NDRS
NATIONAL DISEASE REGISTRATION SERVICE

NDRS Ovarian Cancer Audit Feasibility Pilot

PROFILE AND TREATMENT REPORT

DIAGNOSES 2015-2019

May 2023

ovarian cancer action

BRITISH GYNAECOLOGICAL CANCER SOCIETY

Target Ovarian Cancer

About the NDRS

The National Disease Registration Service (NDRS) is part of NHS England (NHSE). Its purpose is to collect, collate and analyse data on patients with cancer, congenital anomalies, and rare diseases. It provides robust surveillance to monitor and detect changes in health and disease in the population. NDRS is a vital resource that helps researchers, healthcare professionals and policy makers make decisions about NHS services and the treatments people receive.

The NDRS includes:

- the National Cancer Registration and Analysis Service (NCRAS) and
- the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS)

Healthcare professionals, researchers and policy makers use data to better understand population health and disease. The data is provided by patients and collected by the NHS as part of their care and support. The NDRS uses the data to help:

- understand cancer, rare diseases, and congenital anomalies
- improve diagnosis
- plan NHS services
- improve treatment
- evaluate policy
- improve genetic counselling

NDRS
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Report index

In 2020, the Ovarian Cancer Audit Feasibility Pilot (OCAFP) produced two reports that indicated regional disparities across England in both ovarian cancer survival[1] and treatment delivery.[2] Together, these reports provided valuable learning for developing targeted improvements in clinical practice and improved outcomes for patients.

This latest report provides an update to these earlier statistics, reporting results for diagnoses up to the period immediately preceding the Covid-19 pandemic.

There is continued evidence of incidence remaining reasonably stable in England, and survival improving. However, variation in incidence, mortality rates and stage at diagnosis can be seen across sub-ICBs and Cancer Alliances. Additionally, marked geographic inequalities in access to treatment remain, even after accounting for regional differences in patient and tumour characteristics.

These refreshed findings provide a new opportunity for identifying recent examples of best practice that could be disseminated to areas where treatment rates and patient survival are poor comparative to national averages.

Ovarian Cancer Audit Feasibility Pilot Steering Group

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This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the NDRS, which is part of NHS England.

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Introduction

About the Ovarian Cancer Audit Feasibility Pilot

The Ovarian Cancer Audit Feasibility Pilot (OCAFP) has been a four-year collaboration between the gynaecological oncology clinical community, the charity sector and NHS England (NHSE). Between 2019 and 2023, a range of outputs on ovarian cancer have been reported. The primary objective of the OCAFP has been to explore the feasibility of undertaking meaningful analyses of routinely collected data for the purpose of improving treatment and outcomes for women diagnosed with ovarian cancer in England – the leading cause of gynaecological cancer death for women in the UK.

An additional objective of the collaboration has been to demonstrate the potential for ovarian cancer data analysis to reduce inequalities in health and care provision, supporting calls for a publicly funded national ovarian cancer audit. This ambition was achieved when the Healthcare Quality Improvement Partnership (HQIP) announced a national ovarian cancer audit in 2022.

The methods, successes, limitations, and associated intelligence from the OCAFP should be used to inform the development of the national ovarian cancer audit, which has the potential to extend the achievements of the OCAFP over the coming years. A project summary report was published by NHSE in 2023 and details the methodological successes, challenges and limitations identified during the OCAFP.

The OCAFP has been jointly funded by the British Gynaecological Cancer Society, Target Ovarian Cancer and Ovarian Cancer Action, and delivered by analysts within NHSE's NDRS.

About the Profile and Treatment Reports

The first publication from the OCAFP was the Disease Profile report[1] for ovary, fallopian tube and primary peritoneal carcinomas ('ovarian cancer') diagnosed in England. This described incidence, mortality and stage for 2015-2017 diagnoses, and survival for cases diagnosed 2013-2017. Amongst its many findings, the report showed marked geographic variation in cancer survival across England at a Cancer Alliance level.

One hypothesis for such disparity was the possibility of variation in the local clinical management of disease. To explore this, a follow-up report was produced to quantify the extent to which ovarian cancer treatment differed between Cancer Alliances in England, and the degree to which such differences might be explained by variations in tumour and patient characteristics.[2] Results from this Geographic Treatment Variation report analysing cases diagnosed between 2016 and 2018 supported the hypothesis of regional variations in the probability of accessing surgery and chemotherapy across England, even after accounting for differences in patient and tumour characteristics.

Given the importance of these findings, this latest report and final OCAFP output, updates key data from the Disease Profile and Geographic Treatment Variation publications. It begins with updated incidence, mortality, stage and survival results for ovarian cancers diagnosed between 2015 and 2019, before moving on to report regional variation in treatment. This latter set of results focuses on diagnoses made in 2019 only, highlighting more recent disparities in access to treatment. For comparison against the updated survival statistics, treatment variation results are also be reported for the period 2015-2019. These updated survival analyses found that one-year net survival for ovary, fallopian tube and primary peritoneal carcinomas (excluding borderline tumours) had increased from 57.6% for 2001 to 2005 diagnoses to 68.4% for 2015 to 2019 diagnoses. Similarly marked improvements were also found for five-year net survival.

The methods and limitations underlying all analyses are included at the end of the report.

Incidence

Incidence of ovary, fallopian tube and primary peritoneal carcinomas, 2015 to 2019

There were 6,959 ovary, fallopian tube or primary peritoneal carcinoma diagnoses of per year on average in England in 2015 to 2019 (34,796 over the five-year period), including tumours with borderline malignant potential. For simplicity, the term 'ovarian cancer' is utilised throughout the report to refer to this group of diseases. The ICD-10 and ICD-O-2 codes used to define the cohort are detailed in **Appendix 1**. The overall crude incidence rate for the period was 24.7 cases per 100,000 person-years.

Age standardisation was used to enable comparison of sub-Integrated Care Boards (sub-ICBs) with different age profiles. Age standardised incidence rates in the 106 sub-ICBs ranged from 20.8 to 32.1 cases per 100,000 person-years.

Incidence data by sub-ICB, Integrated Care Board (ICB), Cancer Alliance and for all of England are available in **Table 1** and **Table 2** of the accompanying Excel workbook.

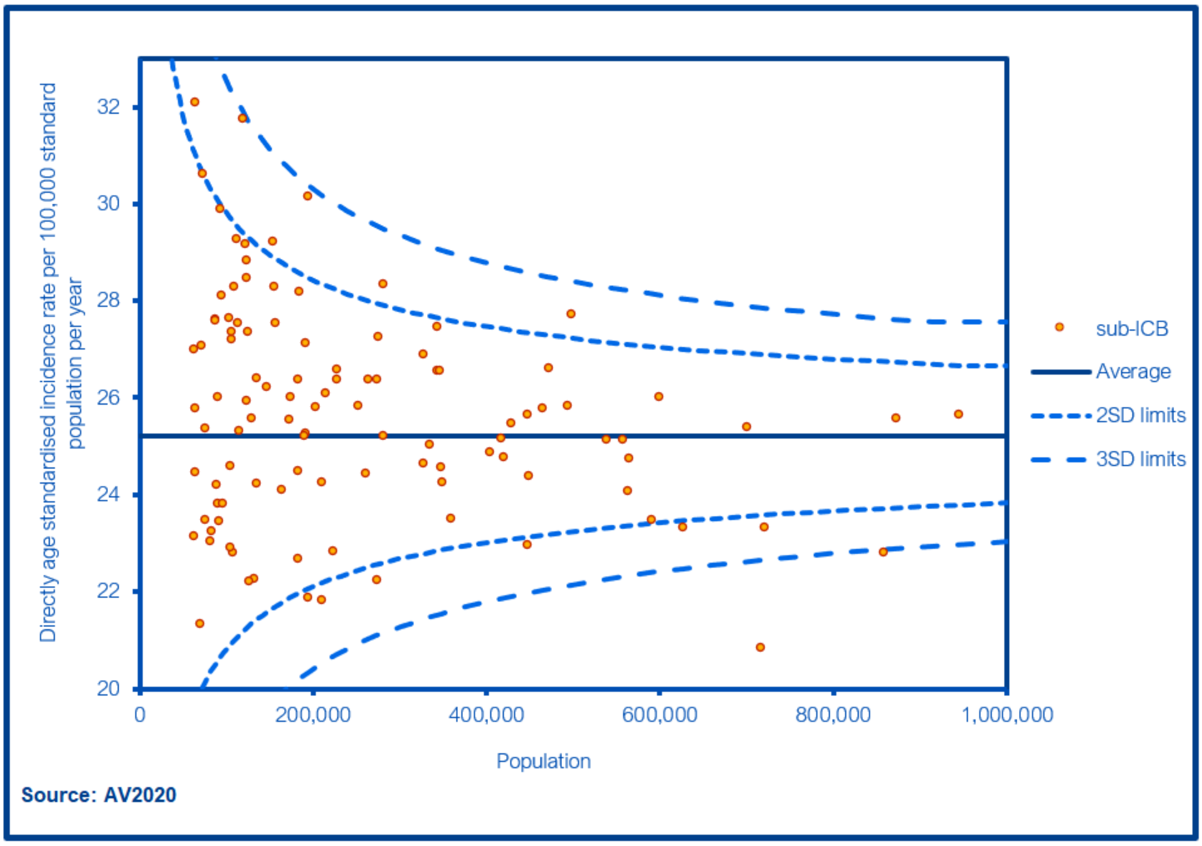


Figure 1. Ovary, fallopian tube and primary peritoneal carcinomas: directly age standardised incidence rates by sub-ICB, 2015 to 2019

Each point on the funnel plot represents a geographical area (in this case, sub-ICB). The population of each sub-ICB is presented on the horizontal axis and the (age standardised) incidence rate of ovarian cancer is shown on the vertical axis. Some random variation in rates between areas is expected, but the estimate of the incidence rate is likely to be more precise for a larger area than for a smaller one. This precision level is represented by the 'funnel' dashed lines. Points that lie outside of the dashed lines indicate that such variation may not be explained solely by randomness but may be due to real differences in incidence between areas.

Age standardised incidence rates in the 21 Cancer Alliances ranged from 20.8 to 26.8 cases per 100,000 person-years.

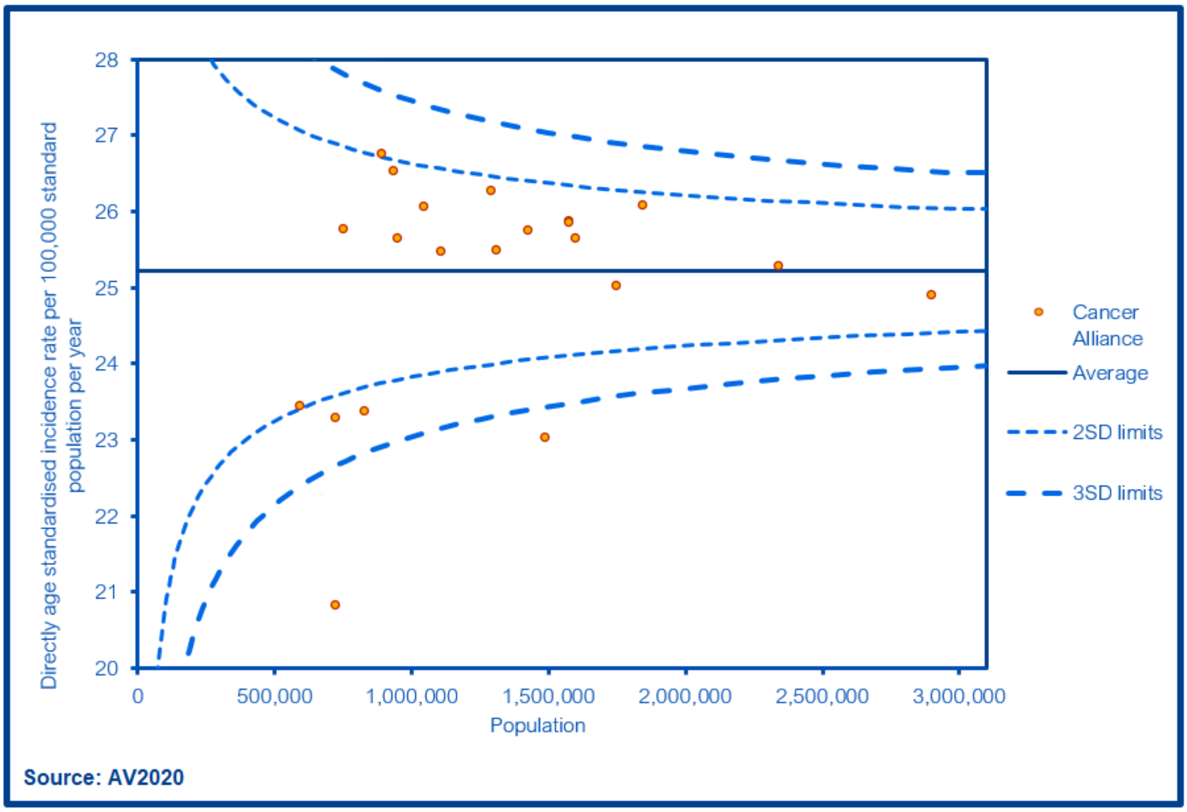


Figure 2. Ovary, fallopian tube and primary peritoneal carcinomas: directly age standardised incidence rates by Cancer Alliance, 2015 to 2019

These funnel plots show variation in the incidence of ovarian cancer among local geographies (identified by sub-ICBs) and regional geographies (identified by Cancer Alliances). It had previously been thought that regional variation in incidence may reflect differences in the methods and conventions used for distinguishing between ovary, fallopian tube and primary peritoneal carcinomas at diagnosis. However, the new methodology, which includes all of these diseases in the analysis, negates this as a confounding factor. Age standardisation removes the impact of differences in population age profile on incidence rates, but variation in ethnicity, and in particular clusters of ethnicities with higher genetic predisposition factors such as BRCA gene mutations, could impact on these results. Regional variation in other disease risk factors such as use of hormonal contraception may also partially explain local and regional variations in ovarian cancer incidence.

Incidence of ovary, fallopian tube and primary peritoneal carcinomas, 2001 to 2019

The crude incidence rate of ovarian cancer in England has fluctuated at around 25 cases per 100,000 women between 2001 and 2019. The crude rate in 2001 was 25.5 cases per 100,000 women and in 2019 it was observed to be 24.9 cases per 100,000 women. There was no significant trend in the crude incidence of ovarian cancer over the period 2001-2019.

The age-standardised rate, which accounts for the differences in age distribution of the population over time, shows a slight downward trend, with 27.8 cases per 100,000 women in 2001 to 25.1 cases per 100,000 women in 2019. A trend of convergence between the crude and age-standardised estimates is consistent with the age distribution of women in the general population more closely matching the 2013 European Standard Population by 2019. Whilst the overall risk of ovarian cancer had generally decreased over the period, the crude incidence rate remained fairly stable due to the ageing nature of the underlying population. Ovarian cancer risk is higher in older age groups, so with the increase in the percentage of the population that is older, more cases are occurring in some older age groups so this balances out the decreasing risk overall.

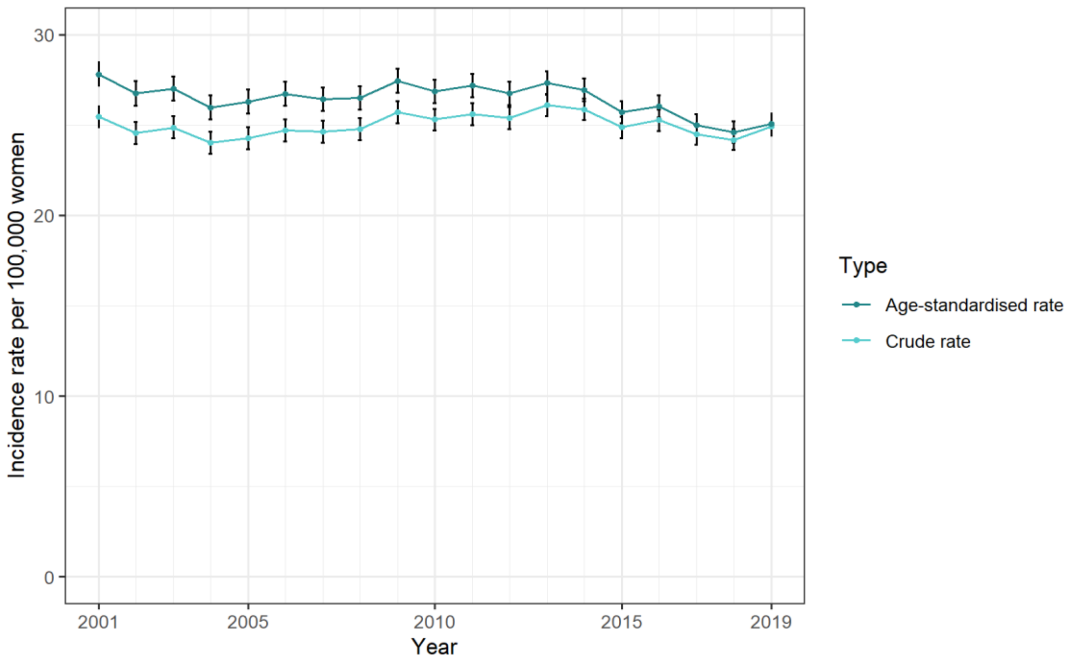


Figure 3. Crude and age-standardised rates of ovary, fallopian tube and primary peritoneal carcinomas in England, 2001 to 2019 (Source: CAS AV2020 and ONS2020)

Mortality

Mortality from ovarian and fallopian tube cancer, 2015 to 2019

There were 3,522 deaths from ovarian and fallopian tube cancer (C56-C57 in ICD-10) per year on average in 2015 to 2019 (17,610 over the five-year period). The overall crude mortality rate was 12.5 deaths per 100,000 person-years. See Appendix 1 for a full cohort definition, including an explainer for why only C56 and C57 could be reported for mortality.

