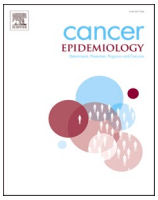
Cancer Epidemiology 96 (2025) 102778

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep



Are there inequalities in ovarian cancer diagnosis and treatment in England? A population-based study

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ARTICLE INFO

Keywords:
Ovarian Cancer
Socioeconomic Inequalities
Treatment
Delays

ABSTRACT

Introduction: Ovarian cancer ranks as the sixth leading cause of cancer-related mortality among women. Notably, there is a deprivation gradient in survival rates, with individuals from more affluent socioeconomic groups more likely to be alive at five years following diagnosis. This study examines disparities in treatment received and the timeliness of diagnosis and treatment across different socioeconomic groups in England, a country with universal healthcare.

Methods: The Cancer Registry identified a retrospective cohort of patients diagnosed with ovarian cancer in England between 2016 and 2017. Registry data were linked to Hospital Episode Statistics, Cancer Pathway, Systematic Anti-Cancer Dataset, and Diagnostic Imaging Datasets. The odds of surgery and chemotherapy were evaluated using logistic regression. The secondary care diagnostic interval methodology was used to calculate the starting point for the measurement of time to diagnosis and treatment and was analysed using quantile regression. All analyses were conducted using Stata v17. The study was registered on ClinicalTrials.gov (NCT05185388).

Results: A total of 9572 patients were included in the analysis. Area deprivation was a significant predictor of receipt of surgery and chemotherapy. The odds of having surgery and chemotherapy were 0.68 (95 % CI 0.57–0.82) and 0.68 (95 % CI 0.56–0.81), respectively, for patients from the most deprived quintile, adjusting for other factors. The interval measured from the beginning of the diagnostic pathway to treatment was significantly longer for patients from the most, compared with the least deprived areas after adjusting for important factors (median difference 4.50 days [95 % CI 2.72–6.28]).

Conclusion: In this large cohort of patients with ovarian cancer in England, we demonstrated that patients from more deprived areas are less likely to receive surgery or chemotherapy and wait longer to commence treatment. Further research is needed to understand why and what evidence-based actions can reduce these inequalities in treatment and timeliness.

1. Introduction

Ovarian cancer remains one of the leading causes of cancer-related mortality among women worldwide [1]. It is the 6th most common cause of cancer-related death among women [2]. Survival rates in the United Kingdom (UK) lag behind those in comparable countries [3]. A socioeconomic gradient also exists in ovarian cancer survival, with individuals from the most compared with the least affluent areas more likely to survive 5 years (55.8 % vs 49.2 % net survival) following diagnosis [4–6].

Disparities in outcomes have been partially attributed to inequalities in access to treatment and delays in diagnosis and treatment among those from more deprived areas [7]. Previous research documents inequalities in treatment for lung and gastrointestinal cancers, indicating that patients from more deprived backgrounds are less likely to receive cancer treatment [8–11]. Moreover, patients residing in more deprived

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https://doi.org/10.1016/j.canep.2025.102778
Received 30 October 2024; Received in revised form 2 February 2025; Accepted 16 February 2025
Available online 8 March 2025

areas encounter barriers to timely diagnosis [9, 12–16].

Factors influencing treatment decisions include fitness, age, stage, comorbidities, and individual perceptions of treatment benefits and side effects [17–19]. While previous studies highlight treatment inequalities in ovarian cancer, gaps remain concerning the time to diagnosis and treatment [9].

Existing research relies on historical cohorts and lacks comprehensive adjustment for confounding factors. This study addresses these gaps by analysing a recently diagnosed cohort of patients in England while accounting for potential confounders. This study also presents the first comprehensive evaluation of diagnostic and treatment intervals for nearly every patient diagnosed with ovarian cancer in England. Specifically, we investigate inequalities in cancer-directed surgery and chemotherapy and examine three timelines associated with quality care, including the secondary care diagnostic interval (SCDI) using the methodology described by Pearson et al. [20], the interval from diagnosis to the initiation of treatment, and the overall timeline from the onset of the SCDI to the initiation of treatment. This study adheres to the RECORD statement for reporting (Appendix 1) [21].

1.1. Patient and public involvement

The study design was informed by a collaborative process involving members of Involve Hull, a patient and public engagement group.

2. Materials and methods

2.1. Data availability and exclusions

This study used cancer registration data from the National Cancer Registration and Analysis Service (NCRAS) [22], Public Health England (PHE) to identify ovarian cancers (ICD10 codes: D39.1, C48, C56-C57) diagnosed in individuals aged 18–99 in England during 2016 and 2017.

Eligible patients were individuals diagnosed with ovarian cancer whose basis of diagnosis was not solely via death certificate, had no prior invasive malignancy, did not present with synchronous or metachronous ovarian cancer, were not diagnosed with borderline ovarian cancer or sarcoma and were female. Detailed exclusion criteria are provided in Appendix 2. The study was registered with ClinicalTrials.gov (NCT05185388) and received ethical approval from the Hull York Medical School Ethics Committee.

2.2. Data linkage

Data linkage was conducted by NCRAS, primarily using patient's NHS numbers [22]. Data linkage integrated the Cancer Registry data with additional population-based electronic health datasets, which provided comprehensive information on treatment and timelines of diagnostic and outpatient events, including:

2.3. Hospital Episode Statistics (HES): Surgical treatments [23]

- Diagnostic Imaging Dataset: Radiological imaging
- Cancer Pathway: Incorporating data from the Systemic Anticancer Therapy Dataset (SACT) [24], Routes to Diagnosis and Cancer Waiting Times datasets, providing data on chemotherapy and outpatient events

NCRAS provided the linked, pseudonymised data, subsequently stored in the Data Safe Haven at the University of Hull.

