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Impact of cancer service centralisation on the radical treatment of men with high-risk and locally advanced prostate cancer: A national cross-sectional analysis in England

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In many countries, specialist cancer services are centralised to improve outcomes. We explored how centralisation affects the radical treatment of high-risk and locally advanced prostate cancer in the English NHS. 79,085 patients diagnosed with high-risk and locally advanced prostate cancer in England (April 2014 to March 2016) were identified in the National Prostate Cancer Audit database. Poisson models were used to estimate risk ratios (RR) for undergoing radical treatment by whether men were diagnosed at a regional co-ordinating centre ('hub'), for having surgery by the presence of surgical services on-site, and for receiving high dose-rate brachytherapy (HDR-BT) in addition to external beam radiotherapy by its regional availability. Men were equally likely to receive radical treatment, irrespective of whether they were diagnosed in a hub (RR 0.99, 95% CI 0.91–1.08). Men were more likely to have surgery if they were diagnosed at a hospital with surgical services on site (RR 1.24, 1.10–1.40), and more likely to receive additional HDR-BT if they were diagnosed at a hospital with direct regional access to this service (RR 6.16, 2.94–12.92). Centralisation of specialist cancer services does not affect whether men receive radical treatment, but it does affect treatment modality. Centralisation may have a negative impact on access to specific treatment modalities.

Introduction

Approximately one third of all men with a new diagnosis of prostate cancer in England have locally advanced disease.[1] These men have a high risk of disease progression and cancer-related mortality, highlighting the importance of radical treatment in this group.[2,3] Contemporary data from the National Prostate Cancer Audit (NPCA) suggest that 27% of men with high-risk or locally advanced prostate cancer do not receive radical treatment with surgery or radiotherapy.[4] According to the NPCA[1] and the National Institute for Health and Care Excellence[5] risk stratification, high-risk localised disease is classified in the same group as 'locally advanced' disease.

There is a clear survival benefit for the combination of external beam radiation therapy (EBRT) and androgen deprivation

Key words: prostate cancer, under-treatment, centralisation, inequity, access
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What's new?

More than one-quarter of men with high-risk or locally advanced prostate cancer in England do not receive radical treatment with radiotherapy or surgery, potentially owing to differences in treatment access. Here, prostate cancer service centralisation in England was investigated for potential impacts on treatment access. Among English patients in the National Prostate Cancer Audit database, centralisation had no impact on decisions to use radical treatment. It did, however, affect treatment option availability, with potential consequences for patient outcome. Patients were more likely to undergo surgery or high dose-rate brachytherapy when diagnosed at hospitals with direct links to these services.

therapy (ADT), over either treatment alone, and this combination is a standard of care for men with locally advanced prostate cancer.[6–8] Current UK National Institute for Health and Care Excellence (NICE) guidelines (2014) and European Association of Urology (EAU) guidelines (2017) also recommend combining high-dose rate brachytherapy (HDR-BT) with EBRT, for suitable men with high-risk prostate cancer.[5,9] Recently reported observational data are now beginning to favour combination therapy in terms of disease progression and mortality but utilisation of this treatment strategy has not been previously reported in England.[10]

Radical prostatectomy (RP) has historically been reserved for clinically localised disease but there is increasing evidence that it has a positive effect in high-risk men, and even in more advanced cases.[11] It is currently used in 22% of men with high-risk or locally advanced patients in England (2015/16).[4] Optimal use of RP as part of a multimodal approach is yet to be established but current guidelines advocate its use for selected patients.[12]

For over a decade, specialist radiotherapy and radical prostatectomy services for prostate cancer have been centralised in England, which has restricted the number of centres providing these specialist services and in turn increased the centres' average volume of procedures. The rationale for this centralisation is to optimise the quality of care men receive and to improve patient outcomes by focussing treatment in high-volume centres.[13,14] To co-ordinate access to these specialist services 48 specialist Multi-Disciplinary Teams (MDT) were set up across England. Each specialist MDT is made up of a regional referral network of hospitals within a specific geographical area of the country. Hospitals assigned as the lead of each regional referral network, or 'hub' site, act as regional co-ordinating centres. Each hub is usually a specialist centre for either radiotherapy, surgery or both and the other hospitals within the network act as 'spoke' hospitals. Most spoke hospitals are non-specialist centres and therefore have to refer to specialist centres for radical treatment, but a few provide one or more treatment modalities on-site.

