

**Usage of cancer drugs approved by NICE  
Report of Review undertaken by the  
National Cancer Director**

**Gateway number: 7124  
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### Introduction

1. Cancer continues to be a major issue in England as elsewhere in the world. More than 227,000 new cases of cancer were diagnosed and over 127,000 people died from cancer in England in 2003. Nevertheless, the latest figures show that cancer mortality rates in the under 75s fell by 14% in between 1996 and 2003 which equates to around 43,000 lives saved over that period. Survival rates for patients diagnosed with cancer in this country are improving but there is still progress to be made if we are to be amongst the best in Western Europe.
2. The NHS Cancer Plan (2000) set out for the first time a 10 year national strategy for cancer in England focusing on prevention, diagnosis and treatment. This has already reformed the way in which cancer services are delivered, has standardised care and led to improvements in patients' experience of care. There remains more to do but cancer remains a top priority for both the Government and the NHS.

### *Background to this report*

3. One of the key areas of public, media and clinical concern over recent years has been that access to some of the newer and more expensive cancer treatments has been dependent more on where someone lives than their clinical needs. The National Institute for Health & Clinical Excellence (NICE) was set up in 1999 to provide national guidance on treatments and care for use in the NHS in England and Wales. There is a legal obligation on Primary Care Trusts (PCTs) to make funding available for the implementation of NICE's technology appraisals within three months of their publication. This should address inequalities in access to cancer and other treatments.
4. Since 2000, NICE has appraised a wide range of drugs – around a quarter of its appraisals to date have been on cancer drugs. The large majority of these drugs have received a positive appraisal from NICE and many thousands of cancer patients are benefiting as a result.

### *2004 report – findings and recommendations*

5. However, during 2003 several pharmaceutical companies expressed concerns that variations in usage of cancer drugs continued between the 34 cancer networks in England even after a positive NICE appraisal was published. In response, the then Secretary of State for Health asked the National Cancer Director to investigate and identify what, if any, action needed to be taken to ensure that all patients have appropriate access to cancer drugs approved by NICE.

6. In June 2004, the outcome of this investigation was published. It showed that overall usage of cancer drugs generally increased following a positive NICE appraisal. However, it also found that considerable variation in usage of cancer drugs remained between cancer networks that could not be accounted for by differences in casemix or cross boundary flows alone. The reasons for variations were complex but did not appear to be associated with funding restrictions on the use of these drugs. The main impact on usage seemed to be constraints in service capacity and differences in clinical practice although the variation in usage did appear to lessen over time.
7. The report set out a number of recommendations to address, what was considered to be, the unacceptable variation in access to NICE approved cancer drugs. One of the recommendations was to ensure that cancer networks, with their Strategic Health Authorities, developed action plans to respond to the report findings. These plans were encouraging, confirming that the profile of implementing NICE appraisals had increased and that, where problems had been identified they had been, or were in the process of being, addressed. It was also recommended that a repeat analysis would be undertaken in 2005 to confirm whether variations had reduced as a result of the action taken.
8. This report sets out the findings of this repeat analysis.

## Overall findings of 2005 review

9. Overall findings of the 2005 analysis show:
  - a. a continued increase in uptake of cancer drugs following a positive NICE appraisal. The increase since the last exercise in the median rate of usage of all NICE approved cancer drugs ranged from 11% for the drugs Vinorelbine and Fludarabine to 120% for Temozolomide. The median of the increases in the median rate for 14 drugs was 47%. [*Tegafur Uracil was excluded since it had median usage of zero and Raltitrexed, which was not approved by NICE, was also excluded.*]
  - b. a reduction in variation in the usage of all 15 NICE approved drugs since the last analysis.

## Approach to 2005 review

10. As in 2003, this review has considered the 16 cancer drugs appraised by NICE (15 of which received a positive appraisal) plus four standard cancer drugs as comparators (see **Annex 1** for details).
11. As DH does not collect data centrally about the prescription and administration of chemotherapy drugs in hospitals, IMS Health kindly

provided the initial data used for this exercise as they did for the last exercise.

12. IMS Health collects information from NHS Trusts on drugs used in hospitals. They currently collect data from hospitals containing around 93% of acute beds in the UK. In most of these sites, including almost all of the major cancer centres in England, IMS collects information relating to the usage of drugs used to treat cancer. The data provided for the original exercise was for the six month period July to December 2003. For this exercise, the six month period from January to June 2005 was used. This was 12-18 months on from the last exercise and, as such, the results take account of any actions networks took in response to the last report. (see **Annex 2a** for further details on methodology).
13. The information provided by IMS Health has some limitations (see **Annex 2b**) so in both exercises cancer networks were given the opportunity to validate the information and provide alternative figures if necessary. Where cancer networks provided revised figures, these were used in preference to the IMS Health data. The final dataset used is therefore a mixture of IMS Health and network data. Although not perfect, it is the best information available. IMS Health is currently investigating the differences between its data and networks' data to ensure improvements in data quality.
14. A number of analyses were carried out on the final dataset to identify the national picture in early 2005 and how it has changed since late 2003. The main analysis was the 90:10 ratio (ratio of the 90<sup>th</sup> percentile to the 10<sup>th</sup> percentile of the distribution of estimated usage per head of population by cancer network) which provides a single measure of variability in usage of each drug across networks excluding the results of networks at each extreme (ie very high and very low users). For simplicity this ratio is referred to as "X fold variation" in this report. A high X fold variation figure indicates a lot of variation with a low number indicating little variation.

## Findings

### *Trends in usage of cancer drugs approved by NICE*

15. The IMS Health Hospital Pharmacy Audit data used in the first exercise showed that usage of cancer drugs generally increased following a positive appraisal from NICE. This pattern has continued as illustrated by the examples (Trastuzumab, Imatinib, Rituximab & Oxaliplatin) at **Annex 3a**.
16. The increase since the last exercise in the median rate of usage of all NICE approved cancer drugs (excluding Tegafur Uracil as its median was zero) ranged from 11% for the drugs Vinorelbine and Fludarabine to 120% for Temozolomide. The median of the increases in the median rate for 14 drugs was 47%. The percentage increase for each NICE approved

drug is set out in the following table and a more detailed table setting out the information on which the percentages are based is at **Annex 3b**.

NICE approved cancer drug	Percentage increase in median usage (Jul-Dec 03 to Jan-Jun 05)
Rituximab	87%
Imatinib	70%
Gemcitabine	39%
Fludarabine	11%
Docetaxel	65%
Capecitabine	64%
Oxaliplatin	68%
Irinotecan	26%
Paclitaxel	24%
Trastuzumab	55%
Vinorelbine	11%
Peg Lip Dox	21%
Temozolomide	120%
Topotecan	15%

*Changes in variation between cancer networks between July – December 2003 and January – June 2005*

17. In the 2003 exercise variations in usage were wider for some NICE drugs than others and the same is still true. Also, the two drugs that had the widest variation in the 2003 exercise still have the widest variation in this latest review. However, the variations for all drugs has reduced. The following tables shows variation for each drug in 2003 compared to 2005. A more detailed table is at **Annex 4** along with corresponding charts at **Annexes 5 & 6**.

### Comparator drugs

Comparator drugs	Ratio of 90 <sup>th</sup> /10 <sup>th</sup> percentile: X-fold variation in usage		Difference between 03 & 05	% Difference (reduction in variation)
	Jul-Dec 03	Jan-Jun 05		
Carboplatin for multiple cancer types	2.3	2.1	-0.2	7
Cisplatin for multiple cancer types	2.3	2.1	-0.1	6
Doxorubicin for multiple cancer types	2.7	2.5	-0.1	5
Epirubicin for multiple cancer types	2.4	2.1	-0.3	13

Note: differences due to rounding

### NICE approved drugs

NICE approved drugs	Ratio of 90 <sup>th</sup> /10 <sup>th</sup> percentile: X-fold variation in usage		Difference between 03 & 05	% Difference (reduction in variation)
	Jul-Dec 03	Jan-Jun 05		
Capecitabine (Xeloda) for breast & bowel cancer	3.6	3.3	-0.3	9
Docetaxel (Taxotere) for breast & lung cancer	3.3	2.7	-0.6	17
Fludarabine (Fludara) for leukaemia (CLL)	3.2	2.2	-0.9	30
Gemcitabine (Gemzar) for lung and pancreatic cancer	3.0	2.5	-0.5	16
Imatinib (Glivec) for chronic myeloid leukaemia	2.9	2.5	-0.4	15
Irinotecan (Campto) for bowel cancer	3.7	2.5	-1.2	33
Oxaliplatin (Eloxatin) for bowel cancer	3.7	3.0	-0.7	19
Paclitaxel (Taxol) for breast, ovarian & lung cancer	3.8	3.1	-0.7	17
Pegylated Liposomal doxorubicin (Caelyx) for ovarian cancer	9.7	5.8	-3.9	40
Rituximab (Mabthera) for non-Hodgkin's lymphoma	2.6	2.3	-0.3	11
Temozolamide (Temodal) for brain cancer	11.6	9.5	-2.1	18
Trastuzumab (Herceptin) for breast cancer	4.2	2.8	-1.4	33
Vinorelbine (Navelbine) for breast & lung cancer	8.1	3.1	-5.0	62

Note: differences due to rounding

Note: Raltitrexed(Tomodex) for bowel cancer has been excluded from the table as it did not receive a positive appraisal from NICE. Tegafur uracil (Uftoral) for bowel cancer and Topotecan (Hycamptin) for ovarian cancer have also been excluded as their low national usage across the country (probably due to the range of NICE and non-NICE alternatives for these conditions) gives a 10<sup>th</sup> percentile value of zero.

18. In summary, the tables show that:
- a. the variation between the comparator drugs remains the smallest with a 2.1-2.5 fold variation in the period January to June 2005 compared to 2.3-2.7 in July to December 2003.
  - b. The majority of NICE approved cancer drugs (all but 2) now have a 2.2-3.3 fold variation in use compared to a range of 2.6-8.1 in July to December 2003. Five of these NICE approved drugs are in the range 2.2-2.5 – very similar to the comparators.
  - c. One of the most high profile drugs over recent months Trastuzumab (Herceptin) saw a 4.2 fold variation in use in the period in 2003 reduced to a 2.8 fold variation in use in January to June 2005. It should be noted that this use will predominantly be for advanced breast cancer as this review was carried out prior to the release of trial data on the use of herceptin for early breast cancer.
  - d. One of the NICE approved drugs had a reduction in variation of 9%, 7 had a reduction of 10-19%, 4 had a reduction of 20-40% and 1 had a reduction of over 60%.
  - e. The two drugs with the biggest variations in the period July to December 2003 (Pegylated Liposomal Doxorubicin (PLD) for ovarian cancer and Temozolomide for glioma – a form of brain cancer (9.7 and 11.6 fold respectively)) still had the largest variation but this has reduced to 5.8 and 9.5 fold respectively – this implies a 40% and an 18% reduction in variation respectively. Whilst these variations may still seem large compared to the other NICE approved drugs there may be legitimate reasons for these drugs to have a slightly wider variation in use:
    - i. **PLD** – there are a number of drug options for treatment of ovarian cancer and some patients may choose to have one of these alternatives (including non-NICE drugs) after discussing the different side effect profiles with their doctor. They may also choose to be entered into a clinical trial which does not include PLD as a treatment option.
    - ii. **Temozolomide** – glioma is a relatively uncommon brain tumour and some networks will refer their patients to neighbouring networks for specialist treatment of this condition. This particularly applies to networks on the outskirts of London which will often refer patients to London hospitals for treatment ie. some networks may appear low users but their patients will still have access to the drug.
19. Usage of each of the 16 drugs appraised by NICE and the 4 comparators by each cancer network is shown in the series of charts at **Annex 7**. These charts set out the estimated usage for each network along with

“margins of error” to reflect factors which might impinge on the comparisons between networks. These charts show, as they did in the period July to December 2003, that most networks have a spread of drugs for which they are high, low or middle users.

20. A comparison was carried out to see how a network that was frequently a high, average or low prescriber in 2003 compared in 2005. To do this, for each drug, networks were allocated to one of five bands according to where they are in relation to the median for both periods:
  - a. Band 1- those more than 1.5 times the median rate,
  - b. Band 2 - those more than 1.25 times the median rate but not exceeding 1.5 times,
  - c. Band 3 - those more than 0.75 times the median rate but not exceeding 1.25 times,
  - d. Band 4 - those more than 0.5 times the median rate but not exceeding 0.75 times
  - e. Band 5 - those less than 0.5 times the median rate.
  
21. However small the variation is, one network will have to have the lowest rate and one the highest. However, allocating networks in relation to the median gives a more objective approach and could result in every network sitting within the middle band if variation is minimal. Having put the results for each drug within each network on a scale of 1-5 it was easy to look across all drugs to see whether a network was frequently a high, average or low prescriber during January-June 2005. Then, by summing over all drugs, an overall “score” was derived for each network. Networks were then ranked with a low number rank indicating high usage and vice versa. This method can also give rise to “ties” between networks.
  
22. The resulting charts are set out at **Annex 8**. These show that:
  - a. in July to December 2003 for most drugs there were 11-17 networks within 25% of the median rate (ie. in band 3) but in January to June 2005 for most drugs there were 16- 22 networks within this band ie. as the median rate has increased more networks are now closer to the median usage value.
  
  - b. comparing usage across the two periods shows that:
    - i. 8 networks were generally high users in both the 2003 and 2005 reviews (South West London, Dorset, Greater Manchester & Cheshire, Peninsula, West Anglia, 3 Counties, North East London and Norfolk & Waveney)
    - ii. 4 networks were low users in 2003 but high users in 2005 (Central South Coast, Arden, Derby/Burton, Black Country)
    - iii. 17 networks had variable usage in 2003 and had generally average usage in 2005 (North Trent, Avon, Somerset & Wiltshire, Mid Anglia, South East London, Humber & Yorkshire Coast, North West Midlands, Pan Birmingham, Leicestershire,

Northamptonshire and Rutland, Sussex, Yorkshire, West London, Surrey, West Sussex & Hampshire, Northern, Merseyside & Cheshire and Mid Trent)

- iv. 2 networks had high usage in 2003 but lower usage in 2005 in relation to the median (North London and Kent & Medway)
  - v. 5 networks had generally low usage compared to other networks in both reviews (Mount Vernon, Thames Valley, Lancashire & South Cumbria, Teesside, South Durham & North Yorkshire and South Essex)
23. It is important not to misinterpret the information at paragraph 22. No matter how small the variation between networks there will always be a network that has the lowest usage and one that has the highest. Being the highest or lowest user is not necessarily an indicator of a high or low quality service. There may well be legitimate reasons for a network being a low user of a certain drug. For example, there may be alternative drugs (including NICE approved alternatives) that patients, following discussion with their doctor about side effects etc choose to have. There may also be networks that refer patients to other networks for more specialist treatments and some networks that choose to refer patients to other networks for the majority of chemotherapy if a specialist centre is near by. There may also be clinical trials open to patients where they will be given alternative treatment options. In addition, it should be remembered that there are some data quality issues (see **Annex 2b**) so there will be a margin of error with these figures.

## Level of Variations

24. There will always be some variation in drug usage across the country and this is expected given the different needs and choices of local communities and patients. The department has not, and has no plans to, set a benchmark for what is an acceptable level of variation.
25. This exercise has shown that the majority of NICE approved drugs now have a 2.2-3.3 fold variation in use. This is a major improvement from the position in 2003 and networks should be congratulated on this. Cancer networks now need to remain on top of this issue through adequate planning and monitoring. It should be possible over time to reduce the variation further. For example, the comparator drugs in the exercise (older drugs that have been in use for many years) had a 2.1-2.5 fold variation in use and it might be possible to reduce variation to a similar order for NICE approved drugs.
26. For the two drugs (Pegylated Liposomal Doxorubicin and Temozolomide) where there was widest variation there may be legitimate reasons for this (as set out in para 18e). However, there is likely to be scope to reduce these variations still further.

## Recommendations

27. There is no evidence that patients are being denied access to NICE approved cancer drugs and this must remain the case. The level of variation is reducing but there may be scope to reduce this level further. Implementing the following recommendations should ensure that variation is kept to a minimum.

### *Capacity Planning*

28. It is important that cancer networks plan ahead to ensure that they are aware of what cancer drugs are in the pipeline so that they can take the necessary action to address capacity and demand issues in good time. This is particularly important as the recent introduction of the new NICE single technology appraisal process will mean that NICE guidance on a range of new cancer drugs will become available within weeks of drugs being licensed. The NICE website ([www.NICE.org.uk](http://www.NICE.org.uk)) clearly sets out their programme of work including when draft and final guidance on particular drugs can be expected. ***It is recommended that cancer networks and their stakeholders keep track of the position on this website if they do not already do so.***
29. The 2004 report recommended that a capacity planning model for chemotherapy be developed. Such a tool would support both the providers of chemotherapy (eg. NHS Trusts) and those who commission these services (PCTs) to identify the local implications of using potential new drugs and plan ahead for their routine introduction when appropriate. A Pharmaceutical Oncology Initiative Partnership was set up in 2005. This is a partnership between the Association of British Pharmaceutical Industries (ABPI), the Department of Health/Cancer Action Team and the NHS/Cancer Services Collaborative. One of the first tasks of the Partnership has been the development of the capacity planning tool. This tool should be ready for roll out to cancer networks in October and ***it is strongly recommended that cancer networks and their stakeholders use this tool to improve forward planning for cancer drugs both before and after appraisal by NICE.***

### Information

30. Information remains a key lever to change clinical practice and standardise care across the country - electronic prescribing systems will be key. Work is underway to develop the national strategic ePrescribing solutions and it is currently anticipated that these will be deployed in 2008/10, with some trial implementations taking place before then. In the meantime, agreement has been reached that cancer networks should be allowed to implement interim solutions for oncology ePrescribing if they wish providing this can be done in sufficient time to ensure a reasonable return on investment.
31. Capital has been made available centrally to support the purchase of oncology ePrescribing software against which cancer centres/units have

already been invited to bid. Business cases, supported by Strategic Health Authorities, are due to be submitted to Connecting for Health by 30<sup>th</sup> September 2006. This is a voluntary exercise but ***it is recommended that those networks that already have advanced plans to procure local chemotherapy e-prescribing systems capitalise on this initiative.***

### **Monitoring implementation of NICE guidance**

32. Most networks took the opportunity, following the 2003 exercise to strengthen their arrangements for ensuring appropriate implementation of NICE appraisals. ***All cancer networks should ensure that there are local arrangements in place that include the regular monitoring and reporting to network boards of the uptake of NICE approved cancer drugs.***
33. Until e-prescribing is nationally available ***it is recommended that this exercise is repeated periodically to ensure that the level of variation is reduced as much as possible – it is suggested that the exercise should next be carried out in late 2007/early 2008 and that this should include any new drugs approved by NICE in the interim.***

### **Conclusion**

34. Cancer networks and their stakeholders should be congratulated on the progress they have made in reducing the variation across the country in usage of cancer drugs approved by NICE. It is now important that they remain on top of this issue through adequate planning and regular monitoring and seek to make further reductions in variation where possible.

