Supplementary material

File S1 – Interview guide

Consent

Before starting the interview, we ask for your consent to use the information collected. We remind you that your participation is voluntary and you can interrupt the interview at any time. Furthermore, we would like to ask your permission to record this interview, in order to ensure the quality of information gathering.

Introductory remarks

Thank you for your time […]. The aim of this project is […]. We anticipate that the interview will take no longer than one hour.

Throughout the interview process, we will make written notes on your responses to the various questions. Please bear with us if there are short pauses between questions while we note your replies.

We would like to begin, by learning more about you. What's your current role, affiliation and experience in the management of prostate cancer?

Clinical pathway

Before proceeding with the interview, we would like to share with you a definition of the setting to which we will refer from now on.

By patients with castration-resistant non-metastatic prostate cancer we mean patients with testosterone <50ng/dl, in biochemical progression (who have had at least three increases in PSA, the last of which was> 2ng/ml) during treatment with ADT, but who still have no detectable metastases with CT scan or scintigraphy. We define patients with non-metastatic castration-resistant prostate cancer as high-risk when they exhibit PSA doubling time ≤ 10 months.

1. In what respect is non-metastatic castration-resistant prostate cancer different from non-metastatic castration-sensitive prostate cancer?
2. In what respect is non-metastatic castration-resistant prostate cancer different from metastatic castration-resistant prostate cancer?
3. Could you explain how to make a diagnosis of non-metastatic castration-resistant prostate cancer?
    a. In what respect is the diagnosis different from metastatic castration-resistant prostate cancer? (hint: Is the diagnosis of nmCRPC and mCRPC imaging-based, test-based or also based on clinical symptoms? Which symptoms are specific to metastasis free rather than non-metastatic disease?)
4. What is the clinical pathway according to your experience with this patient population? (hint: what is the sequence of events occurring to the patient since the establishment of a diagnosis till

confirmed progression? Which doctors intervene in the process of care? Are there inpatient or outpatient services required?)

5. Who is in charge of the patient's treatment choice in non-metastatic castration resistant prostate cancer? Who is in charge of the patient's treatment choice in all steps of the patient pathway described above? (hint: only one specialist and which one, or a team of more specialists? Which ones?)
    a. In case there is a multi-disciplinary team (TMD) involved, when does it take responsibility on the patient? According to which criteria (if any) a patient is in charge of the TMD or a single specialist?
6. How do you currently treat non-metastatic castration-resistant prostate cancer patients?
    a. Which factors influence the choice of one treatment option over the other? In case of hormonal manipulation, how does it work, how many lines are prescribed and on which criteria are chosen?
    b. In what respect is the treatment different from metastatic castration-resistant prostate cancer?
    c. With the introduction of new therapeutic options in this setting, which factors will influence the choice of one treatment over the others, beside efficacy? Please rank the below factors and add any additional factor you value as relevant.
        - Patient profile
        - QoL
        - Safety/tolerability
        - Sequencing
        - Interference with subsequent treatments
        - New drug on the market
        - Other: please specify
7. In your opinion, is there a gap in clinical guidelines with respect to the management of this patient population?
    a. Is there a specific clinical pathway (PDTA) in place at your hospital for the management of this patient population?

Health state description

Interviewer: In our study, we would like to estimate disability weights of patients living with non-metastatic and metastatic castration-resistant prostate cancer. To do so, we will submit to a panel of judges, both clinicians and health economists, a vignette with the description of health states, on which individuals will be asked to express their preferences. Ultimately, these preferences will be used to estimate disability weights and calculate DALYs.

For the realization of these vignettes, we would like to take advantage of your expertise on the disease. We would therefore ask you to provide us with a description of the health status of patients with castration-resistant prostate cancer, both metastatic and non-metastatic.

Closing remarks

We have reached the conclusion of the interview. Do you have any questions or observations that you would wish to make?

If you wish to know about the results of this project we will notify you once the report and related publication will be available.

File S2 - PTO and VAS exercises

PTO exercise

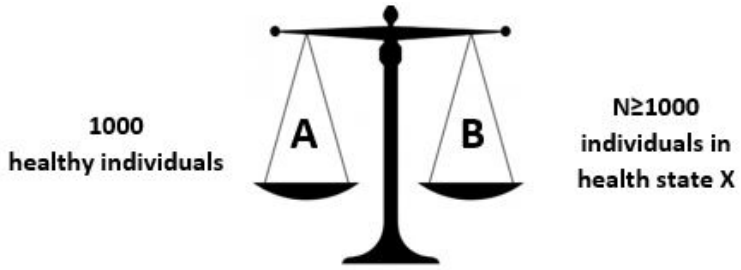
Imagine you are a decision maker. You have sufficient funds to finance a single health policy intervention. You have to make a choice between two mutually exclusive interventions, A and B.

By choosing intervention A, the life of 1000 healthy individuals will be extended by one year, after which the individual will die. If you do not choose intervention A, all healthy individuals will die immediately.

By choosing intervention B, the lives of N individuals in a health state X, lower than the state of perfect health, will be extended by one year, after which all individuals will die. If you do not choose intervention B, all individuals in a health state X will die immediately.

Objective:

Identify the number N of subjects in the state of health X for which the extension of one year of life is equal, from his point of view, to the extension of one year of life for 1000 healthy individuals. The number N is the point of indifference between the two options and is always greater than or equal to 1000.



If you choose N = 1000, it means that the health state X is equal to perfect health. If you choose N = 100000, it means that you value the health state X as very bad. Your choice of N can be placed anywhere between these two extremes (1000≤N≤100000).

VAS exercise

Step 1

By dragging the health state, please order the health states from the best (on the top) to the worst (on the bottom).

