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Geographic, socioeconomic and demographic inequalities in the incidence of metastatic prostate cancer at time of diagnosis in England: a population-based evaluation

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ABSTRACT

Objective To evaluate the area-based incidence of metastatic prostate cancer at diagnosis, reflecting the risk of late-stage diagnosis, and overall prostate cancer incidence, reflecting the risk of over-diagnosis, in a country without a formal screening programme.

Methods and analysis National study of annual prostate cancer incidence between 2015 and 2019. Mixed-effects regression estimated area-based incidence, adjusted for age, ethnicity and socioeconomic deprivation. Linear regression assessed the association between metastatic and overall cancer incidence.

Results National annual incidence of metastatic prostate cancer was 5.7 per 10 000 men and overall incidence was 43.9. Higher incidence of both metastatic and overall cancer were observed in areas with older populations and with more men with black ethnicity (both p<0.0001). Greater socioeconomic deprivation was linked to higher metastatic but lower overall cancer incidence (p<0.0001). Metastatic incidence varied across the country from 4.0 to 6.8, and prostate cancer overall from 37.9 to 50.1 per 10 000 men. Areas with higher metastatic cancer incidence had lower overall cancer incidence (p<0.0001).

Conclusions There is significant geographic variation in metastatic prostate cancer incidence at diagnosis, with a higher incidence of metastatic cancer observed in areas with a lower overall prostate cancer incidence and in more socioeconomically deprived neighbourhoods, which likely contributes to poorer long-term outcomes. The findings highlight the need for a targeted, risk-based diagnostic approach as well as improved diagnostic facilities and referral pathways. Further research is needed to understand the factors driving this variation in order to reduce metastatic presentations and tackle inequalities in prostate cancer outcomes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ International guidelines stress the importance of detecting prostate cancer while it is still localised and treatable. The UK currently lacks a formal prostate cancer screening programme, although some advocate for increased PSA testing. We compared the rates of metastatic prostate cancer and overall prostate cancer incidence across different geographic areas in England, defined by the 21 Cancer Alliances that coordinate cancer care within the National Health Service. We searched MEDLINE and Embase with the following terms: "national", "metastatic", "prostate cancer" and "incidence" and for publication between 1 January 1990 and 29 August 2024. No studies were found that report geographic differences in incidence rates of metastatic prostate cancer at diagnosis and overall prostate cancer, while adjusting for differences in sociodemographic characteristics.

WHAT THIS STUDY ADDS

⇒ This is the first national study that examined the association of the incidence of metastatic prostate cancer at diagnosis with the overall incidence of prostate cancer across different areas. Areas with a lower incidence of metastatic prostate cancer at diagnosis tended to have a higher incidence of prostate cancer diagnoses overall, suggesting that geographic differences in PSA testing, as well as practice patterns and diagnostic availability might be influencing these results. The study also provides evidence of socioeconomic inequality, with higher incidence of metastatic disease and lower incidence of prostate cancer overall in more deprived neighbourhoods.

INTRODUCTION

In England, around 50 000 new cases of prostate cancer are diagnosed annually, with approximately 19% of these being metastatic at initial diagnosis.[1] The 5-year overall survival rate of men diagnosed with localised prostate cancer is reported to be 95%, but it is only 50% for men diagnosed with metastatic disease.[2] Metastatic prostate cancer is

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Geographic and sociodemographic inequalities in cancer diagnosis exist for prostate cancer, affecting long-term outcomes. Our findings highlight the importance of a targeted, risk-based diagnostic strategy alongside enhanced diagnostic facilities and referral pathways. Additional research is essential to understand the factors behind this variation, reduce metastatic diagnoses and address inequalities in prostate cancer outcomes.

associated with significant morbidity, including complications from locoregional and metastatic progression, and the toxicities of lifelong systemic treatment,[3 4] which, collectively, incur high healthcare costs.[5]

International guidelines highlight the importance of detecting prostate cancer at a stage when it is still locally confined and potentially curable.[6–9] These guidelines highlight that the risk of men being diagnosed with metastatic prostate cancer increases with their age, level of socioeconomic deprivation and having a minority-ethnic background. However, this risk will also depend strongly on screening and early detection practices. Currently, the UK does not recommend a formal screening programme for prostate cancer,[10 11] although independent research organisations and patient advocacy groups argue for increased prostate-specific antigen (PSA) testing.[12 13]

This national population-based study compares the incidence of metastatic prostate cancer at diagnosis and the incidence of prostate cancer overall across geographic areas in England, defined by the boundaries of the 21 Cancer Alliances, within which cancer care pathways in the National Health Service (NHS) are regionally coordinated.[14] The study uses national cancer registry data and area-based information on population size and characteristics. We also examined the association of the area-based incidence of metastatic prostate cancer at the time of diagnosis with the incidence of overall prostate cancer, while adjusting for differences in sociodemographic characteristics.

