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Impact of the Covid-19 pandemic on the diagnosis and treatment of men with prostate cancer

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ABSTRACT

Objective

To determine the impact of the Covid-19 pandemic on diagnostic and treatment activity in 2020 across hospital providers of prostate cancer (PCa) care in the English National Health Service.

Methods

Diagnostic and treatment activity between March 23rd (start of first national lockdown in England) and December 31st 2020 was compared with same calendar period in 2019. Patients newly diagnosed with PCa were identified in national rapid cancer registration data linked to other electronic healthcare datasets.

Results

There was a 30.8% reduction (22,419 versus 32,409) in the number of men with newly diagnosed PCa in 2020 after the start of the first lockdown, compared with the corresponding period in 2019. Men diagnosed in 2020 were typically at more advanced stage (21.2% versus 17.4%, stage IV) and slightly older (57.9% versus 55.9% \geq 70 years, p<0.001). Prostate biopsies in 2020 were more often performed through using transperineal routes (64.0% versus 38.2%). The number of radical prostatectomies in 2020 was reduced by 26.9% (3,896 versus 5,331) and the number treated by external beam radiotherapy (EBRT) by 14.1% (9,719 versus 11,309). Other changes included an increased use of EBRT with hypofractionation and reduced use of docetaxel chemotherapy in men with hormone-sensitive metastatic PCa (413 versus 1,519) with related increase in the use of enzalutamide.

Conclusion

We found substantial deficits in the number of diagnostic and treatment procedures for men with newly diagnosed PCa after the start of the first lockdown in 2020. The number of men diagnosed with PCa decreased by about one third and those diagnosed had more advanced disease. Treatment patterns shifted towards those that limit the risk of Covid-19 exposure including increased use of transperineal biopsy, hypofractionated radiation, and enzalutamide. Urgent concerted action is required to address the Covid-19-related deficits in PCa services to mitigate their impact on long-term outcomes.

INTRODUCTION

Covid-19 has had a profound impact on care provided to patients diagnosed with cancer, with delays in diagnosis and treatment due to steps taken to mitigate viral transmission, changes to provision of services in response to capacity pressures, and patients being reluctant to seek care [1]. In England, the National Health Service increased capacity to treat patients infected with Covid-19 by cancelling elective procedures but it stated at the time that 'emergency admissions, cancer treatment and other clinically urgent care should continue unaffected' [2].

Most European countries have had disrupted cancer services during the initial phase of the pandemic [3] and significant delays in the diagnosis and treatment of cancer have been reported worldwide [1]. During the first national lockdown period in England (between March 23rd March and July 4th 2020), urgent referrals for suspected cancer are reported to have decreased by up to 84% [4].

Prostate cancer (PCa), the commonest urological malignancy and second commonest cause of cancer death in men in the United Kingdom, is a heterogeneous disease. At the time of diagnosis it can range from very low- risk localised cancer to high-burden metastatic disease. The prevalence is higher in older men, in those with a Black and South Asian ethnic background and in those with comorbidities. These characteristics are also key risk factors for Covid-19 related mortality [5]. This demonstrates the challenge faced by clinicians, public health specialists and policy makers who tried to control the spread of Covid-19 infection while minimising delays in the diagnosis and treatment of cancer patients.

One study reported a significant reduction in PCa diagnoses between March and July 2000 in a specific English region [6]. In the same period, a national study found markedly decreased prostate radiotherapy (RT) activity in England [7]. However, to date, there has not been a comprehensive assessment of the Covid-19 pandemic's impact on the entire treatment pathway for PCa care in England.

We used electronic healthcare data from the National Prostate Cancer Audit to evaluate the impact of the Covid-19 pandemic on the diagnosis and treatment of men with PCa in 2020 in England. This evaluation aims to quantify the proportion of the "at risk" population who have experienced delays or changes in the diagnosis and treatment of PCa. These finding are important as they will inform the

development of strategies to mitigate the negative impact of the Covid-19 pandemic on PCa outcomes.

METHODS

Population and data sources

We determined diagnostic and treatment activity across all NHS hospital providers of PCa care in England using national data sets linked at patient level: rapid Cancer Registration Data (rCRD), the Cancer Waiting Times data set (CWT), Hospital Episode Statistics (HES), the National Radiotherapy Data Set (RTDS), and the Systemic Anti-Cancer Therapy data set (SACT).

