Public Health England

BRITISH GYNAECOLOGICAL CANCER SOCIETY

Ovarian Cancer Audit Feasibility Pilot

Geographic variation in ovarian, fallopian tube and primary peritoneal cancer treatment in England

November 2020

ovarian cancer action

TARGET OVARIAN CANCER

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Data for this report is based on patient- and tumour-level information collected by the NHS, as part of the care and support of cancer patients. The data is collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is part of Public Health England (PHE).

Contents

Introduction

About the Ovarian Cancer Audit Feasibility Pilot

The Ovarian Cancer Audit Feasibility Pilot is a collaboration between the gynaecological oncology clinical community, the charity sector and Public Health England, with the aim of performing meaningful analyses of routinely collected data for the purpose of improving treatment and outcomes for women diagnosed with ovarian cancer in England. The Ovarian Cancer Audit Feasibility Pilot is jointly funded by the British Gynaecological Cancer Society, Target Ovarian Cancer and Ovarian Cancer Action, and is being delivered by analysts at the National Cancer Registration and Analysis Service (NCRAS), which is part of Public Health England. The pilot will run for two years from 2019 and publish a range of outputs on ovarian cancer, including a final report on the audit and its findings, bringing all of the analyses into one place. Outputs can be found on the project webpages.

Building on the disease profile report and this report looking at geographic variation, future analyses will include a closer examination of surgery and an exploration of the factors associated with short-term mortality. This will bring together an impressive new body of evidence in relation to ovarian cancer treatment and outcomes in England and provide the baseline of data and structures needed for a continuing ovarian cancer audit.

About the Geographic Variation report

The first publication from the Ovarian Cancer Audit Feasibility Pilot was the Disease Profile in England report,[1] which describes incidence, mortality, stage and survival for ovary, fallopian tube and primary peritoneal carcinomas (‘ovarian cancer’) diagnosed in England.

Amongst its many findings, the report showed marked geographic variation in cancer survival across England at a Cancer Alliance level. Excluding borderline diagnoses, five-year net survival ranged between 29% and 50% across the 19 Cancer Alliances in England for the period 2013 to 2017.

One possible reason for such disparity was variation in the local clinical management of disease. To explore this hypothesis, this geographic variation report describes differences in treatment between Cancer Alliances in England, and the extent to which these might be explained by variation in tumour and patient characteristics.

Beginning with a description of how treatment differed according to stage at diagnosis, patient age, tumour morpohology and comorbidities, the report moves on to look at regional variation in

treatment at Cancer Alliance level. In addition to unadjusted (crude) results, models are presented that control for confounding variables (including age, stage and morphology) that may differ between regions, helping isolate any variation that may be attributable to clinical decision making.

Results from these analyses indicate that the probability of accessing surgery and chemotherapy varies between regions within England, even after accounting for differences in patient and tumour characteristics. These findings indicate an opportunity for identifying examples of best practice that could be disseminated to Cancer Alliances where treatment probabilities are lower, leading to improvements in therapy and better outcomes for women with ovarian cancer. Methods underlying these results are described at the end of the report.

Treatment variation by stage, age, tumour morphology and Charlson comorbidity score

Describing the cohort

The following analyses are based on ovarian cancers diagnosed in England between 2016 and 2018. Borderline cases were not included as such tumours are routinely managed surgically and there was likely to be minimal regional variation in management. Of 20,676 ovarian cancers diagnosed during the period, 17,307 (83.7%) were non-borderline cases. From these, tumours diagnosed via death certificate were also excluded, as clinicians had no opportunity to provide treatment. This left an analytical cohort of 17,155 (98.9%) ovarian cancers. Results are reported according to the tumour rather than patient, hence reference throughout to tumours and cancers when describing the cohort, characteristics and treatment.

Where data were available, each tumour was linked to information describing the delivery of systemic anti-cancer therapy or major surgical resection during the primary (i.e. first) course of treatment, defined here as the nine months following diagnosis. For simplicity, these treatment types are referred to throughout the text of this report as chemotherapy and surgery, respectively. Surgery is either performed at the start of the treatment pathway (primary surgery) or following chemotherapy (neoadjuvant chemotherapy with interval debulking surgery). Chemotherapy that follows surgery is referred to as adjuvant chemotherapy.

Based on the type of treatment and the order in which treatment was received, each tumour was assigned to one of the following categories:

1. No surgery or chemotherapy
2. Primary surgery with adjuvant chemotherapy (i.e. surgery followed by chemotherapy)
3. Neoadjuvant chemotherapy with interval debulking surgery (i.e. chemotherapy followed by surgery)
4. Chemotherapy but no surgery
5. Primary surgery but no chemotherapy

The distribution of key patient and tumour characteristics across these treatment groups is described below for the 17,155 ovarian cancers selected. A complete table of patient demographics and tumour characteristics is available in Appendix 1, and summarised below.

Treatment variation by stage

Following a cancer diagnosis, mutlidisciplinary teams make an assessment as to the best course of treatment, based on factors including how far the cancer has spread (referred to as the ‘stage’ of the cancer), and patient choice. Stages range from 1 to 4, with smaller values indicating less advanced disease. For example, a stage 1 cancer is localised and has not spread to the abdomen, pelvis, lymph nodes, or distant sites.

Typically, for ovarian cancers, surgery offers the best long term prognosis. For women with early stage disease, where the cancer has not spread, surgery alone may be sufficient, but most women will receive a combination of surgery and chemotherapy. For women with more advanced disease, such as in cases where cancer has spread beyond the pelvis, chemotherapy may be used ahead of surgery (neoadjuvant) to help reduce the tumour size prior to operating. While research to date has not shown a difference in survival between neoadjuvant chemotherapy or surgery followed by chemotherapy, it has indicated a lower risk of surgical complications and morbidity for women who undergo chemotherapy prior to surgery.[2] Research is ongoing to establish the characteristics of cases that may be best managed by the two treatment options. Finally, in some advanced cases, chemotherapy on its own may be used to provide palliative care and to ease symptoms.

Within the cohort of 17,155 ovarian tumours, treatment delivery varied by disease stage (p=<0.001). As shown in Figure 1, within stage 1 cancers, primary surgery without chemotherapy was the most commonly delivered treatment type (54.9%, n=1,763), while stage 2-3 tumours and stage 4 tumours received primary surgery but no chemotherapy in just 7.2% (n=521) and 2.6% (n=103) of cases respectively. In contrast, chemotherapy on its own was the treatment method typically delivered to tumours diagnosed at a more advanced stage of disease, at 34.4% (n=1,344) of stage 4 tumours compared to 0.9% (n=28) of stage 1 cancers.

Treatment with surgery or chemotherapy was much less common for higher-stage tumours than for early stage disease, with 28.2% (n=1,104) of stage 4 tumours receiving neither treatment versus 2.2% (n=70) of stage 1 ovarian cancers. The proportion was highest for cancers with no valid staging information (60.7%; n=1,723), suggesting that this sub-group likely represents tumours that were diagnosed at a point where either the disease was too advanced or the patient was too unwell for treatment. Overall, of the diagnoses analysed for this report, 21.9% (n=3,751) received no surgery or chemotherapy.

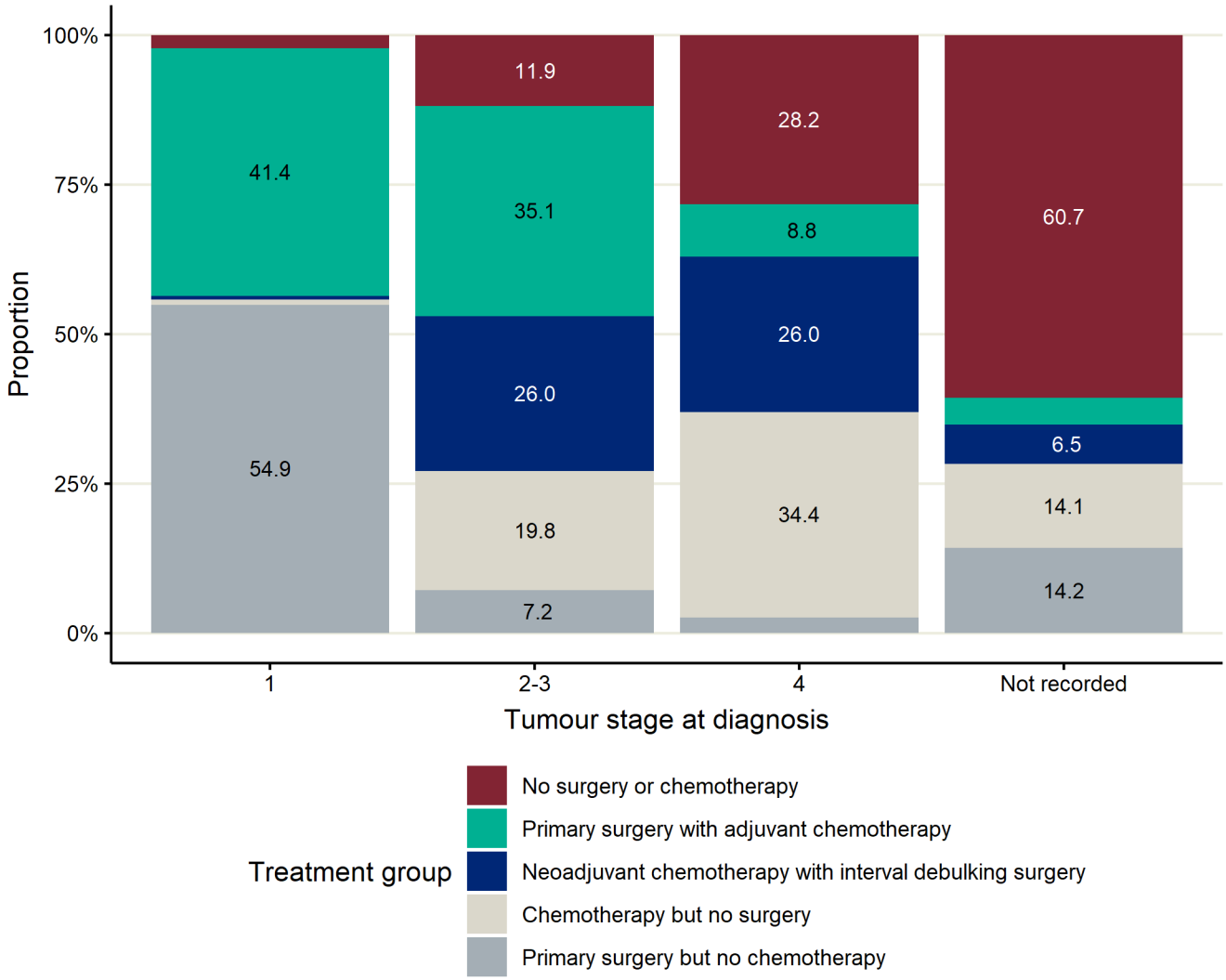


Figure 1 Treatment by stage at diagnosis, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Treatment variation by age

Treatment also differed between age groups (p=<0.001). Notably, tumours in women aged >79 were the least likely to receive any treatment, with 60.1% (n=1,987) receiving neither chemotherapy nor surgery (Figure 2). The use of primary surgery without chemotherapy was more common for cancers in younger women, at 51.6% (n=196) of tumours in patients aged <30 years at diagnosis compared to 8.3% (n=274) of tumours in patients aged >79 years at diagnosis. Conversely, the use of chemotherapy without surgery increased with age, at 20.8% (n=687) of tumours in patients aged >79 years at diagnosis compared to 6.3% (n=24) of tumours in patients aged <30 years at diagnosis.

These variations could in part reflect differences in the biology of ovarian cancer across age groups, as well as increases in the prevalence of underlying medical conditions in older age. For example, women aged >70 years are more likely to have multiple comorbities, which may explain why diagnoses in older patients were less likely to be treated with any surgery and

more likely to receive chemotherapy without surgery compared to younger age groups. Moreover, more than half of the cases of sex cord stromal and germ cell tumours occur in women under the age of 50 years.[3] As Figure 3 shows, almost three quarters of such cancers are treated with surgery alone.

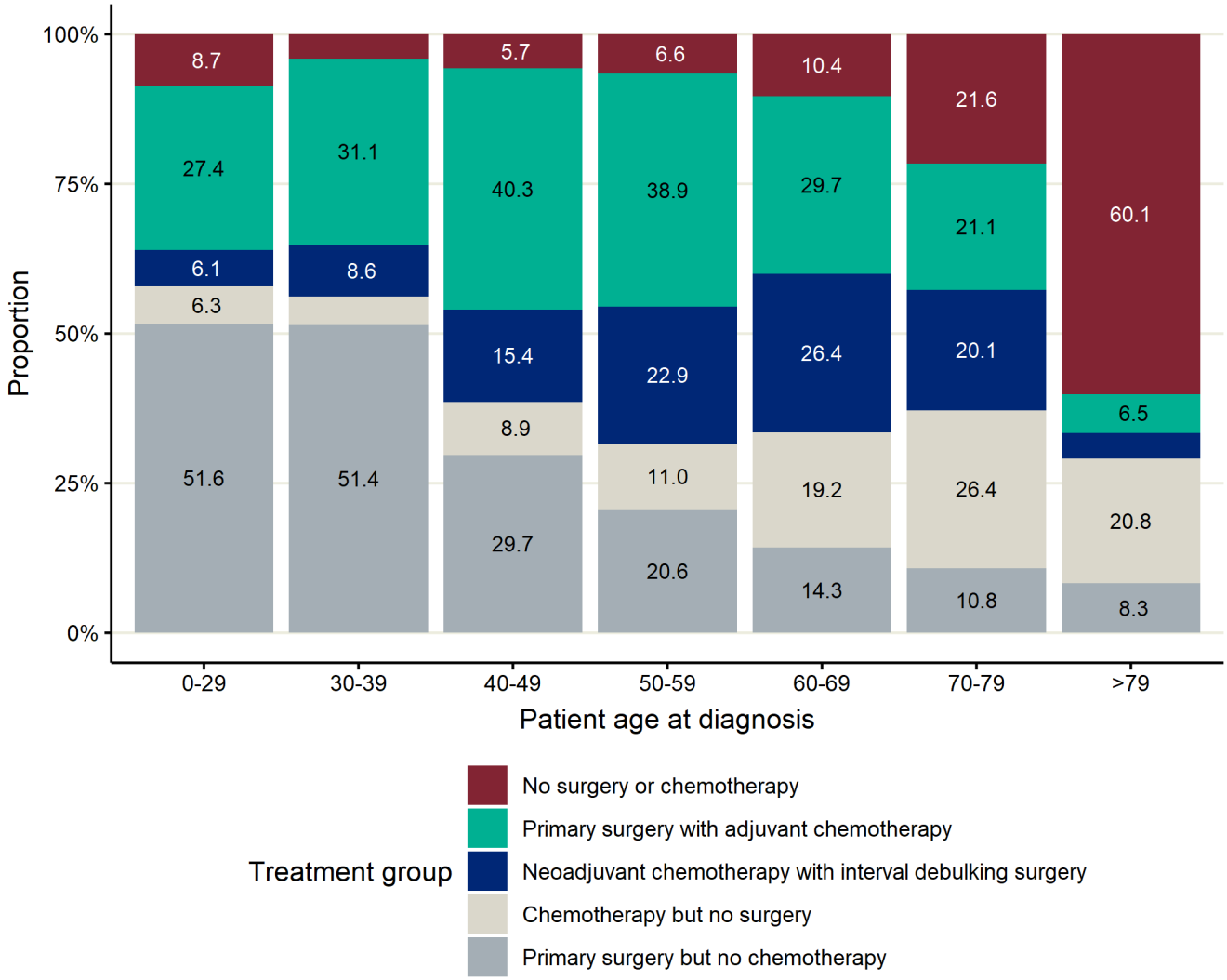


Figure 2 Treatment by age group at diagnosis, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Treatment variation by morphology

Figure 3 shows marked differences in treatment by the type of cell in which the cancer developed, referred to as tumour 'morphology' (p=<0.001). For example, mucinous carcinoma (63.3%, n=620) and sex cord-stromal and germ cell (73.0%, n=675) morphologies were most commonly treated with primary surgery but no chemotherapy, while primary surgery with adjuvant chemotherapy was the treatment most often delivered to clear cell (66.5%, n=489) and endometrioid (55.7%, n=546) carcinomas. Serous carcinomas, accounting for over half of all tumours under consideration (n=9,231), were most commonly treated with neoadjuvant chemotherapy followed by surgery (29.8%, n=2,750), while 11.8% (n=1,087) did not receive any surgery or chemotherapy. Miscellaneous or unspecified tumours (89.1%, n=1,379) and

tumours of non-specific site (71.0%, n=44) were the two morphology categories that most often received no surgery or chemotherapy. These tumours were likely to reflect diagnoses for women who presented too unwell to undergo full diagnostic and staging pathway investigations.

