussex and East Surrey
- 32 Frimley Health and Care
- 33 Surrey Heartlands
- 34 Buckinghamshire, Oxfordshire and Berkshire West
- 35 Hampshire and the Isle of Wight

South West

- 36 Cornwall and the Isles of Scilly
- 37 Devon
- 38 Somerset
- 39 Bristol, North Somerset and South Gloucestershire
- 40 Bath and North East Somerset, Swindon and Wiltshire
- 41 Dorset
- 42 Gloucestershire



RESULTS

The following results come from NHS Trusts, including data from 2016 to 2018.

Incidence rates of cancer and VTE

Proportion of patients diagnosed with cancer and VTE in England

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	394,133	6,133	1.6%
2017	412,142	6,172	1.5%
2018	446,155	6,258	1.4%

Proportion of patients diagnosed with cancer and VTE in North East and Yorkshire

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	48,316	712	1.5%
2017	50,356	762	1.5%
2018	52,719	708	1.3%

Proportion of patients diagnosed with cancer and VTE in North West

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	97,540	691	0.7%
2017	102,539	712	0.7%
2018	109,901	735	0.7%

Proportion of patients diagnosed with cancer and VTE in East of England

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	28,262	612	2.1%
2017	29,801	572	1.9%
2018	39,771	646	1.6%

Proportion of patients diagnosed with cancer and VTE in London

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	49,204	832	1.7%
2017	50,890	730	1.4%
2018	52,779	849	1.7%

Proportion of patients diagnosed with cancer and VTE in Midlands

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	47,506	317	0.7%
2017	51,922	343	0.7%
2018	57,245	329	0.6%

Proportion of patients diagnosed with cancer and VTE in South East

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	88,658	2,021	2.3%
2017	91,714	2,119	2.3%
2018	98,233	2,114	2.2%

Proportion of patients diagnosed with cancer and VTE in South West

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2016	34,647	948	2.8%
2017	34,920	934	2.7%
2018	35,507	877	2.5%

RESULTS

Proportion of patients treated for cancer who had a diagnosis of VTE in the past three years who were receiving chemotherapy

Year	Number of patients treated for cancer
2016	16,092
2017	16,187
2018	17,136

Proportion of patients treated for cancer who had a diagnosis of VTE in the past three years who had metastatic disease

Year	Number of patients who had metastatic disease
2016	8,074
2017	8,169
2018	8,589

Proportion of patients treated for cancer who had a diagnosis of VTE in the past three years who were had localised disease

Year	Number of patients who had localised disease
2016	1,963
2017	1,930
2018	1,917

Proportion of patients treated for cancer who had a diagnosis of VTE in the past three years who were treated for cancer [Cancer type listed below]

Year	Brain cancer	Lung cancer	Uterine cancer	Bladder cancer
2016	242	2,027	467	741
2017	240	2,343	418	650
2018	282	2,652	433	785

Year	Pancreatic cancer	Stomach cancer	Kidney cancer
2016	712	429	337
2017	754	411	489
2018	811	475	444

RESULTS

Mortality rates involving cancer and VTE in England

Proportion of patients where cancer (of any type) was listed as the primary cause of death in the last three years

Year	Number of patients where cancer was listed as primary cause of death
2016	11,891
2017	12,123
2018	10,911

Proportion of patients where VTE as well as cancer was listed as a cause of death in the last three years

Year	Number of patients who had cancer and VTE listed as a cause of death
2016	402
2017	353
2018	291

Proportion of patients who died with VTE and cancer listed as a cause of death who were receiving chemotherapy

Year	Number of patients who died with VTE and cancer listed as a cause of death who were receiving chemotherapy
2016	84
2017	66
2018	38

Proportion of patients who died with VTE and cancer listed as a cause of death who were treated for cancer [Types outlined below]

Year	Brain cancer	Lung cancer	Uterine cancer	Bladder cancer
2016	7	58	8	12
2017	7	59	8	1
2018	1	34	3	1

Year	Pancreatic cancer	Stomach cancer	Kidney cancer
2016	21	8	1
2017	24	7	4
2018	15	3	3

RESULTS

Advice given to patients

Are ambulatory cancer patients who are receiving chemotherapy routinely risk assessed for their risk of developing CAT /VTE?