METHODS

Conceptual framework

We chose to study the annual area-based incidence of metastatic prostate cancer at the time of diagnosis, measured as the annual number of men diagnosed with metastatic disease divided by the number of men living in each area. This incidence measure, rather than the proportion of men diagnosed with metastatic disease in all men diagnosed with prostate cancer,[15] provides a more accurate measure of the risk of being diagnosed with metastatic prostate cancer in men living in a particular geographic area. This is because a geographic area might have a lower proportion of metastatic disease among men with newly diagnosed prostate cancer due to a higher number of men diagnosed with localised disease, a lower number diagnosed with metastatic disease or a combination of both.

Prostate cancer diagnoses

Men with newly diagnosed prostate cancer were identified from the English National Cancer Registration dataset[16] using the C61 code from the International Classification of Diseases, 10th Edition.[17] Data items from the cancer registry were used to obtain information about the tumour (T), node (N) and metastasis (M) stage of each prostate cancer.

Patients with metastatic disease at diagnosis were identified from the recorded TNM status (M1). For cases with missing M-status, validated clinical assumptions were used to impute this data[18]: if N-status was recorded but M-status was missing, the patient was assumed to be M0, as they were likely investigated for metastases with none found. Additionally, patients with T1/T2 disease were also classified as M0 due to the low likelihood of metastatic disease.

We identified men with prostate cancer diagnoses aged between 50 and 90 years from 1 January 2015 to 31 December 2019. This period was chosen as it was the most recent before the COVID-19 pandemic: this provided sufficient numbers of events to estimate annual incidence rates accurately.

Population data

Population data for England in 2017 were used as it was midway through the 5-year inclusion period.[19] The smallest geographic area used was the postcode-based lower-layer super output area (LSOA), of which there are about 34 000 in England, each including about 1600 people or 650 households.[20] We refer to these LSOAs as 'neighbourhoods.

For each LSOA, the number of people in defined age and sex categories and the reported proportion of the population within defined ethnic categories are publicly available.[19] LSOAs were also ranked by socioeconomic deprivation using the Index of Multiple Deprivation (IMD).[21] We collated these data for the male population aged between 50 and 90 years and grouped age in four 10-year categories. Ethnicity was classified as 'white', 'Asian (including Chinese and Indian)', 'black' and 'other (including missing)'. Socioeconomic deprivation levels were divided into quintiles of the national distribution of the LSOAs' IMD rankings (IMD 1 to IMD 5: 1=least deprived; 5=most deprived).[22] Each patient was assigned to an LSOA based on their residence at the time of the prostate cancer diagnosis. LSOAs were categorised as rural, urban or part of an urban conurbation, by the Office of National Statistics.[22] Cancer Alliances in England are 21 geographic regions, where cancer care pathways within the NHS are regionally coordinated.

Statistical methods

The national annual incidence of prostate cancer overall and the incidence of metastatic prostate cancer at diagnosis was calculated by dividing the number of cases from

1 January 2015 to 31 December 2019 by five times the mid-year population in 2017.

Mixed-effects logistic regression models with geographic area (Cancer Alliance) as a random effect were used to estimate the national annual incidence from an unadjusted model and to calculate empirical-Bayes estimates of the age-adjusted annual incidence for each of 21 geographic areas, also adjusting for ethnicity and socioeconomic deprivation by including these variables as fixed effects in the model.

Mixed-effects models were used rather than spatial correlation models: Cancer Alliances were created in England to coordinate service provision in geographic areas, and mixed-effects models recognise this grouping. The Alliances cover large geographic areas and function independently of one another. Consequently, we assumed that there is no a priori reason to expect one Alliance to affect the performance of its neighbours.

The logistic models used the population in each of four age groups of an LSOA as the denominator, and the number of cases with prostate cancer or metastatic prostate cancer in that LSOA's age group as the numerator. An example of the data structure is provided in online supplemental appendix table 3. Each LSOA has eight rows of data, two for each age group.