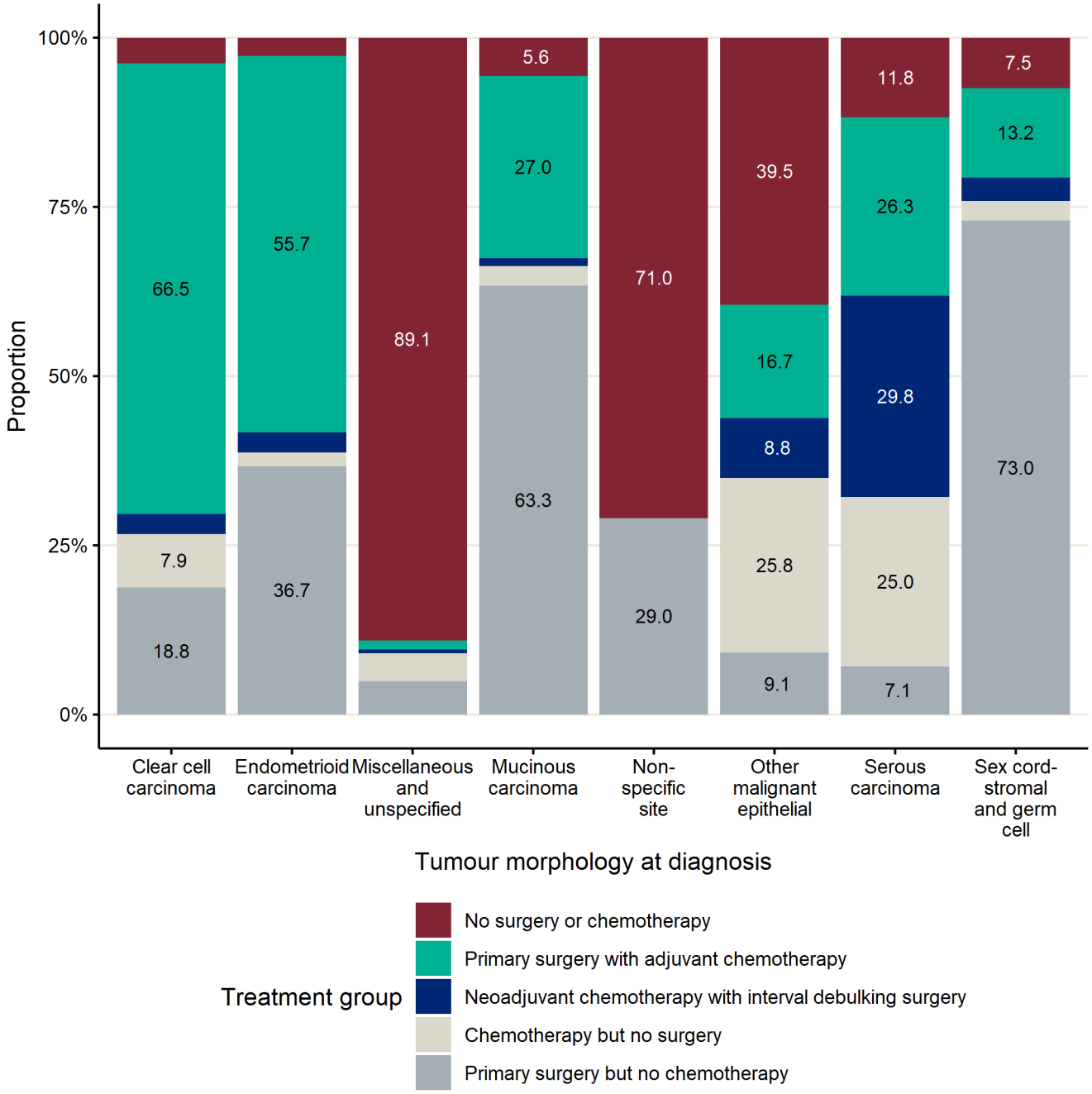


Figure 3 Treatment by morphology at diagnosis, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Treatment variation by Charlson comorbidity score

Comorbidities are pre-existing conditions that affect a patient's prognosis and ability to undergo treatment. For this report, the burden of comorbidity is described using the Charlson comorbidity index. A score is assigned to each tumour by identifying the patient within whom

the cancer occurred and looking for a number of pre-defined chronic health conditions documented within the cancer registry and hospital inpatient episodes. These conditions include dementia, liver disease and other primary cancer diagnoses. Higher scores are indicative of a greater burden of comorbid disease, though the index is not comprehensive; comorbid conditions not considered by the Charlson comorbidity index or otherwise only documented within an outpatient or primary care setting are not identified. Of the 17,155 tumours in the cohort, 14,196 (82.8%) were recorded as having been diagnosed in patients with no comorbidity according to the Charlson comorbidity index (a score of zero).

Figure 4 shows variation in treatment by Charlson comorbidity score (p=<0.001). Treatments were approximately evenly distributed among tumours in patients with a comorbidity score of zero, with the use of chemotherapy without surgery being largely consistent regardless of comorbidity burden. Conversely, the proportions that did not receive any surgery or chemotherapy were greater the higher the burden of comorbidity.

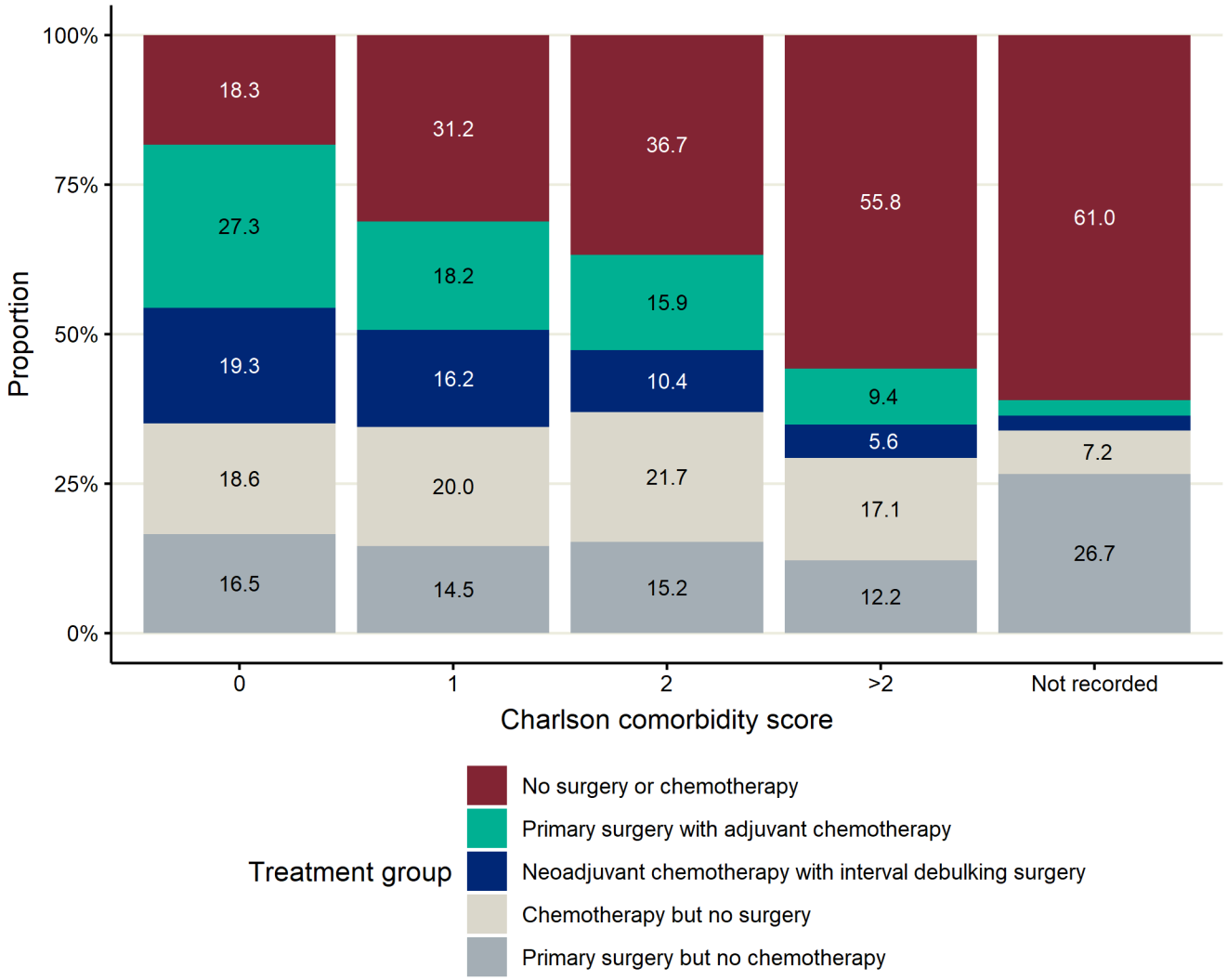


Figure 4 Treatment by Charlson comorbidity score at diagnosis, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Treatment variation by stage, age, tumour morphology and Charlson comorbidity score: summary

The findings presented in Figures 1-4 and Appendix 1 demonstrate marked variations in treatment according to the stage and morphology of ovarian cancers, as well as the age and comorbidity burden of patients. They show that tumours in older women, advanced stage disease and a greater burden of comorbidity were more likely to result in women not receiving any surgery or chemotherapy. These differences may represent valid differences in clinical decision making. Given that these factors may be distributed unevenly across the country, attempts to investigate the independent relationship between geography and ovarian cancer treatment will control for these variables to provide a clearer picture of treatment variation between Cancer Alliances in England.

Treatment variation by Cancer Alliance

This section describes an analysis of variation in treatment between the 19 Cancer Alliances defined for England in 2018. Cancer Alliances are geographic areas that bring together clinicians and managers from different hospital trusts and other health and social care organisations with the aim of coordinating the diagnosis and treatment of cancer patients in the local area. A map of these Cancer Alliances is shown in Figure 5.*

1. North East and Cumbria
2. Lancashire and South Cumbria
3. West Yorkshire and Harrogate
4. Humber, Coast and Vale
5. Greater Manchester
6. Cheshire and Merseyside
7. South Yorkshire, Bassetlaw, North Derbyshire, Hardwick
8. West Midlands
9. East Midlands
10. East of England
11. North West and South West London (RM Partners)
12. North Central and North East London (UCLH Cancer Collaborative)
13. South East London
14. Somerset, Wiltshire, Avon and Gloucestershire
15. Thames Valley
16. Peninsula
17. Wessex
18. Surrey and Sussex
19. Kent and Medway

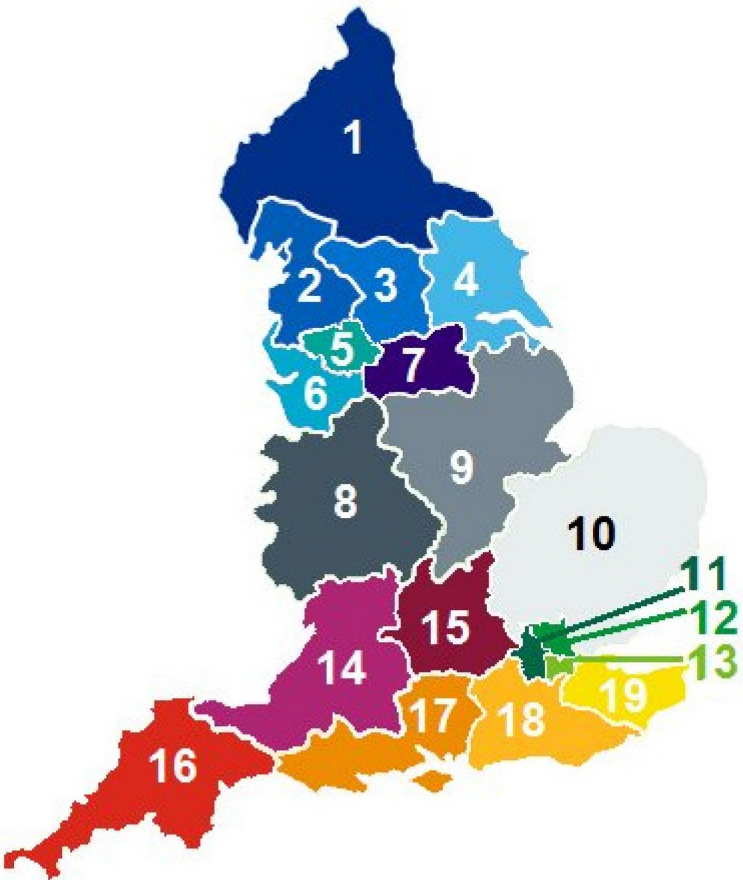


Figure 5 Map of Cancer Alliances in England, as defined by NHS England in 2018

* Image source NHS England.

The analysis of geographic variation in treatment selected only stage 2-4 and stage unknown cancers. Stage 1 tumours were excluded as, unlike in stage 2-4 tumours, trial evidence has not demonstrated a major survival benefit of chemotherapy for low-grade stage 1 tumours. As 96.3% (n=3,091) of stage 1 tumours were treated with primary surgery only or surgery with adjuvant chemotherapy, this suggests minimal variation in treatment pathways (Figure 1). Owing to how few were present in the cohort, tumours with a non-specific site morphology were also removed (n=62; 0.4%). This left a cohort for analysis of 13,889 tumours. Patient demographics and tumour characteristics for the analytical sample are provided in Appendix 2 .

Findings are presented below as both funnel plots and results tables. Each point on a funnel plot represents a geographical area (in this case, a Cancer Alliance). The standard error is shown on the horizontal axis and provides an indication of the number of tumours diagnosed within the Cancer Alliance. Estimates from Cancer Alliances with a greater number of tumours are more precise, appearing further to the right-hand side of the plot and represented by bigger red markers than Cancer Alliances with fewer tumour diagnoses. The percentage difference in the probability of a treatment or treatment combination is shown on the vertical axis relative to the population average (all tumours combined). A Cancer Alliance with an estimate above the average (indicated by a solid black horizonal line) suggests that tumours within the geography were more likely to receive treatment than the population average, with estimates below the line indicating a lower probability.

Two pairs of dashed lines are included on each funnel plot that represent the bounds of statistical confidence around the average value. The inner set of dashed lines represents two standard deviations (SD) from the population average and the outer set represents three SD, being approximately equivalent to 95.0% and 99.7% confidence intervals, respectively. Any observation plotted outside of these dashed lines will have a confidence interval that does not include the average value, and may therefore indicate a systematic deviation in clinical practice that warrants further investigation. However, some random variation in the probability of treatment is expected between regions such that some points will sit outside the dashed lines through chance alone. This should be taken into consideration when interpreting funnel plots (for example, five out of every 100 observations are likely to lie outside the two SD funnel).

Within each accompanying table, Cancer Alliances highlighted in blue had treatment probabilities that were significantly higher ($p=<0.05$) than the average, and those highlighted in red had significantly lower probabilities. These represent Cancer Alliances that fall outside the innermost pair of dashed lines in the corresponding funnel plot (two SDs).

Given the variation in treatment across patient and tumour characteristics, as shown in Figures 1-4, three different models were developed for each of the treatment scenarios reported through this section:

- Model 1 represents an unadjusted analysis, which compares crude treatment probabilities for tumours diagnosed by each Cancer Alliance.

- Model 2 adds adjustment for differences between Cancer Alliances in the distribution of patient age, tumour morphology and tumour stage.
- Model 3 adjusts for the same factors as Model 2, plus area income deprivation and Charlson comorbidity score.

While funnel plots are shown for the minimally (Model 1) and maximally (Model 3) adjusted models only, findings from all three models are presented in table form to allow comparisons according to differing levels of covariate adjustment.

Treatment variation by Cancer Alliance: any treatment versus no treatment

Ovarian cancer is an aggressive disease and long-term survival relies on access to treatment. This initial analysis looks at differences between Cancer Alliances in the proportions of diagnosed tumours that received any treatment, defined here as surgery or chemotherapy either alone or in combination.

The weighted average probability of a stage 2-4 and unknown stage ovarian cancer receiving any treatment was 73.8% (Table 1). Despite adjustment for a range of factors associated with differences in the treatment pathway, funnel plot B in Figure 6 shows that geographic variation in treatment delivery remained. Moreover, the probability of any treatment fell more than two SDs below the population average for four Cancer Alliances, while five Alliances had probabilities more than two SDs greater than the average. These results indicate not just that there is marked variation in overall treatment between Cancer Alliances in England, but that some of these differences may not be explained by chance alone and warrant further investigation. A complete table of coefficients is reported in Appendix 3.

