NPCA
National Prostate Cancer Audit

Using the Cambridge Prognostic Groups for risk stratification of prostate cancer in the National Prostate Cancer Audit:

How could it impact our estimates of potential 'over-treatment'?

NPCA: Short Report

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Background

Several risk stratification tools exist which are used in different countries and contexts to classify prostate cancer. Studies have shown that these have differing abilities to predict prostate cancer death and other outcomes. A recently developed system, the five-tiered Cambridge Prognostic Group (CPG) classification (1), shows potential to replace the three-tiered D'Amico risk stratification system currently used in the NICE guidelines (2). Work by the National Prostate Cancer Audit (NPCA) has shown the CPG to be accurate in predicting outcomes and has potential for assessing the appropriateness of treatment allocation.

The NPCA has reported results for several years for men who have been traditionally classified as having low-risk disease and who receive radical treatment (surgery, chemotherapy or radiotherapy). Using the new CPG classification is likely to change the level of this potential 'over-treatment' estimate, as there will be more men in the lowest risk category (CPG1) than were included in the previous low-risk group.

This report compares the characteristics of men classified by both the existing NPCA classification and the CPG. It aims to show the impact of using the new way of stratifying the risk of prostate cancer on the way that potential 'over-treatment' is measured in the NPCA.

Methods

The NPCA database is made up of English Cancer Registry data and information from the Cancer Information System for Wales (CaNISC), linked at patient level to radiotherapy and hospital administrative databases. This database was used to classify men diagnosed with prostate cancer between 1 April 2017 and 31 March 2018, according to the modified D'Amico risk stratification algorithm and using CPG criteria.

The relative proportions of men assigned to each tier in each classification were compared. The demographic characteristics of the men in the lowest risk tiers (low-risk and CPG1 respectively) were compared. The distribution across providers, of the receipt of radical treatment by men in both these lowest risk tiers, was displayed in funnel plots.

Results

41,724 men were included in the cohort. The low-risk group makes up 6.1% of the whole cohort (2,537 men) while CPG1 includes 14.7% (6,137 men). After excluding men with metastatic disease and pelvic node involvement (which are not included in the CPG classification) and removing the cases with missing data there were 25,246 men in the CPG classification. The CPG categories were roughly similar in size to each other, with CPG3 somewhat smaller (CPG1=24.3%; CPG2=19.2%; CPG3=12.8%; CPG4=19.3%; CPG5=24.5%). In the current stratification, for which 31,897 men could be assigned a risk group, the two higher risk groups are roughly even with a very small low-risk group (high-risk/locally advanced group=48.4%, intermediate-risk group=43.6% and low-risk group=8.0%).

4.3% (109/2,537) of men classified in the low-risk group had radical treatment, compared to 9.8% (603/6,137) of those classified in the CPG1 category. The demographic characteristics of men in these lowest risk tiers were similar to each other, whether they received radical treatment or not.

There was more variation apparent across providers in the provision of radical treatment for men in CPG1 compared to in the low-risk group, and there were more outliers outside the funnel plot limits.

Conclusion

The new CPG classification can be used to stratify men's prostate cancer for the NPCA going forward. There will be a noticeable change in the proportion of men in the lowest risk category and thus an impact on the potential 'over-treatment' indicator used to monitor the use of radical treatment for these men. However, due to the higher numbers, this indicator will now be more robust, highlighting wider variation among providers than was previously apparent, allowing further improvement to the quality of care.

Key Messages

- A new risk stratification tool, the Cambridge Prognostic Grouping (CPG) has been developed which classifies men into five tiers according to their Gleason score, PSA and tumour characteristics (T,N,M).
- This tool will be used to classify men's prostate cancer risk in future National Prostate Cancer Audit reporting, replacing the current three-tiered system of low-, intermediate- and high-risk groups.
- This will impact the NPCA indicator measuring potential 'over-treatment' which monitors the proportion of men in the low-risk group receiving radical treatment, when the guidelines advocate active surveillance for most of this tier.
- Although their demographic characteristics are shown to be similar, there are more men in the lowest risk tier in the new stratification (CPG1) than in the low-risk group and this leads to an overall higher proportion of men identified as potentially 'over-treated'
- The higher numbers, however, allow for more robust assessment of the variation between providers, with more providers identified as lying outside the expected range of values, potentially leading to further improvements in the quality of care.

Patient Summary

Currently, the risk associated with a man's prostate cancer is classified as low-, intermediate- or high-risk. A new stratification tool (the Cambridge Prognostic Grouping, CPG) classifies men into five categories based on more detailed information about the clinical features of their disease. These classifications help inform the decisions made about the management of men's prostate cancer.

Active surveillance is generally advised for men with the lowest risk rather than being given radical treatment. Whether a patient has received radical treatment is therefore one of the indicators for quality of care which is assessed in the National Prostate Cancer Audit (NPCA). This potential 'over-treatment' can lead to unnecessary side effects. There may be situations where patients choose and/or clinicians advise radical treatment for low-risk prostate cancer, but the variation in the proportion of men potentially 'over-treated' across providers is of concern.

This report aims to show the impact of using the new way of stratifying the risk of prostate cancer on the way that potential 'over-treatment' is measured in the NPCA. Using English and Welsh hospital data from previous audits, this report shows how the new CPG compares to the current risk stratification. It shows that more men are placed in the lowest risk (CPG1) category compared to the current low-risk group, but that the characteristics of the men (such as age and deprivation) are similar across these tiers. The proportion of men potentially 'over-treated' goes up (from 4% of men in the low-risk group to 10% in CPG1), but it also shows us the variation between providers more clearly, with more providers being identified as outside the expected range.