**Annex 1****Cancer Drugs appraised by NICE**

<b>Drug</b>	<b>Company</b>	<b>Indication</b>
Capecitabine (Xeloda)	Roche	Breast & Bowel
Docetaxel (Taxotere)	Sanofi-Aventis	Breast & Lung
Fludarabine (Fludara)	Schering Health	Leukaemia (CLL)
Gemcitabine (Gemzar)	Lilly	Lung & Pancreas
Imatinib (Glivec)	Novartis	Leukaemia (CML)
Irinotecan (Camppto)	Sanofi-Aventis	Bowel
Oxaliplatin(Eloxatin)	Sanofi-Aventis	Bowel
Paclitaxel (Taxol)	Bristol-Myers Squibb	Breast, Ovary & Lung
Pegulated Liposomal doxorubicin (Caelyx)	Schering-Plough	Ovary
Raltitrexed(Tomudex)	AstraZeneca	Bowel
Rituximab (MabThera)	Roche	Lymphoma (NHL)
Tegafur uracil (Uftoral)	Bristol Myers Squibb	Bowel
Temozolamide (Temodal)	Schering-Plough	Brain
Topotecan(Hycamptin)	Merck	Ovary
Trastuzumab (Herceptin)	Roche	Breast
Vinorelbine (Navelbine)	Pierre Fabre	Breast & Lung
<b>Comparator Drugs</b>		
Cisplatin	Non-proprietary	Multiple cancer types
Carboplatin (Paraplatin)	Bristol Myers Squibb	Multiple cancer types
Doxorubicin	Pharmacia/Upjohn	Multiple cancer types
Epirubicin (Pharmorubicin)	Pharmacia/Upjohn	Multiple cancer types

## Approach to this review

1. This review has considered the 16 cancer drugs appraised by NICE plus four standard cancer drugs as comparators (see **Annex 1** for details).

### *Data*

2. There is no routine national data collection in relation to cancer chemotherapy prescribed and administered in hospitals. This contrasts with the detailed information on drugs prescribed in the community available from the Prescribing Pricing Authority database. Other sources have therefore had to be used to inform this review.

### *IMS Health*

3. IMS Health has kindly provided the initial data used for this exercise. IMS Health collect information on drugs used in hospitals (direct from NHS Trusts). At present the data they collect covers hospitals containing around 93% of acute beds in the UK. This includes almost all of the major adult cancer centres in England.
4. IMS Health data on the usage of the 20 drugs considered in this exercise was sent to each network for validation as it was in the 2003 exercise. The validation process consisted of each of the 34 cancer networks being provided with a spreadsheet showing their usage (unprojected IMS figures) of the 16 NICE appraised cancer drugs and 4 comparator chemotherapy drugs for the 6 month period January to June 2005. In addition they were given information to show the allocation of trusts that were assumed to be part of their network, allocation of PCTs to derive the network population and information on the coverage of the IMS data. Exact details of the coverage of the IMS data for each network were given. Networks were not given each others' usage data.
5. All 34 cancer networks responded either revising all the IMS figures provided (19 networks), some of the IMS figures (7 networks) or accepting the IMS figures (8 networks). Some networks accepted IMS figures because they did not have the time or capacity to validate the figures – in these cases they had not necessarily agreed that the IMS data accurately reflected usage in their network.
6. More networks revised their usage figures in this exercise than previously. Where networks revised figures, these were used throughout the analysis. Revision by a network of IMS' figures has not necessarily meant that IMS figures are incorrect. Validation carried out

by IMS has subsequently indicated that some networks may have made errors in calculating their revised figures.

7. In some cases, the differences between the IMS and network figures were large. Some of the differences could be explained by coverage of IMS data. However, even for networks where IMS believed they had good coverage of a networks' usage, there were still some significant differences. IMS is investigating these differences with network pharmacists in order to try and improve the data quality for the future.

**Data Limitations**

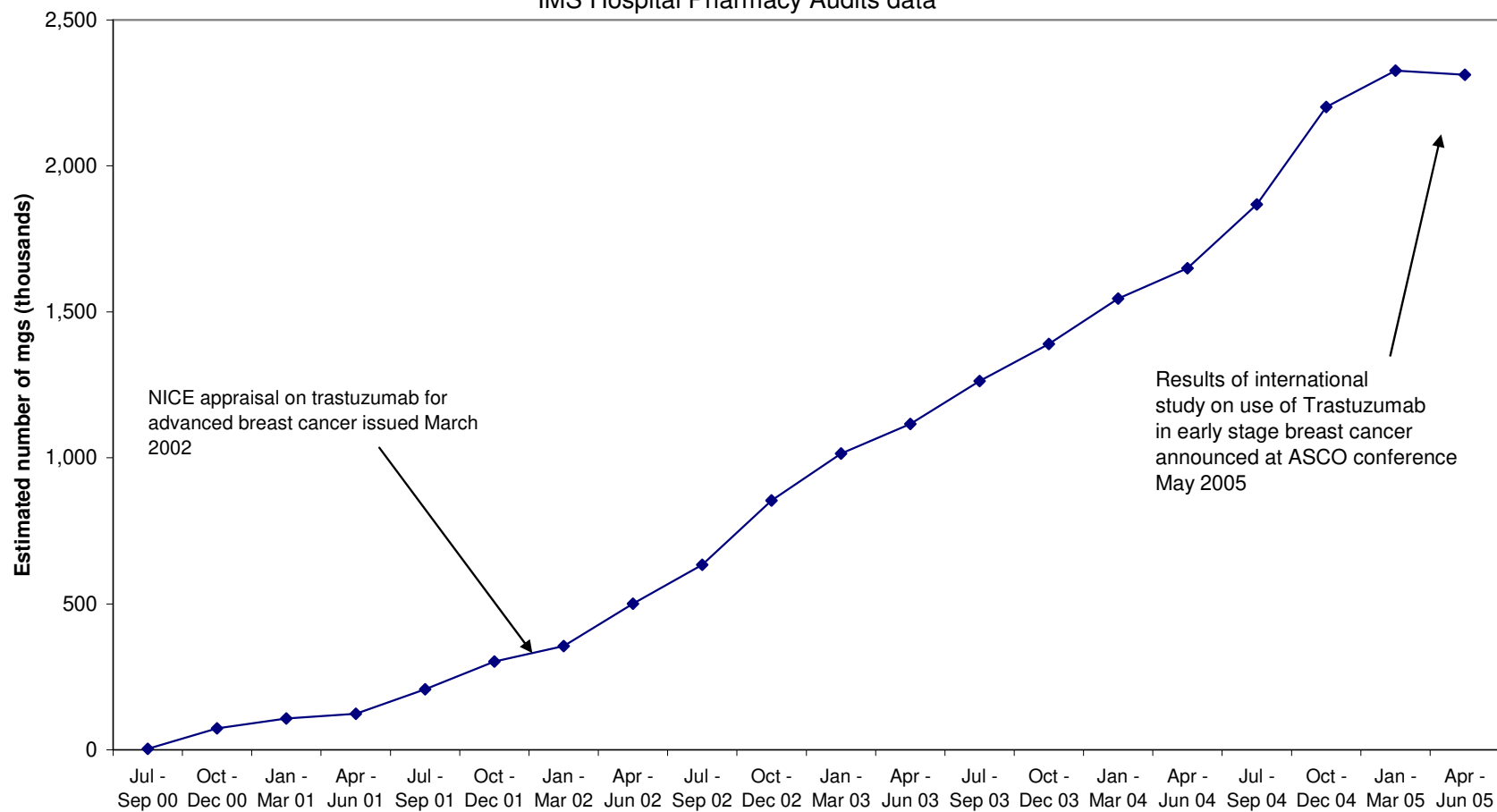
The information on which this report is based (whether IMS or network data is used) has some limitations:

- a) The IMS data used in this report is based on unprojected figures (ie. if some Trust data was missing, IMS did not extrapolate to take account of this). However, when networks considered this unprojected data they had the opportunity to include data from missing trusts in order to get the most accurate data. They also had the opportunity to ensure the allocation of trusts (including primary care trusts) used to calculate a network's population was correct. For those networks that accepted the IMS data there may be issues if the coverage of IMS data was not very good for that network although there will be some variation between networks in the effect of these issues. Further details on the coverage of IMS data can be provided if required.
- b) It was not possible in the IMS data provided to differentiate between drugs prescribed for NHS patients and those prescribed to private patients within NHS trusts. Networks were therefore asked to provide an estimate of the proportion of overall usage which related to the treatment of private patients since ideally private usage would be excluded from the analysis. Some networks were able to give the proportion of private usage by drug which has been taken into account in the analysis. Some networks indicated that no private usage is included in the figures. However many networks did not indicate the proportion of private usage therefore the data is likely to be overestimated.
- c) The information does not take into account patient flows across network boundaries i.e. that patients residing in x network may receive y drug at a Trust in z network. Therefore x network may appear a low user of y drug even though its patients do have access to it.
- d) Some networks have indicated that the data they provided was purchasing data (i.e. when hospitals buy in "bulk") rather than issue data ie. drugs issued from the hospital pharmacy to specific clinics, wards or patients. For the remaining networks we can not be sure that they have provided issue data therefore usage of drugs as reported by networks may not reflect the true usage of drugs actually issued in the six month period.
- e) No information is available on the numbers of patients treated or on the type of cancer for which the drugs are being used – it is not therefore possible to tell if a NICE appraised cancer drug has a high usage for one indication but a low usage for another. IMS data is likely to be for all indications. Some of the network data may only be for the NICE indications.

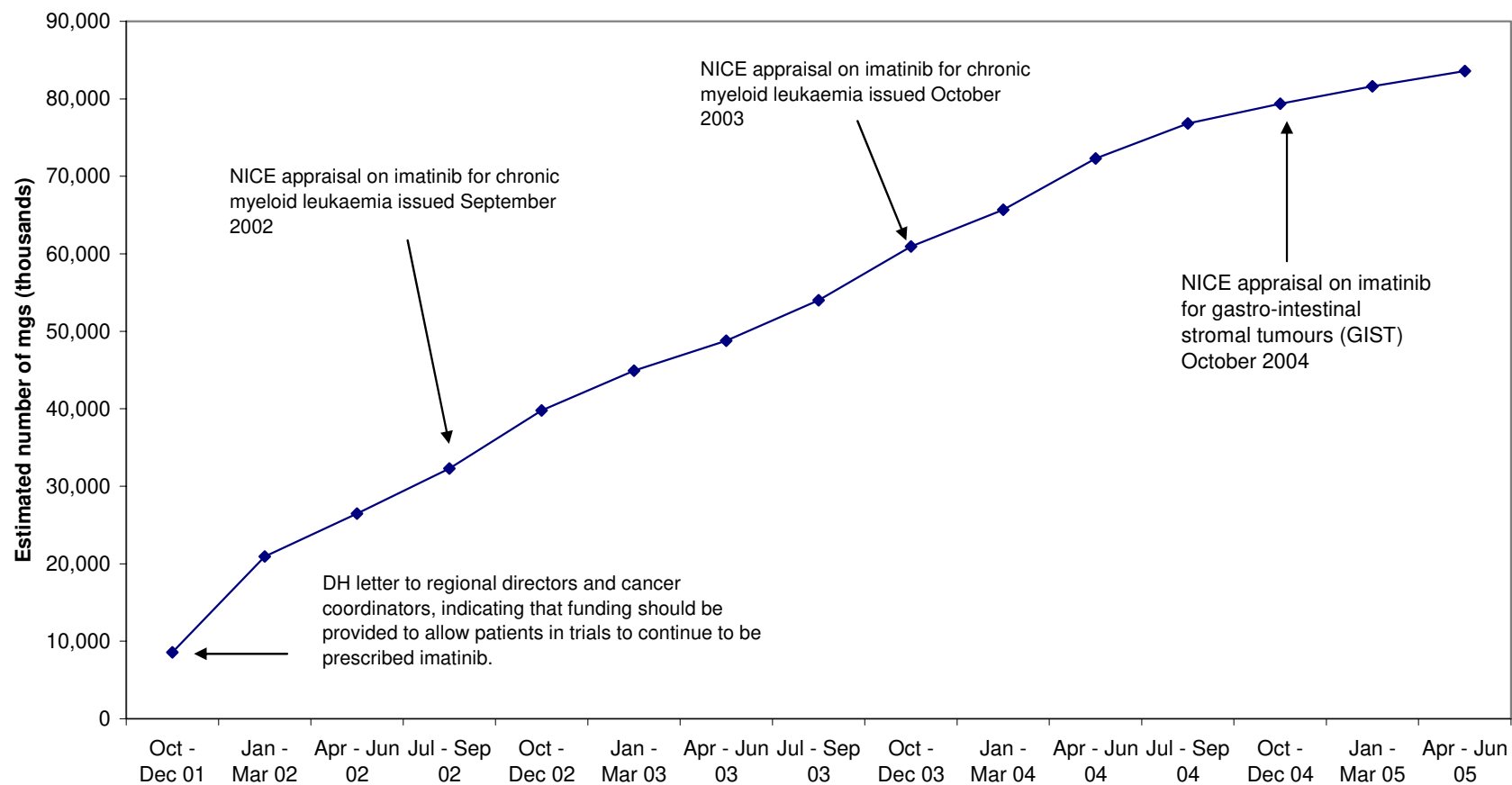
- f) Where networks are, or have been, involved in clinical trials of drugs these drugs may be supplied direct to the chemotherapy units and not through the hospital pharmacy so will be excluded from the IMS data. IMS data may therefore be lower than usage in the network, although it is suspected that this proportion is small. Some networks commented that clinical trial usage was included in their figures which could explain the difference between the IMS and network data.
- g) Drugs prescribed in the community are not included in the IMS figures (though these are available from Prescription Pricing Authority database). However, community prescribing is negligible and has only a minimal impact on the NICE approved cancer drugs.
- h) It is believed that a proportion of drug usage supplied by Homecare companies under hospital contract is excluded from the data supplied to IMS Health. Networks were asked in their returns to indicate the level of Homecare usage in their network by drug. In the few cases where this information was provided, the majority of networks indicated that there was no or negligible homecare usage in their network. It is not clear whether, where there is Homecare usage, this is included or excluded from the data but it is not thought to be a big issue since homecare usage appears to be negligible.
- i) For a few networks, it appears that they have derived their usage figures by applying the list price costs to their actual expenditure, rather than base it on their contract price. This will have the effect of underestimating usage.
- i) Some networks have indicated that they have only revised figures where there is significantly different usage to the IMS data. In most cases where this has happened, there is no indication what significantly different means.

These limitations may impact on figures for usage in some/all networks eg. artificially deflating their figures. There will be some variation between networks in the effect of these issues. For this reason ***it is inappropriate to regard small differences between networks as significant***. Estimated range bars, for each network, have been shown on the charts at Annex 7 to allow for the data limitations and to give some indication of the likely variation.