We estimated 99.8% credibility intervals for the empirical-Bayes estimate of the annual incidence in each of the geographic areas and 95% CIs for ORs estimating the associations between annual incidence and the adjustment variables. Analyses were performed using Stata V.17[23] and maps were generated with QGIS.[24]

To investigate the association between metastatic incidence and all incidence at Cancer Alliance level, we used linear regression with empirical-Bayes estimates of metastatic incidence in each geographic area as the dependent variable and all incidence as the independent variable, weighting according to population size in each area.

Sensitivity analysis

The ethnic proportion of each LSOA population is assumed to be the same across the four age groups. A sensitivity analysis to check the impact of this assumption was carried out by modifying the proportions of the black population in each of the four age groups in such a way that black ethnicity was more prevalent in the youngest and less prevalent in the oldest age group. Further details of this sensitivity analysis can be found in online supplemental appendix table 4.

Patient involvement

The National Prostate Cancer Audit's Patient and Public Involvement Forum provided advisory support informing the conceptualisation and the design for this study, and their comments contributed to the interpretation of the results.[25]

RESULTS

Description of the cohort

Between 1 January 2015 and 31 December 2019, 212 507 men aged between 50 and 90 years were newly diagnosed with prostate cancer in England. Their sociodemographic characteristics and those of men diagnosed with metastatic prostate cancer at the time of initial diagnosis are summarised in table 1. With a mid-year population size in 2017 of the number of men aged 50—90 years of 9 679 729,[19] the national annual incidence of prostate cancer was 43.9 cases per 10 000 men. Among these, 28 558 men were diagnosed with metastatic prostate cancer at diagnosis, giving a national annual incidence of 5.7 cases per 10 000 men. This is a slight underestimate of the risk of being diagnosed with metastatic cancer because the metastatic status of 18 294 of the 212 507 patients diagnosed with prostate cancer (8.6%) could not be determined. Of the 165 655 M0 patients, 15 524 had missing M status but were classified as M0 using their T and N status and our clinical assumption rules.

Patient demographic and prostate cancer incidence

The populations in the geographic areas differed in terms of age, ethnicity, socioeconomic deprivation and rurality. The areas covering the London conurbation included younger populations while areas in the south, the southwest, the east and the north had older populations (online supplemental table 1). The areas covering the London conurbation also had the most ethnically diverse populations and several of these areas had relatively large Asian populations. Socioeconomic deprivation was highest in areas in the north and lowest in areas covering the west of the London conurbation.

Table 2 shows that a higher level of socioeconomic deprivation was associated with a higher incidence of metastatic disease at diagnosis (OR 1.11, 95% CI 1.02 to 1.20, for men living in the most deprived quintile of neighbourhoods, compared with those living in the least deprived quintile), but this was associated with a lower incidence of prostate cancer overall (corresponding OR 0.81, 95% CI 0.78 to 0.83). This table also demonstrates that the inverse relationship of metastatic prostate cancer and overall prostate cancer incidence was not seen for age or ethnicity: older age and a black ethnic background were associated with both a higher incidence of metastatic prostate cancer and a higher incidence of overall prostate cancer.

The association with rurality was less clear, with some evidence that overall prostate cancer diagnosis rates were lower in urban cities and towns than in either urban conurbations or rural areas, but with no significant association between rurality and metastatic disease at the time of diagnosis.

Area-based incidence of metastatic prostate cancer and overall prostate cancer

There was considerable geographic variation in the annual incidence of metastatic prostate cancer after

Table 1 Sociodemographic characteristics of men aged between 50 and 90 years diagnosed with metastatic prostate cancer and overall prostate cancer in England between 2015 and 2019