Introduction

'Risk stratification'

Risk stratification is used by clinicians to classify men's prostate cancer to inform clinical decision-making and to give prognostic information. Various stratification tools exist which are used in different countries and contexts, and studies have shown that these have differing abilities to predict prostate cancer death and other outcomes (3-5). Some use five strata, for example the National Comprehensive Cancer Network's guidelines for staging prostate cancer used in the US (6), others use three, such as that in the NICE guidelines (2), used in England and Wales.

One system shown more recently to have good discrimination in terms of mortality is the five-tiered prostate cancer risk classification system that has been developed for non-metastatic cancer: the Cambridge Prognostic Group (CPG) classification (1). This has strong potential to replace the 'traditional' three-tiered risk stratification (low-, intermediate- and high-risk or locally advanced disease) (2), given its better accuracy in predicting outcomes and its potential for assessing the appropriateness of treatment allocation (7).

The CPG has been developed from representative 'real-world' registry data, and validated with external datasets. Its five tiers classifies men into sub-groups of those who have different mortality and disease progression outcomes compared to those predicted from the three-tiered stratification (4, 5). This is because the CPG follows a more 'nuanced' risk classification, taking into account a wider range of combinations of Gleason biopsy score (Appendix 1, Table A1), pre-treatment serum prostate-specific antigen (PSA) and clinical stage (based on MRI results, using T, N, M – Appendix 1, Table A2) (8). Table 1 shows how risk tiers are categorised using these scores for the NICE guidelines (2) and CPG criteria from Gnanapragasam et al (4, 5). Henceforth, we will use the term 'risk group' for the current 3-tiered system and 'category' for the 5-tiered system, as in Table 1.

CPG1 encompasses more men than the existing low-risk group according to the three-tiered stratification as it includes all stage T2 tumours, not just those at stage T2a. The D'Amico risk stratification (adapted by the NPCA (9)) relies upon a sub-classification of T stage, which has not been available in the NPCA dataset. Therefore for the low-risk group, the NPCA currently only includes patients with T1 tumours (and with a PSA <10ng/ml and Gleason score of ≤6) but excludes patients with stage T2a tumours.

In fact, in the NPCA data we do not have access to a reliable sub-classification of T stage which the D'Amico risk relies on. Therefore up until now we have only included in the low-risk group men with T1 (and with a PSA <10ng/ml and Gleason score of ≤6), and we were unable to include the patients with stage T2a tumours. However, it has been shown that there is little difference in outcomes for T1 and T2 (as long as other scores are low) and also that this level of staging is known to be frequently inaccurate (10, 11).

Another major difference is in the intermediate-risk group where the Gleason score is subdivided to allow a more accurate assessment of risk categorisation. The CPG classification picks up the difference, for instance, between Gleason score 7 made up of 3+4 (more grade 3 cells than grade 4 cells) versus one made up of 4+3. This is clinically significant, as the former grade of cancer grows more slowly than the latter. This difference is reflected in the split of CPG2 and CPG3, which are both within the 'original' intermediate-risk group.

CPG4 and CPG5 also allow for a split between men who were all previously classified as having high-risk localised or locally-advanced disease. Men with higher grade prostate cancer (Gleason score 9-10) or a stage T4 tumour, or those with a combination of Gleason score 8, PSA >20ng/ml or Stage 3, are in a separate category from men whose cancer has only one of these latter three features.

These more clearly defined categorisations allow for better decision-making, ensuring disease management strategies are dictated by the clinical features of the patient's cancer. For instance, men in CPG2 and CPG3 should be managed differently from each other, with more men in the CPG2 category (who would all have been classified as having 'intermediate-risk' disease) being potentially eligible for active surveillance while men in CPG3 are more likely to need definitive treatment (7). Active surveillance should be considered for all men in the new CPG1 category, some of whom would previously have been classified in the intermediate-risk group.

'Over-treatment'

There has been concern over the years that some patients classified with the traditionally-used categorisation as having low-risk disease, who can generally be safely monitored with active surveillance, are being given radical treatment early and sometimes unnecessarily. Although patient choice and other circumstances will mean that some men in the lowest risk category will receive treatment, this potential 'over-treatment' can result in avoidable side-effects such as reduced sexual function, or urinary or bowel problems.

The level of men with low-risk disease having radical treatment as opposed to active surveillance has reduced steadily over the years of the NPCA: the proportion was an average of 8% across England in 2015-16 (12), an improvement from 12% in 2014-15 (9). As the 2017 NPCA report stated, this suggests that findings from studies recommending more active surveillance "such as PIVOT (13) and Protect (14) are being disseminated into national practice" (p.43 (12)). The most recent reports (15, 16) found that the proportion potentially 'over-treated' had fallen to 4% for men diagnosed 2016-17, and remained stable for men diagnosed 2017-18, although there is still substantial variation between providers (0 to 16%).

When the NPCA adopts the CPG for assigning risk categories to men, as is suggested for future years of the annual reports, there is likely to be a change in the level of potential 'over-treatment' we estimate, as there will be more men in the lowest risk category (CPG1) than were included in the previous low-risk group.

This short report uses recent prostate cancer audit data to compare how men were stratified by the existing NPCA risk classification and how they would now be classified using the CPG. It then focuses on the difference between men receiving radical treatment in each of the lowest risk tiers (low risk and CPG1) to examine what the impact of changing the classification would be on the potential 'over-treatment' performance indicator.

Methods

Using NPCA data, all men newly diagnosed with prostate cancer between 1 April 2017 and 31 March 2018 were identified in the English Cancer Registry and Welsh Cancer Intelligence and Surveillance Unit using the ICD-10 diagnosis code C61 (17) and the corresponding date of diagnosis. These data were linked at the

level of individual patients with the Hospital Episode Statistics (HES) database (18) and the National Radiotherapy Data Set (RTDS) (19).