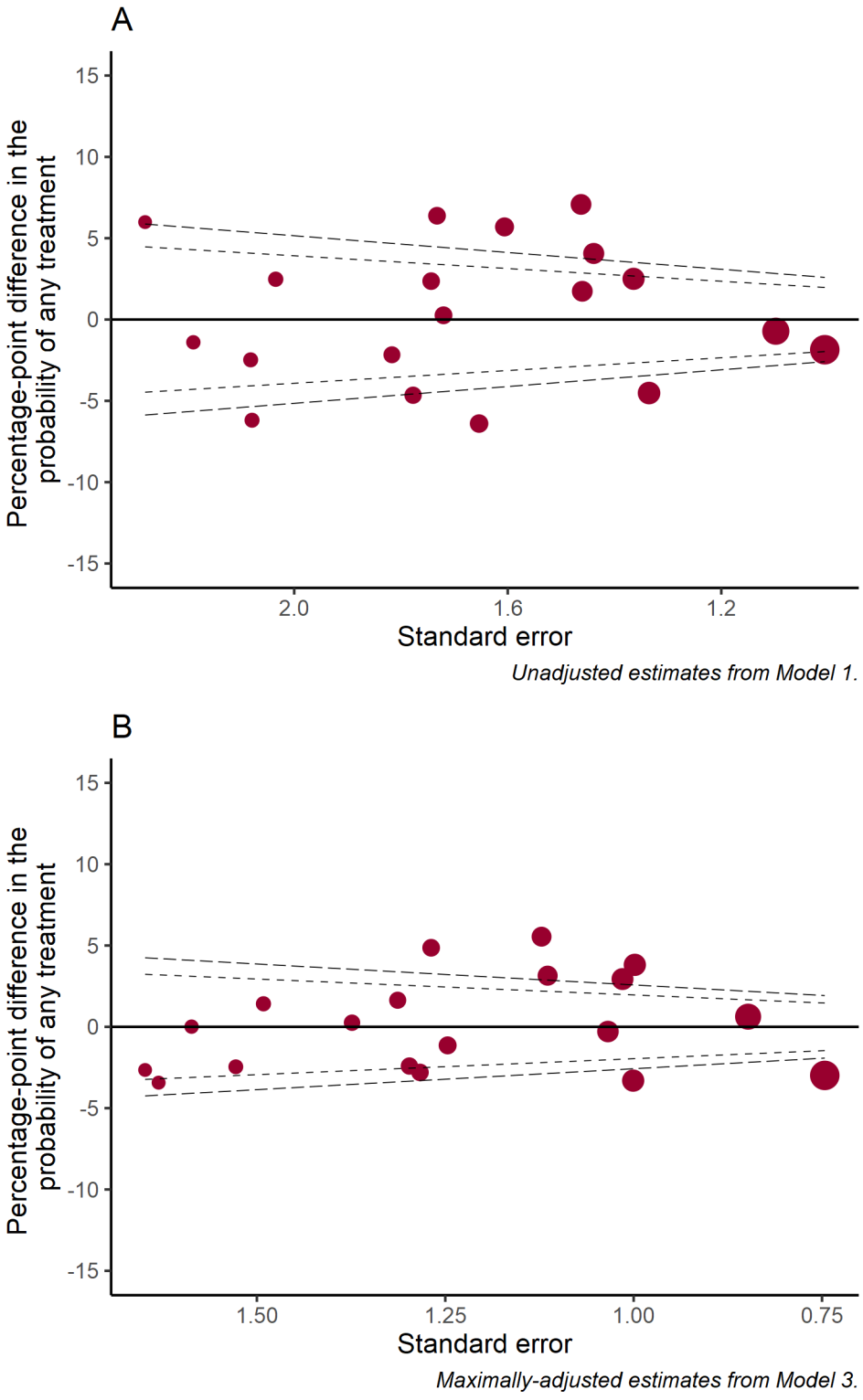


Figure 6 Geographic variation in the probability of receiving any treatment versus no treatment, excluding stage 1 disease, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Table 1 Probability of receiving any treatment versus no treatment, excluding stage 1 disease

	Model 1* (n=13,889)		Model 2* (n=13,889)		Model 3* (n=13,889)	
Variables	**Estimate**	**p-value**	**Estimate**	**p-value**	**Estimate**	**p-value**
Cohort average (intercept)	73.8	0.000	73.8	0	73.8	0.000
Cancer Alliance						
Cheshire and Merseyside	-4.7	0.009	-2.6	0.048	-2.4	0.063
East Midlands	-4.5	0.001	-3.3	0.001	-3.3	0.001
East of England	-1.9	0.065	-2.7	0.000	-3.0	0.000
Greater Manchester	0.3	0.880	-3.6	0.005	-2.8	0.029
Humber, Coast and Vale	-1.4	0.522	-2.5	0.106	-2.5	0.108
Kent and Medway	-2.5	0.234	-3.1	0.059	-3.4	0.035
Lancashire and South Cumbria	2.5	0.223	1.0	0.502	1.4	0.342
North Central and North East London	6.4	0.000	-1.2	0.380	0.3	0.853
North East and Cumbria	1.7	0.234	-0.9	0.411	-0.3	0.780
North West and South West London	7.1	0.000	5.0	0.000	5.5	0.000
Peninsula	-2.2	0.233	5.1	0.000	4.9	0.000
Somerset, Wiltshire, Avon and Gloucestershire	4.1	0.005	3.9	0.000	2.9	0.004
South East London	6.0	0.009	-0.9	0.562	0.0	0.994
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-6.2	0.003	-3.2	0.058	-2.7	0.108
Surrey and Sussex	2.5	0.067	4.9	0.000	3.8	0.000
Thames Valley	2.4	0.176	2.8	0.032	1.6	0.213
Wessex	-6.4	0.000	-0.3	0.808	-1.1	0.361
West Midlands	-0.7	0.513	0.1	0.935	0.6	0.462
West Yorkshire and Harrogate	5.7	0.000	2.9	0.010	3.1	0.005

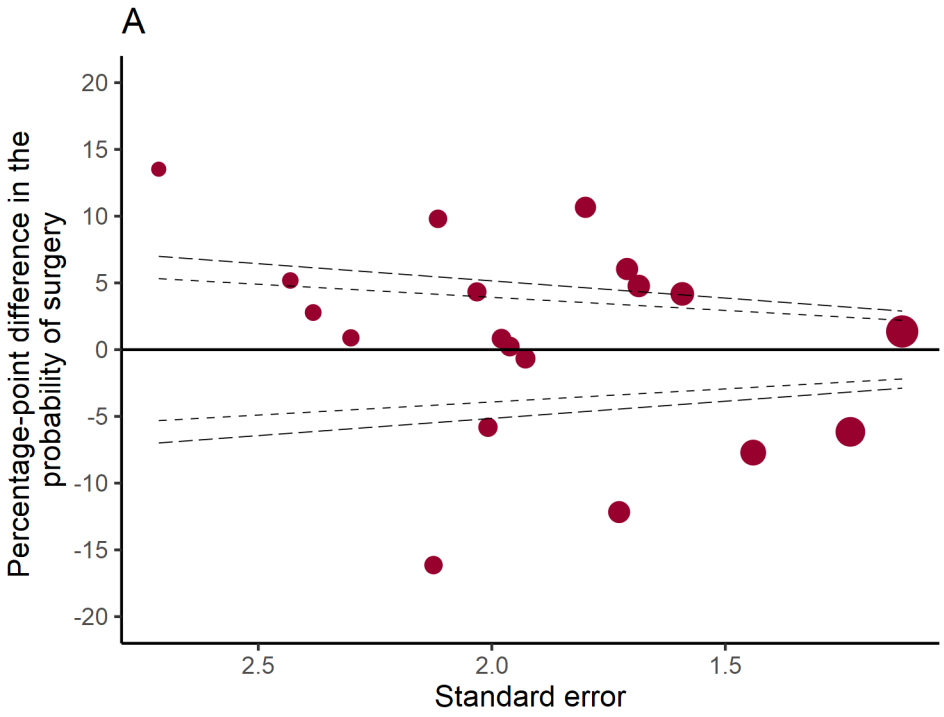
The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate. Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.

Treatment variation by Cancer Alliance: any surgery versus no surgery

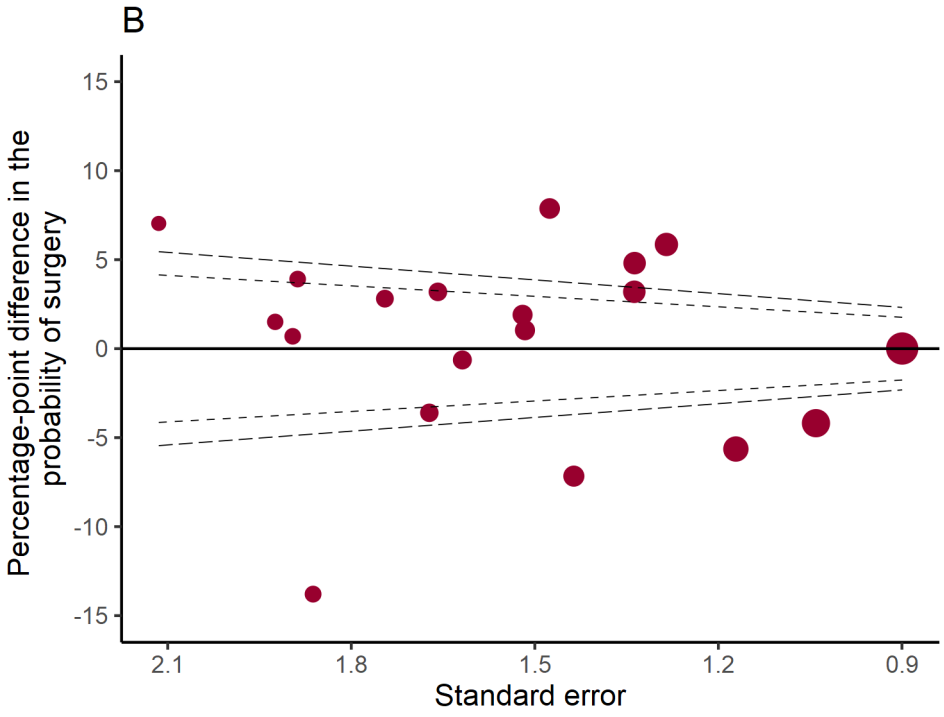
The nature of ovarian cancer means that surgery is essential in the large majority of cases to remove (debulk) the tumour. While the results above provide an indication of variation in women receiving any treatment, the analysis below looks specifically at the probability of surgery either alone or in combination with other therapies.

The average probability of Stage 2-4 and unknown stage ovarian cancer being treated with any surgery was 51.0% (Table 2). The funnel plots in Figure 7 indicate large geographic variation in the delivery of surgery between Cancer Alliances, even after adjustment for other factors, where six Cancer Alliances had surgery probabilities two SDs above the average and five had

probabilities two SDs below the average (Figure 7b). A full table of coefficients is provided in Appendix 4. The probability of treatment with surgery was particularly low in one Cancer Alliance and warrants investigation to determine whether the figure represents true regional variation in clinical practice or is the product of either poor treatment reporting or unadjusted differences in the type of tumour or patient being treated.



Unadjusted estimates from Model 1.



Maximally-adjusted estimates from Model 3.

Figure 7 Geographic variation in the probability of receiving any surgery versus no surgery, excluding stage 1 disease, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Table 2 Probability of receiving any surgery versus no surgery, excluding stage 1 disease

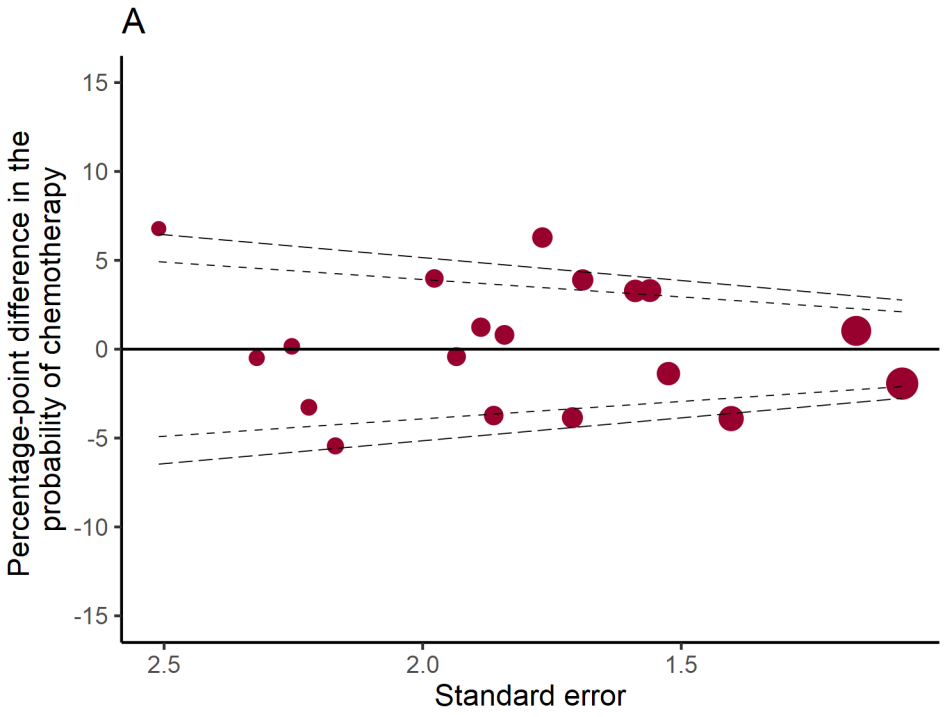
	Model 1* (n=13,889)		Model 2* (n=13,889)		Model 3* (n=13,889)	
Variables	**Estimate**	**p-value**	**Estimate**	**p-value**	**Estimate**	**p-value**
Cohort average (intercept)	51.0	0.000	51.0	0.000	51.0	0.000
Cancer Alliance						
Cheshire and Merseyside	-0.7	0.731	0.6	0.683	1.0	0.495
East Midlands	-7.7	0.000	-5.6	0.000	-5.6	0.000
East of England	1.4	0.225	0.5	0.568	0.0	0.993
Greater Manchester	0.2	0.906	-4.7	0.004	-3.6	0.031
Humber, Coast and Vale	5.2	0.033	3.8	0.044	3.9	0.038
Kent and Medway	0.9	0.701	1.2	0.533	0.7	0.714
Lancashire and South Cumbria	2.8	0.243	1.0	0.613	1.5	0.434
North Central and North East London	9.8	0.000	1.1	0.544	2.8	0.108
North East and Cumbria	4.8	0.005	2.3	0.086	3.2	0.017
North West and South West London	10.7	0.000	7.4	0.000	7.9	0.000
Peninsula	-5.8	0.004	2.3	0.134	1.9	0.211
Somerset, Wiltshire, Avon and Gloucestershire	6.0	0.000	5.9	0.000	4.8	0.000
South East London	13.5	0.000	5.8	0.007	7.0	0.001
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-16.1	0.000	-14.5	0.000	-13.8	0.000
Surrey and Sussex	4.2	0.009	7.1	0.000	5.9	0.000
Thames Valley	4.3	0.033	4.5	0.007	3.2	0.054
Wessex	-12.2	0.000	-6.2	0.000	-7.2	0.000
West Midlands	-6.2	0.000	-4.8	0.000	-4.2	0.000
West Yorkshire and Harrogate	0.8	0.676	-0.9	0.562	-0.6	0.694

The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate. Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.

