








Are evidence-based guidelines translating into clinical practice? A national population-based study of the use of treatment intensification in metastatic hormone-sensitive prostate cancer (mHSPC) in England

Joanna Dodkins^{a,b,*} , Adrian Cook^a, Emily Mayne^a , Marina Parry^a , Matthew G. Parry^a ,
Jemma Boyle^a , Julie Nossiter^{a,b}, Thomas E. Cowling^{a,b}, Alison Tree^c, Noel Clarke^d,
Jan van der Meulen^{a,b,1}, Ajay Aggarwal^{a,b,e,1}

^a National Cancer Audit Collaborating Centre, Clinical Effectiveness Unit, Royal College of Surgeons of England, London, UK

^b Department of Health Services Research & Policy, London School of Hygiene & Tropical Medicine, London, UK

^c The Royal Marsden NHS Foundation Trust and the Institute of Cancer Research, London, UK

^d The Christie and Salford Royal NHS Trusts, Manchester, Manchester, UK

^e Guy's Cancer Centre, Guy's and St Thomas' NHS Foundation Trust, London, UK

ARTICLE INFO

Keywords:
Metastatic
Prostate
Cancer
Treatment
Intensification
Utilisation

ABSTRACT

Background and objective: International guidelines recommend treatment intensification combining docetaxel or androgen receptor pathway inhibitors with androgen deprivation therapy for metastatic hormone-sensitive prostate cancer (mHSPC). However, evidence suggests underuse in many high-income countries. This study evaluates the use of treatment intensification in the English National Health Service (NHS) and explores patient and hospital-level factors associated with variation.

Methods: All men diagnosed with mHSPC in England between January 2018 and December 2022 were identified through the national cancer registry. Treatment intensification within six months of diagnosis was assessed using hospital and systemic anti-cancer therapy data. Multilevel regression models explored associations between treatment intensification and sociodemographic factors including age, comorbidities, frailty, ethnicity, socioeconomic status, rurality, and year of diagnosis. Variation among the 47 specialist multidisciplinary teams (sMDTs), responsible for coordinating prostate cancer care in England, was also evaluated.

Key findings and limitations: Among 29,713 mHSPC patients, treatment intensification use was 39.0%. Treatment intensification use decreased with age, comorbidities, frailty, socioeconomic deprivation, and among black patients (p always < 0.05). 59.8% ($n = 9184$) of men aged 75 or younger had a record of treatment intensification, compared to only 16.8% ($n = 2404$) of men older than 75. The use of treatment intensification across sMDTs ranged from 20.3% to 53.7%, with greater variation in older patients, particularly those older than 75.

Conclusions and clinical implications: There is potential underuse of treatment intensification for mHSPC patients, particularly among older, black, and socioeconomically deprived patients. Significant variation in practice exists between specialist prostate cancer teams (sMDTs) nationally, especially in older populations, indicating that many patients may not receive optimal care.

1. Introduction

Prostate cancer represents 15% of all cancers and is the second most common cancer diagnosed worldwide in men [1,2]. Every year there are approximately 50,000 new cases of prostate cancer in England (UK

which has a population of 57 million people [3,4]. Of these, around 19% are diagnosed with metastatic disease at the time of initial diagnosis [4]. Prior to 2015, the treatment for metastatic hormone-sensitive prostate cancer (mHSPC) was androgen-deprivation therapy (ADT). Since 2015, trials have demonstrated that mHSPC patients treated with docetaxel [5,

* Correspondence to: London School of Hygiene & Tropical Medicine, UK.

E-mail address: joanna.dodkins@lshtm.ac.uk (J. Dodkins).

@joannadodkins (J. Dodkins)

¹ Joint Senior Authors.

6], or androgen receptor pathway inhibitors (ARPIs) such as enzalutamide [7,8], abiraterone [9,10] or apalutamide [11], in addition to ADT, have a significant improvement of their overall survival, compared to those treated with ADT alone.

As a consequence, international and national clinical practice guidelines now recommend intensification of ADT as first line treatment for men with mHSPC at time of diagnosis [12,13]. NICE and NHS England have issued recommendations for treatment intensification for the following: Docetaxel (January 2016) [14], Enzalutamide (June 2021) [15], Apalutamide (October 2021) [16], and Abiraterone (December 2024, currently available under an NHS England interim clinical commissioning policy while awaiting NICE guidance) [17]. Additionally, during the COVID-19 pandemic, NHS England's interim guidance permitted the use of enzalutamide or abiraterone in 2020. Emerging evidence supports the use of "triplet therapy" — combining either darolutamide [18] or abiraterone [19] with docetaxel and ADT — for the treatment of mHSPC.

Despite level 1 evidence and treatment intensification being recommended in international guidelines, a recent systematic review demonstrated that rates of treatment intensification for potentially eligible patients remain very low [20], with use varying from 9 % to 38 % across high income countries [21–25].

To get a better understanding of the factors associated with underuse of treatment intensification we used data available to the National Prostate Cancer Audit (NPCA) [26], consisting of routinely collected national data linked at patient level, covering all National Health Service (NHS) hospitals delivering prostate cancer treatments in England. The aim of this study was to identify both evidence of hospital level variation and inequalities in treatment intensification to inform interventions to improve uptake of evidence-based treatment.

2. Methods

2.1. Patient population

We identified all men diagnosed with prostate cancer in England between 1 January 2018 and 31 December 2022 using data from the English Cancer Registry, according to the International Classification of Diseases, 10th Edition (ICD-10) code for prostate cancer (C61) [27]. Data were linked to records of Hospital Episode Statistics (HES), an administrative dataset with records of all care episodes provided by NHS hospitals [28], and to the Systemic Anti-Cancer Therapy (SACT) dataset [29].

2.2. Data sources

The SACT dataset, mandatory for all NHS providers since April 2014, includes details on all systemic anti-cancer treatments delivered in inpatient, day-case and outpatient settings. We used cancer registry data, including information on tumour (T), node (N), and metastasis (M) stages, to identify patients presenting with metastatic disease at diagnosis. Those with de novo metastatic disease and no prior treatment are referred to as having mHSPC throughout the paper. We applied two validated clinical assumptions to impute missing data about the presence of metastatic disease: 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 [30].

2.3. Patient characteristics

English cancer registry data were used to determine diagnosis date, age, ethnicity and NHS hospital of diagnosis. Age (in years) was grouped into ten categories; < 50, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, ≥ 90. The Royal College of Surgeons (RCS) Charlson

score was used to identify any comorbid conditions captured in the HES record of hospital admissions within one year before diagnosis [31]. The secondary care administrative records frailty (SCARF) index was used to capture frailty according to 32 deficits that cover functional impairment, geriatric syndromes, problems with nutrition, cognition and mood, and medical comorbidities, within two years of diagnosis derived from HES [32]. Patients without a HES record within two years of their diagnosis were classified as "missing" for frailty. Frailty was grouped into four categories: fit, mild, moderate, and severe frailty.