Registry data were used to identify the diagnosing hospital, the date of diagnosis, cancer characteristics (TNM stage, PSA level, Gleason score), and age at diagnosis for each man. The HES (Hospital Episode Statistics) or PEDW (Patient Episode Database for Wales) record for each man was used to identify any comorbid conditions during the year prior to diagnosis, applying The Royal College of Surgeons (RCS) algorithm for assigning the Charlson Co-morbidity Score (20). Socioeconomic deprivation status was determined from the HES/PEDW record of postcode of residence using the Index of Multiple Deprivation (IMD) divided according to quintiles of the national distribution (21, 22). Self-reported ethnicity data were only available for men diagnosed in England. These men were classified into two groups: 'White' and 'All other ethnic groups combined'[a]. Age, deprivation, ethnicity and comorbidities were used to compare the proportions represented within the different classifications.

Men were classified according to the NPCA's three-tiered stratification and into the five CPG categories. Neither classification includes men with metastatic disease but the NICE risk groups do include men with lymph node involvement. Three-tiered groupings were based on the modified D'Amico risk stratification algorithm developed previously by the NPCA (9); and a five-tiered categorisation was based on the CPG criteria from Gnanapragasam et al (4, 5), developed for the NPCA by Parry et al (7).

Descriptive analyses showed the relative proportions of men in each of the tiers, which were used to assess how patient characteristics compare across the two classifications. The proportions of men in the low risk and CPG1 categories who received radical treatments were compared. The funnel plots in Figures 2 and 3 show how the two categorisation systems impact the distribution of potential 'over-treatment' across providers for men in these lowest risk tiers who are receiving radical treatment.

Results

41,724 men diagnosed in England and Wales between 1 April 2017 and 31 March 2018 were included in the cohort. Table 2 shows how the distribution of men in the risk groups compares to that in the CPG categories, showing all men (including those with metastatic disease, nodal involvement and with missing risk information). In the CPG classification, it was not possible to assign a category to 8,329/41,724 (20.0%) men, while in the risk groups 3,555/41,724 (8.5%) are missing. The low-risk group makes up 6.1% of the whole cohort (2,537/41,724 men) while CPG1 includes 14.7% (6,137/41,724 men). Men with metastatic disease and pelvic lymph node involvement made up a total of 8,149/41,724 men (19.5% of the cohort). Men with pelvic nodal involvement are included in the high-risk/locally advanced group (1,877/15,437 men, 12.2% of this group) and so are also shown in Table 2.

Metastatic disease, pelvic node involvement and missing cases were excluded in the final CPG classification, leaving 25,246 men. After these exclusions, the CPG categories are roughly similar in size with CPG3 somewhat smaller than the others (N=25,246: CPG1 = 6,137 men, 24.3%; CPG2 = 4,836, 19.2%; CPG3 = 3,228, 12.8%; CPG4 = 4,869, 19.3%; CPG5 = 6,176, 24.5%). The high-risk/locally advanced group includes men with node involvement: of the 31,897 men assigned a risk group, 15,437 men were in this group (48.4%); the intermediate-risk group contained 13,923 men (43.6%) and the low-risk group 2,537

[a] As recommended by https://www.ethnicity-facts-figures.service.gov.uk/style-guide/writing-about-ethnicity

men (8.0%). The comparison in tiers after missing data from both classifications was excluded is shown below in Figure 1 – this shows that the three lower CPG categories (CPG1 + 2 + 3) are equivalent to the low- and intermediate- risk groups (Appendix 2, Table A3).

Comparing the classifications for men who had radical treatment

Table 3 compares the classifications among men who received radical treatment. Men with metastatic disease were excluded from both classifications, but men with pelvic node involvement were included in the high-risk/locally advanced group, so these men are shown in this table. Men who could not be assigned to one or other of the risk classifications were also included as 'missing'.

As per Table 2 and 3, within the currently used risk groups, 109/2,537 men with low-risk disease (4.3%) had radical treatment. 6,596/13,923 men (50.0%) in the intermediate-risk group had radical treatment, while in the high-risk/locally advanced group the number was 10,554/15,437 men (68.4%). 558/18,177 men (3.1%) who had radical treatment could not be assigned to one of these risk groups.

In the CPG classification: 603/6,137 (9.8%) of men in the CPG1 risk category had radical treatment. 109/603 men (18.1%) were already in the low-risk group and 408/603 (67.7%) were added from the intermediate-risk group (86/603, 14.3% had been classed as missing).

In CPG2, 2,746/4,836 men (56.8%) had radical treatment. These men were all previously part of the intermediate-risk group, making up 39.5% (2,746/6,956) of all intermediate-risk men who had radical treatment. The CPG3, CPG4 and CPG5 categories included 2,401/3,228 (74.4%), 3,867/4,869 (79.4%) and 4,559/6,176 men (73.8%), respectively, who had radical treatment (data from Tables 2 and 3). In CPG3, these men made up 34.5% (2,401/6,956) of the intermediate-risk group who had radical treatment, while in CPG4 and CPG5 they made up 36.6% (3,867/10,554) and 43.2% (4,559/10,554) respectively of the high-risk/locally advanced group who had radical treatment (Table 3).

953/1,877 (50.8%) men with node involvement (who are not included in CPG) had radical treatment (Tables 2 and 3). They made up 9.0% (953/10,554) of those classified in the high-risk/locally advanced group who had radical treatment, representing 5.2% (953/18,177) of all men who had radical treatment (Table 3).