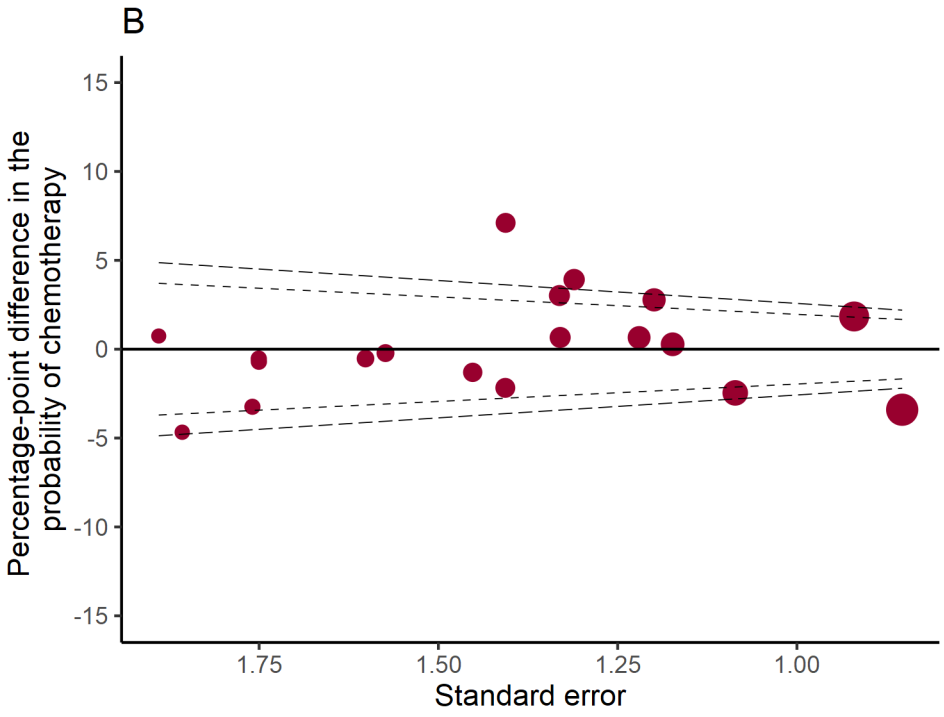
Treatment variation by Cancer Alliance: any chemotherapy versus no chemotherapy

All women with an ovarian cancer diagnosis should receive chemotherapy to treat and help manage the disease, with the exception of stage 1 cancers (for which primary surgery only is typical), certain less common tumour types, circumstances where the risks from chemotherapy may outweigh the benefits (such as due to comorbidity), and patient choice.

Of tumours in the stage 2-4 and unknown stage cohort, the average probability of treatment with chemotherapy was 66.5% (Table 3). Following adjustment for a broad range of factors, including patient age and tumour morphology, funnel plot B in Figure 8b shows five Cancer Alliances with chemotherapy rates two SDs above the average (one notably so) and three with chemotherapy rates two SDs below the average. A full table of coefficients is provided in Appendix 5.



Unadjusted estimates from Model 1.



Maximally-adjusted estimates from Model 3.

Figure 8 Geographic variation in the probability of receiving any chemotherapy versus no chemotherapy, excluding stage 1 disease, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Table 3 Probability of receiving any chemotherapy versus no chemotherapy, excluding stage 1 disease

	Model 1* (n=13,889)		Model 2* (n=13,889)		Model 3* (n=13,889)	
Variables	**Estimate**	**p-value**	**Estimate**	**p-value**	**Estimate**	**p-value**
Cohort average (intercept)	66.5	0.000	66.5	0.000	66.5	0.000
Cancer Alliance						
Cheshire and Merseyside	-3.7	0.045	-1.5	0.303	-1.3	0.370
East Midlands	-3.9	0.005	-2.4	0.028	-2.5	0.024
East of England	-1.9	0.071	-3.1	0.000	-3.4	0.000
Greater Manchester	0.8	0.662	-2.9	0.040	-2.2	0.122
Humber, Coast and Vale	-0.5	0.831	-3.2	0.068	-3.2	0.066
Kent and Medway	-3.3	0.141	-4.3	0.021	-4.7	0.012
Lancashire and South Cumbria	0.2	0.943	-1.2	0.508	-0.7	0.687
North Central and North East London	4.0	0.044	-1.9	0.244	-0.5	0.742
North East and Cumbria	3.3	0.035	-0.2	0.851	0.3	0.814
North West and South West London	3.9	0.021	3.4	0.011	3.9	0.003
Peninsula	1.2	0.513	7.4	0.000	7.1	0.000
Somerset, Wiltshire, Avon and Gloucestershire	3.3	0.039	3.6	0.002	2.8	0.021
South East London	6.8	0.007	-0.2	0.928	0.7	0.695
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-5.4	0.012	-1.0	0.573	-0.5	0.761
Surrey and Sussex	-1.4	0.367	1.6	0.177	0.7	0.591
Thames Valley	-0.4	0.829	0.8	0.594	-0.2	0.889
Wessex	-3.9	0.024	1.5	0.267	0.7	0.620
West Midlands	1.0	0.375	1.3	0.162	1.8	0.045
West Yorkshire and Harrogate	6.3	0.000	2.7	0.041	3.0	0.023

The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate. Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.

Treatment variation by Cancer Alliance: primary surgery with adjuvant chemotherapy versus neoadjuvant chemotherapy with interval debulking surgery

Chemotherapy is increasingly used prior to surgery (neoadjuvant). This approach is often used in two cases which are specific to advanced disease. Firstly, if a patient is too unwell to undergo surgery, chemotherapy can start to treat the tumour while waiting

for the patient to recover. Secondly, if the multidisciplinary team (MDT) considers it unlikely that complete tumour resection (removal) will be feasible during primary surgery, neoadjuvant chemotherapy may be used to make the tumour more operable, reducing the risk of surgical complications and morbidity.[2]

The following analysis explores geographic variation in the probability of receiving primary surgery with adjuvant chemotherapy versus neoadjuvant chemotherapy with interval debulking surgery. Accordingly, the analysis was restricted to the 6,065 tumours within the cohort of stage 2-4 and unknown stage cancers that were assigned to one of these two treatment groups.

Of these tumours, the probability of primary surgery and adjuvant chemotherapy was 49.4% on average (Table 4). Figure 9b shows regional variation after adjustment for patient demographics and tumour characteristics associated with treatment, with three Cancer Alliances falling two SD above the average and five regions falling two SDs below the average. The maximally-adjusted probability of treatment with primary surgery and adjuvant chemotherapy of one Cancer Alliance was markedly higher than others and requires further investigation. A full table of coefficients from the underlying models can be viewed in Appendix 6.

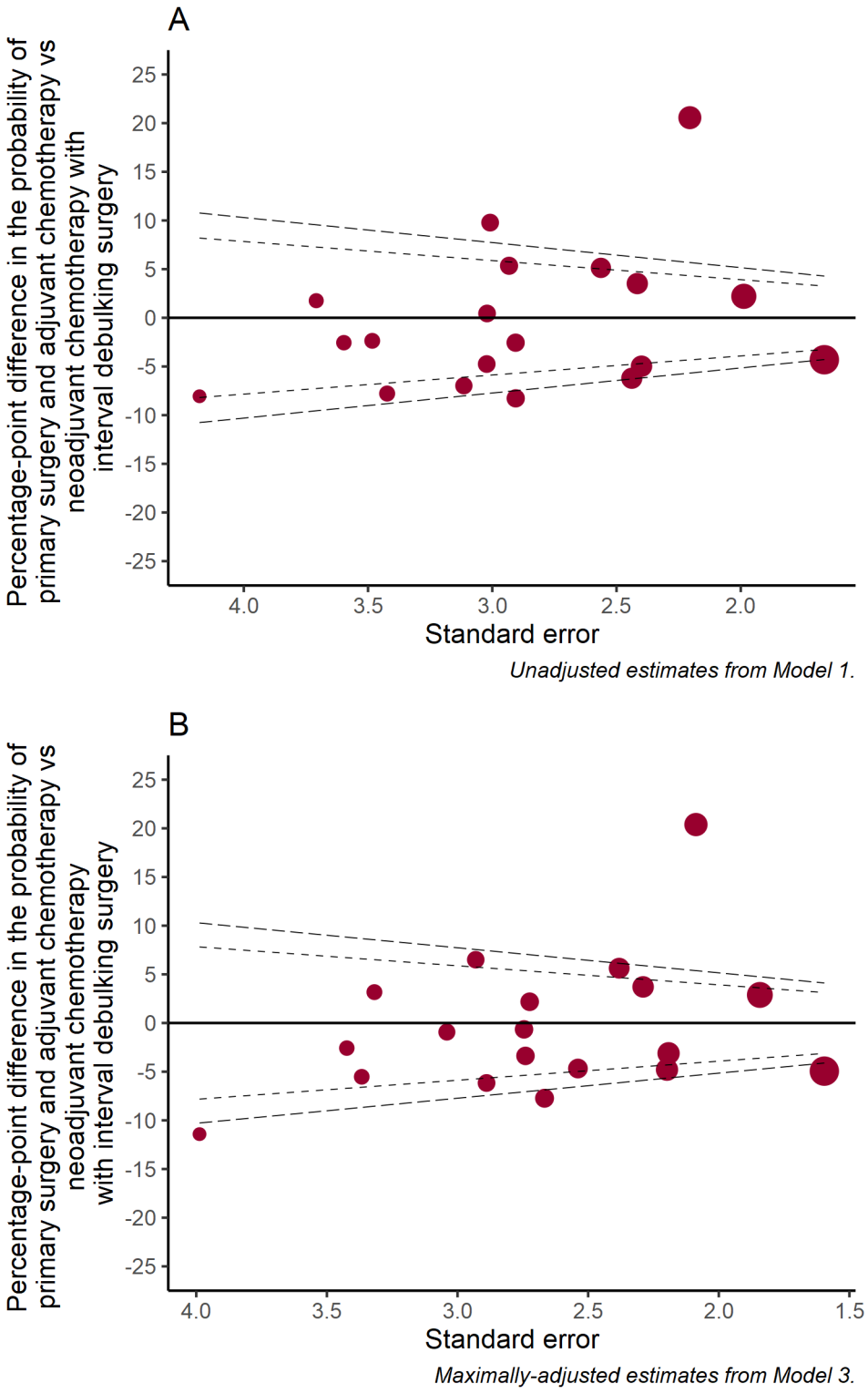


Figure 9 Geographic variation in the probability of receiving primary surgery and adjuvant chemotherapy versus neoadjuvant chemotherapy with interval debulking surgery, excluding stage 1 disease, 2016 to 2018 (Source: CAS AV2018, HES, SACT)

Table 4 Probability of receiving primary surgery with adjuvant chemotherapy versus neoadjuvant chemotherapy and interval debulking surgery, excluding stage 1 disease

	Model 1* (n=6,065)		Model 2* (n=6,065)		Model 3* (n=6,065)	
Variables	**Estimate**	**p-value**	**Estimate**	**p-value**	**Estimate**	**p-value**
Cohort average (intercept)	49.4	0.000	49.4	0.000	49.4	0.000
Cancer Alliance						
Cheshire and Merseyside	-2.6	0.379	-4.8	0.059	-4.7	0.066
East Midlands	3.5	0.146	3.9	0.092	3.7	0.105
East of England	-4.3	0.010	-5.1	0.001	-4.9	0.002
Greater Manchester	5.3	0.068	2.3	0.389	2.2	0.423
Humber, Coast and Vale	-7.8	0.023	-5.4	0.108	-5.5	0.101
Kent and Medway	-2.4	0.497	-0.9	0.758	-0.9	0.760
Lancashire and South Cumbria	-2.6	0.477	-2.3	0.492	-2.6	0.452
North Central and North East London	0.4	0.883	-0.5	0.864	-0.7	0.812
North East and Cumbria	20.6	0.000	20.6	0.000	20.4	0.000
North West and South West London	5.1	0.045	5.6	0.019	5.6	0.018
Peninsula	-7.0	0.025	-5.8	0.043	-6.2	0.033
Somerset, Wiltshire, Avon and Gloucestershire	-6.2	0.011	-5.0	0.022	-4.8	0.029
South East London	1.8	0.635	3.1	0.348	3.2	0.339
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-8.1	0.054	-11.6	0.004	-11.4	0.004
Surrey and Sussex	-5.0	0.038	-3.1	0.154	-3.1	0.156
Thames Valley	-4.7	0.116	-3.7	0.172	-3.4	0.218
Wessex	9.8	0.001	6.5	0.026	6.5	0.027
West Midlands	2.2	0.267	3.0	0.106	2.9	0.118
West Yorkshire and Harrogate	-8.3	0.004	-7.8	0.003	-7.7	0.004

The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate. Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.

Treatment variation by Cancer Alliance: summary table

Table 5 shows the maximally-adjusted results from Table 1 (any treatment), Table 2 (any surgery) and Table 3 (any chemotherapy). Collectively, they indicate pronounced geographic variation in treatment delivery after accounting for differences in the regional distribution of various patient demographics and tumour characteristics.

Table 5 Summary of maximally-adjusted geographic variation in any treatment, surgery and chemotherapy (Model 3)

	Any treatment (n=13,889)		Any surgery (n=13,889)		Any chemotherapy (n=13,889)	
Variables	**Estimate**	**p-value**	**Estimate**	**p-value**	**Estimate**	**p-value**
Cohort average (intercept)	73.8	0.000	51.0	0.000	66.5	0.000
Cancer Alliance						
Cheshire and Merseyside	-2.4	0.063	1.0	0.495	-1.3	0.370
East Midlands	-3.3	0.001	-5.6	0.000	-2.5	0.024
East of England	-3.0	0.000	0.0	0.993	-3.4	0.000
Greater Manchester	-2.8	0.029	-3.6	0.031	-2.2	0.122
Humber, Coast and Vale	-2.5	0.108	3.9	0.038	-3.2	0.066
Kent and Medway	-3.4	0.035	0.7	0.714	-4.7	0.012
Lancashire and South Cumbria	1.4	0.342	1.5	0.434	-0.7	0.687
North Central and North East London	0.3	0.853	2.8	0.108	-0.5	0.742
North East and Cumbria	-0.3	0.780	3.2	0.017	0.3	0.814
North West and South West London	5.5	0.000	7.9	0.000	3.9	0.003
Peninsula	4.9	0.000	1.9	0.211	7.1	0.000
Somerset, Wiltshire, Avon and Gloucestershire	2.9	0.004	4.8	0.000	2.8	0.021
South East London	0.0	0.994	7.0	0.001	0.7	0.695
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-2.7	0.108	-13.8	0.000	-0.5	0.761
Surrey and Sussex	3.8	0.000	5.9	0.000	0.7	0.591
Thames Valley	1.6	0.213	3.2	0.054	-0.2	0.889
Wessex	-1.1	0.361	-7.2	0.000	0.7	0.620
West Midlands	0.6	0.462	-4.2	0.000	1.8	0.045
West Yorkshire and Harrogate	3.1	0.005	-0.6	0.694	3.0	0.023

The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate. Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.

Conclusion

This second report of the Ovarian Cancer Audit Feasibility Pilot examines variation in the treatment of cases of ovarian, tubal and peritoneal cancer diagnosed in England between 2016 and 2018. The report describes differences in treatment by stage, age, morphology and comorbidity, then explores geographic variation in treatment with adjustment for these factors.

With regard to patient demographics and tumour characteristics (Appendix 1), findings from this report confirm what previous research and clinical practice have indicated, including that:

- Women with stage 4 disease or no stage recorded, and tumours classed as miscellaneous and unspecified, were much less likely to receive any treatment.
- Women with underlying medical conditions, identified by the Charlson comorbidity index, were less likely to receive surgery.
- Older women were more likely to have chemotherapy alone or not receive any chemotherapy or surgery.

Some of these differences can be explained by a range of underlying factors. For example, younger women may be more likely to have surgery without adjuvant chemotherapy due to a greater prevalence of certain tumour types among younger women. Likewise, tumours classed as miscellaneous and unspecified, or where no stage is recorded, can reflect disease that is too advanced for surgery, classification and staging.

Findings also point to worrying patterns of variation, especially in relation to age. Results reported in Appendix 3 indicate that the likelihood of receiving surgery may be far lower for older age cohorts than younger women, even after accounting for factors including stage and morphology. Some of this variation may be explained by factors including the burden of comorbidities not captured by the Charlson comorbidity index, poor performance status, and patient choice (such as opting for chemotherapy over surgery; Appendix 5). Research is needed to explore the reasons for diagnoses in older age groups having a lower probability of surgery.

In terms of geographic variation, differences beyond those that may be explained by random variation alone were present for all treatments investigated (any treatment versus no treatment; surgery versus no surgery; chemotherapy versus no chemotherapy; adjuvant versus neoadjuvant chemotherapy). This variation was particularly apparent for surgery, with cancers in six Cancer Alliances showing an above average probability and five showing a below average probability of surgery out of a total of 19 Cancer Alliances. These regional variations may be attributable to a variety of factors not accounted for in the maximally-adjusted models, including differences in access to primary care enabling early diagnosis and timely referral to secondary care. However, differences may also reflect real variation between gynaecological

cancer centre multidisciplinary teams in the efficiency of diagnostic pathways or preparedness to perform radical surgery and/or administer chemotherapy to women with advanced disease.

While stressing differences in the time coverage, covariate adjustment and cohort definitions of the two sets of analyses, cross-referencing results from this study with the outputs of the first report of the Ovarian Cancer Audit Feasibility Pilot (Disease Profile in England: Incidence, mortality, stage and survival for ovary, fallopian tube and primary peritoneal carcinomas)[4] indicates that Cancer Alliances that were less likely to undertake treatment generally had lower than average five year survival figures, and that this relationship may be particularly pronounced for surgery. Together, these findings present an opportunity for further work to better understand the reasons for variation in treatment between areas, the impact of this variation on patient health outcomes, and the steps that can be taken to address it.