Response	% of patients
Yes	35.7%
No	54.7%

Are ambulatory cancer patients who are receiving chemotherapy AND deemed at high risk of developing CAT/VTE offered pharmacological thromboprophylaxis with?

Response	% of patients
Not held	9.5%
Low-molecular-weight heparin (LMWH)	45.2%
Direct Oral Anticoagulants (DOAC)	28.6%
Aspirin	10.4%
Warfarin	5.2%
Other	0%
None	6%
No response	36.5%

DISCUSSION AND OBSERVATIONS

The incidence rate for patients diagnosed with cancer and VTE has declined steadily from 1.6% in 2016 to 1.4% in 2018. While most NHS regions reported stagnant or modestly declining figures, in the East of England there was a 0.5% decrease from 2016-18, the largest of any region during this timescale. The last cancer report published by the APPTG found that 2.4% of cancer patients from 2012-14 were diagnosed with VTE, meaning that there has been a significant fall in the intervening years. This decline is worrying when you take into account that the number of patients treated for cancer has increased by around 50,000 from 2012-18, which would suggest that appropriate risk assessments are not being undertaken. This point is backed up by data that shows that only 27.6% of patients who are receiving chemotherapy are routinely risk assessed for CAT /VTE.

The region with the largest proportion of patients diagnosed with cancer and VTE was the South West. The incidence rate reduced slightly from 2.8% to 2.5% from 2016-18, which is in line with the nationwide results. The South East also had a high average incidence rate of 2.3% from 2016 to 2018. Given the average for patients diagnosed with cancer and VTE across England was 1.4% in 2018, the figures from South West and South East are extremely high. This also aligns with what was found in the annual survey where the South East and West had much higher average cases of confirmed Hospital Associated Thrombosis (HAT) than other regions, a few trusts within these areas also had a higher number of patients not receiving thromboprophylaxis prior to developing HAT. In contrast, the regions with the lowest proportion of patients diagnosed with cancer and VTE were the North West and the Midlands, both with an average incidence rate of 0.7%. This widespread regional variation is a persistent feature that we have seen in previous reports, and should form the basis of future work to ensure that patients across the country have equal access to appropriate treatment.

This year's FOI request also asked about the proportion of patients treated for cancer who had a diagnosis of VTE and a number of different co-morbidities, as well as those receiving chemotherapy. Of the ten co-morbidities, eight of them saw increases in the number of patients who were treated on a three-year cumulative basis.

Only the number of patients treated for localised disease and uterine cancer saw a decrease, although in both instances the decrease was minimal.

The three-year cumulative total number of patients receiving chemotherapy increased from 16,092 in 2016 to 17,136 in 2018. Aside from chemotherapy lung cancer (an increase of 625) and metastatic disease (an increase of 515) saw the largest cumulative rise in total patients receiving treatment from 2016 to 2018. For the rest of the co-morbidities listed, there were modest increases, although none of these indicate a significant rise in the number of patients treated for any specific condition. It should also be noted that this question received a low response rate, which could affect the results described above.

For those ambulatory cancer patients who are receiving chemotherapy and deemed at high risk of developing CAT /VTE, our results outline that just under 50% (45.2%) are offered pharmacological thromboprophylaxis with LMWH, the highest % of any treatment option. Direct oral anticoagulants (DOACs) are used as treatment in 28.6% of patients, compared to 10.4% for aspirin and only 5.2% for Warfarin. 6% of patients were given none of these treatment options, although again the low response rate for this section of the FOI means that firm conclusions cannot be drawn.