Age standardisation was used to enable comparison of sub-ICBs with different age profiles. Age standardised mortality rates in the 106 sub-ICBs ranged from 8.7 to 18.3 per 100,000 person-years.

Mortality data by sub-ICB, ICB and Cancer Alliance and for all of England are available in Table 3 of the accompanying Excel workbook.

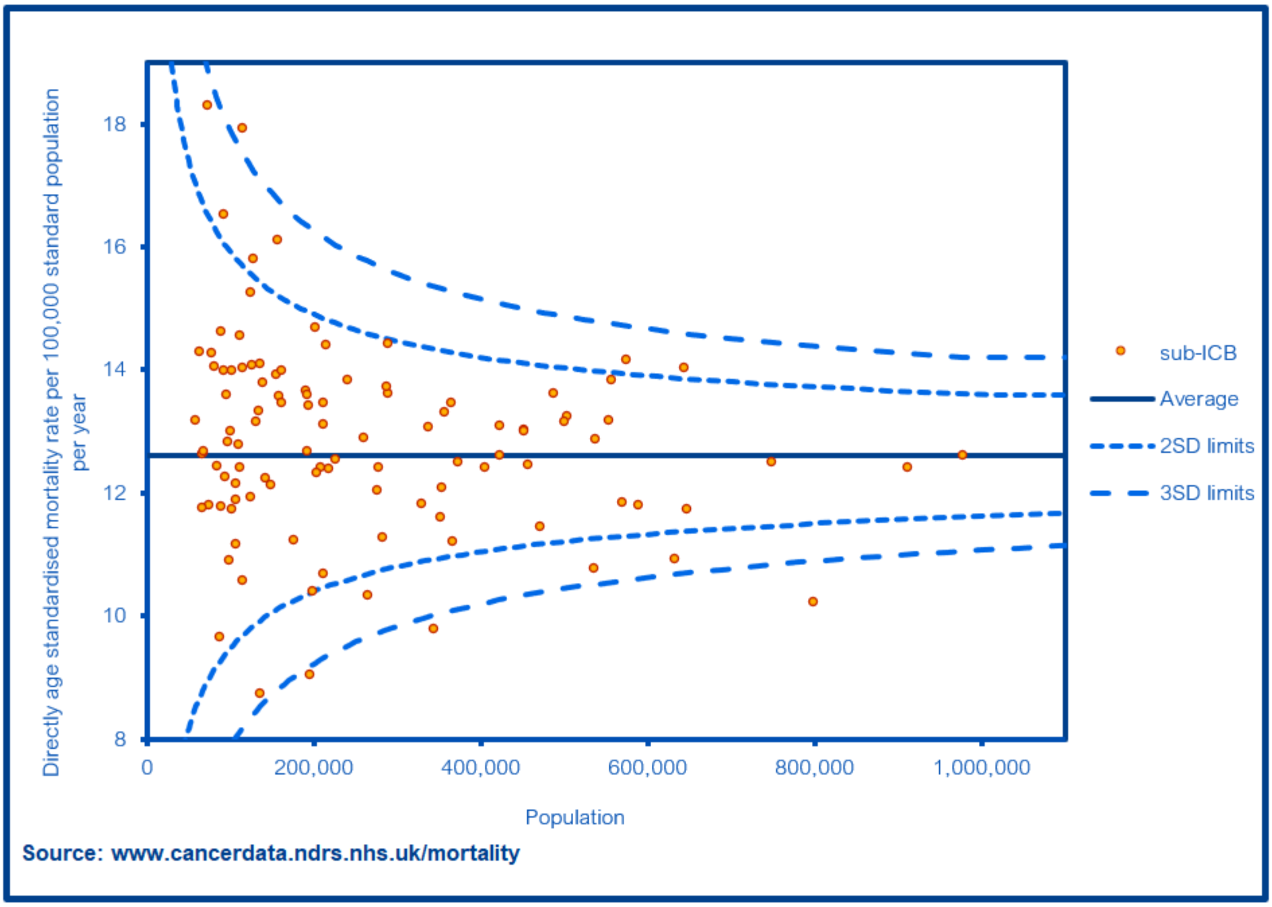


Figure 4. Ovarian and fallopian tube cancer: directly age standardised mortality rates by sub-ICB, 2015 to 2019

Mortality rates from cancer are driven by many factors including incidence rates (how many patients get cancer), stage (how advanced their disease is at the time of diagnosis), comorbidities (other health conditions) and treatments received. Mortality rates do not specify how long patients survive after diagnosis or treatment.

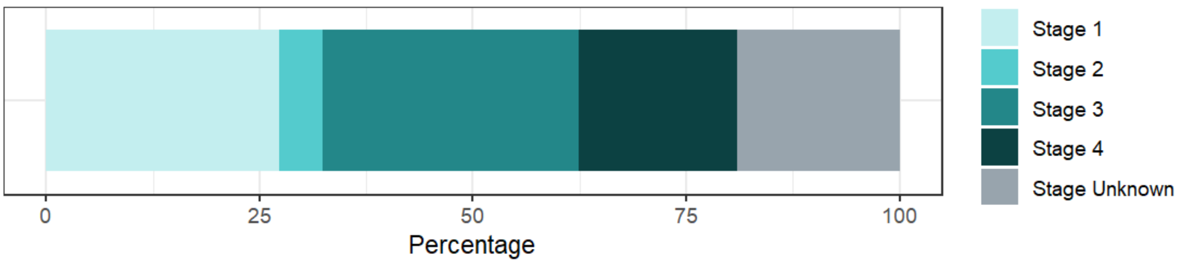
Stage

The stage of a cancer describes the extent and pattern of spread, with stage 1 disease confined to the organ of origin and stages 3 and 4 defining disease which has spread to distant organs. Disease staging is fundamental to the management of cancer cases, and all diagnosed cases of ovarian cancer should be staged by the multidisciplinary team (MDT) managing the case. When the patient is too unwell at the time of diagnosis (due to very advanced disease or comorbidities) to undergo full investigations and/or surgery, it may not be possible for the MDT to record stage data.

Stage presented in this report is based on the FIGO 2014 staging system. For more detailed information on staging and its derivation, see Appendix 2. Staging data are reported for all ovary, fallopian tube and primary peritoneal carcinomas, including borderline tumours. See Appendix 1 for a full cohort definition.

Stage data by sub-ICB, ICB and Cancer Alliance and for all of England are available in Table 4 of the accompanying Excel workbook.

Stage at diagnosis of ovary, fallopian tube and primary peritoneal carcinomas in England, 2015 to 2019



	Stage 1	Stage 2	Stage 3	Stage 4	Stage Unknown
England	27.2%	5.1%	30.0%	18.5%	19.1%

Figure 5. FIGO stage at diagnosis of ovary, fallopian tube and primary peritoneal carcinomas in England, 2015 to 2019 (Source: CAS AV2020)

Variation in stage at diagnosis of ovary, fallopian tube and primary peritoneal carcinomas by sub-ICB, 2015 to 2019

The proportion of tumours diagnosed at Stage 1 ranged from 16.1% to 38.4% the 106 sub-ICBs.

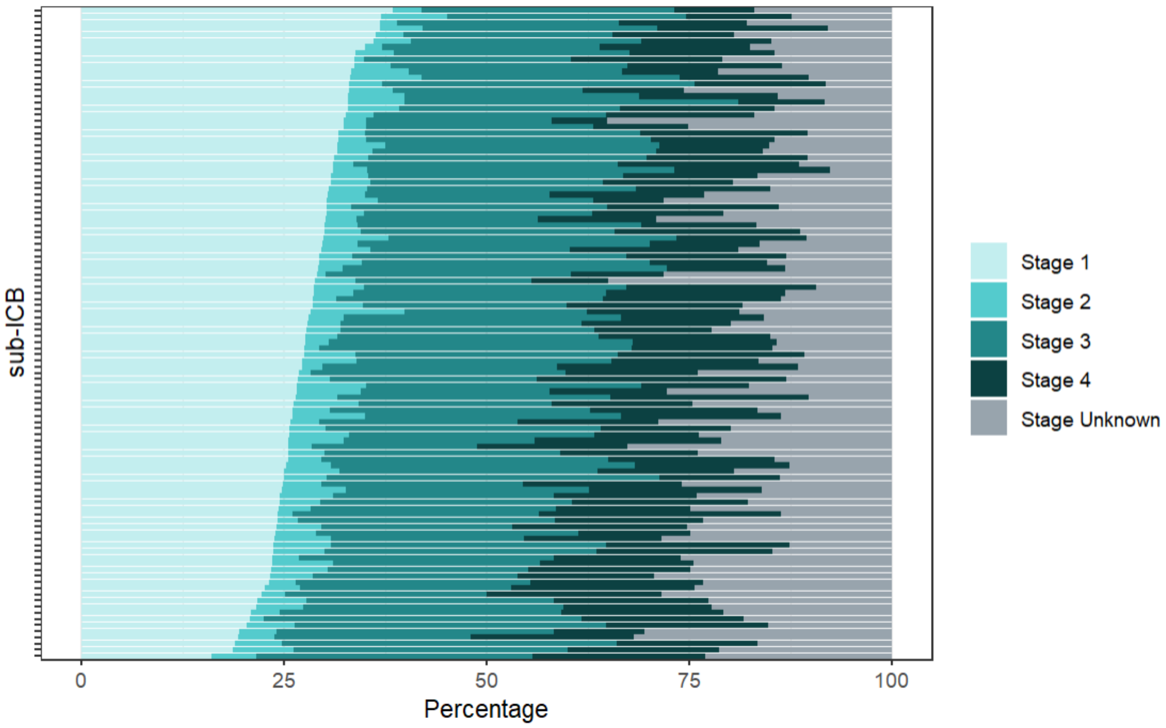


Figure 6. Stage at diagnosis of ovary, fallopian tube and primary peritoneal carcinomas by sub-ICB, 2015 to 2019 (Source: CAS AV2020)

There are substantial differences in the stage profile across different geographies. Regional variation in stage data should be interpreted with care. Differences may be driven by how the data has been recorded or by real variation in the profile of cases diagnosed in different regions. Potential explanations for any real variation in stage profiles include differences in diagnostic pathways between regions, varying patterns of the time taken for patients to seek to consult their GP after first experiencing symptoms, inequality in ease of access in primary care to consult a GP for assessment of symptoms, variations in referral practices amongst GPs, and regional differences in primary care access to investigations such as ultrasound.

Variation in proportion of ovary, fallopian tube and primary peritoneal carcinomas with stage recorded by sub-ICB, 2015 to 2019

The proportion of tumours registered with stage recorded ranged from 92.4% to 64.9% amongst the sub-ICBs.

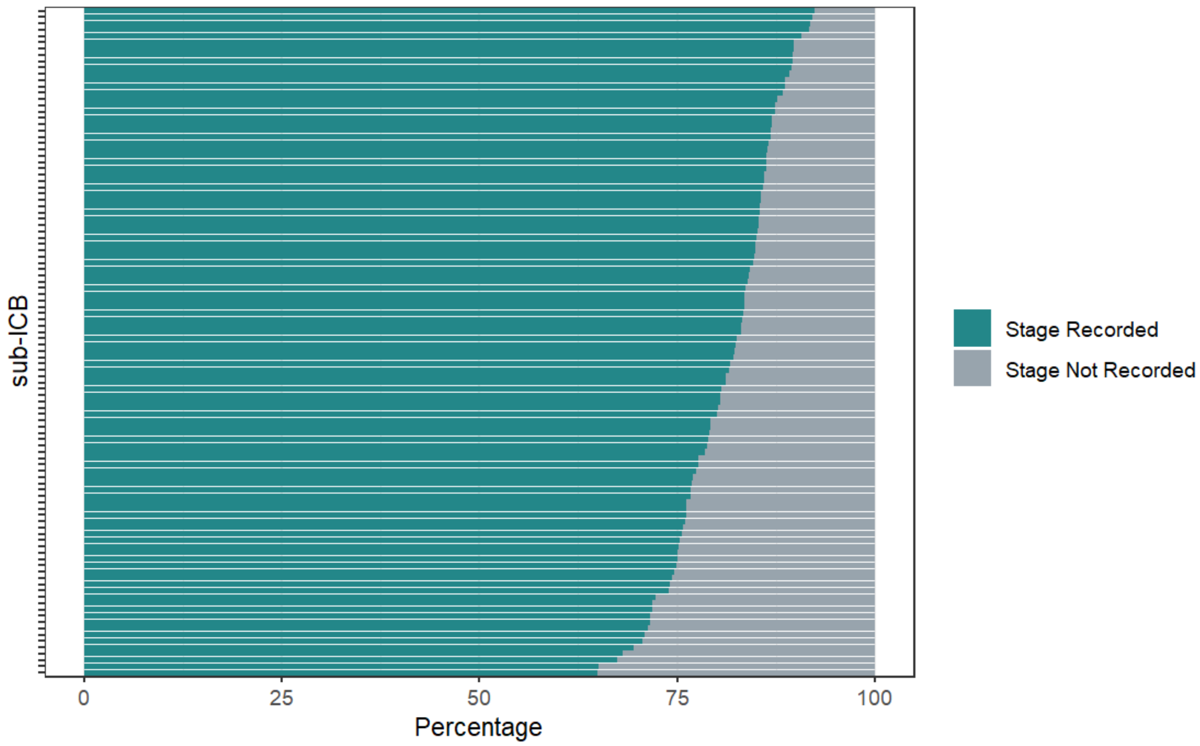


Figure 7. Ovary, fallopian tube and primary peritoneal carcinomas with stage recorded by sub-ICB, 2015 to 2019 (Source: CAS AV2020)

A total of 19.1% of cases considered in this report do not have stage recorded; this varies geographically with up to 35.1% of cases in some sub-ICBs having unknown stage.

The Ovarian Cancer Audit Feasibility Pilot reports the completeness of stage data in the datasets uploaded to the cancer registry by MDTs on a routine basis, with the aim of improving the completeness of this data where this is clinically appropriate. This information is available at provider level to NHS staff via the CancerStats website.

Variation in proportion of ovary, fallopian tube and primary peritoneal carcinomas diagnosed at early stage vs late stage amongst tumours with stage recorded by sub-ICB, 2015 to 2019.

The proportion of tumours diagnosed at early stage (stages 1 and 2) in England was 32.4% and ranged from 27.6% to 54.2% amongst the sub-ICBs.