Ethnicity was recorded using the categories of the 2021 Census and was grouped into white, Asian, black, mixed and other. Index of Multiple Deprivation (IMD) was used to measure socioeconomic deprivation based on quintiles of the national distribution of neighbourhoods (i.e. Lower Super Output Areas [33] [34]). A patient's IMD score (ranging from 1 indicating least deprived and 5 most deprived) was based on the recorded residential area at the time of diagnosis. A patient's residential area was classified as "rural" or "urban" according to a classification of the Office for National Statistics [35].

In the English NHS, hospital-level care is provided by hospital organisations ('hospital trusts'). Prostate cancer care provided by hospital trusts is coordinated within 47 specialist multidisciplinary teams (sMDTs), which are composed of one or more hospital trusts offering the full range of prostate cancer treatments in a hub and spoke model [36]. Usually there will be one main prostate cancer surgical centre and radiotherapy centre (hub) within each sMDT, with other hospitals (spokes) referring patients in for evaluation and treatment [37]. One or more Trust (hub or spoke) within the sMDT will provide SACT. Patients were assigned to a sMDT based on the diagnosing hospital trust.

2.4. Outcome variable

Patients who received treatment intensification within six months of diagnosis were identified using the SACT dataset. Relevant treatments included docetaxel or ARPIs (enzalutamide, abiraterone or apalutamide), reflecting current practice guidelines for mHSPC [38].

2.5. Statistical analysis

A multilevel multivariable logistic regression model, with sMDT at diagnosis as a random intercept, was used to estimate associations between treatment intensification and patient characteristics. The statistical significance of each characteristic was tested by a likelihood ratio test comparing nested models. Patients with missing data on either frailty or ethnicity were included using separate "missing" categories, and all other variables were complete. Since treatment intensification was commonly used (i.e. > 10 %) in some sub-groups, the results are presented as risk ratios rather than odds ratios, estimated from the regression model [39].

Funnel plots were used to graphically explore sMDT variation in the use of treatment intensification by establishing whether the sMDT variation in the proportion of patients receiving treatment intensification was greater than expected by chance alone [40]. The 46 sMDTs that had 10 or more patients eligible for treatment intensification per year were included in the funnel plots.

The intra-class correlation coefficient (ICC) quantified the variation between sMDTs according to the fully adjusted multilevel logistic regression model. The ICC is an index (ranging from 0 to 1) which represents the proportion of the total variance that is between sMDTs. The larger the value, the greater the sMDT variation.

To identify factors influencing sMDT variation, ICCs were estimated separately for subgroups based on age (≤ 75 versus > 75 years); comorbid conditions (men with 0 versus one or more comorbid conditions); socioeconomic deprivation (men in the lowest three national neighbourhood quintiles versus men in the two highest quintiles of IMD), and frailty (fit versus mild/moderate/severe frailty). Ethnicity was not explored in this way due to relatively low patient numbers in the

groups with a minority-ethnic background. We compared the ICC between strata using an independent samples *t*-test to estimate two tailed p-values, with a p-value of 0.05 considered statistically significant. All analyses were performed using Stata, StataCorp 2021, Release 17 [19].

2.6. Sensitivity analysis

A sensitivity analysis compared treatment intensification data from 2018 to 2021 captured in the SACT dataset with information from the HES and Cancer Waiting Times (CWT) datasets to ensure no treatment episodes were missed. Further detail of this validation step is in the [Methods Appendix](#).

3. Results

Between 1 January 2018 and 31 December 2022, 234,377 men were diagnosed with prostate cancer. Of these, 30,920 men (13.2 %) with missing data for cancer stage at the time of diagnosis, after imputation of missing data about metastatic disease using the clinical rules (see methodology), were excluded ([Appendix Fig. A1](#)). Of the 203,457 patients included, 29,713 (14.6 %) had mHSPC. The baseline characteristics of the patients with mHSPC are summarised in [Table 1](#).

Table 1
Distribution of patient characteristics and use of treatment intensification.

	Total		Received treatment intensification		p value	Adjusted relative risk (RR)	p value
	n = 29,713	%	n = 11,588	%			
Year					X ²	RR 95 % CI	
2018	6393	21.5	2160	33.8	< 0.001	1	< 0.001
2019	5689	19.1	1998	35.1		1.054 (0.995–1.115)	
2020	5746	19.3	2171	37.8		1.213 (1.150–1.277)	
2021	6189	20.8	2693	43.5		1.441 (1.377–1.506)	
2022	5696	19.2	2566	45.1		1.455 (1.389–1.521)	
Age (year)					< 0.001		< 0.001
< 50	146	0.5	118	80.8		1	
50–54	463	1.6	320	69.1		0.846 (0.712–0.959)	
55–59	1324	4.5	944	71.3		0.886 (0.766–0.985)	
60–64	2395	8.1	1616	67.5		0.847 (0.724–0.952)	
65–69	3857	13.0	2455	63.7		0.806 (0.679–0.917)	
70–74	5881	19.8	3150	53.6		0.688 (0.557–0.813)	
75–79	5729	19.3	2185	38.1		0.499 (0.379–0.629)	
80–84	4942	16.6	700	14.1		0.196 (0.138–0.282)	
85–89	3389	11.4	93	2.7		0.042 (0.027–0.066)	
≥ 90	1587	5.3	7	0.4		0.008 (0.003–0.018)	
Charlson score (number of comorbidities)					< 0.001		< 0.001
0	23,348	78.6	10,324	44.2		1	
1	2749	9.3	760	27.7		0.942 (0.883–1.002)	
≥ 2	3616	12.2	504	13.9		0.800 (0.737–0.865)	
Frailty (SCARF index)					< 0.001		< 0.001
Fit	14,228	47.8	7412	52.1		1	
Mild frailty	5257	17.7	2182	41.5		0.840 (0.805–0.875)	
Moderate frailty	4797	16.1	1170	24.4		0.613 (0.576–0.651)	
Severe frailty	4061	13.7	330	8.1		0.298 (0.265–0.335)	
Missing	1370	4.6	494	36.1		0.688 (0.630–0.748)	
Ethnicity					0.002		< 0.001
White	26,125	87.9	10,011	38.3		1	
Mixed	114	0.4	60	52.6		1.078 (0.820–1.356)	
Asian/Asian British	417	1.4	149	35.7		0.930 (0.791–1.080)	
Black/black British	780	2.6	313	40.1		0.761 (0.670–0.858)	
Other	326	1.1	145	44.5		0.884 (0.740–1.039)	
Missing	1951	6.6	910	46.6		1.013 (0.946–1.082)	
Socioeconomic deprivation (quintiles of national distribution of neighbourhoods)					< 0.001		< 0.001
1-least deprived	6756	22.7	2759	40.8		1	
2	6773	22.8	2684	39.6		0.952 (0.903–1.000)	
3	6279	21.1	2477	39.5		0.876 (0.829–0.924)	
4	5226	17.6	2028	38.8		0.876 (0.826–0.927)	
5-most deprived	4679	15.8	1640	35.1		0.756 (0.708–0.806)	
Rurality					< 0.001		0.071
Urban	22,370	75.3	8583	38.4		1	
Rural	7343	24.7	3005	40.9		1.038 (0.997–1.080)	

