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Prostate cancer progression: a scoping review, pharmacoeconomic assessment, and evaluation of quality of life

Rute Dinis de Sousa[a,b], Daniela Mariana Zagalo[a], Miguel Gouveia[c], Luís Gomes[a], José Santos Dias[d], André Mansinho[e,f], Susana Santos[g], José Mariano[g], Helena Canhão[a,b,h] and Ana Rodrigues[a,b,i]

[a]CHRC, NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa, Lisboa, Portugal; [b]Episaúde - Associação Científica, Évora, Portugal; [c]Católica Lisbon School of Business and Economics, Universidade Católica Portuguesa, Lisboa, Portugal; [d]Instituto da Próstata, Lisboa, Portugal; [e]START Center for Cancer Care, Hospital de Santa Maria, Unidade Local de Saúde Santa Maria, Lisboa, Portugal; [f]Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; [g]Johnson & Johnson Innovative Medicine, Oeiras, Portugal; [h]Unidade Local de Saúde São José, Hospital Santo Antonio Capuchos, Lisboa, Portugal; [i]Hospital dos Lusíadas, Lisboa, Portugal

ABSTRACT

Aims/background: Prostate cancer is the most common malignancy in men and a leading cause of cancer-related death. Progression from non-metastatic castration-resistant prostate cancer (nmCRPC) to metastatic CRPC (mCRPC) significantly worsens health-related quality of life (HRQoL), increases mortality, and raises healthcare costs. This study assessed the impact of avoiding or delaying progression to mCRPC on HRQoL, mortality, and economic outcomes, incorporating patients' lived experiences and unmet needs.

Methods: Three complementary studies were conducted. Study 1 was a scoping review of HRQoL and functional outcomes across disease stages, analyzing 56 studies (27 RCTs, 29 observational). Study 2 used a pharmacoeconomic survival-partition model of apalutamide, calibrated for the Portuguese healthcare system, to estimate utility gains, mortality impacts, and healthcare costs associated with delaying progression (excluding drug costs). Study 3 comprised two virtual focus groups ($n = 5$) exploring patient experiences, including symptom burden, psychological impact, daily life disruption, coping strategies, and care-related unmet needs.

Results: High-risk nmCRPC patients had higher HRQoL and better function than mCRPC patients. Symptomatic mCRPC had the lowest HRQoL (EQ-5D 0.63–0.90 vs 0.85–0.86; FACT-P 93–123 vs 109–121). Delaying progression yielded an estimated utility gain of 0.192, reduced annual mortality (0.1% vs 19.1%), and 4.4-fold lower healthcare costs. Focus groups confirmed greater physical symptoms, emotional distress, and social disruption in mCRPC, while nmCRPC experiences centered on monitoring and uncertainty. Patients identified gaps in supportive care, including psychosocial, sexual, and functional needs.

Conclusions: Delaying progression from nmCRPC to mCRPC confers substantial HRQoL, survival, and economic benefits. Patient perspectives highlight gaps in supportive care and the value of early targeted interventions.

Limitations: Small qualitative sample, reliance on baseline HRQoL without longitudinal adjustment, heterogeneity across studies, and exclusion of nmCRPC treatment costs may limit generalizability and precision.

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CONTACT Rute Dinis de Sousa rute.sousa@nms.unl.pt CHRC, NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa, Campo Mártires da Pátria, 130, 1169-056 Lisboa, Portugal

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Introduction

Prostate cancer remains the most commonly diagnosed cancer among men worldwide. In the United States alone, it is estimated that there will be 313,780 new cases and 35,770 deaths from prostate cancer in 2025[1]. Similarly, in 2022, prostate cancer was the third most commonly diagnosed cancer in the European Union, with an estimated 330,000 new cases, accounting for 12.1% of all cancer diagnoses[2]. In Portugal, prostate cancer was the most prevalent cancer among men in 2022, with an incidence of 7,529 new cases (19.9%) and a mortality of 2,083 (10.7%)[3]. The age-standardized incidence rate of prostate cancer in Portugal was 62.6 cases per 100,000 men in 2022, slightly higher than the European average of 59.9[4]. Conversely, Portugal's mortality rate was 11.1 per 100,000, closely aligning with the European average of 11.2[4].

Prostate cancer risk is shaped by a multifactorial interplay of non-modifiable and modifiable determinants. Well-established non-modifiable risk factors include advancing age, African ancestry, a familial history of the disease, and specific hereditary genetic conditions, such as Lynch syndrome and mutations in the BRCA1 and BRCA2 genes. In parallel, increasing evidence supports the influence of modifiable exposures, particularly behavioral and lifestyle factors, on disease initiation and progression. These include tobacco use, alcohol consumption, dietary patterns, obesity, and insufficient physical activity. Moreover, the use of specific pharmacological agents and occupational exposure to carcinogenic substances may further elevate the risk of developing clinically aggressive and potentially lethal forms of prostate cancer[5–7].

Table 1 summarizes key data from the Portuguese National Oncological Registry (RON) for 2001, 2009, and 2019[8–10]. Between 2001 and 2019, new cases increased by 77.5%, with the crude incidence rate rising by 77.3%. This growth is largely attributed to the aging population, as the incidence rate tends to rise with age. This pattern is shown in Figure 1, which highlights the sharp rise in incidence with age[8–10].

Table 1. Prostate cancer incidence in Portugal.[8–10]

Year	2001[8]	2009[9]	2019[10]
New Cases	3895	5433	6912
Crude rate per 100,000 men	80.2	107.3	142.2
Standardized Rate per 100,000 men, ESP	66.8	82.4	90.9
Standardized Rate per 100,000 men, WSP	44.5	56.1	61.7

Standardized incidence rate per 100,000 men using a European Standard Population (ESP); Standardized incidence rate per 100,000 men using a World Standard Population (WSP).

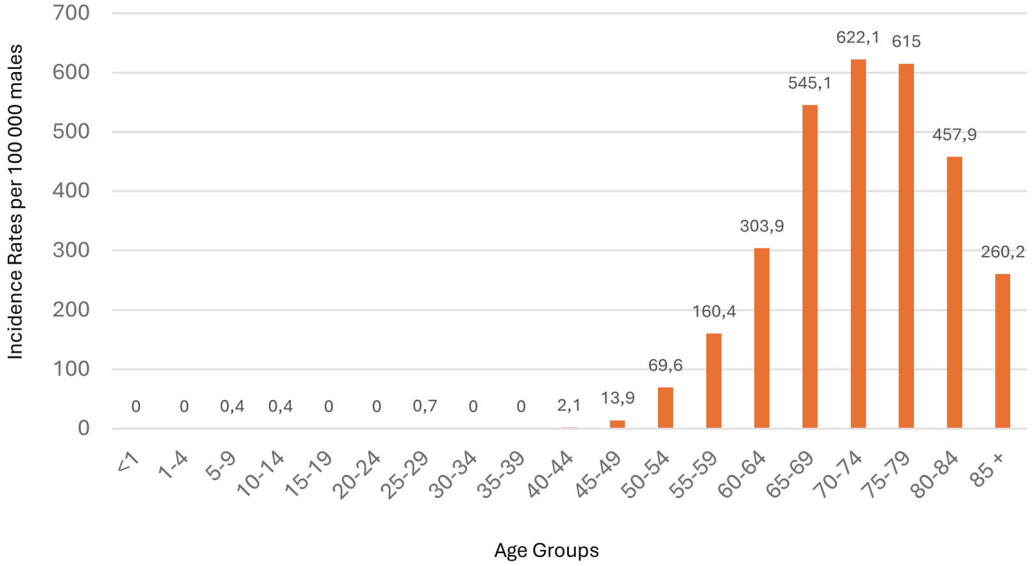

Figure 1. Incidence rates by age of prostate cancer in Portugal, per 100,000 males[10].

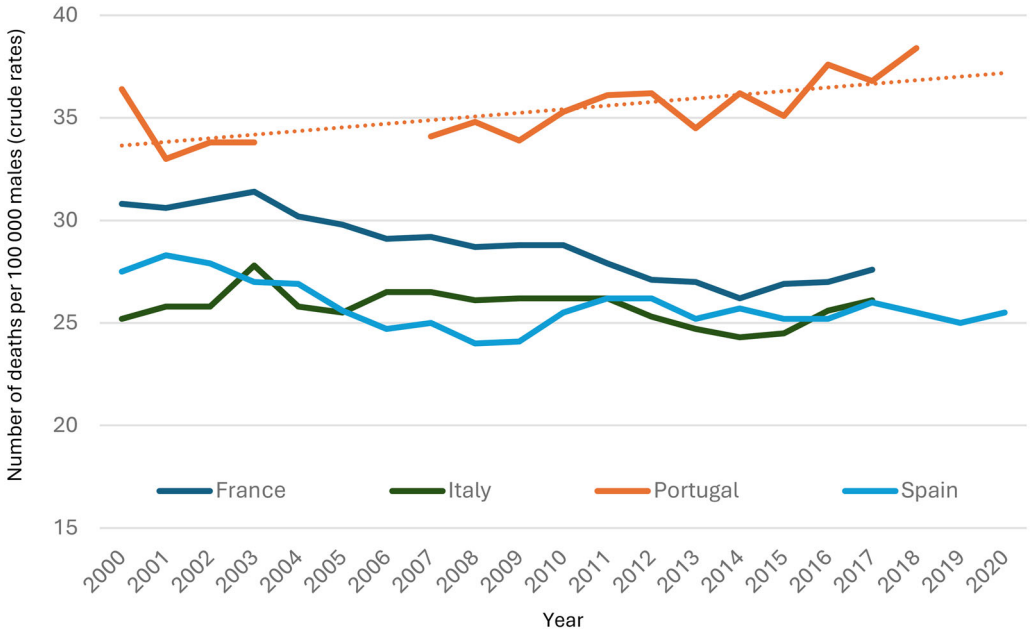

Figure 2. Malignant neoplasms of prostate, deaths per 100,000 males (crude rates)[11].
Crude mortality rates represent the number of deaths from malignant neoplasms of the prostate per 100,000 males in the total male population of each country, regardless of age. The denominator includes all males who were alive for at least one day of each year. Crude rates are not adjusted for differences in age distribution across countries or over time. *Source:* OECD Health Statistics—Malignant Neoplasms of Prostate[11].