With this analysis indicating geographic variation in the treatment of ovarian, tubal and peritoneal cancer after adjusting for important variables, future outputs of the Ovarian Cancer Audit Feasibility Pilot will start to answer some of the outstanding questions outlined above, focusing in greater detail on treatment variation and seeking to better understand the treatment pathway of those patients with the poorest survival.

The analysis presented in this report is based on data collected prior to the COVID-19 pandemic and provides a baseline measure of access to treatment across England. The pandemic has already had an immense impact on cancer diagnoses and access to treatment[5] and, while it is too early to quantify its full impact on cancer diagnosis and treatment, it makes the need for a continuing and fully-funded ovarian cancer audit even more pressing given the worrying picture presented within this report.

Limitations

Residual confounding

The maximally-adjusted models described throughout this report accounted for differences in the distribution of numerous patient demographics and tumour characteristics between Cancer Alliances that might confound the main association under study. Despite this adjustment, geographic variation in treatment was observed for a number of treatment types. However, some of these geographic differences may be attributable to residual confounding rather than real disparities in clinical practice, such as differential routes to diagnosis (unavailable at the time of analysis), variation in the proportion of patients who died before the primary course of treatment could be started or concluded, or geographic differences in patient frailty.

Private healthcare data

Additionally, reported analyses do not consider treatments provided in private healthcare settings. Due to the absence of private healthcare data, tumours in private patients will have been incorrectly assigned to the 'no major surgical resection or chemotherapy' category. Accordingly, the true proportion of tumours that received treatment will be higher than reported, and with the possibility of differences in private treatment access between Cancer Alliances. If present, such differences will explain some of the variation observed between Cancer Alliances in analyses where tumours assigned to the 'no major surgical resection or chemotherapy' category are included. We are not aware of any data sources that allow for a reliable estimate of the degree to which this misclassification occurred.

Major surgical resections

A further point to note is that this report defines surgery as the delivery of at least one major resection during the primary course of treatment. A list of such procedures is provided in Appendix 7, and was developed in consultation with experienced clinicians. Major surgical resections do not encompass all surgical procedures delivered to ovarian tumours, for example excluding procedures for diagnostic biopsies. If a broader definition of surgery were to be applied, treatment rates in these patient groups would be expected to exceed those described in this report. Major surgical resections were selected because they constitute the main surgical intervention for the treatment of ovarian cancer.

Charlson comorbidity scores

Charlson comorbidity scores were defined for each tumour by linking to non-ovarian primary cancers in the cancer registry or a pre-defined comorbid medical condition documented within an inpatient setting prior to the diagnosis of ovarian cancer. A list of medical conditions considered and the scoring assigned to each is described in Appendix 8. This derivation is such

that the score is dependent on the recording of particular diagnoses during patient admission, and may therefore underestimate the burden of index-relevant comorbidity by missing diagnoses in Appendix 8 that are exclusively documented in outpatient or primary care settings. However, a comparison of Charlson comorbidity indexes derived for a fixed general population cohort of adults aged >20 years found that an index based on secondary care data performed at least as well as one that utilised primary care data for the prediction of case-mix adjusted all-cause mortality.[6]

Despite this, the index may not reflect the true burden of all comorbid disease that may influence clinical decision making. For instance, Appendix 1 shows that 82.8% (n=14,196) of tumours in the cohort were assigned a Charlson comorbidity score of zero, representing tumours in patients without any record of another primary cancer in the cancer registry or a pre-defined comorbid medical condition documented within an inpatient setting prior to the diagnosis of ovarian cancer. That more than four-fifths of tumours in the cohort received a comorbidity score of zero sits at odds with the age profile of the ovarian cancer cohort, and research elsewhere for other tumour sites that demonstrated a broad range of comorbid medical conditions.[7] Nevertheless, the Charlson comorbidity index captures at least some of the variation in the probability of treatment, whereby tumours in patients with higher scores were reported as having lower probabilities of any treatment (Appendix 3), any surgery (Appendix 4) or any chemotherapy (Appendix 5).

Cancer Alliance at diagnosis

Finally, this report described geographic variations in treatment according to the Cancer Alliance of residence at the time of diagnosis. It is possible that some tumours may have received treatments from multiple Cancer Alliances over the course of treatment, which may have differed from the Cancer Alliance at diagnosis. As the Cancer Alliance at treatment can vary over time and according to treatment type, Cancer Alliance at diagnosis was reported for simplicity.

Method

Defining the ovarian cancer cohort

Ovary, fallopian tube and primary peritoneal carcinomas ('ovarian cancers') were selected into the cohort from the national cancer registry for England[8] if diagnosed between January 2016 and December 2018. Cases were identified according to the following ICD-10/O-2 codes:

- C56 (malignant neoplasm of ovary); or,
- C57 (malignant neoplasm of other and unspecified female genital organs); or,
- C48 (malignant neoplasm of retroperitoneum and peritoneum), excluding sarcomas: 8693, 8800, 8801, 8802, 8803, 8804, 8805, 8806, 8963, 8990, 8991, 9040, 9041, 9042, 9043, 9044, 8810, 8811-8921, 9120-9373, 9490, 9500, 9530-9582; or,
- D39.1 (neoplasm of uncertain or unknown behaviour of ovary).

Only tumours diagnosed within female patients were included in the cohort.

For the purpose of this report, 'borderline' malignancies were excluded as the treatment pathway for this sub-group can look quite different and only a minority of such tumours receive systemic anti-cancer therapy – a key treatment type of interest . Tumours identified via death certificate only are also excluded as these diagnoses would not have been referred for treatment.

Tumours with an ICD-10 site code of C56, C57 or C48 were defined as 'borderline' if their morphology code in ICD-O-2 was 8442, 8444, 8451, 8463, 8473, 8472 or 8462. Tumours with ICD-10 site code D39.1 were defined as 'borderline' if their morphology code in ICD-O-2 was 8144, 8260, 8313, 8380, 8381, 8440, 8441, 8460, 8470, 8480, 8481, 9000, 9013, 9014 or 9015.

Defining cancer treatment

Treatment dates for each tumour were extracted from multiple data sources in a manner consistent with internal PHE standard operating procedures. Briefly, dates of systemic anti-cancer therapy administrations and major surgical resections were extracted at a tumour level from the cancer registry if they occurred during the primary course of therapy (defined for ovarian cancer as the period between one month prior and up to nine months following diagnosis). Where patients with tumours selected selected into the cohort were known to have not received another primary cancer diagnosis during the 18 months before or after the primary tumour of interest, information from the cancer registry was supplemented with any additional dates available at a patient level from the Systemic Anti-Cancer Therapy (SACT) dataset[9] and Hospital Episode Statistics (HES) admitted patient care dataset.[10] SACT and HES data are otherwise not used as they are patient-linked datasets where the precise tumour a treatment

relates to is not identified. A list of major surgical resections is provided in Appendix 7 and referred to as 'surgery' within the body of this report.

Systemic anti-cancer therapies were excluded from the analysis if they pertained exclusively to a supportive regimen, such as the delivery of anti-emitic or analgesic medication for the treatment of cancer symptoms. Throughout the main body of the report, systemic anti-cancer therapy is referred to as 'chemotherapy'. Radiation therapy was not considered as it is rarely prescribed for ovarian cancers.

Once all relevant treatment dates were extracted, each tumour was assigned to one of the following five groups according to the order in which treatments were delivered:

1. No surgery or chemotherapy
2. Primary surgery with adjuvant chemotherapy (i.e. surgery followed by chemotherapy)
3. Neoadjuvant chemotherapy with interval debulking surgery (i.e. chemotherapy followed by surgery)
4. Chemotherapy but no surgery
5. Primary surgery but no chemotherapy

Based on the above treatment groups, four binary comparison groups were created for use in the treatment analyses described in the main body of this report:

1. Any treatment (groups two to five) versus no treatment (group one)
2. Surgery (groups two, three and five) versus no surgery (groups one and four)
3. Chemotherapy (groups two, three and four) versus no chemotherapy (groups one and five)
4. Primary surgery with adjuvant chemotherapy (group two) versus neoadjuvant chemotherapy with interval debulking surgery (group three).

Defining patient demographics and tumour characteristics

A number of patient and tumour chracteristics were likely to be associated with clinical decision-making concerning how best to treat a particular cancer. Analyses were therefore adjusted for the following variables:

- Tumour morphology (the histological type of the malignancy, e.g. clear cell carcinoma);
- Stage at diagnosis (the size and spread of the tumour);
- Patient age at diagnosis;
- Charlson comorbidity index (the burden of comorbid health conditions);
- Area income deprivation

As described later, a sensitivity analysis of any treatment versus no treatment was undertaken that included adjustment for performance status (Appendix 9). This variable was not included in the main set of analyses owing to a high proportion of missing data (57.9%; Appendix 1).

Performance status is a measure of a patient's ability to undertake daily living acitivities. It is scored according to the adult Eastern Cooperative Oncology Group (ECOG) scale,[11] which rates physical function from 0 to 4, with a score of 4 indicating complete disability and total confinement to a bed or chair.

Stage at diagnosis was that defined by the cancer registry based on information from multiple sources. Cancer registration staff take FIGO staging data provided by the diagnosing trust via the MDT and review it alongside information from pathology reports and clinical investigations to record the most accurate stage at diagnosis possible. If insufficient staging data were available at the time of analysis, a tumour was defined for this report as 'stage not recorded'. Tumour stages are numbered from 1 to 4, with a higher value indicating more advanced disease.

Finally, a Charlson comorbidity score was derived for each tumour, drawing on diagnosis data from the cancer registry and the HES admitted patient care dataset. Consistent with a PHE standard operating procedure, comorbid diagnoses were selected if they occurred between three and 27 months prior to the cancer diagnosis of interest. As shown in Appendix 8, a total of 15 medical conditions were considered and assigned values between one and six. Comorbid conditions included myocardial infarction (heart attack), dementia and liver disease. The final index ranged from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score was assigned.

Area income deprivation is reported in quintiles according to the income component of the Index of Multiple Deprivation, which provides a relative measure of income deprivation in the area of a patient's residence. It was defined for each patient by linking their postcode at the time of diagnosis to a 2011 ONS census Lower Super Output Area (LSOA).[12] This LSOA was then linked to the associated Ministry of Housing, Communities & Local Government 2015 income deprivation quintile.[13]

Defining geography

Geographic variation in treatment was analysed at the Cancer Alliance level according to regions defined in 2018. As shown in Figure 5, these disaggregate England into 19 geographic areas that bring together clinicians and managers from different hospital trusts and other health and social care organisations with the aim of coordinating the diagnosis and treatment of cancer patients in the local area. The Cancer Alliance for each tumour was assigned according to the main residence of the patient on the date of diagnosis.

Statistical analysis

Descriptive statistics

The statistical significance of differences in the crude distribution of treatment groups by patient demographics and tumour characteristics was estimated using the chi-squared test.

Linear probability models

Each binary treatment comparison group detailed above was added as an outcome variable in separate linear probability models. Covariates were then introduced as explanatory variables in three stages:

- Model 1: Cancer Alliance only.
- Model 2: as Model 1, plus adjustment for differences between Cancer Alliances in the distribution of patient age, tumour morphology and tumour stage.
- Model 3: as Model 2, plus area income deprivation and Charlson comorbidity score.

Linear probability models are equivalent to linear regression with a binary outcome, where standard errors, confidence intervals and p-values are adjusted for heteroskedasticity (residuals that violate the normal distribution assumption due to the outcome for each tumour only taking one of two values). A linear approximation of probabilities when using a binary outcome is considered appropriate when probabilities fall between values of 0.2 and 0.8, representing the range within which a logistic function is largely linear.[14] This requirement held for all models under study. Importantly, in contrast to logistic probability models, which are conventionally used in analyses of binary outcome data, linear regression permits the direct comparison of estimates from nested models as new covariates are introduced.[15]

Weighted effect coding[16] was applied to each linear probability model such that the sum of all estimates from variable categories reported in each model was equal to zero. Estimates are then interpretable as percentage-point deviations from the sample mean (i.e. from the average probability for the tumour cohort as a whole, weighted according to the number of observations within each category reported by the respective model).

Tumours assigned to a non-specific site morphology were dropped from all linear probability models owing to small numbers (0.4%; n=62; Appendix 1). Tumours with stage 1 disease at diagnosis were also excluded as little regional variation in treatment decisions was expected, given 96.3% (n=3,091) of such tumours were treated with primary surgery only or surgery with adjuvant chemotherapy.

Analyses were undertaken using R version 3.5.3.

Sample sizes

From the original cohort of 17,155 tumours, removal of stage 1 tumours and tumours of non-specific site morphologies left an analytical sample of 13,889 ovarian cancers. In the final main analysis, which concerned the probability of primary surgery with adjuvant chemotherapy versus neoadjuvant chemotherapy with interval debulking surgery, the cohort was restricted to the sub-set of patients who received either of the two treatment combinations (n=6,065).

Funnel plots

For each binary treatment comparison group, Cancer Alliance estimates from Model 1 and Model 3 were extracted and presented on funnel plots. Each point on a funnel plot represents a Cancer Alliance. The standard error is shown on the horizontal axis and provides an indication of the number of tumours diagnosed within the Cancer Alliance. Estimates from Cancer Alliances with a greater number of tumours are more precise, appearing further to the right-hand side of the plot. Each Cancer Alliance is plotted with a radius proportional to the inverse of its estimate's standard error, providing a quick visual indication as to differences in the size of each plotted Cancer Alliance, as represented by the number of tumours.

The percentage difference in the probability of treatment (overall or a particular combination) is shown on the vertical axis relative to the population average (all tumours combined). A Cancer Alliance with an estimate above the middle line suggests that tumours within the geography were more likely to receive treatment than the population average, with estimates below the line indicating a lower probability.

Two pairs of dashed lines are included on each funnel plot that represent the bounds of statistical confidence around the average value. The inner set of dashed lines represents two standard deviations (SD) from the population average and the outer set represents three SD, being approximately equivalent to 95.0% and 99.7% confidence intervals, respectively. Any observation plotted outside of these dashed lines will have a confidence interval that does not include the average value, and may therefore indicate a systematic deviation in clinical practice that warrants further investigation. However, some random variation in the probability of treatment is expected between regions such that some points will sit outside the dashed lines through chance alone. This should be taken into consideration when interpreting funnel plots (for example, five out of every 100 observations are likely to lie outside the two SD funnel).

Sensitivity analysis

Owing to a sizeable proportion of missing data for patient performance status at diagnosis (57.9%; Appendix 1), this variable was not included in the main analyses reported. Instead, its contribution to a reduction in treatment variation between Cancer Alliances was investigated via a sensitivity analysis. This sensitivity analysis constrained the cohort to the 5,823 tumours documented within patients with a known performance status value at diagnosis, then reported estimates for the 'any treatment versus no treatment' model with and without the inclusion of performance status alongside all other *a priori* covariates. Results from the sensitivity analysis are reported in Appendix 9 and show a strong and expected inverse relationship between performance status and the probability of treatment. Variation between Cancer Alliances from the population average were shifted by between 0.2 and 3.2 percentage points.

