



VENOUS THROMBOEMBOLISM (VTE) IN CANCER PATIENTS

CANCER, CHEMOTHERAPY AND CLOTS

OCTOBER 2016

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AntiCoagulation Europe pays Insight Consulting Group to act as the group's secretariat from grants received from the Pfizer-BMS Alliance, Bayer, Leo Pharmaceuticals and FirstKind Ltd.





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).

The thrombus or its part can break off, travel in the blood system and eventually block an artery in the lung. 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 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.

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 its inception in 2006, the APPTG has produced reports to support the implementation of best practice in VTE prevention in the NHS. Drawing on evidence gathered by surveys of Acute Trusts and CCGs, local case studies and official national statistics, our reports provide a comprehensive overview of progress in implementing best practice; identify areas for future improvement; and offer recommendations on what more can be done to ensure that NHS services are underpinned by high quality VTE prevention and management.

The APPTG has long been concerned about the risks of VTE in cancer patients, and in particular that awareness of the issue is low in the NHS. Our 2015 report *Venous Thromboembolism (VTE) in Cancer Patients: Cancer, Chemotherapy and Clots* found that an average of 4,000 cancer deaths per year in England and Wales may actually be caused by preventable blood clots. Despite this, we found that many hospitals are not taking appropriate action to reduce the risk to patients.

The report's findings painted a worrying picture across the whole of England and Wales for cancer patients. Potentially avoidable deaths from VTE are occurring in our hospitals; a risk that could be

alleviated by increasing clinical awareness and by providing patients with basic information as has been done for the majority of hospital inpatients already.

In order to verify our findings and identify four-year trends in mortality statistics, the APPTG conducted further research to produce this updated version of our VTE in Cancer Patients report. Our new findings show that cancer deaths linked to VTE are clearly a growing problem, with a higher average annual increase than that of overall cancer deaths. Our new findings also indicate that the incidence of VTE in cancer patients may be higher than previously estimated.

More needs to be done for patients with cancer, many of whom are treated as outpatients, where mandatory risk assessment and prophylaxis policies do not apply. It is a tragedy that in today's NHS a patient can beat their cancer, only to then die of a clot. We hope that by raising awareness of this overlooked issue, we can drive up patient safety and provide better outcomes for patients.

I hope you find our report informative and that it inspires you to continue your work in helping to spread awareness of best practice in VTE prevention and management, whatever your role in the health system.

Andrew Gwynne MP
Outgoing Chair, All-Party
Parliamentary Thrombosis Group

SUMMARY OF FINDINGS

Cancer and VTE Diagnosis

The number of patients diagnosed with both cancer and VTE has remained relatively constant over the previous three years; averaging around 2.4% across England.

Incidence and Variation

The South of England region has an incidence rate of 2.2% and the North of England has a significantly higher rate of 2.6%.

Mortality

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. The average annual increase in cancer deaths where VTE is implicated is over four times higher than the average annual increase in overall cancer deaths.

High Risk Cancers

Death rates for patients who died of brain, lung and bladder cancers - where VTE was also implicated – were particularly high, recorded at 2.9%, 2.9% and 2.5% respectively (in 2015).

Patient Information

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, what symptoms to look out for and what action they should take if they suspect a Deep Vein Thrombosis or Pulmonary Embolism.

VTE Cancer Policies

Only 35% of Trusts have a dedicated policy or pathway for the management of suspected VTE in patients receiving chemotherapy.

AIMS AND OBJECTIVES

This report seeks to further establish the known link between the treatment of cancer patients and the increased risk of venous thromboembolism (VTE). It aims to build on previous APPTG research published in 2015 through analysis of newly available data, and to cross-reference earlier findings with data gathered from additional sources.

Background

The links between VTE and patients with cancer have been well established, and represent a major cause of morbidity and mortality in such patients. VTE is the second most common cause of death in patients with cancer. Population-based case-control studies have shown that the two year cumulative incidence of VTE is between 0.8 and 8% (Chew HK, 2006).