While crude rates reflect raw population growth and aging, standardized rates adjust for demographic changes. As shown in Table 1, the standardized incidence rate rose by only 36.1% (European standard), implying that the remaining 41.2% growth is age-related. Importantly, regardless of the causes, the incidence rates of prostate cancer have been increasing in Portugal[8–10].

On the other hand, Figure 2 presents crude prostate cancer mortality rates in France, Italy, Portugal, and Spain. While France, Italy, and Spain have seen declines, Portugal's crude mortality rate has increased, again reflecting population aging[11].

Figure 3 shows that standardized mortality rates are declining faster than crude rates in those countries, and even in Portugal, standardized mortality is decreasing, despite the crude rate increase[11].

Although the aforementioned statistics might be perceived as disconcerting, it is important to highlight that Portugal's mortality/incidence ratio has dropped significantly, from 41.2% in 2001 to 23.7% in 2019, suggesting progress in diagnosis and treatment[8–10].

This progress can be largely attributed to significant advances in early detection and therapeutic innovation over recent decades. In Portugal, prostate cancer screening is integrated into the National Cancer Screening Program, with Prostate-Specific Antigen (PSA) testing recommended for individuals aged 50 to 75 years[12]. Declining standardized mortality and, more notably, the reduced mortality/incidence ratio signal substantial health gains through improved diagnostic and therapeutic strategies[8–10].

Across different stages of prostate cancer, available treatments include androgen deprivation therapy (ADT), radical prostatectomy, radiotherapy, and novel agents such as androgen receptor pathway inhibitors (e.g. abiraterone, apalutamide, enzalutamide, and darolutamide). However, measuring health gains solely by mortality reduction overlooks a significant portion of these gains. The crucial point is that, considering survival, there may be substantial health improvements derived from enhancements in Health-related quality of life (HRQoL).

While many men with prostate cancer experience a favorable prognosis and near-normal life expectancy, the disease and its management can impose significant physical, psychological, and social burdens. These impacts vary depending on cancer stage, grade, and treatment type, affecting not only patients' quality of life but also that of their caregivers or partners[13–18].

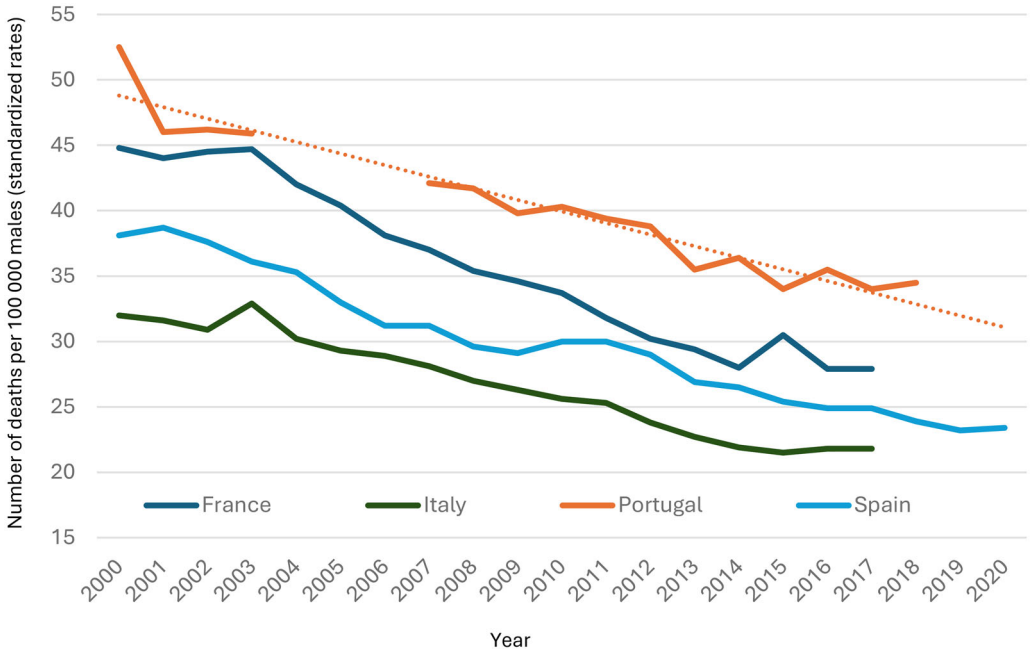

Figure 3. Malignant neoplasms of prostate, deaths per 100,000 males (standardized rates)[11].
Age-standardized mortality rates represent the number of deaths from malignant neoplasms of the prostate per 100,000 males, adjusted to the 2015 OECD population structure. This standardization allows for accurate comparisons between countries and over time by accounting for differences in age distribution. The denominator includes all males in the general population, not just those diagnosed with prostate cancer. *Source:* OECD Health Statistics—Malignant Neoplasms of Prostate[11].

The evaluation of HRQoL in prostate cancer aims to quantify the essential physical and psychological burden of the disease and its treatment for evaluating patient status, encompassing urinary, sexual, and bowel functions, hormonal function, psychological well-being, and general health perception[15–17,19–34].

The main objective of this article was to conduct a comprehensive and in-depth investigation into the impact of the absence of disease progression to the metastatic stage in prostate cancer concerning HRQoL, mortality rates, and cost savings to the healthcare system. The combination of qualitative and pharmacoeconomic studies in this field yields a more thorough understanding of the potential impact of the disease and its treatment on the quality of life of patients with and without disease progression to the metastatic phase, providing equally valuable insights into the unmet needs within the healthcare system. Consequently, it facilitates a more informed discussion on the development and implementation of new policies, patient support initiatives, and additional strategies designed to ensure enhanced clinical practice and side-effect management for individuals with this illness.

Methodology

Three distinct studies were conducted to assess the impact of the absence of disease progression to the metastatic stage in prostate cancer. These studies integrate multidisciplinary perspectives, including those of health professionals, health economists, and patients themselves. In the initial phase, a review analysis was conducted on the bibliographic corpus, with a focus on analyzing HRQoL and function data over the course of disease progression from study populations (high-risk non-metastatic castration-resistant prostate cancer (nmCRPC) and metastatic castration-resistant prostate cancer (mCRPC) patients) (Study 1, Scoping Review). Subsequently, an apalutamide pharmacoeconomic model was employed to quantify the health gains achieved through the postponement of disease progression (Study 2, Pharmacoeconomic Assessment). Last, a qualitative research design with focus groups was conducted to obtain an interpretive understanding of the experiences of patients with and without disease progression to the metastatic phase (Study 3, Qualitative Study).

Study 1—scoping review

The primary aim of this scoping review was to evaluate the impact of disease progression, specifically, the development of metastases, on HRQoL and functional outcomes in adult men diagnosed with castration-resistant prostate cancer at high risk of metastasis. Our focus on nmCRPC is justified by its role as a pivotal stage where metastasis-free survival can be extended through targeted therapies, thereby preventing the high costs and HRQoL declines associated with metastatic disease. Notably, nmCRPC benefits from approved androgen receptor inhibitors like apalutamide, enzalutamide, and darolutamide, which improve MFS and OS, whereas high-risk localized disease lacks such specific data-supported interventions beyond standard multimodal therapy. This aligns with recent therapeutic advancements and addresses a gap in evidence for this understudied subgroup.

Thus, the review had the following specific objectives: (a) Explore and characterize HRQoL and functional outcomes in patients with nmCRPC at high risk of progression to metastatic disease; (b) Explore and characterize HRQoL and functional outcomes in patients with mCRPC; (c) Examine differences in HRQoL and functional outcomes across subgroups of patients, including high-risk nmCRPC, asymptomatic mCRPC, and symptomatic mCRPC[33].

Literature search strategy

A comprehensive electronic search was conducted in MEDLINE (*via* PubMed) in June 2022 to identify peer-reviewed primary studies relevant to the review objectives. The search included randomized controlled trials, non-randomized controlled studies, and observational studies. To ensure that the review reflects contemporary clinical practice and incorporates the evolving understanding of CRPC, only studies published between June 2012 and June 2022 were deemed eligible for inclusion.

The process was conducted following the methodology established in the Preferred Reporting Items for Scoping Reviews (PRISMA-ScR)[35]. The search strategy was developed in collaboration with an experienced information specialist and combined Medical Subject Headings (MeSH) with free-text terms related to prostate cancer, castration resistance, metastasis, HRQoL, and functional outcomes (see Appendix A in Supplemental Materials).

To ensure consistency in data interpretation and reporting, the search was restricted to articles published in English. Only original research articles presenting primary data were eligible for inclusion.

Study selection process

A structured two-step screening process was implemented by an experienced reviewer according to predefined eligibility criteria. This process accounted for potential heterogeneity in the definitions and classification of castration-resistant and metastatic disease across studies.