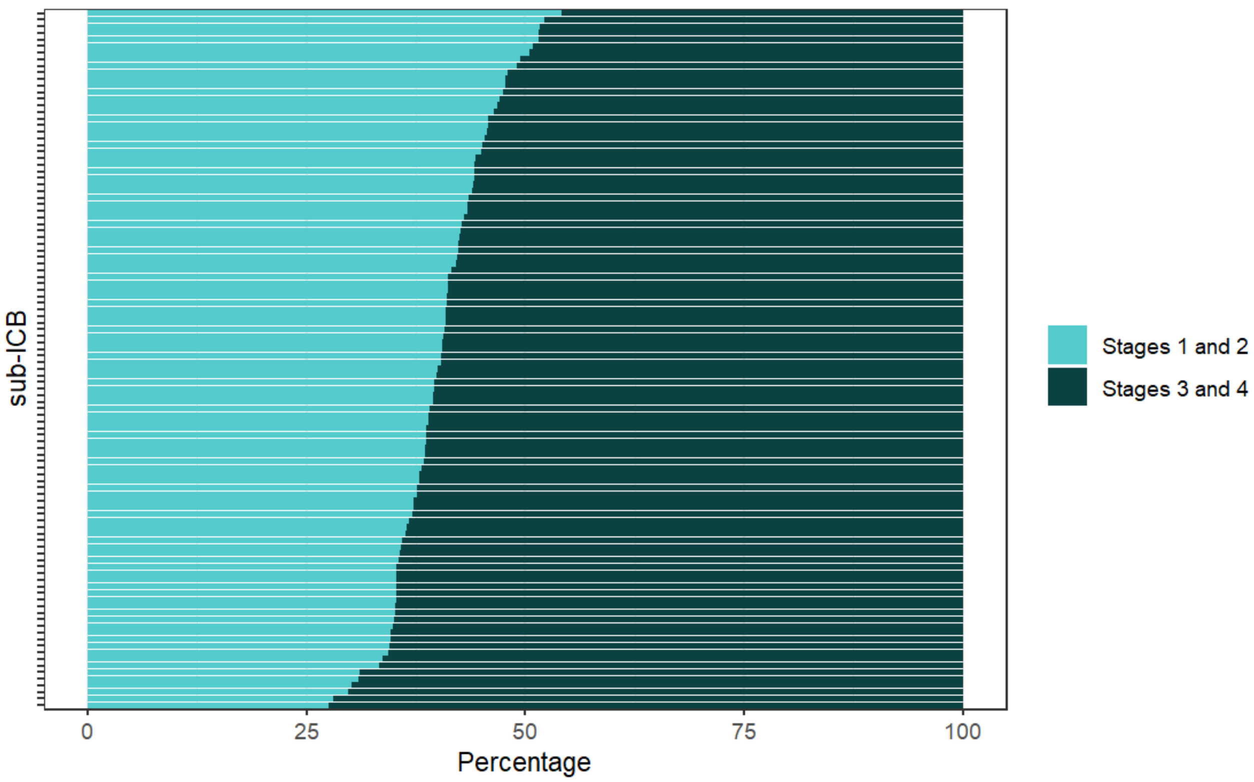


Figure 8. Ovary, fallopian tube and primary peritoneal carcinomas diagnosed at early or late stage by sub-ICB, 2015 to 2019 (Source: CAS AV2020)

There are substantial differences in the stage profile across different geographies. Potential explanations for this variation include differences in stage completeness, as well as referral and diagnostic pathways.

Survival

Net survival rates for 2015 to 2019 diagnoses of ovary, fallopian tube and primary peritoneal carcinomas excluding borderline tumours

The following are net survival rates for 2015 to 2019 diagnoses in England of ovary, fallopian tube and primary peritoneal carcinomas (C56-C57, C48 excluding sarcomas), excluding all borderline tumours and all tumours coded to D39.1 in ICD-10. See **Appendix 1** for a full cohort definition. All rates are net rates, age standardised with International Cancer Survival Standard (ICSS) weights. Net survival rates compare the survival of cancer patients with that of the general population. See **Appendix 4** for more information on the survival methodology applied.

Survival data by ICB, Cancer Alliance, NHS Region and for all of England are available in **Table 5** and **Table 6** of the accompanying Excel workbook.

Net survival rates of patients with ovary, fallopian tube and primary peritoneal carcinomas excluding borderlines at one and five years, 2015 to 2019 diagnoses

For ovary, fallopian tube and primary peritoneal carcinomas, excluding borderlines in all of England, the one-year net survival rate was 68.4%, and the five-year net survival rate was 35.1%.

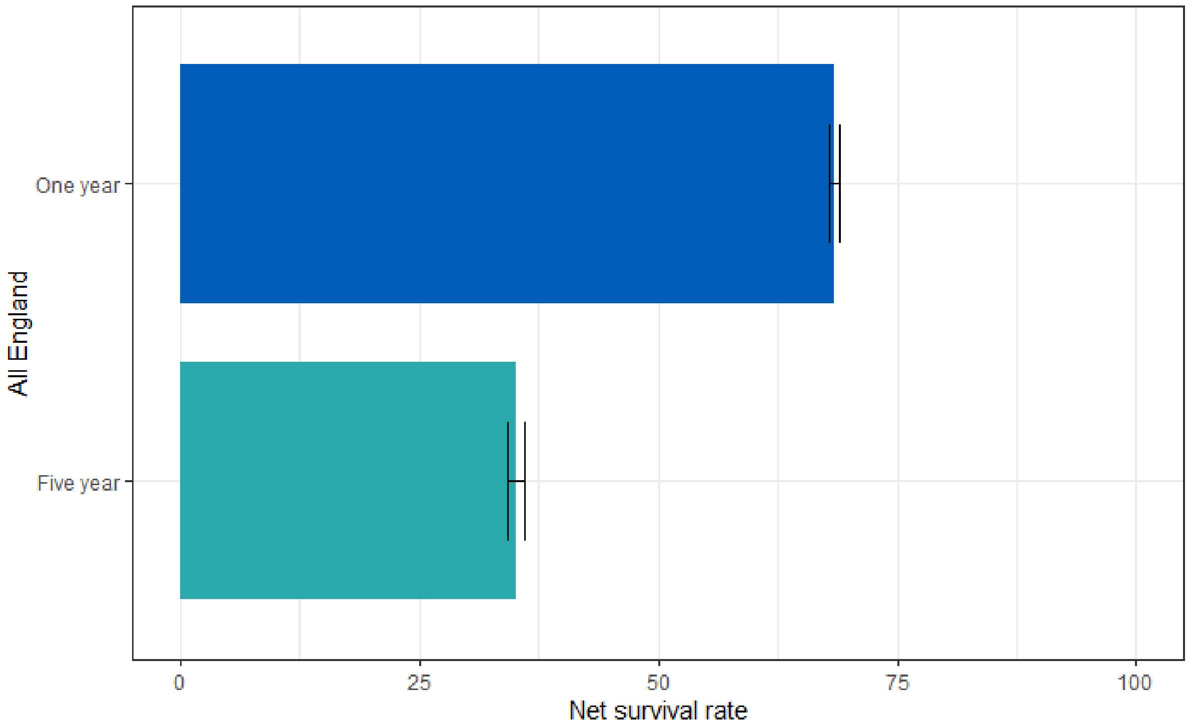


Figure 9. Net survival rates of patients with ovary, fallopian tube and primary peritoneal carcinomas excluding borderlines at one and five years, England, 2015 to 2019 diagnoses (Source: CAS AV2020)

Net survival rates of patients with ovary, fallopian tube and primary peritoneal carcinomas excluding borderlines at one and five years by Cancer Alliance, 2015 to 2019 diagnoses

One-year net survival for the 21 Cancer Alliances varied between 60.9% and 75.8%, five-year net survival varied between 27.8% and 47.5%.

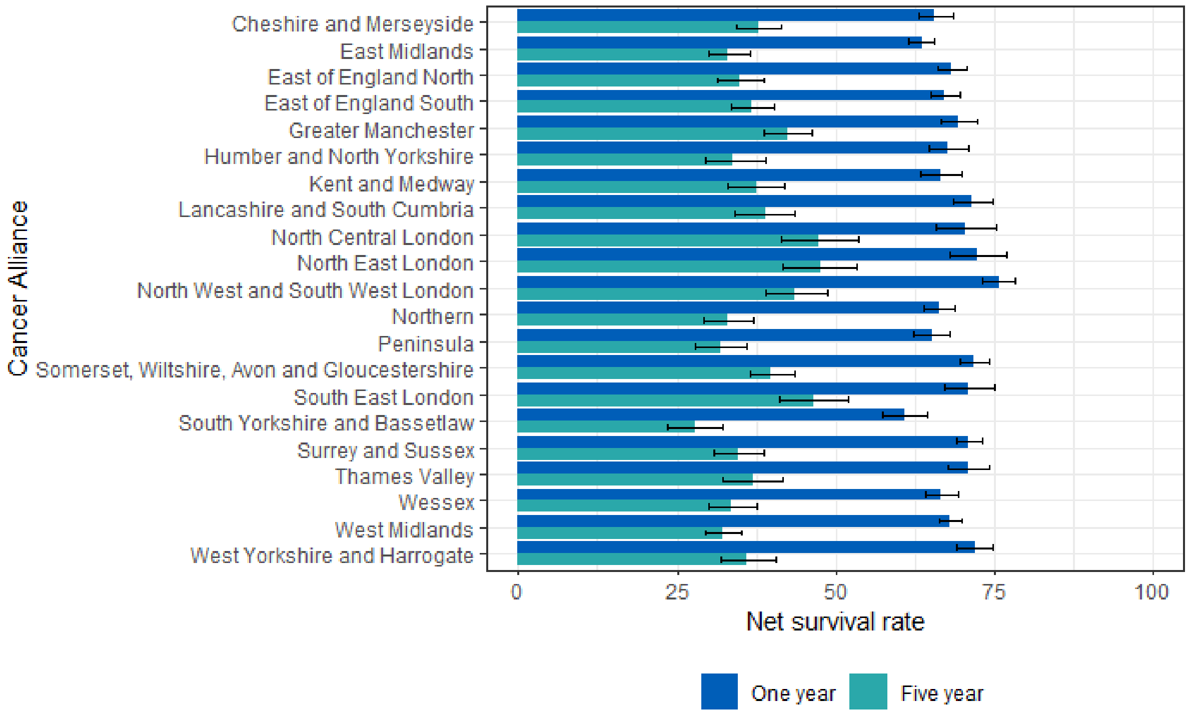


Figure 10. Net survival rates of patients with ovary, fallopian tube and primary peritoneal carcinomas excluding borderlines at one and five years by Cancer Alliance, 2015 to 2019 diagnoses (Source: CAS AV2020)

Variation in survival between regions may suggest possible variation in the quality of treatment (surgery and chemotherapy) between different gynaecological cancer centres. However, survival is also dependent on many other factors, including the profile of the population being treated and access to care. For example, there are differences in age, general health (including comorbidities), ethnicity and socioeconomic profiles of different regional populations across England, which could all impact on survival following a diagnosis of ovarian cancer. Additionally, there may be variation in the provision of primary care which would impact on referral into secondary care for diagnosis and treatment.

One-year survival is often considered to be an indicator of late presentation of malignancy, with poor one-year survival associated with diagnosis at late stage. Five-year survival is more likely to reflect the quality of treatment administered by the gynaecological cancer MDTs, in addition to the other associated factors mentioned above.

One of the principal aims of the Ovarian Cancer Audit Feasibility Pilot is to explore these complex factors in order to understand variations in treatment approaches between Cancer Alliances. We go on to explore whether the survival variation seen in these charts can be fully explained by population factors, or whether there are examples of best practice in ovarian cancer management in some areas of the country which could be extended to other regions in order to improve outcomes for patients.

Net survival rates of patients with ovary, fallopian tube and primary peritoneal carcinomas including and excluding borderlines at one and five years, 2001 to 2019 diagnoses

One-year net survival for ovary, fallopian tube and primary peritoneal carcinomas excluding borderline tumours has increased from 57.6% for 2001 to 2005 diagnoses to 68.4% for 2015 to 2019 diagnoses. Five-year net survival estimates have also improved, from 25.9% for patients diagnosed in 2001 to 2005 up to 35.1% for patients diagnosed in 2015 to 2019.

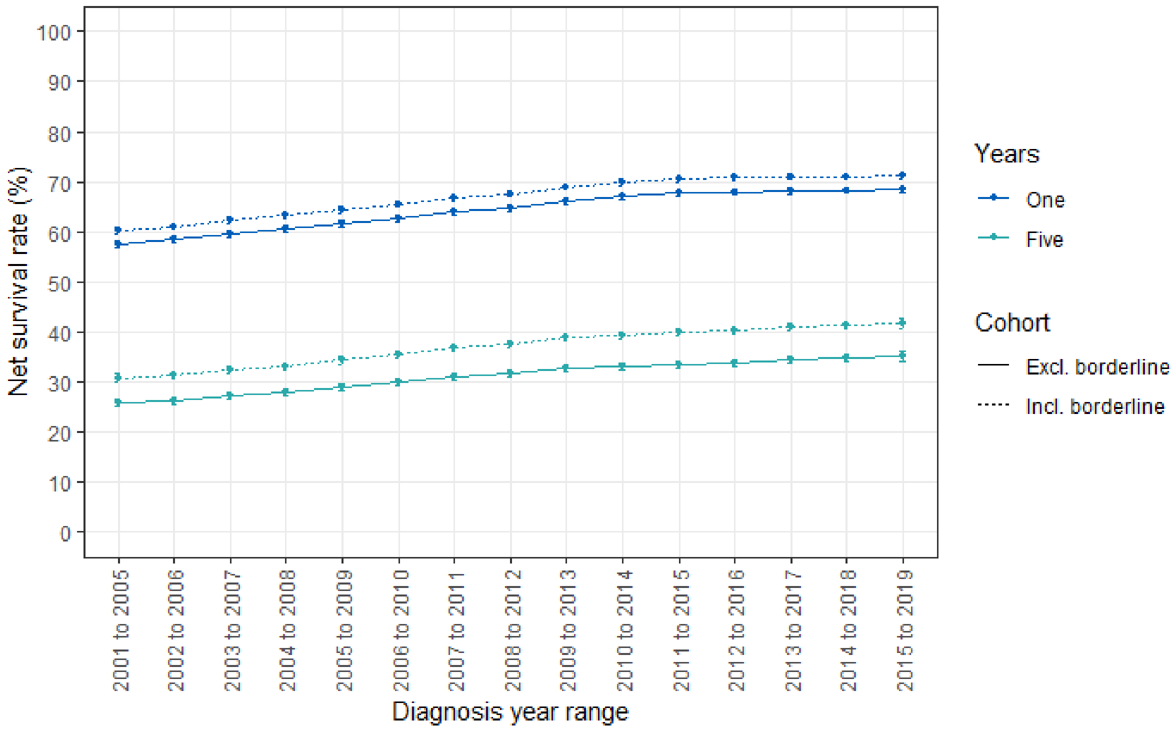


Figure 11. Net survival rates of patients with ovary, fallopian tube and primary peritoneal carcinomas including and excluding borderlines at one and five years, 2001 to 2019 diagnoses (Source: CAS AV2020)

The steady improvement in both one and five-year survival rates likely represents improvements in various aspects of care in England since the turn of the century. Between 2000 and 2005 specialist gynaecological oncology centres with specialist MDTs were established throughout the country, providing access to centralised specialist surgery for all women regardless of where they live.

The major barrier to one-year survival remains access to timely diagnosis. Cancer registration data analyses such as the OCAFP publications and the Get Data Out programme indicate that patients diagnosed at stage 4 have lower survival rates and lower treatment rates than those diagnosed with earlier stage disease. This suggests that a proportion of women may be presenting too unwell from advanced disease to enable the specialist teams to administer effective chemotherapy or surgery. The improvement in one-year survival suggests that we may be starting to impact on this issue, likely due to increased awareness of symptoms amongst women and primary care practitioners, and improved diagnostic and early treatment pathways in secondary care.

The improvement in five-year survival likely reflects not only improving access to treatment, but also increased treatment effectiveness. There are likely to have been real improvements in the quality of surgery available to women following the publication of the NHS Cancer Plan in 2000, with the establishment of specialist gynaecological cancer centres throughout England. Ovarian cancer surgery is now performed throughout the country by subspecialist accredited gynaecological oncology surgeons with specialist cancer surgery training. Surgical radicality for ovarian malignancies has generally increased during the past two decades, and there have been several improvements in chemotherapy treatments for newly diagnosed and recurrent disease. Over recent years women have had access to new maintenance treatments which help to prevent disease recurrence, and the impact of these treatments will be increasingly seen in five-year survival data during the coming years. The precise contributions of each of the factors described above are unknown, but they have all likely had an impact in the improvement of five-year survival, and further improvements in diagnostic pathways, surgical and medical treatments will hopefully continue the upward trend in one- and five-year survival rates in the future.

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

Describing the cohort

The following analyses are based on ovary, fallopian tube and primary peritoneal carcinomas (hereafter 'ovarian cancers') diagnosed in England in 2019. Borderline cases were not included as such tumours are routinely managed surgically and there was likely to be minimal regional variation in management. Of 7,039 ovarian cancers diagnosed in 2019, 5,994 (85.2%) were non-borderline cases. From these, tumours diagnosed via death certificate were also excluded, as clinicians had no opportunity to provide treatment. This left a cohort of 5,813 (82.6%) ovarian cancers.