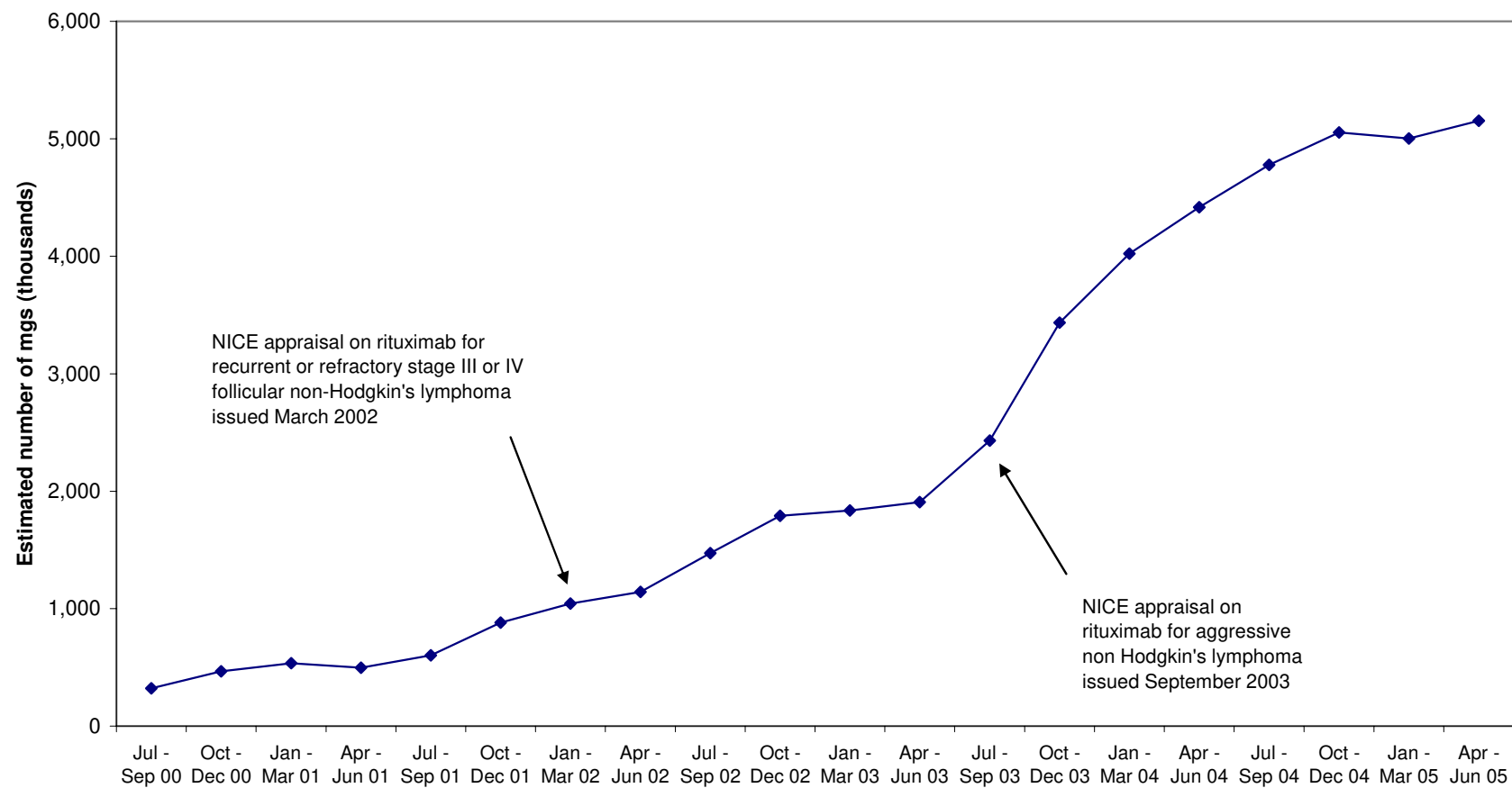
**Estimated volume of Trastuzumab used in hospitals in England, July 2000 to June 2005**  
 IMS Hospital Pharmacy Audits data



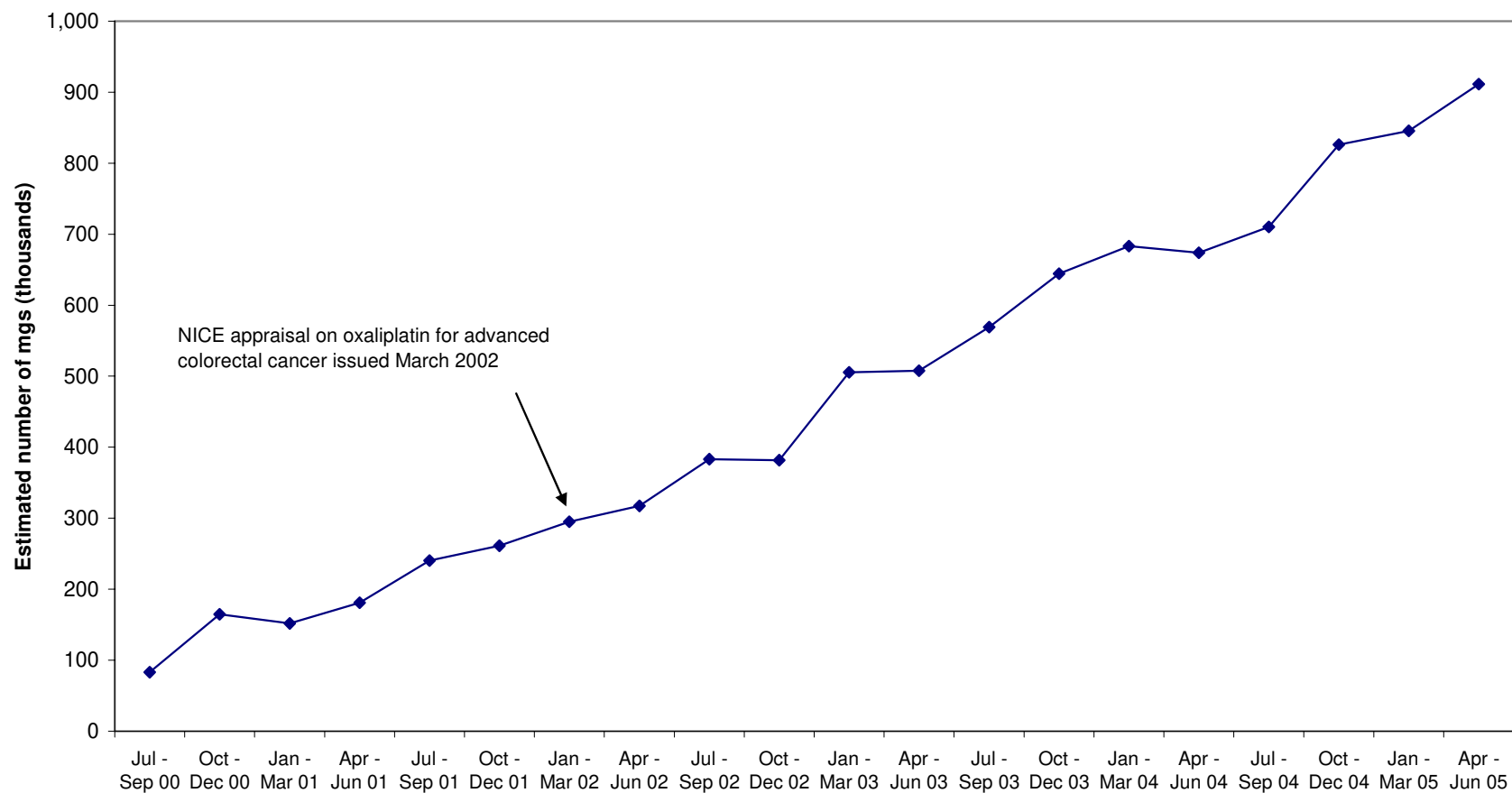
**Estimated volume of Imatinib used in hospitals in England, Oct 2001 to June 2005**  
 IMS Hospital Pharmacy Audits data



**Estimated volume of Rituximab used in hospitals in England, July 2000 to June 2005**  
IMS Hospital Pharmacy Audits data



**Estimated volume of Oxaliplatin used in hospitals in England, July 2000 to June 2005**  
 IMS Hospital Pharmacy Audits data



**Average growth in usage of Cancer drugs, based on the median rate usage of each drug, between July to December 2003 and January to June 2005**

This information has been supplied by IMS Health and the cancer networks.

Drug	Median rate (mg per 1000 population)		Percentage change (Jul-Dec 03 to Jan - Jun 05)
	Jul- Dec 03	Jan - Jun 05	
RITUXIMAB	111.5	207.9	87%
IMATINIB	1,843.7	3,140.4	70%
GEMCITABINE	846.9	1,178.1	39%
FLUDARABINE	21.5	23.8	11%
DOCETAXEL	13.9	23.0	65%
CAPECITABINE	13,976.7	22,982.9	64%
OXALIPLATIN	20.0	33.7	68%
IRINOTECAN	46.5	58.4	26%
PACLITAXEL	44.3	55.0	24%
TRASTUZUMAB	47.5	73.4	55%
VINORELBINE	6.8	7.5	11%
PEG LIP DOX	2.3	2.7	21%
TEMOZOLOMIDE	28.4	62.5	120%
TOPOTECAN	0.1	0.1	15%
RALTITREXED	-	-	N/A
URACIL/TEGAFUR	-	-	N/A
CISPLATIN*	46.2	46.4	0%
CARBOPLATIN*	307.7	363.1	18%
EPIRUBICIN*	70.9	79.0	12%
DOXORUBICIN*	42.3	39.9	-6%

**The median of the increases in median rate between Jul-Dec 03 and Jan-Jun 05:**

All NICE drugs (excluding Raltitrexed and Uracil/Tegafur) 47%

\* These drugs have not been appraised by NICE and have been included in this work as comparators.

Notes:

1. All figures are estimated mg used per 1000 population
2. Raltitrexed, and Uracil / Tegafur have been excluded as their low usage gives a median value of zero.
3. All analyses have been undertaken in relation to the estimated population served by the relevant network. Cancer network populations were estimated using population data from the Census (2003 resident PCT estimates based on 2001 Census) and the allocations of PCTs to networks were checked with the cancer policy team and networks. Several networks commented about the population data used for the denominator.
4. The figures in the table are based on information provided by IMS Health and validated by cancer networks. Network figures were used in place of IMS figures where provided.
5. An overall median rate for all drugs cannot be calculated from the information in this table.

## Annex 4

### National Variation in usage of all drugs in the study (Jan to Jun 2005) Median and 90%ILE/10%ILE compared with Jul - Dec 03 data.

This information has been supplied by IMS Health and the cancer networks.

Drug	Minimum	25th percentile	75th percentile	Maximum	Mean	Median	Median - Jul- Dec 03	Percentage increase in median (Jul- Dec 03 to Jan Jun 05)	90%ILE/ 10%ILE	90%ILE/ 10%ILE Jul - Dec 03
RITUXIMAB	108.0	162.0	246.0	439.0	218.1	207.9	111.5	87%	2.3	2.6
IMATINIB	1,225.0	2,704.7	3,685.2	11,008.0	3,626.9	3,140.4	1,843.7	70%	2.5	2.9
GEMCITABINE	646.8	1,010.4	1,482.8	2,591.5	1,307.6	1,178.1	846.9	39%	2.5	3.0
FLUDARABINE	8.1	20.4	27.3	37.6	24.2	23.8	21.5	11%	2.2	3.2
DOCETAXEL	7.2	16.9	29.7	73.5	25.6	23.0	13.9	65%	2.7	3.3
CAPECITABINE	9,163.4	19,191.2	32,038.7	56,758.0	24,324.9	22,982.9	13,976.7	64%	3.3	3.6
OXALIPLATIN	15.0	29.3	49.7	78.9	40.0	33.7	20.0	68%	3.0	3.7
IRINOTECAN	14.5	42.1	77.2	242.9	65.5	58.4	46.5	26%	2.5	3.7
PACLITAXEL	25.8	44.6	73.4	177.0	63.4	55.0	44.3	24%	3.1	3.8
TRASTUZUMAB	30.9	57.8	94.8	222.0	85.1	73.4	47.5	55%	2.8	4.2
VINORELBINE	1.8	5.2	11.4	16.3	8.5	7.5	6.8	11%	3.1	8.1
PEG LIP DOX	0.4	1.6	4.2	8.2	3.2	2.7	2.3	21%	5.8	9.7
TEMOZOLOMIDE	2.0	35.1	112.0	152.3	71.6	62.5	28.4	120%	9.5	11.6
TOPOTECAN	0.0	0.0	0.2	0.7	0.2	0.1	0.1	15%	N/A	N/A
RALTITREXED	0.0	0.0	0.0	0.4	0.0	0.0	0.0	N/A	N/A	N/A
URACIL/TEGAFUR	0.0	0.0	0.0	403.9	16.8	0.0	0.0	N/A	N/A	N/A
CISPLATIN*	8.0	41.9	59.4	199.0	57.4	46.4	46.2	0%	2.1	2.3
CARBOPLATIN*	81.0	313.4	407.3	1,458.6	383.1	363.1	307.7	18%	2.1	2.3
EPIRUBICIN*	43.0	64.7	93.6	164.0	83.7	79.0	70.9	12%	2.1	2.4
DOXORUBICIN*	18.0	31.1	48.9	277.5	48.3	39.9	42.3	-6%	2.5	2.7

\* These drugs have not been appraised by NICE and have been included in this work as comparators.

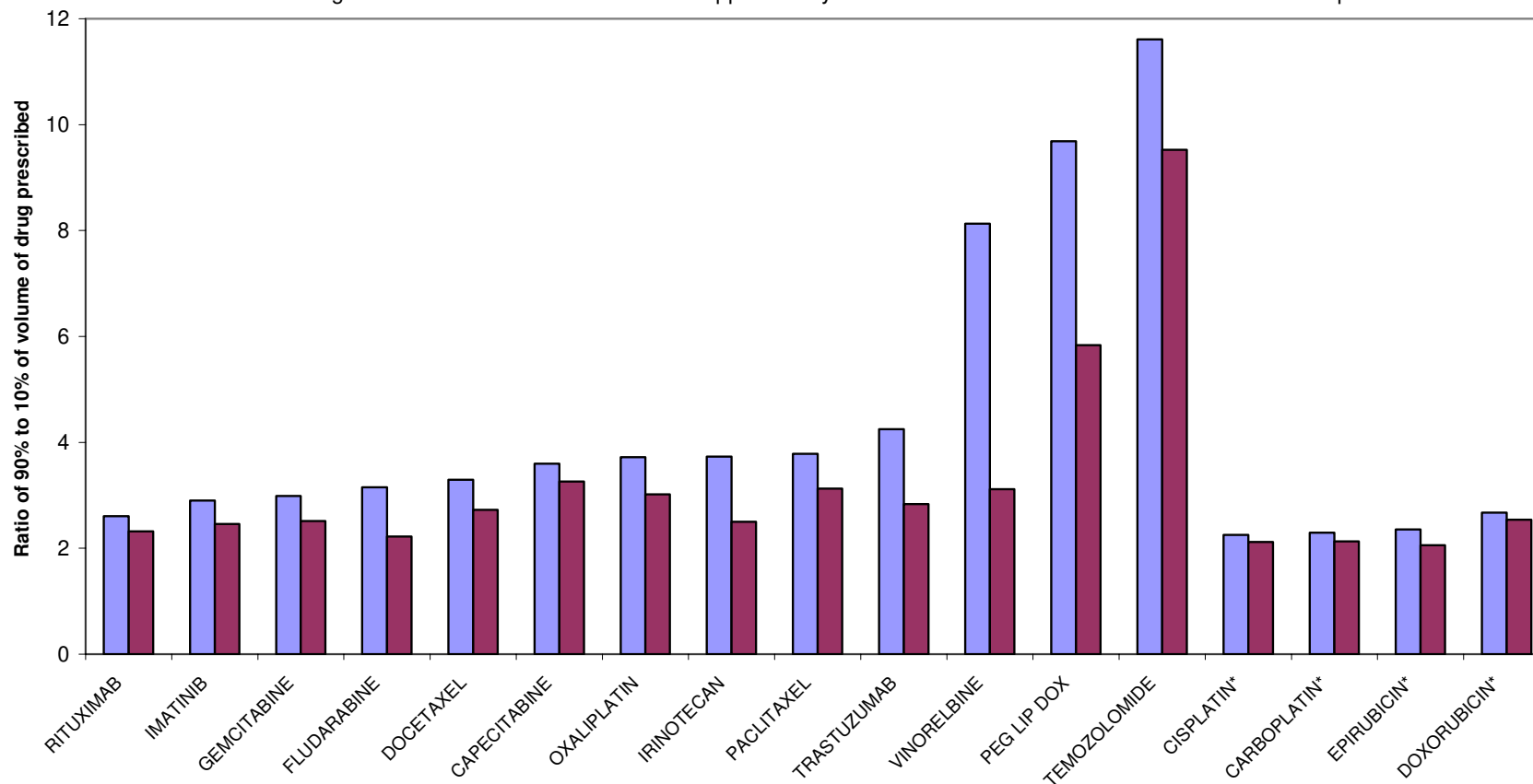
#### Notes:

1. All figures are estimated mg used per 1000 population
2. Minimum - lowest usage among networks
3. 25th percentile - 25% of networks lie below this point
4. 75th percentile - 25% of networks lie above this point
5. Maximum - highest usage among networks
6. 90%ILE/ 10%ILE - the 90/10 ratio is the ratio of the 90th percentile to the 10th percentile of the distribution of usage per head of population by cancer network. This provides a single measure of variability in usage of each drug across networks (a higher number indicates a wider variation). It excludes results of networks at each extreme to minimise the impact of networks with highest and lowest usage.
7. All analyses have been undertaken in relation to the estimated population served by the relevant network. Cancer network populations were estimated using population data from the Census (2003 resident PCT estimates based on 2001 Census) and the allocations of PCTs to networks were checked with the cancer policy team and networks. Several networks commented about the population data used for the denominator.
8. The figures in the table are based on information provided by IMS Health and validated by cancer networks. Network figures were used in place of IMS figures where provided.

