Mapping Health-Related Quality of Life (HRQoL) Measures to Preference-Based Measures in Metastatic Hormone-Sensitive Prostate Cancer (mHSPC): A Systematic Literature Review

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INTRODUCTION

- Prostate cancer is among the most commonly diagnosed cancers in men[1,2] and despite advances in early detection and treatment, a considerable proportion of cases progress to advanced stages, including metastatic hormone-sensitive prostate cancer (mHSPC).[3]
- Health-related quality of life (HRQoL) is clinically and statistically significantly lower in patients with metastatic disease compared with localised disease, with fatigue and pain the most important factors associated with poor HRQoL.[4]
- Generic preference-based measures (PBMs) typically consist of a standardised HRQoL questionnaire and are commonly administered in clinical trials[5]; such instruments include the EQ-5D and the Health Utilities Index Mark 2 and 3.
- PBMs help aid decision-makers in resource allocation by the generation of health state utility values, which can be used to calculate quality-adjusted life years and allow comparisons to be made across different diseases and patient groups.
- In the absence of robust PBM data collected directly from patients, health technology assessment (HTA) bodies may accept the mapping of or elicitation from disease-specific/generic HRQoL data to a generic PBM.[6]
- Functional Assessment of Cancer Therapy – Prostate (FACT-P) is a disease-specific HRQoL measure widely used in prostate cancer studies, comprised of the Functional Assessment of Cancer Therapy – General (FACT-G) and a prostate cancer subscale (PCS)[7]:
  - The generic FACT-G measure consists of 27 items across 5 subscales measuring physical, functional, social/family, and emotional well-being, in addition to satisfaction with doctor–patient relationship.
  - The PCS includes 12 items specifically designed to measure HRQoL in patients with prostate cancer.
- The Brief Pain Inventory (BPI) is a self-administered assessment tool used in pain management, which provides information on the intensity of pain, along with the degree to which the pain interferes with the everyday functioning of life.

OBJECTIVE

- The aim of the current systematic literature review (SLR) is to identify mapping algorithms for HRQoL data, with a primary focus on algorithms that allow mapping of FACT-P and BPI to PBMs, conducted or verified in patients with mHSPC.

METHODS

- The SLR was conducted according to published guidance from the Cochrane Collaboration and the Centre for Reviews and Dissemination.[8,9]
- Systematic searches of Embase®, MEDLINE®, MEDLINE Epub Ahead of Print (In-Process & Other Non-Indexed Citations), and Evidence-Based Medicine Reviews (EBMR) were conducted on 13th December 2023.
- Electronic database searches were complemented by reviewing several recent conference proceedings (past 3 years), HTA websites (with a focus on National Institute for Health and Care Excellence [NICE] technology appraisals [TAs]), the Health Economics Research Centre database of mapping studies, and reference lists of included publications.
- Results from the searches were downloaded into an Excel® database and citations were screened for eligibility by two analysts at title/abstract and full publication review stages.
- Eligible publications included algorithms reporting mapping of one of the following tools onto PBMs **(Table 1)**:
  - FACT-P
  - BPI
- Due to the anticipated paucity of eligible records for patients with mHSPC, broader prostate cancer populations were eligible for consideration.
- Eligible mapping algorithms were 'quality assessed' using a published checklist of essential items to consider when reporting mapping studies.[10]