3.1. Change in use of treatment intensification over time

The number of patients receiving treatment intensification within six months after diagnosis is shown in [Fig. 1](#) and in [Appendix Table A1](#). Of the 29,713 patients with mHSPC at diagnosis, 11,588 (39.0 %) had a record of treatment intensification in the SACT dataset. Of these patients 6212 (53.6 %) received docetaxel, 4076 (35.2 %) enzalutamide, 954 (8.2 %) apalutamide, and 346 (3.0 %) abiraterone. These results are naturally influenced by the timing and nature of NICE recommendations for treatment intensification (i.e. the approval of Docetaxel in 2016 and Enzalutamide and Apalutamide in 2021).

[Fig. 1](#) demonstrates the change over time in different regimens. The use of treatment intensification increased over time from 33.8 % in 2018 to 45.1 % in 2022. Docetaxel use peaked in 2018 but fell sharply with the approval of enzalutamide and apalutamide in 2021, coinciding with the onset of the COVID-19 pandemic and related guideline updates. Abiraterone use was low throughout: its use increased only slightly from 2020, likely related to prescribing restrictions in England for this drug in this context.

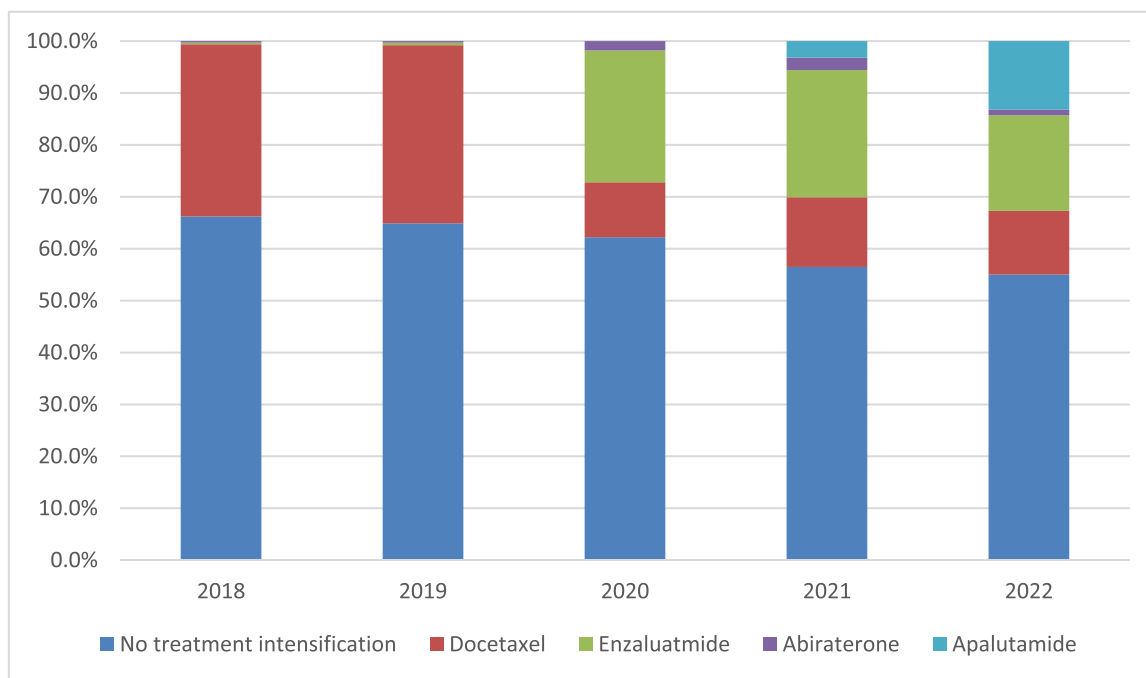


Fig. 1. Use of treatment intensification over time.

3.2. Determinants of use of treatment intensification

Table 1 shows that the use of treatment intensification significantly decreased with increasing age from 80.8 % in men younger than 50 years, 63.7 % in men aged between 65 and 69 (adjusted risk ratio RR [aRR] = 0.806 [95 % confidence interval 0.679–0.917]), 38.1 % in men between 75 and 79 years (aRR = 0.499 [0.379–0.629]), and 14.1 % in men aged 80–84 years (aRR 0.196 [0.138–0.282]) (p < 0.05).

Between the ages of 70 and 80 years, there was a sharp decline in the use of treatment intensification (Fig. 2). Of the 15,357 patients aged 75

or younger, 9184 (59.8 %; range 32.8–73.8 % across sMDTs) received treatment intensification. In contrast, among the 14,356 men aged older than 75, only 2404 (16.8 %; range 3.6–30.5 % across sMDTs) received treatment intensification (Appendix Fig. A2).