Distribution of characteristics for men in CPG1 compared to the low-risk group

Patient characteristics in the two 'lowest risk' tiers (CPG1 and low-risk) were compared for all men, and for those receiving radical treatment (Table 4). The distribution of these characteristics appeared similar for all variables.

Provider-level results

Using the CPG classification, the average proportion of potential 'over-treatment' is 9.8% (Figure 2) compared to 4.3% with the low-risk grouping (Figure 3). These estimates range across providers from 0% to 21.9% for CPG1 (Figure 2) and 0% to 16.1% for the low-risk group (Figure 3). As there are more men included in the CPG1 than in the low-risk group, there is a wider range of numbers of patients seen (as shown on the x-axis of Figure 2), however the funnel plots take the number of patients into account by having narrower limits as numbers increase. Using the CPG classification, there are more providers who are

negative outliers: two Welsh and three English providers are above the expected range of values (Figure 2), compared with one outlier when the low-risk grouping is used (Figure 3). This one outlier is not an outlier using the CPG classification.

Discussion

This report has used existing audit data to compare the current risk groups with the newer CPG classification for stratifying men's prostate cancer risk. This highlighted the apparent increase in potential 'over-treatment' when we compare the low-risk groups and CPG1 (from 4.3 to 9.8% respectively). The CPG redistributes men to risk categories according to more detailed risk profiling than the previously-used classification, reassigning some intermediate-risk men to CPG1 – the lowest risk category in that classification. CPG2 and CPG3 'share' the rest of the intermediate-risk men between them. CPG4 and CPG5 separate the high-risk men, also removing men with node involvement from the classification.

There are more men with a missing CPG category than have a missing risk group as the CPG requires more elements of the characteristics of a patient's cancer in order to assign a risk tier. There was no reason to believe that the missing data impacted the clinical relevance of the classifications however (7).

The new CPG classification has implications for the evaluation of treatment management of men with prostate cancer, and this has been addressed particularly for CPG2 to CPG5 in recent research by Parry et al (7). The current report is not intended to direct clinical practice, but as an early warning that when the NPCA reports radical treatment in the lowest risk tier in future (which will be the CGP1 category), there will be a higher proportion to report than previously (in the low-risk group). The 'broader' definition of CPG1 compared to the low-risk group explains the difference in the size of the tiers, but despite this difference, the patient characteristics were similar in each. These extra numbers make our assessment of potential 'over-treatment' more robust so more of the variation between providers can be identified. The apparent 'jump' from preceding years will need to be carefully explained, but it will reflect more accurately that clinical practice may be 'over-treating' some men for whom active surveillance would be appropriate. The new classification has led to more, and different, providers being classed as outliers, outside the expected range of the proportion of radical treatments given to the lowest risk men (in this case, in CPG1). Although this will be of concern to those outlier providers at first, this change may help drive quality improvement.

It is important to note, however, that the categories do not replace the need for individual assessment and decision-making. For instance, there will be men with stage T2c tumours, Gleason score of 6 and a PSA<10ng/ml who will be classed as CPG1, but who clinicians may feel are candidates for radical treatment. Therefore, on a patient level this broad classification may not always be appropriate, and we would not expect receipt of radical treatment by men in the lowest risk tier to ever reach zero.

Treatment guidelines support the use of active surveillance for men in the low-risk group but there is less clarity about its use for men with intermediate-risk disease, some of whom would fall into the CPG1 category. Some guidelines do not sub-divide the intermediate-risk group into 'favourable' and 'unfavourable' disease at all. This is now a well-established distinction with men in the 'favourable' group having one intermediate risk factor, a Gleason score of 3+4=7 (or less) and less than 50% positive biopsy cores; while the 'unfavourable' group have more than one risk factor, a Gleason score of 4+3=7 and 50% or more positive biopsy cores (23). Some guidelines that do use this subdivision, do not encompass those in the favourable category (which the CPG1 men would fall into) in their inclusion criteria for active

surveillance (2, 24). However, other guidelines, such as those supported by Prostate Cancer UK (25) and those used in North America (6, 26), do indicate that active surveillance is suitable for these men. Thus, many of the men to be included in the CPG1 category would be suitable. The NICE 2019 Quality Statement 2 requires that even "people with low-risk localised prostate cancer for whom radical treatment is suitable are offered a choice between active surveillance, radical prostatectomy or radical radiotherapy" (27), and that will also be relevant for the men who make up CPG1.

It seems likely that in certain providers, too many men who could be on active surveillance (including most of those in CPG1, as well as some others) are still having radical treatment. The literature suggests that this could be improved going forward by improving the stratification of risk to help clinical decision-making and by ensuring that patients are aware of potentially severe and permanent side effects of treatment. Studies have shown the positive long-term outcomes of management with active surveillance for appropriate groups of men (24, 28-30) and that its use can reduce 'over-treatment' (31). Active surveillance has also been shown to be safe for men with what is currently classified as intermediate-risk disease, where this is judged to be 'favourable' (32-35).

The use of this new, more nuanced classification has been shown to better reflect clinical features of men's prostate cancer, and thus can inform clinical practice and decision-making so that more men and their clinicians may feel able to choose an active surveillance strategy (7). From the audit's perspective, using the CPG allows for classification using more granular information which also adds more men to the lowest risk category. This makes the audit indicator more able to identify real variation between providers so that the potential 'over-treatment' of patients can be appropriately addressed.

Tables and Figures

Table 1: Patient characteristics of men diagnosed with non-metastatic prostate cancer according to the NICE three-tiered risk stratification (2) and the Cambridge Prognostic Group classification (CPG) (4).

