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A Comprehensive National Survey of Prostate-specific Antigen Testing and Prostate Cancer Management in France: Uncovering Regional and Temporal Disparities

Olivier Cussenot[a,b,*], *Yoann Taille*[c], *Jean-Jacques Portal*[c], *Géraldine Cancel-Tassin*[b,d], *Morgan Roupret*[b,d], *Alexandre de la Taille*[e], *Guillaume Ploussard*[f], *Romain Mathieu*[g], *Freddie C. Hamdy*[a], *Eric Vicaut*[c]

[a] *Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK;* [b] *CeRePP, Paris, France;* [c] *Clinical Research Unit, AP-HP. Nord - University Paris Cité, Paris, France;* [d] *GRC n°5 Predictive Onco-Urology, AP-HP, Sorbonne Université, Paris, France;* [e] *Department of Urology, AP-HP, Hopitaux Universitaires Henri Mondor, University of Creteil, Créteil, France;* [f] *Department of Urology, La Croix du Sud Hospital, Quint Fonsegrives, France;* [g] *Department of Urology, CHU Rennes, Rennes, France*

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Abstract

We report nationwide real-life practice in the management of prostate cancer (PC) in France in a population of 4 936 750 men. All prostate-specific antigen (PSA) blood tests performed between 2006 and 2018 were recorded in a National Health registry, which allowed to identify 692 516 men diagnosed with PC and a control population consisting of 3 899 509 men without PC. PSA tests, age at diagnosis, treatments, and survival were analysed. Their management was analysed by age range and compared in the different French regions. Disparities were found in age at PSA testing and management approaches (surveillance, and local and systemic therapies). We found that 50% of men had received five PSA blood tests, but the first PSA test was taken late in life, with a peak in the decade between 65 and 75 yr of age. Adoption of monitoring was low (12%). Older men appeared to receive a late diagnosis with reduced chances of curative therapy and a subsequent increase in mortality, but cautious interpretation of our data is warranted in view of competing morbidities and other causes of death. The incidence of metastases at diagnosis, indicated by the use of systemic therapies, increased progressively from 2011 onwards.

Patient summary: In this study, we report nationwide real-life practice in the management of prostate cancer (PC) in France in a population of 4 936 750 men, including 692 516 patients with PC. We found that the first prostate-specific antigen test is taken too late in life, leading to a late diagnosis with reduced chances of curative therapy and a subsequent increase in mortality.

* Corresponding author. Nuffield Department of Surgical Sciences, University of Oxford, Old Road Campus Research Building (off Roosevelt Drive) Headington, Oxford OX3 7DQ, UK. Tel. +33 1 56 01 76 46; Fax: +33 1 56 01 76 47.
E-mail address: o.cussenot@cerepp.org (O. Cussenot).

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Prostate cancer (PC) is a leading cause of cancer-related deaths in Europe, with a standardised death rate of approximately 37.4 per 100 000 male residents of the European Union in 2019 [1]. The management of PC, including the use of prostate-specific antigen (PSA) testing for early detection and initial therapeutic strategies, remains controversial [2]. Although health care authorities and professional societies have provided guidelines to reduce the harms associated with PSA testing in primary care, metastatic disease continues to be diagnosed at an increasing rate [3], despite a paradoxical decline in disease-specific mortality in recent years. Furthermore, there are still significant regional disparities in the incidence of PC and disease-specific mortality, which may be influenced by a range of factors, including variations in medical practice. In this study, we present data from a French national registry of medical practices that provide real-life insight into trends in PSA testing, management of PC, and disease-specific mortality.

Between 2006 and 2018, the study identified 692 516 men with PC and 3 899 509 control men (Supplementary material [Methods], Supplementary Table 1, and Supplementary Fig. 1). During this period, 37 640 010 PSA blood tests were performed, 1 860 156 before the diagnosis of a PC and 15 685 675 for men without PC. We found that 50% of men had received at least five PSA blood tests, but the first one was taken late in life, with a peak in the decade between 65 and 75 yr of age (Fig. 1). In the control men, the median age for first PSA testing decreased from 69 yr (interquartile range [IR]: 62–75) in 2006 to 64 yr (IR: 57–71) in 2018. The youngest median ages for the first PSA test were 59 (IR: 53–65) and 61 (IR: 54–69) yr in Martinique and Guadeloupe, respectively (Supplementary Table 2). The proportion of PC diagnosed in the population having undergone PSA tests was 15.1% in continental regions, with a greater proportion observed in the West Indies, including Martinique (21.6%) and Guadeloupe (20.8%; Supplementary Table 3).

Of the PC cases, 28% were detected at the first PSA test. In men aged 50–70 yr, 23.3% had locally advanced or metastatic disease, and 61.2% were first treated by radical prostatectomy (RP), associated in 88% of cases with pelvic lymphadenectomy. Distribution of first-line treatment is presented by age groups and year of inclusion in Supplementary Table 4 and Supplementary Figure 2, and by administrative regions in Supplementary Figure 3. During the observed period, administration of androgen deprivation therapy (ADT) by medical or surgical castration and chemotherapy, including new hormonal therapy (CHM), increased, while active surveillance and watchful waiting (ASWW) remained stable (Fig. 2).