In the first phase, titles and abstracts were screened for relevance based on the target population, outcomes of interest, and appropriateness of study design. Studies were included if they reported primary data on HRQoL or functional outcomes in patients with CRPC. Excluded at this stage were studies focusing on androgen-sensitive or metastatic castration-sensitive prostate cancer, as well as secondary sources such as systematic reviews, commentaries, editorials, and narrative reviews.

In the second phase, full-text articles of potentially eligible studies were assessed against the inclusion criteria. Studies were required to report population characteristics and clearly defined HRQoL or functional outcome measures. Only articles published between June 2012 and June 2022 were retained. Studies were excluded if the full text was unavailable, if they were published in a language other than English, or if they provided insufficient data for assessment. When multiple publications originated from a single study cohort, they were consolidated and treated as one data source to prevent duplication.

Studies were excluded at either screening phase for the following reasons:

1. Population: Studies were excluded if the target population did not align with the predefined eligibility criteria—for example, those focusing on general prostate cancer populations, androgen-sensitive disease, or metastatic castration-sensitive prostate cancer, or where castration resistance or metastatic status was inadequately defined.

2. Outcomes: Studies that did not assess outcomes relevant to the review objectives—specifically, those lacking measures of HRQoL or functional status—were excluded. These included studies reporting solely on survival, biochemical recurrence, or treatment feasibility without incorporating HRQoL metrics.
3. Study Design: Articles that did not present original primary data, such as systematic reviews, narrative reviews, editorials, commentaries, study protocols, or methodological papers, were excluded.
4. Publication Date: Studies published outside the predefined time frame (June 2012 to June 2022) were excluded.
5. Other Reasons: Additional exclusions included duplicate publications or studies where insufficient information was available to determine eligibility.

The complete study selection process, including the number of records identified, screened, assessed for eligibility, and included in the final synthesis, is illustrated in the PRISMA flowchart diagram (Figure 12)[17,25,27,30–34,36–91].

Data extraction and synthesis

Data extraction was performed independently by two reviewers using a standardized and piloted extraction form developed specifically for this review. Extracted variables included study characteristics (e.g. first author, year of publication, study design), population details (sample size, inclusion and exclusion criteria), interventions or exposures, HRQoL instruments and functional outcome measures, and key findings. Where available, baseline data on HRQoL and functional domains—including sexual, urinary, and bowel function—were also collected.

Given the aim of mapping and summarizing findings from original research, which is expected to be heterogeneous in methods, a narrative analysis was conducted. This summarized reports of HRQoL and functional outcomes in patients with high-risk nmCRPC and mCRPC, highlighting variation in baseline measures across populations. Comparative analysis focused on the reported range (i.e. minimum and maximum mean values) of outcomes for each domain. Where data permitted, the synthesis also explored associations between clinical disease severity (e.g. symptom burden, metastatic site involvement) and reported outcomes.

Study 2—pharmacoeconomic assessment

A pharmacoeconomic model was used to estimate the HRQoL gains achieved by delaying the progression of nmCRPC. The model used in this study was designed to assess the cost-effectiveness of Erleada® (apalutamide), a pharmaceutical product indicated for the treatment of nmCRPC patients at high risk of developing metastatic disease[92,93]. This specific version of the model was calibrated with the costs of the Portuguese healthcare system in 2019 and was accepted by Infarmed, the Portuguese National Authority of Medicines and Health Products[92,93]. The objective of this study is to utilize this officially accepted model to extract valuable information regarding the consequences of prostate cancer progression, including estimates of time spent in nmCRPC and mCRPC, as well as the utility and costs associated with each stage. Our goal is to highlight the benefits of delaying progression, independent of the intervention used to achieve this delay.

The clinical parameters of the pharmacoeconomic model were calibrated with data from the SPARTAN clinical trial[36]. The calibration of the CE model was carried out by its authors with access to individual level data. The mean age of patients was 73.9 (Standard Deviation (SD) 8). This model is a survival-partition model, commonly used in oncology, where transitions between health states are determined by estimates of Overall Survival (OS) curves, which provide information about mortality rates over time, and Metastasis-Free Survival (MFS) curves, capturing the progression of patients to the metastatic stage over time. The model operates on monthly cycles and considers two mutually exclusive health states before death: nmCRPC and mCRPC. The estimates of the percentage of patients in the mCRPC health state and the time spent there are derived from the difference between OS and MFS. Progression in the model is irreversible, meaning patients cannot revert back to nmCRPC once in the mCRPC health state. Naturally, estimates of OS and MFS curves depend on treatment choices.

One of the primary variables under scrutiny for capturing the benefits of avoiding progression is the alteration in HRQoL during the transition from nmCRPC to mCRPC. The model utilizes EQ-5D (EuroQoL Five-Dimensions) instruments to measure utilities. Utility measures are cardinalized such that a value of 1 corresponds to perfect health (complete absence of health problems), while a value of zero is equivalent to being deceased[94]. The higher the utility, the better the HRQoL. Given that the model considers two health states, it assigns a utility level to each. The utility level for the nmCRPC state in the CE model was estimated from data generated by the SPARTAN study, where the EQ-5D-3L (three levels for possible answers) was applied at all scheduled visits and 1 year after discontinuation of therapy[36]. The estimated utility level for time spent in nmCRPC was 0.822. The utility estimated for the mCRPC health state was extracted from the LATITUDE study, where the EQ-5D-5L (version with five levels for possible answers) was utilized[95]. To mitigate potential variations in results due to the use of different instruments (3 L versus 5 L), the builders of the CE model found it was necessary to convert the results of the EQ-5D-5L to EQ-5D-3L results, as recommended by the National Institute for Health and Care Excellence (NICE). The estimated utility level for time in mCRPC was 0.630.

Healthcare costs associated with progression are another aspect that needs to be considered. To obtain estimates of the costs avoided by preventing or delaying progression, it was necessary to refer to the cost-effectiveness model for apalutamide and utilize the information with which it was calibrated.

In the case of Portugal, the CE model builders and adaptors use of resources (including medicinal products, exams, tests, consultations, inpatient admissions, and emergencies) was determined by the consensus of two expert panels, one for nmCRPC and the other for mCRPC. The unit costs for medicines were based on prices derived from public tenders, while the unit costs for other resources were established according to the National Health Service price lists, as outlined in the Ordinances governing NHS invoicing and the application of Diagnosis-Related Group (DRG) classifications. Additionally, some unit costs were sourced from the list of government-defined prices for the long-term care national network (RNCCI).

The information on costs provided by the apalutamide cost-effectiveness model requires careful consideration to align with the purpose of assessing the gains from avoiding or delaying prostate cancer progression. First, in the context relevant to the analysis the costs should not be discounted. The concern is not with the present value of costs referenced to the moment of treatment initiation, but rather with how the flow of costs and health per period changes when comparing the nmCRPC and mCRPC stages. Second, the relevant costs are costs per unit of time, standardized as costs per year. This standardization is crucial because the model computes costs incurred during the nmCRPC and mCRPC stages considering the total duration of the stages. As the durations are significantly asymmetrical, these total cost estimates are not suitable for comparing the two stages. The relevant comparison is between costs accrued during 1 year of time spent in nmCRPC and costs accrued during 1 year in mCRPC, despite the actual durations being different. For the record, the "no discounting" choice generates overall costs per year that are 2.8% lower compared to the estimates of costs per year when discounting at 4%.

Other assumptions are needed. One assumption is that the cost estimates will be based on a scenario without apalutamide, as this provides the most relevant information on the pure impact of progression on costs. Another assumption is that end-of-life costs are not included in the analysis. This is a conservative assumption given the very large differences between mortality rates in nmCRPC and in mCRPC. The assumption is made since patients will eventually die, i.e. death will occur even if we completely avoid progression and with zero discounting, the timing of death is of secondary importance as far as costs are concerned. Importantly, in this analysis, the acquisition costs of therapies used to delay nmCRPC progression, including apalutamide, enzalutamide, or darolutamide, were not included. This choice allows the model to isolate the impact of disease progression itself on healthcare costs, independent of the treatment used.

A final assumption pertains to the costs of treatment-related adverse events. The model only specifies these costs for the nmCRPC stage, assuming zero costs for mCRPC. This is conceptually unimportant for the cost-effectiveness analysis the model was designed to do, but not for our objective of quantifying the gains in cost savings by not having prostate cancer progression. To restore symmetry, our analysis assumes that the costs of adverse reactions are null at both stages. Since these costs are small, this assumption has very little impact on the results.

Study 3—qualitative study

The third study developed encompasses two primary objectives: first, to comprehend the experiences of patients with prostate cancer, both with and without disease progression to the metastatic phase, regarding quality of life, physical function, pain, and psychological health; and second, to expand the understanding of the unmet needs identified by patients with and without disease progression to the metastatic phase. Given the nature of the objectives and research questions, a qualitative study was designed using two virtual focus groups. The groups were composed of (1) two patients with a previous diagnosis of prostate cancer without progression to the metastatic stage and (2) three patients with a previous diagnosis of prostate cancer with progression to the metastatic stage. For the purpose of this study, two virtual focus groups were organized using Zoom Colibri—Zoom Video Communications, Inc. Copyright © 2012–2023. The virtual sessions with focus groups lasted between 60 and 90 min and were conducted by a psychologist specialist in clinical and health psychology, accredited by the Portuguese Psychologists' Association, accompanied by a research assistant, following an open interview script. All research participants previously signed informed consent forms to participate in this qualitative study. Recordings were transcribed verbatim.