2.4. Outcome variables

Our outcome variables were:

- Receipt of cancer-directed surgery (binary)
- Receipt of chemotherapy (binary)
- Secondary care diagnostic interval (measured in days)
- Treatment interval (measured in days)
- Whole interval (measured in days)

2.4.1. Defining surgery and chemotherapy

Cancer-directed surgery was determined via relevant OPCS-4 codes captured within the Cancer Registry, supplemented by HES data (Appendix 3) [25]. Cancer-directed surgery was defined as a relevant operation recorded between 30 days prior and nine months post-diagnosis, thereby minimising the inclusion of procedures to treat new malignancies. Receipt of chemotherapy was captured from the Cancer Registry, supplemented by SACT data for regimens we designated as used in the first-line treatment of ovarian cancer (Appendix 4) [26,27].

2.4.2. Defining the secondary care diagnostic interval, treatment and whole intervals

Diagnostic and treatment pathways were delineated using methodologies established by Pearson et al. (2019), mirroring approaches applied in the Routes to Diagnosis study [20,28]. The SCDI commenced with the earliest relevant event identified within six months before diagnosis. It concluded with the date of cancer diagnosis, determined by the European Network of Cancer Registry (ENCR) rules (See Fig. 1) [29]. However, an alternative indicator of the diagnosis date, such as a date of a Multi-Disciplinary Team meeting or referral for treatment or treatment initiation, was used if this date was within three months preceding the ENCR-defined diagnosis date. This is because, in practice, diagnosis may be reached before this date. Potential first events were defined by PHE methodology, including relevant imaging (Appendix 5), date referred to secondary care, or date first seen in secondary care [30,31].

The treatment interval was calculated as the duration from the diagnosis date to the initiation of the first treatment received. The whole interval, encompassing the SCDI and treatment interval, was measured in days from the commencement of the SCDI to the initiation of the first treatment.

2.5. Covariates

The exposure of interest was area-level socioeconomic status, using the income domain from the 2015 Index of Multiple Deprivation, categorised into quintiles. Quintile one reflects the most affluent areas, and quintile five the most deprived [32].

Stage was classified according to the International Federation of Gynaecology and Obstetrics (FIGO) staging system 2014 [33]. This comprises stage I (limited to the ovary), II (pelvic extension), III (peritoneal metastases beyond the pelvis), and IV (distant metastasis) [33].

The Cancer Registry provided a weighted comorbidity score based on the Charlson Comorbidity Index (CCI). This index counts the number of defined conditions based on inpatient admissions recorded in HES data 6–72 months before the diagnosis of ovarian cancer, using a well-established methodology (Appendix 6) [34,35]. Based on the observed distribution, the score was categorised as 0, 1, or $\geq$ 2 comorbidities.

The Cancer Registry provided the route to diagnosis by integrating multiple data sources [28]. Eight routes have been identified through which patients are diagnosed (e.g. urgent GP referral with a suspicion of cancer [two-week wait], GP referral [routine and urgent referrals not under two-week wait]).

The morphological subgroup was included to account for biological variations among deprivation quintiles. Ovarian cancer tumour types were defined using relevant morphology codes (ICD-O3) [36]. Similar to other publications, they were classified into serous, endometroid, clear cell, mucinous, germ cell and sex cord-stromal tumours, miscellaneous and unspecified, and other malignant epithelial types (Appendix 7) [37, 38].

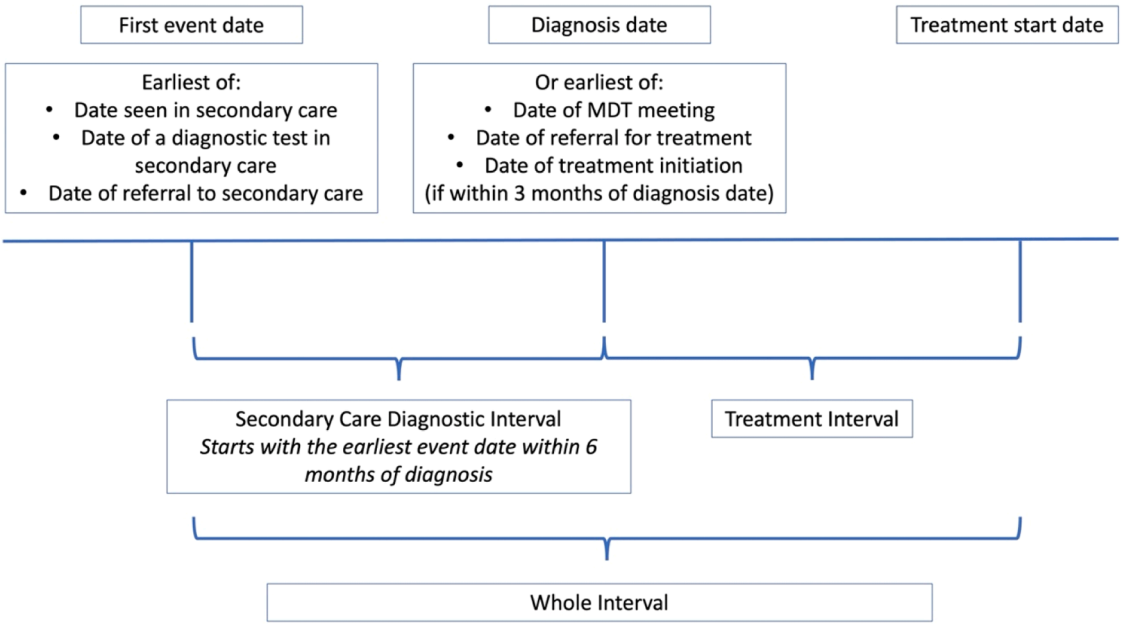

Fig. 1. Pathways to diagnosis and treatment – based on the Aarhus statement and SCDI methodology by Pearson et al. [20,49].

