Systematic Literature Review on Economic Evaluations and Health Economic Models in the Field of Metastatic Castration-Sensitive Prostate Cancer

SA50

Nguyen TT[1,2], Ameyaw D[2], Obeng GD[2], Amuah R[2], Józwiak-Hagymásy J[2], Dóczi T[2], Mezei D[2], Németh B[2], Tordai A[3], Alanya A[4], Grisay G[5], Csanádi M[2]

1) Center for Health Technology Assessment, Semmelweis University, Budapest, Hungary; 2) Syreon Research Institute, Budapest, Hungary, 3) Department of Transfusion Medicine, Semmelweis University, Budapest, Hungary, 4) Quality of Life Department, European Organization for Research and Treatment of Cancer (EORTC), Brussels, Belgium, 5) Department of Medical Oncology, Centres Hospitaliers Universitaires HELORA, La Louvière, Belgium

Contact email: tu.nguyen@syreon.eu

INTRODUCTION

➢ Prostate cancer is among the most common types of cancer among men in Europe and in the United States [1,2].

➢ At diagnosis, all prostate cancer is sensitive to androgen deprivation; these patients are usually referred to as *castration-sensitive prostate cancer patients*. However, as a result of hormonal therapy, eventually, all prostate cancer will advance into castration resistance, which is called castration-resistant prostate cancer.

➢ In the past, androgen deprivation therapy (ADT) was the standard of care for metastatic castration-sensitive prostate cancer (mCSPC) patients, whereas maximal androgen blockade in a form of intensified ADT was considered rather for metastatic castration-resistant prostate cancer (mCRPC). However, nowadays, it is also used for mCSPC as it showed significantly improved survival [3,4,5].

➢ The use of intensified ADT leads to increased costs because of the costs of the additional treatments as well as costs to manage adverse events [6]. In addition, the quality of life of patients is affected. Therefore, there is a need for better understanding of the cost and effectiveness of managing mCSPC with the available treatment options.

OBJECTIVES

This systematic review aimed to review the available economic evaluations and health economic models of mCSPC treatments in Europe or North America.

METHODS

Search Strategy

➢ Medline (via PubMed), Embase, Scopus databases were searched on 8th of September 2023.

➢ Studies were searched from 2008 with no restrictions on the intervention (i.e. treatment, diagnosis or screening) or on the stage of the disease.

➢ Snowball sampling of relevant articles were conducted.

➢ Grey literature: related documents were searched from ISPOR, NICE, and CADTH.

Study selection

➢ Title and abstract screening, full-text screening, and data extraction were conducted by two researchers independently, using Covidence and Excel.

➢ At the full-text screening, first we included all health economic evaluations of prostate cancer treatments; then we focused on mHSPC treatments for data extraction and synthesis.

Data extraction and synthesis

➢ Study characteristics, information on patients and treatment, and the evaluation / modelling method were extracted using an Excel form. Then a narrative synthesis were performed.

RESULTS

➢ Our search resulted in the following hits: Medline (n=2 089); EMBASE (n=1 671); Scopus (n=2 877). Duplications were detected automatically (n = 2 947), so 3 690 records were reviewed.

➢ The title and abstract screening resulted in 416 potentially relevant records without limiting to specific patient population or type of intervention.

➢ *Full-text screening resulted in the inclusion of 18 health economic evaluations of mCSPC treatments (see Table 1). The PRISMA flow diagram is presented in the supplemental material.*

➢ Majority of the economic evaluations (13 studies) used deterministic Markov structure; either Markov cohort or partitioned survival models. Besides, 3 studies applied Markov simulation and 1 study had a hybrid model structure.

➢ We identified 3 conference material from the ISPOR database, which did not overlap with the above publications (see Table 2). All of these economic evaluations used a partitioned survival model with 3 health states: progression free, progressed disease, and death.

➢ We identified 7 health economic evaluations from NICE and CADTH (see supplemental material). Five of these studies presented details about modeling, and all used partitioned survival models.

➢ Majority of found health economic evaluations investigated various types of ADT based combinations comparing the addition of androgen receptor pathway inhibitors, chemotherapy agents, or radiation therapy to ADT alone.