Thematic analysis was performed manually by two independent researchers using an inductive coding process, followed by triangulation with researcher field notes. While qualitative data analysis software was not used due to the limited sample size, the process adhered to established qualitative research standards.

Recruitment limitations, particularly among patients with advanced disease, posed a challenge. Some participants declined due to fatigue, digital illiteracy, or emotional burden. Although only five participants were ultimately included, thematic saturation was observed in key domains such as pain, fatigue, psychological distress, and support needs. This limitation is acknowledged in the discussion and suggests that future studies should consider mixed-methods longitudinal approaches with broader recruitment strategies.

Results

Study 1

The electronic search found 611 references, of which 243 full texts were evaluated for inclusion. A total of 56 studies with 64 reports were included in this review: 27 were RCTs and 37 were observational studies (See Figure 12, Appendix A in Supplemental Materials). The main reasons for exclusion were the type of population, the type of study, and the year of publication. Reasons for the exclusion of 179 references can be found in Table 4 (see Appendix A in Supplemental Materials).

The characteristics of the included studies can be found in Table 5 (see Appendix B in Supplemental Materials). Regarding population, only four studies (three RCTs and one observational) met the eligibility criteria for the nmCRPC population at high risk of disease progression; 53 for the mCRPC population (18 RCTs and 35 observational). Regarding population characteristics in baseline, only three studies (three RCTs) met the eligibility criteria for the nmCRPC population at high risk of disease progression; 52 for the mCRPC population (18 RCTs and 34 observational); and one for both populations (1 observational). The specificity associated with the classification "high risk" of metastasis contributed greatly to the reduced number of studies considering the nmCRPC population. Given that this is a recent classification, the studies identified were also the most recent within the search period, having been published between 2018 and 2022. In contrast, the publication dates of the mCRPC studies ranged from 2013 to 2022. For these studies, the eligibility criteria were generally poorly described, which centrally limited the potential for subgroup analysis: only 16 studies considered the presence of symptoms, 13 the life expectancy, and eight the location of metastasis. Since the eligibility criteria considered by the different studies regarding life expectancy and location of metastasis were similar, subgroup analysis was performed only for the presence of symptoms (high-risk nmCRPC vs. asymptomatic mCRPC vs. symptomatic mCRPC). This characteristic was determined based on the authors' reports in the eligibility criteria (explicit inclusion of 'symptomatic' or 'asymptomatic' mCRPC).

Regarding outcomes, the Functional Assessment of Cancer Therapy—Prostate (FACT-P) was the most used measurement instrument, having been used in 35 studies (four for nmCRPC and 32 for mCRPC patients). The remaining most used instruments were the EuroQoL group 5-dimension 3-level or 5-level

(EQ-5D-3L or 5 L) (16 studies: three for nmCRPC and 13 for mCRPC patients), The European Organization for Research and Treatment of Cancer QoL Core questionnaire C-30 (EORTC QLQ C-30) (14 studies: 0 for nmCRPC and 14 for mCRPC patients), and EORTC QLQ Prostate Cancer Module (EORTC QLQ PR25) (6 studies: 2 for nmCRPC and 4 for mCRPC patients).

Finally, instruments such as the 8-Dimension Assessment of Quality of Life (AQoL-8D) questionnaire (one study: mCRPC patients), Edmonton Symptom Assessment System (ESAS) (one study: mCRPC patients), The Functional Assessment of Chronic Illness Therapy (FACIT-F) (one study: mCRPC patients), FACT-Cognitive Function (FACT-Cog) (two studies: mCRPC patients), International Index of Erectile Function (IIEF) (one study: mCRPC patients), International Positive and Negative Affect Schedule Short-Form (I-PANASSF) (one study: mCRPC patients), Karanofsky Performance Status (KPS) (one study: mCRPC patients), National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy - Prostate Symptom Index-17 (NCCN-FACT-FPSI-17) questionnaire (one study: mCRPC patients), and Short-Form Health Survey 36 Item (SF36) (two studies: mCRPC patients) were also used to assess HRQoL and function.

Baseline HRQoL and function analysis in high-risk nmCRPC and mCRPC populations

HRQoL and function baseline data from both study populations (nmCRPC and mCRPC) were analyzed according to the instruments used. Three of these instruments (FACT-P, EORTC QLQ PR25, EQ-5D) were used in both populations (Table 6), while the remaining were used only in the mCRPC population (Table 7).

The comparison of the minimum and maximum mean values for the instruments used in both high-risk nmCRPC and mCRPC populations of included studies can be found in Table 8. In general, the population with nmCRPC has higher HRQoL and function both for the overall and specific domain scores of included instruments. Regarding the FACT-P (total score), the mean baseline values for the nmCRPC population ranged between 108.6 and 120.8, while for the mCRPC population it ranged between 93.3 and 122.6 (Figure 4). In the EQ-5D, the mean index for the nmCRPC population ranged between 0.85 and 0.86, while for the mCRPC population it ranged between 0.63 and 0.90. In the EQ-5D VAS, the variation was 76.2–77.5 and 56.2–77.7 for the nmCRPC and mCRPC populations, respectively (Figure 5). Lastly, the following results were found for the EORTC QLQ PR25 subscales in the nmCRPC population: bowel symptoms ranged from 4.7 to 6.0; hormonal treatment-related symptoms ranged from 14.9 to 17.0; incontinence aid usage ranged from 12.0 to 15.0; sexual activity ranged from 89.0 to 90.0; sexual function ranged from 44.0 to 46.0; and urinary symptoms ranged from 20.0 to 24.0. The results of the

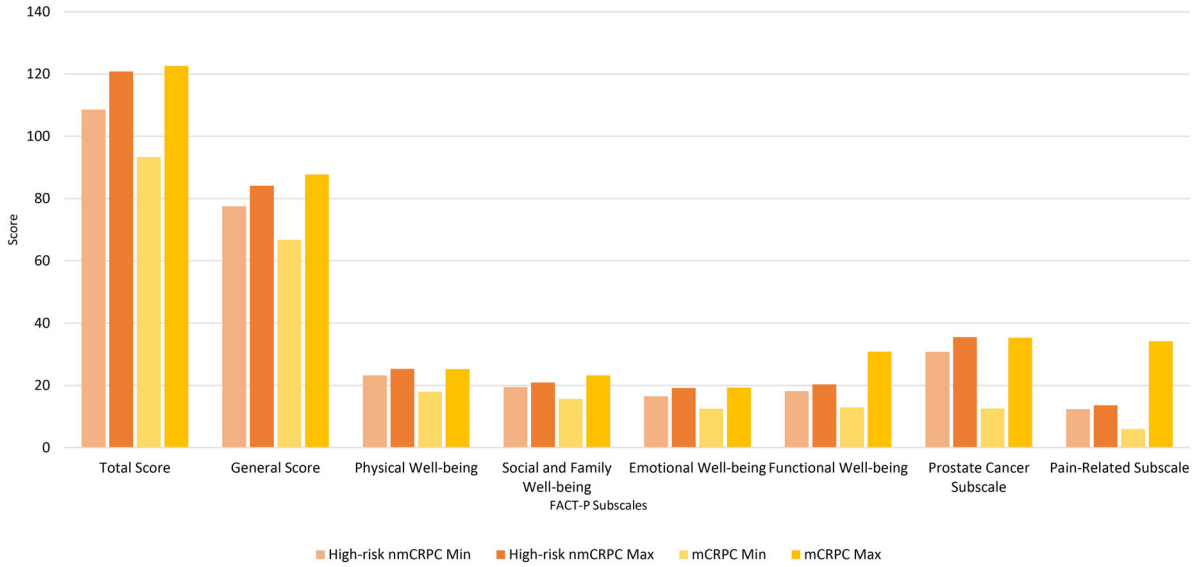

Figure 4. HRQoL baseline data of RCTs (FACT-P total and subscale baseline min-max score).
FACT-P, Functional Assessment of Cancer Therapy–Prostate; HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; min, minimum; max, maximum. Higher FACT-P scores indicate better HRQoL.

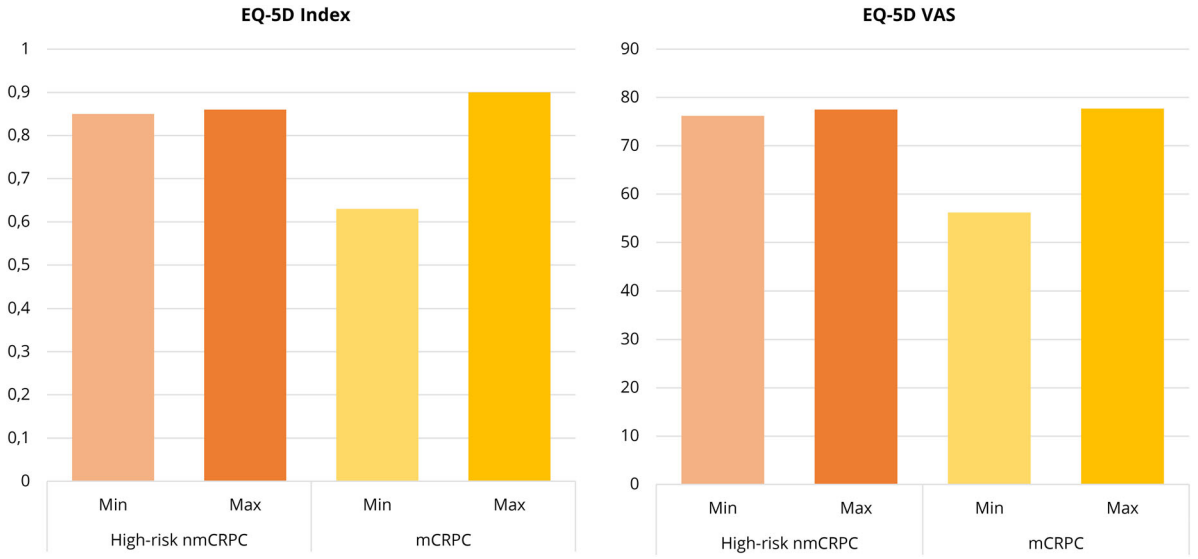

Figure 5. HRQoL baseline data of RCTs (EQ-5D index and VAS baseline min-max score).
EQ-5D-3L/5L, EuroQol 5-Dimension 3-Level or 5-Level; VAS, visual analogue scale; HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; min, minimum; max, maximum. Higher EQ-5D and VAS scores indicate better HRQoL.