NICE risk group	Criteria	CPG category	Criteria
Low-risk disease	Gleason score ≤ 6 *AND* PSA < 10 ng/ml *AND* stages T1-T2a	***1***	Gleason score 6 (Grade Group 1) *AND* PSA < 10 ng/ml *AND* stages T1-T2
Intermediate-risk disease	Gleason score 7 **OR** PSA 10-20 ng/ml **OR** Stage T2b	***2***	Gleason score 3 + 4 = 7 (Grade Group 2) **OR** PSA 10-20 ng/ml *AND* stages T1-T2
		3	Gleason score 3 + 4 = 7 (Grade Group 2) *AND* PSA 10-20 ng/ml *AND* stages T1-T2 **OR** Gleason score 4 + 3 = 7 (Grade Group 3) *AND* stages T1-T2
High-risk or locally advanced disease	Gleason score 8-10 **OR** PSA > 20 ng/ml **OR** Stage ≥T2c	***4***	***One* of:** Gleason score 8 (Grade Group 4) **OR** PSA > 20 ng/ml **OR** Stage T3
		5	**Any *combination* of:** Gleason score 8 (Grade Group 4), PSA > 20 ng/ml or Stage T3 **OR** Gleason score 9-10 (Grade Group 5) **OR** Stage T4

Footnote: PSA = prostate specific antigen; T = tumour stage

Table 2: CPG compared to risk groups in all men, including those with node involvement or metastatic disease using the NICE three-tiered risk stratification (columns) (2) and the CPG classification (rows) (4)

	Low-risk		Intermediate-risk		High-risk/locally advanced		Metastatic		*Missing*		Total	
	N	%	N	%	N	%	N	%	N	%	**N**	**%**
CPG1	2,537	100.0	3,070	22.0	0	0.0	0	0.0	*530*	*14.9*	**6,137**	**14.7**
CPG2	0	0.0	4,836	34.7	0	0.0	0	0.0	*0*	*0.0*	**4,836**	**11.6**
CPG3	0	0.0	3,228	23.2	0	0.0	0	0.0	*0*	*0.0*	**3,228**	**7.7**
CPG4	0	0.0	0	0.0	4,853	31.4	0	0.0	*16*	*0.5*	**4,869**	**11.7**
CPG5	0	0.0	0	0.0	6,176	40.0	0	0.0	*0*	*0.0*	**6,176**	**14.8**
Nodes	0	0.0	0	0.0	1,877	12.2	0	0.0	*0*	*0.0*	**1,877**	**4.5**
Metastatic	0	0.0	0	0.0	0	0.0	6,272	100.0	*0*	*0.0*	**6,272**	**15.0**
Missing	*0*	*0.0*	*2,789*	*20.0*	*2,531*	*16.4*	*0*	*0.0*	*3,009*	*84.6*	***8,329***	***20.0***
Total	**2,537**	**100.0**	**13,923**	**100.0**	**15,437**	**100.0**	**6,272**	**100.0**	***3,555***	***100.0***	**41,724**	**100.0**

Table 3: CPG categories (4) compared to risk groups (2) for men who had radical treatment (excluding those with metastatic disease)

	Low-risk		Intermediate-risk		High-risk/locally advanced		*Missing*		Total	
	N	%	N	%	N	%	N	%	**N**	**%**
CPG1	109	100.0	408	5.9	0	0.0	*86*	*15.4*	**603**	**3.3**
CPG2	0	0.0	2,746	39.5	0	0.0	*0*	*0.0*	**2,746**	**15.1**
CPG3	0	0.0	2,401	34.5	0	0.0	*0*	*0.0*	**2,401**	**13.2**
CPG4	0	0.0	0	0.0	3,867	36.6	*3*	*0.5*	**3,870**	**21.3**
CPG5	0	0.0	0	0.0	4,559	43.2	*0*	*0.0*	**4,559**	**25.1**
Nodes	0	0.0	0	0.0	953	9.0	*0*	*0.0*	**953**	**5.2**
Missing	*0*	*0.0*	*1,401*	*20.1*	*1,175*	*11.1*	*469*	*84.1*	***3,045***	***16.8***
Total	**109**	**100.0**	**6,956**	**100.0**	**10,554**	**100.0**	***558***	***100.0***	**18,177**	**100.0**

Table 4: Demographic characteristics of men in the CPG1 and low-risk groups

	All				Men receiving radical treatment			
	CPG1		Low-risk		CPG1		Low-risk	
	N	**(%)**	**N**	**(%)**	**N**	**(%)**	**N**	**(%)**
Total	**6,137**	**100.0**	**2,537**	**100.0**	**603**	**100.0**	**109**	**100.0**
Age group								
<60	1,410	23.0	578	22.8	193	32.0	39	35.8
60-69	2,506	40.8	1,048	41.3	248	41.1	45	41.3
70-79	1,891	30.8	757	29.8	153	25.4	24	22.0
80+	330	5.4	154	6.1	9	1.5	1	0.9
Deprivation quintile								
1 - Least deprived	1,536	25.0	663	26.1	153	25.4	30	27.5
2	1,483	24.2	641	25.3	135	22.4	22	20.2
3	1,252	20.4	477	18.8	153	25.4	23	21.1
4	1,010	16.5	403	15.9	85	14.1	13	11.9
5 - Most deprived	811	13.2	335	13.2	74	12.3	20	18.3
Missing	*45*	*0.7*	*18*	*0.7*	*3*	*0.5*	*1*	*0.9*
Co-morbidity score								
0	4,541	74.0	1,810	71.3	464	76.9	79	72.5
1	1,074	17.5	485	19.1	99	16.4	23	21.1
2+	485	7.9	227	8.9	39	6.5	7	6.4
Missing	*37*	*0.6*	*15*	*0.6*	*1*	*0.2*	-	-
Ethnicity								
White	4,578	74.6	1,937	76.4	452	75.0	77	70.6
All other ethnic groups combined	410	6.7	129	5.1	39	6.5	6	5.5
Missing (England)	*658*	*10.7*	*301*	*11.9*	*31*	*5.1*	*6*	*5.5*
*Not available (Wales)**	*491*	*8.0*	*170*	*6.7*	*81*	*13.4*	*20*	*18.3*

* There were no data available for ethnicity in the Welsh dataset.

