Identifying Patients with Metastatic Castration-Resistant Prostate Cancers (mCRPC) in the SNDS database: CAMERRA study

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Background

➢ **Prostate cancer**
- Most common cancer in men, with more than 53 900 new cases in 2011 in France (INCa 2016)
- Slow but unavoidable disease progression to metastatic and/or castration-resistant stage

➢ **Major changes in metastatic castration-resistant prostate cancer (mCRPC) management**
- In 2012 and 2013, abiraterone acetate and enzalutamide obtained respectively a European marketing authorization for the treatment of mCRPC patients previously treated by docetaxel
- High potential changes in mCRPC patients care pathway

➢ **CAMERRA study**
- Aims to assess the therapeutic strategic changes for mCRPC between 2012 and 2014 from data of the French nationwide claims and hospital database (SNDS)
- However, no direct markers are available to identify mCRPC in the database

Objective: To design an algorithm for mCRPC identification in the SNDS in 2014

Methods

➢ **Data source**: EGB (*Echantillon Généraliste des Bénéficiaires*)
- 1/97th representative sample of SNDS, which covers 99% of the French population (66.6 million people)
- Includes individual anonymous information on reimbursed outpatients claims, national hospital-discharge summaries, and national death registry

➢ **Study period:** 01/01/2009 to 12/31/2014

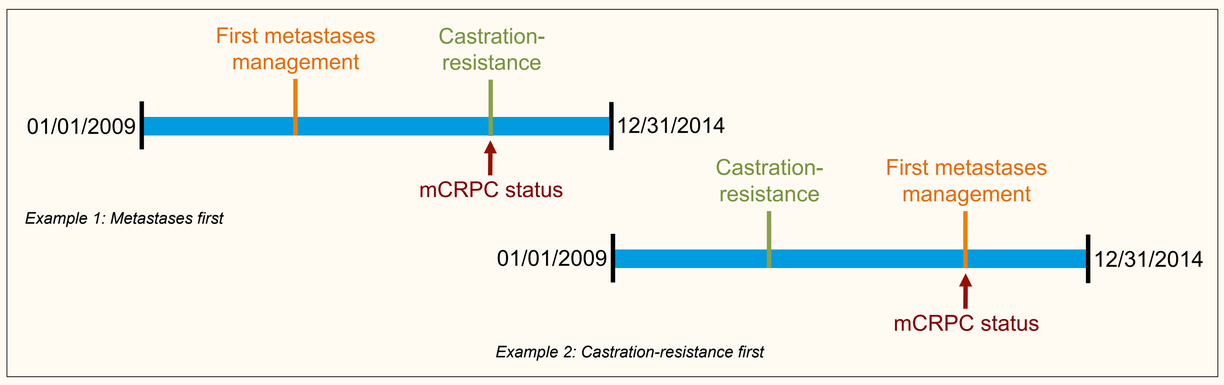

Figure 1. Chronology between first metastases management, castration-resistance and mCRPC status

➢ **4 steps to identify prevalent mCRPC cases**

- **Step 1 = Identification of prostate cancer**

  Inclusion criteria
  - Men ≥ 40 years old and alive on 01/01/2014, covered by the national health insurance "*Régime Général*" without any gap > 1 year in their 5-year healthcare history
  - With a prostate cancer indicator:
    i. Long-term disease registration (LTD) for prostate cancer (ICD10 = C61)
    ii. Hospital stay in 2014 with a diagnosis of prostate cancer (C61 as primary, related or associated diagnosis), and a prostate cancer specific treatment between 2009 and 2014 (radical prostatectomy, brachytherapy, hormonotherapy, *etc.*)
    iii. Dispensing in 2014 of prostate cancer specific treatment: androgen deprivation therapy (GnRH analogs/antagonists or antiandrogens), new generation hormonotherapy (e.g. abiraterone, enzalutamide), estramustine, or chemotherapy

  Exclusion criteria
  - Patients without LTD registration or hospitalization for prostate cancer and having:
    i. LTD registration for persistent delusional disorders (F22), specific personality disorders (F60), unspecified mental retardation (F79), or gender identity disorders (F64)
    ii. Androgen deprivation therapy with less than 3 PSA tests

- **Step 2 = Identification of metastatic cases**

  Date of first metastases management based on specific drug or procedures:
  - Radiotherapy session for metastases
  - Hospital stay with "secondary malignant neoplasm" as diagnosis (ICD10 = C77, C78, C79) associated with a LTD or a diagnostic code for prostate cancer
  - Dispensing of bone metastases targeted therapy: denosumab, zoledronic acid, hepatic radiofrequency ablation, beta particle emitting radionuclides (e.g. strontium-89, samarium-153, radium-223)
  - Initiation of a GnRH analog within 2 months of prostate cancer diagnosis in young patient (< 70 years old) without any local prostate cancer treatment prior
  - Initiation of a specific mCRPC treatment if preceded by at least 3 months of continuous androgen deprivation therapy and within 4 months after a specified medical imaging procedure