We identified all patients in England newly diagnosed with PCa between January 1st 2019 and December 31st 2020 according to the rCRD, using the C61 code of the 10th revision of the International Classification of Diseases (ICD-10). The rCRD also provided information on age at diagnosis, ethnicity, tumour stage ranging from stage I (cancer contained within prostate with PSA < 10 ng/ml) to stage IV (cancer spread to lymph nodes or other parts of the body) [8], Charlson comorbidity score [9], and the Index of Deprivation (IMD). The IMD is an area-level measure which combines seven domains of deprivation (income, employment, education, healthcare, housing, and living environment) into a single measure [10]. Patients were categorised into five socioeconomic groups (1=least deprived; 5=most deprived) according to national quintiles of IMD rankings of 32,844 Lower Super Output Areas, containing typically 1500 people. In addition, information on receipt of androgen-deprivation therapy (ADT) as a first treatment was derived from the cancer treatment modality data item in the CWT data set.

OPCS-4 Classification of Interventions and Procedures Procedure codes in HES, the administrative data set of all episodes in English NHS hospitals, were used to determine specific procedures. The M70.2 code was used to identify patients who had a transperineal (TP) biopsy and the M70.3 to identify patients who had a transrectal (TR) biopsy using both inpatient and outpatient HES. For each patient, the biopsy with a date closest to the date of diagnosis was taken. The M61 OPCS-4 code was used to identify men undergoing radical prostatectomy (RP). Additional OPCS-4 codes were used to identify robotic-assisted RP: 'Y753', 'Y765' and laparoscopic RP: 'Y508', 'Y751', 'Y752', 'Y763', 'Y768'.

The OPCS-4 code X67.1 in the RTDS was used to identify men who had radical RT for non-metastatic PCa and other RTDS data items provided information about whether men had received external beam RT (EBRT) or brachytherapy (BT). Combinations of OPCS-4 codes in HES (M70.6.and X65.3 and Y36.3, M70.6 and X65.3, or M71.2 and X65.3) were also used to identify men who had BT. The RTDS

also provided information on the RT region (prostate bed only/whole pelvis), RT doses, number of attendances, and fractionation regimen (standard, hypofractionation, or ultra-hypofractionation on the basis of United Kingdom RT dose fractionation guidance) [11].

The SACT data set was used to identify men who received systemic treatment with docetaxel, enzalutamide, or abiraterone. Linkage of SACT to the rCRD identified men with hormone-sensitive metastatic PCa who had treatment within 16 weeks of diagnosis. The SACT data also provided information on age at diagnosis, ethnicity, tumour stage, Charlson score, and the IMD for the procedure-based cohorts (see below).

Data analysis

We analysed a *diagnosis-based cohort* including patients newly diagnosed with PCa in England between January 1st 2019 and December 31st 2020 according to the rCRD and a number of *procedure-based cohorts* including patients with PCa who had a RP, RT, ADT or chemotherapy between January 1st 2019 and December 31st 2020.

We considered patients to be diagnosed or treated in the initial phase of the pandemic if the date of their diagnosis or treatment was between March 23rd 2020 and 4th July 2020 (the start and end date of the first 'lockdown period' in the UK). We compared the number of patients diagnosed with or treated for PCa in particular periods in 2020 with corresponding calendar periods in 2019.

We used Stata version 15 to perform chi-squared tests to test if proportions are consistent with a null hypothesis of no difference.

This study was exempt from NHS Research Ethics Committee approval because it involved analysis of de-identified linked data collected for the purpose of service evaluation.

RESULTS

Number of men diagnosed with prostate cancer

There was a 48.3% reduction (6,247 versus 12,066) in PCa diagnoses in England during the first formal lockdown period (between March 23rd March and July 4th 2020) compared with the same calendar period in 2019 (Figure 1a). Although the monthly number of diagnoses increased after

lockdown restrictions were lifted in July 2020, overall there was a 30.8% reduction (22,419 versus 32,409) in PCa diagnoses after the start of the first lockdown period (between March 23rd to December 31st December 2020) compared with the same calendar period in 2019 (Table 1). In this period men were likely to be diagnosed at a more advanced stage (p<0.001) and were slightly older (p<0.001) than those diagnosed during the same calendar period in 2019 (Table 2).