		Metastatic prostate cancer		Overall prostate cancer		Missing metastatic status	
		N=28 558	(100%)	N=212 507	(100%)	N=18 294**	(100%)
Age group (years)	50–59	1696	(5.9%)	24 897	(11.7%)	1528	(8.4%)
	60–69	6517	(22.8%)	70 413	(33.1%)	3723	(20.4%)
	70–79	11 149	(39.0%)	82 543	(38.8%)	5727	(31.3%)
	80–90	9196	(32.2%)	34 654	(16.3%)	7316	(40.0%)
Ethnic background	White	25 476	(94.5%)	183 190	(92.8%)	14 875	(92.6%)
	Asian	390	(1.5%)	3749	(1.9%)	366	(2.3%)
	Black	687	(2.6%)	6904	(3.5%)	535	(3.3%)
	Other	414	(1.5%)	3473	(1.8%)	290	(1.8%)
	Missing	1591		15 191		2228	
Socioeconomic deprivation (neighbourhood quintiles)††	1 (least deprived)	6285	(22.0%)	52 830	(24.9%)	4934	(27.0%)
	2	6585	(23.1%)	51 611	(24.3%)	4362	(23.8%)
	3	6116	(21.4%)	44 586	(21.0%)	3847	(21.0%)
	4	5075	(17.8%)	35 493	(16.7%)	3060	(16.7%)
	5 (most deprived)	4497	(15.8%)	27 987	(13.2%)	2091	(11.4%)
Rurality	Urban	12 961	(45.4%)	92 966	(43.8%)	7888	(43.1%)
	Conurbation	8763	(30.7%)	67 148	(31.6%)	6055	(33.1%)
	Rural	6834	(23.9%)	52 393	(24.7%)	4351	(23.8%)

*Not including 15 524 patients who had missing M status imputed from T and N status.
†Quintiles of the national distribution of the Multiple Index of Deprivation in neighbourhoods defined according to lower super output areas (see the Methods section).

adjustment for age, ethnicity and socioeconomic deprivation (figure 1A). The highest incidence was observed in an area in the southwest (annual incidence 6.84, 99.8% credibility interval 6.29 to 7.44, per 10 000 men) and the lowest in an area in the London conurbation (4.02, 3.45 to 4.69, per 10 000 men) (table 3, figure 1A and online supplemental table 2). There was also considerable geographic variation in the adjusted incidence of overall prostate cancer (figure 1B) with the highest adjusted annual incidence seen in an area in the London conurbation (50.1, 47.9 to 52.4, per 10 000 men) and the lowest in an area in the north east (37.9, 36.8 to 39.1, per 10 000 men). The variation between Cancer Alliances in both metastatic incidence and overall incidence is more than expected from the random-effect component of the adjusted mixed models (table 2), indicating the existence of systematic underlying differences.

Figure 2 demonstrates an inverse association between the annual incidence of metastatic prostate cancer and the annual incidence of overall prostate cancer in the 21 geographic areas (p<0.0001). The regression line shows that in an area where the incidence of overall prostate cancer is 10 per 10 000 men higher, the corresponding incidence of metastatic prostate cancer would be approximately 1 per 10 000 men lower (−0.919, 95% CI −0.920 to −0.918, p<0.0001).

Sensitivity analysis

The results of the sensitivity analysis are presented in online supplemental appendix table 4. They show that modifying the proportions of the population with black ethnicity in such a way that black ethnicity is more prevalent in the younger age groups had minimal impact on the ORs for ethnicity.

DISCUSSION

This study reveals significant geographic variation in the annual incidence of prostate cancer that is metastatic at the time of diagnosis in England. The highest area-based annual incidence (7 per 10 000 men) was more than 60% higher than the lowest incidence (around 4 per 10 000 men). It is important to note that areas with a higher incidence of metastatic prostate cancer at diagnosis typically had a lower incidence of prostate cancer diagnosed overall. It is unlikely that this geographic variation is due to differences in population characteristics because the incidence estimates were adjusted for age, ethnicity and

Table 2 Association between sociodemographic characteristics and incidence of metastatic prostate cancer and overall prostate cancer

		Metastatic prostate cancer		Overall prostate cancer	
		OR (95% CI)	P value	OR (95% CI)	P value
Age group (years)	50–59	1	<0.0001	1	<0.0001
	60–69	4.82 (4.50 to 5.16)		3.61 (3.49 to 3.74)	
	70–79	11.29 (10.58 to 12.05)		5.80 (5.55 to 6.07)	
	80–90	17.98 (16.66 to 19.40)		4.66 (4.40 to 4.94)	
Ethnic background (percentage of neighbourhood population: see the Methods section)*	Asian	0.97 (0.94 to 0.99)	0.002	0.96 (0.95 to 0.97)	<0.0001
	Black	1.11 (1.08 to 1.14)	<0.0001	1.12 (1.08 to 1.17)	<0.0001
	Other	0.97 (0.88 to 1.06)	0.456	0.95 (0.91 to 0.99)	0.017
Socioeconomic deprivation (neighbour quintile)†	1 (least deprived)	1	=0.0001	1	<0.0001
	2	1.06 (1.01 to 1.12)		0.96 (0.94 to 0.97)	
	3	1.06 (1.00 to 1.12)		0.92 (0.91 to 0.94)	
	4	1.07 (1.00 to 1.14)		0.88 (0.85 to 0.91)	
	5 (most deprived)	1.11 (1.02 to 1.20)		0.81 (0.78 to 0.83)	
Rurality	Urban	1	0.544	1	<0.0001
	Conurbation	0.98 (0.91 to 1.05)		1.04 (0.99 to 1.09)	
	Rural	0.99 (0.95 to 1.04)		1.05 (1.03 to 1.08)	
Random effect (Cancer Alliance)		Coefficient	(95% CI)	Coefficient	(95% CI)
Variance (constant)		0.018	(0.007 to 0.050)	0.006	(0.003 to 0.010)