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 5,813 selected ovarian cancers diagnosed during the year 2019. A complete table of patient demographics and tumour characteristics is available in Table 7 of the accompanying Excel workbook and summarised below.

Treatment variation by stage

Following a cancer diagnosis, multidisciplinary teams make an assessment as to the best course of treatment, based on factors including tumour stage and patient choice.

Typically, for ovarian cancers, a treatment pathway which includes surgery offers the best long-term prognosis. Surgery alone may be sufficient for women with stage 1 disease where the cancer has not spread, but most women will receive a combination of surgery and chemotherapy. For women with advanced disease, chemotherapy may be used ahead of surgery (neoadjuvant chemotherapy) to help reduce the extent of the tumour and improve the health of the patient 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. However, there are likely to be some women with advanced stage disease who would have a best long-term outcome from undergoing surgery prior to chemotherapy, and 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 5,813 ovarian tumours diagnosed in 2019, treatment delivery varied by disease stage (p=<0.001). As shown in **Figure 12**, primary surgery without chemotherapy was the most delivered treatment type for stage 1 tumours (56.9%, n=598), while stage 2-3 tumours and stage 4 tumours received primary surgery but no chemotherapy in just 8.5% (n=179) and 2.7% (n=34) of cases respectively. In contrast, chemotherapy without surgery was the treatment method most commonly delivered for stage 4 disease (33.7%, n=430).

27.6% (n=352) of stage 4 tumours received neither surgery nor chemotherapy, compared to just 3.3% (n=35) of stage 1 ovarian cancers. The proportion to receive neither treatment was highest for cancers with no valid staging information (48.2%, n=670), suggesting that the unstaged sub-group likely represents tumours that were diagnosed at a point where either the disease was too advanced and / or the patient too unwell for treatment. Overall, the proportion of patients who received no treatment was 22.2% (n=1,288).

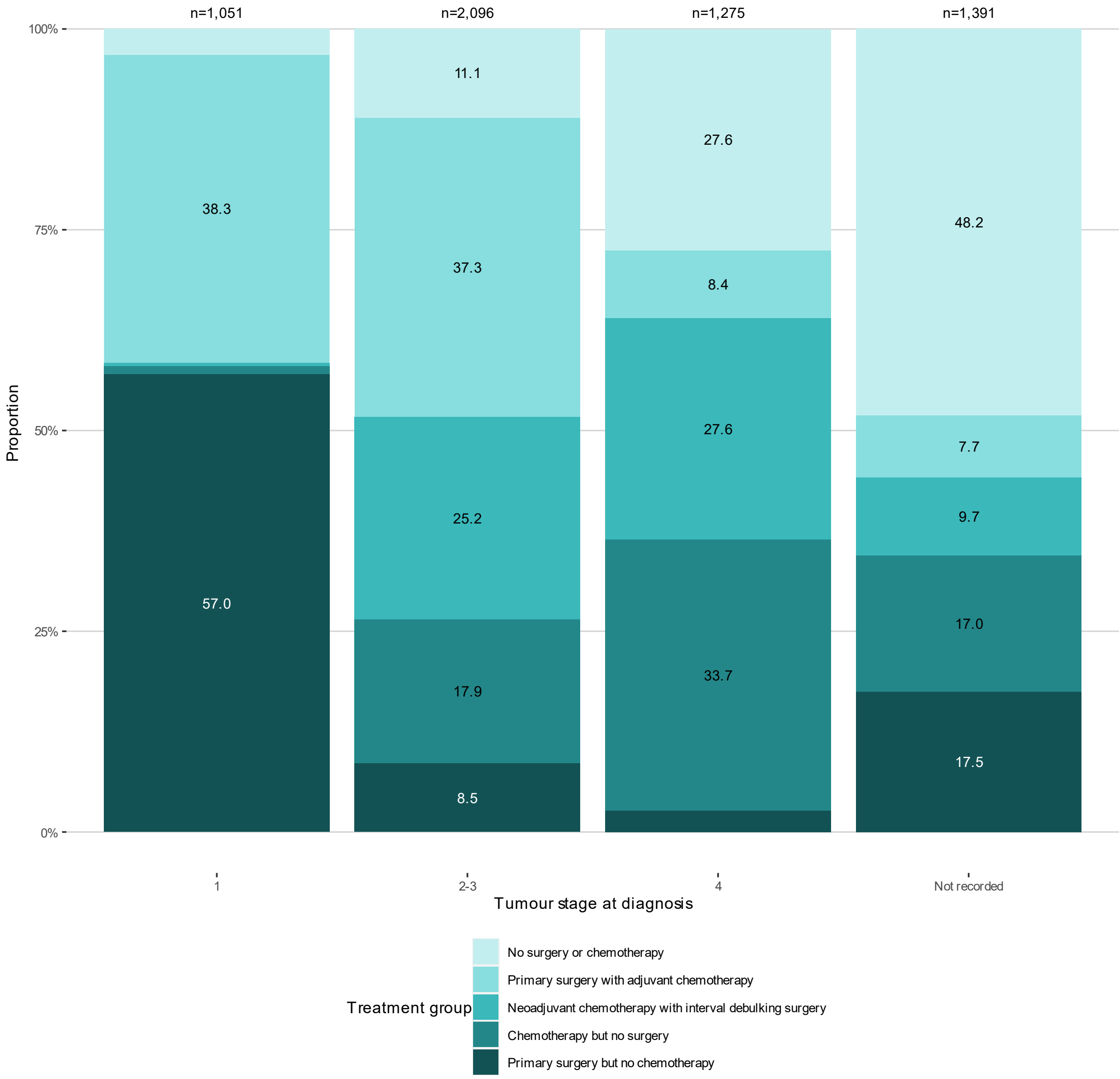


Figure 12 Treatment by stage at diagnosis, 2019

Treatment variation by age

Treatment also differed between age groups (p=<0.001). Notably, tumours in women aged >79 years at diagnosis were the least likely to receive any treatment, with 58.0% (n=618) receiving neither chemotherapy nor surgery (**Figure 13**). The use of primary surgery without chemotherapy was more common for cancers in younger women, at 56.5% (n=91) of tumours in patients aged <30 years at diagnosis compared to 9.6% (n=102) of tumours in patients aged >79 years at diagnosis. Conversely, the use of chemotherapy without surgery increased with age, at 21.9% (n=233) of tumours in patients aged >79 years at diagnosis compared to 6.2% (n=10) 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 comorbidities, 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. As **Figure 14** shows, almost three quarters of such cancers were treated with surgery alone.

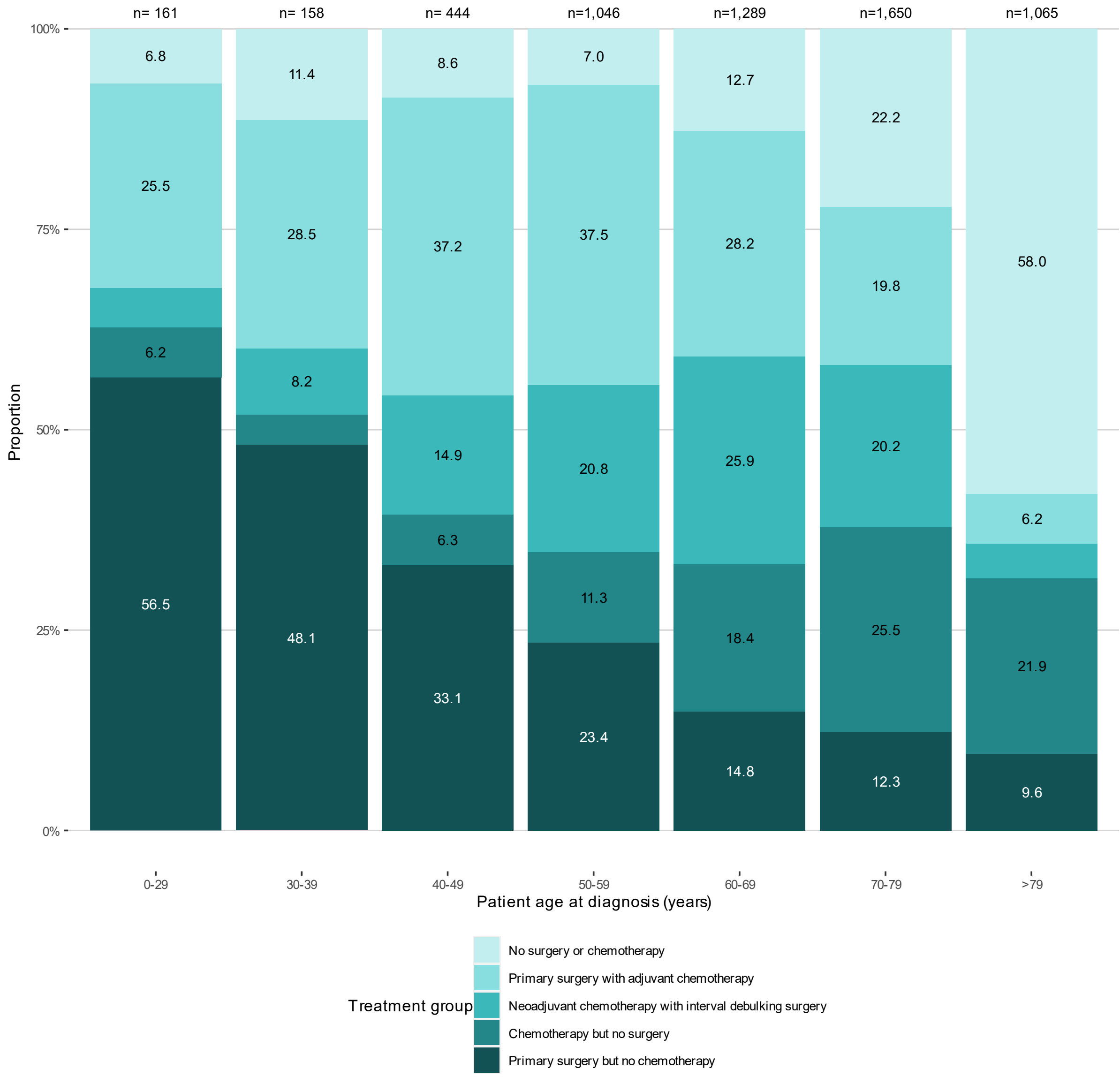


Figure 13 Treatment by age group at diagnosis, 2019

Treatment variation by morphology

Figure 14 indicates 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 (66.6%, n=227) was most commonly treated with primary surgery but no chemotherapy, while primary surgery with adjuvant chemotherapy was the treatment most often delivered to clear cell (63.6%, n=150) and endometrioid (49.1%, n=165) carcinomas. Serous carcinomas, accounting for over half of all tumours under consideration (n=3,210), were most commonly treated with neoadjuvant chemotherapy followed by surgery (28.8%, n=926), while 13.5% (n=434) did not receive any surgery or chemotherapy. Miscellaneous or unspecified tumours (77.6%, n=387) and tumours of non-specific site (70.6%, n=84) 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.

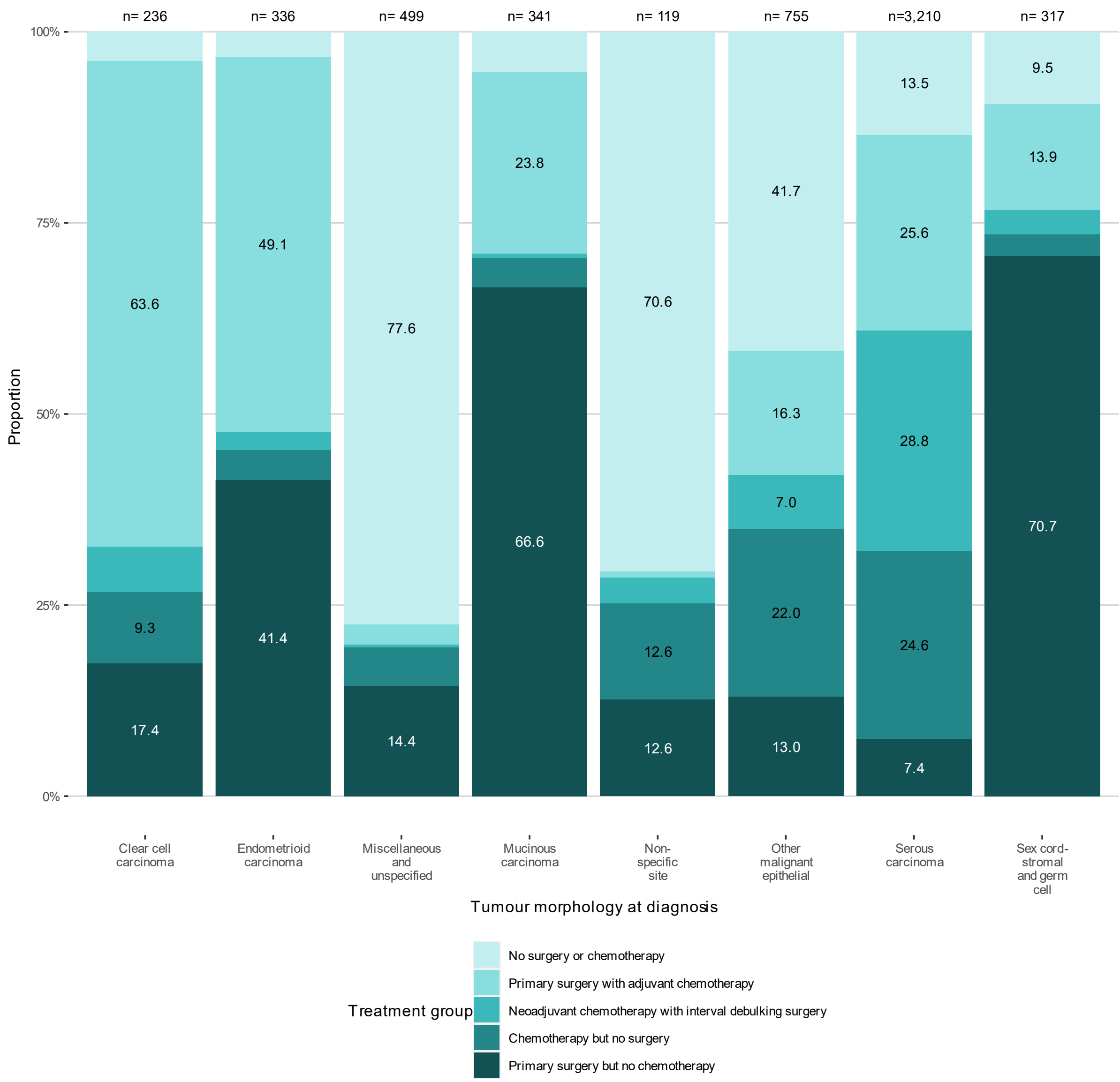


Figure 14 Treatment by tumour morphology at diagnosis, 2019

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 was assigned to each tumour by identifying the patient within whom the cancer occurred and looking for 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 index or otherwise only documented within an outpatient or primary care setting are not identified.

Of the 5,813 tumours in the cohort, 83.4% (n=4,846) were recorded as having been diagnosed in patients with no comorbidity according to the Charlson comorbidity index (a score of zero). This low rate of comorbidities for ovarian cancer patients does not reflect the clinical experience of the multidisciplinary teams who care for these women, confirming the lack of sensitivity of the methodology for capturing comorbidity from inpatient hospital episode statistics (HES).

Figure 15 shows variation in treatment by Charlson comorbidity score (p=<0.001). The five different treatment combinations were approximately evenly distributed among tumours in patients with a comorbidity score of zero. Conversely, the proportions that did not receive any surgery or chemotherapy were greater the higher the burden of comorbidity, rising from 18.5% (n=897) of those with a score of zero, to 54.3% (n=120) of those with a score >2.