Among the men diagnosed with PC, 21% received a secondary line of management and 12% a third line (Supplementary Fig. 4). Salvage pelvic radiotherapy (external beam radiotherapy [EBRT]) and ADT were used, respectively, in 7.4% and 16.8% of men who received a primary RP, with the majority of treatments (55.9% and 64.8%, respectively) given within 2 yr from surgery (Supplementary Table 5). EBRT was mainly given with neoadjuvant ADT. Long-term ADT was given as first treatment in 43.4% of men, and complemented with chemotherapy in 12.6%. Of the 12.0% of men receiving ASWW initially, 25.4% received a second treatment as follows: RP (4.45%), EBRT (1.62%), and ADT (18.93%; Supplementary Table 6). The mean ages for the initiation of treatment were 65.9 (standard deviation [SD]: 6.9), 69.9 (SD: 7.5), 64.4 (SD: 6.3),

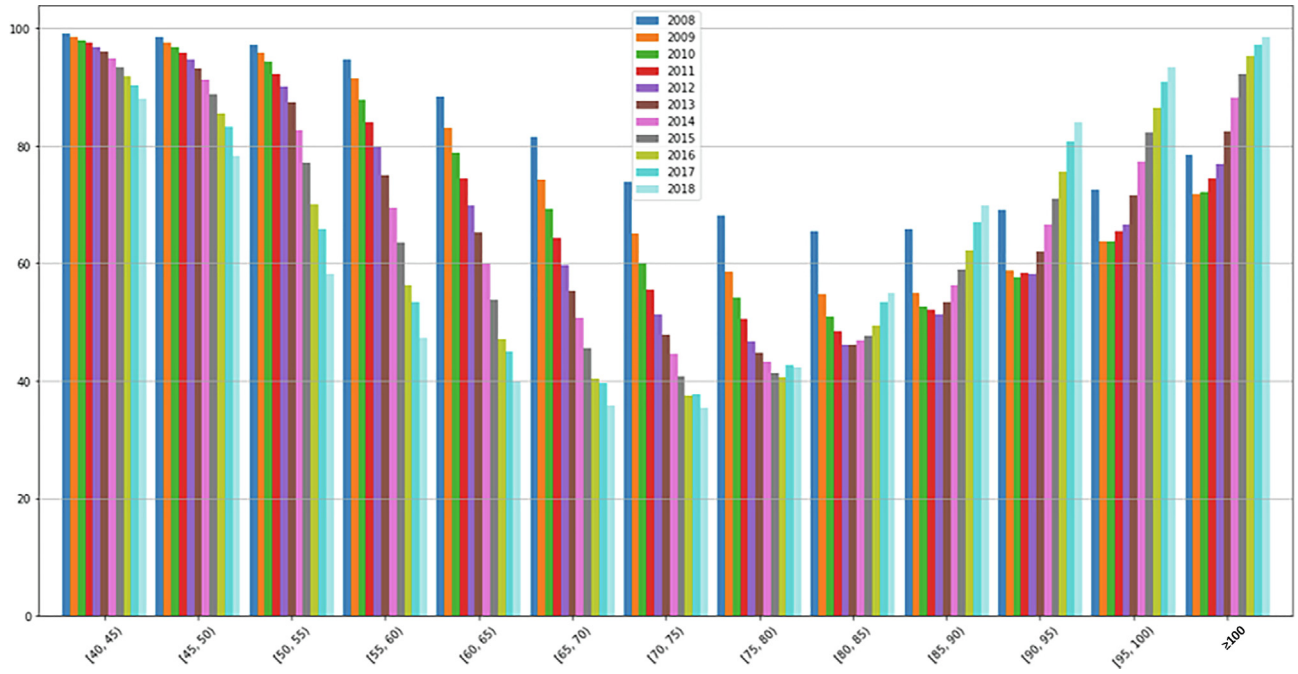

Fig. 1 – Percentage of men without PSA test according to age group and year of inclusion. PSA = prostate-specific antigen.