RESULTS

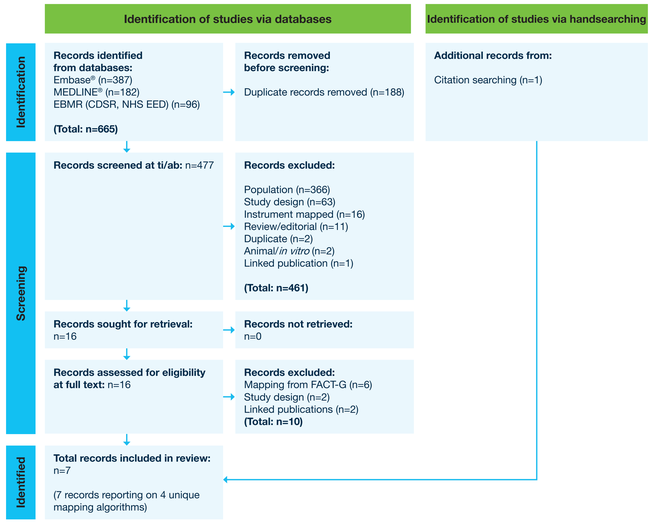
- Following de-duplication, 477 records were screened on the basis of title and abstract, with 16 records selected for full paper retrieval. A further 10 records were excluded at this stage, with a single record included from supplementary searches **(Figure 1)**. Therefore, 7 studies relating to 4 unique mapping algorithms were eligible for inclusion **(Table 2)**.[11-17]
  - No studies mapped condition-specific non-PBMs to PBMs in an mHSPC population; rather all studies were conducted in a metastatic castration-resistant prostate cancer (mCRPC) population.
  - All four algorithms mapped FACT-P to EQ-5D (EQ-5D-3L, n=3) and no mapping algorithms mapping the BPI to a PBM in prostate cancer were identified.
- Algorithms employed a variety of datasets from multinational trials (observational, n=3; randomised controlled trial (RCT) [AFFIRM], n=1) and used UK preference weights to estimate EQ-5D (Spencer and Diels (2011)[12] employed value sets for eight countries, including UK) **(Table 2)**.
  - All studies explored multiple mapping models using regression methods; in general, ordinary least squares (OLS) regression models were the best performing.

TABLE 1. SLR ELIGIBILITY CRITERIA

CRITERIA	INCLUSION	EXCLUSION
Population	• Adult patients (age ≥18 years) with mHSPC • mHSPC synonym – castrate-sensitive, hormone-dependent, hormone-naïve patients • Patients with prostate cancer other than mHSPC (due to anticipated paucity of data in a mHSPC population)	• Female • Healthy volunteers • Paediatric population • Patients with benign, localised, or locally advanced prostate cancer
Interventions	No restrictions	None
Comparators	No restrictions	None
Outcomes	• Studies reporting mapping of one of the following tools onto a preference-based utility measure: – FACT-P – BPI	Other disease-specific/generic tools
Study design/ publication date/ territory	No limits	None
Language	English language only	Non-English language

Abbreviations: BPI, Brief Pain Inventory; FACT-P, Functional Assessment of Cancer Therapy – Prostate; mHSPC, metastatic hormone-sensitive prostate cancer; SLR, systematic literature review.

FIGURE 1. PRISMA FLOW DIAGRAM



Abbreviations: CDSR, Cochrane Database of Systematic Reviews; EBMR, Evidence-Based Medicine Reviews; FACT-G, Functional Assessment of Cancer Therapy – General; NHS EED, National Health Service Economic Evaluation Database; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ti/ab, title/abstract.

Spencer and Diels (2011)[12]

- Patient-level data were obtained from the Adelphi Prostate Cancer Disease Specific Programme, a multi-national, cross-sectional study of prostate cancer patients across France, Germany, Italy, Spain, and the UK.
- The authors estimated EQ-5D values based on value sets for eight countries (Belgium, Denmark, Germany, New Zealand, Spain, the Netherlands, UK, and US) and Europe.
- Predictive validity of the FACT-P subscales and demographics were tested using OLS, median, Gamma, and Tobit multivariate regression models, in addition to predictive algorithms developed to convert FACT-P to EQ-5D utilities for the different country value sets.
  - OLS and Tobit regressions were the best-performing models.

Wu et al (2007)[11]

- Data were obtained from a multi-national, prospective observational study of mCRPC patients conducted from 2002 to 2004.
- Three prediction models based on OLS regression (all patients versus observations with EQ-5D summary score <1) or median regression were used to estimate EQ-5D values from FACT-P and European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire-30 (EORTC QLQ-C30) data and FACT-P data alone.
  - The OLS regression using the individual component scores of FACT-P and EORTC QLQ-C30 and no interaction terms was the best-performing model, explaining 58.2% of the observed EQ-5D variation in the validation sample.
- One limitation of using the proposed algorithm is that some predicted EQ-5D values fell outside of the EQ-5D-3L range (-0.594, 1.000), so truncation is required.