Patients with fewer comorbidities, those who were less frail, those from a non-black ethnic background and those from less socioeconomically deprived neighbourhoods were significantly more likely to receive treatment intensification (p always < 0.05). For example, use of treatment intensification significantly decreased with increasing comorbidities from 44.2 % in men with a Charlson score of 0, 27.7 % in

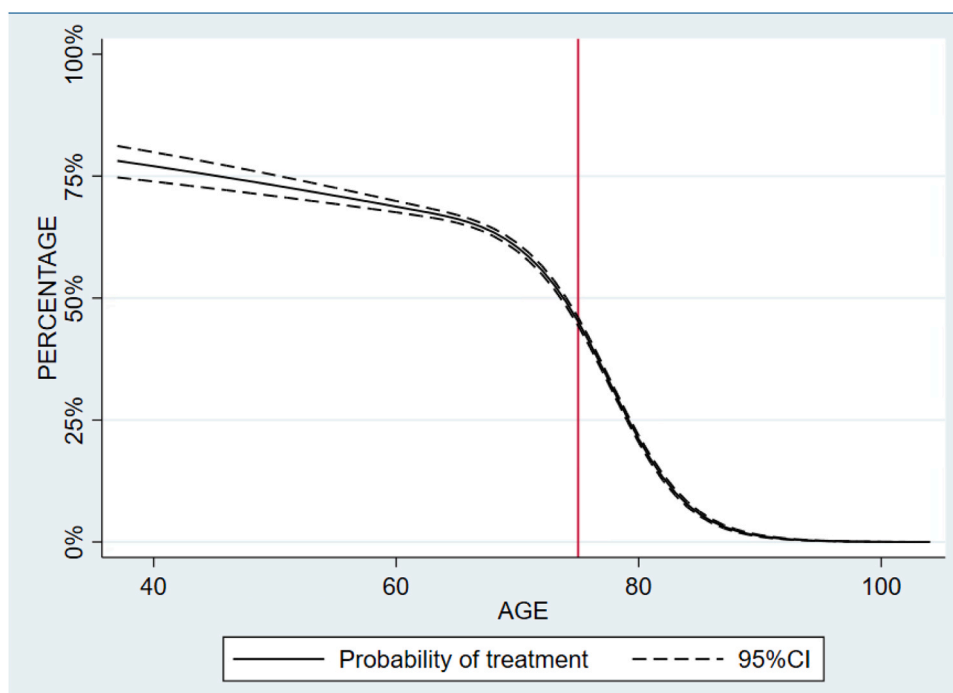


Fig. 2. Percentage of men with mHSPC who receive treatment intensification within six months of diagnosis (with 95 % confidence intervals) according to age. Vertical line at age 75.

men with a Charlson score of 1 (aRR = 0.942 [0.883–1.002]) and 13.9 % in men with Charlson score of 2 or more (aRR 0.800 [0.737–0.865]). Use of treatment intensification also significantly decreased with increasing socioeconomic deprivation, from 40.8 % in men living in the least deprived neighbourhoods to 35.1 % in men living in the most deprived neighbourhoods (aRR = 0.756 [0.708–0.806]). Treatment intensification use did not seem to vary according to rurality. Appendix Table A4 shows that docetaxel was more commonly given to younger, fitter patients with fewer comorbidities, while older, frailer patients with more comorbidities were more likely to receive ARPIs,

with minimal differences across ethnicity, socioeconomic status, and rurality.

3.3. Variation between sMDTs

The proportion of patients receiving treatment intensification ranged by sMDT from 20.3 % to 53.7 % (Fig. 3a). Substantial sMDT variation remained even after adjustment for age, co-morbidity, frailty and year of diagnosis (proportion after adjustment ranged from 19.5 % to 50.8 % by sMDT). The use of treatment intensification was below the 99.8 %

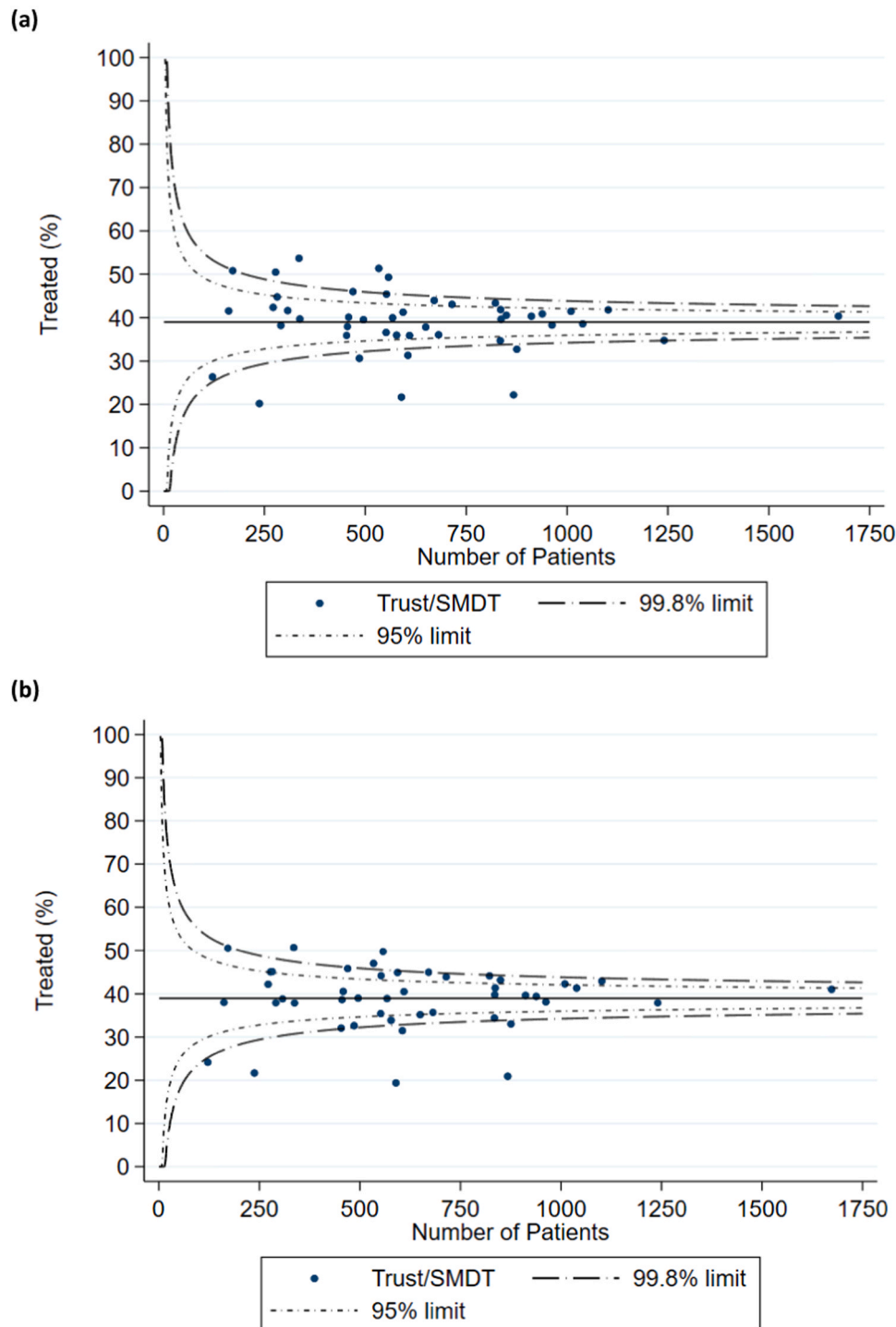


Fig. 3. Funnel plots showing the percentage of patients with mHSPC who received treatment intensification in each sMDT within which prostate cancer care is coordinated, (a) without adjustment and (b) with adjustment for year of diagnosis, age, number of comorbidities and level of frailty.

funnel plot limit (i.e., more than three standard deviations from the national level of treatment intensification use) for six sMDTs after adjustment (Fig. 3b). A funnel plot, now also adjusted for socioeconomic deprivation, in addition to the variables mentioned above, demonstrated only very small changes compared to this funnel plot (Appendix Fig. A3).