The NPCA collected information regarding the organisation of prostate cancer services for each regional referral network and the specialist treatment services available on-site at each hospital.[15] Between April 2014 and March 2016, 138 hospitals in the English National Health Service (NHS) provided diagnostic facilities for prostate cancer, of which 53 were specialist surgical centres, 51 were specialist radiotherapy centres and 19 were specialist HDR-BT centres. Access to radiotherapy and surgical centres is available to every hospital within England *via* one of the 48 regional referral networks, however HDR-BT services are only available to hospitals within 24 of these regions, either directly or externally *via* a neighbouring regional referral network. HDR-BT has therefore become a super-specialised treatment modality within the complex, centralised system for prostate cancer care in England.

The hub-and-spoke model for prostate cancer care aims to improve outcomes while aiming to guarantee appropriate access, irrespective of the hospital where a patient is diagnosed. Despite this, studies have started to emerge highlighting that this centralisation process has led to an inequity of access to surgery in the treatment of other cancers, such as lung cancer and liver metastases in colorectal cancer.[15–17]

We therefore aim to assess whether cancer service centralisation impacts on the access to radical treatment, or on the specific type of radical treatment that men with high-risk and locally advanced prostate cancer receive in the English NHS.

Materials and Methods

Study population

The NPCA is a national clinical audit assessing the quality of services and care provided to men with prostate cancer in England and Wales. The NPCA has been reporting about the treatment and outcomes of all patients newly diagnosed with prostate cancer since April 2014.

All patients newly diagnosed with prostate cancer between April 1st 2014 and March 31st 2016 were identified in the NPCA database. This database includes relevant data items from the English Cancer Registry and data items specific to the NPCA, both supplied by Public Health England's National Cancer Registration and Analysis Service (NCRAS). Disease status was assigned according to a risk stratification algorithm previously described by the NPCA[1], and based on the NICE criteria[5], which uses NPCA data items for each cancer characteristic (Gleason score, PSA and TNM). TNM data used preferentially clinical cancer registry items and then pathological cancer registry items, in line with the Union for International Cancer Control (UICC) TNM 7th edition, taking staging information that was updated as much as possible by cancer registry staff. Gleason scores were based on prostate biopsy information. The patient cohort was restricted only to men with non-metastatic, high-risk or locally advanced disease

defined as any one of: Gleason score ≥ 8, PSA > 20 ng/mL or T3/T4 (±N1).

The NPCA database was linked at patient-level with two routine databases. Hospital Episode Statistics (HES) is a database of all hospital admissions in the English NHS and is a source of surgery-specific information about operation type and date.[18] The National Radiotherapy Data Set (RTDS) is a national database that contains standardised data from all NHS hospital providers of radiotherapy services in England.[19] 1495 men without a documented diagnosing hospital were excluded.

Baseline characteristics

English Cancer Registry data was used to identify the diagnosing hospital, the date of diagnosis, cancer characteristics, ethnicity and age at diagnosis for each man. Cancer characteristics were used for stratifying disease status but also to provide baseline information.

The Royal College of Surgeons (RCS) Charlson score was used to identify co-morbid conditions in the HES record based on co-morbidities that were recorded one year before a patient's prostate cancer diagnosis.[20] The Index of Multiple Deprivation (IMD) was used to categorise patients into five socioeconomic groups (1 = least deprived; 5 = most deprived) based on the areas in which they lived. The IMD ranks 32,482 areas, and each area covers a mean population of around 1500 people or 400 households. The five categories were fifths of the national IMD ranking of these areas.[21]

Outcome variables

The OPCS Classification of Interventions and Procedures (OPCS-4) code 'M61' was used to identify the men in the HES record who underwent an RP and the date of their operation.[22] The RTDS data item 'treatment modality' was used to select men who underwent EBRT and/or brachytherapy and the date of their treatment. Brachytherapy dosing information was used to identify the men who received HDR-BT.

Three binary outcome measures were used. The first was whether men with high-risk or locally advanced prostate cancer received any radical treatment (EBRT, brachytherapy, RP or a combination) within one year of diagnosis. The second was whether surgery was selected for the men who received radical treatment. The third was whether HDR-BT was provided for the men who received radiotherapy. Radical treatment was defined as the first treatment selected and therefore men receiving additional salvage treatment were included within the group according to their primary treatment.