Table 1: Summary of health economic evaluations of mHSPC treatments in peer-reviewed publications

Reference	Investigated therapies	Modelling approach	Study outcome	Study country	Time horizon
Iannazzo, 2011	1) Leuprorelin lower dose vs. 2) Leuprorelin higher dose vs. 3) Triptorelin vs. 4) Buserelin vs. 5) Goserelin	**Markov simulation model** • Health states in a Markov chain: alive or death; • Identical patients were simulated through the five treatment branches	Cost / life-month gained	Italy	Lifetime
Hird, 2020	1) ADT with initial docetaxel chemotherapy vs. 2) ADT with initial abiraterone acetate and prednisone	**Markov simulation model** • Health states: 1st line; 2nd line; 3rd line; Palliation; Death • Events: treatment-associated complications, treatment-related death, disease progression	Cost / QALY	Canada	Lifetime
Lester-Coll, 2021	1) ADT + Prostate Radiation Therapy vs. 2) ADT alone	**Markov simulation model** • Health states: stable disease after initial treatment; progression; 2nd progression; death	Cost / QALY	USA	37 months to mirror the trial + Lifetime
Lu, 2012	1) Degarelix vs. 2) Triptorelin + short-term flutamide + cyproterone or bicalutamide	**Hybrid model** • Decision tree: 1 month to capture treatment complications • Markov health states: in response; in progressive disease; dead;	Cost / QALY	United Kingdom	10 years
Barbier, 2022	1) ADT + docetaxel vs. 2) ADT + abiraterone vs. 3) ADT + apalutamide vs. 4) ADT+ enzalutamide vs. 5) ADT alone	**Markov cohort** • Health states: Progression-free disease, progressive disease, death	Cost / QALY	Switzerland	30 years
Bleser, 2020	1) Metastasis-directed therapy with delayed ADT vs. 2) Surveillance with delayed ADT vs. 3) Immediate ADT	**Markov cohort (assumed)** • Health states: ADT-free, ADT-state, castration-resistant prostate cancer, death	Cost / QALY	Belgium	5 years
Parikh, 2020	1) Metastasis-directed therapy followed by AAP + ADT, followed by docetaxel + ADT vs. 2) AAP + ADT followed by ADT + docetaxel vs. 3) ADT + docetaxel followed by ADT + AAP	**Markov cohort (assumed)** • Health states: Low-volume M1; High-volume mHSPC; castrate resistance prostate cancer; death (prostate cancer); death (other)	Net Monetary Benefit	USA	10 years
Pelloux-Prayer, 2021	Asymptomatic or mildly symptomatic patients 1) ADT + AAP → ADT + enzalutamide vs. 2) ADT + AAP → ADT + docetaxel vs. 3) ADT + docetaxel → ADT + abiraterone vs. 4) ADT + docetaxel → 5)ADT + enzalutamide vs. Symptomatic patients): 1) ADT + AAP → ADT + docetaxel vs. 2) ADT + docetaxel → ADT + cabazitaxel vs. 3) ADT + docetaxel →ADT + docetaxel	**Markov cohort (assumed)** • Health states: mHSPC, mHRPC, death	Cost / LYG	France	Lifetime
Ramamurthy, 2019	1) ADT + Abiraterone acetate vs. 2) ADT + Docetaxel vs. ADT alone	**Markov cohort** • Model 1: stable disease without AE, stable disease with fatigue; stable disease treatment discontinuation, disease progression / death • Model 2: stable disease with neutropenia, stable disease neutropenic fever; stable disease no AE, stable disease post-chemo disease, progression / death	Cost / progression-free quality-adjusted life years	USA	3 years
Saad, 2022	1) ADT + Enzalutamide vs. 2) ADT + Apalutamide vs. 3) ADT alone	**Markov cohort (assumed)** • Health states: mHSPC, mHRPC, death	Cost / QALY	Canada	15 years
Sathianathen, 2019	1) ADT + Docetaxel vs. 2) ADT + Abiraterone vs. 3) ADT alone	**Markov cohort** • Health states: mHSPC; mHRPC, prostate-cancer death, all-cause death	Cost / QALY	USA	Lifetime
Sung, 2021	1) ADT + Docetaxel vs. 2) ADT + Abiraterone vs. 3) ADT + Enzalutamide vs. 4) ADT + Apalutamide vs. 5) ADT alone	**Markov cohort** • Health states: Progression free; progression; death	Cost / QALY	USA & China	Lifetime
Zhang, 2021	1) Enzalutamide + ADT vs. 2) ADT alone	**Markov cohort (assumed)** • Health states: Progression-free survival, progressive disease, death	Cost / QALY	USA & China	20 years
Beca, 2019	1) ADT + docetaxel vs. 2) ADT alone	**Partitioned survival model** • Health states: mHSPC, mHRPC, death	Cost / QALY Cost / LYG	Canada	15 years
Parmar, 2021	1) ADT + Apalutamide vs. 2) ADT alone	**Partitioned survival model (assumed)** • Health states: Progression-free, progressive disease, death	Cost / QALY Cost / LYG	Canada	Lifetime
Yoo, 2023	1) ADT + Docetaxel vs. 2) ADT + AAP vs. 3) ADT + Apalutamide vs. 4) ADT + Enzalutamide vs. 5) ADT + Darolutamide and Docetaxel vs. 6) ADT + Enzalutamide and Docetaxel vs. 7) ADT alone	**Partitioned survival model** • Health states: Progression-free, progression to mHRPC, death	Cost / QALY	USA	10 years
Wang, 2022	1) ADT + docetaxel vs. 2) ADT + AAP vs. 3) ADT + enzalutamide vs. 4) ADT + apalutamide vs. 5) ADT alone	**Partitioned survival model** • Health states: mHSPC, mHRPC, death	Cost / QALY	USA	Lifetime
Esteban, 2017	1) ADT + docetaxel vs. 2) ADT alone	• Incremental drug costs were divided by overall survival increment based on the CHAARTED and STAMPEDE studies	Cost / LYG	Spain	Non-applicable