Figure 1: Final CPG categories (4) and risk groups (2) (data in Appendix 2); adapted from Parry et al (7), using data in this analysis.

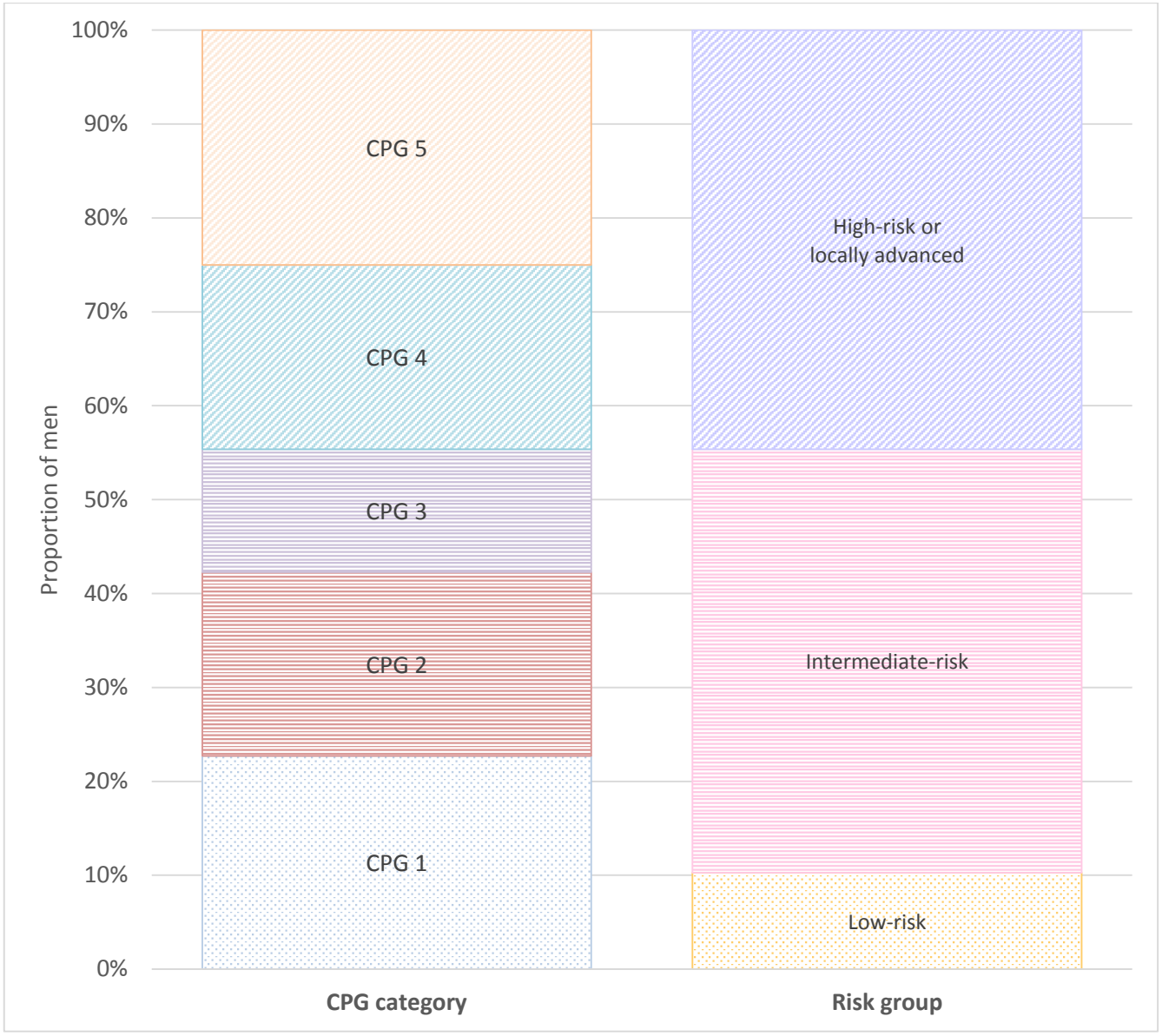


Figure 2: Variation of proportion of men in the CPG1 category undergoing radical treatment across providers