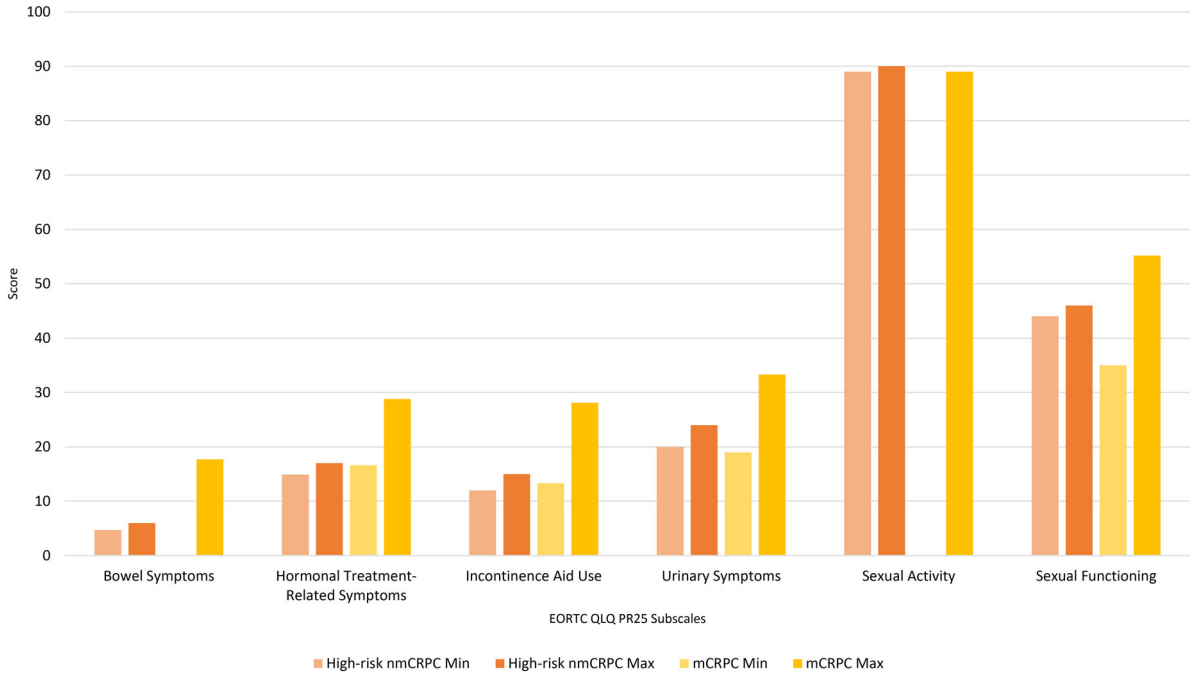

Figure 6. HRQoL baseline data of RCTs (EORTC QLQ PR25 subscales baseline min-max scores).
EORTC QLQ-PR25, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Prostate Cancer Module; HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; min, minimum; max, maximum. For the EORTC QLQ-PR25, higher functional scores (e.g. sexual activity and function) indicate better functioning, while higher symptom scores indicate greater symptom burden.

mCRPC population ranged from 0.0 to 17.7 for bowel symptoms, 16.6 to 28.8 for hormonal treatment-related symptoms, 13.3 to 28.1 for incontinence aid use, 0.0 to 89.0 for sexual activity, 35.0 to 55.2 for sexual function, and 19.0 to 33.3 for urinary symptoms (Figure 6). The single study which followed up the same patients before and after disease progression, found that HRQoL (EQ-5D-5L) and function (FACT-P) declined for those who developed distant or symptomatic metastasis[31,36]. Data extraction showed an important proportion of missing data. Despite the authors having reported measuring

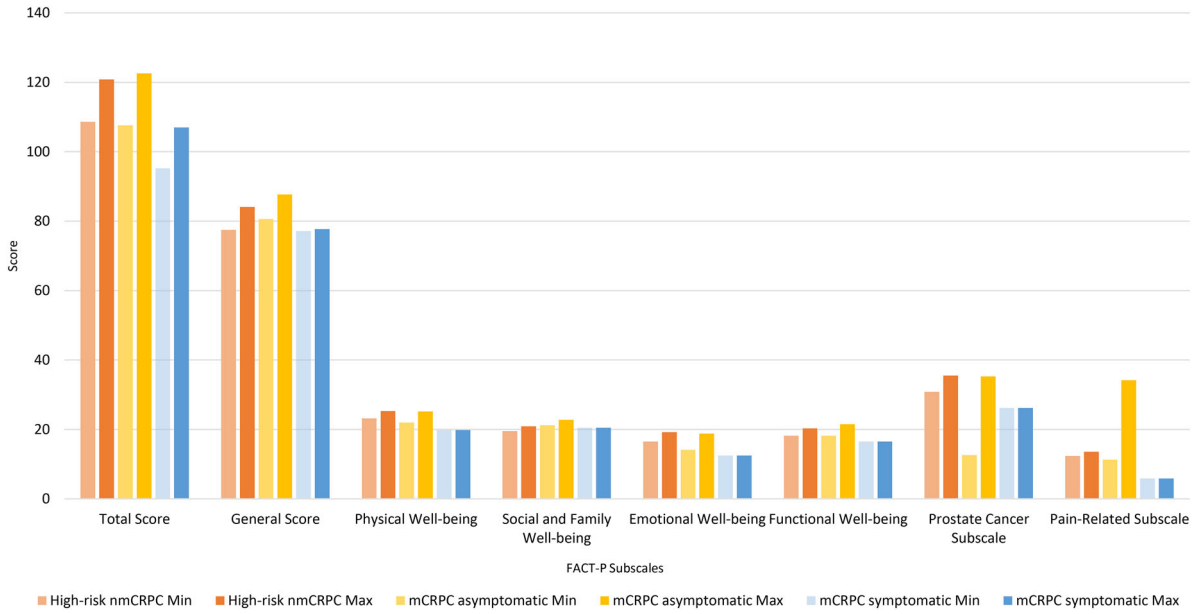

Figure 7. Subgroup analysis of HRQoL baseline data of RCTs (FACT-P total and subscale baseline min-max scores).
FACT-P, Functional Assessment of Cancer Therapy–Prostate; HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; min, minimum; max, maximum. Higher FACT-P scores indicate better HRQoL.

baseline HRQoL and function data, it was not provided or was only graphically described for some of the included studies which prevented the full analysis. Specifically, 26% (9/35) of studies considering FACT-P did not provide absolute baseline data; 19% (3/16) did not provide absolute baseline EQ-5D data; 17% (1/6) did not provide absolute baseline EORTC QLQ PR25 data; and finally, 57% (8/14) did not provide absolute baseline EORTC QLQ C30 data.

Regarding the preliminary subgroup analysis (Table 9), baseline HRQoL and function scores were compared among three different subgroups: nmCRPC, asymptomatic mCRPC, and symptomatic mCRPC. Results suggested that symptomatic mCRPC patients have lower HRQoL compared with nmCRPC. No differences seem to exist between nmCRPC and asymptomatic mCRPC patients (Figure 7, Figure 8, Figure 9).

Burden analysis of disease progression

To estimate the burden of disease progression, the mean EQ-5D scores were utilized and compared between patients with nmCRPC and mCRPC. Additionally, a preliminary subgroup analysis was also performed to explore differences between subgroups of patients with symptomatic and asymptomatic mCRPC. The results of this analysis are presented in Table 10.

The EQ-5D-3L or 5 L index and VAS means for nmCRPC were 0.853 ($n = 1,173$) and 76.52 ($n = 2,500$), respectively, with one study contributing to the index mean and two studies to the VAS mean. For mCRPC, the EQ-5D-3L or 5 L index and VAS mean were 0.76 ($n = 4,920$) and 69.35 ($n = 16,850$), respectively, with 9 studies contributing to the index mean and 11 studies to the VAS mean. When considering the subgroups of mCRPC, the EQ-5D-3L or 5 L index and VAS means for patients with asymptomatic mCRPC (from 4 studies) were 0.84 ($n = 2,596$) and 75.87 ($n = 2,596$), respectively. For patients with symptomatic mCRPC (from 1 study), the EQ-5D-3L or 5 L index and VAS means were 0.63 ($n = 50$) and 56.2 ($n = 50$), respectively.