Mixed-effects multivariable logistic regression models for metastatic and all prostate cancer (separate models), with Cancer Alliance as a random effect.
*ORs shown are the estimated change in prostate cancer incidence associated with a 10% increase in ethnic background of the population.
†Index of Multiple Deprivation neighbourhood quintile.

socioeconomic deprivation. Given the high mortality rate associated with metastatic prostate cancer,[26] these findings suggest geographic inequalities in prostate cancer mortality in the future.

Another key study outcome is the different pattern of association between metastatic prostate cancer and overall prostate cancer incidence according to socioeconomic deprivation on the one hand and according to age and ethnicity on the other. Areas with higher socioeconomic deprivation had a higher incidence of metastatic cancer but a lower overall prostate cancer incidence, whereas older age and a black ethnic background were associated with both a higher incidence of metastatic prostate cancer and a higher incidence of overall prostate cancer. These results suggest a similar interpretation for both the observed geographic and the socioeconomic variation.

The reasons for the geographic, socioeconomic and demographic variation in the annual incidence rates of metastatic prostate cancer and overall prostate cancer are complex, but it is likely that they are linked, at least in part, to variation in the opportunistic use of PSA testing and other early detection methods.[27 28] Lower rates of PSA testing may decrease overall prostate cancer incidence and detect cancer at later stages, as observed in the US following directives that limited access to PSA testing.[29 30] However, higher rates of PSA testing, particularly in those who are asymptomatic and without a family history of prostate cancer, can lead to overdiagnosis and overtreatment, with minimal clinical benefits but higher treatment risks.[31 32] Other factors that may contribute to the variation in metastatic and overall prostate cancer incidence include differences in access to and quality of healthcare provision,[33] differences in potential risk factors (such as a family history of prostate cancer), prevalence of comorbidities that can mask symptoms and health behaviours,[34–36] health literacy[37 38] as well as delays