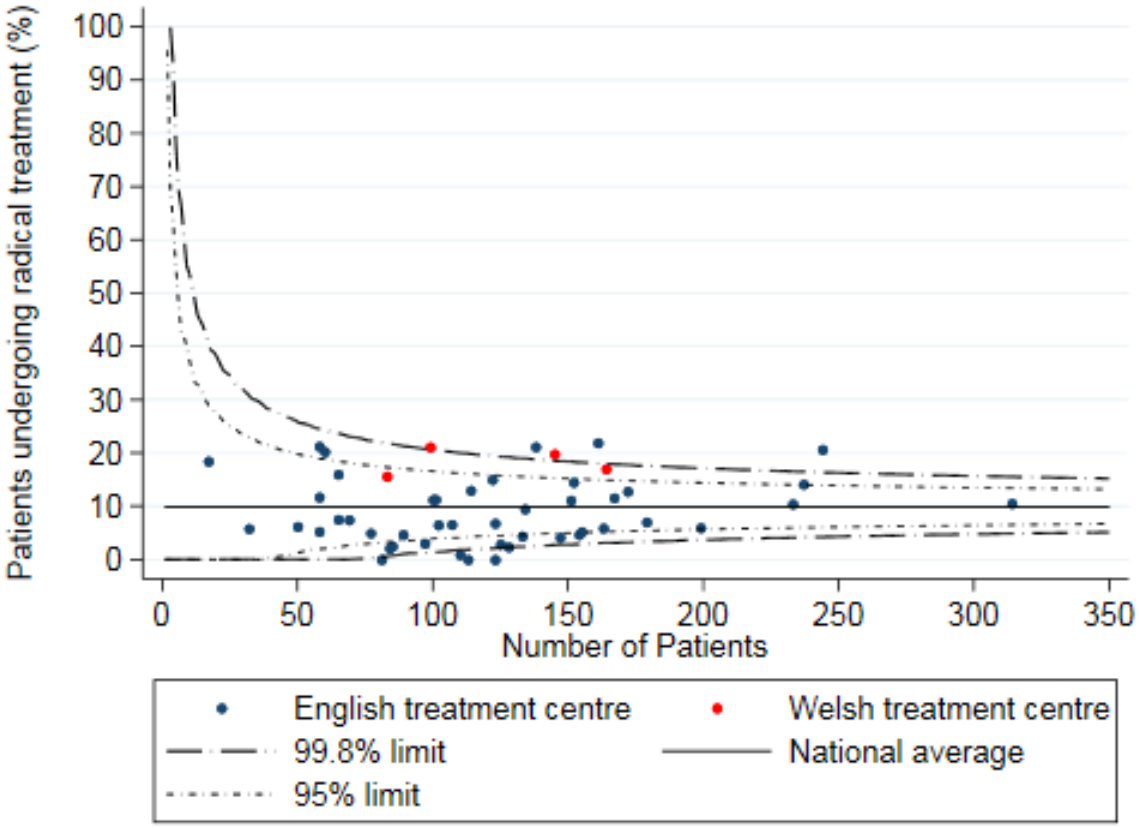
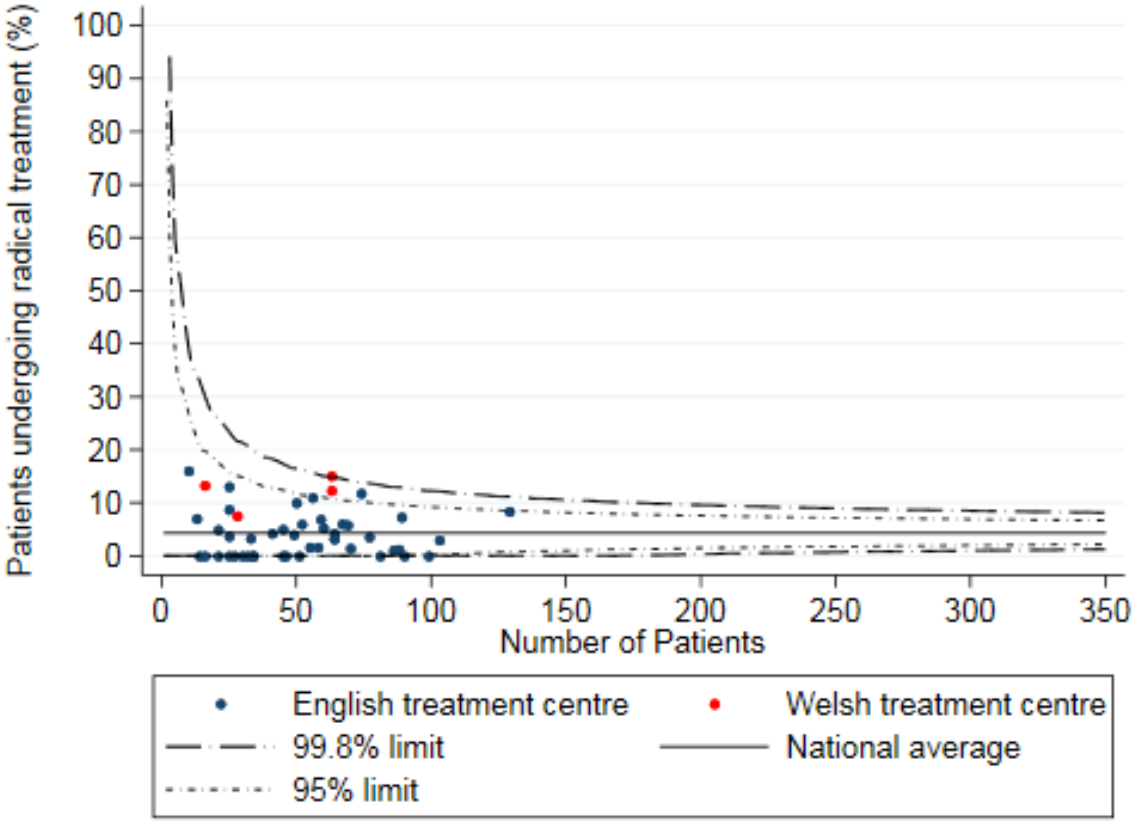


Figure 3: Variation of proportion of men in the low-risk group undergoing radical treatment across providers (scale kept the same as above for comparison)



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Appendices

Appendix 1: Details of TNM staging classification and Gleason scoring system (see also Glossary)

The Gleason score is determined by adding the two most common cell grades identified by the pathologist, 1 being most like normal cells and 5 being the most abnormal. The score is an indication of how aggressive the prostate cancer is likely to be.