Before the first lockdown period in 2020 (between January 1st 2020 and March 23rd 2020), the number of prostate biopsies was slightly higher than in the same calendar period in 2019 (Figure 2). However, the monthly number of prostate biopsies dropped rapidly during the first formal lockdown (between March 23rd March and July 4th 2020) and there was a 48.8% reduction (3,076 versus 6,010) in the number of biopsies compared with the same calendar period in 2019.

An increase in biopsy activity was evident after restrictions were lifted in July 2020, although it did not reach the same level as seen in the same calendar period in 2019. Of the biopsies performed during the first lockdown period (March 23rd March to July 4th 2020), there was a 30.4% point increase (2,825/4,318 versus 3,333/9,511) in the use of the TP approach compared with the same calendar period in 2019 (Figure 2). Overall (between March 23rd March and December 31st 2020), 64.0% of the biopsies performed (10,592 of 16,551) after the start of the first lockdown period in 2020 were by the TP approach compared with 38.2% (9,918 of 25,936) in the same calendar period in 2019.

Surgery

Markedly fewer men underwent RP in 2020 than in 2019. There was a 46.3% reduction (1,076 versus 2,005) in the number undergoing RP during the first lockdown (March 23rd March to 4th July 2020) compared with the same calendar period in 2019 (Figure 1b). By June 2020, surgical activity had increased to 2019 levels although a further decline in activity was evident from August 2020 onwards.

Overall, there was a 26.9% reduction (3,896 versus 5,331) in the number of men undergoing surgery during 23rd March – 31st December 2020 compared with the same calendar period in 2019 (Table 1). Cancer stage in men who had a RP during this period in 2020 was typically less advanced than in those treated in 2019 (Stage 1, 36.3% versus 30.3%; Stage 2, 26.2% versus 27.1%; Stage 3, 34.8% versus 39.6%; Stage 4, 2.8% versus 3.0%, p<0.001), but differences in other patient and tumour characteristics were small (see Supplementary Table 1).

Radiotherapy

The number of men undergoing EBRT fell by 45.4% (2,339 versus 4,287) during the first lockdown period (between March 23rd and July 4th 2020) compared with same calendar period in 2019 (Figure 1c). There was a substantial escalation in activity from July 2020. However, activity fell below 2019 levels from October 2020 onwards. Overall, there was a 14.1% reduction (9,719 versus 11,309) in the number men starting radical RT in 2020 (23rd March – 31st December) compared with the same calendar period in 2019 (Table 1). Men who had EBRT in this period in 2020 were younger (p<0.001) and received a hypofractionated regimen more often (83.1% versus 78.1%), compared with those treated in 2019, with only small difference in other patient and tumour characteristics (see Supplementary Table 2).

The number of men undergoing BT during the first lockdown period in 2020 (between March 23rd March and July 4th 2020) decreased by 56.4% compared with those treated in the same calendar period in 2019 (Figure 1d). Although BT activity increased from May 2020, it never regained prepandemic levels.

Androgen-deprivation therapy

The number of newly diagnosed men receiving ADT after the start of the first formal lockdown period (March 23rd March to Dec 31st 2020) declined by 26.3% (11,789 versus 15,993) compared with the same calendar period in 2019. There are only small differences in the patient and tumour characteristics between men who received ADT in this period and those treated in the same calendar period in 2019 (see Supplementary Table 3).

Systemic treatments

Overall, there was a 72.8% reduction (413 versus 1,519) in the number of men with hormone-sensitive metastatic PCa who received docetaxel after the start of the first lockdown period (March 23rd to December 31st 2020) compared with those treated in the same calendar period in 2019 (Figure 6a). Conversely, there was a marked increase in men receiving enzalutamide after the start of the lockdown period (1,040), March 23 to December 31st 2020) compared to the same calendar period in 2019 (5; Figure 6b). The uptake of abiraterone between March 23rd and November 30th 2020 was limited to 68 patients.

DISCUSSION

To our knowledge, this is the first comprehensive, national evaluation quantifying the impact of Covid-19 on patterns of PCa care. In this population-based study in the English NHS there was a substantial reduction in the number of men who were diagnosed with, or who underwent treatment for PCa during the first formal lockdown period (March 23rd – July 4th 2020). There was also an increased number of men presenting with more advanced cancer after the start of the first lockdown period. Although there was an increase in activity immediately following the end of the first lockdown period, there were substantial 'diagnostic and treatment deficits' by the end of 2020.