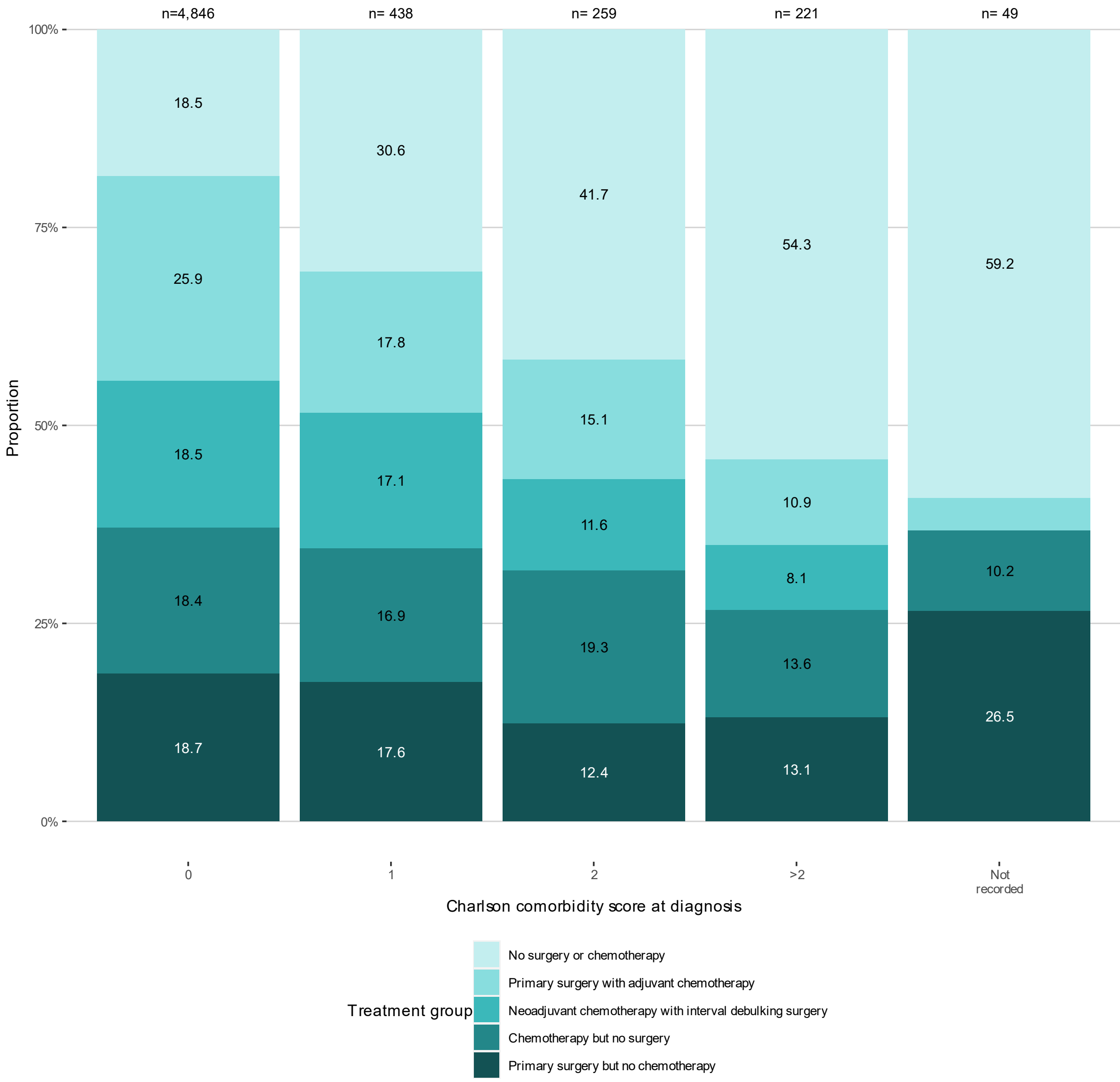


Figure 15 Treatment by Charlson comorbidity score at diagnosis, 2019

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

The findings presented between Figure 11 and Figure 15, and presented in full in Table 7, 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, the following section investigates the independent relationship between geography and ovarian cancer treatment by controlling for differences in patient demographics and tumour characteristics between Cancer Alliances in England.

Treatment variation by Cancer Alliance

Introduction

This section describes an analysis of variation in treatment between the 21 Cancer Alliances defined for England in 2022 (see Appendix 3).

Consistent with the previous Geographic Treatment Variation report, stage 1 tumours were excluded from these analyses as the management of early-stage tumours is consistent throughout the United Kingdom: 95.2% (n=1,001) of stage 1 tumours were treated with either primary surgery only or surgery with adjuvant chemotherapy, with minimal variation in treatment pathways expected between specialist gynaecological cancer centres or Cancer Alliances (Figure 12). This exclusion left a cohort for analysis of 4,762 tumours. Patient demographics and tumour characteristics for this analytical sample are provided in Table 8 of the accompanying Excel workbook.

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 sampled 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 observed across a range of patient demographics and tumour characteristics (Table 8), three different models were developed, each with an increasing level of adjustment for these factors:

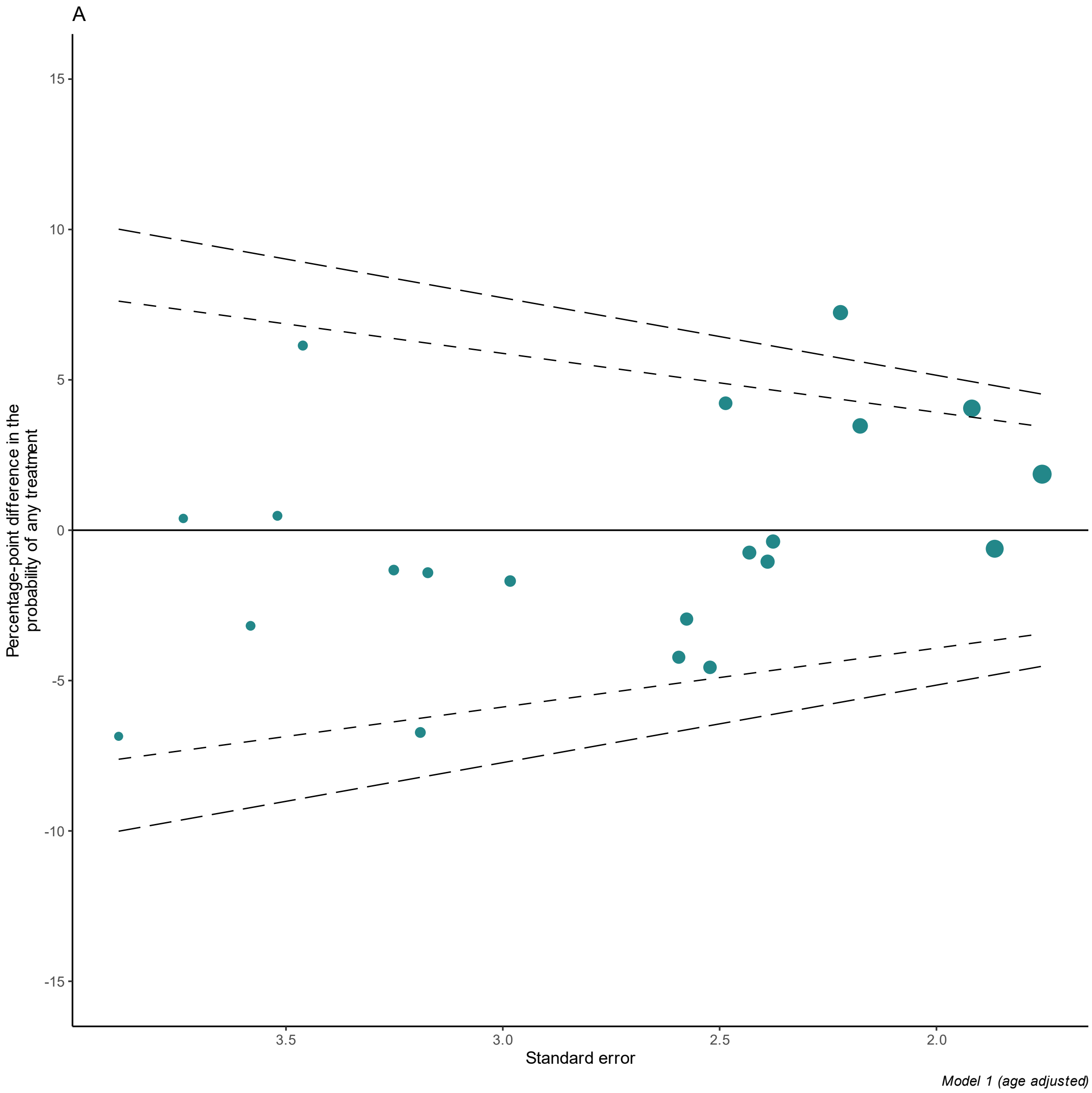
- Model 1: adjusts treatment probabilities within each Cancer Alliance for differences between regions in the distribution of the patient age at diagnosis.
- Model 2: adds adjustment for differences in tumour morphology and tumour stage between Cancer Alliances.
- Model 3: further adjusts for area deprivation and Charlson comorbidity score.

While funnel plots are only shown for the age adjusted (Model 1) and maximally adjusted (Model 3) models, findings from all three models are presented in a single table to allow comparisons according to differing levels of covariate adjustment. Note that these three models adjusted for confounding factors in a different order from that applied within the preceding report. For instance, Model 1 was formerly unadjusted rather than age-adjusted.

Treatment variation by Cancer Alliance: any treatment versus no treatment

This first analysis looks at differences between Cancer Alliances in the proportions of 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 having received any treatment during the first nine months following diagnosis was 73.7%, almost identical to the rate reported in the Treatment report (73.8%) for the preceding three years (Table 9 of the accompanying Excel workbook).



A
Percentage-point difference in the probability of any treatment
15
10
5
0
-5
-10
-15
3.5
3.0
2.5
2.0
Standard error
Model 1 (age adjusted)

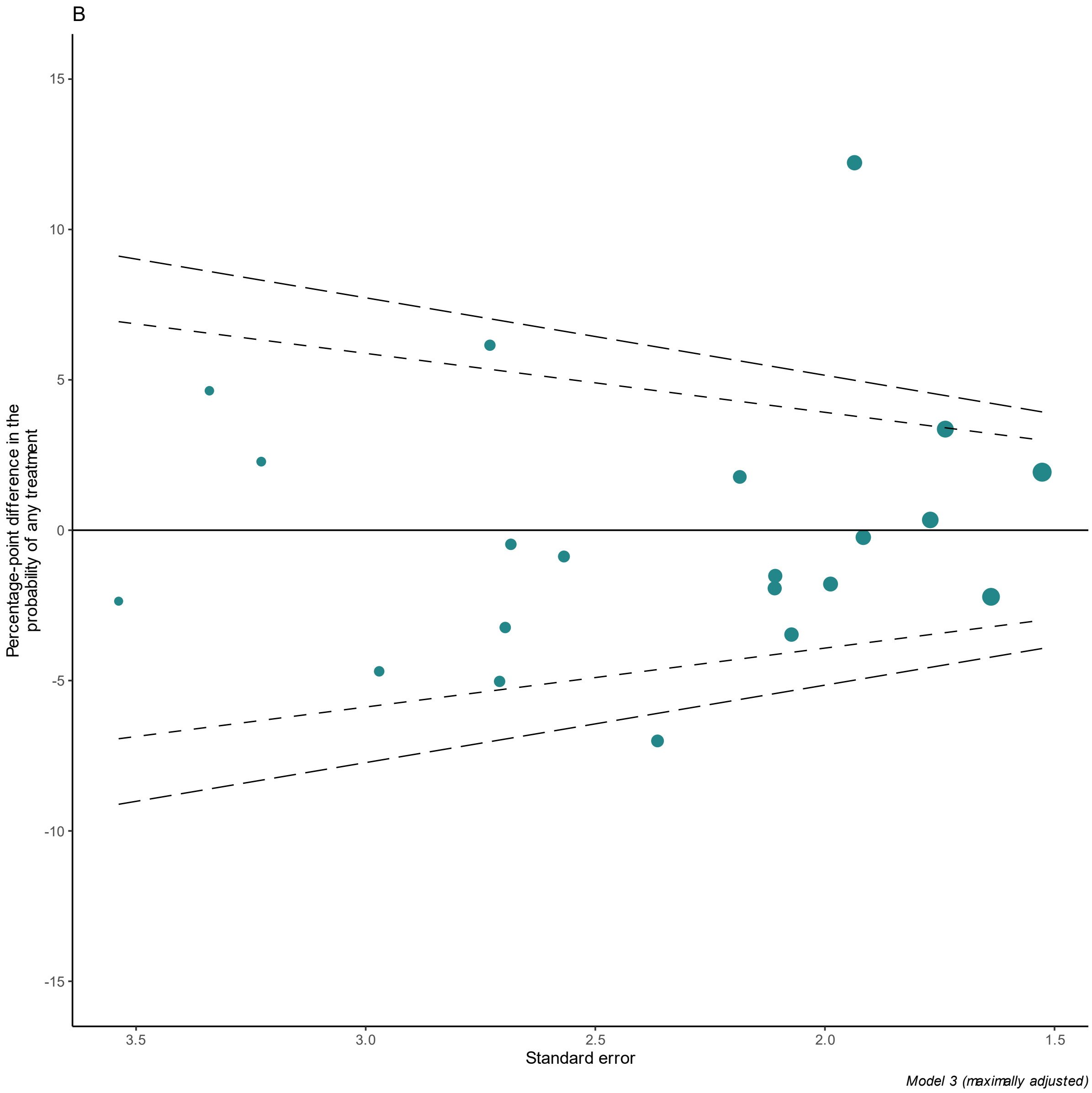


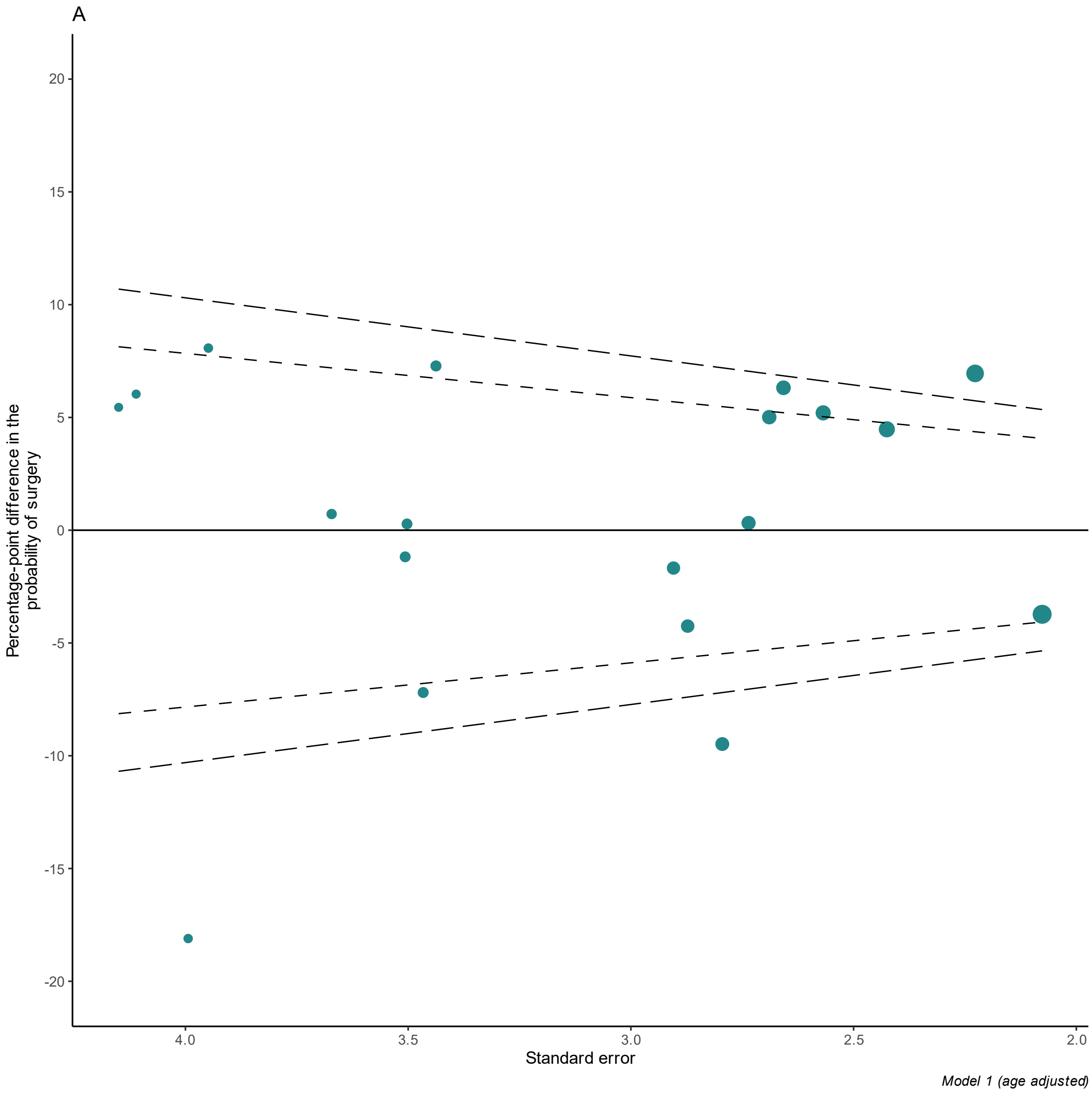
Figure 16 Geographic variation in the probability of any treatment versus no treatment, excluding stage 1 disease, 2019

Figure 16 shows that geographic variation in treatment remained following adjustment for a range of factors associated with differences in the treatment pathway. The probability of any treatment fell more than two SDs below the population average for one Cancer Alliance, while two Alliances had probabilities more than two SDs greater than the average. These results indicate variation in overall treatment between Cancer Alliances in England to a degree that may not be explained by chance alone and warrants further investigation. Notwithstanding, comparison with the Geographic Treatment Variation report suggests that regional variation in access to any treatment was less marked in 2019 than in the previous three years. In the Treatment report maximally adjusted analysis of 2016-2018 diagnoses there were four Cancer Alliances with statistically significant low rates of 'any treatment', sitting below the -2SD line on the funnel plot. For 2019 data, only the Greater Manchester Cancer Alliance remained a low statistical outlier for this parameter. The treatment report also demonstrated 5 Cancer Alliances with 2016-2018 'any treatment' rates more than 2SD above the national average. Comparison of data is complicated by adjustments of Cancer Alliance configuration in London, but for 2019 diagnoses just two Alliances (North West London and North East London) were demonstrated as high performing outliers on the maximally adjusted analysis. A complete table of coefficients is reported in **Table 10** of the accompanying Excel workbook.