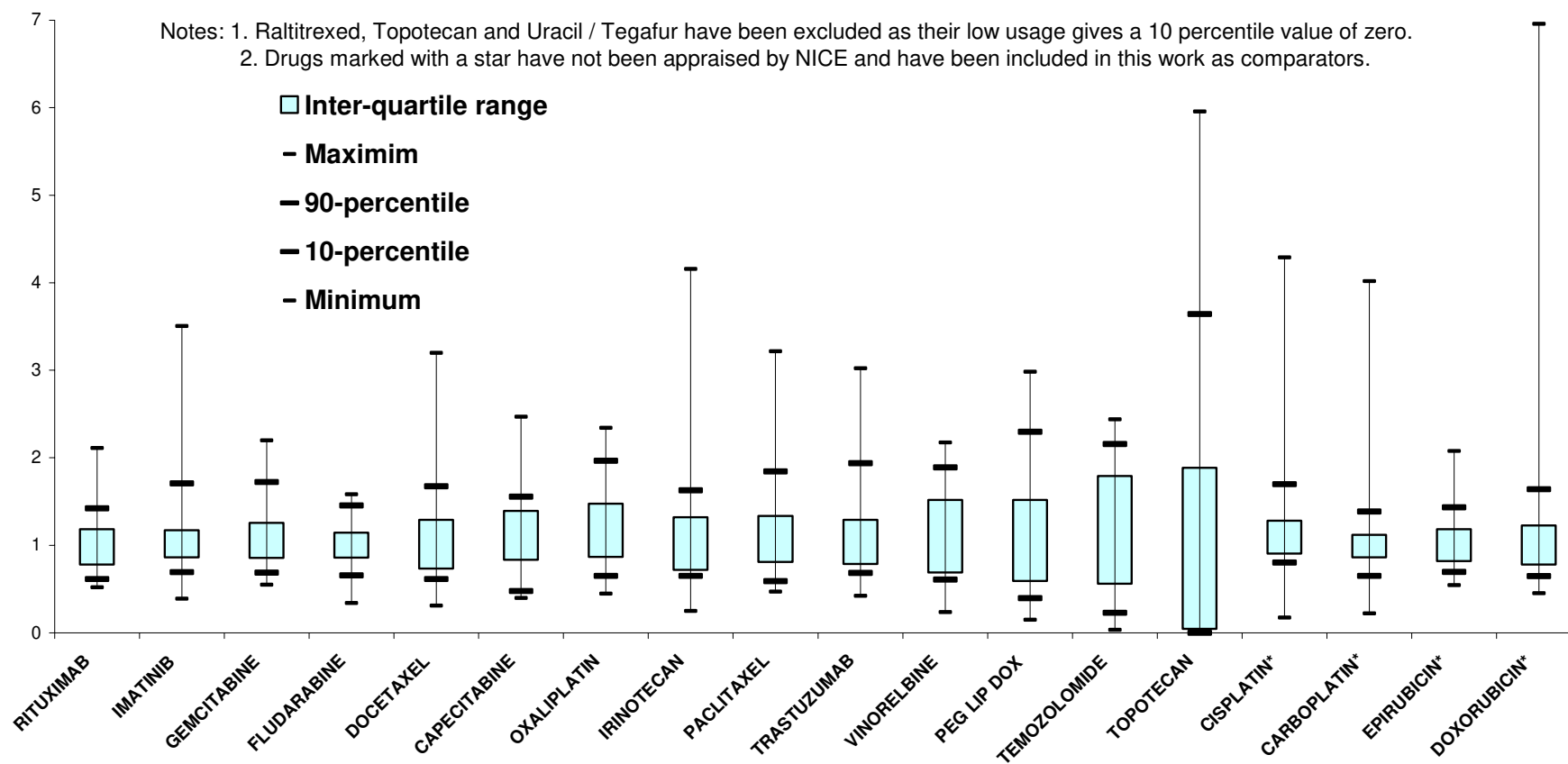
**Ratio of 90-percentile to 10-percentile of volumes of drugs prescribed, indicating the spread of values across networks. Jul to Dec 2003 and Jan to Jun 2005**

Jul to Dec 2003      Jan to Jun 2005

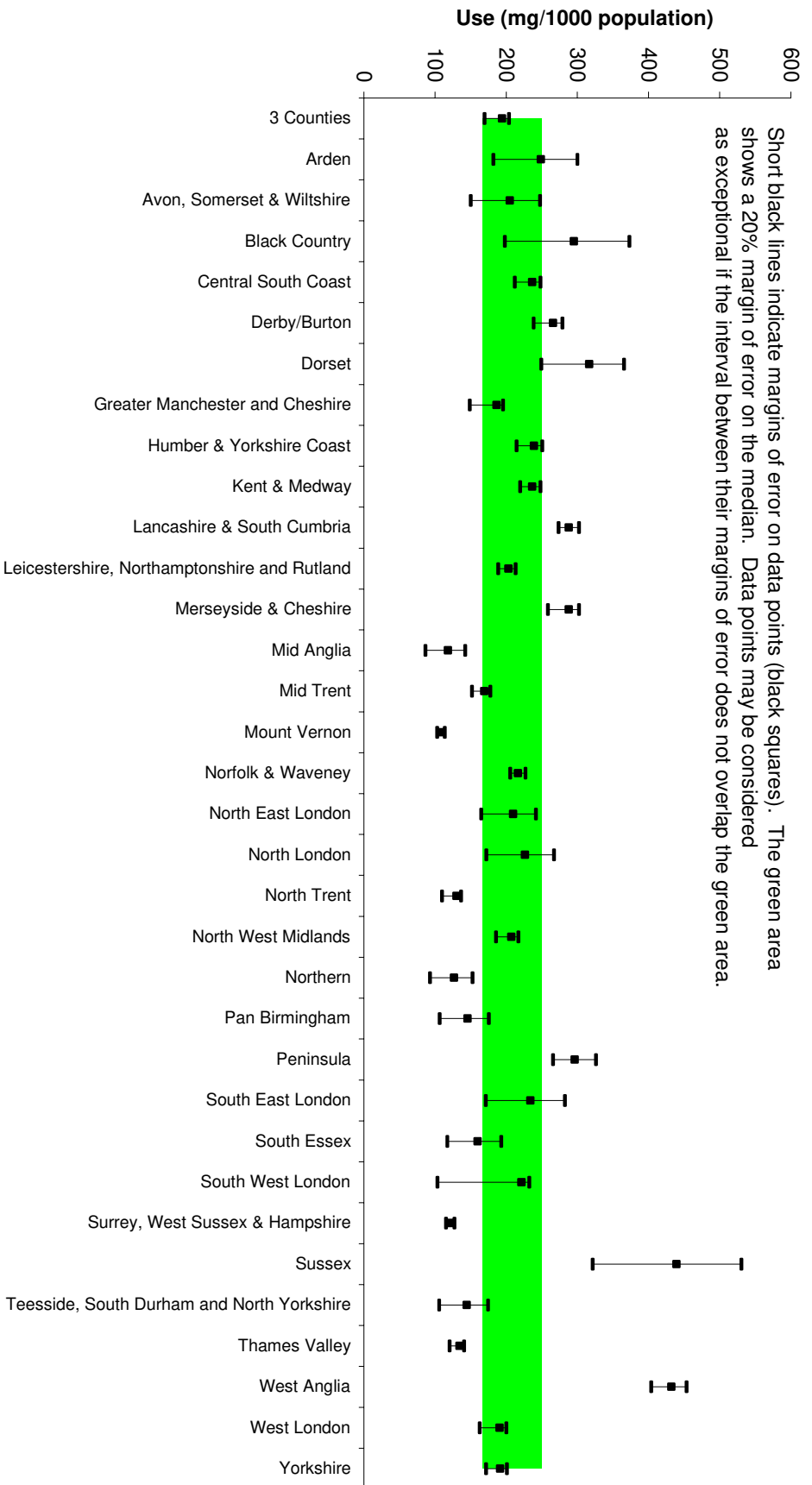
Notes: 1. Raltitrexed, Topotecan and Uracil / Tegafur have been excluded as their low usage gives a 10 percentile value of zero.  
 2. Drugs marked with a star have not been appraised by NICE and have been included in this work as comparators.

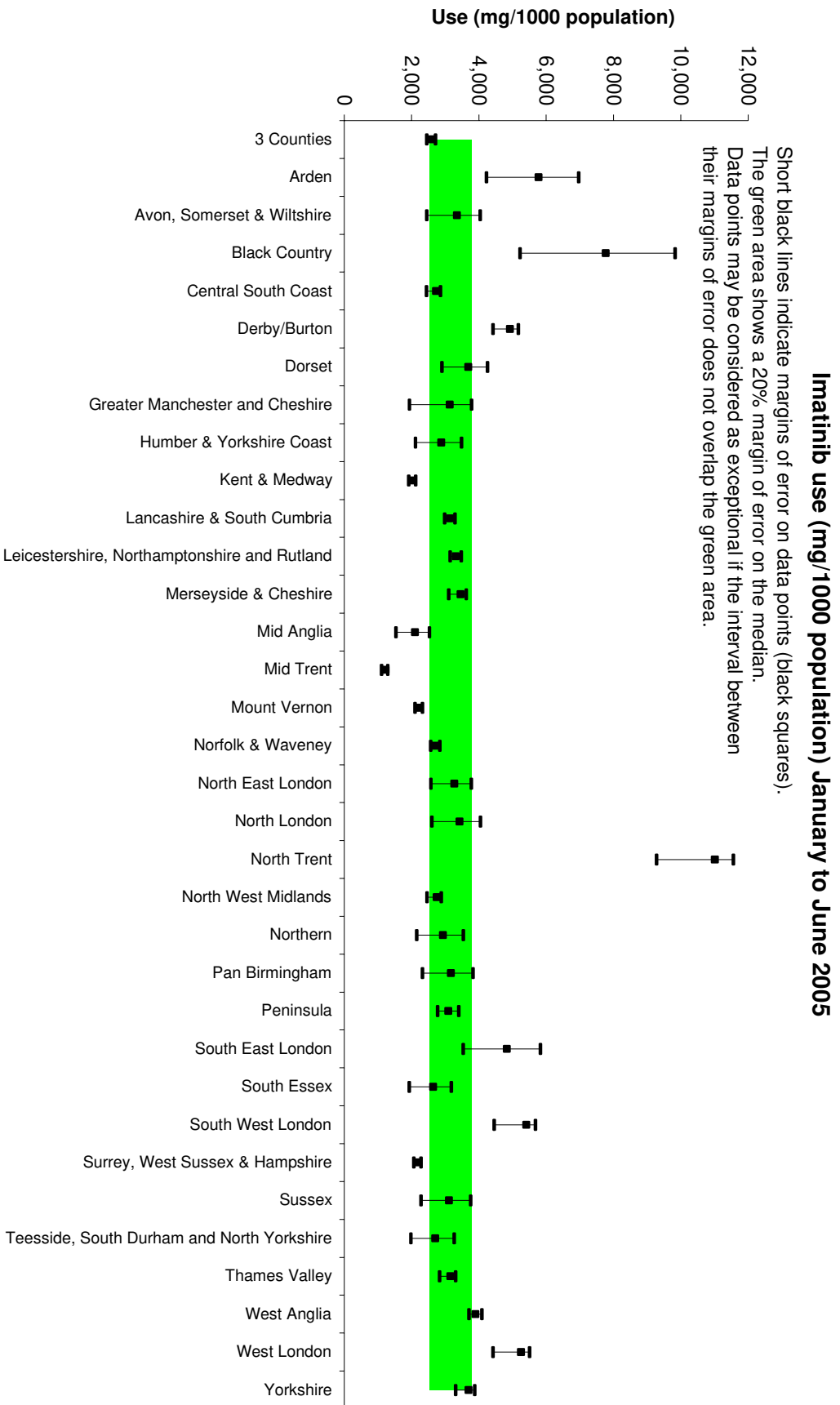


### Distribution of drugs used per thousand population across cancer networks (Jan to Jun 2005), scaled so that median value is 1

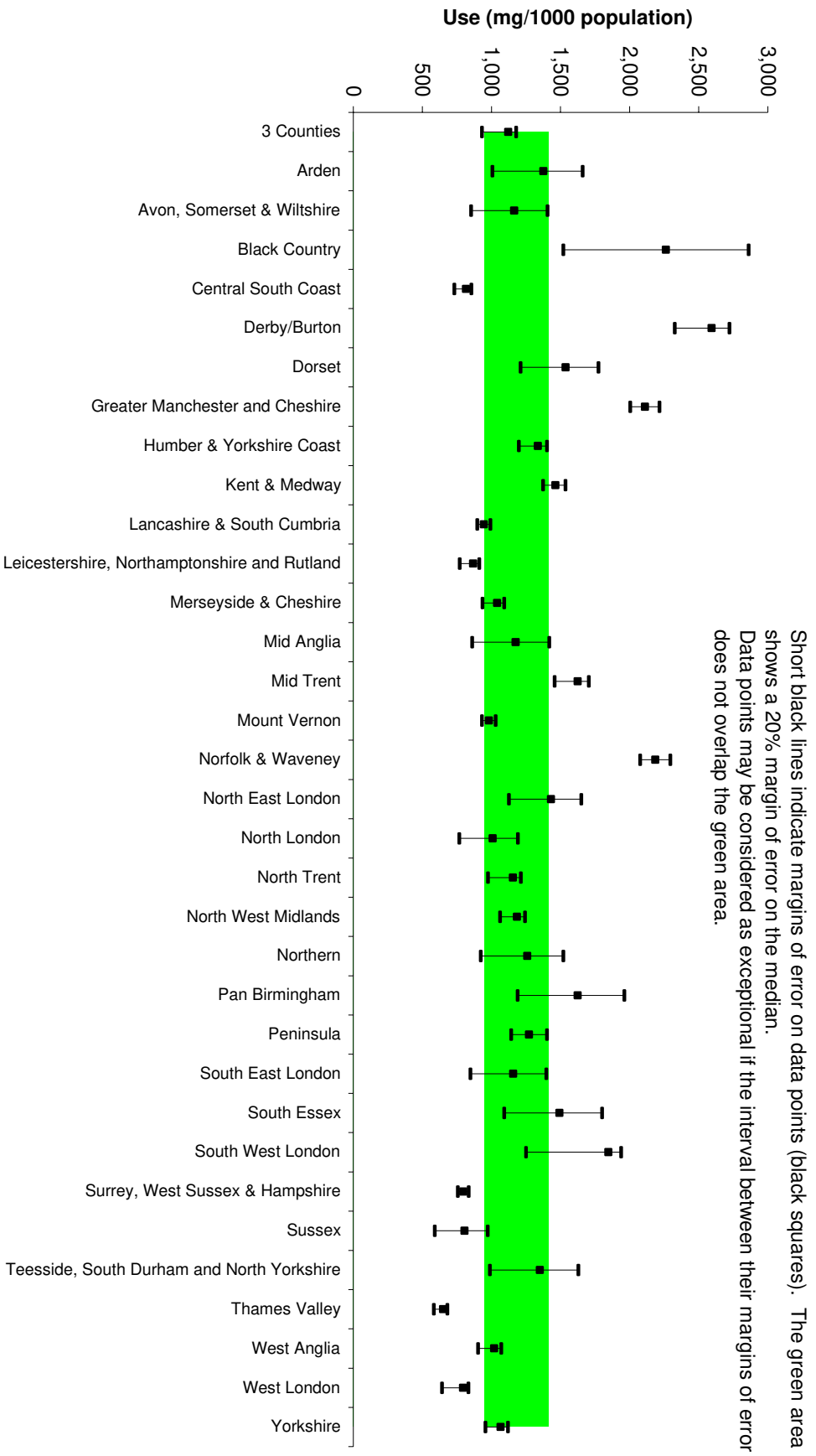


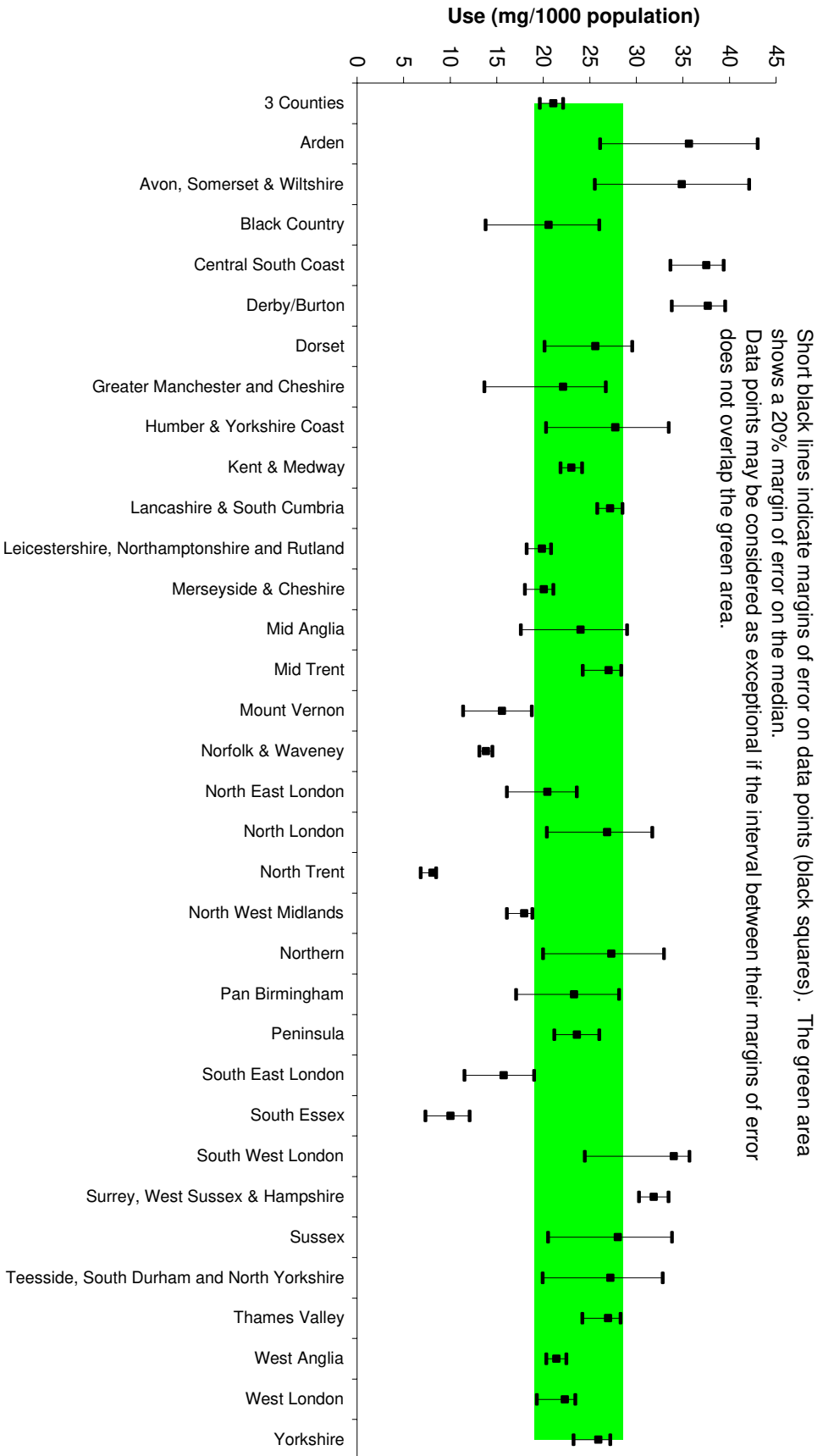
**Rituximab use (mg/1000 population) January to June 2005**