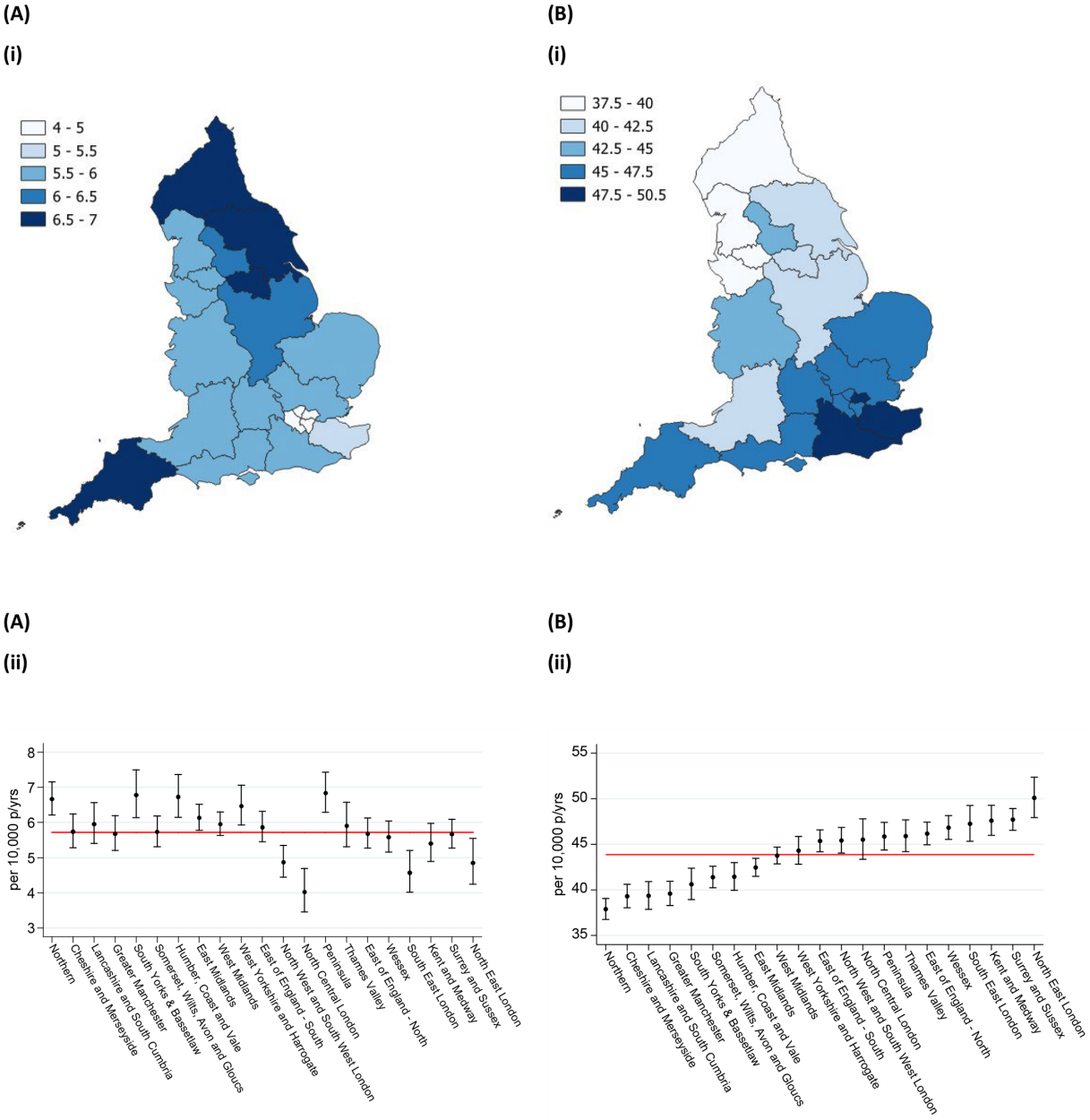

Figure 1 Adjusted annual incidence of metastatic prostate cancer (A) and prostate cancer overall (B) at time of diagnosis in 21 geographic areas ('Cancer Alliances') between 2015 and 2019. (i) Map of England with geographic areas colour-coded according to annual incidence categories. (ii) Annual incidence estimates (99.8% credibility intervals), adjusted for neighbourhood-based measures of ethnicity and socioeconomic deprivation (see the Methods section).

in seeking care due to sociocultural beliefs or financial constraints.[39] In addition, despite adjusting for age, ethnicity and socioeconomic deprivation in our study, it cannot be excluded that residual confounding explains some of the association of these factors with the variation in metastatic and overall cancer incidence.

In many high-income countries, there is ongoing debate about the clinical and cost-effectiveness of formal prostate cancer screening programmes.[40–42] In the UK, there is no national prostate formal cancer screening programme,[10] although organisations, such as NHS England and Prostate Cancer UK, a major patient and research charity, are promoting risk assessment and PSA testing for men aged between 50 years and 70 years old and for those at higher risk due to family history or ethnic background.[43] A recent clinical guideline, developed in the UK following an explicit consensus method, recommends proactive approaches to testing in higher-than-average risk groups.[44] However, evidence suggests that cancer screening programmes, for example, in colorectal cancer, do not necessarily eliminate social and geographic inequalities.[45 46]

Our results could serve as a prompt to revisit current national prostate cancer detection strategies. Recommendations against a formal screening programme using relatively low PSA thresholds are often based on studies from

Table 3 Annual incidence* of metastatic prostate cancer and overall prostate cancer by geographic area ('Cancer Alliance')