Patients with the highest one year incidence rate of VTE are those with advanced disease of the brain, lung, uterus, bladder, pancreas, stomach and kidney. In these cancers, the rate of VTE is 4–13 times higher among patients with metastatic disease as compared with those with localized disease. While receiving chemotherapy, cancer patients have a seven fold risk of developing VTE as compared with other patients without cancer. (Mandala M, 2011).

For the general population, the standard treatment for acute VTE consists of initial therapy with a low-molecular-weight heparin (LMWH) followed by longer-term treatment (3–6 months) with an oral vitamin K antagonist (VKA). Although this approach can be effective for many patients, cancer patients have a substantial risk of recurrent VTE (Lee et al., 2013). The National Institute for Health and Care Excellence pathway '*Venous thromboembolism: patients with cancer*' recommends pharmacological prophylaxis for ambulant patients receiving oncological treatment who are at increased risk of VTE (NICE, 2011).

The APPTG published the first edition of its *VTE in Cancer Patients* report on World Thrombosis Day (13th October) 2015. Informed by a Freedom of Information request sent to 157 Hospital Trusts in England and Wales, and information provided by the Office of National Statistics, the report's key findings were:

- Up to 4,000 cancer deaths per year may be caused by preventable blood clots.
- On average, 1.7% of patients treated for cancer in England and Wales were diagnosed with VTE between 2012 and 2014.
- Only 41% of Trusts had a dedicated policy or pathway for the management of suspected VTE in patients receiving chemotherapy.
- Just under half of Trusts are providing patients with both written and verbal information about the risk of developing VTE during chemotherapy, what symptoms to look out for and what action they should take if they suspect a Deep Vein Thrombosis or Pulmonary Embolism.

Methodology

To cross-reference the data gathered from Hospital Trusts on the incidence of VTE in cancer patients, the APPTG approached Public Health England for data on the number of patients diagnosed with cancer who were subsequently diagnosed with VTE within a year of their cancer diagnosis. This data pertains to England only for the years 2012, 2013 and 2014, and was calculated by linking Hospital Episode Statistics to the Cancer Registry.

A Freedom of Information Request was sent to the Office for National Statistics asking the following:

In England and Wales, in the years 2012, 2013 and 2014:

1. How many people had cancer listed as a cause of death on their death certificate?
2. How many people had cancer and Venous thromboembolism (VTE) listed as a cause of death on their death certificate?

Freedom of Information requests were also sent to 150 Hospital Trusts in England and 7 Hospital Trusts in Wales asking:

1. Are patients who receive chemotherapy provided with written and verbal information about the risk of developing VTE during chemotherapy? Is this information provided to chemotherapy inpatients only, chemotherapy outpatients only, or both in and outpatients?
 2. Are patients who receive chemotherapy provided with written and verbal information which outlines the symptoms suggestive of VTE? Is this information provided to chemotherapy inpatients only, chemotherapy outpatients only, or both in and outpatients?
 3. Are patients who receive chemotherapy provided with written and verbal information regarding what action they should take if they suspect a Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE)? Is this information provided to chemotherapy inpatients only, chemotherapy outpatients only, or both in and outpatients?
 4. Does your Trust have a 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 4 NHS England regions: North of England, Midlands and East of England, London and the South of England. The maps below from NHS England's regional teams' web pages show the area boundaries.