New diagnoses of prostate cancer

Our study demonstrates the substantial effect that the Covid-19 pandemic had on the number of men diagnosed with PCa: nearly half of the expected diagnoses were not made in the first lockdown period in England. A similar reduction was observed in a regional study in England including three NHS hospitals [6] and in a study in the United States including 20 healthcare institutions (London et al. 2020). An even more marked reduction (75%) was observed in an Italian study including 3 secondary care hospitals [12].

Although the monthly numbers of PCa diagnoses increased after the end of the first lockdown period in England (from July 4th 2020), these numbers were always lower than in corresponding periods in 2019, creating a 'diagnostic deficit' of almost 10,000 men by the end of 2020. An important concern is the potential for a stage-shift in these men when they are finally diagnosed and their prognosis may be significantly worse.

We also observed an increase in the use of the TP biopsy method after the start of the lockdown period in 2020. The reduction in the overall number of biopsies undertaken reflects British Association of Urological Surgeons and European Association of Urology guidelines recommending to limit the use of invasive procedures and general anaesthesia [13,14]. The shift towards using TP biopsies started before the Covid-19 pandemic, most likely in response to the lower rates of sepsis associated with this technique compared with TR [15], and it accelerated after the start of the Covid-19 pandemic in response to guidance to avoid TRUS where possible [13,14].

Our results are in line with the findings of a survey of 268 urologists in the UK in April and May 2020, just after the start of the first lockdown period in England, which reported that prostate biopsies

were restricted to patients who were suspected to have high-risk disease and that a TP biopsy with a local anaesthetic was typically the preferred method [16].

Radical treatment

Pre-Covid-19 guidance advocated active surveillance in the first instance for patients with low-risk disease [17] and the Covid-19 pandemic simply reinforced this approach [18]. However, the impact of the Covid-19 pandemic on the treatment of men with high-risk disease is more complex and recommendations for these men in response to the Covid-19 pandemic varied from immediate radical treatment to a delay of radical treatment with immediate initiation of ADT [13, 14, 18, 19].

The number of men undergoing RP during the first lockdown period in England fell sharply by almost 50% compared with 2019. A similar reduction in the surgical management of PCa (53%) was reported in a global survey on the impact of Covid-19 on urological services in the first week of April 2020 [20]. In July 2020, English NHS hospitals were asked to put plans in place to restore cancer services to pre-pandemic levels [21]. Although surgical activity reached 2019 levels by June 2020, activity levels dropped again and as a result a 'surgical deficit' was created of just under 1,500 men by the end of December 2020.

There was concern during the pandemic about laparoscopic or robotic surgery due to the potential of aerosol generation and increased viral transmission [22]. However, our results demonstrate that where surgery took place robotic-assisted surgery remained the predominant modality in the English NHS. Men undergoing RP had less advanced disease compared with the same period in 2019.

A systematic review of guidelines and recommendations for urology practice during the Covid-19 pandemic highlighted a lack of agreement about the impact of postponing RP in men with high-risk PCa [18]. ADT was considered as an option to delay disease progression when surgery for high-risk is deferred despite the lack of evidence in this setting [14]. With further follow-up, the National Prostate Cancer Audit will determine the impact of delaying RP for high-risk disease on patient outcomes with and without ADT.

The number of patients receiving EBRT in the English NHS fell sharply by more than 50% during the first lockdown period. Guidance published at the outset of the Covid-19 pandemic advocated avoidance of EBRT in patients with low or favourable intermediate cancer risk, or deferral of EBRT and an extended period of ADT in patients with unfavourable intermediate risk, high-risk or locally

advanced disease, who are commonly initiated on ADT prior to EBRT [19]. Similarly, the decrease in the use of BT during lockdown is in keeping with recommendations to use BT with caution during the pandemic [19].

Although there was a rapid increase of RT activity between July to September 2020 to levels above those observed in 2019, activity levels fell again from October 2020. Overall, there was a 'radiotherapy deficit' of 1,500 men by December 2020. Patients receiving EBRT in 2020 were younger (<70 years), reflecting concerns for an increased risk of Covid-19 for older patients.

During the pandemic, increased use of hypofractionation was seen and there was also some evidence of an increased use of ultra-hypofractionation. These changes followed guidance for the safe maintenance of RT services without reducing treatment effectiveness [19, 23]. These results are similar to those from a national study, carried out in the English NHS and based on unlinked RT data, which reported a rapid uptake of hypofractionation across multiple cancer sites, including treatment for localised PCa, during the pandemic [7].