DISCUSSION AND OBSERVATIONS

NICE Guideline NG89 states that VTE prophylaxis should not be offered to patients with cancer who are receiving cancer-modifying treatments such as radiotherapy, chemotherapy or immunotherapy and who are mobile, unless they are also at increased risk of VTE because of something other than the cancer. While our data does not show us the reasons that patients were offered prophylaxis, a large proportion of patients were, which raises questions as to the degree to which guidance is being followed.

In terms of mortality figures, many trusts were unable to provide comparable data due to the information being unavailable. This was anticipated due to a similar situation having occurred the last time this report was published in 2016. However, while a comparison with previous data is difficult to undertake, some general trends relating to mortality rates can be drawn, as well as the recommendation that trusts introduce procedures to effectively record mortality data in order to analyse trends over time.

Of the trusts that responded to this portion of the FOI request, the total number of patients where cancer of any type was listed as the primary cause of death over a cumulative three-year period declined from 11,891 in 2016 to 10,911 in 2018. Likewise, the number of patients who had cancer and VTE listed as a cause of death decreased from 402 in 2016 to 291 in 2018. Additionally, we asked trusts to disclose their mortality data for VTE and specific co-morbidities. In nine out of ten comorbidities, the number of deaths decreased from 2016 to 2018, with only kidney cancer seeing a slight increase.

CONCLUSIONS AND APPTG RECOMMENDATIONS

The APPTG's findings should be met with concern across England. VTE is an important co-morbidity for many cancer patients and yet unfortunately sufficient action is not being taken to mitigate risks.

These results demonstrate how diagnosis rates are falling year-on-year, with only 35% of cancer patients routinely risk assessed for VTE. Risk assessment models need to be updated in order to capture at-risk cancer patients. This was highlighted in the Brenner, B. et al (2019) study, which concluded that 'patients with cancer need better VTE risk assessment tools to tailor primary thromboprophylaxis to tumour types and disease stages, and the potential for drug–drug interactions needs to be considered.'¹¹

Our results also demonstrate that there is significant regional variation between the proportion of patients diagnosed with cancer and VTE. Trusts should therefore be encouraged to share best practice in treatment and care nationwide in order to reduce this variation gap and associated healthcare inequalities. This has been delivered at an international level through the International Initiative on Thrombosis and Cancer, an academic working group that has developed evidence-based clinical practice guidelines, which are available online and through mobile applications.

A key step that could also be implemented by trusts to effectively manage chemotherapy patients who are suspected of having VTE, is to develop specific written policies for the management of such patients. While NICE guideline NG89 sets out advice on this, it is open to interpretation in some places. By setting out a series of written policies, each trust can make their treatment plans clear, which will further assist with the sharing of best practice.

This work could also be supported by ensuring that all chemotherapy and cancer clinical nurse specialists are trained in pre and post registration oncology training on the importance of VTE prevention and management. This recommendation was included in the previous iteration of this report in October 2016, however little action has been taken on this to date.

Based upon the findings of this report, the APPTG recommends the following:

- A platform should be developed to encourage NHS trusts to actively share best practice in VTE cancer care in order to reduce variation in diagnosis and treatment across the country.
- CCGs should implement measures to ensure that trusts are following NICE guidelines regarding mandatory risk assessments for VTE patients.
- Trusts should develop specific written policies for the management of suspected VTE in patients receiving chemotherapy.
- New models of risk assessment should be tested and developed to ensure that there are adequate risk assessment tools, which can tailor primary thromboprophylaxis to tumour types, disease stages and drug-to-drug interactions.
- Trusts should note in their hospital associated root cause analysis reports whether a patient with a diagnosis of cancer or undergoing cancer treatment, also has/had VTE.
- VTE prevention and management should be included on the curriculum for both pre and post-registration oncology training, as well as in the training for chemotherapy and cancer clinical nurse specialists.
- More needs to be done to raise awareness of cancer patients' increased risk of developing VTE and the dangers posed by this. This could be achieved through patient literature and interactive materials hosted on prominent cancer charities' websites or social media platforms.

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