		Metastatic prostate cancer at diagnosis		Overall prostate cancer diagnosis	
NHS Region	Cancer Alliance	Rate*	99.8% CI	Rate*	99.8% CI
East of England	East of England—North	5.68	(5.27, 6.12)	46.2	(45.0, 47.4)
	East of England—South	5.87	(5.45, 6.32)	45.4	(44.2, 46.6)
London	North Central London	4.02	(3.45, 4.69)	45.5	(43.4, 47.8)
	NE London	4.85	(4.24, 5.55)	50.1	(47.9, 52.4)
	NW and SW London	4.87	(4.44, 5.34)	45.4	(44.0, 46.9)
	SE London	4.57	(4.01, 5.20)	47.3	(45.3, 49.3)
Midlands	East Midlands	6.14	(5.77, 6.52)	42.5	(41.5, 43.5)
	West Midlands	5.95	(5.63, 6.30)	43.8	(42.9, 44.7)
North East and Yorkshire	Humber, Coast and Vale	6.73	(6.15, 7.37)	41.4	(40.0, 43.0)
	Northern	6.67	(6.21, 7.16)	37.9	(36.8, 39.1)
	Yorkshire and Bassetlaw	6.79	(6.14, 7.50)	40.6	(38.9, 42.4)
	Yorkshire and Harrogate	6.47	(5.93, 7.06)	44.3	(42.8, 45.9)
North West	Cheshire and Merseyside	5.74	(5.28, 6.24)	39.3	(38.0, 40.6)
	Greater Manchester	5.68	(5.21, 6.19)	39.6	(38.3, 40.9)
	Lancashire and South Cumbria	5.95	(5.40, 6.56)	39.4	(37.9, 40.9)
South East	Kent and Medway	5.40	(4.89, 5.97)	47.6	(46.0, 49.3)
	Surrey and Sussex	5.67	(5.27, 6.09)	47.7	(46.5, 48.9)
	Thames Valley	5.91	(5.31, 6.57)	45.9	(44.2, 47.7)
	Wessex	5.58	(5.16, 6.05)	46.8	(45.5, 48.2)
South West	Peninsula	6.84	(6.29, 7.44)	45.9	(44.4, 47.4)
	Somerset, Wilts, Avon and Gloucs	5.73	(5.31, 6.19)	41.4	(40.2, 42.6)
England		5.72		43.9	

*Empirical Bayes estimates per 10 000 men, adjusted for age, neighbourhood-based measures of ethnicity and socioeconomic deprivation (see the Methods section).

more than two decades ago.[47–49] It is likely that ongoing advancements in MRI, active surveillance approaches for low-risk and some intermediate-risk cancers, potential revisiting of critical PSA thresholds for investigation and improved surgical and oncological treatments have enhanced benefits of radical treatment while reducing side effects. Recent calls for a national comprehensive risk-based prostate cancer detection programme[42] are supported by our findings. The new £42 million prostate cancer screening study in the UK will provide much-needed updated evidence on screening strategies,[50] but it may take years before this study can influence policy.

A limitation of our study is the lack of cancer stage information for nearly 9% of patients, potentially leading to an underestimation of metastatic prostate cancer incidence. Also, because the incidence of overall prostate cancer is the sum of the incidences of localised and metastatic prostate cancer, one would expect a direct association between the incidence of overall prostate cancer and the incidence of metastatic prostate cancer, even if the incidences of localised and metastatic prostate cancer are uncorrelated. However, we found an inverse association between the incidence of metastatic prostate cancer and the incidence of prostate cancer, which only strengthens our interpretation that more intensive risk-based diagnostic approaches may reduce the incidence of metastatic disease. By using population data on age and ethnicity, we had to assume that within each neighbourhood the ethnic breakdown was the same in each age group, which could introduce a small degree of error in estimating the association between prostate cancer incidence and ethnicity. However, given the high level of data granularity—covering approximately 34 000 neighbourhoods in England—any resulting bias is likely to be very small, which was confirmed by a sensitivity analysis where we made black ethnicity more prevalent in the younger age groups. Another limitation of the study is the assumption that incidences within Cancer Alliances are independent or, in other words, that there is no 'spill-over effect' between neighbouring Alliances. While this assumption is