Although fewer men received radical treatment during 2020, there was only a small difference in the distribution of the type of radical treatment received compared with 2019 (RP: 27.7% versus 30.5%; RT: 64.9% versus 69.0%; Brachytherapy: 4.5% versus 3.3%: 2019 versus 2020, respectively).

Systemic treatments

Although docetaxel provides significant survival benefits in patients presenting with primary metastatic PCa [24], there were concerns that the related immunosuppression would increase the risk of patients becoming severely ill with Covid-19. In April 2020, national rapid guidance was published in the UK on systemic anticancer therapy, recommending swapping docetaxel for enzalutamide or abiraterone in men with newly-presenting hormone-sensitive disease, given that these treatments are less immunosuppressive and can be administered at home [25]. This is reflected in our results showing a rapid and marked fall in docetaxel use and a concomitant marked increase in the use of enzalutamide. In the UK, these treatment recommendations will be reviewed in the second half of 2021 [25].

Strengths and limitations

A key strength of our study is that we report outcomes in an unselected national population, including all men with a new diagnosis of PCa recorded in the rCRD, a national data set that allowed

rapid access to data on patients diagnosed with cancer, linked to other national data sets that capture hospital activity in the NHS, which provides cancer care for 95% of men diagnosed with PCa in England [26].

There are limitations associated with the rCRD, the rapid cancer registry data that we used to identify PCa patients, including under-ascertainment and incomplete information on cancer stage [27]. An unpublished preliminary analysis, carried out by the NPCA comparing the rCDR with standard cancer registry data for PCa diagnoses between January 1st 2018 and March 31st 2019, suggests an under-ascertainment of about 7%. As the rCRD was used to compare activity in both 2019 and 2020, the relative differences that we report are valid. However, the absolute numbers representing the diagnostic and treatment deficits will under-report the backlog in diagnostic and therapeutic activity to the same extent.

Also, Gleason scores and PSA levels are unavailable in the rCRD, so we were not able to risk stratify the patient cohorts into low, intermediate or high-risk groups, which would have reflected the men's cancer risk at the time of diagnosis more accurately.

Clinical and policy implications

The Covid-19 pandemic has caused unprecedented disruption to NHS services. However, the extent of the diagnostic and treatment deficits that were built up by December 2020 demonstrate that it will take significant additional capacity for the NHS to address this backlog. Potential positive effects are that it seems to have accelerated the uptake of TP, increased the use of hypofractionation, and initiated a rapid switch from the use of docetaxel to enzalutamide.

There was a diagnostic deficit of approximately 10,000 men who now have potential to experience a stage a shift to more advanced disease when they are finally diagnosed. Therefore, there should be a focus on increasing public trust in the safety of cancer services, irrespective of the state of the Covid-19 pandemic and better provision of reassurance to patients who may be reluctant to visit primary care and hospital services. In England, the introduction of integrated imaging networks is being considered which will provide support to radiology teams and diagnostic hubs in the community, so that imaging capacity can be increased at sites away from hospitals [28].

From a relative perspective, the therapeutic deficit was greatest for patients receiving surgical treatment. Approaches to reduce the surgical deficit could use the example of 'Covid-light surgical

centres' that have been established in every region in the English NHS [29]. For RT, although the use of ultra-hypofractionation techniques was recommended to limit potential Covid-19 exposure by reducing the number of hospital visits [19], its adoption was still limited. Evolution of the evidence for this approach, coupled with the development of the relevant technical and physical infrastructure and quality assurance processes, has the potential to strengthen its role.

A further consideration is that the Covid-19 pandemic will lead to an increasing number of men diagnosed with more advanced disease which will have a negative impact on their prognosis. Treating patients with locally advanced or metastatic disease is also likely to be more costly than treating those with less advanced disease [30]. All this indicates that urgent concerted action is required to address the diagnostic and treatment deficits in PCa services in order to control the clinical, economic and welfare costs to society.

Conclusions

Our study provides comprehensive national evidence on the impact of the Covid-19 pandemic on PCa care in England. Although diagnostic and therapeutic activity rapidly increased after the end of the first national lockdown period, we found ongoing diagnostic and treatment deficits by December 2000.

During the Covid-19 pandemic, PCa care changed and shifted towards patterns that limit the risk of Covid-19 exposure for patients during their treatment, including increased use of TP biopsy and hypofractionated RT regimens as well as the substitution of docetaxel with enzalutamide. We hope that these observations provide important information for patients and the wider public to help to increase their understanding of and trust in the safety of cancer services, irrespective of the phase of the Covid-19 pandemic.