Treatment variation by Cancer Alliance: surgery versus no surgery

The optimal management of ovarian cancer requires surgery in the large majority of cases to remove (debulk) the tumour. While the results above indicate variation in the receipt of any treatment, the analysis below looks specifically at the probability of surgery either alone or in combination with chemotherapy.

The average probability of stage 2-4 or unknown stage ovarian cancers being treated with surgery was 51.8% (**Table 11** of the accompanying Excel workbook), similar to the rate for diagnoses in 2016-2018 as reported in the Geographic Treatment Variation report (51.0%). The funnel plots in **Figure 17** show large geographic variation in the delivery of surgery between Cancer Alliances, even after adjustment for other factors. Six Cancer Alliances had surgery probabilities two SDs above the average and four had probabilities two SDs below the average. Comparison with 2016-2018 data suggests that the marked regional variation demonstrated in the Treatment report remains equally profound in relation to cases diagnosed in 2019. All four Cancer Alliances with low 2019 surgery rates (South Yorkshire and Bassetlaw, East Midlands, West Midlands and Wessex) also had significantly low surgery rates for cases diagnosed 2016-2018 in the Treatment report. Whilst Cancer Alliance reconfigurations limits direct comparison between 2016-2018 data and 2019 data for some regions, it appears that surgery rates in London alliances, the North East and Surrey & Sussex have remained high in both analysis periods. A full table of coefficients is provided in **Table 12** of the accompanying Excel workbook.


A
Percentage-point difference in the probability of surgery
20
15
10
5
0
-5
-10
-15
-20
4.0
3.5
3.0
2.5
2.0
Standard error
Model 1 (age adjusted)

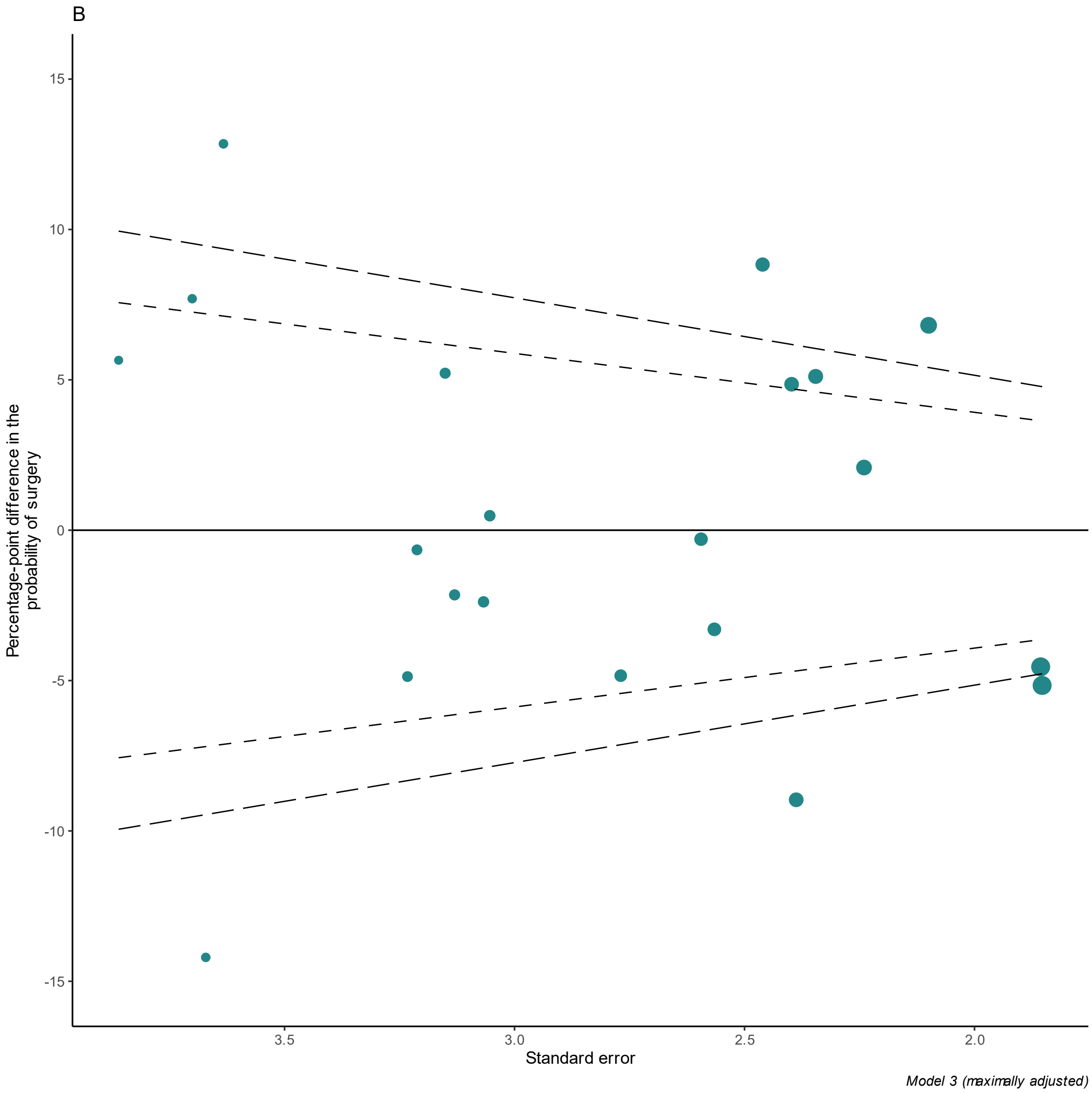


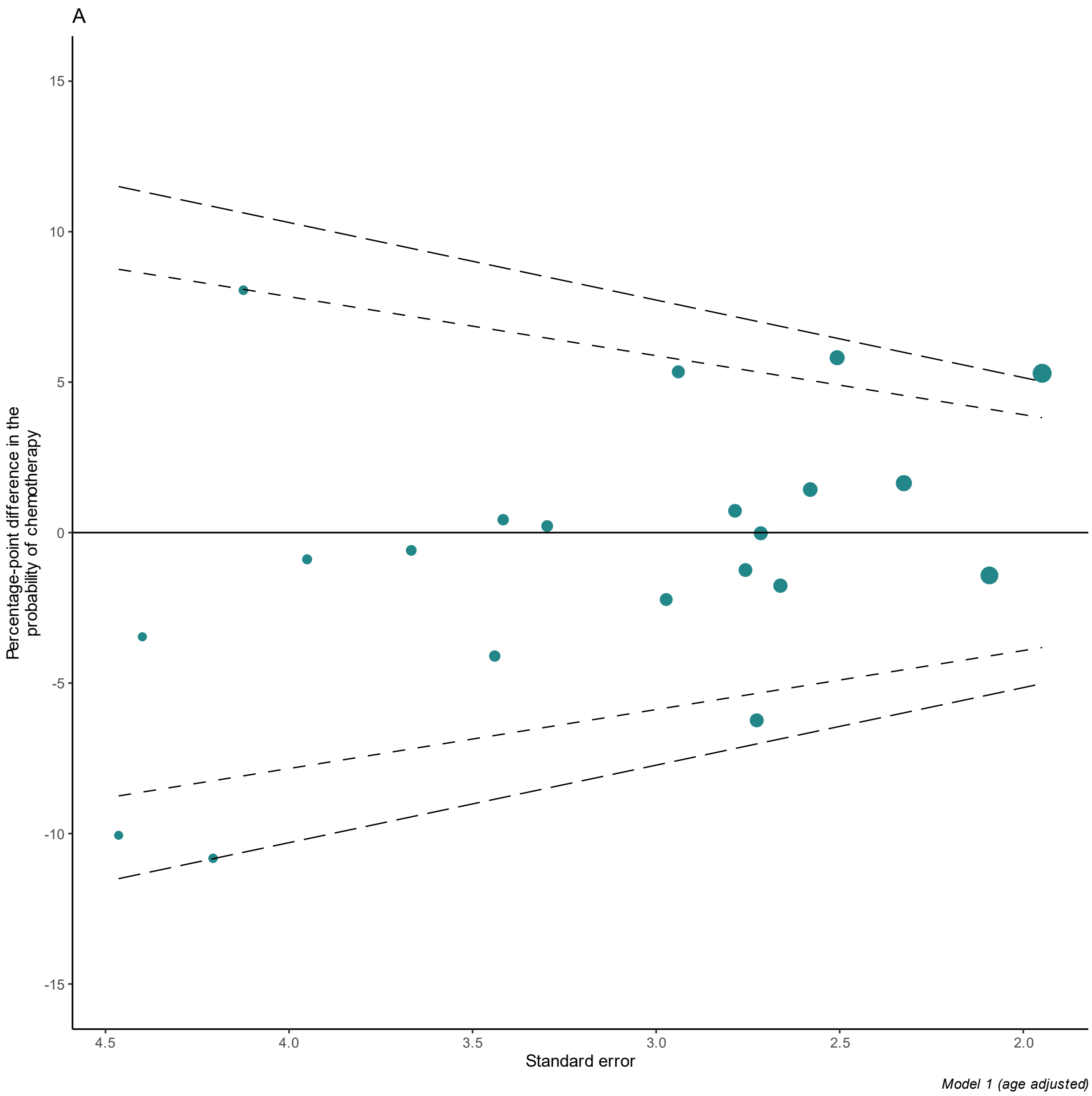
Figure 17 Geographic variation in the probability of surgery versus no surgery, excluding stage 1 disease, 2019

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.

Treatment variation by Cancer Alliance: chemotherapy versus no chemotherapy

The majority of women with an ovarian cancer diagnosis should receive chemotherapy to treat and help manage the disease. Exceptions to this include some histological types and grades of stage 1 disease, where surgery alone may be adequate to provide a high chance of disease cure. Additionally, there are circumstances where risks from chemotherapy may outweigh the benefits, and where patients may decline chemotherapy treatments.

Of stage 2-4 and unknown stage ovarian cancers, the average probability of treatment with chemotherapy was 64.1%, compared to 66.5% demonstrated in the Treatment table for 2016-2018 diagnoses (**Table 13** of the accompanying Excel workbook).



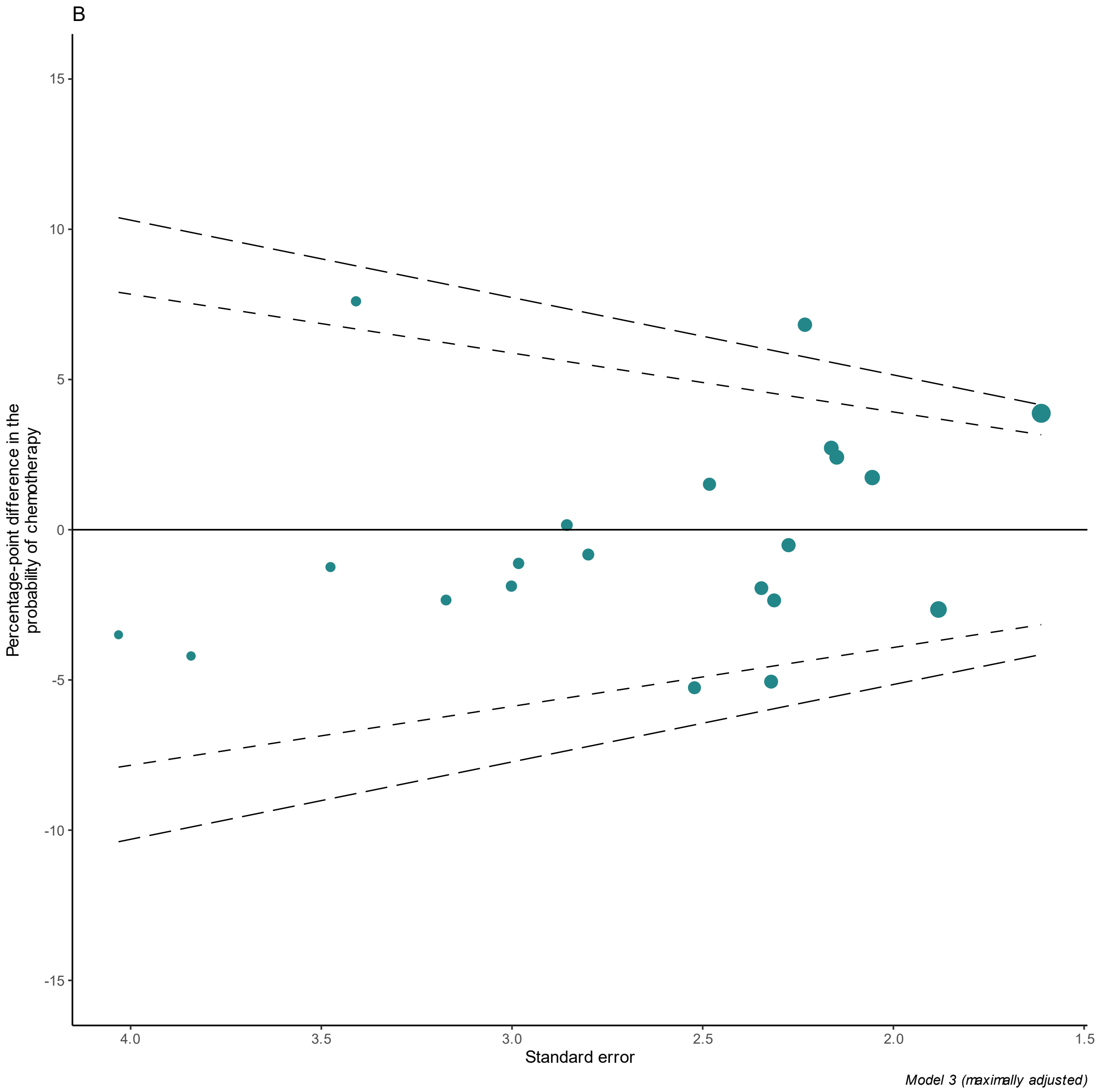


Figure 18 Geographic variation in the probability of chemotherapy versus no chemotherapy, excluding stage 1 disease, 2019