Appendices

Appendix 1 Tumour characteristics and patient demographics of the full cohort (n=17,155)

	Treatment groups†						
Descriptives	**No surgery or chemotherapy (N, %)**	**Primary surgery with adjuvant chemotherapy (N, %)**	**Neoadjuvant chemotherapy with interval debulking surgery (N, %)**	**Chemotherapy but no surgery (N, %)**	**Primary surgery but no chemotherapy (N, %)**	**Total (N, %)**	**p-value**
Total tumours (N, %)*	3751 (21.9)	4322 (25.2)	3091 (18.0)	3200 (18.7)	2791 (16.3)	17155 (100.0)	
Tumour characteristics							
Site							
C48	303 (26.6)	56 (4.9)	316 (27.8)	420 (36.9)	43 (3.8)	1138 (6.6)	<0.001
C56	3145 (22.1)	3554 (24.9)	2347 (16.5)	2682 (18.8)	2523 (17.7)	14251 (83.1)	
C57	248 (15.3)	705 (43.5)	428 (26.4)	98 (6.0)	141 (8.7)	1620 (9.4)	
D39	55 (37.7)	7 (4.8)	0 (0.0)	0 (0.0)	84 (57.5)	146 (0.9)	
Morphology							
Clear cell carcinoma	28 (3.8)	489 (66.5)	22 (3.0)	58 (7.9)	138 (18.8)	735 (4.3)	<0.001
Endometrioid carcinoma	26 (2.7)	546 (55.7)	29 (3.0)	20 (2.0)	360 (36.7)	981 (5.7)	
Miscellaneous & unspecified	1379 (89.1)	20 (1.3)	9 (0.6)	64 (4.1)	76 (4.9)	1548 (9.0)	
Mucinous carcinoma	55 (5.6)	264 (27.0)	11 (1.1)	29 (3.0)	620 (63.3)	979 (5.7)	
Non-specific site	44 (71.0)	0 (0.0)	0 (0.0)	0 (0.0)	18 (29.0)	62 (0.4)	
Other malignant epithelial	1063 (39.5)	451 (16.7)	238 (8.8)	696 (25.8)	246 (9.1)	2694 (15.7)	
Serous carcinoma	1087 (11.8)	2430 (26.3)	2750 (29.8)	2306 (25.0)	658 (7.1)	9231 (53.8)	
Sex cord-stromal & germ cell	69 (7.5)	122 (13.2)	32 (3.5)	27 (2.9)	675 (73.0)	925 (5.4)	
Stage at diagnosis							
1	70 (2.2)	1328 (41.4)	20 (0.6)	28 (0.9)	1763 (54.9)	3209 (18.7)	<0.001
2-3	854 (11.9)	2525 (35.1)	1869 (26.0)	1427 (19.8)	521 (7.2)	7196 (41.9)	
4	1104 (28.2)	343 (8.8)	1016 (26.0)	1344 (34.4)	103 (2.6)	3910 (22.8)	
Not recorded	1723 (60.7)	126 (4.4)	186 (6.5)	401 (14.1)	404 (14.2)	2840 (16.6)	
Patient demographics							
Age at diagnosis (years)							
0-29	33 (8.7)	104 (27.4)	23 (6.1)	24 (6.3)	196 (51.6)	380 (2.2)	<0.001
30-39	20 (4.1)	151 (31.1)	42 (8.6)	23 (4.7)	250 (51.4)	486 (2.8)	
40-49	73 (5.7)	516 (40.3)	197 (15.4)	114 (8.9)	380 (29.7)	1280 (7.5)	
50-59	195 (6.6)	1151 (38.9)	676 (22.9)	326 (11.0)	610 (20.6)	2958 (17.2)	

60-69	412 (10.4)	1182 (29.7)	1052 (26.4)	766 (19.2)	568 (14.3)	3980 (23.2)	
70-79	1031 (21.6)	1004 (21.1)	958 (20.1)	1260 (26.4)	513 (10.8)	4766 (27.8)	
>79	1987 (60.1)	214 (6.5)	143 (4.3)	687 (20.8)	274 (8.3)	3305 (19.3)	
Cancer Alliance at diagnosis							
Cheshire & Merseyside	201 (24.7)	189 (23.2)	151 (18.6)	121 (14.9)	151 (18.6)	813 (4.7)	<0.001
East Midlands	345 (25.7)	343 (25.5)	189 (14.1)	288 (21.4)	180 (13.4)	1345 (7.8)	
East of England	494 (23.6)	506 (24.2)	429 (20.5)	345 (16.5)	315 (15.1)	2089 (12.2)	
Greater Manchester	174 (21.3)	230 (28.2)	126 (15.4)	144 (17.6)	143 (17.5)	817 (4.8)	
Humber, Coast & Vale	117 (24.2)	116 (24.0)	118 (24.4)	66 (13.6)	67 (13.8)	484 (2.8)	
Kent & Medway	137 (23.8)	140 (24.3)	106 (18.4)	89 (15.5)	103 (17.9)	575 (3.4)	
Lancashire & South Cumbria	106 (18.2)	146 (25.0)	100 (17.1)	98 (16.8)	134 (22.9)	584 (3.4)	
North Central & North East London	105 (15.8)	160 (24.0)	133 (20.0)	102 (15.3)	166 (24.9)	666 (3.9)	
North East & Cumbria	206 (20.1)	363 (35.4)	124 (12.1)	162 (15.8)	170 (16.6)	1025 (6.0)	
North West & South West London	139 (16.5)	248 (29.4)	164 (19.4)	135 (16.0)	158 (18.7)	844 (4.9)	
Peninsula	168 (23.6)	151 (21.2)	142 (19.9)	159 (22.3)	92 (12.9)	712 (4.2)	
Somerset, Wiltshire, Avon & Gloucestershire	183 (19.4)	239 (25.3)	221 (23.4)	168 (17.8)	134 (14.2)	945 (5.5)	
South East London	67 (16.1)	126 (30.4)	88 (21.2)	47 (11.3)	87 (21.0)	415 (2.4)	
South Yorkshire, Bassetlaw, North Derbyshire, Hardwick	158 (26.2)	104 (17.3)	82 (13.6)	160 (26.6)	98 (16.3)	602 (3.5)	
Surrey & Sussex	222 (20.7)	244 (22.7)	223 (20.8)	194 (18.1)	191 (17.8)	1074 (6.3)	
Thames Valley	141 (20.3)	160 (23.0)	147 (21.1)	121 (17.4)	127 (18.2)	696 (4.1)	
Wessex	252 (27.6)	221 (24.2)	107 (11.7)	216 (23.7)	117 (12.8)	913 (5.3)	
West Midlands	403 (22.3)	477 (26.4)	278 (15.4)	415 (22.9)	237 (13.1)	1810 (10.6)	
West Yorkshire & Harrogate	133 (17.8)	159 (21.3)	163 (21.8)	170 (22.8)	121 (16.2)	746 (4.3)	
Charlson comorbidity index[§]							
0	2594 (18.3)	3880 (27.3)	2740 (19.3)	2637 (18.6)	2345 (16.5)	14196 (82.8)	<0.001
1	463 (31.2)	270 (18.2)	240 (16.2)	297 (20.0)	216 (14.5)	1486 (8.7)	
2	265 (36.7)	115 (15.9)	75 (10.4)	157 (21.7)	110 (15.2)	722 (4.2)	
>2	310 (55.8)	52 (9.4)	31 (5.6)	95 (17.1)	68 (12.2)	556 (3.2)	
Not recorded	119 (61.0)	5 (2.6)	5 (2.6)	14 (7.2)	52 (26.7)	195 (1.1)	
Area income deprivation[‡]							
Quintile 1 (least deprived)	751 (19.8)	970 (25.5)	755 (19.9)	740 (19.5)	582 (15.3)	3798 (22.1)	<0.001
Quintile 2	775 (20.7)	964 (25.7)	711 (19.0)	714 (19.1)	581 (15.5)	3745 (21.8)	
Quintile 3	814 (22.4)	954 (26.2)	676 (18.6)	645 (17.7)	553 (15.2)	3642 (21.2)	
Quintile 4	736 (23.1)	745 (23.3)	552 (17.3)	599 (18.8)	560 (17.5)	3192 (18.6)	
Quintile 5 (most deprived)	675 (24.3)	689 (24.8)	397 (14.3)	502 (18.1)	515 (18.5)	2778 (16.2)	
Performance status at diagnosis							
0	119 (3.6)	1313 (39.8)	721 (21.9)	477 (14.5)	666 (20.2)	3296 (19.2)	<0.001
1	191 (8.1)	639 (27.2)	656 (27.9)	615 (26.2)	248 (10.6)	2349 (13.7)	
2	201 (22.4)	114 (12.7)	186 (20.8)	320 (35.7)	75 (8.4)	896 (5.2)	
3	264 (49.2)	33 (6.1)	62 (11.5)	150 (27.9)	28 (5.2)	537 (3.1)	

4	125 (86.8)	1 (0.7)	2 (1.4)	11 (7.6)	5 (3.5)	144 (0.8)	
Not recorded	2851 (28.7)	2222 (22.4)	1464 (14.7)	1627 (16.4)	1769 (17.8)	9933 (57.9)	

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Borderline tumours and cases diagnosed via death certificate are excluded. Patient demographics are reported at a tumour level. The age at diagnosis for two tumours diagnosed on the same day within a single patient will therefore be identical.

† Treatment data are compiled from the cancer registry, the Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the Neoadjuvant anti-cancer therapy treatment group.

§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the ‘baseline’ period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.

‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 2 Tumour characteristics and patient demographics of the analytical cohort, FIGO Stage 2-4 (n=13,889)

	Treatment groups†						
Descriptives	**No surgery or chemotherapy (N, %)**	**Primary surgery with adjuvant chemotherapy (N, %)**	**Neoadjuvant chemotherapy with interval debulking surgery (N, %)**	**Chemotherapy but no surgery (N, %)**	**Primary surgery but no chemotherapy (N, %)**	**Total (N, %)**	**p-value**
Total tumours (N, %)*	3637 (26.2)	2994 (21.6)	3071 (22.1)	3172 (22.8)	1015 (7.3)	13889 (100.0)	
Tumour characteristics							
Site							
C48	303 (26.6)	56 (4.9)	316 (27.8)	420 (36.9)	43 (3.8)	1138 (8.2)	<0.001
C56	3078 (27.4)	2337 (20.8)	2329 (20.7)	2656 (23.6)	839 (7.5)	11239 (80.9)	
C57	248 (16.8)	599 (40.6)	426 (28.9)	96 (6.5)	105 (7.1)	1474 (10.6)	
D39	8 (21.1)	2 (5.3)	0 (0.0)	0 (0.0)	28 (73.7)	38 (0.3)	
Morphology							
Clear cell carcinoma	23 (7.1)	196 (60.1)	22 (6.7)	55 (16.9)	30 (9.2)	326 (2.3)	<0.001
Endometrioid carcinoma	22 (6.1)	241 (67.1)	25 (7.0)	17 (4.7)	54 (15.0)	359 (2.6)	
Miscellaneous & unspecified	1363 (90.7)	19 (1.3)	9 (0.6)	64 (4.3)	47 (3.1)	1502 (10.8)	
Mucinous carcinoma	48 (19.1)	85 (33.9)	11 (4.4)	24 (9.6)	83 (33.1)	251 (1.8)	
Non-specific site	-	-	-	-	-	-	
Other malignant epithelial	1051 (43.4)	324 (13.4)	235 (9.7)	690 (28.5)	124 (5.1)	2424 (17.5)	
Serous carcinoma	1082 (12.5)	2067 (23.9)	2739 (31.7)	2297 (26.6)	459 (5.3)	8644 (62.2)	
Sex cord-stromal & germ cell	48 (12.5)	62 (16.2)	30 (7.8)	25 (6.5)	218 (56.9)	383 (2.8)	
Stage at diagnosis							
1	-	-	-	-	-	-	<0.001
2-3	854 (11.9)	2525 (35.1)	1869 (26.0)	1427 (19.8)	521 (7.2)	7196 (51.8)	
4	1103 (28.2)	343 (8.8)	1016 (26.0)	1344 (34.4)	103 (2.6)	3909 (28.1)	
Not recorded	1680 (60.3)	126 (4.5)	186 (6.7)	401 (14.4)	391 (14.0)	2784 (20.0)	
Patient demographics							
Age at diagnosis (years)							
0-29	19 (11.0)	54 (31.4)	22 (12.8)	22 (12.8)	55 (32.0)	172 (1.2)	<0.001
30-39	11 (4.8)	84 (36.7)	40 (17.5)	22 (9.6)	72 (31.4)	229 (1.6)	
40-49	70 (8.6)	323 (39.7)	197 (24.2)	109 (13.4)	114 (14.0)	813 (5.9)	
50-59	181 (8.5)	740 (34.8)	671 (31.6)	321 (15.1)	212 (10.0)	2125 (15.3)	
60-69	398 (12.2)	837 (25.7)	1046 (32.1)	759 (23.3)	220 (6.7)	3260 (23.5)	
70-79	1013 (24.0)	787 (18.7)	953 (22.6)	1256 (29.8)	207 (4.9)	4216 (30.4)	

>79	1945 (63.3)	169 (5.5)	142 (4.6)	683 (22.2)	135 (4.4)	3074 (22.1)	
Cancer Alliance at diagnosis							
Cheshire & Merseyside	198 (30.8)	132 (20.6)	150 (23.4)	121 (18.8)	41 (6.4)	642 (4.6)	<0.001
East Midllands	335 (30.7)	211 (19.3)	188 (17.2)	284 (26.0)	73 (6.7)	1091 (7.9)	
East of England	486 (28.0)	351 (20.3)	428 (24.7)	340 (19.6)	128 (7.4)	1733 (12.5)	
Greater Manchester	161 (25.9)	151 (24.3)	125 (20.1)	142 (22.9)	42 (6.8)	621 (4.5)	
Humber, Coast & Vale	112 (27.6)	84 (20.7)	118 (29.1)	66 (16.3)	26 (6.4)	406 (2.9)	
Kent & Medway	131 (28.7)	94 (20.6)	106 (23.2)	89 (19.5)	37 (8.1)	457 (3.3)	
Lancashire & South Cumbria	101 (23.7)	88 (20.7)	100 (23.5)	96 (22.5)	41 (9.6)	426 (3.1)	
North Central & North East London	102 (19.8)	131 (25.4)	132 (25.6)	100 (19.4)	50 (9.7)	515 (3.7)	
North East & Cumbria	200 (24.4)	286 (35.0)	123 (15.0)	162 (19.8)	47 (5.7)	818 (5.9)	
North West & South West London	133 (19.1)	194 (27.9)	162 (23.3)	134 (19.3)	73 (10.5)	696 (5.0)	
Peninsula	167 (28.4)	103 (17.5)	140 (23.8)	156 (26.5)	23 (3.9)	589 (4.2)	
Somerset, Wiltshire, Avon & Gloucestershire	175 (22.1)	167 (21.1)	220 (27.8)	165 (20.9)	64 (8.1)	791 (5.7)	
South East London	62 (20.2)	91 (29.6)	87 (28.3)	47 (15.3)	20 (6.5)	307 (2.2)	
South Yorkshire, Bassetlaw, North Derbyshire, Hardwick	158 (32.4)	57 (11.7)	81 (16.6)	160 (32.8)	32 (6.6)	488 (3.5)	
Surrey & Sussex	216 (23.7)	178 (19.5)	223 (24.5)	193 (21.2)	102 (11.2)	912 (6.6)	
Thames Valley	137 (23.8)	116 (20.2)	144 (25.0)	120 (20.9)	58 (10.1)	575 (4.1)	
Wessex	246 (32.6)	152 (20.1)	105 (13.9)	216 (28.6)	36 (4.8)	755 (5.4)	
West Midlands	392 (26.9)	295 (20.2)	277 (19.0)	412 (28.3)	81 (5.6)	1457 (10.5)	
West Yorkshire & Harrogate	125 (20.5)	113 (18.5)	162 (26.6)	169 (27.7)	41 (6.7)	610 (4.4)	
Charlson comorbidity index[§]							
0	2523 (22.2)	2686 (23.6)	2723 (23.9)	2615 (23.0)	839 (7.4)	11386 (82.0)	<0.001
1	446 (36.0)	186 (15.0)	237 (19.1)	294 (23.7)	76 (6.1)	1239 (8.9)	
2	257 (42.0)	74 (12.1)	75 (12.3)	156 (25.5)	50 (8.2)	612 (4.4)	
>2	304 (60.9)	44 (8.8)	31 (6.2)	95 (19.0)	25 (5.0)	499 (3.6)	
Not recorded	107 (69.9)	4 (2.6)	5 (3.3)	12 (7.8)	25 (16.3)	153 (1.1)	
Area income deprivation[‡]							
Quintile 1 (least deprived)	735 (23.5)	666 (21.3)	748 (24.0)	734 (23.5)	240 (7.7)	3123 (22.5)	<0.001
Quintile 2	754 (24.5)	675 (21.9)	709 (23.0)	708 (23.0)	232 (7.5)	3078 (22.2)	
Quintile 3	793 (26.8)	662 (22.4)	673 (22.7)	637 (21.5)	196 (6.6)	2961 (21.3)	
Quintile 4	711 (27.6)	528 (20.5)	548 (21.3)	596 (23.1)	192 (7.5)	2575 (18.5)	
Quintile 5 (most deprived)	644 (29.9)	463 (21.5)	393 (18.3)	497 (23.1)	155 (7.2)	2152 (15.5)	
Performance status at diagnosis							
0	108 (4.7)	854 (36.8)	719 (31.0)	471 (20.3)	167 (7.2)	2319 (16.7)	<0.001
1	185 (9.1)	478 (23.6)	651 (32.2)	615 (30.4)	94 (4.6)	2023 (14.6)	
2	198 (24.0)	89 (10.8)	186 (22.5)	320 (38.7)	33 (4.0)	826 (5.9)	
3	258 (50.2)	27 (5.3)	61 (11.9)	149 (29.0)	19 (3.7)	514 (3.7)	
4	123 (87.2)	0 (0.0)	2 (1.4)	11 (7.8)	5 (3.5)	141 (1.0)	
Not recorded	2765 (34.3)	1546 (19.2)	1452 (18.0)	1606 (19.9)	697 (8.6)	8066 (58.1)	