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Author Contributions

Conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results: JN, AA, JvM, HP, NWC.

Drafted or revised the manuscript: JN, MM, MGP, AS, PC, AA, JvM, HP, NWC.

Approved the final version: JN, MM, MGP, AS, PC, AA, JvM, HP, NWC.

Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: JN, MM, MGP, AS, PC, AA, JvM, HP, NWC.

JN had full access to the data in the study and final responsibility for the decision to submit for publication.

Conflict of interest and financial disclosures

JN, MM, MGP, AS, PC, AA, JvM, HP, NWC are members of the Project Team of the National Prostate Cancer Audit (www.npca.org.uk) which is commissioned by the Healthcare Quality Improvement Partnership (www.hqip.org.uk) as part of the National Clinical Audit and Patient Outcomes Programme, and funded by NHS England and the Welsh Government. 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. The researchers had full independence from the Healthcare Quality Improvement Partnership.

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References

- 1. Sharpless NE. COVID-19 and cancer. Science 2020; 368 (6487): 1290.
- 2. NHS England 2020a. Next steps on the NHS response to Covid-19. Letter from Simon Stevens and Amanda Pritchard, 17th March 2020. https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/20200317-NHS-COVID-letter-FINAL.pdf
- 3. World Health Organisation, 2021 https://news.un.org/en/story/2021/02/1083552
- 4. Sud A, Torr B, Jones ME, Broggio J, Scott S, Loveday C, Garrett A, Gronthoud F, Nicol DL, Jhanji S, Boyce SA. Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study. Lancet Oncology. 2020 Aug 1;21(8):1035-44.
- 5. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehrkar A, Evans D, Inglesby P, Cockburn J, McDonald HI, MacKenna B, Tomlinson L, Douglas IJ, Rentsch CT, Mathur R, Wong AYS, Grieve R, Harrison D, Forbes H, Schultze A, Croker R, Parry J, Hester F, Harper S, Perera R, Evans SJW, Smeeth L, Goldacre B. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020 Aug; 584(7821):430-436.
- 6. Purushotham A, Roberts G, Haire K, Dodkins J, Harvey-Jones E, Han L, Rigg A, Twinn C, Pramesh C, Ranganathan P, Sullivan R. The impact of national non-pharmaceutical interventions ('lockdowns') on the presentation of cancer patients. ecancermedicalscience. 2021;15.
- 7. Spencer K, Jones CM, Girdler R, Roe C, Sharpe M, Lawton S, Miller L, Lewis P, Evans M, Sebag-Montefiore D, Roques T. The impact of the COVID-19 pandemic on radiotherapy services in England, UK: a population-based study. The Lancet Oncology. 2021 Mar 1;22(3):309-20.
- 8. Prostate cancer stages. American Cancer Society. https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/staging.html
- 9. Armitage JN and van der Meulen J. Identifying co-morbidity in surgical patients using administrative data with the Royal College of Surgeons Charlson Score. Br J Surg **97**(5): 772-81 (2010).
- 10. Smith T, Noble M, Noble S, Wright G, McLennan D and Plunkett E. The English indices of deprivation. London: Department for Communities and Local Government, 2015.
- 11. The Royal College of Radiologists. Radiology dose fractionation, third edition. London: The Royal College of Radiologist, 2019.

brfo193 radiotherapy dose fractionation third-edition.pdf (rcr.ac.uk)

- 12. London JW, Fazio-Eynullayeva E, Palchuk MB, Sankey P, McNair C. Effects of the COVID-19 pandemic on cancer-related patient encounters. JCO Clinical Cancer Informatics. 2020 Jul;4:657-65.
- 13. BAUS, 2020. Covid-19 strategy for the interim management of prostate cancer. https://wmcanceralliance.nhs.uk/images/Documents/Covid-19 2020/COVID-19 BAUS Oncology Prostate final 1.pdf