Ethnicity data were self-reported through hospital administration systems and recorded in the cancer registry based on the UK Government census ethnic groups 2011 [39]. For this study, ethnic groups were grouped into white (e.g. English), other specified ethnic groups (e.g. Asian), and ethnic backgrounds otherwise unspecified.

2.6. Data analysis

Descriptive statistics outlined the distribution of surgery and chemotherapy across deprivation quintiles, stage, age, CCI, route to diagnosis, morphology, and ethnicity. Univariable and multivariable logistic regression models were used to evaluate the relationship between treatment receipt and deprivation quintile, adjusting for relevant a priori covariates based on clinical experience and the literature [40]. The covariates evaluated were IMD quintile, stage, age (modelled as linear and quadratic continuous variables), CCI, route to diagnosis, morphology, and ethnicity.

The diagnostic and treatment intervals were examined using quantile regression models. This technique is similar to least-squares regression but minimises the sum of absolute residuals and estimates the conditional distribution of the dependent variable. It can be used when parametric assumptions are unmet (e.g., right-skewed distributions) and is robust to outliers [41]. Quantile regression has previously examined time intervals in ovarian, colorectal, and breast cancers [42–44]. The covariates evaluated were IMD quintile, age (continuous variable), CCI, route to diagnosis, ethnicity, and treatment first received. Owing to their position on the causal pathway, adjustments for stage and morphology were intentionally excluded, thus avoiding known biases [45].

2.7. Missing data

Stage, route to diagnosis, ethnicity (other backgrounds unspecified), and morphology (within the category "miscellaneous and unspecified") had missing data points. Analyses were initially conducted with missing data in the covariates labelled "unknown". We also performed sensitivity analyses with multiple imputation using chained equations, which uses a separate conditional distribution for each imputed variable (Appendix 8) [46]. We assumed the data were Missing at Random and generated 30 imputed datasets. Results from both approaches were compared [47]. All analyses were conducted using Stata v17 [48].

3. Results

Between January 2016 and December 2017, 9860 patients were registered with ovarian cancer in the Cancer Registry. There were 9572 patients for the analyses of treatment inequalities after 288 patients were excluded. A further 462 patients were excluded from the analyses of diagnostic and treatment pathways due to a lack of events pre-diagnosis (Fig. 2). Those excluded from the analysis of the pathways had a higher proportion of the most affluent group, missing stage, aged $\geq$ 80, comorbidities, other epithelial morphology and those from other unspecified ethnic backgrounds (Appendix 9).

There were 1609 (16.8 %) patients diagnosed with ovarian cancer

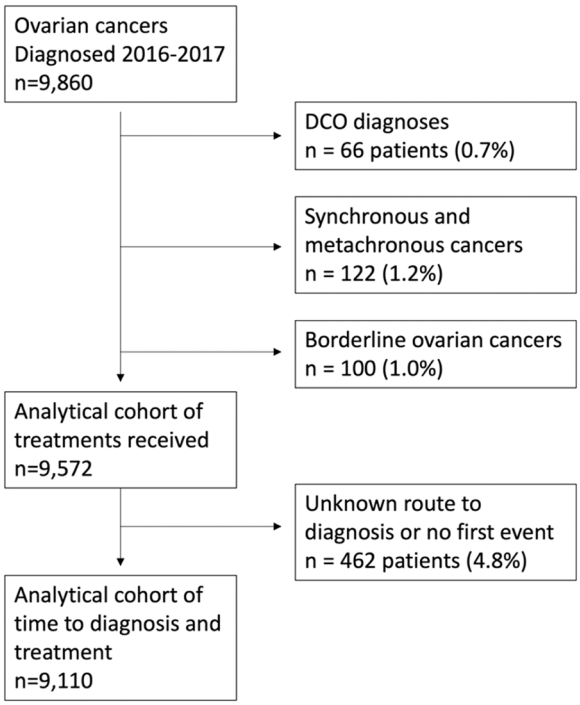

Fig. 2. Flow diagram to show exclusions applied to the cohort.

from the most deprived quintile. Those from the most deprived quintile were younger (median age 64 compared to 68 among the most affluent). There were higher proportions of comorbidity; 11.4 % had a CCI of ≥ 2 compared with 5.9 % among the most affluent quintile. There was a higher proportion of patients diagnosed following an emergency presentation (33.7 %) compared with the most affluent quintile (27 %) (Table 1).

3.1. Receipt of cancer-directed surgery

Table 2 displays the results from unadjusted and adjusted logistic regression models, evaluating the odds of receiving surgery. There were no statistically significant univariable associations between the odds of surgery and deprivation quintile. However, after adjustment for the covariates (Table 2), compared with patients from the most affluent quintile, the odds of surgery for patients from the most deprived quintile were 0.68 (95 % CI 0.57–0.82, $p < 0.001$).

We conducted additional analyses to elucidate why the inequalities by deprivation group observed in crude analysis were weaker compared to the fully adjusted analysis. Such additional analyses used a sequence of models where adjustment was made for deprivation alongside each other case-mix variable in pair-wise combinations. They demonstrated that inequalities in odds of surgery by deprivation group were accentuated most strongly when adjustment was also made for age (OR 0.69, 95 % CI 0.59–0.80, $p < 0.001$) or stage at diagnosis (OR 0.78, 95 % CI 0.67–0.92, $p < 0.002$) (Appendix 10). Sequential adjustment of deprivation differences also adjusting for either Charlson comorbidity score, or route to diagnosis, or morphology orethnicity (each added pairwise in models alongside deprivation group) on the other hand attenuated the strength of inequalities by deprivation (Appendix 11).