The biggest determinant of the sMDT variation in use of treatment intensification was age i.e. the management of patients over 75 varied substantially depending on which sMDT they were treated in, even after adjusting for frailty, comorbidity, socioeconomic deprivation (patients 75 years and under: ICC = 0.045, [95 % CI 0.029–0.070]: patients older than 75; ICC = 0.092, [0.058–0.142], P < 0.05). Differences in between-sMDT variation (as measured with the ICC) according to comorbidity, frailty or socioeconomic deprivation were not statistically significant (Fig. 4).

3.4. Capture of treatment intensification within other datasets

In the sensitivity analysis based on HES, 5037 patients (21 %) had treatment intensification recorded in both datasets, 3971 patients (17 %) according to SACT alone, 280 patients (1 %) according to HES alone and 14,597 (61 %) had no treatment intensification in either dataset (Appendix Table A2). In the sensitivity analysis based on CWT, 4957 patients (21 %) had treatment intensification recorded in both datasets, 4051 patients (17 %) according to SACT alone, 588 patients (2 %) according to CWT alone and 14,289 (60 %) had no treatment intensification in either dataset (Appendix Table A3). Due to the very small numbers, patients who showed evidence of receiving treatment intensification in either HES or CWT alone were not included in the analysis.

4. Discussion

4.1. Main findings

This national study examined patients diagnosed with mHSPC in the English NHS from 2018 to 2022, revealing that only 39 % of patients received treatment intensification within six months of diagnosis. This is despite national and international guidelines recommending its use

[41]. Older age emerged as the strongest determinant of whether patients received treatment, even after adjusting for comorbidity, frailty, ethnicity, and socioeconomic factors. While the use of treatment intensification increased over the study period (34 % in 2018 to 45 % in 2022), it remains low, with marked variation across prostate cancer specialist teams (sMDTs) ranging from 20 % to 51 %, after risk-adjustment for age, co-morbidity and frailty.

This is the largest study to date exploring treatment intensification in mHSPC patients. The findings demonstrate that practice-changing clinical trials are not fully translated into routine practice in the English NHS, a healthcare system which provides care for 57 million people, where care is free at the point of use funded through general taxation and national insurance contributions [42–44]. Implementation of treatment intensification is influenced by the timing and nature of NICE and NHS recommendations in England and explains the relatively high use of docetaxel initially (approved 2016) before its subsequent decrease in utilisation after enzalutamide and apalutamide were approved (2021). Our results align with data from the US, where 37 % of mHSPC patients received treatment intensification between 2015 and 2021 [45]. Comparable or lower rates are reported in Australia (25 %) [24], Scotland (38 %) [21] and Canada (13 %) [46]. Two studies from Sweden, specifically examining ARPI use, found utilisation rates of 10–12 % among the eligible population [23,25].

The 2022 Advanced Prostate Cancer Consensus Conference (APCCC) panel agreed that most fit patients with mHSPC should receive combination systemic therapy rather than ADT alone. However they recommended not to use docetaxel unless it is administered in combination with an ARPI [47]. A recent systematic review supports the survival benefit of adding an ARPI to ADT in mHSPC patients receiving docetaxel, with the greatest OS advantage seen when ARPI is given concurrently with chemotherapy [48]. As new therapies continue to be approved for mHSPC, it is crucial to assess how quickly and effectively new evidence and national guidelines on treatment intensification are implemented in real-world clinical practice.

4.2. Potential reasons for low uptake of treatment intensification

While the exact reasons for the low uptake of treatment intensification in mHSPC remain unclear, both patient- and provider-level factors

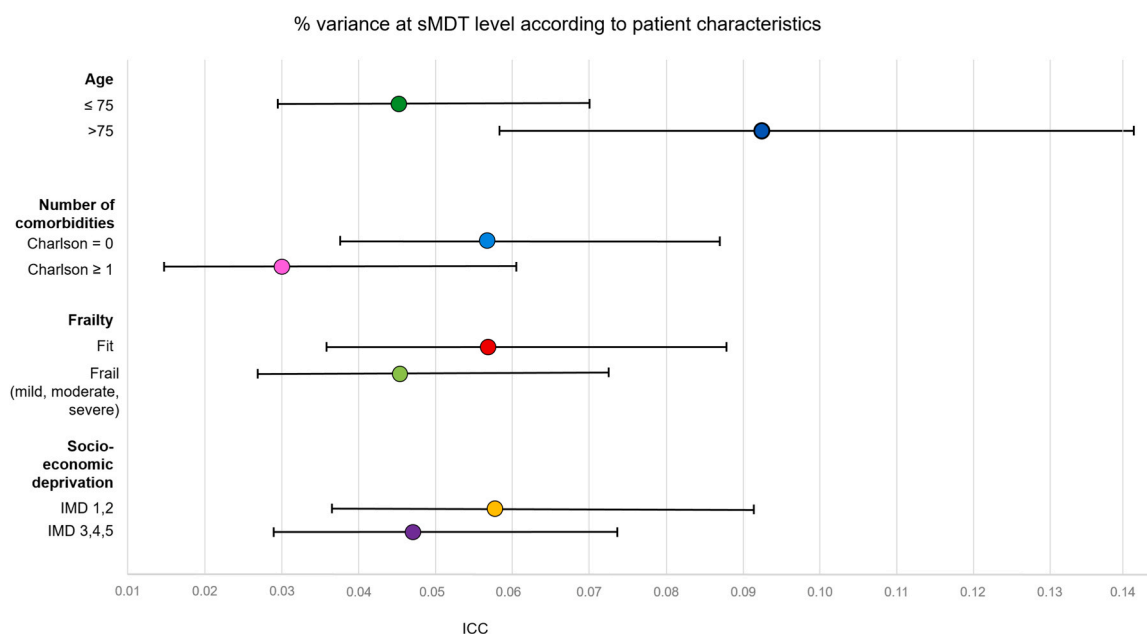


Fig. 4. The intraclass correlation (ratio of the between-sMDT variance to the total variance) according to age, number of comorbidities, level of frailty and socioeconomic deprivation.

are likely contributors. Patient level factors such as comorbidities and frailty present significant barriers to treatment adoption, a pattern consistent with other studies [20,49]. Drug costs, clinicians' familiarity with newer therapies and concerns about side effects also hinder uptake [50]. This is despite evidence of cost-effectiveness for both docetaxel and ARPIs [51,52]. Moreover, patient-reported outcomes suggest that concerns of poor tolerability and quality-of-life impacts are unfounded [53].