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Borderline, stage 1 and diagnoses of a non-specific site were excluded, along with cancers diagnosed via death certificate. Patient demographics are reported at a tumour level. The age at diagnosis for two tumours diagnosed on the same day within a single patient will therefore be identical.
† Treatment data are compiled from the cancer registry, the Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the Neoadjuvant anti-cancer therapy treatment group.
§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the 'baseline' period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.
‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 3 Probability of receiving any treatment versus no treatment

	Model 1* (n=13,889)			Model 2* (n=13,889)			Model 3* (n=13,889)		
Variables	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**
Cohort average (intercept)	73.8	0.4	0.000	73.8	0.3	0.000	73.8	0.3	0.000
Cancer Alliance									
Cheshire and Merseyside	-4.7	1.8	0.009	-2.6	1.3	0.048	-2.4	1.3	0.063
East Midlands	-4.5	1.3	0.001	-3.3	1.0	0.001	-3.3	1.0	0.001
East of England	-1.9	1.0	0.065	-2.7	0.7	0.000	-3.0	0.7	0.000
Greater Manchester	0.3	1.7	0.880	-3.6	1.3	0.005	-2.8	1.3	0.029
Humber, Coast and Vale	-1.4	2.2	0.522	-2.5	1.5	0.106	-2.5	1.5	0.108
Kent and Medway	-2.5	2.1	0.234	-3.1	1.6	0.059	-3.4	1.6	0.035
Lancashire and South Cumbria	2.5	2.0	0.223	1.0	1.5	0.502	1.4	1.5	0.342
North Central and North East London	6.4	1.7	0.000	-1.2	1.4	0.380	0.3	1.4	0.853
North East and Cumbria	1.7	1.5	0.234	-0.9	1.0	0.411	-0.3	1.0	0.780
North West and South West London	7.1	1.5	0.000	5.0	1.2	0.000	5.5	1.1	0.000
Peninsula	-2.2	1.8	0.233	5.1	1.3	0.000	4.9	1.3	0.000
Somerset, Wiltshire, Avon and Gloucestershire	4.1	1.4	0.005	3.9	1.0	0.000	2.9	1.0	0.004
South East London	6.0	2.3	0.009	-0.9	1.6	0.562	0.0	1.6	0.994
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-6.2	2.1	0.003	-3.2	1.7	0.058	-2.7	1.6	0.108
Surrey and Sussex	2.5	1.4	0.067	4.9	1.0	0.000	3.8	1.0	0.000
Thames Valley	2.4	1.7	0.176	2.8	1.3	0.032	1.6	1.3	0.213
Wessex	-6.4	1.7	0.000	-0.3	1.3	0.808	-1.1	1.2	0.361
West Midlands	-0.7	1.1	0.513	0.1	0.9	0.935	0.6	0.8	0.462
West Yorkshire and Harrogate	5.7	1.6	0.000	2.9	1.1	0.010	3.1	1.1	0.005
Tumour morphology									
Clear cell carcinoma				9.1	1.4	0.000	8.2	1.4	0.000
Endometrioid carcinoma				9.3	1.2	0.000	9.2	1.2	0.000
Miscellaneous and unspecified				-43.5	1.0	0.000	-42.3	1.0	0.000
Mucinous carcinoma				4.1	2.2	0.067	4.5	2.2	0.040

Other malignant epithelial		-12.1	0.8	0.000	-11.8	0.8	0.000
Serous carcinoma		9.5	0.3	0.000	9.3	0.3	0.000
Sex cord-stromal and germ cell		12.9	2.0	0.000	12.5	1.9	0.000
Tumour stage at diagnosis							
Stage 2-3		7.6	0.3	0.000	7.3	0.3	0.000
Stage 4		-2.7	0.5	0.000	-3.0	0.5	0.000
Stage not recorded		-15.7	0.8	0.000	-14.8	0.8	0.000
Age at diagnosis (years)							
0-29		12.2	2.6	0.000	12.2	2.6	0.000
30-39		16.1	1.6	0.000	16.2	1.6	0.000
40-49		12.0	0.9	0.000	12.6	0.9	0.000
50-59		10.9	0.6	0.000	10.8	0.6	0.000
60-69		8.8	0.5	0.000	8.6	0.5	0.000
70-79		0.1	0.4	0.811	0.1	0.4	0.878
>79		-22.1	0.7	0.000	-22.0	0.7	0.000
Charlson comorbidity index[§]							
Charlson 0					1.3	0.1	0.000
Charlson 1					-2.5	1.0	0.011
Charlson 2					-3.2	1.4	0.025
Charlson >2					-11.3	1.6	0.000
Not recorded					-27.0	3.2	0.000
Area income deprivation[‡]							
Quintile 1 (least deprived)					2.0	0.5	0.000
Quintile 2					1.2	0.5	0.020
Quintile 3					0.4	0.5	0.404
Quintile 4					-1.0	0.6	0.084
Quintile 5 (most deprived)					-4.1	0.7	0.000

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate.
Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.
§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the 'baseline' period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.
‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 4 Probability of receiving any surgery versus no surgery

	Model 1* (n=13,889)			Model 2* (n=13,889)			Model 3* (n=13,889)		
Variables	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**
Cohort average (intercept)	51.0	0.4	0.000	51.0	0.3	0.000	51.0	0.3	0.000
Cancer Alliance									
Cheshire and Merseyside	-0.7	1.9	0.731	0.6	1.5	0.683	1.0	1.5	0.495
East Midlands	-7.7	1.4	0.000	-5.6	1.2	0.000	-5.6	1.2	0.000
East of England	1.4	1.1	0.225	0.5	0.9	0.568	0.0	0.9	0.993
Greater Manchester	0.2	2.0	0.906	-4.7	1.7	0.004	-3.6	1.7	0.031
Humber, Coast and Vale	5.2	2.4	0.033	3.8	1.9	0.044	3.9	1.9	0.038
Kent and Medway	0.9	2.3	0.701	1.2	1.9	0.533	0.7	1.9	0.714
Lancashire and South Cumbria	2.8	2.4	0.243	1.0	1.9	0.613	1.5	1.9	0.434
North Central and North East London	9.8	2.1	0.000	1.1	1.8	0.544	2.8	1.7	0.108
North East and Cumbria	4.8	1.7	0.005	2.3	1.3	0.086	3.2	1.3	0.017
North West and South West London	10.7	1.8	0.000	7.4	1.5	0.000	7.9	1.5	0.000
Peninsula	-5.8	2.0	0.004	2.3	1.5	0.134	1.9	1.5	0.211
Somerset, Wiltshire, Avon and Gloucestershire	6.0	1.7	0.000	5.9	1.3	0.000	4.8	1.3	0.000
South East London	13.5	2.7	0.000	5.8	2.2	0.007	7.0	2.1	0.001
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-16.1	2.1	0.000	-14.5	1.9	0.000	-13.8	1.9	0.000
Surrey and Sussex	4.2	1.6	0.009	7.1	1.3	0.000	5.9	1.3	0.000
Thames Valley	4.3	2.0	0.033	4.5	1.6	0.007	3.2	1.7	0.054
Wessex	-12.2	1.7	0.000	-6.2	1.4	0.000	-7.2	1.4	0.000
West Midlands	-6.2	1.2	0.000	-4.8	1.0	0.000	-4.2	1.0	0.000
West Yorkshire and Harrogate	0.8	2.0	0.676	-0.9	1.6	0.562	-0.6	1.6	0.694
Tumour morphology									
Clear cell carcinoma				9.8	2.2	0.000	8.8	2.3	0.000
Endometrioid carcinoma				20.6	1.7	0.000	20.5	1.7	0.000
Miscellaneous and unspecified				-23.0	0.9	0.000	-21.8	0.9	0.000

Mucinous carcinoma		14.8	2.6	0.000	15.0	2.6	0.000
Other malignant epithelial		-15.5	0.8	0.000	-15.1	0.8	0.000
Serous carcinoma		5.7	0.3	0.000	5.4	0.3	0.000
Sex cord-stromal and germ cell		23.5	2.3	0.000	23.2	2.3	0.000
Tumour stage at diagnosis							
Stage 2-3		11.7	0.4	0.000	11.5	0.4	0.000
Stage 4		-12.6	0.6	0.000	-12.8	0.6	0.000
Stage not recorded		-12.6	0.8	0.000	-11.8	0.8	0.000
Age at diagnosis (years)							
0-29		12.6	3.5	0.000	12.4	3.5	0.000
30-39		24.2	2.3	0.000	24.4	2.3	0.000
40-49		20.1	1.3	0.000	20.6	1.3	0.000
50-59		19.6	0.8	0.000	19.5	0.8	0.000
60-69		10.4	0.7	0.000	10.2	0.7	0.000
70-79		-5.2	0.6	0.000	-5.3	0.6	0.000
>79		-25.3	0.7	0.000	-25.1	0.7	0.000
Charlson comorbidity index[§]							
Charlson 0					1.3	0.2	0.000
Charlson 1					-2.9	1.1	0.007
Charlson 2					-5.8	1.5	0.000
Charlson >2					-9.5	1.6	0.000
Not recorded					-20.4	3.1	0.000
Area income deprivation[‡]							
Quintile 1 (least deprived)					2.1	0.6	0.001
Quintile 2					1.8	0.6	0.006
Quintile 3					1.4	0.6	0.032
Quintile 4					-1.8	0.7	0.014
Quintile 5 (most deprived)					-5.4	0.8	0.000

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate.
Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.
§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the 'baseline' period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.
‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 5 Probability of receiving any chemotherapy versus no chemotherapy

	Model 1* (n=13,889)			Model 2* (n=13,889)			Model 3* (n=13,889)		
Variables	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**
Cohort average (intercept)	66.5	0.4	0.000	66.5	0.3	0.000	66.5	0.3	0.000
Cancer Alliance									
Cheshire and Merseyside	-3.7	1.9	0.045	-1.5	1.5	0.303	-1.3	1.5	0.370
East Midlands	-3.9	1.4	0.005	-2.4	1.1	0.028	-2.5	1.1	0.024
East of England	-1.9	1.1	0.071	-3.1	0.9	0.000	-3.4	0.9	0.000
Greater Manchester	0.8	1.8	0.662	-2.9	1.4	0.040	-2.2	1.4	0.122
Humber, Coast and Vale	-0.5	2.3	0.831	-3.2	1.8	0.068	-3.2	1.8	0.066
Kent and Medway	-3.3	2.2	0.141	-4.3	1.9	0.021	-4.7	1.9	0.012
Lancashire and South Cumbria	0.2	2.3	0.943	-1.2	1.8	0.508	-0.7	1.8	0.687
North Central and North East London	4.0	2.0	0.044	-1.9	1.6	0.244	-0.5	1.6	0.742
North East and Cumbria	3.3	1.6	0.035	-0.2	1.2	0.851	0.3	1.2	0.814
North West and South West London	3.9	1.7	0.021	3.4	1.3	0.011	3.9	1.3	0.003
Peninsula	1.2	1.9	0.513	7.4	1.4	0.000	7.1	1.4	0.000
Somerset, Wiltshire, Avon and Gloucestershire	3.3	1.6	0.039	3.6	1.2	0.002	2.8	1.2	0.021
South East London	6.8	2.5	0.007	-0.2	1.9	0.928	0.7	1.9	0.695
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-5.4	2.2	0.012	-1.0	1.8	0.573	-0.5	1.8	0.761
Surrey and Sussex	-1.4	1.5	0.367	1.6	1.2	0.177	0.7	1.2	0.591
Thames Valley	-0.4	1.9	0.829	0.8	1.6	0.594	-0.2	1.6	0.889
Wessex	-3.9	1.7	0.024	1.5	1.3	0.267	0.7	1.3	0.620
West Midlands	1.0	1.2	0.375	1.3	0.9	0.162	1.8	0.9	0.045
West Yorkshire and Harrogate	6.3	1.8	0.000	2.7	1.3	0.041	3.0	1.3	0.023
Tumour morphology									
Clear cell carcinoma				8.6	1.9	0.000	7.6	1.9	0.000
Endometrioid carcinoma				3.5	2.0	0.074	3.3	2.0	0.093
Miscellaneous and unspecified				-37.9	1.0	0.000	-36.7	1.0	0.000

Mucinous carcinoma		-19.9	2.9	0.000	-19.4	2.9	0.000
Other malignant epithelial		-10.2	0.8	0.000	-9.8	0.8	0.000
Serous carcinoma		11.1	0.3	0.000	10.8	0.3	0.000
Sex cord-stromal and germ cell		-34.3	2.3	0.000	-34.6	2.3	0.000
Tumour stage at diagnosis							
Stage 2-3		7.7	0.3	0.000	7.4	0.3	0.000
Stage 4		0.6	0.5	0.270	0.3	0.5	0.558
Stage not recorded		-20.6	0.8	0.000	-19.6	0.8	0.000
Age at diagnosis (years)							
0-29		22.2	4.0	0.000	22.1	4.0	0.000
30-39		6.6	2.9	0.026	6.7	2.9	0.024
40-49		7.2	1.3	0.000	7.7	1.3	0.000
50-59		8.8	0.7	0.000	8.6	0.7	0.000
60-69		8.5	0.5	0.000	8.4	0.5	0.000
70-79		1.3	0.5	0.007	1.3	0.5	0.008
>79		-20.6	0.7	0.000	-20.4	0.7	0.000
Charlson comorbidity index[§]							
Charlson 0					1.4	0.2	0.000
Charlson 1					-2.2	1.0	0.039
Charlson 2					-5.2	1.6	0.001
Charlson >2					-10.6	1.7	0.000
Not recorded					-30.3	2.9	0.000
Area income deprivation[‡]							
Quintile 1 (least deprived)					1.8	0.6	0.003
Quintile 2					0.8	0.6	0.199
Quintile 3					1.0	0.6	0.101
Quintile 4					-1.0	0.7	0.122
Quintile 5 (most deprived)					-3.8	0.8	0.000

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate.
Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.
§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the 'baseline' period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.
‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 6 Probability of receiving primary surgery with adjuvant chemotherapy versus neoadjuvant chemotherapy with interval debulking surgery

	Model 1* (n=6,065)			Model 2* (n=6,065)			Model 3* (n=6,065)		
Variables	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**
Cohort average (intercept)	49.4	0.6	0.000	49.4	0.6	0.000	49.4	0.6	0.000
Cancer Alliance									
Cheshire and Merseyside	-2.6	2.9	0.379	-4.8	2.5	0.059	-4.7	2.5	0.066
East Midlands	3.5	2.4	0.146	3.9	2.3	0.092	3.7	2.3	0.105
East of England	-4.3	1.7	0.010	-5.1	1.6	0.001	-4.9	1.6	0.002
Greater Manchester	5.3	2.9	0.068	2.3	2.7	0.389	2.2	2.7	0.423
Humber, Coast and Vale	-7.8	3.4	0.023	-5.4	3.4	0.108	-5.5	3.4	0.101
Kent and Medway	-2.4	3.5	0.497	-0.9	3.0	0.758	-0.9	3.0	0.760
Lancashire and South Cumbria	-2.6	3.6	0.477	-2.3	3.4	0.492	-2.6	3.4	0.452
North Central and North East London	0.4	3.0	0.883	-0.5	2.7	0.864	-0.7	2.7	0.812
North East and Cumbria	20.6	2.2	0.000	20.6	2.1	0.000	20.4	2.1	0.000
North West and South West London	5.1	2.6	0.045	5.6	2.4	0.019	5.6	2.4	0.018
Peninsula	-7.0	3.1	0.025	-5.8	2.9	0.043	-6.2	2.9	0.033
Somerset, Wiltshire, Avon and Gloucestershire	-6.2	2.4	0.011	-5.0	2.2	0.022	-4.8	2.2	0.029
South East London	1.8	3.7	0.635	3.1	3.3	0.348	3.2	3.3	0.339
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-8.1	4.2	0.054	-11.6	4.0	0.004	-11.4	4.0	0.004
Surrey and Sussex	-5.0	2.4	0.038	-3.1	2.2	0.154	-3.1	2.2	0.156
Thames Valley	-4.7	3.0	0.116	-3.7	2.7	0.172	-3.4	2.7	0.218
Wessex	9.8	3.0	0.001	6.5	2.9	0.026	6.5	2.9	0.027
West Midlands	2.2	2.0	0.267	3.0	1.8	0.106	2.9	1.8	0.118
West Yorkshire and Harrogate	-8.3	2.9	0.004	-7.8	2.7	0.003	-7.7	2.7	0.004
Tumour morphology									
Clear cell carcinoma				35.5	2.0	0.000	35.6	2.0	0.000
Endometrioid carcinoma				35.7	1.8	0.000	35.7	1.8	0.000