Those with more advanced ovarian cancers (stages III & IV), as well as those with unknown stage, had significantly lower odds of having surgery compared with patients with stage I cancer. There was a complex association between age and the odds of resection, with increasing and then decreasing odds of surgery with increasing age. Those with CCI scores of 1 and 2 or more had reduced odds of surgery compared with those with a score of 0. Compared to those referred by a two-week wait, patients diagnosed following an emergency admission, GP referral, inpatient elective, and unknown routes had significantly lower odds of undergoing surgery (Table 2). The results of the analysis repeated in multiply imputed datasets are shown in Appendix 12. No statistically significant differences were observed.

Table 1
Baseline characteristics of patients diagnosed with ovarian cancer by deprivation quintile.

		Deprivation Quintile				
	Total (%)	1 Least deprived (%)	2 (%)	3 (%)	4 (%)	5 Most deprived (%)
Total number (%)	9572 (100)	2054 (21.5)	2048 (21.4)	2025 (21.2)	1836 (19.2)	1609 (16.8)
Year of diagnosis (%)						
2016	4940 (51.6)	1104 (53.8)	1010 (49.3)	1088 (53.7)	948 (51.6)	790 (49.1)
2017	4632 (48.4)	950 (46.3)	1038 (50.7)	937 (46.3)	888 (48.4)	819 (50.9)
Stage						
I	1741 (18.2)	350 (17.0)	352 (17.2)	353 (17.4)	350 (19.1)	336 (20.9)
II	589 (6.2)	116 (5.7)	139 (6.8)	120 (5.9)	119 (6.5)	95 (5.9)
III	3556 (37.2)	763 (37.2)	782 (38.2)	773 (38.2)	635 (34.6)	603 (37.5)
IV	2211 (23.1)	501 (24.4)	455 (22.2)	456 (22.5)	451 (24.6)	348 (21.6)
Unknown	1475 (15.4)	324 (15.8)	320 (15.6)	323 (16.0)	281 (15.3)	227 (14.1)
Median age at diagnosis (IQR)	68 (56–77)	68 (58–77)	69 (59–77)	69 (57–77)	67 (55–77)	64 (53–75)
Age group, years						
18–59 years	2970 (31.0)	565 (27.5)	531 (25.9)	604 (29.8)	634 (34.5)	636 (39.5)
60–64 years	1002 (10.5)	223 (10.9)	196 (9.6)	210 (10.4)	199 (10.8)	174 (10.8)
65–69 years	1322 (13.8)	308 (15.0)	323 (15.8)	270 (13.3)	219 (11.9)	202 (12.6)
70–74 years	1359 (14.2)	299 (14.6)	343 (16.8)	297 (14.7)	227 (12.4)	193 (12.0)
75–79 years	1186 (12.4)	261 (12.7)	279 (13.6)	255 (12.6)	221 (12.0)	170 (10.6)
80–99 years	1733 (18.1)	398 (19.4)	376 (18.4)	389 (19.2)	336 (18.3)	234 (14.5)
Charlson comorbidity index score						
0	7512 (78.5)	1694 (82.5)	1628 (79.5)	1589 (78.5)	1426 (77.7)	1175 (73.0)
1	1268 (13.3)	239 (11.6)	262 (12.8)	277 (13.7)	240 (13.1)	250 (15.5)
≥ 2	792 (8.3)	121 (5.9)	158 (7.7)	159 (7.9)	170 (9.3)	184 (11.4)
Route to diagnosis						
Emergency presentation	2867 (30.0)	554 (27.0)	585 (28.6)	609 (30.1)	593 (32.3)	526 (32.7)
GP referral	1764 (18.4)	385 (18.7)	376 (18.4)	370 (18.3)	327 (17.8)	306 (19.0)
Inpatient elective	106 (1.1)	23 (1.1)	24 (1.2)	17 (0.8)	20 (1.1)	22 (1.4)
Other outpatient	902 (9.4)	188 (9.2)	182 (8.9)	195 (9.6)	185 (10.1)	152 (9.5)
Two week wait	3580 (37.4)	803 (39.1)	802 (39.2)	752 (37.1)	664 (36.2)	559 (34.7)
Unknown	353 (3.7)	101 (4.9)	79 (3.9)	82 (4.1)	47 (2.6)	44 (2.7)
Morphology						
Serous	5089 (53.2)	1153 (56.1)	1109 (54.2)	1051 (51.9)	946 (51.3)	830 (51.6)
Endometrioid	560 (5.9)	111 (5.4)	123 (6.0)	135 (6.7)	100 (5.5)	91 (5.7)
Clear Cell	427 (4.5)	97 (4.7)	102 (5.0)	76 (3.8)	81 (4.4)	71 (4.4)
Mucinous	554 (5.8)	108 (5.3)	104 (5.1)	106 (5.2)	128 (7.0)	108 (6.7)
Germ Cell and SCST	436 (4.6)	77 (3.8)	79 (3.9)	100 (4.9)	83 (4.5)	97 (6.0)
Miscellaneous & Unspecified	857 (9.0)	149 (7.3)	166 (8.1)	210 (10.4)	182 (9.9)	150 (9.3)
Other Malignant Epithelial	1649 (17.2)	359 (17.5)	365 (17.8)	347 (17.1)	316 (17.2)	262 (16.3)
Ethnicity						
White	8289 (86.6)	1835 (89.3)	1850 (90.3)	1748 (86.3)	1544 (84.1)	1312 (81.5)
Other Specified Backgrounds	742 (7.8)	88 (4.3)	92 (4.5)	139 (6.9)	198 (10.8)	225 (14.0)
Other Backgrounds Unspecified	541 (5.7)	131 (6.4)	106 (5.2)	138 (6.8)	94 (5.1)	72 (4.5)
Treatment						
Surgery received	5643 (59.0)	1222 (59.5)	1232 (60.2)	1196 (59.1)	1063 (57.9)	930 (57.8)
Chemotherapy received	6061(63.3)	1365 (66.5)	1345 (65.7)	1276 (63.0)	1113 (60.6)	962 (59.8)
Both surgery and chemotherapy received	4250 (44.4)	960 (46.7)	942 (46.0)	907 (44.8)	775 (42.2)	666 (41.4)
No treatment received	2118 (22.1)	427 (20.8)	413 (20.2)	460 (22.7)	435 (23.7)	383 (23.8)

Table 2
Odds ratios, 95 % confidence intervals and p-values (from unadjusted and adjusted logistic regression) of receiving cancer-directed surgery for patients with ovarian cancer.