Exposure variables

One key aim of the NPCA was to assess the configuration and availability of specialist prostate cancer services in England. In 2014, the NPCA undertook an organisational survey of all NHS hospitals across England. Questionnaires established the availability and location of core diagnostic, treatment and support services for the management of non-metastatic prostate cancer. The survey was updated in December 2016 to reflect changing service organisation.

This organisational survey was used to provide information about available services at each hospital with regards to RP, EBRT and HDR-BT, as well as other services. Binary variables were created to express the hub or spoke status of each diagnosing hospital, the provision of RP services on-site at each diagnosing hospital, and the availability of HDR-BT services in each regional referral network. These three variables were the main exposure variables for our study.

Statistical analysis

Multivariable multilevel Poisson regression, with robust standard errors, was used to estimate the risk ratio of receiving radical treatment by whether men were diagnosed at a hub or spoke hospital, adjusted for age, ethnicity, socioeconomic deprivation status, Charlson score, T-stage, N-stage, Gleason score and PSA value.[23] A random intercept was modelled for each hospital to adjust for clustering within hospitals.[24]

A second regression model was performed for a cohort of men who received radical treatment to estimate the likelihood of receiving RP according to whether surgery was available on-site at the diagnosing hospital. A final regression model was performed for a cohort of men who received radiotherapy to estimate the likelihood of receiving HDR-BT according to whether these services were regionally available.

Missing data for ethnicity (6.6%), Charlson score (8.0%), T-stage (1.6%), N-stage (6.7%), Gleason score (26.3%) and PSA (19.9%) were imputed with statistical imputation using chained equations to create ten data sets. Rubin's rules were then used to combine the risk ratios across all ten data sets.

Results

79,085 newly diagnosed patients were identified from the NPCA database between April 1st 2014 and March 31st 2016. 1495 men (1.9%) and 7840 men (9.9%) were excluded as there was insufficient information available to ascertain their diagnosing hospital or cancer stage, respectively. The patient cohort was further restricted to a final cohort of 27,248 men (48.8%) with high-risk or locally advanced prostate cancer (Fig. 1).

Most men (56.3%) were diagnosed at a spoke hospital (Table 1). There was no significant difference in the characteristics of those diagnosed at a hub or spoke hospital (age, ethnicity, socioeconomic deprivation status, number of co-morbidities, T stage, N stage, Gleason score and PSA).

66% of the men received radical treatment for their high-risk or locally advanced disease (Table 2). The variation between the 48 regional referral networks that co-ordinate specialist prostate cancer services ranged from 43.4% to 84.9%. Radical treatment was performed just as frequently, irrespective of whether the diagnosing hospital was a hub or a