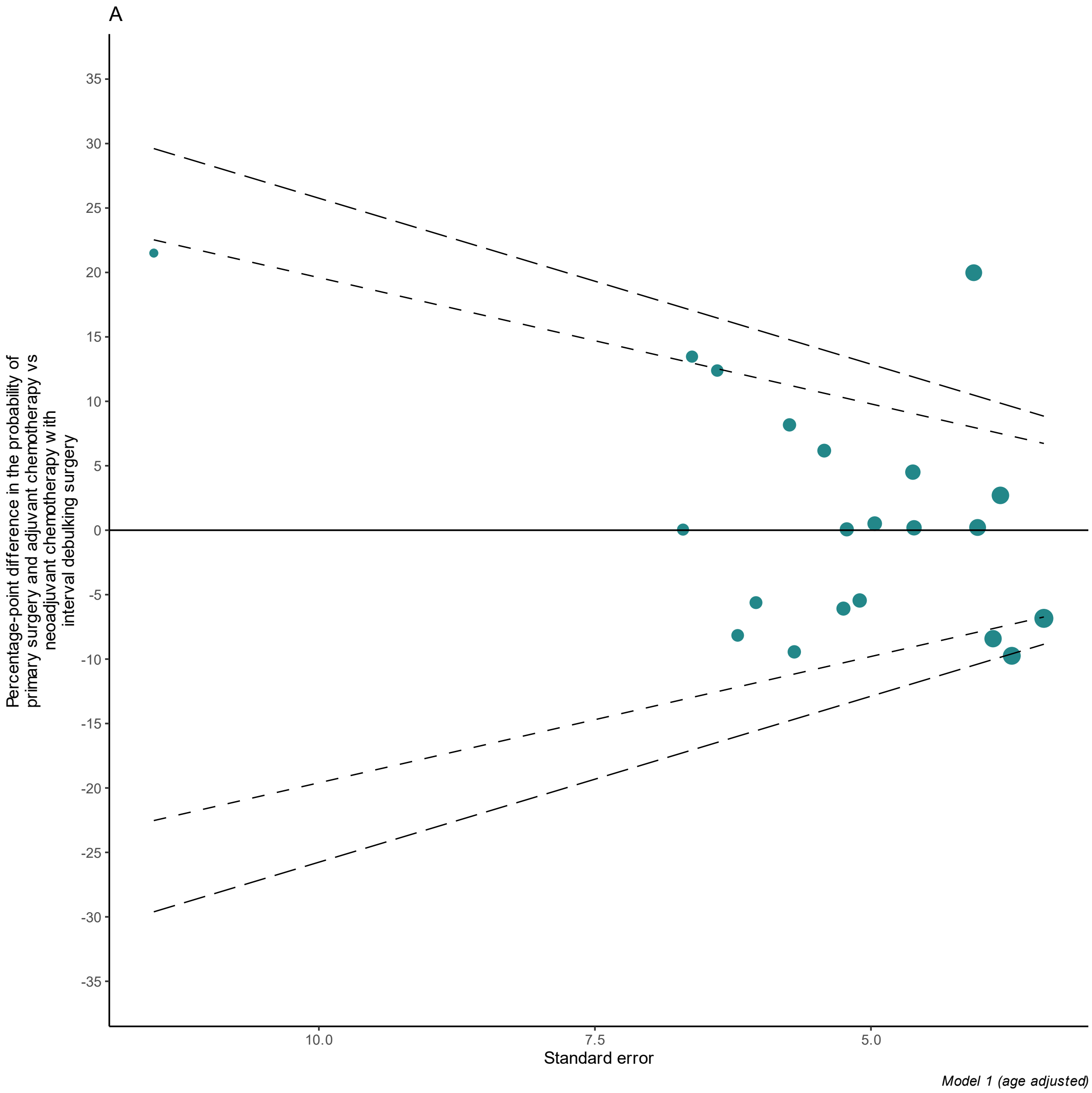
Following adjustment for a broad range of factors, including patient age and tumour morphology, **Figure 18** shows three Cancer Alliances with chemotherapy rates two SDs above the average and two with chemotherapy rates two SDs below the average. As previously reported for 2016-2018 diagnoses, there was markedly less regional variation in chemotherapy treatment rates throughout England compared to surgery rates. There were no Cancer Alliances with statistically significant low chemotherapy rates in both the original treatment report (diagnoses 2016-2018) and the current analysis (2019 diagnoses), with little evidence of consistently high chemotherapy treatment rates across the two reports except for the West Midlands Alliance and Alliances in the north of London. A full table of coefficients is provided in **Table 14** of the accompanying Excel workbook.

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 applied in two circumstances specific to advanced disease. Firstly, if a patient is very unwell at the time of diagnosis, chemotherapy can start to treat the cancer and support improvement in the overall health and performance status of the patient before undergoing surgery. 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.[3]

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 2,010 tumours within the cohort of stage 2-4 and unknown stage cancers that received one of these two treatment combinations.

Within this subsample, the probability of primary surgery and adjuvant chemotherapy was 49.6% on average (**Table 15** of the accompanying Excel workbook), compared to the rate of 49.4% for cases diagnosed 2016-2018, as described in the Geographic Treatment Variation report.


A
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
Percentage-point difference in the probability of primary surgery and adjuvant chemotherapy vs neoadjuvant chemotherapy with interval debulking surgery
10.0
7.5
5.0
Standard error
Model 1 (age adjusted)

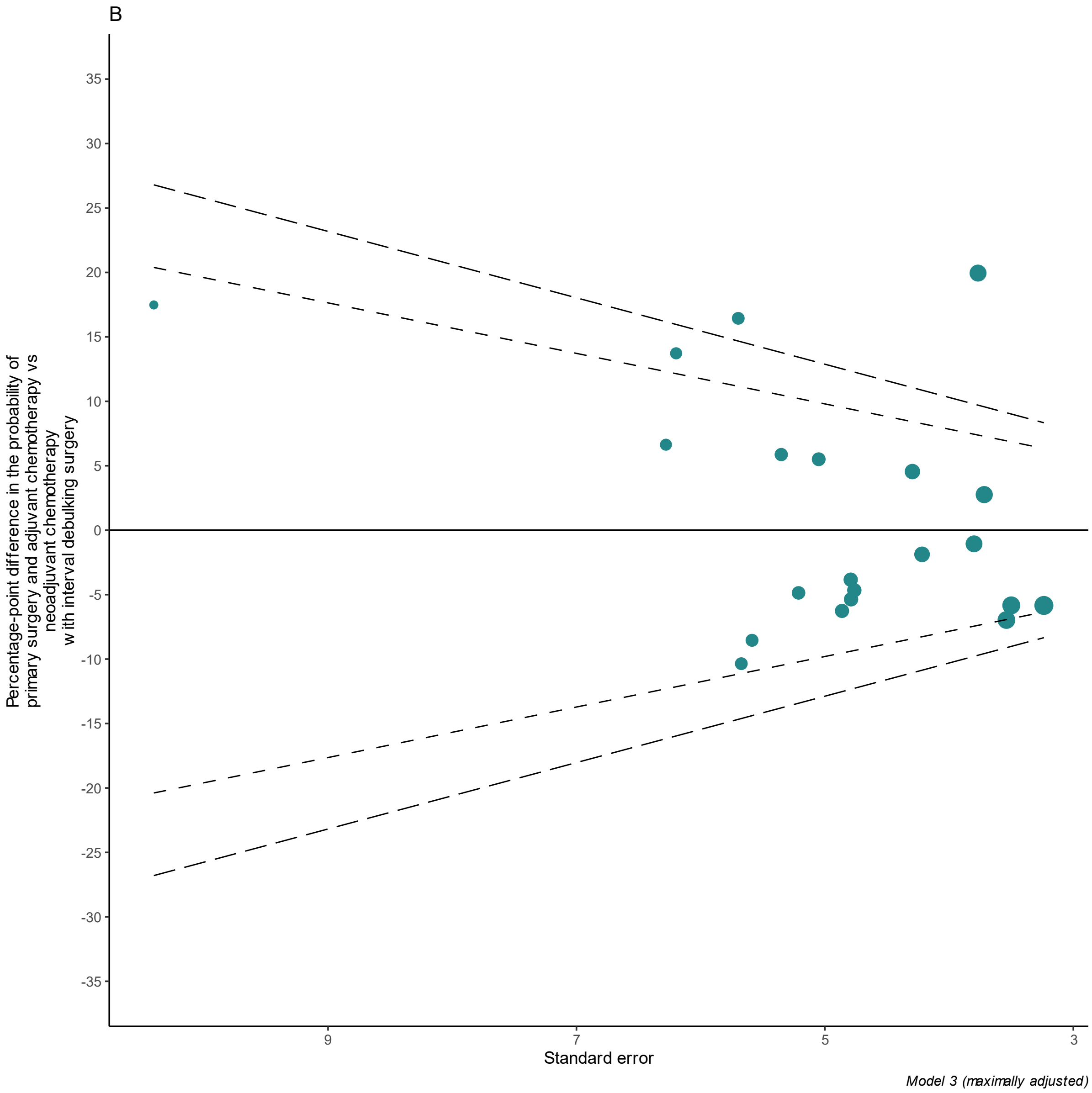


Figure 19 Geographic variation in the probability of primary surgery and adjuvant chemotherapy versus neoadjuvant chemotherapy with interval debulking surgery, excluding stage 1 disease, 2019

Figure 19 shows regional variation following adjustment for patient demographics and tumour characteristics associated with treatment, with three Cancer Alliances falling two SD above the average and one region falling two SDs below the average. The maximally adjusted probability (Model 3) was markedly higher in one Cancer Alliance than others. The former Cancer Alliance North East and Cumbria had primary surgery and adjuvant chemotherapy proportion that was 20.4 percentage points higher than the national average for the 2016-2018 diagnoses described in the Geographic Treatment Variation report, while the newly defined Northern Cancer Alliance remained the most marked outlier for diagnoses in 2019 (20 percentage points higher). Generally, there was markedly less variation in the proportion of cases having upfront surgery versus neoadjuvant chemotherapy compared to the extensive variation in actual surgical resection rates. A full table of coefficients from the underlying models can be viewed in Table 16 of the accompanying Excel workbook.

Treatment variation by Cancer Alliance: summary tables

Table 17 of the accompanying Excel workbook (also reproduced below) pulls together the maximally adjusted results from Table 9 (any treatment), Table 11 (any surgery) and Table 13 (any chemotherapy). Collectively, they indicate geographic variation in treatment delivery after accounting for differences in the regional distribution of various patient demographics and tumour characteristics.

Table 17 Summary of maximally-adjusted geographic variations in any treatment, surgery and chemotherapy (Model 3; diagnosed 2019)

To supplement these 2019 geographic variation in treatment data, Table 18 reports the variation in treatment over time for England as a whole. Specifically, the proportions of patients selected into each treatment category, stratified by year of diagnosis (2015 and 2019). This analysis suggests stable patterns and rates of treatment across England between 2015 and 2019. Very little variation in treatment was observed over time at a country level beyond a small fall in the proportion of patients who received any chemotherapy (2015: 65.2%; 2019: 64.1%).

To assist comparison against the refreshed age-standardised survival statistics presented earlier in this report for cases diagnosed 2015-2019, age-adjusted geographic variation treatment is presented in Table 19 of the accompanying Excel workbook (also reproduced below) for tumours diagnosed during the same five-year period. This supplementary analysis excludes borderline and D391 cases, consistent with the survival cohort for the period.

Table 19 Summary of age-adjusted geographic variation in any treatment, surgery and chemotherapy for tumours diagnosed between 2015 and 2019, excluding D391 and borderline disease (Model 1)

In turn, Table 20 of the accompanying Excel workbook presents the patient demographics for the patients in Table 19. It should be noted that the count of patients in the treatment tables (28,478 tumours for 28,351 patients) is slightly larger than presented in the survival tables for the period (28,189) patients. The reasons for this discrepancy are as follows:

- The survival method excludes patients with vital status data quality issues. Vital status was not a consideration for treatment variation analyses, and so this exclusion criterion was not applied.
- The survival method considers ovarian cancer patients aged 15-99 years at diagnosis, while the treatment analysis was restricted to patients aged ≥18 years at the time of diagnosis.

- Both sets of analyses selected on the earliest tumour documented per patient. However, while the treatment analysis applied this rule exclusively to the period 2015-2019, the survival method applied a rolling five-year analysis from 2001-2019. Thus, for patients with multiple diagnoses that were dated either side of 01/01/2015, there will be a discrepancy in how each analysis flagged the earliest tumour.
- The survival method selected on tumours documented with a behaviour code of 3 (i.e., confirmed as primary, invasive, and malignant), while the treatment analysis applied no such condition when selecting on tumours.
- The survival method excluded patients with missing or imputed gender, date of diagnosis, date of birth or age information.
- The survival method excludes ovarian cancers documented with a morphology of 8320, which is not a valid entry for ovarian cancer.

Conclusion

This report provides an update to two prior publications that described both trends in the incidence, mortality and survival of ovarian cancer,[1] and geographic variation in treatment delivery for cases diagnosed between 2015 and 2019.[2]

Conclusions from the refreshed Disease Profile analysis

This disease profile reviews the latest data (up to 2019 diagnoses) on incidence, mortality, stage at diagnosis and survival of patients with ovarian cancer in England.

Main findings:

- The crude incidence rate in England has remained reasonably stable, and the age standardised incidence rate has reduced, since 2001.
- Crude incidence and mortality rates vary among sub-ICBs and Cancer Alliances, with variation beyond what might be expected by random chance, suggesting that there may be genuine differences between areas.
- The proportions of patients diagnosed at early and late stages vary considerably around the country; some of this variability was likely due to data completeness but other factors should also be considered. These may relate to population and tumour characteristics geographical variation but may also reflect variation in access to diagnostic pathways relating to more frequent late diagnosis in some regions.
- Completeness of stage data varied by geography; there is some room for improvement which would lead to better data quality for reporting.
- Survival of patients has been gradually improving since 2001. Improving one-year survival may reflect progress in diagnosing the disease sooner, with increased awareness of the symptoms amongst women and primary care practitioners, and improved diagnostic pathways, enabling more women to be diagnosed while still well enough to undergo treatment. Increased five-year survival may additionally reflect improvements in surgical and chemotherapy treatments. Assessment of geographic variation in survival rates may help to identify areas of best practice and improve the outlook for all patients.

By using NDRS data to analyse cohorts of ovarian cancers (including or excluding borderline tumours as appropriate), we have been able to make clear comparisons between geographies and over time.

Building on this new understanding, the forthcoming national ovarian cancer audit will gain further insight into the factors behind the observed geographic variation and into best practices in diagnosis and treatment, aiming for improved outcomes for patients.

Reporting on data completeness back to clinical staff in the NHS via the CancerStats website has been an ongoing part of the ovarian cancer audit feasibility pilot work. It is recommended that similar efforts be undertaken by the forthcoming national audit; improving the quality of data available to NDRS about patient performance status, stage, residual disease and surgeon grade will enable further valuable analyses to be undertaken.

Conclusions from the refreshed Geographic Variation analysis

Regarding patient demographics and tumour characteristics (Table 7 of the accompanying Excel workbook), findings from the refresh of the Geographic Variation report correspond with previous research and evidence from clinical practice, 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. Results shown in Table 12 indicate that the likelihood of receiving surgery was far lower for older age cohorts than for younger women, even after accounting for factors including stage and morphology. This variation may be explained by factors including comorbidities not captured by the Charlson comorbidity index, poor performance status, or patient choice (such as opting for chemotherapy over surgery; Appendix 11). Research is needed to clarify the reasons for diagnoses in older age groups having a lower probability of surgery.
- There was very marked regional variation in surgical resection rates for cases of FIGO stage 2-4 and unrecorded stage ovarian cancer diagnosed in 2019.

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 that enable early diagnosis, timely referral to secondary care and patient characteristics such as performance status which the models have not been able to control for. However, observed variation may also reflect real differences between gynaecological cancer centre multidisciplinary teams in the efficiency of diagnostic pathways or preparedness to perform radical surgery or administer chemotherapy to women with advanced disease.

Cross-tabulating age-adjusted results from this refresh of the Geographic Variation report (Table 18) against age-standardised net survival statistics from the refreshed Disease

Profile report (**Table 5**) indicates that Cancer Alliances with lower probabilities of any treatment also exhibited lower five-year survival estimates (2015-2019 diagnoses). This correlation was weak, however (Pearson's r=0.29).

Final thoughts

Taken together, these refreshed results present an opportunity to target future studies designed to better understand the reasons for variation in the diagnosis and treatment of ovarian cancer patients between areas of England, as well as the impact of this variation on patient survival. Past results have already been used by consultants to push through positive changes in clinician practice, as summarised in **Appendix 9**.

The treatment pathway and survival of some patients analysed for this refreshed report will have been impacted to some degree by the COVID-19 pandemic, which had an immense impact on cancer diagnoses and access to treatment.[4,5] For example, for patients diagnosed in late 2019, their ovarian treatment pathways may have coincided with the initial COVID-19 lockdown starting in March 2020. It is expected that the fuller impact of the pandemic on cancer diagnosis and treatment will be captured in the forthcoming national ovarian cancer audit, which will analyse cases diagnosed and further analysis of treatments administered during 2020 onwards.