TABLE 2. OVERALL SUMMARY OF STUDIES REPORTING MAPPING ALGORITHMS FOR FACT-P TO EQ-5D (N=4)

AUTHOR (YEAR)	INDICATION	TOOLS MAPPED	DATA SOURCE	STUDY DESIGN	COUNTRY	NO. OF PARTICIPANTS	MAPPING MODELS INVESTIGATED
Diels et al (2015)[14]	mCRPC	FACT-P to EQ-5D-3L	NR	Observational, multi-national, cross-sectional	Belgium, France, Germany, Sweden, the Netherlands, UK (UK preference weights)	602	OLS regression (median regression, GLM, and Tobit regression models also explored)
Skaltsa et al (2014)[13] (Related article: Ivanescu et al (2014)[15])	mCRPC	FACT-P to EQ-5D-3L	AFFIRM (NCT00974311)	Double-blind, placebo-controlled, multinational, Phase 3 RCT	France, Germany, Italy, Spain, UK (UK preference weights)	236	GEE (two-part model, GSM also explored; separate GEE models for good and poor health)
Spencer and Diels (2011)[12]	mCRPC	FACT-P to EQ-5D (EQ-5D levels NR)	Adelphi Prostate Cancer DSP	Observational, multi-national, cross-sectional	France, Germany, Italy, Spain, UK (Preference weights applied from Belgium, Denmark, Germany, New Zealand, Spain, the Netherlands, UK, US, and Europe)	291	OLS regression (median regression, GLM, and Tobit regression models also explored)
Wu et al (2007)[11] (Related articles: Cella et al (2012)[16] and Wu et al (2012)[17])	mCRPC	FACT-P to EQ-5D-3L	NR	Prospective observational, multinational	North America (Canada and US), Europe (France, Germany, Italy, UK), and Australia (UK preference weights)	276	OLS regression (group-specific OLS regression, median regression models also explored)

Abbreviations: DSP, disease specific programme; FACT-P, Functional Assessment of Cancer Therapy – Prostate; GEE, generalised estimating equation; GLM, generalised linear model; GSM, group-specific model; mCRPC, metastatic castration-resistant prostate cancer; NR, not reported; OLS, ordinary least squares; RCT, randomised controlled trial.

Diels et al (2015)[14]

- Collected HRQoL data (FACT-P) in an observational, multinational, cross-sectional study of 699 adult patients with confirmed mCRPC across six countries.
- Predictive validity was tested using four different regression models: OLS regression, median regression, generalised linear models (GLMs) with log link and Gamma, and Tobit multivariate regression.
- Across treatment status and for all patients, the OLS and Tobit regression models were shown to have the best fit between the predicted utility values and the observed data, but the Tobit model was considered to have greater limitations.
- Hence, the authors developed an algorithm to map the disease-specific FACT-P measure to the generic preference-based EQ-5D instrument, based on data collected from mCRPC patients, using OLS regression, which was considered to be the best-performing model.

Skaltsa et al (2014)[13]

- FACT-P data were obtained from a double-blind, placebo-controlled, multinational, Phase 3 RCT enrolling mCRPC patients (AFFIRM; NCT00974311).
  - Mapping model was developed on 236 patients with mCRPC in a post-chemotherapy setting.
- Of the three statistical techniques compared: (i) generalised estimating equation (GEE); (ii) a two-part model combining logistic regression and GEE; and (iii) separate GEE models in two subsets of data for patients with poor versus good health (referred to as the group-specific model [GSM]), the GSM had the best predictive performance.
- Ivanescu et al (2014)[15] evaluated the predictive performance of the Skaltsa et al (2014)[13] algorithm on a sample of asymptomatic or minimally to mildly symptomatic chemotherapy-naïve mCRPC patients who had progressed on androgen deprivation therapy (data from Phase 3 PREVAIL RCT).
  - The validation exercise confirmed that the algorithm (developed in the post-chemo setting) performed well in a pre-chemo setting in mCRPC patients (although overpredicted for severe states).