ADT: androgen deprivation therapy; AAP: abiraterone acetate plus prednisone QALY: quality-adjusted life years; LYG: life year gain; mHSPC: metastatic hormone-sensitive prostate cancer; mHRPC: metastatic hormone-resistant prostate cancer; AE: adverse events.

Table 2: Summary of health economic evaluations of mHSPC treatments identified in the ISPOR database

Reference	Investigated therapies	Modelling approach	Study outcome	Study country	Time horizon
Katta, 2023	1) ADT + Enzalutamide vs. 2) ADT + Apalutamide vs. 3) ADT + Abiraterone acetate	• Partitioned survival model • Progression free, Progressed disease, Death	Cost / QALY	USA	Lifetime
Madani, 2023	1) ADT Abiraterone acetate + Prednisone vs. 2) ADT alone	• Partitioned survival model • Pre-progression, Post-progression, Dead	Cost / QALY	UK	Lifetime
Nwogu, 2023	1) ADT + Darolutamide + Docetaxel vs. 2) ADT + Docetaxel	• Partitioned survival model • Progression free, Progressed disease, Death	Cost / QALY	USA	Lifetime

ADT: androgen deprivation therapy; QALY: quality-adjusted life years.

CONCLUSION

➢ Health economic evaluations in the field of prostate cancer are widely published and there are a large number of publications even in the specific sub-group of mCSPC.

➢ In this sub-group, the majority of health economic evaluations compared intensified ADT with ADT alone.

➢ Regardless of the investigated interventions, most studies apply similar methodologies and simulate patients from mCSPC state until the development of mCRPC and death.

SUPPLEMENTAL MATERIAL

Scan the QR code to visit the supplemental material

REFERENCES

1. European Cancer Information System. Cancer statistics [accessed 2024 Oct 22]. Available from: https://ecis.jrc.ec.europa.eu/en
2. American Cancer Society. Cancer facts for men [accessed 2024 Oct 22]. Available from https://www.cancer.org/cancer/risk-prevention/understanding-cancer-risk/cancer-facts/cancer-facts-for-men.html#:~:text=Prostate%20cancer%20is%20the%20most,death%20(after%20lung%20cancer
3. Wala, J., Nguyen, P., & Pomerantz, M. (2023). Early treatment intensification in metastatic hormone-sensitive prostate cancer. *Journal of Clinical Oncology, 41*(20), 3584-3590.
4. Ong, S., O'Brien, J., Medhurst, E., Lawrentschuk, N., Murphy, D., & Azad, A. (2021). Current treatment options for newly diagnosed metastatic hormone-sensitive prostate cancer—a narrative review. *Translational Andrology and Urology, 10*(10), 3918.
5. Blas, L., Shiota, M., & Eto, M. (2022). Current status and future perspective on the management of metastatic castration-sensitive prostate cancer. *Cancer Treatment and Research Communications, 32*, 100606.
6. Olsen, T. A., Filson, C. P., Richards, T. B., Ekwueme, D. U., & Howard, D. H. (2023). The cost of metastatic prostate cancer in the United States. *Urology Practice, 10*(1), 41-47.

Presented at the ISPOR Europe 2024 Conference, 17 – 20 NOVEMBER 2024 BARCELONA, SPAIN

Funded by the European Union

Scan the QR code to visit the DE-ESCALATE website