- 14. Ribal MJ, Cornford P, Briganti A, Knoll T, Gravas S, Babjuk M, Harding C, Breda A, Bex A, Rassweiler JJ, Gözen AS. European Association of Urology Guidelines Office Rapid Reaction Group: an organisation-wide collaborative effort to adapt the European Association of Urology guidelines recommendations to the coronavirus disease 2019 era. European urology. 2020 Jul 1;78(1):21-8.
- 15. Berry B, Parry MG, Sujenthiran A, Nossiter J, Cowling TE, Aggarwal A, Cathcart P, Payne H, van der Meulen J, Clarke W. Comparison of complications after transrectal and transperineal prostate biopsy: a national population-based study. BJU International. 2020 Mar 2;126(1):97-103.
- 16. Stroman L, Cathcart P, Lamb A, Challacombe B, Popert R. A cross-section of UK prostate cancer diagnostics during the COVID-19 era-a shifting paradigm? BJU International. 2020.
- 17. NICE, 2019. Prostate cancer: diagnosis and management. NICE guideline [NG131], 2019 <u>NICE</u> <u>Guideline [NG131], 2019</u>
- 18. Heldwein FL, Loeb S, Wroclawski ML, Sridhar AN, Carneiro A, Lima FS, Teoh JY. A systematic review on guidelines and recommendations for urology standard of care during the COVID-19 pandemic. European urology focus. 2020 Sep 15;6(5):1070-85.
- 19. Zaorsky NG, James BY, McBride SM, Dess RT, Jackson WC, Mahal BA, Chen R, Choudhury A, Henry A, Syndikus I, Mitin T. Prostate cancer radiation therapy recommendations in response to COVID-19. Advances in radiation oncology. 2020 Nov 1;5:26-32.
- 20. Teoh JY, Ong WL, Gonzalez-Padilla D, Castellani D, Dubin JM, Esperto F, Campi R, Gudaru K, Talwar R, Okhunov Z, Ng CF. A global survey on the impact of COVID-19 on urological services. European urology. 2020 Aug 1;78(2):265-75.
- 21. NHS England 2020b. Stepping back up of key reporting and management functions. Letter from Amanda Pritchard, 6th July 2020. https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0634-stepping-back-up-of-key-reporting-and-management-functions-letter.pdf
- 22. Mottrie A. ERUS (EAU Robotic Urology Section) guidelines during COVID-19 emergency. European Association of Urology. 2020;25:1-6.
- 23. NICE, 2020b. NHS England interim treatment changes during the Covid-19 pandemic. NICE guideline [NG161], 2020 <u>NICE Guideline [NG161], 2020. NHS England interim treatment changes during the COVID-19 pandemic</u>
- 24. Clarke NW, Ali A, Ingleby FC, Hoyle A, Amos CL, Attard G, Brawley CD, Calvert J, Chowdhury S, Cook A, Cross W et al. Addition of docetaxel to hormonal therapy in low- and high-burden metastatic hormone sensitive prostate cancer: long-term survival results from the STAMPEDE trial. Ann Oncol. 2019 Dec 1;30(12):1992-2003. doi: 10.1093/annonc/mdz396.
- 25. NICE, 2020a. COVID-19 rapid guideline: delivery of radiotherapy. NICE guideline [NG162], 2020 https://www.nice.org.uk/guidance/NG162
- 26. Barbiere JM, Greenberg DC, Wright KA, et al: The association of diagnosis in the private or NHS sector on prostate cancer stage and treatment. J Public Health (Oxf) 34:108-114, 2012

- 27. NCRAS, 2021. Rapid Registration Dataset, June 2021 monthly snapshot. http://www.ncin.org.uk/collecting and using data/rcrd
- 28. All-Party Parliamentary Group for Radiotherapy. Catch-up with cancer the way forward. May 2021. https://e8604b0e-5c16-4637-907f-3091e4443249.filesusr.com/ugd/b68571 a18ace5b95fa4c3fa3027456b5928faf.pdf
- 29. Royal College of Surgeons of England. A New Deal for Surgery. May 2021. https://www.rcseng.ac.uk/about-the-rcs/government-relations-and-consultation/position-statements-and-reports/action-plan-for-england/
- 30. Sun L, Legood R, dos-Santos-Silva I, Gaiha SM, Sadique Z. Global treatment costs of breast cancer by stage: A systematic review. PLoS One 2018; 13(11): e0207993.

Figure Legends

- **Figure 1.** Monthly number of men (a) newly diagnosed with prostate cancer, (b) undergoing radical prostatectomy, (c) radical external beam radiotherapy or d) brachytherapy in 2019 and 2020.
- **Figure 2.** Monthly number of prostate biopsies and % point change in transperineal biopsies in 2019 and 2020.
- **Figure 3.** Monthly number of men with hormone-sensitive metastatic prostate cancer starting (a) docetaxel and (b) enzalutamide in 2019 and 2020.