Study 2

Health-related quality of life estimates in delaying nmCRPC progression: insights from a pharmacoeconomic model

Study 1 provides a comprehensive literature review on HRQoL for two distinct stages of prostate cancer, as also examined in Study 2. The EQ-5D values derived from the scoping review reveal that the mean

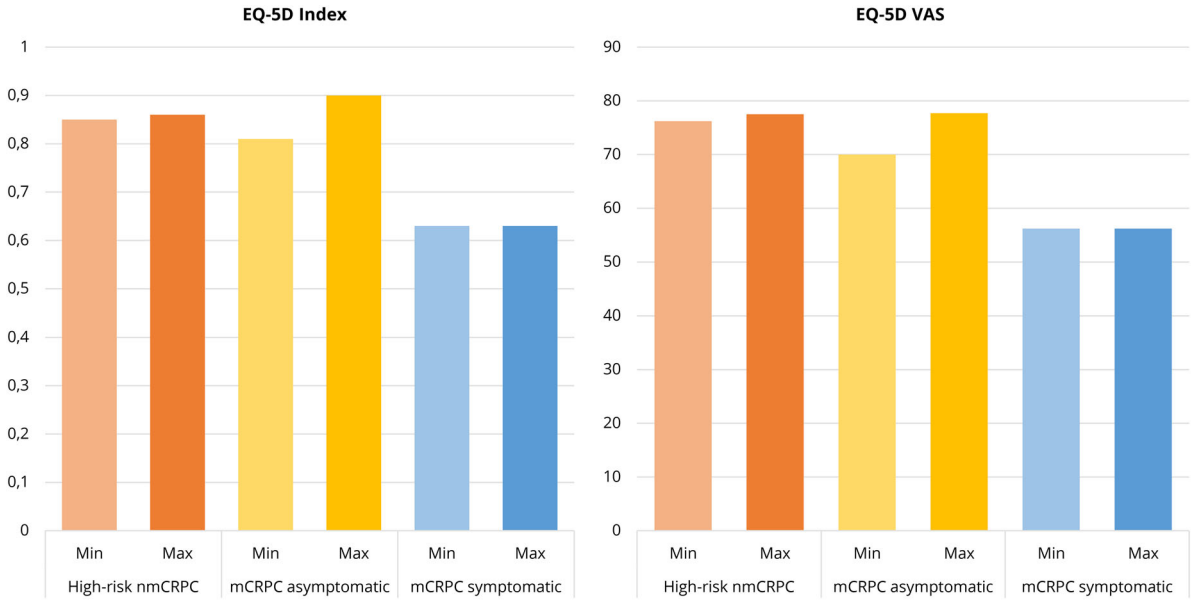

Figure 8. Subgroup analysis of HRQoL baseline data of RCTs (EQ-5D-3L index and VAS baseline min-max scores). EQ-5D-3L/5L, EuroQol 5-Dimension 3-Level or 5-Level; VAS, visual analogue scale; HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; min, minimum; max, maximum. Higher EQ-5D and VAS scores indicate better HRQoL.

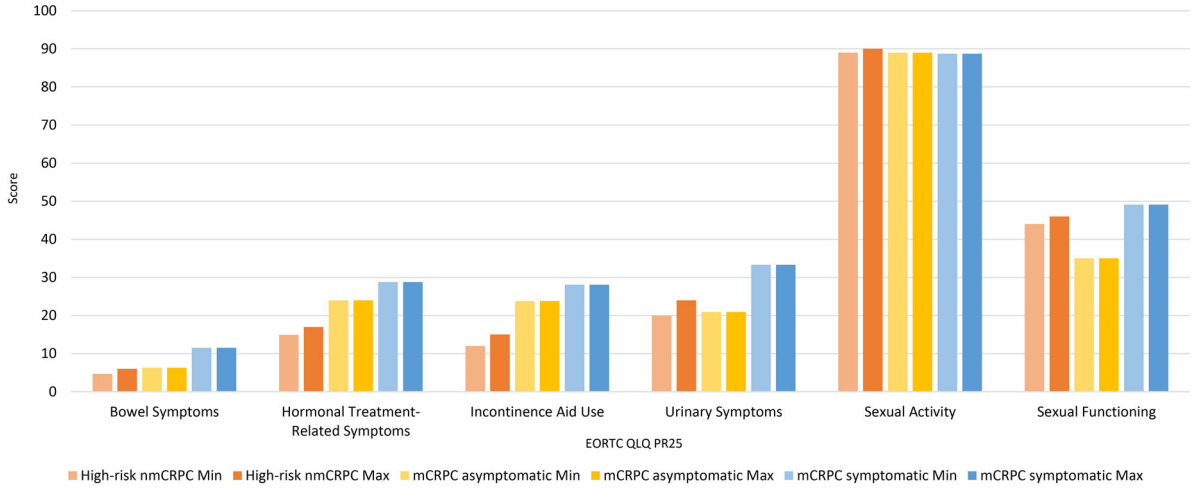

Figure 9. Subgroup analysis of HRQoL baseline data of RCTs (EORTC QLQ PR25 subscales baseline min-max scores). EORTC QLQ-PR25, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Prostate Cancer Module; HRQoL, health-related quality of life; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; min, minimum; max, maximum. For the EORTC QLQ-PR25, higher functional scores (e.g. sexual activity and function) indicate better functioning, while higher symptom scores indicate greater symptom burden.

utility for the nmCRPC population ranged between 0.85 and 0.86, while for the mCRPC symptomatic population it ranged between 0.63 and 0.90.

The CE model estimates indicate that progression to the metastatic stage of prostate cancer leads to a substantial 0.192 decrease in HRQoL.

To provide a more relatable perspective for non-specialists, a comparison based on a more intuitive concept, such as age differences, can be enlightening. An understanding of the value in question can be gleaned by comparing it to population norms of the EQ-5D-3L for the Portuguese population, which illustrates how HRQoL changes with age. The data used for establishing these norms was collected in 2012. The relationship between utility and age for a representative sample of the Portuguese population is depicted in Figure 10[96,97].

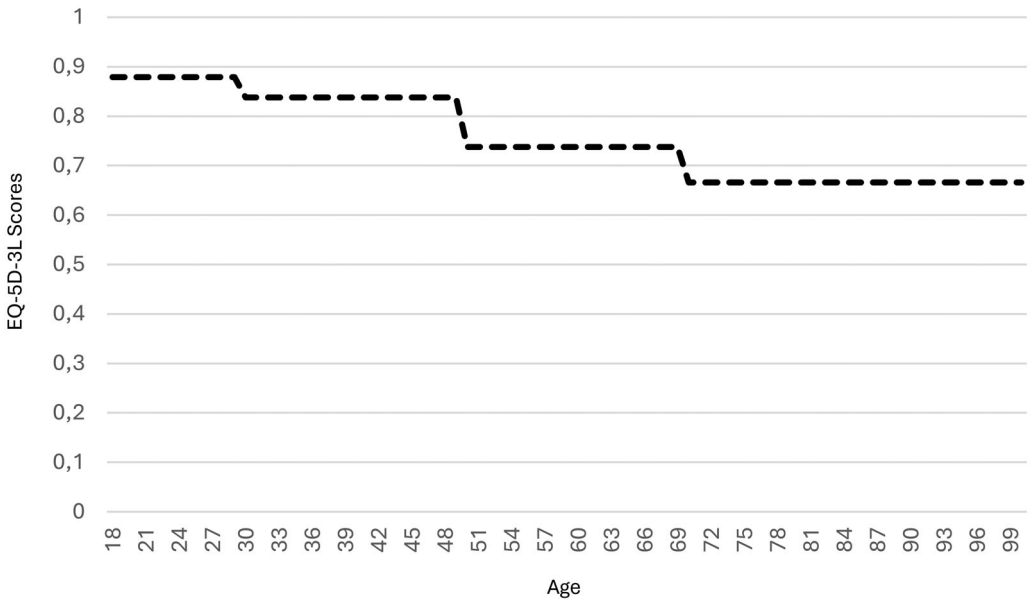

Figure 10. EQ-5D-3L Portuguese male population norms, by age group[96,97].

Considering that the highest age group with available information is 70 and over, an average age of around 80 can be conservatively assumed for this group, given a life expectancy of about 14 years for males aged 70. Conversely, the lowest age group considered was 18 to 29, which can be approximated with an average age of 24.

Based on the population norms represented in Figure 10, on average the aging of a man from 24 to 80 results in a 0.213 loss in utility. This implies that the quality-of-life effect due to prostate cancer progression is similar to approximately 90% of the effect of aging from 24 to 80.

Recently, Ferreira et al. (2023) revisited HRQoL population norms for the Portuguese population using the EQ-5D-5L instrument[98]. The total population norms for both the EQ-5D-3L and the EQ-5D-5L are illustrated in Figure 11[96–98].

With EQ-5D-5L, utility levels at all ages are higher than in the previous norms. However, the loss in utility from age 24 to 80 is smaller, at 0.172. Even accounting for potential variations in utility estimates due to different instruments, this outcome suggests that the 0.192 loss in quality of life due to prostate cancer progression may be greater than the loss attributed to aging from 24 to 80 years of age.

Effects of disease progression on mortality rates in prostate cancer

Having established the significant health gains in HRQoL resulting from preventing or delaying progression, the focus now shifts to the effects on survival, specifically the impact of progression on mortality rates.

As a preliminary background, the cost-effectiveness model introduced a clinically effective intervention that increased total survival from 5.65 years to 6.52 years, namely through an increase in time spent in the nmCRPC health state, from 1.94 years to 4.94 years.