Use of identified algorithms in NICE HTA

- Of the 17 prostate cancer-related TAs identified, three TAs (TA259, TA316, TA387) reported mapping of FACT-P to EQ-5D via the use of internal mapping algorithms:
  - TA259[18] (employed algorithm reported by Spencer and Diels (2011)[12])
  - TA316[19] (employed algorithm reported by Skaltsa et al (2014)[13])
  - TA387[20] (employed algorithm reported by Diels et al (2015)[14])
- Two of the identified TAs (TA259 and TA387) had explicitly considered the use of Wu et al (2007)[11], but believed the algorithm to be unreliable, as it generated utilities greater than one and this consideration was supported by the Evidence Review Group in NICE TA259.[21]
- It was also noted in the NICE TAs that whilst mapping was conducted to obtain utility values directly from HRQoL trial data, all economic models used the mapped utilities in scenario analysis only in order to explore uncertainty in the utility parameters, rather than applying these utilities in the base case.
  - This is due to the consideration that evidence collected directly from a study using PBMs is of better quality than mapped data, due to the uncertainties associated with the mapping process.

Hierarchy of algorithms

- Although the preference would be to conduct mapping using each of the algorithms, if a hierarchy was required, the Wu et al (2007)[11] and Spencer and Diels (2011)[12] algorithms could be deprioritised.
  - Several authors have noted potential 'errors' with the former algorithm (although the authors refute these[17]) and the algorithm by Spencer and Diels (2011)[12] has not been reported in a full publication and therefore has limited information available.
- Both of the remaining algorithms have been using in previous NICE submissions (Diels et al (2015)[14] in TA387[20] and Skaltsa et al (2014)[13] in TA316[19]) and were well reported and seemingly well conducted as per the Petrou et al (2015) checklist.[10]
- External validation of mapping algorithms is, however, recommended to be performed in a variety of out-of-sample populations before their routine use.
  - While such validation is not currently reported for Diels et al (2015)[14], Ivanescu et al (2014)[15] evaluated the predictive performance of the Skaltsa et al (2014)[13] algorithm.
  - Therefore, the Skaltsa et al (2014)[13] algorithm could be considered the algorithm of choice for conducting mapping of FACT-P to EQ-5D in a mHSPC population.

CONCLUSIONS

- Although no studies mapping condition-specific tools to PBMs in a mHSPC population were identified, a small number (n=4) of mapping algorithms were identified in mCRPC.
  - This highlights a need for mapping algorithms to be validated in prostate cancer populations outside of the mCRPC indication.
- As using different mapping algorithms can provide substantially distinct utility estimates, careful consideration should be taken when choosing the appropriate algorithm for the patient population included in the study providing HRQoL data.
- Data mapped from condition-specific, non-preference-based measures is a useful alternative to explore uncertainty in utility parameters and support decision-making.
- Mapping algorithms can also be used to support analyses exploring the impact of key outcomes, e.g. hospitalisations on HRQoL.
- However, mapped utility values would most likely be preferred by an HTA body to be presented as a scenario analysis rather than as the base case utilities.