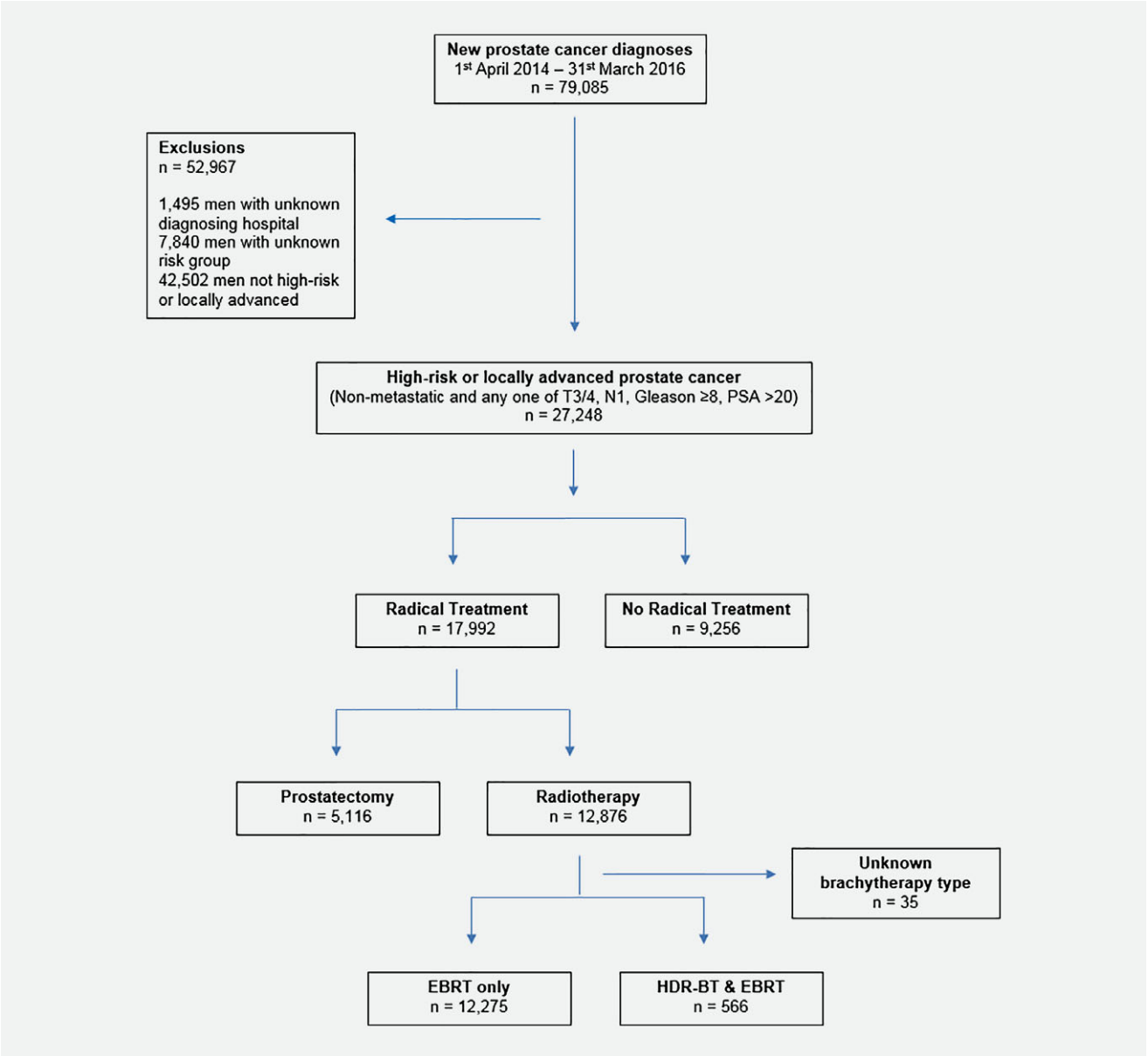

Figure 1. Flow-chart of all men with a new diagnosis of prostate cancer in England from April 1, 2014 to March 31, 2016 and how they were managed. [Color figure can be viewed at wileyonlinelibrary.com]

spoke: 8051 of 11,895 men (67.7%) who were diagnosed at a hub hospital received radical treatment, compared to 9941 of 15,353 (64.8%) who were diagnosed elsewhere (adjusted risk ratio 0.99, 95% CI 0.91 to 1.08).

Men with high-risk or locally advanced disease were less likely to receive radical treatment if they had one or more comorbidity, T1 or T4 stage, lymph node involvement, Gleason score 6, PSA >20 ng/mL, or were aged 70 years or more (p always <0.05), but there was no evidence for an association with ethnicity (Supporting Information Table 1). Although there was a trend toward decreasing socioeconomic deprivation and receipt of radical treatment, this did not reach statistical significance ($p = 0.07$).

Of the 17,992 men who received radical treatment, 5116 (28.4%) underwent surgery. RP was performed more frequently for men who were diagnosed at a hospital which provided surgical services: Of the 9199 men who were diagnosed at a hospital with these services available on-site, 2946 (32.0%) had an RP, compared to 2170 (24.7%) of the 8793 patient who were diagnosed elsewhere (adjusted risk ratio 1.24, 95% CI 1.10 to 1.40) (Table 3). Men were more likely to receive surgery as radical treatment if they had a comorbidity score ≤ 1, T2 or T3 stage, absent lymph node involvement, Gleason score ≤ 7, PSA <10 ng/mL, a lower socioeconomic deprivation score or were younger (p always <0.05). There was no evidence for an association between ethnicity and having surgery (Supporting Information Table 2).