North of England



1. Cumbria, Northumberland, Tyne & Wear
2. Durham, Darlington and Tees
3. North Yorkshire and Humber
4. Lancashire
5. West Yorkshire
6. Merseyside
7. Cheshire, Warrington and Wirral
8. Greater Manchester
9. South Yorkshire and Bassetlaw

Midlands and East of England



1. Shropshire and Staffordshire
2. Derbyshire and Nottinghamshire
3. Leicestershire and Lincolnshire
4. Birmingham and the Black Country
5. Arden, Herefordshire Worcestershire
6. Hertfordshire and South Midlands
7. East Anglia
8. Essex

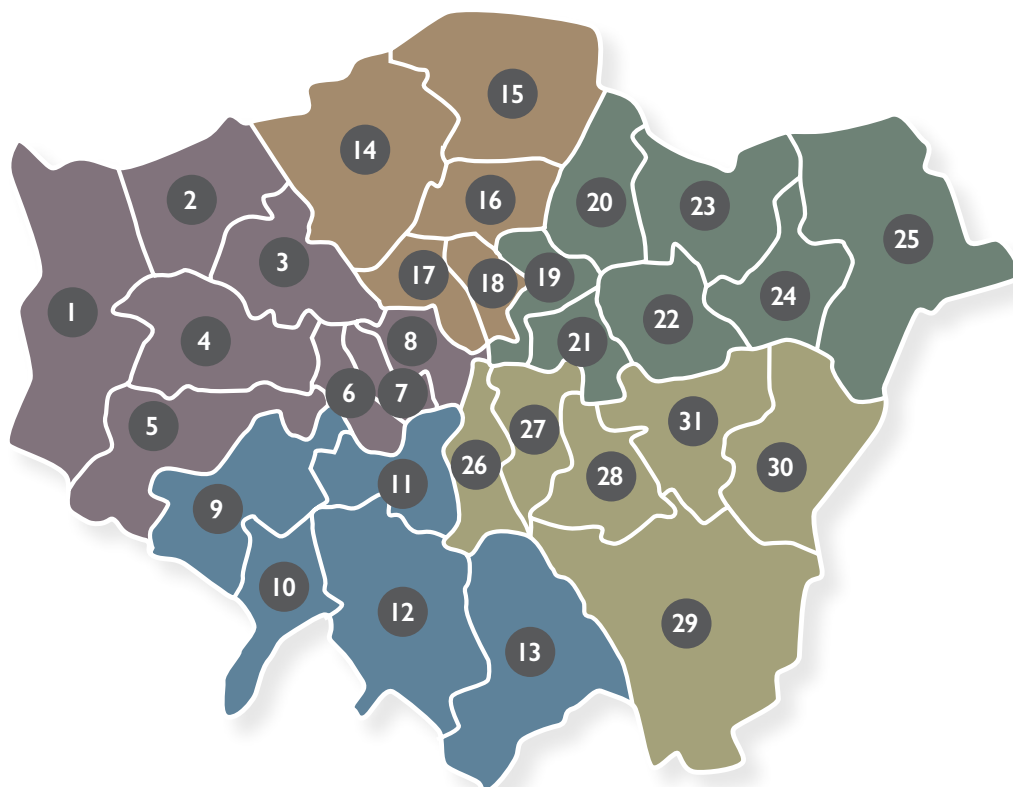
South of England



1. Devon, Cornwall and Isles of Scilly
2. Bristol, North Somerset, Somerset and South Gloucestershire
3. Wessex
4. Bath, Gloucestershire, Swindon and Wiltshire
5. Thames Valley
6. Surrey and Sussex
7. Kent and Medway

London

1. Hillingdon
2. Harrow
3. Brent
4. Ealing
5. Hounslow
6. Hammersmith & Fulham
7. Kensington & Chelsea
8. Westminster
9. Richmond & Twickenham
10. Kingston
11. Wandsworth
12. Sutton & Merton
13. Croydon
14. Barnet
15. Enfield
16. Haringey
17. Camden
18. Islington
19. City & Hackney
20. Waltham Forest
21. Tower Hamlets
22. Newham
23. Redbridge
24. Barking & Dagenham
25. Havering
26. Lambeth
27. Southwark
28. Lewisham
29. Bromley
30. Bexley
31. Greenwich