Likelihood (OR with 95 % CI from logistic regression) of receiving cancer-directed surgery for patients with ovarian cancer							
	Number (%*) receiving surgery	Unadjusted (n = 9572)			Mutually adjusted (n = 9572)		
	n (%)	OR	95 % CI	P Values	OR	95 % CI	P Values
All patients	5643 (59.0)						
Deprivation Quintile							
IMD 1 (Least Deprived)	1222 (59.5)	1.00			1.0		
IMD 2	1232 (60.2)	1.03	0.91–1.16	0.665	1.06	0.90–1.25	0.494
IMD 3	1196 (59.1)	0.98	0.87–1.11	0.779	1.04	0.87–1.23	0.688
IMD 4	1063 (57.9)	0.94	0.82–1.06	0.313	0.88	0.74–1.05	0.150
IMD 5 (Most Deprived)	930 (57.8)	0.93	0.82–1.06	0.301	0.68	0.57–0.82	**< 0.001**
Stage							
Stage I	1647 (94.6)	1.00			1.0		
Stage II	540 (91.7)	0.63	0.44–0.90	0.011	0.99	0.65–1.51	0.970
Stage III	2280 (64.1)	0.10	0.08–0.13	< 0.001	0.14	0.11–0.19	**< 0.001**
Stage IV	837 (37.9)	0.03	0.03–0.04	< 0.001	0.05	0.04–0.07	**< 0.001**
Unknown	339 (23.0)	0.02	0.01–0.02	< 0.001	0.05	0.04–0.07	**< 0.001**
Age categories							
< 60	2467 (83.1)	1.00			-	-	-
60–64	718 (71.7)	0.52	0.44–0.61	< 0.001	-	-	-
65–69	870 (65.8)	0.39	0.34–0.46	< 0.001	-	-	-
70–74	778 (57.2)	0.27	0.24–0.32	< 0.001	-	-	-
75–79	498 (42.0)	0.15	0.13–0.17	< 0.001	-	-	-
≥ 80	312 (18.0)	0.04	0.04–0.05	< 0.001	-	-	-
Age as linear		1.15	1.12–1.17	< 0.001	1.18	1.14–1.21	**< 0.001**
Age as quadratic term		1.00	1.00–1.00	< 0.001	1.00	1.00–1.00	**< 0.001**
Charlson Comorbidity Index Score							
0	4784 (63.7)	1.00			1.0		
1	626 (49.4)	0.56	0.49–0.63	< 0.001	0.82	0.70–0.97	**0.020**
≥ 2	233 (29.4)	0.24	0.20–0.28	< 0.001	0.48	0.38–0.60	**< 0.001**
Route to Diagnosis							
Two Week Wait	2606 (72.8)	1.00			1.0		
Emergency Presentation	1033 (36.0)	0.21	0.19–0.23	< 0.001	0.39	0.34–0.44	**< 0.001**
GP Referral	1150 (65.2)	0.70	0.62–0.79	< 0.001	0.67	0.57–0.78	**< 0.001**
Inpatient Elective	67 (63.2)	0.64	0.43–0.96	0.031	0.56	0.35–0.91	**0.018**
Other Outpatient	658 (73.0)	1.01	0.86–1.19	0.925	0.98	0.79–1.21	0.824
Unknown	129 (36.5)	0.22	0.17–0.27	< 0.001	0.43	0.31–0.60	**< 0.001**
Morphology							
Serous	3245 (63.8)	1.00			1.00		
Endometrioid	528 (94.3)	9.38	6.53–13.46	< 0.001	2.18	1.44–3.31	**< 0.001**
Clear Cell	374 (87.6)	4.01	2.99–5.38	< 0.001	1.01	0.72–1.43	0.942
Mucinous	490 (88.5)	4.35	3.33–5.68	< 0.001	1.16	0.81–1.65	0.417
Germ Cell and SCST	377 (86.5)	3.63	2.74–4.81	< 0.001	1.31	0.90–1.90	0.155
Other Epithelial	578 (35.1)	0.31	0.27–0.34	< 0.001	0.35	0.30–0.40	**< 0.001**
Miscellaneous and Unsp.	51 (6.0)	0.04	0.03–0.05	< 0.001	0.08	0.06–0.12	**< 0.001**
Ethnicity							
White	4872 (58.8)	1.00			1.00		
Other Specified Backgrounds	525 (70.8)	1.70	1.44–2.00	< 0.001	1.25	1.00–1.55	**0.046**
Other Backgrounds Unspecified	246 (45.5)	0.58	0.49–0.70	< 0.001	0.76	0.58–0.99	**0.042**

**Percentages are read as the percentage of all those in that category

3.2. Receipt of chemotherapy

The unadjusted and adjusted odds of chemotherapy for patients from the fourth and fifth most deprived quintiles were reduced compared with those from the most affluent quintile. After adjustment for all the covariates (Table 3), the odds of chemotherapy for patients from the most deprived quintile were 0.68 (95 % CI 0.56–0.81, $p < 0.001$) compared with patients from the most affluent quintile.