The cost-effectiveness model employed is a typical survival-partition model based on overall survival curves (OS) and Metastasis-Free Survival curves (MFS). While this model allows for calculations to estimate outcomes such as the Incremental Cost-Effectiveness Ratio (ICER) of a new cancer medicinal product, it does not explicitly delineate mortality processes by health stage, as seen in state transition models. This type of model does not offer separate mortality curves for before and after progression. This structural limitation has led to criticism of survival-partitioned models, as highlighted in Woods et al. (2017, 2020), emphasizing the absence of a structural link between intermediate clinical endpoints such as disease progression and survival[99,100].

To address this limitation, we sought direct information outside of the model on how progression affects mortality rates and survival. Among the available sources, data from the Surveillance, Epidemiology, and End Results Program (SEER) of the National Cancer Institute in the United States

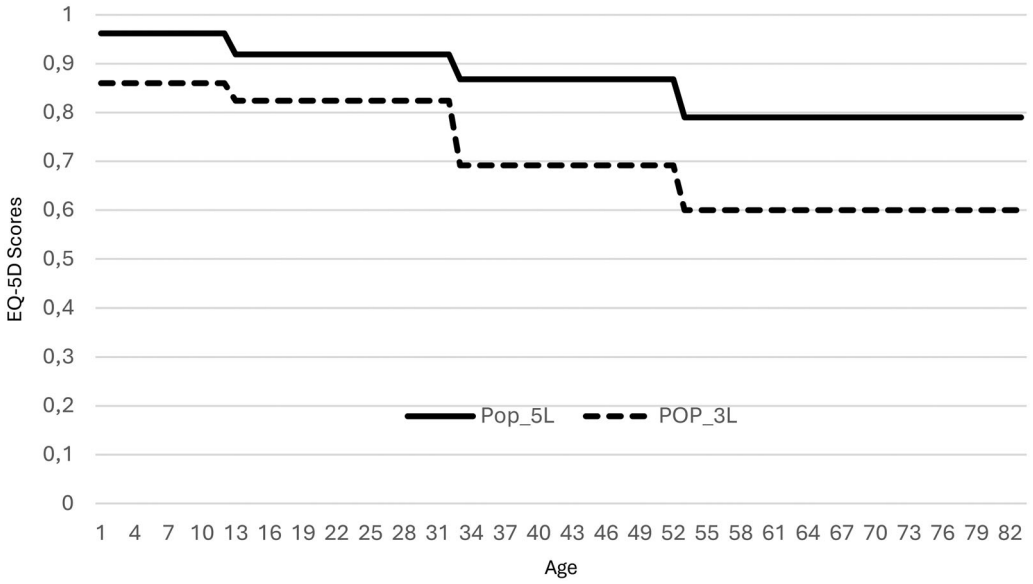

Figure 11. EQ-5D-3L and EQ-5D-5L Portuguese total population norms[96–98].

Table 2. Costs for the nmCRPC and mCRPC stages in Portugal.

	nmCRPC	mCRPC
Treatment costs	€ 1,830	€ 20,470
Follow up costs	€ 5,308	€39,905
Sum	€ 7,138	€ 60,375
Duration (years)	1.94	3.71
Cost per year	€ 3,679	€ 16,273

appeared to be the most relevant. SEER provides comprehensive cancer statistics for the United States (U.S.) population[101].

SEER categorizes prostate cancer into stages: Localized, Regional, Distant, and Unstaged. The 5-year survival rates for the stages Localized and Unstaged have limited relevance for our analysis. Thus, our focus is on the transition between the Regional and Distant stages, which empirically corresponds to progression to a metastatic stage[101].

The pertinent SEER data covering annual data from 2004 to 2018 display empirical annual data points alongside smoothed or modeled estimates (See Figure 13 and Table 11, Supplementary Materials, Appendix C)[101]. These modeled estimates, which reduce statistical noise inherent in the data, form the basis for our estimates of the changes brought about by progression. For Regional prostate cancer, the modeled 5-year relative survival rates slightly improved from 99.1% in 2004 to 99.5% in 2015. Since we are trying to obtain estimates that are relevant to the current situation characterizing prostate cancer in Portugal, we will conservatively use estimate 99.5% from 2015. This survival rate corresponds to an average annual mortality rate from prostate cancer of 0.1% before progression. In contrast, for the Distant stage (considered metastatic), the 5-year survival rate was 29.9% in 2004. However, this rate has shown significant improvement over the years, reaching 33.3% in 2015. Considering potential delays in therapeutic innovation reaching the Portuguese health system compared to the U.S., we assume the current 5-year survival rate for the Distant stage in Portugal lags behind that of the U.S. The SEER data from 2015 provided a modeled survival rate of 34.6%, which we take as a proxy for the current survival rate in Portugal. The corresponding annual mortality rate is 19.1%. With these estimates, we can analyze the mortality consequences of progression. In terms of 5-year survival, progression leads to a 64.9% reduction. Focusing on mortality, the annual mortality rate from prostate cancer increases to a value 190 times larger following progression.

Health care costs of prostate cancer progression

The results of the analysis are shown in Table 2. The line "Treatment costs" refers to the cost of medicinal products and their administration, whereas the line "Follow-up costs" includes the costs of

consultations, tests, in-patient episodes, emergency episodes, and so on. The costs used in the cost-effectiveness model were accepted by the Portuguese regulatory agency, Infarmed, during the process of granting purchase authorization for public hospitals. Costs for nmCRPC-specific drug therapies, such as apalutamide, enzalutamide, or darolutamide, were not included in these estimates, consistent with our aim to assess costs attributable solely to disease progression rather than treatment acquisition. It is assumed that patients will be treated with androgen deprivation therapy (goserelin, leuprorelide, triptorelin, or degarelix) until the end of their life. In the metastatic stage, the three lines of treatment used in the SPARTAN trial are considered, with the duration estimated for the Portuguese health system by a panel of clinical experts. The therapeutic lines include abiraterone, docetaxel, prednisolone, and enzalutamide. The costs of the patients' exams and follow-up were defined by the same Portuguese clinical expert panel. The estimates included an initial study before treatment initiation and a diagnostic for metastasis. The annual follow-up costs before and after progression were also estimated based on information provided by the clinical expert panel.

The most important results are presented in the last line of Table 2, where we see the annual costs of a patient before and after progression. Progression increases costs by a factor of 4.4, making it a very costly development for the healthcare system.

Study 3

A total of five participants were included across two focus groups: two patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and three with metastatic castration-resistant prostate cancer (mCRPC). Ages ranged from early 60s to mid-70s. Three participants were retired, one was on medical leave, and one was still actively working part-time.

Sessions lasted 60–90 min and followed an open script. Audio was transcribed verbatim and inductively coded by two researchers with triangulation of field notes; thematic saturation was reached for core domains (pain, fatigue, psychological distress, support needs). Recruitment proved challenging in advanced disease due to fatigue, limited digital literacy, and emotional burden.

Symptom and function burden

Men with mCRPC consistently described more frequent and intense physical symptoms (pain, fatigue, urinary complications, and bowel changes) often linked to progressive loss of independence and control. By contrast, nmCRPC participants emphasized vigilance and day-to-day management of treatment side effects rather than pervasive functional decline. These patterns mirror the gradient observed in Study 1 between symptomatic mCRPC and earlier stages.

Psychological impact

Across groups, anxiety about progression and feelings of uncertainty were common; however, emotional distress (anxiety/depression, helplessness, perceived loss of control) was more salient in mCRPC, frequently intertwined with symptom escalation and loss of role functioning.

Daily life disruption and social roles

Participants with mCRPC described greater interference with activities of daily living, social withdrawal, difficulties maintaining employment or purposeful routines, and increased dependency on caregivers. nmCRPC participants reported tighter monitoring of health and lifestyle adjustments but fewer disruptions to social/work participation.

Coping strategies and resources

Common coping strategies included family/peer support, graded physical activity, and accessing psychological support when available; some participants sought meaning through volunteering or support groups. Perceived gaps included inconsistent provision of information, fragmented psychosocial care, and variability in access to supportive services.

Care experience and unmet needs

Participants pointed to an "implementation gap" between supportive-care guidelines and real-world delivery—especially for psycho-oncology, continence/sexual health, fatigue management, and navigation of social/financial supports. Online format facilitated participation yet occasionally hindered rapport and was susceptible to technical issues.

In this small, purposive sample, metastatic progression was associated with a sharper decline in physical function, heightened emotional distress, and broader disruption of social/role functioning, whereas nmCRPC experiences centered on uncertainty, monitoring, and side-effect management. These patient-reported patterns align with the quantitative gradient in HRQoL across disease stages identified in Study 1.

Discussion

The findings from the three studies collectively provide a comprehensive and multidimensional understanding of the impact of prostate cancer progression on patients' quality of life, economic outcomes, and lived experiences. Study 1, a scoping review, established the quantitative gradient of HRQoL and functional outcomes across disease stages, demonstrating that patients with high-risk nmCRPC generally maintain higher HRQoL than those with mCRPC, and that symptomatic mCRPC is associated with the lowest quality of life. Building upon these findings, Study 2 translated these HRQoL decrements into health-economic outcomes, quantifying utility losses and the substantial increase in healthcare costs associated with metastatic progression. Study 3 complemented the quantitative analyses by exploring patients' lived experiences and perceived unmet needs through qualitative focus groups. Although the sample was small ($n = 5$), thematic saturation was reached for key domains such as symptom burden, psychological distress, daily functioning, and support needs, providing a patient-centered perspective that mirrors the patterns observed in Studies 1 and 2. By integrating evidence from literature, economic modeling, and patient narratives, the three studies illuminate not only the measurable HRQoL and economic impacts of disease progression but also the real-world experiences and challenges faced by patients. This triangulation reinforces the critical importance of interventions aimed at delaying metastasis, both to improve quality of life and to mitigate healthcare costs, while highlighting areas for enhanced supportive care and service planning.