Table A1: Gleason scoring system

Gleason score	Grade Group	What it means
Gleason score 6 (or 3 + 3 = 6)	Grade Group 1	The cells look similar to normal prostate cells. The cancer is likely to grow very slowly, if at all
Gleason score 7 (or 3 + 4 = 7)	Grade Group 2	Most cells still look similar to normal prostate cells. The cancer is likely to grow slowly
Gleason score 7 (or 4 + 3 = 7)	Grade Group 3	The cells look less like normal prostate cells. The cancer is likely to grow at a moderate rate
Gleason score 8 (or 4 + 4 = 8)	Grade Group 4	Some cells look abnormal. The cancer might grow quickly or at a moderate rate
Gleason score 9 or 10 (or 4 + 5 = 9, 5 + 4 = 9 or 5 + 5 = 10)	Grade Group 5	The cells look very abnormal. The cancer is likely to grow quickly

Source: https://www.cancerresearchuk.org/about-cancer/prostate-cancer/stages/grades

The anatomical extent of a cancer is usually described using by the TNM staging process where "T" represents the local stage, "N" the presence of cancer spread to lymph nodes and "M" spread to metastatic sites.

Table A2: TNM staging classification

Tumour (T) describes the size of the tumour (area of cancer). This is a simplified description of the T stage. There are 4 main stages of cancer size in prostate cancer – T1 to T4.	
T1	The cancer is too small to be seen on a scan, or felt during examination of the prostate. It is divided into T1a, T1b and T1c.
T1a	The cancer is in less than 5% of the removed tissue,
T1b	The cancer is in 5% or more of the removed tissue, might be found during surgery for other reasons
T1c	These cancers are found by biopsy, for example after a raised PSA level
T2	The cancer is completely inside the prostate gland. It's divided into T2a, T2b and T2c.
T2a	the cancer is in only half of one side of the prostate gland.
T2b	The cancer is in more than half of one side of the prostate gland, but not both sides.
T2c	The cancer is in both sides but is still inside the prostate gland.
T3	The cancer has broken through the capsule (covering) of the prostate gland. It's divided into T3a and T3b.
T3a	The cancer has broken through the capsule (covering) of the prostate gland.
T3b	The cancer has spread into the tubes that carry semen (seminal vesicles).
T4	The cancer has spread into other body organs nearby, such as the back passage, bladder, or the pelvic wall.
Node (N) describes whether the cancer has spread to the lymph nodes. N is split into N0 and N1.	
N0	The nearby lymph nodes do not contain cancer cells
N1	There are cancer cells in lymph nodes near the prostate
Metastasis (M) describes whether the cancer has spread to a different part of the body. There are 2 stages of metastasis – M0 and M1.	
M0	The cancer has not spread to other parts of your body.
M1	The cancer has spread to other parts of the body outside the pelvis. It is split into M1a, M1b and M1c.
M1a	There are cancer cells in lymph nodes outside the pelvis
M1b	There are cancer cells in the bone
M1c	There are cancer cells in other parts of the body

Adapted from https://www.cancerresearchuk.org/about-cancer/prostate-cancer/stages/tnm-staging

Appendix 2: CPG and risk groups without missing data or men with pelvic node involvement

Table A3: CPG and risk groups without missing data or men with nodal involvement

CPG	N	%	Risk Group	N	%
CPG1	5,607	22.7%	**Low-risk**	2,537	10.3%
CPG2	4,836	19.6%	**Intermediate-risk**	11,134	45.1%
CPG3	3,228	13.1%	**High-risk/locally advanced**	11,029	44.7%
CPG4	4,853	19.6%	**Total**	**24,700**	**100.0%**
CPG5	6,176	25.0%			
Total	**24,700**	**100.0%**			

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Data for this report is based on patient-level information collected by the NHS, as part of the care and support of cancer patients. The data is collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is part of Public Health England (PHE).

Glossary

Co-morbidity
Medical condition(s) or disease process(es) that are additional to the disease under investigation (in this case, prostate cancer).

Charlson Co-morbidity Score
A commonly used scoring system for medical co-morbidities. The score is calculated based on the absence and presence of specific medical conditions in the Hospital Episode Statistics (HES) database.

Gleason Score
The Gleason score is a microscopic measure assigned by a pathologist to determine how aggressive an individual's prostate cancer is. It is made up of two separate scores which are then added together to make a final score graded between six and ten. Along with PSA and TNM, the Gleason score can be used to predict how a prostate cancer might behave in the future. This process is known as risk stratification.

Healthcare Quality Improvement Partnership (HQIP)
HQIP aims to promote quality improvement in patient outcomes, and in particular, to increase the impact that clinical audit, outcome review programmes and registries have on healthcare quality in England and Wales. HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing and National Voices.

Hospital Episode Statistics (HES)
A database that contains data on all inpatients treated within NHS trusts in England. This includes details of admissions, diagnoses and treatments.

International Classification of Diseases, Tenth Revision (ICD-10)
This is the World Health Organisation international standard diagnostic classification, and is used to code diagnoses and complications within the Hospital Episode Statistics database of the English NHS.

NHS Trust
An NHS organisation that provides acute care services in England which is made up of one or more hospitals.

Patient Episode Database for Wales (PEDW)
A database that contains all inpatient and day case activity undertaken in NHS hospitals in Wales. This includes details of admissions, diagnoses and the treatments.

Royal College of Surgeons of England (RCS)
An independent professional body committed to enabling surgeons to achieve and maintain the highest standards of surgical practice and patient care. As part of this it supports audit and the evaluation of clinical effectiveness of surgery.

Staging/stage
The anatomical extent of a cancer. This determines whether a cancer is confined within its primary site (localised disease) or whether it has spread to other areas of the body (metastatic spread). It is usually denoted by the TNM staging process where "T" represents the local stage, "N" the presence of cancer spread to lymph nodes and "M" spread to metastatic sites.