Metastatic CRPC, asymptomatic or slightly symptomatic
Metastatic CRPC, in progression during or after chemotherapy
Non-metastatic CRPC
Metastatic CRPC, symptomatic

Step 2

Assign a score to health states through the graduated scale, which assumes values from 0 (death or worst health state) to 100 (perfect health).

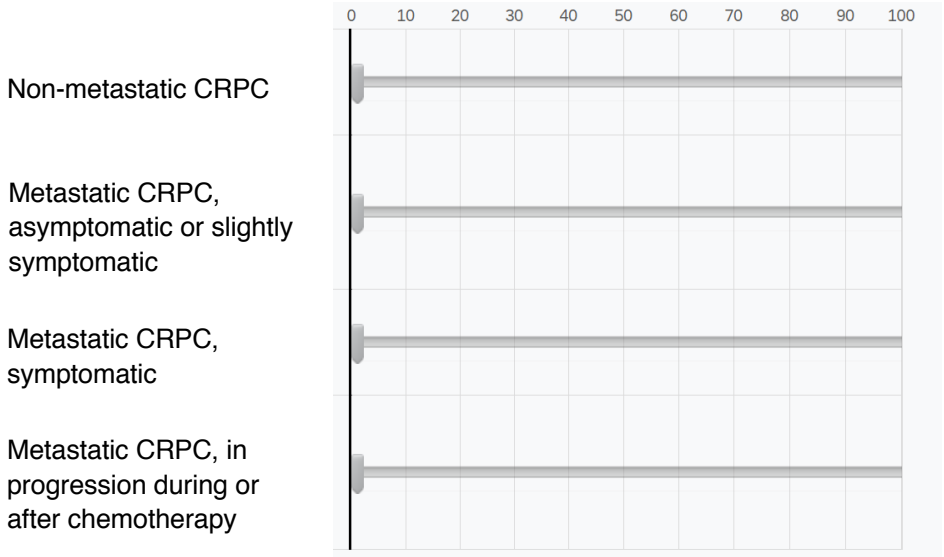


Figure A - Sample identification process for qualitative interviews

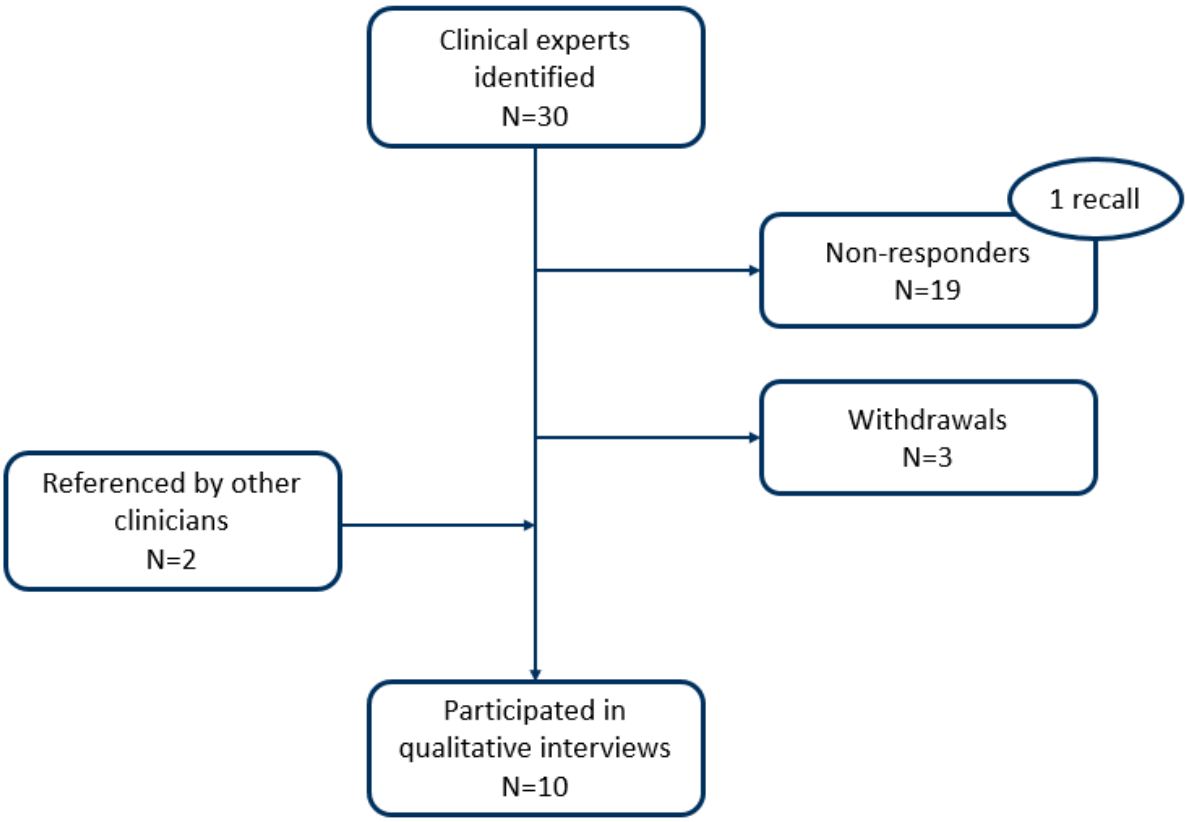


Table A - Interpretation of descriptors used in qualitative interviews analysis

Descriptor	Interpretation
Few	p≤20%
Some	20%<p<50%
Half	p=50%
The majority	p>50%

p is the proportion of responders making a claim or statement out of the total number of experts interviewed