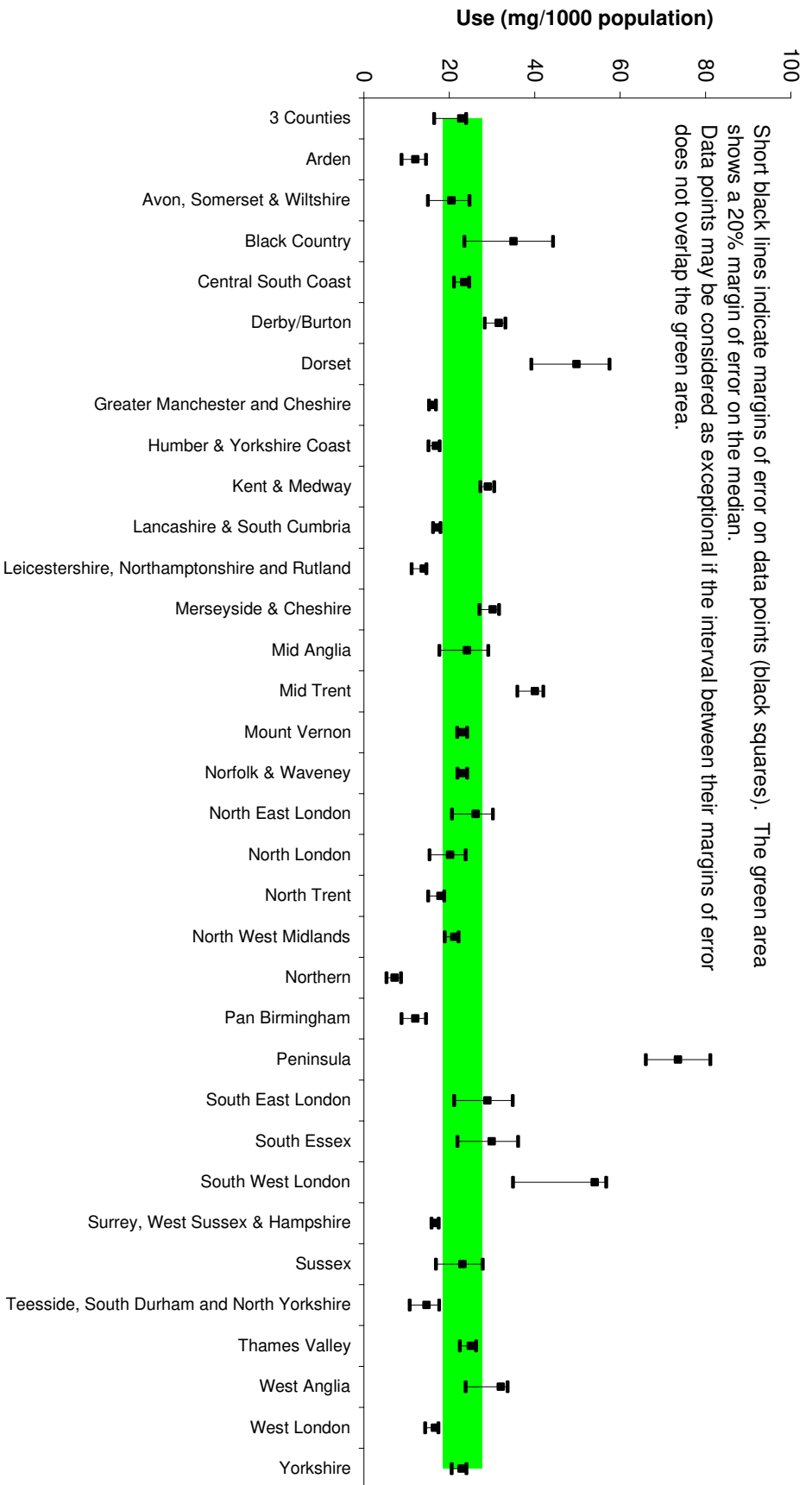


**Gemcitabine use (mg/1000 population) January to June 2005**

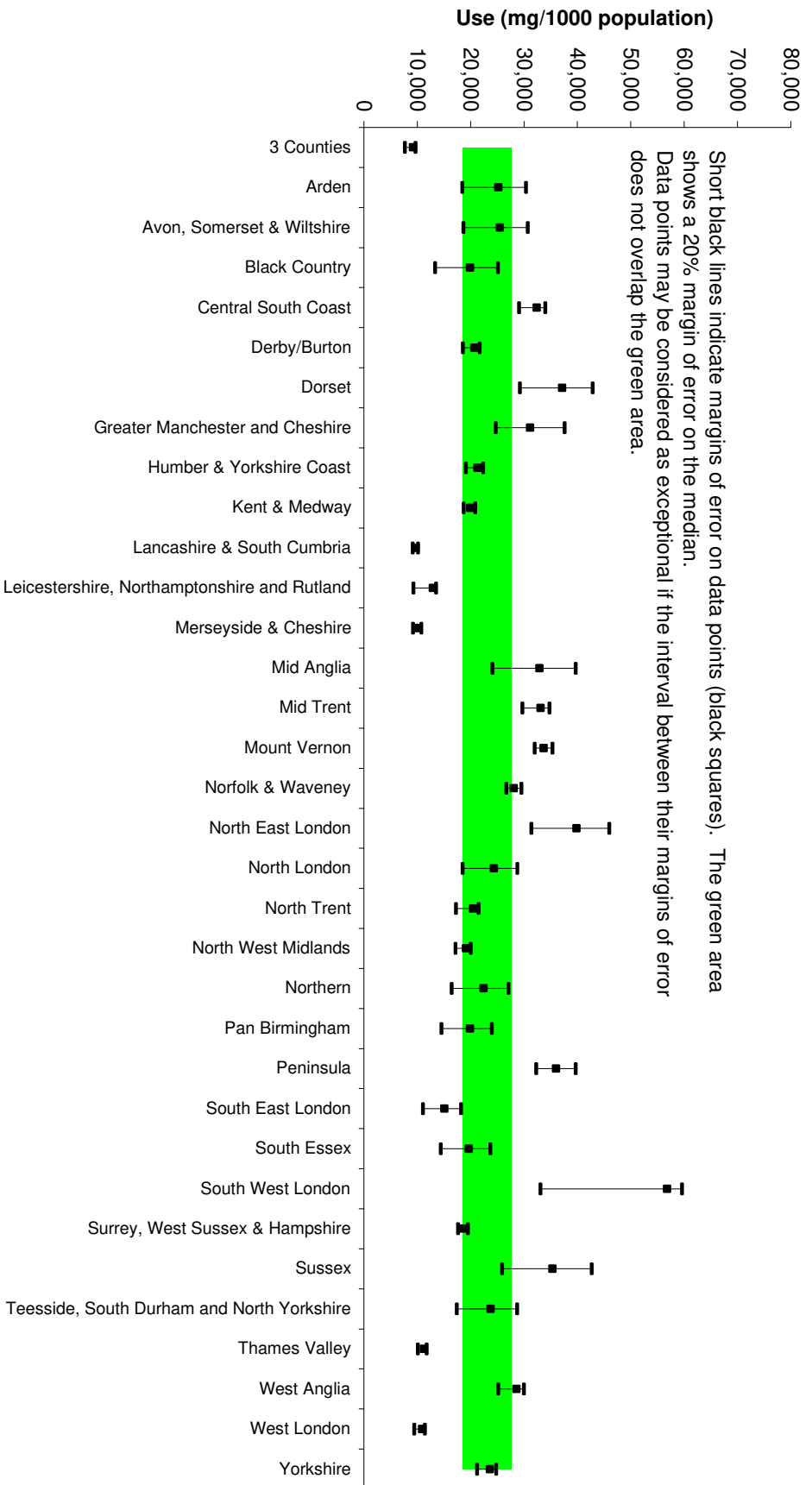




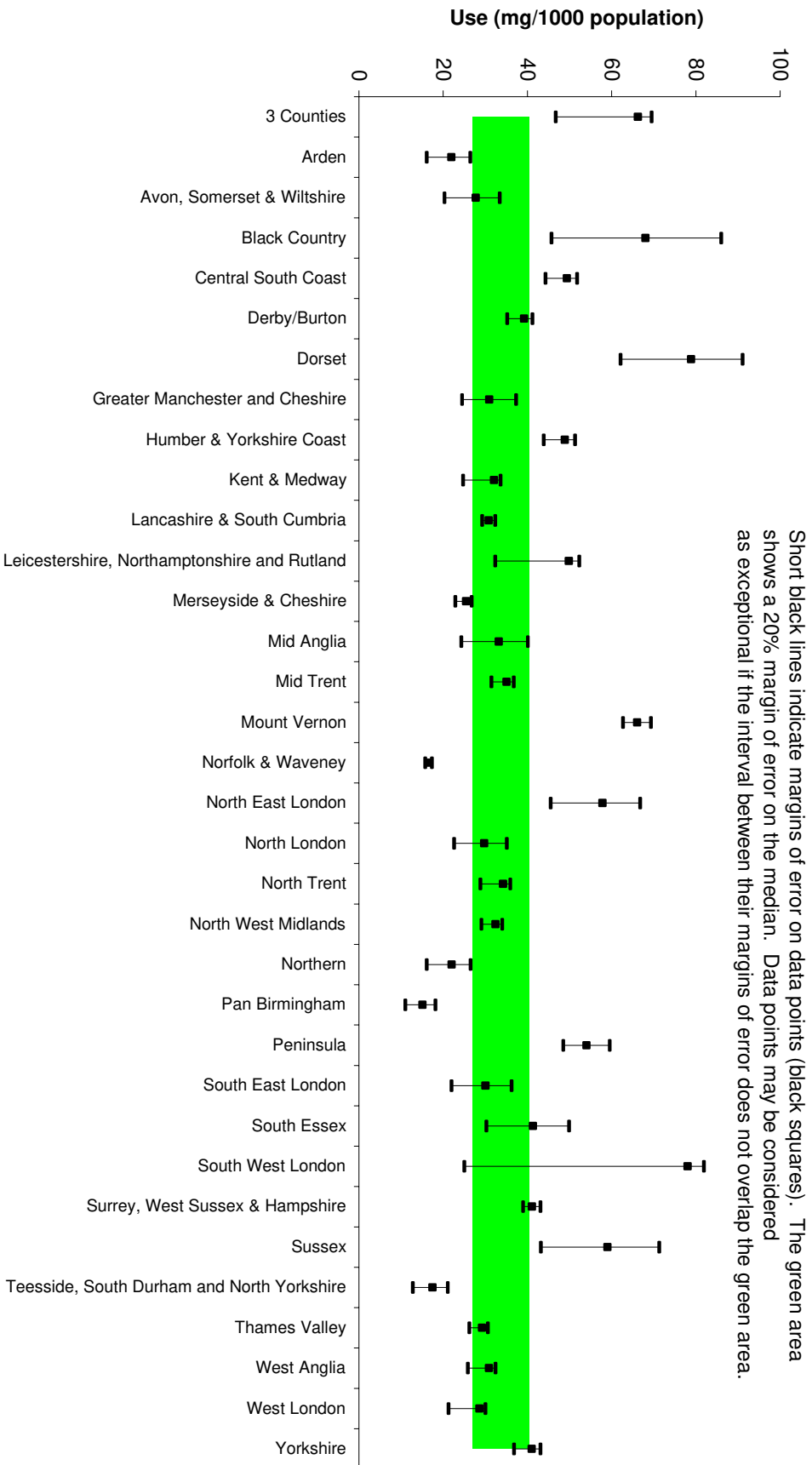
**Docetaxel use (mg/1000 population) January to June 2005**



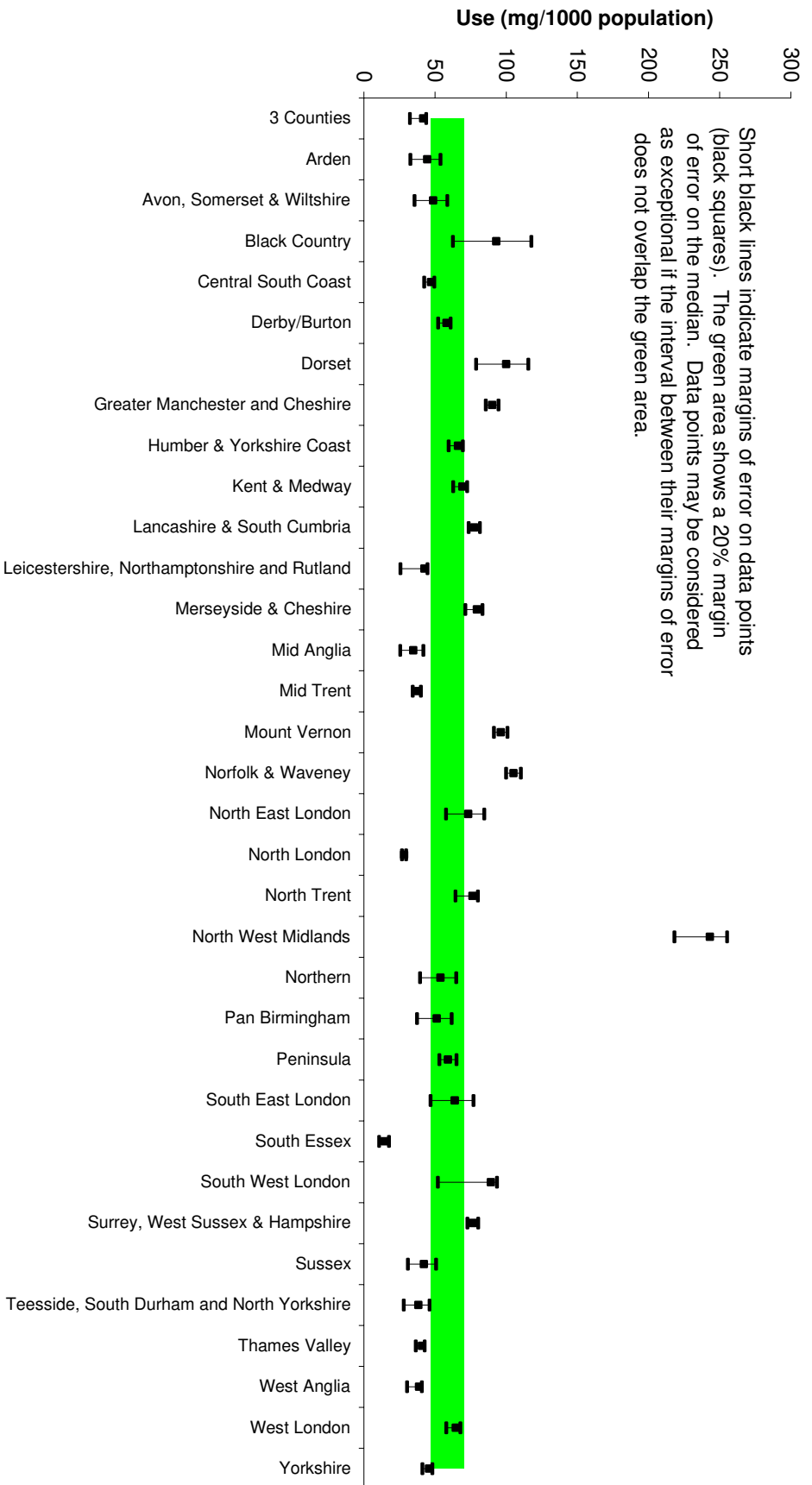
**Capecitabine use (mg/1000 population) January to June 2005**



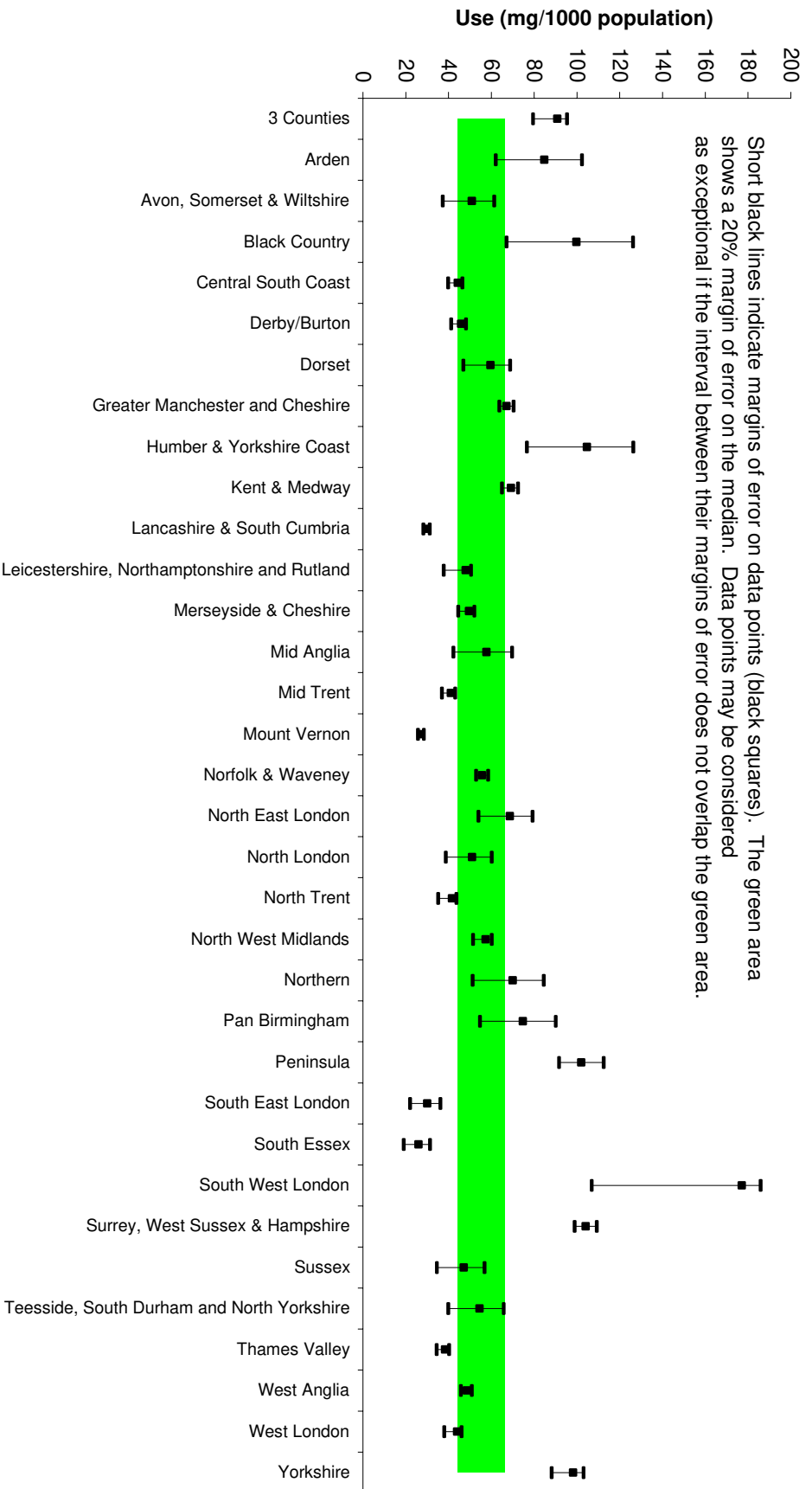
**Oxaliplatin use (mg/1000 population) January to June 2005**