Miscellaneous and unspecified		19.3	9.1	0.034	19.5	9.2	0.034
Mucinous carcinoma		37.1	3.3	0.000	36.7	3.3	0.000
Other malignant epithelial		8.4	1.9	0.000	8.5	1.9	0.000
Serous carcinoma		-5.6	0.3	0.000	-5.6	0.3	0.000
Sex cord-stromal and germ cell		10.6	6.4	0.099	10.5	6.4	0.100
Tumour stage at diagnosis							
Stage 2-3		7.5	0.4	0.000	7.5	0.4	0.000
Stage 4		-21.5	1.1	0.000	-21.6	1.1	0.000
Stage not recorded		-11.5	2.5	0.000	-11.4	2.5	0.000
Age at diagnosis (years)							
0-29		14.2	7.0	0.042	13.8	7.0	0.049
30-39		9.1	3.9	0.019	8.9	3.9	0.022
40-49		8.2	1.8	0.000	8.0	1.9	0.000
50-59		1.8	1.1	0.094	1.7	1.1	0.108
60-69		-3.2	0.9	0.000	-3.1	0.9	0.000
70-79		-2.8	0.9	0.003	-2.7	0.9	0.004
>79		5.8	2.6	0.027	6.2	2.6	0.019
Charlson comorbidity index[§]							
Charlson 0					0.4	0.2	0.076
Charlson 1					-6.1	2.2	0.005
Charlson 2					1.1	3.8	0.781
Charlson >2					6.6	5.2	0.205
Not recorded					-9.1	23.1	0.692
Area income deprivation[‡]							
Quintile 1 (least deprived)					-0.8	1.1	0.465
Quintile 2					0.2	1.1	0.831
Quintile 3					0.1	1.1	0.934
Quintile 4					-0.5	1.3	0.688
Quintile 5 (most deprived)					1.4	1.5	0.333

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate.
Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.
§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the 'baseline' period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.
‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 7 List of major surgical resection codes

OPCS-4 code	Description
H331	Abdominoperineal excision of rectum and end colostomy
H332	Proctectomy and anastomosis of colon to anus
H333	Anterior resection of rectum and anastomosis of colon to rectum using staples
H334	Anterior resection of rectum and anastomosis NEC
H335	Rectosigmoidectomy and closure of rectal stump and exteriorisation of bowel
H336	Anterior resection of rectum and exteriorisation of bowel
H337	Perineal resection of rectum HFQ
H338	Other specified excision of rectum
H339	Unspecified excision of rectum
Q071	Abdominal hysterocolpectomy and excision of periuterine tissue
Q072	Abdominal hysterectomy and excision of periuterine tissue NEC
Q073	Abdominal hysterocolpectomy NEC
Q074	Total abdominal hysterectomy NEC
Q075	Subtotal abdominal hysterectomy
Q078	Other specified abdominal excision of uterus
Q079	Unspecified abdominal excision of uterus
Q081	Vaginal hysterocolpectomy and excision of periuterine tissue
Q082	Vaginal hysterectomy and excision of periuterine tissue NEC
Q083	Vaginal hysterocolpectomy NEC
Q088	Other specified vaginal excision of uterus
Q089	Unspecified vaginal excision of uterus
Q221	Bilateral salpingoophorectomy
Q223	Bilateral oophorectomy NEC
Q231	Unilateral salpingoophorectomy NEC
Q232	Salpingoophorectomy of remaining solitary fallopian tube and ovary
Q235	Unilateral oophorectomy NEC
Q236	Oophorectomy of remaining solitary ovary NEC

Q241	Salpingoophorectomy NEC
Q243	Oophorectomy NEC
Q438	Other specified partial excision of ovary
Q439	Unspecified partial excision of ovary
Q473	Open biopsy of lesion of ovary
Q478	Other specified other open operations on ovary
Q491	Endoscopic extirpation of lesion of ovary NEC
T331	Open excision of lesion of peritoneum
T332	Open destruction of lesion of peritoneum
T338	Other specified open extirpation of lesion of peritoneum
T339	Unspecified open extirpation of lesion of peritoneum
T361	Omentectomy
T362	Excision of lesion of omentum
X141	Total exenteration of pelvis
X142	Anterior exenteration of pelvis
X143	Posterior exenteration of pelvis
X148	Other specified clearance of pelvis
X149	Unspecified clearance of pelvis

Appendix 8 Comorbid conditions and scoring applied for the derivation of a Charlson comorbidity score

Description	Charlson score	Notes
Acute myocardial infarction	1	
Congestive heart failure	1	
Peripheral vascular disease	1	
Cerebral vascular accident	1	
Dementia	1	
Pulmonary disease	1	
Connective tissue disorder	1	
Peptic ulcer	1	
Diabetes	1	Only highest score is counted
Diabetes complications	2	
Paraplegia	2	
Renal disease	2	
Cancer	2	Derived from cancer registry data rather than HES data.
Metastatic cancer	N/A	
Liver disease	1	Only highest score is counted
Severe liver disease	3	
HIV	6	

Appendix 9 Probability of receiving any treatment versus no treatment with and without adjustment for patient performance status

	Without performance status* (n=5,823)			With performance status* (n=5,823)		
Variables	**Estimate**	**SE**	**p-value**	**Estimate**	**SE**	**p-value**
Cohort average (intercept)	85.0	0.4	0.000	85.0	0.4	0.000
Cancer Alliance						
Cheshire and Merseyside	-0.5	1.6	0.729	-1.7	1.5	0.237
East Midlands	0.3	1.6	0.849	-0.4	1.6	0.780
East of England	-3.6	1.0	0.001	-3.4	1.0	0.000
Greater Manchester	-3.4	1.4	0.013	-2.8	1.3	0.034
Humber, Coast and Vale	-2.2	2.1	0.288	1.0	1.9	0.606
Kent and Medway	-5.5	2.2	0.013	-3.3	2.1	0.109
Lancashire and South Cumbria	2.9	1.5	0.054	1.1	1.4	0.427
North Central and North East London	3.0	4.1	0.474	2.3	4.0	0.561
North East and Cumbria	1.1	2.0	0.578	0.4	1.8	0.809
North West and South West London	4.1	1.3	0.002	4.5	1.2	0.000
Peninsula	5.9	1.9	0.002	4.3	1.7	0.014
Somerset, Wiltshire, Avon and Gloucestershire	4.4	1.5	0.004	4.3	1.4	0.002
South East London	2.0	1.5	0.181	2.8	1.6	0.079
South Yorkshire, Bassetlaw, North Derbyshire and Hardwick	-6.0	1.9	0.002	-7.4	1.9	0.000
Surrey and Sussex	0.9	1.6	0.567	0.5	1.5	0.733
Thames Valley	5.3	2.3	0.024	4.8	2.3	0.036
Wessex	1.9	1.6	0.248	-0.1	1.5	0.964
West Midlands	0.1	1.4	0.918	1.1	1.3	0.386
West Yorkshire and Harrogate	3.6	1.2	0.003	5.4	1.1	0.000
Tumour morphology						
Clear cell carcinoma	1.4	1.8	0.433	0.9	1.9	0.636
Endometrioid carcinoma	2.7	1.8	0.146	1.0	1.7	0.581
Miscellaneous and unspecified	-50.7	2.4	0.000	-39.7	2.3	0.000

Mucinous carcinoma	2.4	3.1	0.438	2.5	3.0	0.408
Other malignant epithelial	-9.2	1.2	0.000	-6.6	1.1	0.000
Serous carcinoma	4.9	0.3	0.000	3.8	0.3	0.000
Sex cord-stromal and germ cell	-2.6	3.7	0.483	-2.5	3.8	0.513
Tumour stage at diagnosis						
Stage 2-3	3.7	0.3	0.000	2.9	0.3	0.000
Stage 4	-4.3	0.6	0.000	-3.1	0.6	0.000
Stage not recorded	-9.8	1.7	0.000	-8.1	1.6	0.000
Age at diagnosis (years)						
0-29	16.2	4.0	0.000	13.0	4.3	0.002
30-39	13.6	1.7	0.000	9.6	1.6	0.000
40-49	11.3	0.9	0.000	8.3	0.9	0.000
50-59	7.5	0.7	0.000	5.2	0.7	0.000
60-69	6.6	0.6	0.000	5.1	0.5	0.000
70-79	-1.4	0.6	0.019	-0.3	0.6	0.656
>79	-20.4	1.3	0.000	-16.4	1.2	0.000
Charlson comorbidity index[§]						
Charlson 0	1.0	0.2	0.000	0.6	0.2	0.000
Charlson 1	-3.0	1.4	0.033	-1.9	1.3	0.154
Charlson 2	-2.6	2.2	0.227	0.2	2.0	0.907
Charlson >2	-16.3	3.3	0.000	-12.3	3.1	0.000
Not recorded	-26.9	11.3	0.017	-29.7	11.0	0.007
Area income deprivation[‡]						
Quintile 1 (least deprived)						
Quintile 2	0.8	0.7	0.289	0.2	0.7	0.725
Quintile 3	1.6	0.7	0.028	1.1	0.7	0.106
Quintile 4	0.1	0.7	0.849	0.4	0.7	0.596
Quintile 5 (most deprived)	-0.4	0.8	0.663	-0.4	0.8	0.652
	-3.2	1.0	0.001	-2.0	0.9	0.032

Performance status				
0		5.6	0.5	0.000
1		4.3	0.5	0.000
2		-3.9	1.1	0.001
3		-22.8	1.8	0.000
4		-48.9	3.0	0.000

* The cohort contains cases of ovarian, tubal and primary peritoneal cancer diagnosed between January 2016 & December 2018 inclusive. Stage 1, borderline and non-specific site tumours are excluded, along with cancers diagnosed via death certificate and those with missing performance status information.
Treatment data are compiled from the cancer registry, Hospital Episode Statistics (HES) admitted patient care dataset, and the Systemic Anti-Cancer Therapy (SACT) dataset. Data were captured during the primary course of treatment (the period up to nine months following diagnosis). Treatments dated outside of this window are not considered. In a small minority of cases, tumours were documented as receiving both systemic anti-cancer therapy and major surgical resection on the same day. These cases are coded to the neoadjuvant anti-cancer therapy treatment group.
Model 1 includes Cancer Alliance only; Model 2 as Model 1, plus adjustment for patient age, tumour morphology and tumour stage; Model 3 as Model 2, plus area income deprivation and Charlson comorbidity score.
§ Comorbid diagnoses were abstracted from the cancer registry & Hospital Episode Statistics (HES) admitted patient care dataset for the 'baseline' period between 23 & three months prior to diagnosis. A total of 15 categories of medical condition were considered & assigned values between one & six. Medical conditions include myocardial infarction, dementia & liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. Where a patient had no linkage to HES (as happens for private patients or patients with no inpatient admissions), no score is assigned.
‡ Area income deprivation is reported according to the income component of the English Index of Multiple Deprivation. Further information on the index can be found here: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019

Appendix 10 Glossary

Term	Acronym	Description
Borderline/non-Borderline		Borderline ovarian tumours are abnormal cells that form in the tissue covering the ovary. They are different to ovarian cancer because they do not grow into the supportive tissue of the ovary (the stroma). They tend to grow slowly and in a more controlled way than cancer cells. The main treatment for borderline tumours is surgery. Most women are cured and have no further problems. There is a small risk of the tumour coming back. Very rarely, the borderline tumour cells change into cancer cells.
Cancer Alliances	CA	The 19 Cancer Alliances in England bring together the key organisations in their regions to coordinate cancer care and to plan for and lead delivery of improved outcomes for patients locally.
Cancer registry	NCRAS	The National Cancer Registration and Analysis Service (NCRAS) collects data on all cases of cancer that occur in people diagnosed in England. The data is used to support public health, healthcare and research.
Carcinoma		Category of types of cancer that develop from epithelial cells.
Comorbidity		A disease or condition that someone has in addition to the health problem being studied or treated (i.e. cancer).
Fallopian tube		Fallopian tubes carry eggs from the ovaries to the uterus. Serous carcinomas of the fallopian tube are considered to be the same disease entity as serous cancers of the ovary and primary peritoneal carcinoma, which is why cancers at all 3 sites are collected in this report.
FIGO stage	FIGO	System for staging of gynaecological cancers, published by the International Federation of Gynaecology and Obstetrics (FIGO).
ICD codes	ICD	International Classification of Diseases is a medical classification and coding list for the identification of diseases, signs and symptoms,

		abnormal findings, complaints, social circumstances and external causes of injury or diseases, as maintained by the World Health Organization (WHO). ICD-10 classifies cancers by site and behaviour (malignancy) and ICD-O classifies cancers by site, morphology and behaviour.
Malignant		Malignant tumours are considered to be cancer. Malignant means characterised by the tendency to become progressively worse. Often characterised by anaplasia, invasiveness and /or metastases.
Morphology		Morphology is the type of a tumour, as diagnosed by a pathologist looking at the shape of the cells through a microscope. The morphological type of a tumour can be important in understanding how to treat that tumour and what expected outcomes might be. The morphology categories include the main subtypes of epithelial ovarian cancers (serous, endometrioid, clear cell, mucinous and other epithelial), catagories for cases where the pathology detail was unspecified or the site was unspecified in the data, and the separate category of sex code stromal and germ cell tumours.
Multidisciplinary team	MDT	MDTs bring together experts in specific areas of medicine and care, and usually meet every week to discuss the diagnosis, treatment and care of individual cancer patients.
Performance status		Performance status is an attempt to quantify cancer patients' general well-being and activities of daily life. This is captured as a WHO (World Health Organization) score between 0 and 5.
Peritoneum		The peritoneum is the serous membrane forming the lining of the abdominal cavity.
Primary peritoneal carcinomas	C48	Cancer of the epithelial cells in the peritoneum. Primary peritoneal carcinomas are considered to be the same disease entity as serous carcinomas of the ovarian or fallopian tube, which is why cancers at all 3 sites are collected in this report.
Stage		Stage describes the extent or severity of a person’s cancer. Diagnosis at an earlier stage

		leads to improved prognosis, treatments and outcomes in comparison with cancers diagnosed at a later stage.
Systemic anti-cancer therapy		A collective term to describe the growing number of drugs used to treat cancer
World Health Organization	WHO	The World Health Organization directs and coordinates international health within the United Nations system. The WHO classification systems for cancer sites are used in the cancer registry.

Appendix 11 Useful links

Ovarian Cancer Audit Feasibility Pilot homepage *Information about this project and links to outputs.*	http://ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/gynaecological_cancer/gynaecological_cancer_hub/ovarian_cancer_audit_feasibility_pilot
NCRAS gynae hub ovarian cancer resources *Reports, briefings and other resources on ovarian cancer from NCRAS.*	http://ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/gynaecological_cancer/gynaecological_cancer_hub/resources/ovarian_cancer
CancerData *NCRAS hub for incidence and mortality data by geographies, Routes to Diagnosis and treatment data for cancers including ovary.*	https://www.cancerdata.nhs.uk/incidence https://www.cancerdata.nhs.uk/mortality https://www.cancerdata.nhs.uk/routestodiagnosis https://www.cancerdata.nhs.uk/treatments
CancerStats I *For N3 (NHS) connections only, requires signup. Incidence and mortality with greater geographical granularity than CancerData.*	https://nww.cancerstats.nhs.uk/
CancerStats II *For N3 (NHS) connections only, requires signup.* *Select Audits > OCAFP for project outputs including data completeness report.*	https://cancerstats.ndrs.nhs.uk/

Data Resource Profile: National Cancer Registration Dataset in England *Information about the registry dataset used for this report.*	https://doi.org/10.1093/ije/dyz076
Get Data Out: Ovary, fallopian tube and primary peritoneal carcinomas *Routine data from NCRAS on small groups of ovarian cancer patients since 2013. Incidence, Routes to Diagnosis, treatment, survival.*	https://www.cancerdata.nhs.uk/getdataout/ovary https://www.cancerdata.nhs.uk/getdataout/data
Progress in cancer survival, mortality, and incidence in seven high-income countries 1995–2014 (ICBP SURVMARK-2): a population-based study, The Lancet Oncology, Arnold et al. 2019 *International comparison of cancer incidence, mortality and survival, including ovarian cancer.*	https://doi.org/10.1016/S1470-2045(19)30456-5
Stage breakdown by CCG 2017 *NCRAS stage data for sites including ovary, split by CCG.*	http://www.ncin.org.uk/view?rid=3864

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