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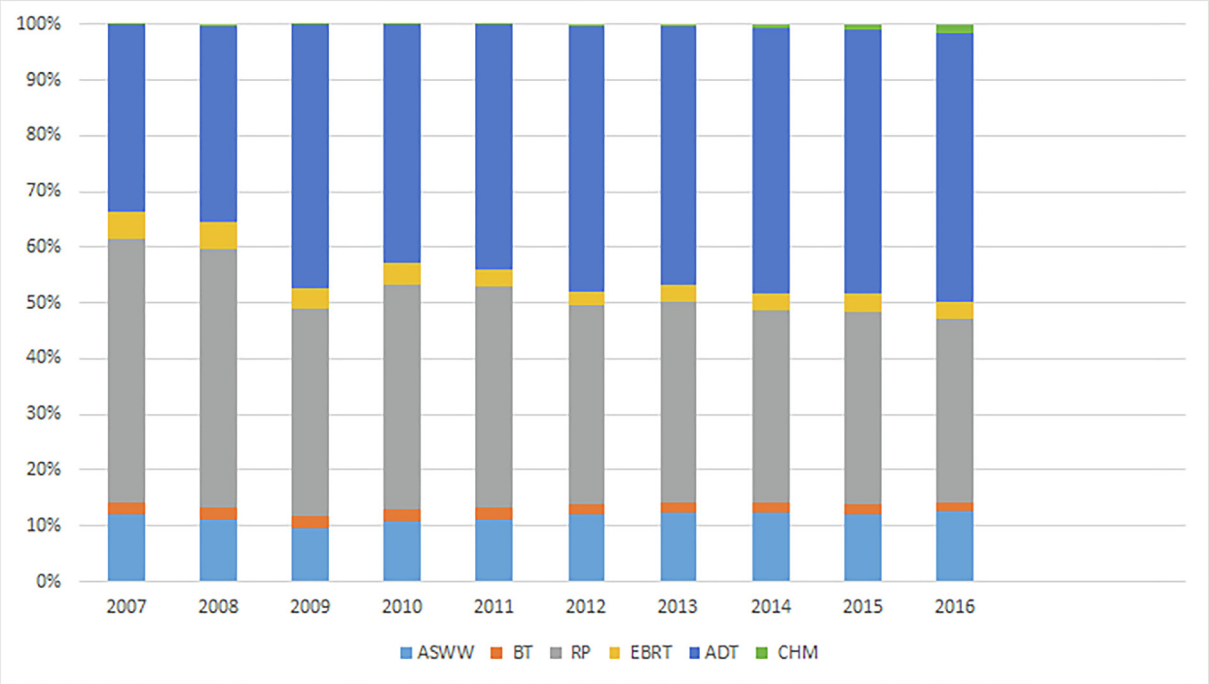

Fig. 2 – Distribution of first-line management of patients with prostate cancer according to the year of diagnosis. ADT = androgen deprivation therapy; ASWW = monitoring by active surveillance or watchful waiting; BT = brachytherapy; CHM = chemotherapy or new hormonal therapy (abiraterone or enzalutamide); EBRT = external beam radiotherapy; RP = radical prostatectomy.

74.4 (SD: 10.3), and 71.9 (SD: 8.4) yr for brachytherapy, EBRT, RP, ADT, and CHM, respectively.

An excess of early mortality in men with PC was observed in all age groups, including after age 80 yr (hazard ratio [HR]: 1.19; 95% confidence interval [95% CI]: 1.19–1.20, $p < 0.0001$; Supplementary Table 7). Earliest death due to PC (matched with control population in the same region) was in Bretagne (HR: 1.26; 95% CI: 1.19–1.25) and the latest in Grand Est (HR: 1.08; 95% CI: 1.06–1.10; Supplementary Table 8 and Supplementary Fig. 5).

The data presented herein were obtained from national registry databases, with their known limitations [4,5]. The patterns of first-line treatment were similar to those reported in the CaPSURE cohort [6], with approximately 50% of RP cases in the 50–75-yr age group. In the CaPSURE cohort, 9% of men received ASWW, with higher mortality in these men than in those receiving radical treatment. We did not observe this mortality difference in the patients of our cohort with ASWW as first-line management (12%), but it is notable that among them, 15% of the men who were managed by watchful waiting died within 3 yr from the diagnosis of PC. This is likely due to competing morbidities and poor health, as 19% of these men were managed for another malignancy. In contrast, the patients who received true active surveillance (AS) had better survival.

In daily practice, management of PC is dictated by prognostic groups based on age, comorbidities, and features of disease aggressiveness, and comparison between treatments is therefore inappropriate and could be misleading. Our analysis suggests that ASWW remains underutilised and was stable in France while increasing in the USA in the same period [7]. The use of radical treatments, such as RP or EBRT, remains stable, while systemic therapies, including long-term ADT and CHM, are increasing, as reported in other countries [3]. These trends suggest an increase in men presenting with metastases at diagnosis, as well as improved detection of small-volume extraprostatic disease. PSA testing continues to increase in France. The observed regional variations in age at death cannot be attributed entirely to PC mortality because of competing causes, illustrated for instance by the low life expectancy observed in the Hauts-de-France region. After adjustment for age at death in the control population, early deaths in the PC group appeared to be higher in western France than in other regions (Supplementary Fig. 5). Health care authorities and professional societies should establish clear guidelines for PSA testing and provide support to primary care physicians in order to implement the recommendations [8]. Finally, efforts should be made to increase the utilisation of AS where appropriate and reduce overtreatment with radical therapies, which can result in significant side effects and reduced quality of life.

***Author contributions*:** Olivier Cussenot had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Cussenot, Vicaut.
Acquisition of data: Taille, Portal, Cancel-Tassin, Cussenot, Roupret, de la Taille, Ploussard, Hamdy, Mathieu.
Analysis and interpretation of data: Taille, Portal, Cussenot, Vicaut.
Drafting of the manuscript: Cussenot, Hamdy, Taille, Cancel-Tassin.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euo.2024.02.008.

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