A major finding is the sharp decline in treatment intensification and the sMDT variation of treatment intensification for older patients, especially those over 75. We found only 16.8 % of patients over 75 receiving treatment intensification compared to 59.8 % of younger patients and this age disparity mirrors trends in the US [54,55]. Treatment decisions for older patients should be based on overall health rather than age alone and this disparity likely stems from professional biases as well as differences in patient comorbidity and frailty levels [22,56,57]. Although some clinical trial data exist on treatment intensification in older patients – with those aged 75 or older making up about a quarter of participants- they were generally fit enough to meet the inclusion criteria). However, the majority of clinical trials focus on younger, fitter patients, creating an “evidence gap” for older and less fit individuals [58,59]. While concerns exist regarding side effects of docetaxel or ARPIs in older patients, the ongoing PEACE-6 Vulnerable trial (NCT04916613) may provide further evidence on the use of darolutamide for patients with limited functional ability and comorbidities deemed ineligible for docetaxel or other ARPIs.

ARPI use requires regular monitoring due to potential side effects such as cognitive impairment and increased fatigue, which can significantly affect the functioning of elderly, particularly frail, patients [60–62]. The International Society of Geriatric Oncology (SIOG) recommends treatment intensification for patients who are “fit enough” [63], supported by standardised geriatric assessment tools [64]. However, only about 10 % of prostate cancer patients in England are diagnosed in hospitals with access to onco-geriatric services [65]. This highlights the limited access to these resources, especially given the high proportion of patients with metastatic disease who are over 75 years old [66] and demonstrates the importance of geriatric assessment tools such as the G8 or the abbreviated comprehensive geriatric assessment (aCGA) [67,68].

Socioeconomic deprivation also significantly affects treatment intensification use which, to the best of our knowledge, has not been identified in previous studies [24,46]. Patients from more deprived neighbourhoods typically have poorer overall health, where comorbidities and frailty are common, alongside lifestyle factors such as poor nutrition and low physical activity [69]. However, even after adjusting for comorbidity and frailty, deprivation remained a strong determinant of treatment disparities. Similarly, patients from a non-black ethnic background were more likely to receive treatment intensification than those from black ethnic groups, a pattern observed in other studies [70, 71]. Additional research is needed to clarify the underlying causes of this disparity.

The observed variation in utilisation of treatment intensification, despite risk adjustment, across prostate cancer sMDTs highlight that provider-level factors are also important to address. Organisational challenges related to the hub-and-spoke structure and how systemic therapy is delivered, alongside prescribing restrictions likely contribute to inconsistencies in treatment practices [72]. For instance, urologists are often restricted from prescribing treatment intensification due to cost constraints and some regions lack sufficient oncology support [73]. While prescribing docetaxel may be less suited to their role, enabling urologists to prescribe ARPIs could improve patient access to these therapies. Given the rising number of metastatic diagnoses and oncologist shortages in certain regions, this remains a significant concern even if urologists were encouraged to also prescribe these therapies. Variations are also influenced by local treatment habits, capacity and policies, underscoring the need for coordinated efforts among

polymakers, healthcare commissioners, and service providers [74].

In terms of solutions, research on practice variation has demonstrated that healthcare performance assessment and assurance is an important step towards improving the quality of clinical care [75,76]. The UK National Prostate Cancer Audit will report on treatment intensification use across England, both national and regionally, to identify variation and guide interventions to improve uptake.

4.3. Strengths and limitations

This study benefits from comprehensive, high-quality national linked datasets for all patients diagnosed with prostate cancer within the English NHS, including detailed systemic therapy information from the SACT dataset. However, the COVID-19 pandemic may have influenced treatment trends and 13 % of patients were excluded due to unknown metastatic status. Additionally, factors such as patient preference, cognitive function and social support, which could impact treatment decisions, were not captured.

To conclude, treatment intensification for mHSPC is at variance with guideline recommendations and the proven effectiveness of adding anti-cancer therapies to standard ADT. The use of treatment intensification was particularly low in certain groups of patients with mHSPC, for example older patients, those from a black ethnic background and those from more deprived neighbourhoods. There was also variation in practice across specialist prostate cancer team nationally. For these groups, an increased uptake of treatment intensification, in line with current guidelines, will improve their survival outcomes.

Funding statement

This study was undertaken alongside the National Prostate Cancer Audit. The audit is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit and Patient Outcomes Programme, funded by NHS England and the Welsh Government (<https://www.hqip.org.uk/national-programmes>). Neither HQIP nor NHS England or the Welsh Government had any involvement in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication. AA receives funding support from the National Institute for Health Research (NIHR Advanced Fellowship, NIHR300599).

Ethical approval was not required for this study as it involved the analysis of anonymised secondary data.

CRedit authorship contribution statement

Parry Matthew G: Writing – review & editing, Methodology. **Boyle Jemma:** Writing – review & editing, Methodology. **Nossiter Julie:** Writing – review & editing. **Cowling Thomas E:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Aggarwal Ajay:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization. **Cook Adrian:** Writing – review & editing, Formal analysis, Data curation. **Mayne Emily:** Writing – review & editing. **Parry Marina:** Writing – review & editing. **Tree Alison:** Writing – review & editing, Supervision. **Clarke Noel:** Writing – review & editing, Supervision. **van der Meulen Jan:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization. **Dodkins Joanna:** Writing – original draft, Visualization, Validation, 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.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ejca.2025.115335](https://doi.org/10.1016/j.ejca.2025.115335).