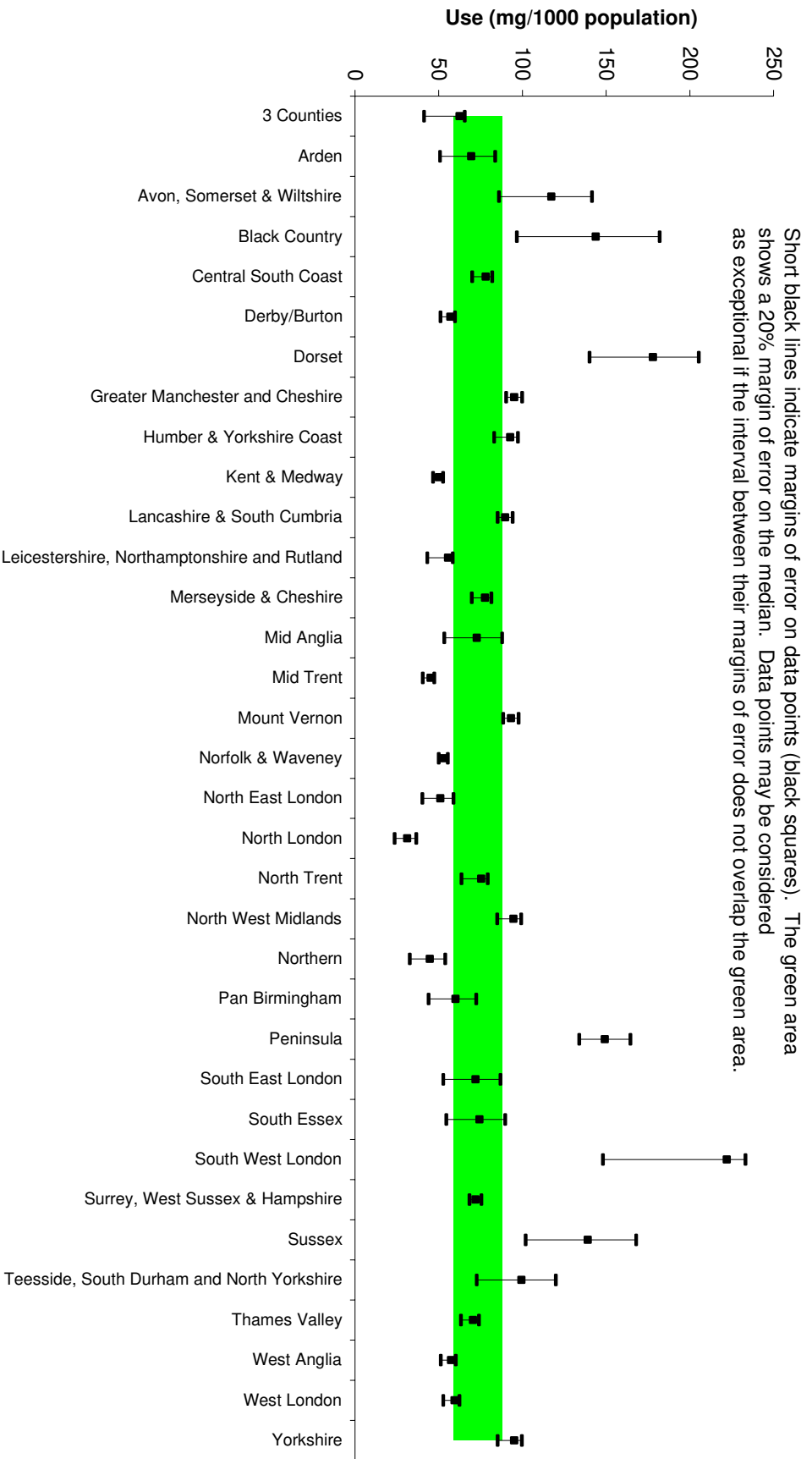
**Irinotecan use (mg/1000 population) January to June 2005**



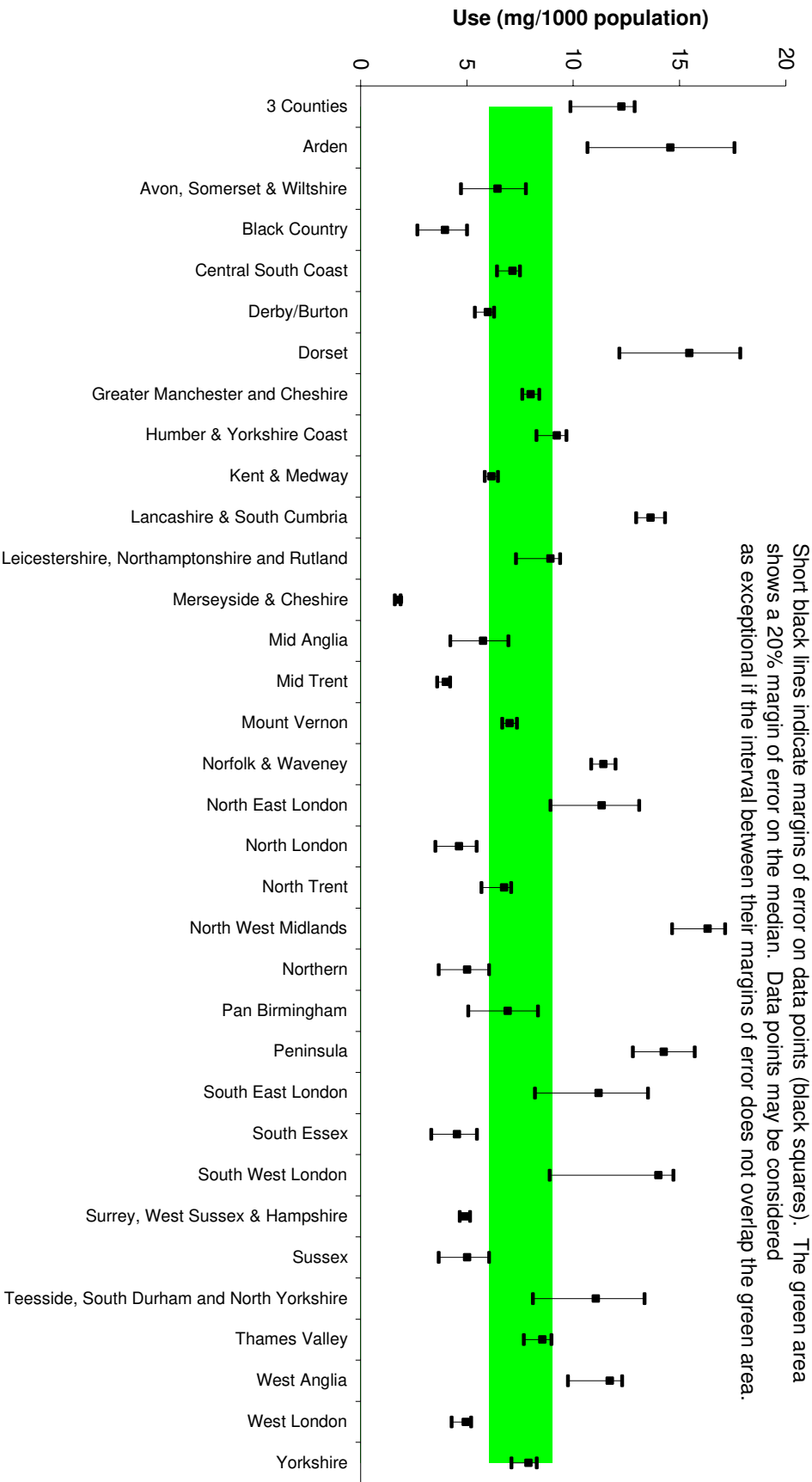
**Pacitaxel use (mg/1000 population) January to June 2005**



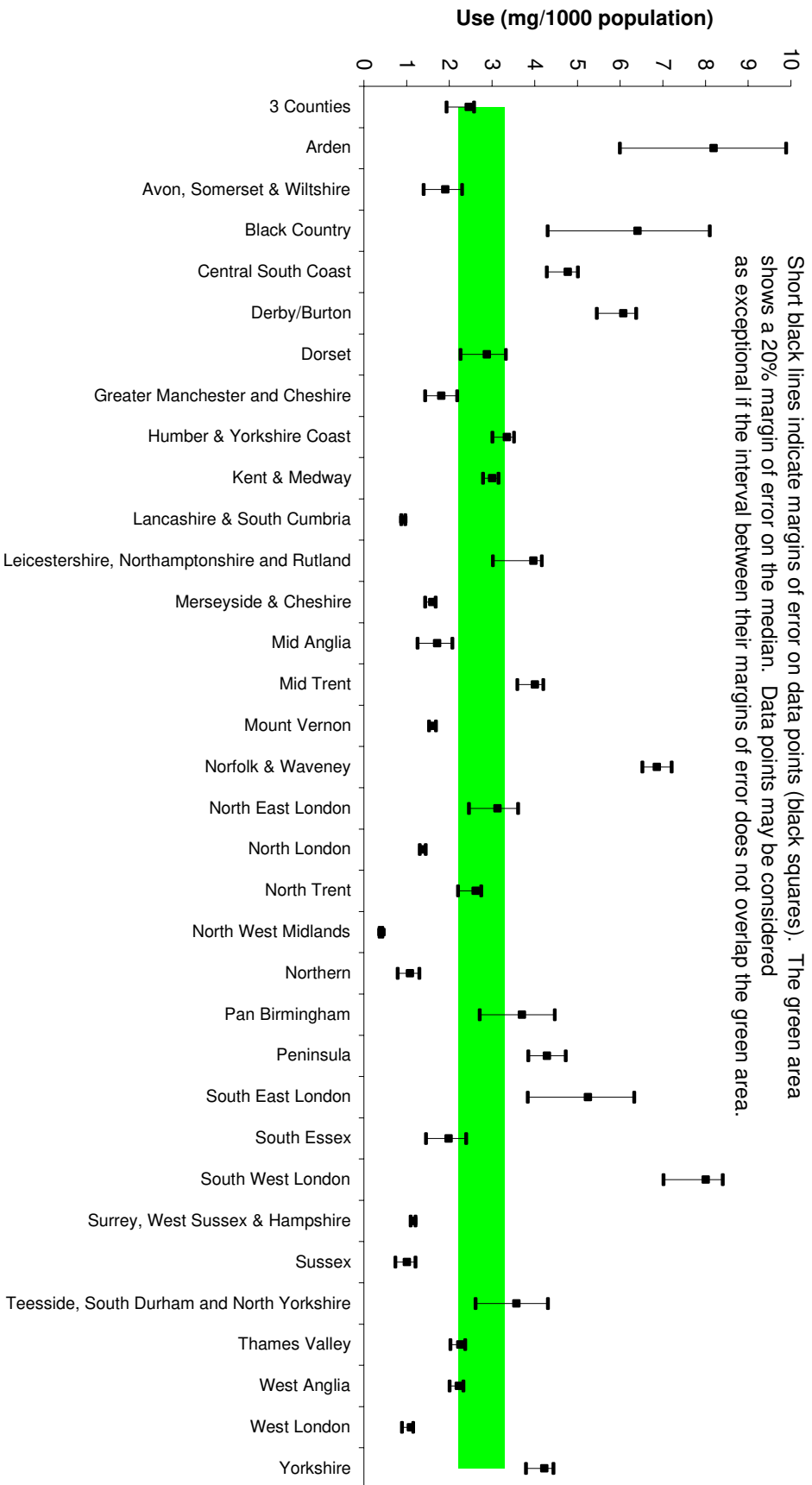
**Trastuzumab use (mg/1000 population) January to June 2005**



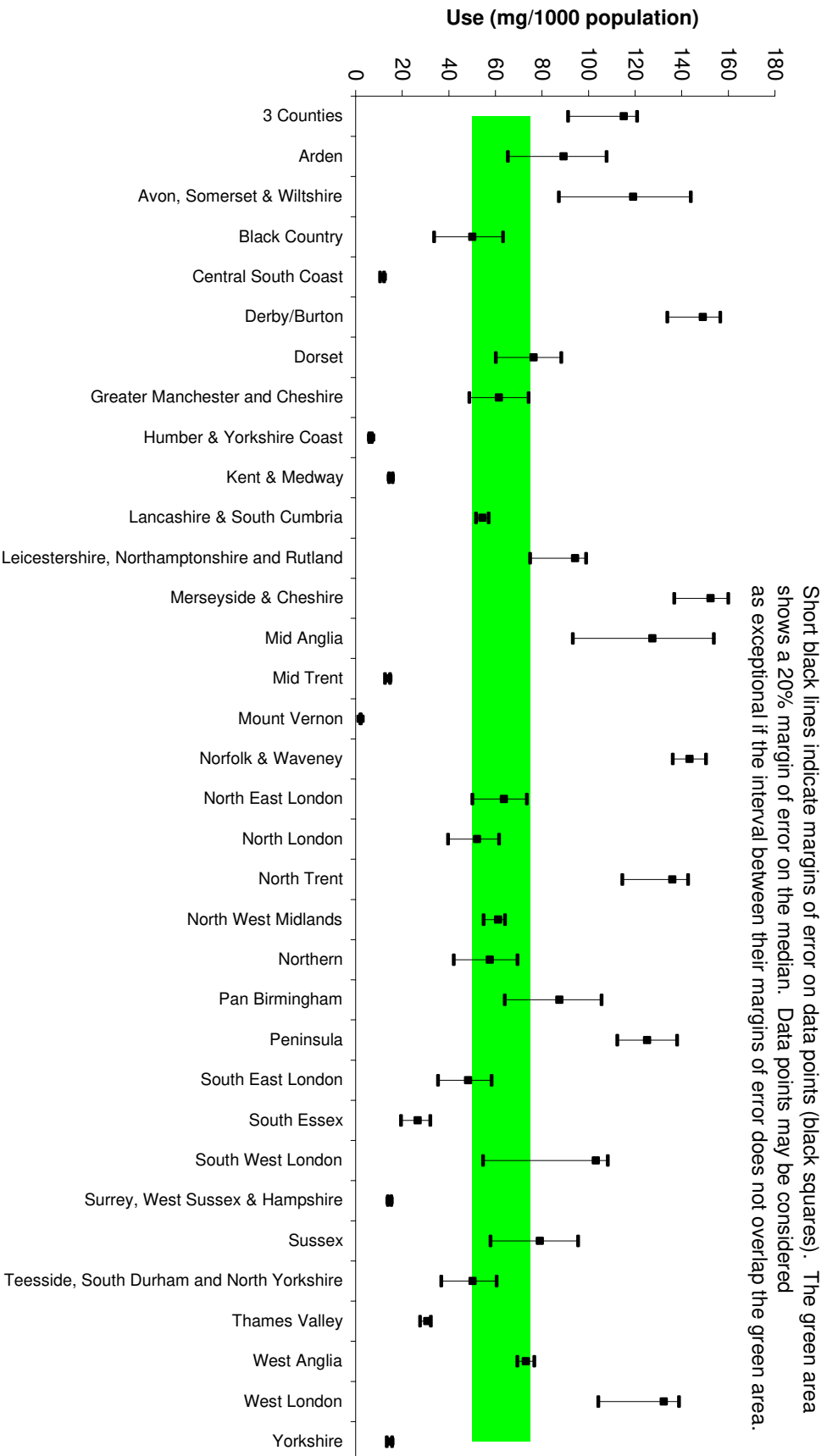
**Vinorelbine use (mg/1000 population) January to June 2005**