- **Step 3 = Identification of castration-resistant cases**

  Date of castration-resistance relying on:
  - Switches between androgen deprivation therapy treatments (anti-androgen, GnRH analog/antagonist)
  - Surgical castration (orchiectomy or testicular pulpectomy)
  - Initiation of estramustine or mCRPC specific treatment

- **Step 4 = Identification of mCRPC cases**

  Patients were considered as mCRPC when a date of first metastases management and a date of castration-resistance were identified in their medical history (Figure 1)

Results

➢ **Identification of prevalent mCRPC cases in 2014 (Figure 2.)**
- A total of 3 192 patients with a prostate cancer were identified in the EGB in 2014. By extrapolation, around 468 142 prostate cancers are expected in the SNDS in 2014 [95%CI: 456 873 – 480 055].
- Among the 3 192 prevalent cases of prostate cancer identified, 273 had metastases and 187 were castration-resistant. Thus, 111 patients were classified as mCRPC in the EGB. By extrapolation, around 16 314 mCRPC cases are expected in the SNDS in 2014 [95%CI: 15 923 – 16 726], i.e. approximately 3.5% of all prostate cancers

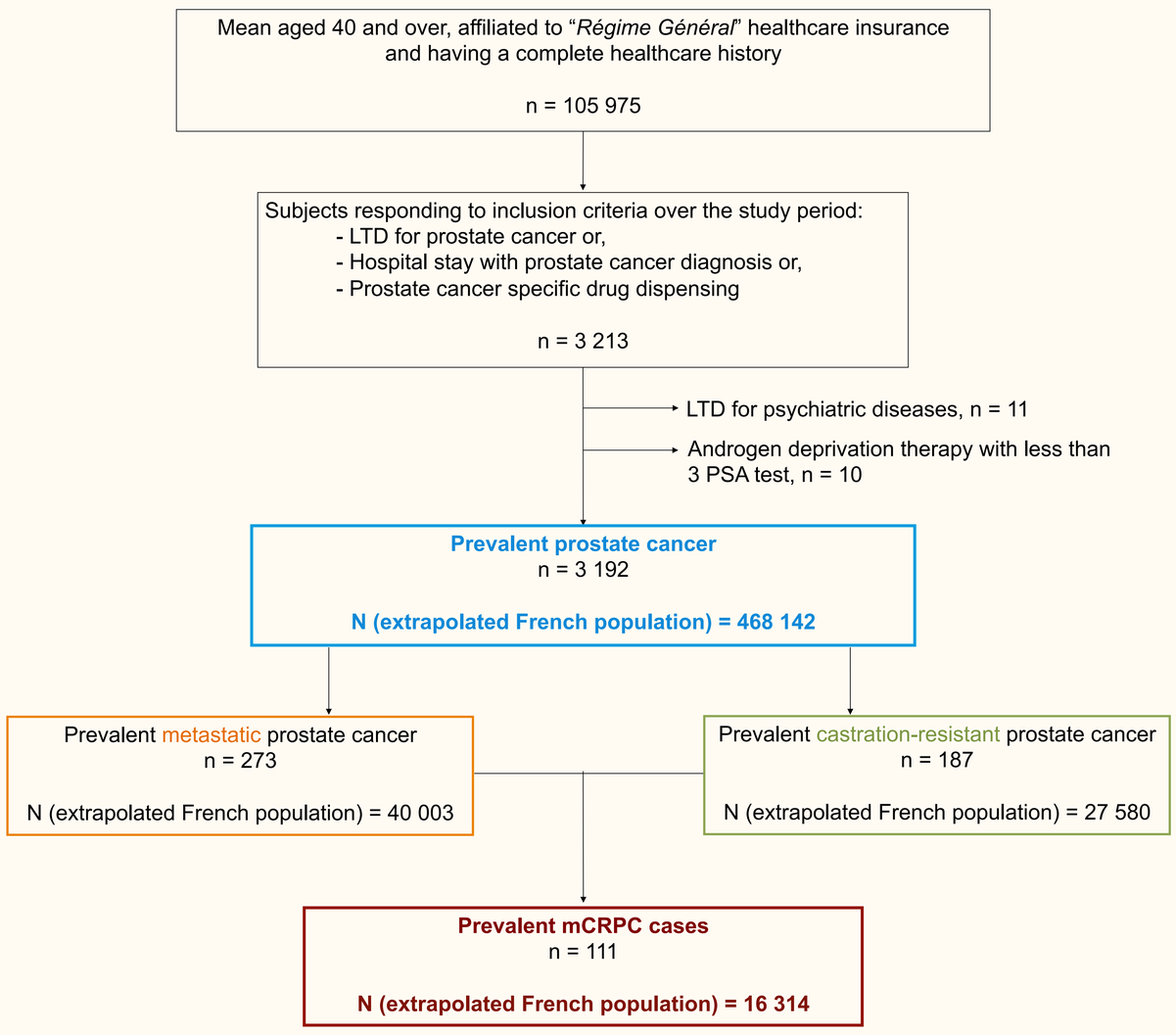

Figure 2 : Flowchart for identification of prevalent mCRPC cases in 2014 from EGB database