Study 1 provided a comprehensive scoping review, highlighting the robustness of its search and selection process as a major strength. Utilizing a sensitive search strategy and an over-inclusion approach, the review aimed to encompass a broad range of relevant literature. Thus, the scoping review concluded that patients with nmCRPC may exhibit higher HRQoL and better function compared to those with mCRPC. Moreover, patients with symptomatic mCRPC tended to have lower HRQoL than those with asymptomatic mCRPC and nmCRPC, suggesting a decline in HRQoL as high-risk nmCRPC progresses toward metastasis. These findings need to be validated in future long-term longitudinal studies monitoring the course of HRQoL over time in patients with different disease stages. In the present review, only one study directly explored the impact of disease progression on patients with high-risk nmCRPC, following up with them before and after disease progression (SPARTAN Study)[31,36].

While the study possesses notable strengths, it also acknowledges some constraints. The use of a single electronic database (MEDLINE) for the search process may have limited the inclusion of all potential references. Furthermore, a single reviewer evaluated reference inclusion, which, associated with some ambiguity in the eligibility criteria for the diagnostic criteria of mCRPC, potentially introduced selection bias. Additionally, the findings of this study should be interpreted with caution due to several key considerations, such as: (1) high inter-study variability; (2) use of only baseline data without adjustment for potential confounders; (3) substantial missing data due to incomplete or graphical-only reporting; and (4) limitations of cross-trial HRQoL comparisons, which should ideally be replaced by intra-study longitudinal assessments within the same cohort before and after metastasis. These limitations are particularly relevant when interpreting economic modeling outcomes.

Given the high-risk nature of nmCRPC, focusing on this smaller population underscores the potential for metastasis prevention *via* approved therapies that enhance OS and MFS, potentially reducing the

economic burden compared with managing the larger cohort of high-risk localized disease, for which robust early-intervention data remain limited.

In Study 2, the focus shifted to the economic impact of prostate cancer progression, particularly to the metastatic stage, using an economic evaluation model (cost-effectiveness) of Erleada® (apalutamide). Progression to the metastatic stage was found to significantly diminish HRQoL, as indicated by a loss of 0.192 in utility. This loss was substantial, close to the impact of aging from 24 to 80 years in the general population. Furthermore, the study highlighted a profound increase in annualized mortality rates (from 0.1% to 19.84%, representing a more than 190-fold increase) and healthcare costs (more than 340%) upon progression to the metastatic stage, underscoring the need for interventions that delay disease progression.

Specifically, the costs of therapies for nmCRPC, such as apalutamide, enzalutamide, or darolutamide, were not included in the treatment cost estimates for the nmCRPC stage. This ensures that the observed increases in healthcare costs are attributable to progression to metastatic disease rather than the choice of pharmacological intervention. While costs for drug therapies in the metastatic stage were included, the acquisition costs of interventions delaying progression in nmCRPC were excluded. Therefore, although delaying progression yields health and economic benefits, the model does not account for the cost of these interventions. Consequently, the results should be interpreted as reflecting the burden of disease progression rather than a full cost-effectiveness evaluation of specific therapies. Despite limitations, such as reliance on a single cost-effectiveness model and incomplete data for adverse events, the model was approved by the national health technology assessment authority, supporting its validity in the Portuguese context.

Study 3, a qualitative investigation, delved into the lived experiences and perspectives of individuals with prostate cancer, focusing on the impact of diagnosis and treatment on HRQoL. This qualitative study complements the scoping and economic analyses by illuminating how progression-related decrements in HRQoL manifest in daily life. The narratives from men with mCRPC—greater pain/fatigue, functional dependency, and role loss—are congruent with Study 1's lower baseline HRQoL in symptomatic mCRPC and with Study 2's utility decrement (−0.192), reinforcing the patient-centered significance of delaying metastasis.

Two implications follow. First, supportive-care interventions (timely psycho-oncology, sexual/urinary rehabilitation, fatigue management, caregiver support) should be systematically embedded earlier in the pathway, with clear referral triggers at signs of progression or symptom escalation. Second, service planning and economic models should account for indirect consequences (productivity loss, caregiver burden) that patients described but are rarely captured in traditional cost-effectiveness frameworks.

Strengths include methodologically transparent thematic analysis with dual independent coding and triangulation, and the juxtaposition of perspectives across two clinically distinct groups. Limitations are the very small sample and online-only format, which may limit rapport and selection representativeness; recruitment in advanced disease was constrained by fatigue and digital barriers. These factors warrant cautious transferability and motivate larger mixed-methods, longitudinal designs that track the same individuals across transition to metastasis, integrating standardized HRQoL measures (e.g. EQ-5D, FACT-P) with qualitative interviewing.

Overall, these findings substantiate the lived-experience counterpart to our quantitative results: progression to mCRPC not only lowers utility and raises costs but also reshapes identity, roles, and support needs—areas where implementation science can bridge the gap between guideline-consistent supportive care and what patients actually receive.

Online focus groups have several advantages over in-person focus groups, as they can be conducted more quickly and easily without coordinating schedules and travel logistics. Additionally, participants can participate from anywhere with an internet connection, providing a larger and more geographically diverse sample. However, the study acknowledged limitations of online focus groups, such as potential challenges in building rapport and trust among participants, technical issues such as internet connectivity or software problems, which can disrupt the flow of the discussion and may require additional resources to resolve, as well as bias factors caused by active involvement in patient associations.

While the themes emerging from qualitative study, such as the importance of a holistic approach, access to information, psychological support, and the need to address emotional, social, and physical

challenges, may reflect well-established practices in oncology, their recurrence in patients' narratives underscores a critical implementation gap. These insights do not aim to introduce novel clinical recommendations, but rather to reaffirm the relevance of such practices from the patient perspective and reveal how inconsistently they are applied across healthcare settings. Importantly, these findings call for implementation of science approaches to bridge the gap between evidence-based supportive-care guidelines and their real-world application in prostate cancer management.

The insights derived from the qualitative analysis further enrich the quantitative findings by illustrating how symptom burden, emotional distress, and perceived lack of support manifest in daily life. Several reported themes—such as social withdrawal, difficulty maintaining employment, and increased dependency on caregivers—are directly linked to dimensions captured by HRQoL instruments (e.g. EQ-5D, FACT-P) and have clear implications for health economics. For instance, loss of productivity and increased caregiver burden may translate into indirect costs that are seldom accounted for in traditional cost-effectiveness models. A more integrated approach that incorporates lived experiences into HRQoL valuation and health resource planning is warranted.

Conclusion

The initial study integrated into this project illustrates that as high-risk nmCRPC progresses to metastases, especially in patients who develop symptomatic mCRPC, there is a noticeable decline in health-related quality of life and vital functions. This information is quantified and contextualized within a life-cycle perspective by the pharmacoeconomic model on which the second study is based. The model not only evaluates the impact of progression on quality of life but also considers its effects on healthcare costs. The findings indicate that as quality of life deteriorates, there is a correlative influx in annual healthcare expenditures necessary for patient treatment and follow-up. Lastly, the third study offers a more humanistic perspective with a focus on a patient-centered view, exploring individual experiences as the disease advances.

Together, these three studies document the repercussions of progression on the substantial financial burden on the healthcare system, the adverse impact on patient quality of life, and additional aspects of patient health, encompassing physical, psychological, and social dimensions. Comprehending the impact of metastatic prostate cancer on patients and the healthcare system is imperative for healthcare providers. This understanding enables informed and collaborative decision-making regarding treatment modalities, the effective management of treatment-related side effects, and the provision of tailored support services to address the unique needs and concerns of each patient. Such endeavors are essential for enhancing the overall well-being and survivorship outcomes of these patients.

Therefore, the findings of this research collectively underscore the critical economic and health benefits that may arise from preventing the progression of prostate cancer to its metastatic stage.

Transparency

Declaration of funding

This work was supported by Johnson & Johnson Innovative Medicine.

Declaration of financial/other relationships

The professional engagements of co-author AM encompass various affiliations with pharmaceutical companies, potentially giving rise to conflicts of interest. He has received honoraria as a consultant and speaker from several prominent entities, including Amgen, Astellas, AstraZeneca, Bayer, B.Braun, Bristol Myers-Squibb, Janssen, Merck-Serono, Merck Sharp & Dohme, Novartis, OMPharma, Pfizer, Pierre Fabre, Roche, and Servier. Additionally, he has received research funding from Bayer and B.Braun. Furthermore, co-authors SS and JM are employees of Johnson & Johnson Innovative Medicine, which sponsored the study. The remaining authors and co-authors have disclosed no potential competing interests.

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Author contributions

Conceptualization: MG, HC, AR; Writing—original draft preparation, DMZ, RDS; Writing—review and editing, DMZ, MG, LG, JD, AM, HC, AR, SS, JM; Design of the figures, MG, LG, DMZ. All authors have read and agreed to the published version of the manuscript.

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Research ethics and informed consent

All research participants previously signed informed consent forms to participate in the qualitative study (Study 3). Both sessions were recorded with the participants' consent for data processing purposes.

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