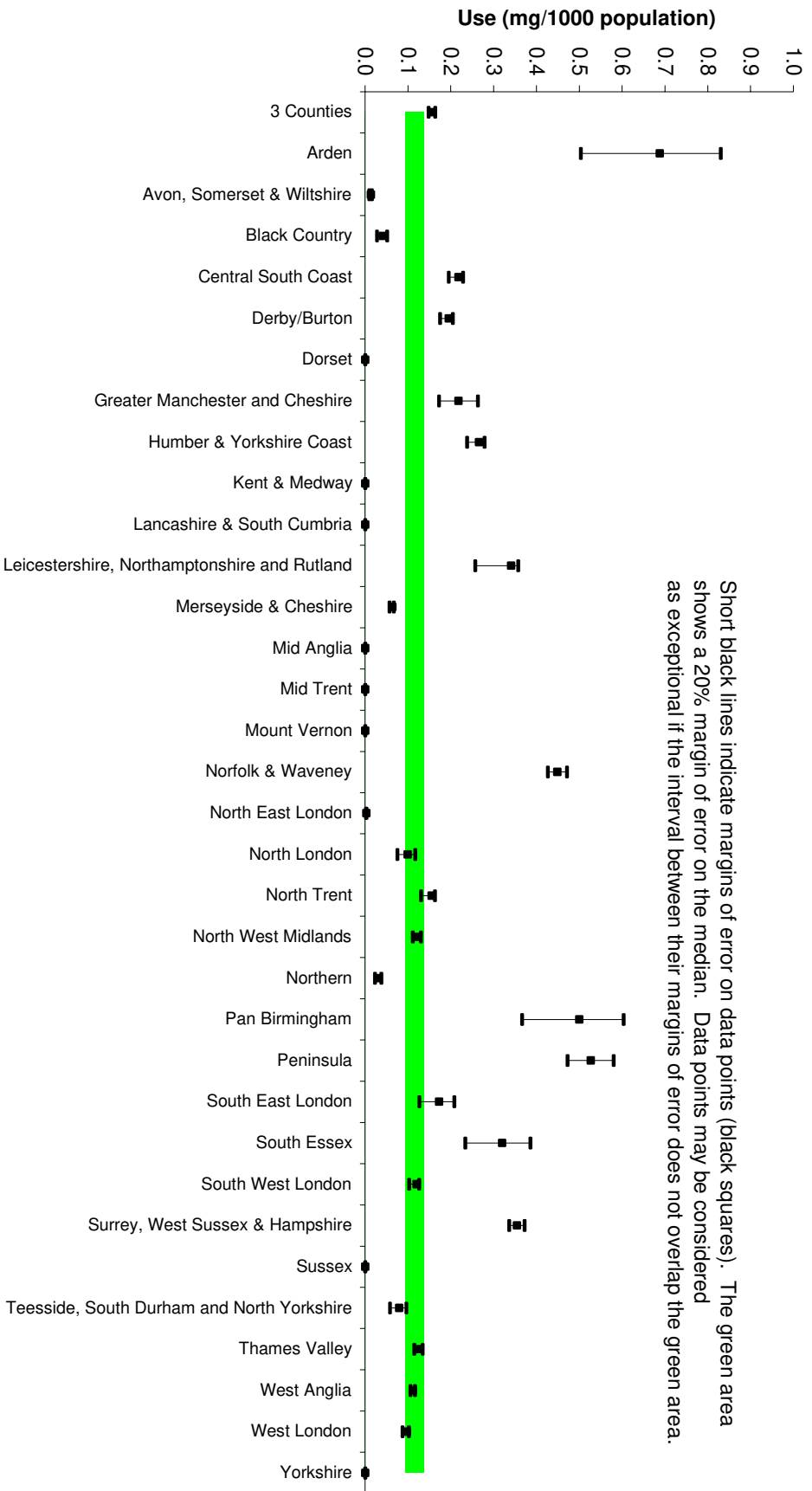
**Pegylated Liposomal Doxorubicin use (mg/1000 population) January to June 2005**



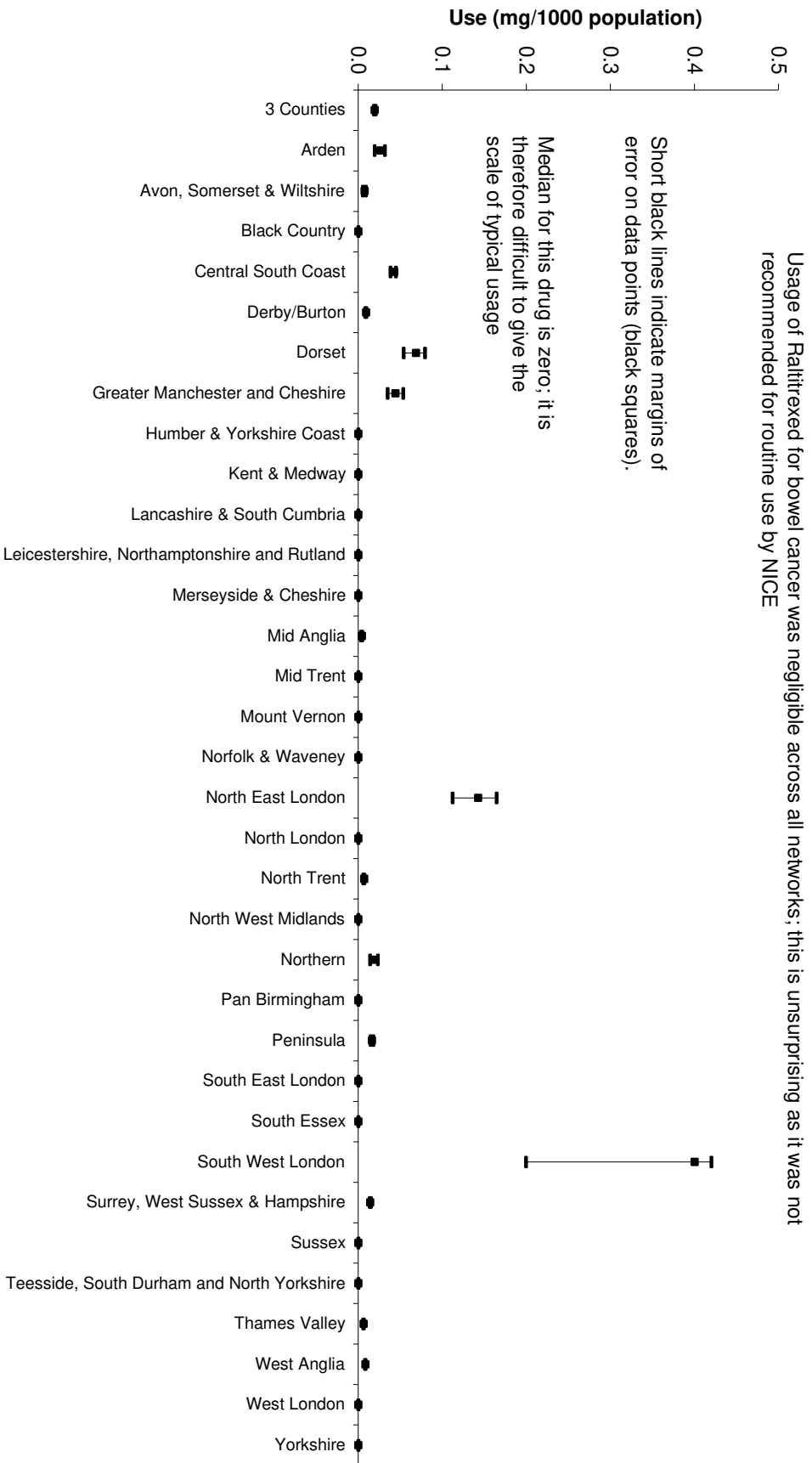
**Temozolomide use (mg/1000 population) January to June 2005**



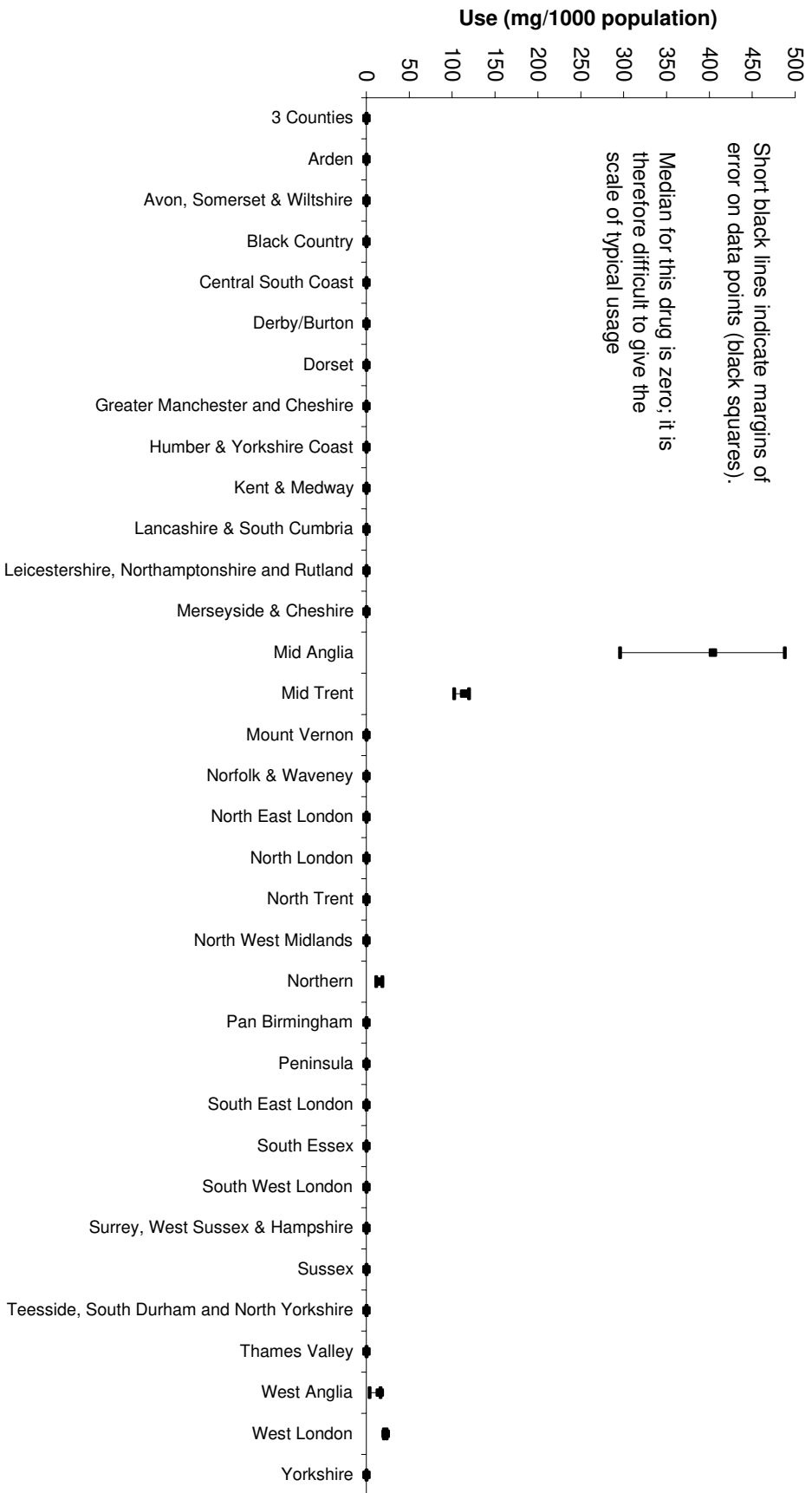
**Topotecan use (mg/1000 population) January to June 2005**



**Ralitrexed use (mg/1000 population) January to June 2005**

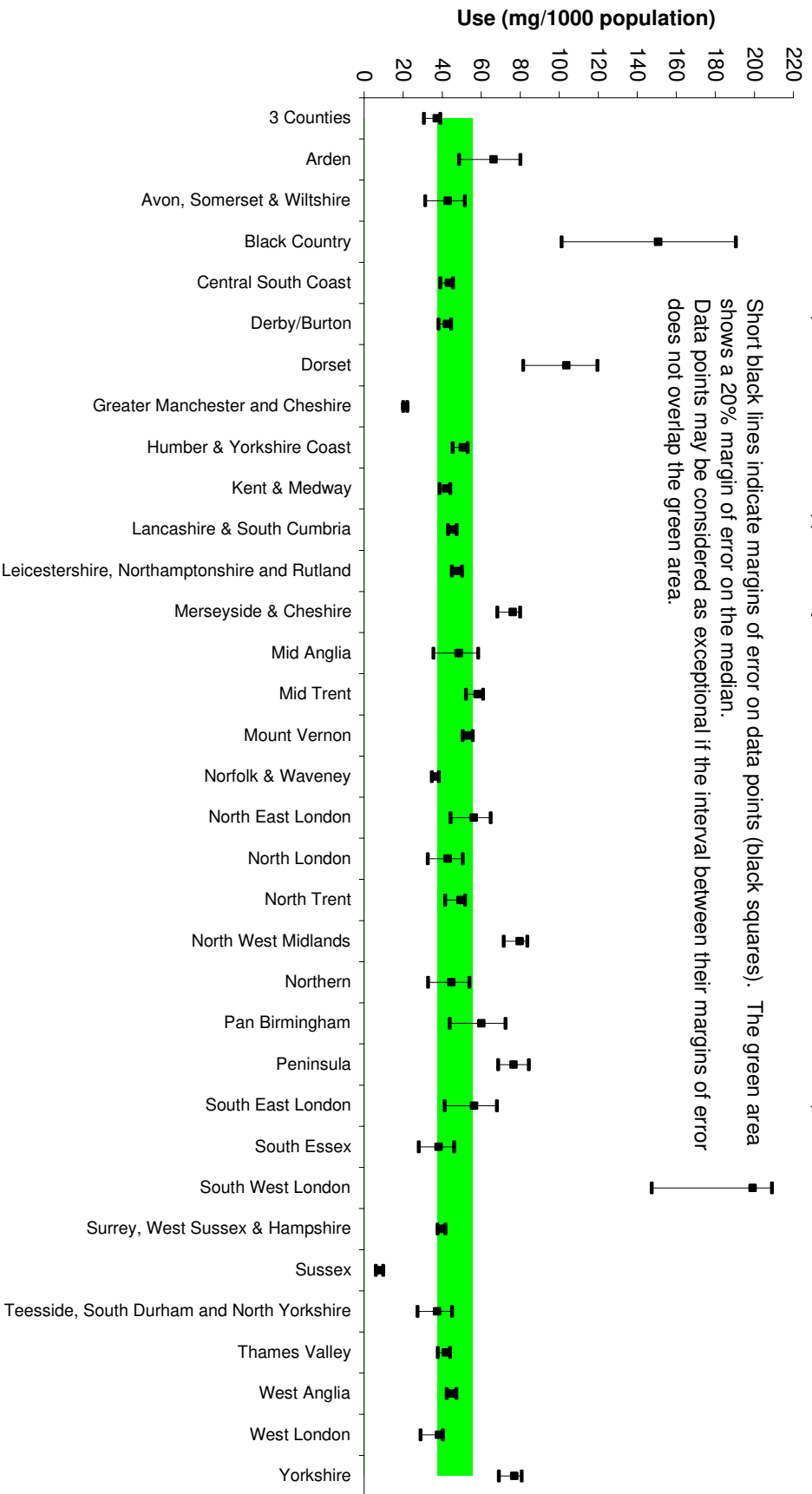


Uracil/Tegafur use (mg/1000 population) January to June 2005



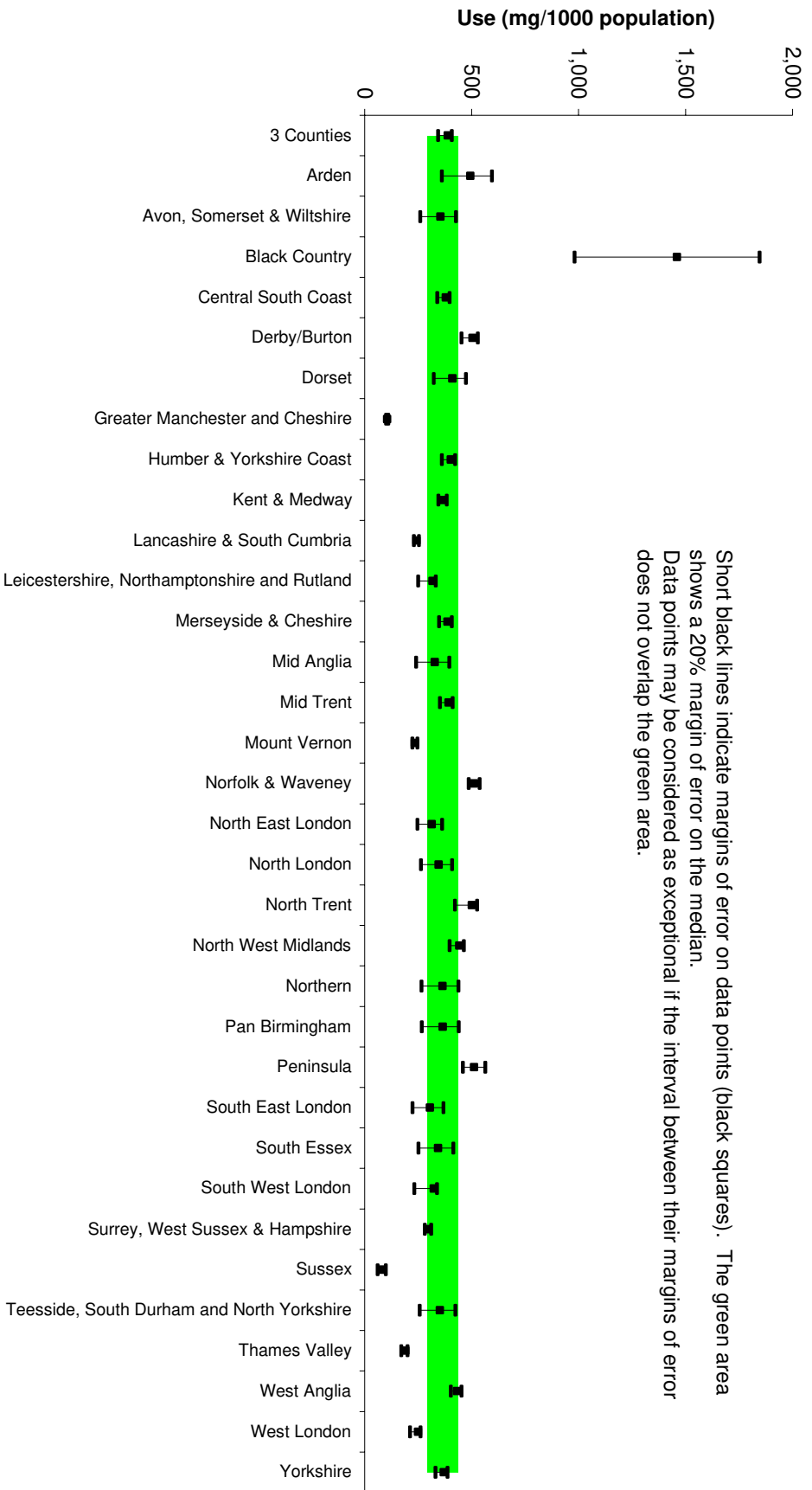
**Cisplatin use (mg/1000 population) January to June 2005**

Note: Cisplatin has not been appraised by NICE and has been included in this work as a comparator