We conducted additional analyses to elucidate why the inequalities by deprivation group observed in crude analysis were weaker compared to the fully adjusted analysis. Such additional analyses used a sequence of models where adjustment was made for deprivatio alongside each other case-mix variable in pair-wise combinations. They demonstrated that inequalities in odds of chemotherapy by deprivation group were accentuated most strongly when adjustment was also made for age (OR 0.67, 95 % CI 0.58–0.78, $p < 0.001$) or stage at diagnosis (OR 0.71, 95 % CI 0.61–0.82, $p < 0.001$) (Appendix 13). Sequential adjustment of deprivation differences also adjusting for either Charlson comorbidity score, or route to diagnosis, or morphology orethnicity (each added pairwise in models alongside deprivation group) on the other hand attenuated the strength of inequalities by deprivation (Appendix 14).

Those with stage II, III and IV cancers had higher odds of receiving chemotherapy compared with patients with stage I cancer. Those with CCI scores of 1 and 2 or more had reduced odds of chemotherapy compared with those with a score of 0. Compared to those referred by two-week wait, patients diagnosed following an emergency admission, GP referral, and unknown routes had reduced odds of receiving chemotherapy (Table 3). Results of the analysis repeated in multiply imputed datasets are shown in Appendix 15. No statistically significant differences were observed.

3.3. Whole interval

A total of 7454 patients underwent either surgery or chemotherapy. Among these, 7212 patients (96.8 %) had a recorded start date for the SCDI, allowing for the calculation of the whole interval. The median interval for the cohort was 55 days, with an interquartile range (IQR) of 39–76 days and a 90th centile of 120 days.

Patients from the most affluent quintile experienced a shorter median interval of 55 days compared to 58 days for those in the most

Table 3
Odds ratios, 95 % confidence intervals and p-values (from unadjusted and adjusted logistic regression) of receiving of receiving chemotherapy for patients with ovarian cancer.

Likelihood (OR with 95 % CI from logistic regression) of receiving chemotherapy for patients with ovarian cancer							
	Number (%*) receiving chemotherapy	Unadjusted (n = 9572)			Mutually adjusted (n = 9.572)		
	n (%)	OR	95 % CI	P Values	OR	95 % CI	P Values
All patients	6061 (63.3)						
Deprivation Quintile							
IMD 1 (Least Deprived)	1365 (66.5)	1.00			1.0		
IMD 2	1345 (65.7)	0.96	0.85–1.10	0.597	0.96	0.81–1.14	0.647
IMD 3	1276 (63.0)	0.86	0.76–0.98	0.021	0.92	0.78–1.09	0.342
IMD 4	1113 (60.6)	0.78	0.68–0.89	0.000	0.76	0.64–0.91	**0.002**
IMD 5 (Most Deprived)	962 (59.8)	0.75	0.66–0.86	0.000	0.68	0.56–0.81	**< 0.001**
Stage							
Stage I	794 (45.6)	1.00			1.0		
Stage II	481 (81.7)	5.31	4.22–6.68	< 0.001	4.61	3.50–6.08	**< 0.001**
Stage III	2879 (81.0)	5.07	4.47–5.75	< 0.001	4.17	3.47–5.02	**< 0.001**
Stage IV	1534 (69.4)	2.70	2.37–3.08	< 0.001	3.01	2.48–3.67	**< 0.001**
Unknown	373 (25.3)	0.40	0.35–0.47	< 0.001	1.01	0.82–1.24	0.958
Age categories							
< 60	2011 (67.7)	1.00			-	-	-
60–64	758 (75.6)	1.48	1.26–1.74	< 0.001	-	-	-
65–69	1038 (78.5)	1.74	1.50–2.03	< 0.001	-	-	-
70–74	980 (72.1)	1.23	1.07–1.42	< 0.001	-	-	-
75–79	735 (62.0)	0.78	0.68–0.89	< 0.001	-	-	-
≥ 80	539 (31.1)	0.22	0.19–0.24	< 0.001	-	-	-
Age as linear		1.35	1.32–1.38	< 0.001	1.16	1.13–1.19	**< 0.001**
Age as quadratic term		1.00	1.00–1.00	< 0.001	1.00	1.00–1.00	**< 0.001**
Charlson Comorbidity Index Score							
0	5024 (66.9)	1.00			1.0		
1	728 (57.4)	0.67	0.59–0.75	< 0.001	0.84	0.71–0.99	**0.032**
≥ 2	309 (39.0)	0.32	0.27–0.37	< 0.001	0.51	0.41–0.62	**< 0.001**
Route to Diagnosis							
Two Week Wait	2870 (80.2)	1.00			1.0		
Emergency Presentation	1470 (51.3)	0.26	0.23–0.29	< 0.001	0.36	0.32–0.42	**< 0.001**
GP Referral	1008 (57.1)	0.33	0.29–0.37	< 0.001	0.43	0.37–0.50	**< 0.001**
Inpatient Elective	66 (62.3)	0.41	0.27–0.61	< 0.001	0.56	0.33–0.92	**0.023**
Other Outpatient	550 (61.0)	0.39	0.33–0.45	< 0.001	0.46	0.38–0.56	0.824
Unknown	97 (27.5)	0.09	0.07–0.12	< 0.001	0.16	0.11–0.22	**< 0.001**
Morphology							
Serous	4189 (82.3)	1.00			1.00		
Endometrioid	357 (63.8)	0.38	0.31–0.46	< 0.001	0.42	0.33–0.53	**< 0.001**
Clear Cell	334 (78.2)	0.77	0.61–0.98	< 0.035	0.79	0.60–1.05	0.104
Mucinous	157 (28.3)	0.08	0.07–0.10	< 0.001	0.11	0.09–0.15	**< 0.001**
Germ Cell and SCST	87 (20.0)	0.05	0.04–0.07	< 0.001	0.08	0.06–0.11	**< 0.001**
Other Epithelial	883 (53.6)	0.25	0.22–0.28	< 0.001	0.38	0.33–0.44	**< 0.001**
Miscellaneous and Unsp.	54 (6.3)	0.01	0.01–0.02	< 0.001	0.05	0.03–0.06	**< 0.001**
Ethnicity							
White	5388 (65.0)	1.00			1.00		
Other Specified Backgrounds	485 (65.4)	1.02	0.87–1.19	0.843	0.94	0.77–1.16	0.581
Other Backgrounds Unspecified	188 (34.8)	0.29	0.24–0.34	< 0.001	0.38	0.30–0.49	**< 0.001**