Limitations

Residual confounding

The linear probability models created for the geographic variation analysis all accounted for differences in the distribution of various patient demographics and tumour characteristics between Cancer Alliances that might have otherwise confounded the main association under study. Despite such adjustment, geographic variation in treatment remained. Rather than representing real disparities in clinical practice, some of these geographic differences may be the result of residual confounding, such as differential routes to diagnosis between regions (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 not captured through the Charlson comorbidity score.

Private healthcare data

The reported analyses did not consider privately funded treatments. Due to the absence of readily accessible private healthcare data, tumours in private patients may have been incorrectly assigned to the ‘no major surgical resection or chemotherapy’ category. Accordingly, the true proportion of tumours that received treatment will likely be higher than reported, with the additional possibility of differences in private treatment access between Cancer Alliances. If present, this 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. The authors are not aware of any data sources that allow for a reliable estimate of the degree to which this misclassification may have occurred.

Major surgical resections

Surgery was defined as the delivery of at least one major resection during the primary course of treatment. Major surgical resections do not encompass all surgical procedures delivered to ovarian tumours, excluding procedures such as 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 score

Charlson comorbidity scores were defined by linking each tumour to pre-defined comorbid medical conditions documented prior to the diagnosis of ovarian cancer. A list of the medical conditions considered and the associated score for each is described in Table 21 of the accompanying Excel workbook. Through a dependence on diagnosis coding within the inpatient setting, the Charlson comorbidity score may underestimate the burden of index-relevant comorbidity by missing diagnoses exclusively documented in outpatient or primary care settings. However, in the context of survival estimation, 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.[6]

Beyond this, through its selection on a specific subset of chronic health conditions, the index may not reflect the full burden of all comorbid disease that may influence clinical decision making. For instance, Table 7 shows that 69.7% (n=898) 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 two-thirds of tumours in the cohort received a comorbidity score of zero sits at odds with the age profile of the ovarian cancer cohort, as well as research elsewhere for other tumour sites that has 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 (Table 10), any surgery (Table 12) or any chemotherapy (Table 14).

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 diagnosing Cancer Alliance. As the Cancer Alliance at treatment can vary over time and according to treatment type, Cancer Alliance at diagnosis was reported for simplicity. Comparison with data from 2016-2018 diagnoses published in the Treatment report is also complicated by the reconfiguration of Cancer Alliances.

Appendices

Appendix 1: Cohort definitions

Defining 'ovarian cancer'

Ovary, fallopian tube and primary peritoneal carcinomas ('ovarian cancers') were selected from the National Cancer Registration Dataset (NCRD)[8] if diagnosed in England between January 2015 and December 2019. Cases were identified according to the following ICD-10 and ICD-O-2 codes:

- C56 (malignant neoplasm of ovary)
- C57 (malignant neoplasm of other and unspecified female genital organs)
- 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
- D39.1 (neoplasm of uncertain or unknown behaviour of ovary)

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

This definition aligns with international ovarian cancer analyses and is designed to capture all ovarian cancers; although there may be variation in the coding of the originating site within this group, in practice their prognosis and treatment are similar. The inclusion of D39.1 means that the cohort includes all 'borderline malignant' ovarian cancer.

Defining 'ovarian cancer' for the incidence analysis

For the incidence analysis, the ovarian cancers were selected if they met the criteria as that outlined above.

Defining 'ovarian cancer' for the mortality analysis

The definition of 'ovarian cancer' used for mortality statistics in this report is C56-C57 in ICD-10. Data on mortality from ovarian cancer are derived from the ONS Mortality Extract which is in turn derived from causes of death recorded on death certificates, which do not include morphology information. Hence the more nuanced cohort descriptions (as used for incidence, stage and survival) which rely on tumour morphology information are not available for this statistic.

Defining 'ovarian cancer' for the survival analysis

Borderline malignant ("borderline") ovarian tumours make up approximately 16% of the overall cohort of ovary, fallopian tube and primary peritoneal carcinomas. These tumours have historically been recorded as ovarian cancers, though their malignant potential is now understood to be lower than the rest of the group.

In this report, survival analysis is presented for cohorts including and excluding borderline tumours. Their exclusion is in line with international ovarian cancer analyses and avoids inflation of the survival estimates due to the better survival of the borderline group. Hence, it gives a clearer picture of the survival of women with non-borderline ovarian cancer.

Cases were identified per the codes under the *"Defining 'ovarian cancer'"* heading, but with the exclusion of all tumours at ICD-10 site code D39.1. This is consistent with National Statistics methodology.

This methodology also applied the following selection criteria:

Include

1. Patients aged between 15-99 years (inclusive)
2. The earliest relevant primary tumour documented during in the period of analysis
3. An invasive, primary, and malignant behaviour code (3) tumour

Exclude

1. Death certificate only (DCO) registrations
2. Missing or imputed gender, date of diagnosis, date of birth or age information

Defining 'ovarian cancer' for the treatment variation analysis

For the geographic variation in treatment analysis, the ovarian cancers were selected if they met the criteria as that outlined above.

Tumours identified via death certificate only were excluded from the analysis of geographic variation in treatment as associated patients would not have been referred for treatment.

Additionally, stage 1 tumours were excluded as trial evidence has not demonstrated a major survival benefit of chemotherapy for low-grade stage 1 tumours.

Appendix 2: Stage

Stage presented in this report is the FIGO 2014 stage at diagnosis of the tumour. Tumour stages are numbered from 1 to 4, with a higher value indicating more advanced disease.

For the analysis of geographic variation in treatment stage 1 tumours were excluded as little regional variation in treatment was expected; almost all such tumours were treated with primary surgery only or surgery with adjuvant chemotherapy. If no staging data were available at the time of analysis, the corresponding tumour was defined as 'stage not recorded'.

Appendix 3: Defining geographies

Geographies were defined according to the borders defined on 1st July 2022.

Geographic variation in treatment was analysed at the Cancer Alliance level according to borders defined in 2022.

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 20** below.

Figure 20 Map of Cancer Alliances in England, as defined by NHS England in 2022. Image source: NHS England

1. Cheshire and Merseyside
2. East Midlands
3. East of England North
4. East of England South
5. Greater Manchester
6. Humber and North Yorkshire
7. Kent and Medway
8. Lancashire and South Cumbria
9. North Central London
10. North East London
11. North West and South West London
12. Northern
13. Peninsula
14. Somerset, Wiltshire, Avon and Gloucestershire
15. South East London
16. South Yorkshire and Bassetlaw
17. Surrey and Sussex
18. Thames Valley
19. Wessex
20. West Midlands
21. West Yorkshire and Harrogate

The Cancer Alliance for each tumour was assigned according to the main residence of the patient on the date of diagnosis.

Appendix 4: Survival methodology

Net cancer survival rates (i.e., estimated survival rates as if cancer were the only possible cause of death) were calculated in a relative survival framework using a complete approach with follow-up to 5th January 2021. Results were age standardised using ICSS weights where numbers permitted. Cancer Survival SOP v11_0 was followed, using stns in Stata 17.

Appendix 5: Variables defined for the treatment variation analysis

Defining cancer treatment

Treatment dates for each tumour were extracted from multiple data sources in a manner consistent with internal NDRS standard operating procedures.

Briefly, dates of systemic anti-cancer therapy administrations and major surgical resection procedures were extracted at a tumour level from the NCRD 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 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, these treatment data were supplemented by patient-level information from the Systemic Anti-Cancer Therapy (SACT)[9] and Hospital Episode Statistics (HES) Admitted Patient Care (APC) and Outpatient (OP) datasets.[10] Consistent with NDRS operating procedures, SACT and HES data were not used if a patient had evidence of multiple primary cancer diagnoses within the 18 months before or after the primary tumour of interest as patient-level linkage is such that the precise tumour to which a treatment relates cannot be reliably identified.

A list of major surgical resections considered is provided in **Table 22** of the accompanying Excel workbook. These are 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 anti-emetic 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 by type of treatment (surgery or chemotherapy), 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

Several patient and tumour characteristics were deemed by the project team as likely to be associated with clinical decision-making. In order to help isolate the relationship between geography and treatment, analyses were adjusted for the following variables:

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

The Eastern Cooperative Oncology Group (ECOG) performance status of patients was also considered as a confounding factor. This rates the physical function of patients from 0 to 4, with a score of 4 indicating complete disability and total confinement to a bed or chair.[11] However, performance status was not included in linear probability models owing to a high degree of missing data (49.7%, n=2,889; Table 7).

A Charlson comorbidity score was derived for each tumour, drawing on diagnosis data from the NCRD and HES APC datasets. Consistent with a NDRS 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 Table 21, a total of 15 medical conditions were considered and assigned values between one and six. Comorbid conditions include myocardial infarction (heart attack), dementia and liver disease. The final index ranges from 0-25, with a higher score indicating a greater burden of comorbid disease. If a patient had no linkage to HES APC (as happens for private patients or patients with no inpatient admissions), and no evidence of another primary cancer diagnosis, a score of zero was assumed.

Area deprivation is reported in quintiles according to the Index of Multiple Deprivation 2019, which provides a relative measure of deprivation for the patient's residence.[12] It is constructed using data spanning seven distinct domains, including income, employment and education. For this study, the index was defined by linking the postcode of each patient at the time of diagnosis to a 2011 Office for National Statistics (ONS) Census Lower Super Output Area (LSOA).[13] Each LSOA is ranked by the ONS according to the derived level of deprivation for the geography, and then assigned to a quintile.

Appendix 6: Statistical analysis for geographic variation in treatment

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 of the four binary treatment comparison groups detailed above was added as an outcome variable in a separate linear probability model. Covariates were then introduced as explanatory variables in three stages:

- Model 1: Cancer Alliance and patient age at diagnosis
- Model 2: as Model 1, plus adjustment for differences between Cancer Alliances in the distribution of tumour morphology and tumour stage
- Model 3: as Model 2, plus area 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 across nested models, allowing readers to assess the impact of adjustment 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, weighted according to the number of observations within each category reported by the respective model).

Estimates are to be interpreted as percentage point differences from the national average.

Analyses were undertaken using R version 4.2.1.

Funnel plots

For each binary treatment comparison group, Cancer Alliance estimates from Model 1 (age adjusted) and Model 3 (maximally adjusted) 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 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).

Appendix 7: Glossary

Age standardised rate, Directly standardised rate	ASR, DSR	Age standardised rates are used to compare rates for different populations accounting for differences in age distribution. They identify differences between populations which are not due to differences of their age distributions. Directly standardised rates are a specific way to calculate age standardised rates using a 'standard' population (European Standard Population 2013) as a reference. Directly standardised rates adjust for age by assuming that the age distribution of the population being studied is the same as that of the standard population. This enables direct comparisons between populations with different age profiles.

		Directly age standardised rates are used for incidence, mortality and survival rates in this report.
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 21 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 Analysis System	CAS, AV	The Cancer Analysis System is the database system maintained and used by the National Cancer Registration and Analysis Service, containing data on all tumours registered in England. Versions of the CAS are indicated by "AV" with a numerical indication of the date of the data. Data in this report are derived from the CAS. Further documentation can be found in the Data Resource Profile cited below.
Cancer registry	NDRS	The National Disease Registration Service (NDRS) 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).
Complete approach		Method of survival analysis that includes all patients diagnosed until the end of a maximum follow up time.

Count		Number of patients or of tumours with relevant characteristics.
Crude rate		Rate derived directly from the counts of relevant patients/tumours and the size of the population. For example, the crude incidence rate of ovary, fallopian tube and primary peritoneal carcinomas in 2019 is the number of such tumours diagnosed divided by the number of women alive in England in that year. Because cancer is not common, this is often multiplied up and expressed as a count per 100,000 person-years.
Emergency Presentation		An emergency presentation is a diagnosis of cancer that arose from an unscheduled (or emergency or unplanned) hospital admission. This is to be contrasted with other Routes to Diagnosis, for example, diagnosis via referral from a GP.
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.
Incidence		The number of new cases of cancer, usually expressed as a rate by dividing by the total population at risk during a certain period.

Integrated Care Board	ICB	The 42 ICBs are areas (covering all of England), are statutory organisations bringing the NHS together locally to improve population health and establish shared strategic priorities within the NHS.
International Cancer Survival Standard weights	ICSS	Weights used for age standardisation of survival data for cancer. The weights reflect the age distribution for the cancer population considered, rather than the population at large.
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.
Mortality		Cancer mortality is the number of deaths from cancer in a specific population within a specific period of time, usually a year. It usually only includes deaths where cancer is mentioned as an underlying cause of death on death certificates. Cancer mortality is often expressed as a crude or age standardised rate. Cancer mortality rates are a standard measure of the frequency of deaths from cancer within a specific period of time relative to a fixed population size, usually 100,000 person-years.
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.
NHS Long Term Plan		The NHS Long Term Plan was published in January 2019 and sets out major goals for the NHS over the following 10 years. This includes some cancer-specific targets, notably a goal to

		diagnose 75% of all cancers at early stage (stages 1 to 2) by 2028.
NHS trusts		NHS hospital trusts are organisational units within the National Health Service in England, providing secondary health services in a particular local area.
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	C48	The peritoneum is the serous membrane forming the lining of the abdominal cavity. 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.
Person-years		The size of the population in each year, summed over years. Using person-years for populations when calculating incidence and mortality rates allow us to compare rates from different lengths of time.
Primary peritoneal carcinomas		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 earlier stage leads to improved prognosis, treatments and outcomes in comparison with cancers diagnosed at a later stage.
Standard population	ESP2013	Standard population is an example distribution of ages in the population and is used for direct age-standardisation. (See “Age standardised rate” above.) This report uses the European Standard Population 2013.
Sub-Integrated Care Boards	Sub-ICBs	A Sub Integrated Care Board Location is a sub-division of an Integrated Care Board's total

		geographic area, required for data disaggregation purposes and to support the electronic health record.
Survival		Crude survival rates are calculated as the number of patients who survive a certain length of time since their diagnosis, divided by the total number of patients in the group. Net survival rates, published here, are survival rates adjusted so that they better estimate the proportion of patients dying of cancer rather than other causes.
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 (ICD-10, ICD-O) and performance status are used in the cancer registry.

Appendix 8: Useful links

Ovarian Cancer Audit Feasibility Pilot homepage *Information about this project and links to outputs.*	Ovarian Cancer Audit Feasibility Pilot
NDRS gynae hub ovarian cancer resources *Reports, briefings and other resources on ovarian cancer from NDRS.*	http://ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/gynaecological_cancer/gynaecological_cancer_hub/resources/ovarian_cancer
CancerData *NDRS 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://www.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 NDRS 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 *NDRS stage data for sites including ovary, split by CCG.*	http://www.ncin.org.uk/view?rid=3864

Appendix 9: Comments on impact from the BCGS membership

Consultant in Leicester

In Leicester and since the results of this Audit we have:

1) Supported our subspecialty trainee to go for a fellowship in Basingstoke and he is currently working as a consultant in Leicester and since then we have significantly increased our cytoreductive surgery rate, and our complete cytoreduction rate. We have moved towards an independent Gynaecological Oncology approach in ultra-staging procedures which has allowed us to:

- Offer CRS to more patients safely and in timely manner.
- Improved our Complete cytoreduction rate.
- We are establishing buddy operating system in our department, as these surgeries can be challenging at times.
- Our new approach so far is progressing well with no significant complications, and very low stoma rate. We are currently auditing our data since this new approach with the aim to be presented very soon.

2) We have taken part in the establishment of a regional MDT lead by ECAG to discuss any ovarian cases in the region that seemed to be not suitable for any treatment at the local MDT level.

I strongly believe that this audit has provided us in Leicester and East midland as a region with a great insight on our performance and areas for improvement.

Consultant in Derby

As we have already discussed before, following the publication of the Ovarian Cancer Feasibility Pilot report, East Midlands Cancer Alliance have funded a Ovarian Cancer East Midlands Regional MDT which is due to start in March 2023.

This is mainly aimed for discussion of ovarian cancer cases that do not have the standard management of Chemotherapy and Surgery or are not offered any treatment. This discussion will be held at Regional level and is collaborative approach with input from all four Cancer centres in East Midlands.

We aim to reduce variation in treatment across East Midlands and hopefully improve survival in the long term

Consultant in West Midlands

The feasibility project has been used to drive the work of the West Midlands Gynaecological Oncology Operational Delivery Network.

Consultant in Bath

We have used this to drive the quality of the data recording in our MDT which has subsequently dramatically improved. Once data recording is consistent we can use it to benchmark improvements.

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