➢ **Partial prevalence of prostate cancer (Table 1.)**
- In the EGB, 1 303 patients were diagnosed with a prostate cancer between 01/01/2010 and 12/31/2014 and were still alive at 12/31/2014. Thus, the 5-years partial prevalence for prostate cancer in the SNDS in 2014 should be around 191 000.
- When considering the mCRPC subpopulation, patients alive at 12/31/2014 and having been diagnosed with a prostate cancer in the 5 years prior were 36 in the EGB. By extrapolation the 5- years partial prevalence for prostate cancer in the mCRPC subgroup should be around 5 000 for the same year in the SNDS.

Table 1. Partial prevalence of prostate cancer among general population and mCPRC population

	Observed population size in EGB in 2014	Expected population size in SNDS in 2014 [95% CI]
Prevalent prostate cancer cases in 2014, n	3 192	468 142 [456 873 - 480 055]
Partial prevalence at 5 years, n	1 303	191 057 [186 887 - 195 439]
Partial prevalence at 3 years, n	724	106 207 [103 927 - 108 601]
Partial prevalence at 1 year, n	252	37 105 [36 320 - 37 929]
Prevalent mCRPC cases in 2014, n	111	16 314 [15 923 - 16 726]
Partial prevalence at 5 years, n	36	5 294 [5 171 - 5 424]
Partial prevalence at 3 years, n	19	2 786 [2 720 - 2 855]
Partial prevalence at 1 year, n	2	309 [298 - 321]

➢ **Identification parameters of mCRPC patients in 2014**

✓ **Metastases (Table 2.)**
- Radiotherapy is the main indicator of metastases among patients with prostate cancer
- The date of first metastases management for mCRPC patients corresponds mainly to diagnostic codes of secondary tumors consecutive to a hospital stay (36%), and to the initiation of a specific mCRPC treatment following an imaging procedure (30%)

Table 2. Indicators to identify the date of 1st metastases management for patients with prostate cancer and for patients with mCRPC in the EGB in 2014

	Prostate cancer n = 3 192		mCRPC n = 111	
Radiotherapy session for metastases, n (%)	98	(3.1)	10	(9.0)
Diagnosis of secondary tumor consecutive to a hospitalization or a LTD registration for prostate cancer, n (%)	85	(2.7)	40	(36.0)
Dispensing of bone metastases targeted treatments: denosumab or zoledronic acid, n (%)	43	(1.3)	16	(14.4)
Targeted beta or alpha particle therapy for bone metastases, n (%)	1	(0.0)	1	(0.9)
Initiation of a mCRPC specific treatment following 3 months of androgen deprivation therapy and a specified imaging procedure, n (%)	33	(1.0)	33	(29.7)
Initiation of a GnRH analog within 2 months of the prostate cancer diagnosis in young patient without any local treatment prior, n (%)	13	(0.4)	11	(9.9)
Radiofrequency ablation of liver metastases, n (%)	0	(0.0)	0	(0.0)

✓ **Resistance (Table 3.)**
- Switches between androgen deprivation therapy treatments (introduction or discontinuation of anti-androgens) are the main indicator of castration-resistance among patients with prostate cancer
- The date of castration-resistance for mCRPC patient relies mainly on the initiation of a specific CRPC or mCRPC treatment (56%) and the switches between androgen deprivation therapy treatments (44%)

Table 3. Indicators to identify the date of castration resistance for patients with prostate cancer and for patients with mCRPC in the EGB in 2014

	Cancer prostate n = 3 192		mCRPC n = 111	
Initiation of a CRPC or mCRPC specific treatment, n (%)	70	(2.2)	62	(55.9)
Introduction for ≥ 2 months of an anti-androgen after a 3 months period with an GnRH analog or antagonist, n (%)	70	(2.2)	30	(27.0)
Discontinuation for ≥ 2 months of an anti-androgen after 3 months of total androgen blockade**, n (%)	47	(1.5)	19	(17.1)
Orchiectomy or testicular pulpectomy after 3 months of androgen deprivation therapy, n (%)	0	(0.0)	0	(0.0)

***provided that cancer is not in remission of disease*

Conclusion

- Preliminary study that has allowed the construction of a **functional algorithm for identifying mCRPC patients** according to complex elements and their sequences
- **Prevalence estimates from EGB in France in 2014** are consistent with the National Cancer Institute (INCa)
  - Expected number of **prostate cancers: 468 100** (508 700 in 2008, INCa)
  - Expected number of **mCRPC: 16 300**
- This algorithm will be assessed through a validation study and applied to SNDS to obtain the actual prevalence of prostate cancer and mCRPC in the overall French population

Declaration of interest: The CAMERRA study is carried out by the Bordeaux PharmacoEpi platform in collaboration with Janssen® company and supervised by a Scientific Committee.

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