* Percentages are read as the percentage of all those in that category

deprived quintile. After adjustment, patients from the most deprived quintile had 4-day longer intervals at the 50th and 75th percentiles than those from the most affluent quintile. Furthermore, older age was associated with longer intervals at the 50th and 75th percentiles. Co-morbidity also played a significant role in prolonging intervals. At the 75th percentile, intervals for those with a score of 2 or more were nearly 11 days longer than those with no comorbidities. (Table 4).

Appendix 16 shows the results of the analysis repeated using multiply imputed datasets. No statistically significant differences were observed. The results of the analysis of the secondary care diagnostic interval and the diagnosis-to-treatment interval are shown in Appendix 17 and 18.

4. Discussion

4.1. Summary of findings and interpretation

This large population-based study demonstrates that during 2016–2017, patients diagnosed with ovarian cancer from the most deprived areas of England were 32 % less likely to receive surgery and chemotherapy compared to their more affluent counterparts. We also found that patients from the most deprived areas experienced an increased whole interval of four days, defined as the period from the start of the secondary care diagnostic interval to commencing treatment. However, this does not have clinical implications. Importantly, this is the first comprehensive evaluation of the hospital interval in England. Understanding delays is vital because early diagnosis and treatment are determinants of better outcomes, including early-stage diagnosis, improved survival and patient experience [12].

Our findings align with more historical cohorts of patients with ovarian cancer in England, where patients from the most deprived areas were less likely to receive surgery or chemotherapy [38, 50–53] and similarly reflect trends across international settings [54,55]. Interestingly, there was no statistically significant univariable association between deprivation quintile and the odds of surgery. However, after adjustment for covariates, patients in the most deprived quintile had significantly lower odds of surgery (OR 0.68 [95 % CI 0.57–0.82, $p < 0.001$]). We observed that the full extent of differences by deprivation in use of either surgery or chemotherapy was not apparent in observed analyses. Our additional analysis indicated that this chiefly

Table 4
Whole interval and quantile regression results (days).

	Whole interval and quantile regression results (days)									
	Number with whole interval	Unadjusted (n = 7212)			Mutually Adjusted Quantile Regression Results For The 50th Centile (n = 7212)			Mutually Adjusted Quantile Regression Results For The 75th Centile (n = 7212)		
		50th	75th	90th	Difference in days	95 % CI	P Value	Difference in days	95 % CI	P Value
All patients	**7212**	**55**	**76**	**120**						
Deprivation Quintile										
IMD 1 (Least Deprived)	1551	55	76	123	Reference					
IMD 2	1583	54	72	113	−0.60	−1.95,0.74	0.378	−2.67	−5.12,−0.22	0.032
IMD 3	1502	55	77	123	1.25	−0.82,3.32	0.236	0.07	−3.57,3.72	0.969
IMD 4	1372	55	75	119	0.44	−1.52,2.39	0.661	−1.86	−4.83,1.11	0.220
IMD 5 (Most Deprived)	1204	58	82	122	4.50	2.72,6.28	**< 0.001**	4.55	1.01,8.09	**0.012**
Age categories										
< 60	2649	52	75	126	-	-	-	-	-	-
60–64	860	52.5	69	113	-	-	-	-	-	-
65–69	1135	55	74	117	-	-	-	-	-	-
70–74	1077	57	76	113	-	-	-	-	-	-
75–79	835	60	82	122	-	-	-	-	-	-
≥ 80	656	60	83	122	-	-	-	-	-	-
Age (continuous)					0.18	0.11,0.24	**< 0.001**	0.15	0.05,0.25	**0.003**
Charlson Comorbidity Index Score										
0	5967	54	73	116	Reference					
1	869	60	89	135	4.45	2.22,6.68	**< 0.001**	7.26	2.78,11.75	**0.002**
≥ 2	376	62	90.5	141	5.04	1.14,8.95	**0.011**	10.87	3.07,18.66	**0.006**
Route to Diagnosis										
Two Week Wait	3323	56	68	92	Reference					
Emergency Presentation	1656	41	60	92	−17.07	−18.79,−15.35	**< 0.001**	−10.58	−13.06,−8.09	**< 0.001**
GP Referral	1390	76	120	170	20.16	16.41,23.90	**< 0.001**	53.59	47.46,59.72	**< 0.001**
Inpatient Elective	91	49	72	119	−7.48	−14.63,−0.33	**0.040**	0.45	−27.92,28.82	0.975
Other Outpatient	752	54	92.5	140	−2.77	−6.40,0.86	0.135	25.76	17.64,33.89	**< 0.001**
Ethnicity										
White	6351	55	76	119	Reference					
Other Specified Backgrounds	618	53	82	133	0.23	−2.48,2.93	0.868	3.74	−1.19,8.68	0.137
Other Backgrounds Unspecified	243	51	67	102	−3.24	−6.05,−0.43	0.024	−2.07	−6.00,1.86	0.301
First Treatment Received										
Surgery	3653	55	77	125	Reference					
Chemotherapy	3559	56	76	115	4.28	2.79,5.77	**< 0.001**	4.85	2.37,7.34	**< 0.001**

reflected confounding by age and stage at diagnosis, with the more deprived patients being of averagely younger age and having tumours of averagely more advanced stage in our sample. Once adjustment for these and other variables was applied, the full extent of inequalities by deprivation became apparent. These observations highlight the importance of using both crude and adjusted analyses in future studies or reports examining inequalities in the management of ovarian cancer. Future research should also explore possible interactions between case-mix variables (for example, between age and comorbidity, or deprivation and ethnicity).