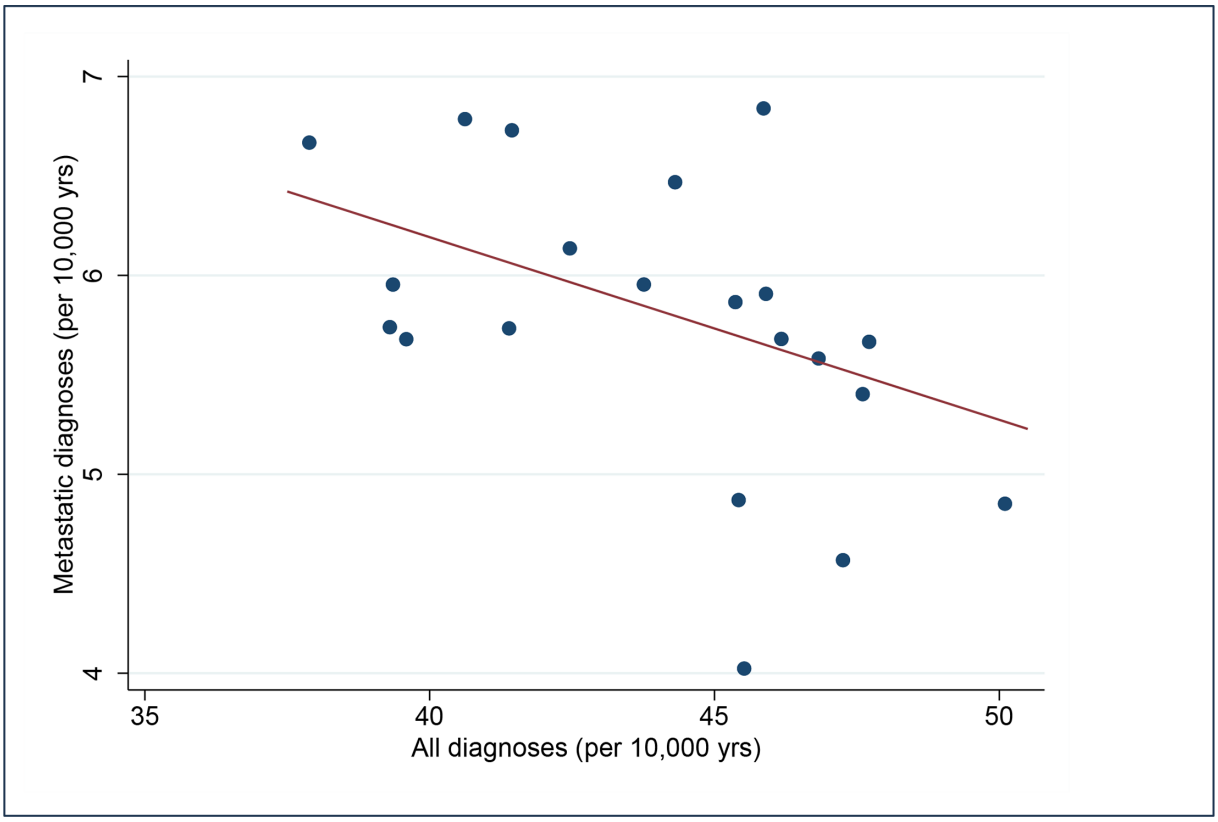

Figure 2 Association between the annual incidence of prostate cancer metastatic at the time of diagnosis and the incidence of prostate cancer overall incidence, adjusted for neighbourhood-based measures of ethnicity and socioeconomic deprivation (per 10 000 men). The figure shows results for 21 geographic areas ('Cancer Alliances'), with fitted line from linear regression model weighted according to population size (p<0.0001).

based on the clear organisational structure of cancer care within defined regional areas, there may still be some effect from cross-border working around the margins of the Alliances.

In conclusion, there is significant geographic variation in the incidence of metastatic prostate cancer at the time of diagnosis, likely leading to poorer long-term outcomes for prostate cancer patients in certain areas. Higher rates of metastatic prostate cancer at diagnosis are observed in regions with a lower overall incidence of prostate cancer. A similar pattern of results is seen among men living in more socioeconomically deprived neighbourhoods. Our results emphasise the need for the strengthening of diagnostic facilities and referral pathways, while awaiting the mortality results of ongoing prostate cancer screening studies that may need at least ten years to report. Furthermore, additional research is crucial to better understand the complex factors driving the variation in the incidence of metastatic prostate cancer, such as patient risk factors, comorbidities, health-seeking behaviours, health literacy and sociocultural beliefs. This would inform the redesign of current detection strategies in the UK, as well as in other countries that currently do not have a formal screening strategy, in order to reduce geographic and socioeconomic variation in the incidence of metastatic presentation and tackle inequalities in long-term prostate cancer outcomes.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study was conducted as part of the National Prostate Cancer Audit (NPCA) which has established regulatory approval, data security and governance procedures. Given that this research involves the use of anonymised secondary data, UK National Research Ethics Committee approval has not been sought in accordance with their guidelines. The study was performed in accordance with the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Data are available from the Data Access Request Service, NHS England (https://digital.nhs.uk/services/data-access-request-service-dars).

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