Table 1. Patient and tumour characteristics of men with high-risk and locally advanced prostate cancer according to whether they were diagnosed at a hub or a spoke hospital.[1]

	Hub n = 11,895		Spoke n = 15,353		All men N = 27,248	
	n	%	n	%	N	%
Age group (years)						
‹65	2,571	21.6	3,038	19.8	5,609	20.6
65–70	2,703	22.7	3,333	21.7	6,036	22.2
70–75	2,625	22.1	3,287	21.4	5,912	21.7
›75	3,996	33.6	5,695	37.1	9,691	35.6
Ethnicity						
White	10,291	92.9	13,476	93.7	23,767	93.4
Black	383	3.5	419	2.9	802	3.2
Other	399	3.6	491	3.4	890	3.5
Missing	822		967		1,789	
Socioeconomic deprivation status (fifth of national distribution)						
1 (least deprived)	1,651	13.9	1,858	12.1	3,509	12.9
2	1,921	16.2	2,649	17.3	4,570	16.8
3	2,386	20.1	3,273	21.3	5,659	20.8
4	2,889	24.3	3,863	25.2	6,752	24.8
5 (most deprived)	3,048	25.6	3,710	24.2	6,758	24.8
Number of co-morbidities (RCS Charlson score)						
0	8,049	75.0	10,305	71.9	18,354	73.2
1	1,911	17.8	2,805	19.6	4,716	18.8
≥2	781	7.3	1,220	8.5	2,001	8.0
Missing	1,154		1,023		2,177	
T stage						
1	587	5.0	837	5.5	1,424	5.3
2	2,737	23.4	3,662	24.2	6,399	23.9
3	7,873	67.3	9,918	65.6	17,791	66.4
4	507	4.3	692	4.6	1,199	4.5
Missing	191		244		435	
N stage						
0	9,659	87.9	12,595	87.2	22,254	87.5
1	1,329	12.1	1,846	12.8	3,175	12.5
Missing	907		912		1,819	
Gleason score						
6	613	7.3	1,170	10.1	1,783	8.9
7	3,900	46.1	5,143	44.3	9,043	45.0
≥8	3,944	46.6	5,306	45.7	9,250	46.1
Missing	3,438		3,734		7,172	
Serum PSA (ng/mL)						
‹10	2,756	30.7	3,767	29.3	6,523	29.9
10–20	2,249	25.0	3,094	24.1	5,343	24.5
›20	3,982	44.3	5,983	46.6	9,965	45.7
Missing	2,908		2,509		5,417	

[1]Hub: hospital assigned as the lead of a regional referral network. Spoke: peripheral hospitals within the regional referral network.

35 men (5.8%) who underwent brachytherapy were excluded as there was insufficient information to differentiate between HDR-BT and low-dose rate brachytherapy (LDR-BT). Of the 12,841 men who received radiotherapy and could potentially be included, 556 (4.4%) underwent HDR-BT. HDR-BT was used more frequently in men who were diagnosed at a hospital with regional access to these services: 490 (7.7%) of the 6390 men had regional access to HDR-BT, compared to 76 (1.2%) of the 6451 men diagnosed in hospitals without regional access (adjusted risk ratio 6.16, 95% CI

Table 2. Results of Poisson regression analysis evaluating the association between the hub or spoke status of the diagnosing hospital and whether radical treatment was received for men with high-risk and locally advanced prostate cancer (n = 27,248).[1]

	Radical Treatment (%)	Adjusted RR	95% CI			P^2
Diagnosing hospital						**0.85**
Hub	67.7	1				
Spoke	64.8	0.99	0.91	-	1.08	

[1]Adjusted for age, ethnicity, socioeconomic deprivation status, RCS Charlson co-morbidity score, T stage, N stage, Gleason score, and PSA.
[2]Wald test.

Table 3. Results of Poisson regression analysis evaluating the association between the availability of surgical services on-site and whether men with high-risk and locally advanced prostate cancer who received radical treatment underwent surgery (n = 17,992).[1]

	Surgery (%)	Adjusted RR	95% CI			P^2
On-site surgery						**<0.01**
No	24.7	1				
Yes	32.0	1.24	1.10	-	1.40	

[1]Adjusted for age, ethnicity, socioeconomic deprivation status, RCS Charlson co-morbidity score, T stage, N stage, Gleason score, and PSA.
[2]Wald test.

2.94 to 12.92) (Table 4). Men were more likely to receive both HDR-BT and EBRT, over EBRT alone, if they had a co-morbidity score ≤ 1, ≤T3 stage, absent lymph node involvement, Gleason score ≤ 7, PSA 10 ng/mL to 20 ng/mL (compared to PSA >20 ng/mL), a lower socioeconomic deprivation score or were younger ($p < 0.05$ for all variables). There was no association between ethnicity or Gleason score and the receipt of HDR-BT (Supporting Information Table 3).