RESULTS

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
2014	416,126	9,926	2.4%
2013	411,269	9,838	2.4%
2012	396,483	9,450	2.4%

Proportion of patients diagnosed with cancer and VTE - London

Year	Number of patients treated for cancer	Number of cancer patients also diagnosed with VTE	Percentage of cancer patients also diagnosed with VTE
2014	38,545	970	2.5%
2013	37,315	935	2.5%
2012	34,311	835	2.4%

Proportion of patients diagnosed with cancer and VTE - Midlands and 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
2014	128,796	3,008	2.3%
2013	126,978	3,040	2.4%
2012	123,273	2,931	2.4%

Proportion of patients diagnosed with cancer and VTE - South 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
2014	122,339	2,726	2.2%
2013	121,738	2,669	2.2%
2012	115,761	2,665	2.3%

Proportion of patients diagnosed with cancer and VTE - North 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
2014	116,716	2,984	2.6%
2013	115,283	2,885	2.5%
2012	113,823	2,732	2.4%

Mortality rates involving cancer and VTE in England and Wales

Cancer deaths

Year	Lung Cancer	Brain Cancer	Bladder Cancer	All Cancers
2015	32,669	3,798	6,284	160,671
2014	33,026	3,793	6,228	159,187
2013	32,724	3,721	6,059	157,848
2012	32,437	3,782	6,110	157,293

Cancer deaths where VTE is also listed as a cause of death on death certificate

Year	Lung Cancer	Brain Cancer	Bladder Cancer	All Cancers
2015	944	110	154	4,224
2014	840	98	145	4,088
2013	850	81	154	4,028
2012	775	78	146	3,848

(Data provided by the Office for National Statistics, September 2016)

RESULTS

Trends over three years

2015	2.6% of patients who died of cancer also had VTE present (4,224 patients)
2014	2.6% of patients who died of cancer also had VTE present (4,088 patients)
2013	2.6% of patients who died of cancer also had VTE present (4,028 patients)
2012	2.5% of patients who died of cancer also had VTE present (3,848 patients)

2015

2015	2.9% of patients who died from brain cancer also had VTE present (110 patients)
2015	2.9% of patients who died from lung cancer also had VTE present (944 patients)
2015	2.5% of patients who died from bladder cancer also had VTE present (154 patients)

Advice given to patients

Are patients who receive chemotherapy provided with written and verbal information about the risk of developing VTE during chemotherapy?

Written and Verbal	47 Trusts (50%)
Written only	11
Verbal only	6

Are patients who receive chemotherapy provided with written and verbal information which outlines the symptoms suggestive of VTE?

Written and Verbal	37 Trusts (39%)
Written only	11
Verbal only	9

Are patients who receive chemotherapy provided with written and verbal information regarding what action they should take if they suspect a Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE)?

Written and Verbal	41 Trusts (44%)
Written only	8
Verbal only	10

Does your Trust have a policy or pathway for the management of suspected VTE in patients receiving chemotherapy?

Yes	33 Trusts (35%)
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DISCUSSION AND OBSERVATIONS

Our new findings not only confirm the scale of the problem of VTE in cancer patients, they show that this is an increasing challenge.

The mortality statistics for 2015 demonstrate a worrying four year trend in cancer deaths linked to VTE. Deaths in England and Wales for which VTE and cancer were recorded as causes of death increased by an average of 3.16% annually between 2012 and 2015. By comparison, overall cancer deaths increased by 0.71% annually during this period. This shows that the average annual increase in cancer deaths linked to VTE is over four times higher than the average annual increase in overall cancer deaths. That suggests that these deaths may have been due to blood clots rather than the cancer itself and could therefore have been prevented.

According to the data obtained from Public Health England, the incidence of VTE in patients diagnosed with cancer in England is higher than previously estimated. Our new findings show that on average, 2.4% of cancer patients were also diagnosed with VTE between 2012 and 2014. Last year, we estimated a lower figure of 1.7%. There are some important differences between the two sources used. The 1.7% figure was calculated from data provided by Hospital Trusts through a Freedom of Information request which had a 60% response rate. The accuracy of data provided by individual Trusts can vary, whereas information from a national register is generally more reliable.