References

- [1] Sung H, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer J Clin* 2021;71(3):209–49.
- [2] James ND, et al. The Lancet Commission on prostate cancer: planning for the surge in cases. *Lancet* 2024;403(10437):1683–722.
- [3] Population estimates for the UK, England, Wales, Scotland, and Northern Ireland: mid-2022; 11.11.24; Available from: (<https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2022>).
- [4] The National Prostate Cancer Audit State of the Nation Report 2023. Available from: (https://www.npca.org.uk/content/uploads/2024/02/REF433_NPCA-SotN-Report_230124_v2.pdf).
- [5] Sweeney CJ, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. *N Engl J Med* 2015;373(8):737–46.
- [6] James ND, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet* 2016;387(10024):1163–77.
- [7] Armstrong AJ, et al. ARCHES: a randomized, phase III study of androgen deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. *J Clin Oncol* 2019;37(32):2974–86.
- [8] Davis ID, et al. Enzalutamide with standard first-line therapy in metastatic prostate cancer. *N Engl J Med* 2019;381(2):121–31.
- [9] James ND, et al. Abiraterone for prostate cancer not previously treated with hormone therapy. *N Engl J Med* 2017;377(4):338–51.
- [10] Fizazi K, et al. Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. *N Engl J Med* 2017;377(4):352–60.
- [11] Chi KN, et al. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med* 2019;381(1):13–24.
- [12] Tilki D, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer. Part II—2024 update: treatment of relapsing and metastatic prostate cancer. *Eur Urol* 2024;86(2):164–82.
- [13] Schaeffer EM, et al. Prostate cancer, version 4.2023, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2023;21(10):1067–96.
- [14] NICE hormone-sensitive metastatic prostate cancer: docetaxel evidence summary [ESUOM50]; 2016 11/02/2025; Available from: (<https://www.nice.org.uk/advice/esuom50>).
- [15] NICE Enzalutamide for treating hormone-sensitive metastatic prostate cancer technology appraisal guidance Reference number:TA712; 2021 11/02/2025; Available from: (https://www.nice.org.uk/guidance/ta712/chapter/1-Recommendations?utm_source=chatgpt.com).
- [16] NICE Apalutamide with androgen deprivation therapy for treating hormone-sensitive metastatic prostate cancer technology appraisal guidance Reference number:TA741; 2021 11/02/2025; Available from: (https://www.nice.org.uk/guidance/ta741/chapter/1-Recommendations?utm_source=chatgpt.com).
- [17] NHS England Interim clinical commissioning policy proposition: Abiraterone acetate and prednisolone for high-risk, hormone sensitive metastatic prostate cancer (adults) [2424]; 2024 11/02/2025; Available from: (https://www.england.nhs.uk/wp-content/uploads/2024/12/2424-Abiraterone-acetate-metastatic-prostate-cancer-interim-clinical-commissioning-policy-proposition-post-pan.pdf?utm_source=chatgpt.com).
- [18] Smith MR, et al. Darolutamide and survival in metastatic, hormone-sensitive prostate cancer. *N Engl J Med* 2022;386(12):1132–42.
- [19] Fizazi K, et al. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. *Lancet* 2022;399(10336):1695–707.
- [20] Dodkins J, et al. Does research from clinical trials in metastatic hormone-sensitive prostate cancer treatment translate into access to treatments for patients in the “real world”? A systematic review. *Eur Urol Oncol* 2023.
- [21] Rulach RJ, et al. Real-world uptake, safety profile and outcomes of docetaxel in newly diagnosed metastatic prostate cancer. *BJU Int*. Vol. 121(no. 2). p. 268–74.
- [22] Freedl, et al. Treatment patterns and survival in metastatic castration-sensitive prostate cancer in the US Veterans Health Administration. *Cancer Med* 2021;10(23):8570–80.
- [23] Fallara G, et al. Rapid ascertainment of uptake of a new indication for abiraterone by use of three nationwide health care registries in Sweden. *Acta Oncol* 2021;60(1):56–60.
- [24] Azad AA, et al. Predictors of real-world utilisation of docetaxel combined with androgen deprivation therapy in metastatic hormone-sensitive prostate cancer. *Int Med J*. Vol. 12. p. 12.
- [25] Gedeberg R, et al. Time on treatment with abiraterone in men with de novo metastatic castration sensitive prostate cancer: a drug utilization study. *Acta Oncol* 2022;61(3):328–32.
- [26] The National Prostate Cancer Audit 09/01/2024; Available from: (<https://www.npca.org.uk/>).
- [27] World Health Organisation. International statistical classification of diseases and related health problems (11th revision); 26/10/2022; Available from: (<https://www.who.int/standards/classifications/classification-of-diseases>).
- [28] National Health Service. Hospital Episode Statistics; 26/10/2022; Available from: (<https://digital.nhs.uk/data-and-information/data-tools-and-services/data-service/hospital-episode-statistics>).
- [29] SACT systemic Anti-cancer therapy dataset; 26/10/2022; Available from: (<http://www.chemodataset.nhs.uk/home>)
- [30] Parry MG, et al. Imputation of missing prostate cancer stage in English cancer registry data based on clinical assumptions. *Cancer Epidemiol* 2019;58:44–51.
- [31] Armitage JN, van der Meulen JH. Identifying co-morbidity in surgical patients using administrative data with the Royal College of Surgeons Charlson Score. *Br J Surg* 2010;97(5):772–81.
- [32] Jauhari Y, et al. Construction of the secondary care administrative records frailty (SCARF) index and validation on older women with operable invasive breast cancer in England and Wales: a cohort study. *BMJ Open* 2020;10(5):e035395.
- [33] Ministry of Housing, Communities and Local Government. Lower layer super output areas (LSOAs); 16/02/2023; Available from: (<https://www.data.gov.uk/dataset/c481f2d3-91fc-4767-ae10-2efdf6d58996/lower-layer-super-output-areas-lsoas>)
- [34] Noble M, The English indices of deprivation 2007; 2008.
- [35] ONS. 2011 rural/urban classification. Available from: (<https://www.ons.gov.uk/methodology/geography/geographicalproducts/ruralurbanclassifications/2011ruralurbanclassification>).
- [36] Aggarwal A, et al. Organisation of prostate cancer services in the English national health service. *Clin Oncol (R Coll Radiol)* 2016;28(8):482–9.
- [37] Elrod JK, Fortenberry JL. The hub-and-spoke organization design: an avenue for serving patients well. *BMC Health Serv Res* 2017;17(1):457.
- [38] Cornford P, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer. Part II-2020 update: treatment of relapsing and metastatic prostate cancer. *Eur Urol* 2021;79(2):263–82.
- [39] Zhang J, Yu KF. What’s the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *Jama* 1998;280(19):1690–1.
- [40] Spiegelhalter DJ. Funnel plots for comparing institutional performance. *Stat Med* 2005;24(8):1185–202.
- [41] National Institute for Health and Care Excellence. Prostate cancer: diagnosis and management; 2019 26/10/2022; Available from: (<https://www.nice.org.uk/guidance/ng131>).
- [42] Bryant J, et al. Examining and addressing evidence-practice gaps in cancer care: a systematic review. *Implement Sci* 2014;9(1):37.
- [43] Uyl-de Groot CA, et al. Unequal access to newly registered cancer drugs leads to potential loss of life-years in Europe. *Cancers* 2020;12(8).
- [44] How health care is funded: the king’s fund; 14.10.2024; Available from: (<https://www.kingsfund.org.uk/insight-and-analysis/long-reads/how-health-care-is-funded#how-is-the-nhs-in-england-currently-funded?>).
- [45] Heath EI, et al. Treatment intensification patterns and utilization in patients with metastatic castration-sensitive prostate cancer. *Clin Genitourin Cancer* 2022;20(6):524–32.
- [46] Wallis CJD, et al. Real-world use of androgen-deprivation therapy: intensification among older Canadian men with de novo metastatic prostate cancer. *JNCI Cancer Spectr* 2021;5(6).
- [47] Gillessen S, et al. Management of patients with advanced prostate cancer—metastatic and/or castration-resistant prostate cancer: report of the Advanced Prostate Cancer Consensus Conference (APCCC) 2022. *Eur J Cancer* 2023;185:178–215.
- [48] Ciccarese C, et al. Triplet therapy with androgen deprivation, docetaxel, and androgen receptor signalling inhibitors in metastatic castration-sensitive prostate cancer: a meta-analysis. *Eur J Cancer* 2022;173:276–84.
- [49] Swami U, et al. The role of physician speciality in the underutilization of standard-of-care treatment intensification in patients with metastatic castration-sensitive prostate cancer. *J Urol* 2023;209(6):1120–31.
- [50] Loeb S, et al. Barriers and facilitators to first-line (1L) treatment intensification (TI) in metastatic castration-sensitive prostate cancer (mCSPC): the IMPLEMENT study. *J Clin Oncol* 2024;42(4 suppl) (224-224).
- [51] Sathianathan NJ, et al. A cost-effectiveness analysis of systemic therapy for metastatic hormone-sensitive prostate cancer. *Eur Urol Oncol* 2019;2(6):649–55.
- [52] Sung WWY, et al. A cost-effectiveness analysis of systemic therapy for metastatic hormone-sensitive prostate cancer. *Front Oncol* 2021;11:627083.
- [53] Stenzl A, et al. Effect of enzalutamide plus androgen deprivation therapy on health-related quality of life in patients with metastatic hormone-sensitive prostate cancer: an analysis of the ARCHES randomised, placebo-controlled, phase 3 study. *Eur Urol* 2020;78(4):603–14.
- [54] Tagawa S, et al. 679P treatment patterns of metastatic castration-sensitive prostate cancer (mCSPC): a real-world evidence study. *Ann Oncol* 2020;31:S541–2.
- [55] Swami U, et al. Treatment pattern and outcomes with systemic therapy in men with metastatic prostate cancer in the real-world patients in the United States. *Cancers* 2021;13(19).
- [56] Jorgensen ML, Young JM, Solomon MJ. Older patients and adjuvant therapy for colorectal cancer: surgeon knowledge, opinions, and practice. *Dis Colon Rectum* 2011;54(3):335–41.
- [57] National Cancer Institute. NCI comorbidity index overview. Available from: (<https://healthcaredelivery.cancer.gov/seermedicare/considerations/comorbidity.html>).
- [58] Beckmann K, et al. The value of real-world data in understanding prostate cancer risk and improving clinical care: examples from Swedish registries. *Cancers* 2021;13(4).