Discussion

The centralisation of prostate cancer services at hubs and the use of regional referral networks in England does not impact on the overall access to radical treatment for men with high-risk/locally advanced prostate cancer. However, there is variation between centres in the type of treatment selected. Men diagnosed at a hospital with surgical facilities were more likely to receive surgery than men diagnosed at a non-surgical centre. Equally, men diagnosed at a hospital where HDR-BT was regionally available were more likely to receive it.

Table 4. Results of Poisson regression analysis evaluating the association between the regional availability of high dose rate brachytherapy (HDR-BT) services and whether men with high-risk and locally advanced prostate cancer who received radical radiotherapy also received HDR-BT (n = 12,835).[1]

	HDR-BT (%)	Adjusted RR	95% CI			P^2
HDR-BT available						**<0.01**
No	1.2	1				
Yes	7.7	6.16	2.94	-	12.92	

[1]Adjusted for age, ethnicity, socioeconomic deprivation status, RCS Charlson co-morbidity score, T stage, N stage, Gleason score, and PSA.
[2]Wald test.

Treatment practices

Our data indicates that between April 2014 and March 2016, 34% of men with high-risk or locally advanced prostate cancer did not receive radical treatment and were potentially undertreated. Latest figures show that this figure continues to drop (27% in men diagnosed between April 2016 and March 2017) but in general these men represent older and more co-morbid or frail patients where radical treatment is contraindicated.[4] These observations are generally consistent with other developed countries where rates of under-treatment are reported at 32% in France (2011)[25], 41% in Germany (2004 to 2012)[26] and 15% in the US (2004 to 2013).[26,27]

EBRT remains the most common primary treatment modality in the UK for the treatment of high-risk or locally advanced prostate cancer (47% had EBRT and 19% surgery). These figures are consistent with the most recent NPCA data (2015/2016) where 49% had EBRT and 22% had surgery.[4] There is currently no clear evidence in favour of using primary RP for these cases but observations from other high-income countries indicate that RP is used more frequently for this patient group (RP 43% and EBRT 42% in the US; RP 37% and EBRT 22% in Germany).[26] Comparisons are difficult due to different inclusion criteria but contemporary figures all indicate that the use of RP in high-risk and locally advanced men is increasing, especially within a multimodal setting.[26–29]

Cancer service centralisation

Cancer services in the UK have been centralised to high-volume centres in order to improve patient outcomes.[13,14] Our data show that the hub-and-spoke model appears to be working as men are equally as likely to receive radical treatment, irrespective of the type of hospital where they were diagnosed. This is in contrast to other centres' experience in the UK and Europe with other cancer types, where service centralisation has had the opposite effect and led to a treatment inequity between hospitals.[16,17]

Data from the US have shown that high-volume centres and hospitals treating high proportions of men with newer technologies (robotic surgery or intensity-modulated radiation therapy) are more likely to treat men radically. Comparisons between the UK and the US are complex however, due to organisational differences in cancer care.[30] US arrangements are more fragmented and less centralised which allows the type of hospital to have more of an effect on the treatment

men receive. In contrast, the creation of the 48 regional referral networks in the UK currently ensures consistent access to radical treatment irrespective of hospital type. The disparity in insurance coverage in the US also contributes to the issue of under-treatment, a problem which is avoided in the UK due to the benefits of a universal healthcare system.[30,31]

Treatment selection—HDR-BT

Combining HDR-BT and EBRT for the treatment of high-risk prostate cancer improves biochemical control over EBRT alone, and it has been included in NICE guidelines since 2014.[5,32] Randomised data is lacking regarding its survival advantage, whereas observational data, including their collation in a meta-analysis, has suggested its superiority.[10,32,33] Despite the growing evidence in support of HDR-BT for high-risk disease, literature is lacking regarding the uptake and availability of this modality in the UK. Only 19 hospitals in England provide HDR-BT services and, of the 12,841 men who underwent radiotherapy in the study period, only 4.4% received multimodal treatment with HDR-BT.

Men were more likely to receive HDR-BT if they were diagnosed at a hospital where it was regionally available, indicating a huge disparity in treatment access. The US has seen declining rates of brachytherapy use, with and without EBRT, and it has been suggested that this is due to changes in referral patterns, advances with alternative therapies or the lack of adequate training.[27] These explanations highlight similarities with our findings where the availability of HDR-BT services is limited to only half of the regional referral networks in England. Expansion of HDR-BT services at other radiotherapy centres across the UK, with additional communication channels between regional referral networks, may improve access in the future.