Table 1. Diagnostic and radical treatment activity in 2019 and 2020 (from March 23rd to December 31st).

Number/year	2019	2020	% reduction
Diagnoses	32,409	22,419	30.8
Radical	5,331	3,896	
prostatectomy			26.9
Radical radiotherapy	11,309	9,719	14.1
Brachytherapy	785	470	40.1

Table 2. Patient and tumour characteristics for men diagnosed with prostate cancer in 2019 and 2020 (from March 23rd to December 31st).

	2019		2020		P-value
	N	%	N	%	
Total diagnosed	32,409		22,419		
Age group (years)					<0.001
0-	4,136	12.8	2,533	11.3	
60-	10,180	31.4	6,900	30.8	
70-	12,915	39.9	9,218	41.1	
80-	5,178	16	3,768	16.8	
Stage					<0.001
1	8,552	36.1	5,465	35.6	
2	3,800	16	2,258	14.7	
3	7,231	30.5	4,374	28.5	
4	4,132	17.4	3,263	21.2	
Missing	8,694		7,059		
Ethnicity					0.03
White	26,096	92.3	17,221	92.5	
Mixed	155	0.5	99	0.5	
South Asian	618	2.2	407	2.2	
Black	1,051	3.7	611	3.3	
Other	349	1.2	275	1.5	
Missing	4,140		3,806		
National quintiles of socioeconomic					
deprivation					0.76
1 - Least deprived	7,828	24.2	5,472	24.4	
2	7,834	24.2	5,461	24.4	
3	6,867	21.2	4,733	21.1	
4	5,511	17	3,811	17	
5 - Most deprived	4,369	13.5	2,942	13.1	
Comorbidities					0.01
0	26,003	80.2	18,198	81.2	
1	3,019	9.3	2,056	9.2	
>=2	3,387	10.5	2,165	9.7	

Figure 1. Monthly number of men (a) newly diagnosed with prostate cancer, (b) undergoing radical prostatectomy, (c) initiating radical external beam radiotherapy or d) undergoing brachytherapy in 2019 and 2020.

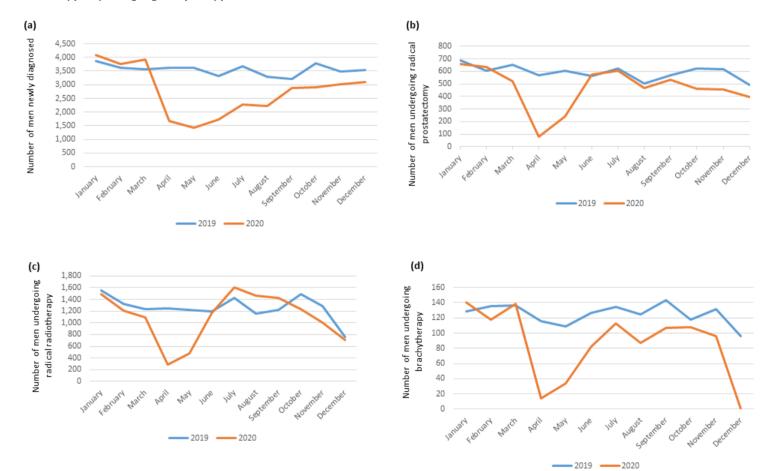


Figure 2. Monthly number of prostate biopsies and percentage point difference in transperineal biopsies in 2019 and 2020.

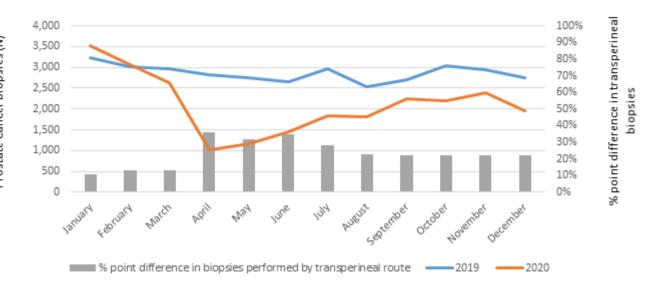


Figure 3. Monthly number of men with hormone-sensitive metastatic prostate cancer starting (a) docetaxel or (b) enzalutamide in 2019 and 2020.