REFERENCES

1 Wang L, et al. Prostate cancer incidence and mortality: global status and temporal trends in 89 countries from 2000 to 2019. Frontiers in public health. 2022;10:811044; 2 Giona S. The epidemiology of prostate cancer. Exon Publications. 2021;1-15; 3 Hamdy FC, et al. Fifteen-year outcomes after monitoring, surgery, or radiotherapy for prostate cancer. NEJM. 2023;388(17):1547-58; 4 Torvinen S, et al. Health-related quality of life in prostate cancer. Acta Oncol. 2013; 52(6):1094-101; 5 Brazier J, et al. A Review of Generic Preference-Based Measures for Use in Cost-Effectiveness Models. Pharmacoeconomics. 2017;35(Suppl 1):21-31; 6 Longworth L, Rowen D. Mapping to obtain EQ-5D utility values for use in NICE health technology assessments. Value Health. 2013 Jan-Feb;16(1):202-10; 7 Esper P, et al. Measuring quality of life in men with prostate cancer using the functional assessment of cancer therapy-prostate instrument. Urology. 1997;50(6):920-8; 8 Higgins JPT, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023); 9 Centre for Reviews and Dissemination. Systematic Reviews: CRD's guidance for undertaking reviews in health care [Internet]. University of York; 2009; 10 Petrou S, et al. The MAPS Reporting Statement for Studies Mapping onto Generic Preference-Based Outcome Measures: Explanation and Elaboration. Pharmacoeconomics. 2015;33(10):993-1011; 11 Wu EQ, et al. Mapping FACT-P and EORTC QLQ-C30 to patient health status measured by EQ-5D in metastatic hormone-refractory prostate cancer patients. Value Health. 2007;10(5):408-14; 12 Spencer M, Diels J. MA2 Mapping FACT-P to country specific patient health status measured by EQ-5D in metastatic castrate resistant prostate cancer patients. Value in Health. 2011;14(7):PA242; 13 Skaltsa K, et al. Mapping the FACT-P to the preference-based EQ-5D questionnaire in metastatic castration-resistant prostate cancer. Value Health. 2014;17(2):238-44; 14 Diels J, et al. Mapping FACT-P to EQ-5D in a large cross-sectional study of metastatic castration-resistant prostate cancer patients. Qual Life Res. 2015;24(3):591-8; 15 Ivanescu C, et al. Mapping Fact-P To EQ-5D In Metastatic Castration-Resistant Prostate Cancer (MCRPC): Performance Of A Previously Developed Algorithm When Applied On A Sample With A Different Disease Stage. Value Health. 2014;17(7):A567; 16 Cella D, Proskorovsky I, Pan F. Approach to fixing the discrepancy found in the Wu et al. FACT-P to EQ-5D questionnaire mapping algorithm. Value Health. 2012;15(5):783-4; 17 Wu EQ, De G. Approach to Fixing the Discrepancy Found in the Wu et al. FACT-P to EQ5D Mapping Algorithm—Reply to Letter to the Editor by David Cella, Irina Proskorovsky, and Feng Pan. Value In Health. 2012;15(5):785; 18 National Institute for Health and Care Excellence. Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen. Technology appraisal guidance; TA259. Published 27 June 2012, last updated 27 July 2016 2012 [Available from: https://www.nice.org.uk/guidance/ta259]; 19 National Institute for Health and Care Excellence. Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen. Technology appraisal guidance; TA316. Published 23 July 2014; 20 National Institute for Health and Care Excellence. Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated. Technology appraisal guidance; TA387. Published 27 April 2016, last updated 27 July 2016 2016 [Available from: https://www.nice.org.uk/guidance/ta387]; 21 Connock M, et al. Abiraterone acetate for the treatment of metastatic, castrate-resistant prostate cancer following previous cytotoxic chemotherapy: A Single Technology Appraisal. 2011.

ABBREVIATIONS

BPI, Brief Pain Inventory; CDSR, Cochrane Database of Systematic Reviews; DSP, disease specific programme; EBMR, Evidence-Based Medicine Reviews; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire-30; FACT-G, Functional Assessment of Cancer Therapy – General; FACT – P, Functional Assessment of Cancer Therapy – Prostate; GEE, generalised estimating equation; GLM, generalised linear model; GSM, group-specific model; HRQoL, health-related quality of life; HTA, health technology assessment; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; NHS EED, National Health Service Economic Evaluation Database; NICE, National Institute for Health and Care Excellence; NR, not reported; OLS, ordinary least squares; PBM, preference-based measure; PCS, prostate cancer subscale; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomised controlled trial; SLR, systematic literature review; TA, technology appraisal; ti/ab, title/abstract.

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