Meanwhile, the times to diagnosis and treatment reported here are the first such comprehensive evaluation of inequalities in time to diagnosis and treatment of ovarian cancer in England. Only two previous studies have been conducted on inequalities among patients with ovarian cancer; one was a relatively small questionnaire, and the other was an unadjusted analysis of cancer waiting times, which will not have captured all patients presenting via non-screening and non-two-week wait routes [56,57]. The present study, therefore, presents an updated and more thorough evaluation of inequalities in the time to diagnosis and treatment of ovarian cancer.

Importantly, factors such as frailty, severity of comorbidities, overall fitness and delayed presentations were unmeasured. The higher prevalence of comorbidities among patients from more deprived areas can impact their fitness for treatment [58–61]. Moreover, access to healthcare can be further constrained if deprivation is associated with the ability to travel for medical care. Consequently, the necessity to travel to access treatment may disproportionately impact those from more deprived areas. Additionally, disparities in access to specialist care and variations in hospital resources and staffing could further impair treatment accessibility [62,63].

Our study did not capture whether patients were actively offered treatments or chose to decline them. It is conceivable that individuals from more deprived backgrounds face competing priorities, such as caring responsibilities, that influence their treatment choices, particularly in instances where the benefits of potentially toxic treatments are marginal. Financial constraints, work commitments, and caregiving duties may all impact decision-making, potentially leading to reduced treatment uptake [64,65].

Although we didn't identify a clinically significant prolongation of intervals within secondary care, it is important to monitor the time to diagnosis and treatment, focusing on inequalities, especially given that waiting times in the UK have deteriorated [66].

4.2. Strengths and limitations

A major strength of this study is the use of a population-based registry linked to multiple other data sources. This linkage provided robust information on ovarian cancer diagnoses, treatments received, potential confounding factors and information on key dates in the diagnostic and treatment pathway. The covariates employed for adjustment were

defined a priori, drawing on the literature [9] and clinical expertise. Unlike other studies exploring the relationship between socioeconomic factors, treatment and delays, which fail to adjust for the route to diagnosis and ethnicity, our analysis incorporates this important data. The Cancer Registry's routine collection of all ovarian cancer diagnoses and demographic and treatment data ensures excellent population coverage, reinforcing the study's external validity [22]. Notably, the characteristics of our sample align closely with those of the Ovarian Cancer Audit, suggesting that our cohort is representative and that our findings are generalisable [38]. We also employed robust decision rules to capture diagnostic and treatment intervals for nearly every patient.

However, we could not capture data on patient preferences or rates of treatment refusal, which restricts our understanding of the influence of patient decision-making. We also could not assess factors such as patient fitness, social support, nutritional status, frailty, cognitive function, and the severity of individual comorbidities. Furthermore, we could not capture a start point of the diagnostic or treatment interval for 4.8 % of the cohort. Those with no route to diagnosis or first event may have different characteristics than those with a measured interval.

Lastly, while widely used, the Charlson Comorbidity Index presents a simplified categorical view of comorbidity that lacks detailed insight into its severity and impact on health [67]. However, while no universally accepted gold standard for measuring comorbidity exists, the CCI score is widely recognised and has demonstrated validity in comparisons with primary care data [68,69].

4.3. Implications for policy and practice

Despite the availability of universal healthcare, patients from the most deprived areas remain at a disadvantage regarding access to surgery and chemotherapy. Addressing disparities and unwarranted variations is paramount in national and international policy agendas. Furthermore, ensuring timely access to care is an essential policy target, and we need to ensure policy changes do not adversely affect patients from more deprived areas.

A particular avenue for further research is how health literacy and decision-making impact treatment inequalities. Shared decision-making is vital for informed patient choice, but this requires patients to understand complex information about treatment options and their associated risks and benefits. Disparities persist if patients experience different levels of involvement in decision-making processes, with poor communication, lack of trust, and insufficient information exacerbating these inequalities [70]. Evidence from the National Cancer Patient Experience Survey has demonstrated that patients from different socioeconomic backgrounds likely experience different levels of involvement with decision-making [71]. Clinicians may, therefore, be able to mitigate some of the effects of deprivation. Strategies may include referring patients for pre-rehabilitation, personalising communication, and ensuring awareness of available financial and transportation support [72].

4.4. Conclusion

In England, a nation with universal healthcare access, our research demonstrates significant inequalities in the provision of surgery and chemotherapy among women with ovarian cancer. It is important to confront the underlying causes of these inequalities.

Ethics Approval

Ethical approval was obtained by the Hull York Medical School Ethics Committee, reference 21.40.

Funding Information

Yorkshire Cancer Research funded this work (award reference number HEND405). It was not involved in any other aspect of the project, such as the design, data collection, analysis, or interpretation.

Funding

Yorkshire Cancer Research (HEND405).

CRediT authorship contribution statement

Lind Michael: Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **Soyiri Ireneous:** Writing – review & editing, Supervision, Software, Resources, Methodology, Formal analysis. **Macleod Una:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Paton Lewis W.:** Writing – review & editing, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Pickwell-Smith Benjamin A.:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The data for this study is based on patient-level information collected by the NHS as part of the care and support of patients with cancer. The National Cancer Registration and Analysis Service, part of Public Health England, collated, maintained, and quality-assured the data. Since 1 February 2023, responsibility for the data has been transferred to NHS England, the data controller.

We thank Helen Roberts and the members of Involve Hull for their expert contributions. We also thank Amy Porter and John Turgoose from the Data Safe Haven at the University of Hull.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2025.102778.

Data Availability

Our data-sharing agreement stipulates that they cannot be shared with any third party.

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