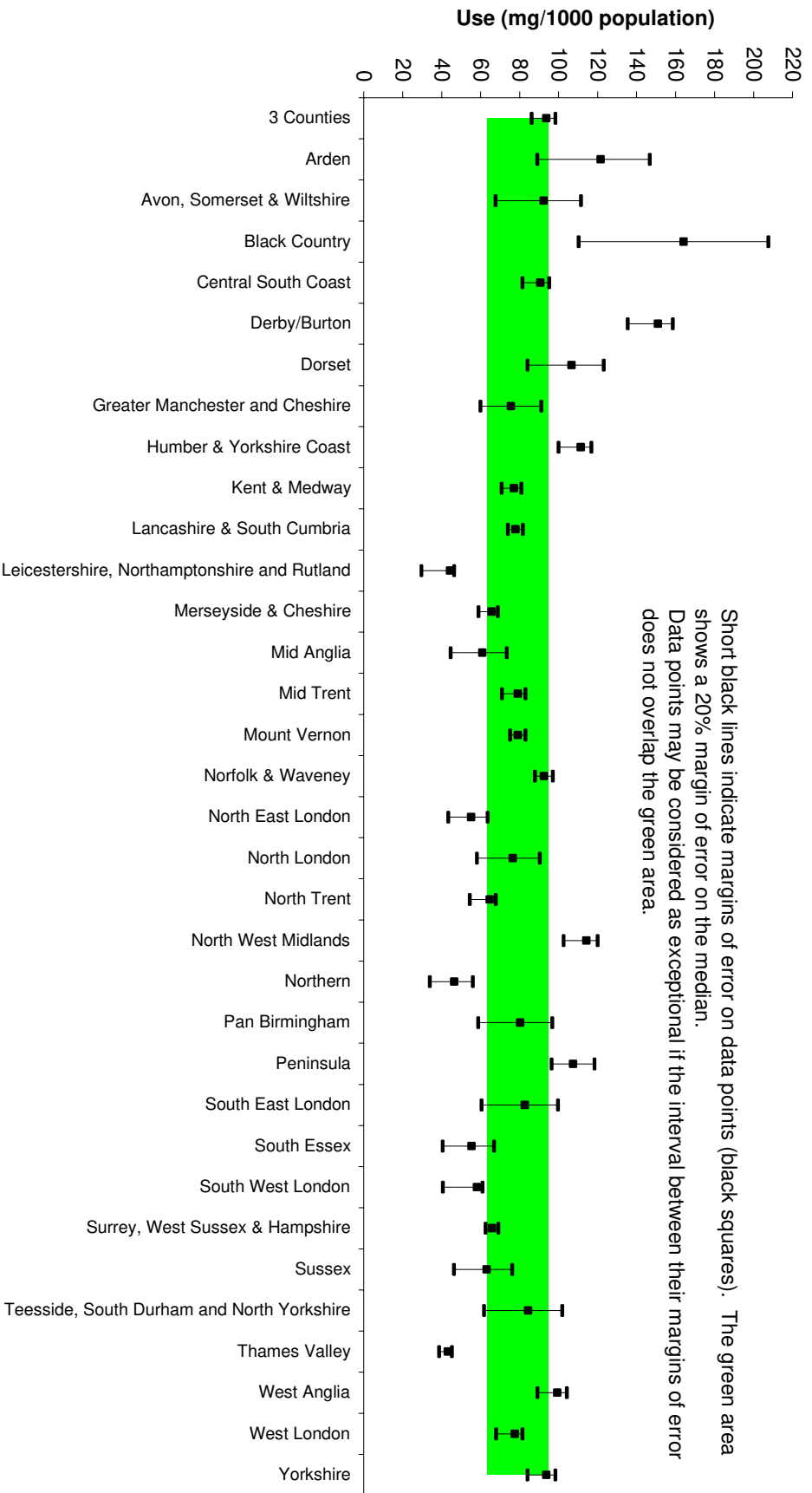
**Carboplatin use (mg/1000 population) January to June 2005**

Note: Carboplatin has not been appraised by NICE and has been included in this work as a comparator



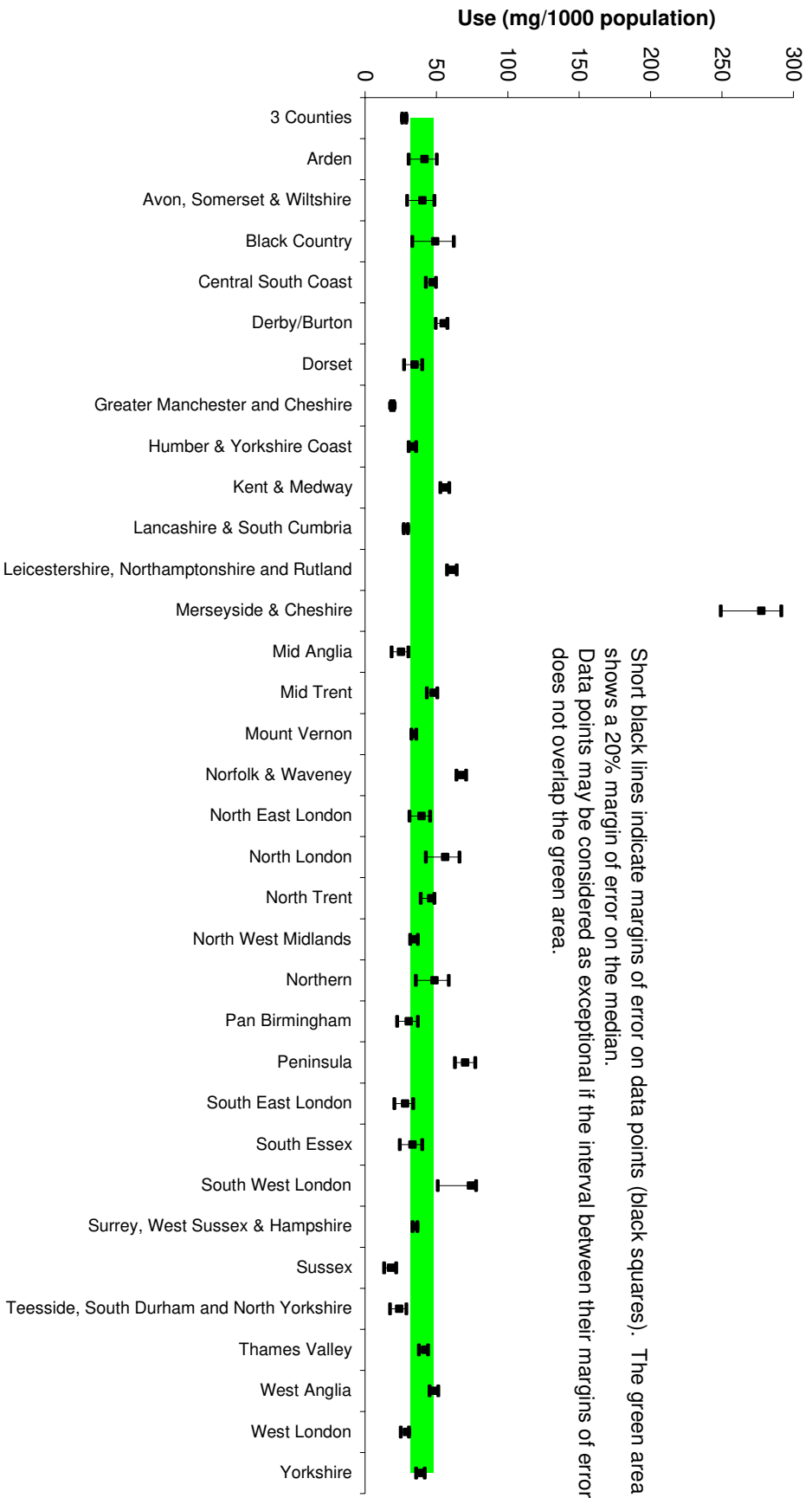
**Epirubicin use (mg/1000 population) January to June 2005**

Note: Epirubicin has not been appraised by NICE and has been included in this work as a comparator



**Doxorubicin use (mg/1000 population) January to June 2005**

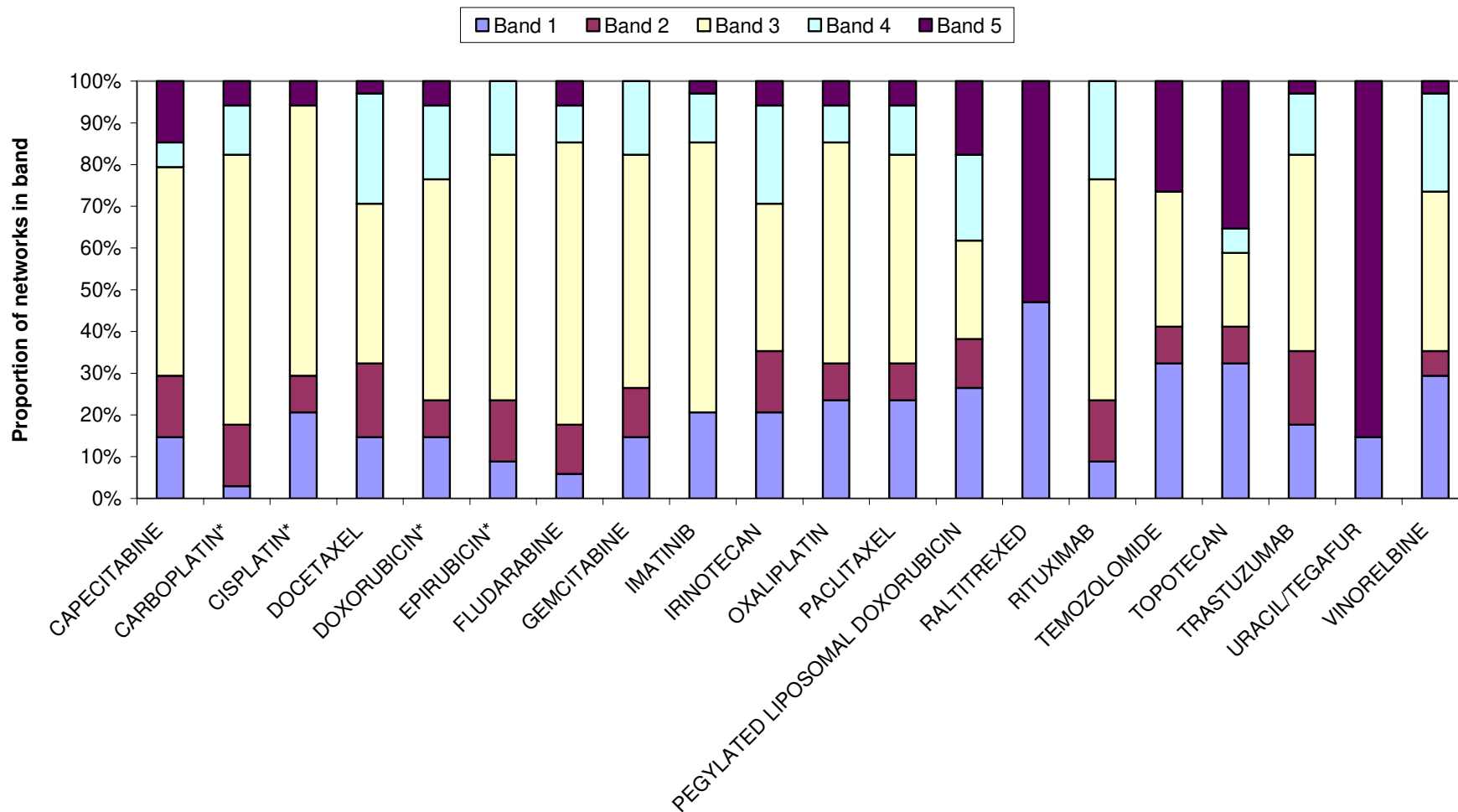
Note: Doxorubicin has not been appraised by NICE and has been included in this work as a comparator



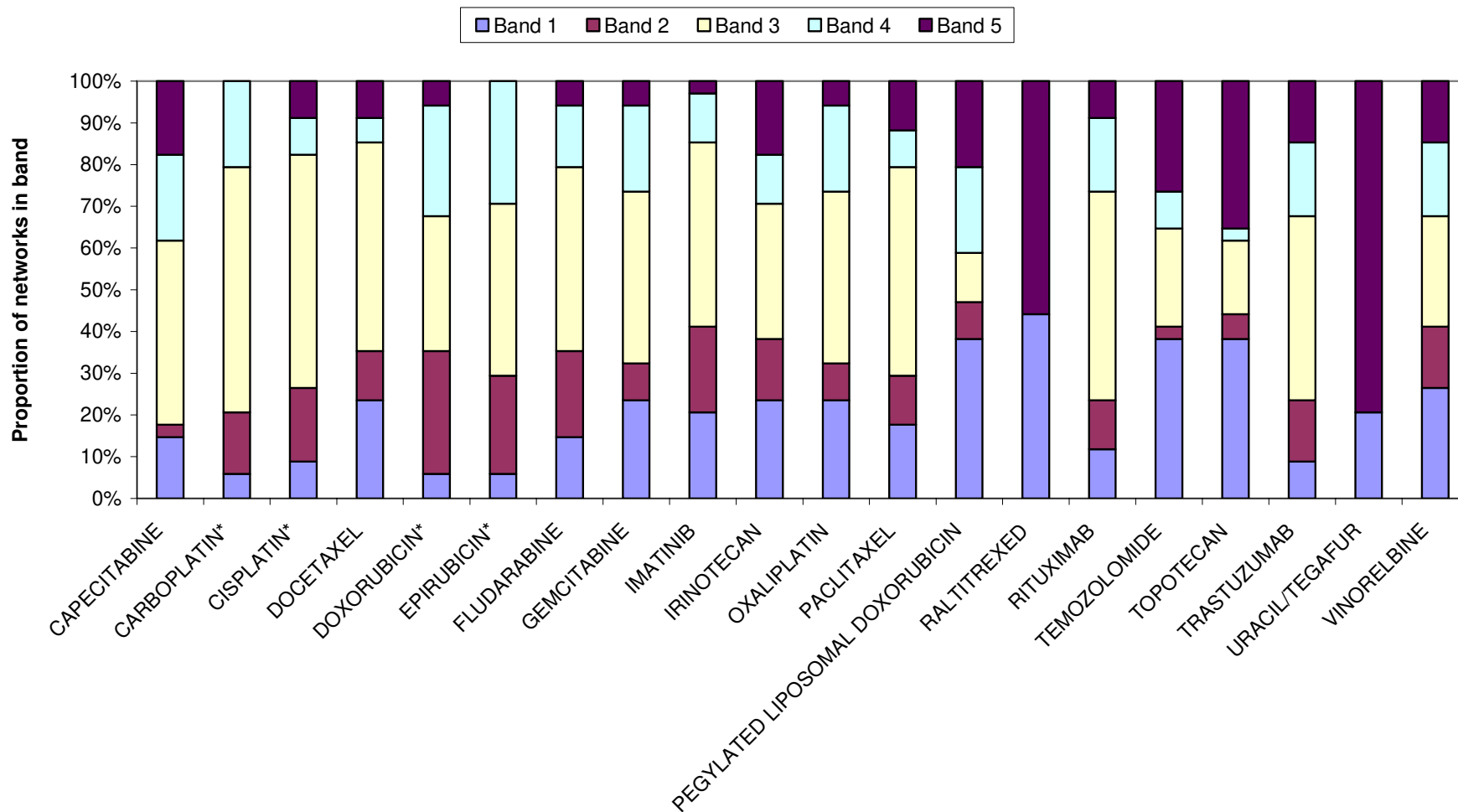
## Changes in variation between cancer networks between July to December 2003 and January to June 2005

	January-June 2005							July-December 2003						
	Count of networks in:					Ratio of 90th percentile rate to 10th percentile rate		Count of networks in:					Ratio of 90th percentile rate to 10th percentile rate	
	Band 1	Band 2	Band 3	Band 4	Band 5		Band 1	Band 2	Band 3	Band 4	Band 5			
CAPECITABINE	5	5	17	2	5	3.3	5	1	15	7	6	3.6		
CARBOPLATIN*	1	5	22	4	2	2.1	2	5	20	7	0	2.3		
CISPLATIN*	7	3	22	0	2	2.1	3	6	19	3	3	2.3		
DOCETAXEL	5	6	13	9	1	2.7	8	4	17	2	3	3.3		
DOXORUBICIN*	5	3	18	6	2	2.5	2	10	11	9	2	2.7		
EPIRUBICIN*	3	5	20	6	0	2.1	2	8	14	10	0	2.4		
FLUDARABINE	2	4	23	3	2	2.2	5	7	15	5	2	3.2		
GEMCITABINE	5	4	19	6	0	2.5	8	3	14	7	2	3.0		
IMATINIB	7	0	22	4	1	2.5	7	7	15	4	1	2.9		
IRINOTECAN	7	5	12	8	2	2.5	8	5	11	4	6	3.7		
OXALIPLATIN	8	3	18	3	2	3.0	8	3	14	7	2	3.7		
PACLITAXEL	8	3	17	4	2	3.1	6	4	17	3	4	3.8		
PEGYLATED LIPOSOMAL DO	9	4	8	7	6	5.8	13	3	4	7	7	9.7		
RALTITREXED	16	0	0	0	18	N/A	15	0	0	0	19	N/A		
RITUXIMAB	3	5	18	8	0	2.3	4	4	17	6	3	2.6		
TEMOZOLOMIDE	11	3	11	0	9	9.5	13	1	8	3	9	11.6		
TOPOTECAN	11	3	6	2	12	N/A	13	2	6	1	12	N/A		
TRASTUZUMAB	6	6	16	5	1	2.8	3	5	15	6	5	4.2		
URACIL/TEGAFUR	5	0	0	0	29	N/A	7	0	0	0	27	N/A		
VINORELBINE	10	2	13	8	1	3.1	9	5	9	6	5	8.1		

Proportion of networks by bandings - Jan to Jun 2005



Proportion of networks by bandings - Jul - Dec 2003



Network band ranks of all NICE drugs