The 1.7% incidence figure also refers to VTE in patients treated for cancer. However, not all patients diagnosed with cancer receive treatment within the space of a year. The data provided from Public Health England reflects VTE in patients diagnosed with cancer, regardless of whether or not they received treatment. This therefore increases the population size examined. Additionally, the data provided by Public Health

England covers England only, whereas last year's incidence data covered Welsh Health Boards as well. The data obtained last year indicated a higher average incidence of 3.6% in Wales.

Despite these risks, our new findings indicate that only one in three Hospital Trusts (35%) have a dedicated policy or pathway for the management of suspected VTE in patients receiving chemotherapy. This is lower than our previous estimate of 41%. While the response rate that our Freedom of Information request received from Hospital Trusts this year was roughly the same as that of the previous year (60%), there were differences in the level of detail that Trusts provided in answer to this question. Some merely provided a 'Yes' or 'No' answer whereas others provided full details of the policies they have in place. While many Trusts indicated that they have a generic VTE management policy or pathway for all patients, few had a policy that was specific to the management of suspected VTE in patients receiving chemotherapy.

Similarly to last year, still less than half of Hospital Trusts (44%) are providing patients with both written and verbal information about the risk of developing a blood clot during cancer treatment, symptoms to look out for and action to take if they suspect a clot. However, additional Trusts do provide this information either verbally or in written form only. The APPTG has heard anecdotal evidence that cancer patients are only being informed of the risk of developing a clot when being treated as inpatients. However, our research findings have not indicated a statistically significant difference in information provided to inpatients versus information provided to outpatients.

CONCLUSIONS AND APPTG RECOMMENDATIONS

The APPTG's findings paint a worrying picture for cancer patients across the whole of England and Wales. VTE is an increasing challenge for cancer patients, yet most Hospital Trusts are not taking sufficient action to mitigate the risk..

As the population of England and Wales ages, increasing the overall risk of VTE, we can expect the four year trend we have observed in VTE-related cancer mortality to continue. For this reason, it is vital that Hospital Trusts recognise that patients undergoing treatment for cancer are at a higher risk of VTE than the general population and that the following three 'C's should be considered in tandem: Cancer, Chemotherapy and Clots.

It is equally vital that cancer patients as well as those providing their treatment are fully aware of the risk of VTE. Patients need to know what they can do to reduce their risk, as well as the warning signs of a clot and the action they should take if one is suspected. Empowering patients to manage their own risk requires both a verbal discussion with their clinician to answer any questions as well as the provision of written information to serve as a reminder of the points discussed.

NHS England is a world leader in overall VTE prevention in hospitals, with risk assessment and thromboprophylaxis now embedded in standard practice. Patients with a unique risk profile, such as cancer patients, should not therefore be overlooked. Ensuring that their risks are appropriately mitigated will require action from all involved in a cancer patient's treatment.

Based upon the findings of this report, the All-Party Parliamentary Thrombosis Group recommends the following:

- Hospital Trusts should develop specific written policies for the management of suspected VTE in patients receiving chemotherapy.
- There should be specific recognition of the VTE risk in Chemotherapy Clinical Reference Group (CRG) service specifications for high risk cancers, with a recommendation for mandatory risk assessment to be undertaken.
- Cancer charities, particularly those focused on tumour types with a higher VTE risk, should develop their own written information for patients on managing their risk of a blood clot.
- Hospital Trusts should note in their mandatory root cause analysis reports for occurrences of VTE in hospital whether the patient had a diagnosis of cancer or was undergoing cancer treatment.

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NHS England

NHS England regional teams

<https://www.england.nhs.uk/about/regional-area-teams/>

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