Treatment selection—surgery

Although service centralisation does not appear to affect access to radical treatment, we have shown that men diagnosed at surgical centres were more likely to undergo radical prostatectomy than those diagnosed elsewhere. This finding was also observed in the US where patients seen at community hospitals, as opposed to high-volume academic institutions or cancer centres, were less likely to have surgery as their initial treatment.[27]

Specialty bias is well documented where physicians and surgeons tend to recommend treatments that they themselves are trained to deliver. In prostate cancer, surgeons are more likely to recommend RP than non-surgeons.[34,35] This bias can be extrapolated to sub-specialty urology whereby urologists who are sub-specialists in pelvic oncology, and work at specialist centres, may be more likely to recommend RP for higher risk men than generalists who adhere to the standard of care. Specialists may be also less risk averse to operating on more elderly patients or men with multiple co-morbidities. Although service centralisation leads to differences in treatment selection between hospitals, clearly this is a multifactorial process involving the complex interplay of patient, clinician, hospital, geographical, socioeconomic and financial factors, where all factors should be taken into account as part of the decision-making process.[35]

Strengths and limitations

Strengths of this population-based study include the high volume of patients included. Data on all men newly diagnosed with prostate cancer are collected by NCRAS and so helps to limit potential selection bias of our study cohort.

A further strength of our study is the accuracy of the routinely collected data used which has been shown to be sufficiently high to support its use for research.[36] It was not possible to differentiate between men who did not have radical treatment and those with missing treatment information. However, this misclassification is likely to be minimal, given the coding completeness, and non-differential between comparator groups, given that the primary purpose of the administrative data used is for reimbursement, and would therefore only lead to an underestimation of the effect. In addition, a validated method was used to identify co-morbidities in the HES record which aids the validity of our adjusted study estimates.[20]

Limitations include the selection bias due to the exclusion of men with an unknown diagnosing hospital (1.9%) or risk group (9.9%). However, the amount of missing data was modest in relation to the overall study size and we therefore feel that the findings remain representative. A further limitation is that because we were using available existing data there was no information on the reasons why men did not undergo radical treatment. Factors may include patient preference, path to diagnosis (PSA testing or symptomatic presentation), travel times, frailty or treatment contraindications, and without adjusting for these factors the value of the term 'under-treatment' has to be interpreted with caution. Equally there are important risk factors which are not routinely collected, such as family history, and may further influence treatment practices.

Conclusions

The centralisation of prostate cancer services does not affect the decision to treat men with high-risk or locally advanced prostate cancer radically. However, the provision of surgical services or specialist HDR-BT units at specific hospitals in England appears to cause differences in treatment selection. Discussions within regional referral networks seem to be focused on whether or not to offer radical treatment but the type of treatment selected remains left to those directly involved in the patient's management. More specifically, the limited regional availability of HDR-BT is likely to be preventing its selection in specific geographical areas of England.

To ensure patient-centred care, more attention should be given to the type of treatment men receive and ensure that all

potential options are considered when newly diagnosed men are discussed within the specialist MDT of a regional referral network. This is particularly relevant for fit, elderly patients where radical treatment may be a good option. Also, access to the HDR-BT services needs to be expanded and inter-region referral pathways established, so these services are more widely available for patients.

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Author contributions

M.G.P. designed the work, analysed and interpreted the data, drafted the article and approved the final version to be published. A.S. designed the work, analysed and interpreted the data, provided critical revision and approved the final version to be published. T.C. analysed and interpreted the data, provided critical revision and approved the final version to be published. J.N. provided critical revision and approved the final version to be published. P.C. provided critical revision and approved the final version to be published. A.A. designed the work, analysed and interpreted the data, provided critical revision and approved the final version to be published. N.W.C. provided critical revision and approved the final version to be published. H.P. provided critical revision and approved the final version to be published. J.v.d.M. designed the work, analysed and interpreted the data, contributed to the drafting of the article, and approved the final version to be published.

Ethics Approval

All patient data used is fully anonymised and is therefore exempt from UK National Research Ethics Committee (NREC) approval.

Availability of Data and Materials

The cancer registry data used for our study are based on information collected and quality assured by Public Health England's National Cancer Registration and Analysis Service (www.ncras.nhs.uk). Access to the data was facilitated by the Public Health England's Office for Data Release. Hospital Episode Statistics were made available by the NHS Health and Social Care Information Centre (© 2012; re-used with the permission of NHS Digital (www.digital.nhs.uk); all rights reserved).

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