- [59] Averitt AJ, et al. Translating evidence into practice: eligibility criteria fail to eliminate clinically significant differences between real-world and study populations. *NPJ Digit Med* 2020;3:67.
- [60] Nowakowska MK, et al. Association of second-generation antiandrogens with cognitive and functional toxic effects in randomized clinical trials: a systematic review and meta-analysis. *JAMA Oncol* 2023;9(7):930–7.
- [61] Huang SW, et al. Risk of cognitive impairment in men with advanced prostate cancer treated with NHAs: a systematic review and network meta-analysis. *Clin Transl Sci* 2023;16(2):313–25.
- [62] Stockler MR, et al. Health-related quality of life in metastatic, hormone-sensitive prostate cancer: ENZAMET (ANZUP 1304), an international, randomized phase III Trial led by ANZUP. *J Clin Oncol* 2022;40(8):837–46.
- [63] Cornford P, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer. Part II—2020 update: treatment of relapsing and metastatic prostate cancer. *Eur Urol* 2021;79(2):263–82.
- [64] Graham LS, et al. Management of prostate cancer in older adults. *Am Soc Clin Oncol Educ Book* 2023;(43):e390396.
- [65] Dodkins J, et al. Organisation and delivery of supportive services for patients with prostate cancer in the National Health Service in England and Wales: a national cross-sectional hospital survey and latent class analysis. *BMJ Open* 2023;13(11):e071674.
- [66] The National Prostate Cancer. Audit short report 2022: patient and tumour characteristics associated with metastatic prostate cancer at diagnosis in England
- [67] Momota M, et al. Geriatric 8 screening of frailty in patients with prostate cancer. *Int J Urol* 2020;27(8):642–8.
- [68] Overcash JA, et al. The abbreviated comprehensive geriatric assessment (aCGA) for use in the older cancer patient as a prescreen: scoring and interpretation. *Crit Rev Oncol Hematol* 2006;59(3):205–10.
- [69] Tomic K, et al. Socioeconomic status and diagnosis, treatment, and mortality in men with prostate cancer. Nationwide population-based study. *Int J Cancer* 2018;142(12):2478–84.
- [70] Freedland SJ, et al. Treatment patterns and survival in metastatic castration-sensitive prostate cancer in the US Veterans Health Administration. *Cancer Med* 2021;10(23):8570–80.
- [71] Beebe-Dimmer JL, et al. Racial differences in patterns of treatment among men diagnosed with de novo advanced prostate cancer: a SEER-Medicare investigation. *Cancer Med* 2019;8(6):3325–35.
- [72] Brooks ES, et al. Inefficiencies of care in hub and spoke healthcare systems: a multi-state cohort study. *Am J Surg* 2024;229:151–5.
- [73] Royal College of Radiologists: clinical oncology census report 2023; 2024 31.10.24; Available from: (<http://rcr.ac.uk/media/j5jmhpju/rcr-census-clinical-oncology-workforce-census-2023.pdf>)
- [74] Chamberlain C, et al. A systematic review of geographical variation in access to chemotherapy. *BMC Cancer* 2015;16(1):1.
- [75] Mays N. Reducing unwarranted variations in healthcare in the English NHS. *BMJ* 2011;342:d1849.
- [76] Aggarwal A, et al. Public reporting of outcomes in radiation oncology: the National Prostate Cancer Audit. *Lancet Oncol* 2021;22(5):e207–15.