Validation of a complex algorithm for the diagnosis of metastatic castration-resistant prostate cancer within a claims database

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Abstract

Background: An algorithm was developed in the French nationwide claims database (SNDS) to identify cases of metastatic castration-resistant prostate cancer (mCRPC). The usual way to validate such an algorithm is to review patients' medical charts. An alternative in an irreversibly pseudonymised database is to use all healthcare use information to identify diagnosis and/or treatment of prostate cancer, then resistant and metastatic stage.
Objectives: To assess and validate mCRPC algorithm using the wealth of data available in SNDS.
Methods: 100 of 14 050 mCRPC patients identified by the algorithm and 100 of 372 273 non-mCRPC patients were randomly selected within SNDS. The 6-year medical history of each of these 200 patients was reconstituted (Long term disease registration [LTD], drug dispensings, procedure codes, hospitalizations, lab tests). These 200 cases were randomly divided into 2 groups of 100 cases. Two groups of independent experts including an urologist and an oncologist each adjudicated blindly the mCRPC status of 100 cases. In case of disagreement within a pair of experts, the 4 experts collegially assessed the case. Positive (PPV) and negative (NPV) predictive values of the algorithm were calculated.
Results: 92 out of 100 mCRPC cases and 93 out of 100 non-mCRPC cases were concordant between the experts and the algorithm, resulting in an algorithm PPV of 0.92 and a NPV of 0.93.
Conclusions: The wealth of data available in the SNDS makes it possible to implement algorithms to detect complex diseases, and to validate them *via* the reconstitution of medical history. The present results show good performance of the algorithm for the identification of mCRPC in the SNDS. In addition, the validation study detected some parameters that could be used to optimize the algorithm's performance.

Declaration of Interest Statement

The CAMERRA study is carried out by the Bordeaux PharmacoEpi platform in collaboration with Janssen® company and supervised by a scientific committee.

Background

➢ **Prostate cancer**
- Most common cancer among men: > 53 900 new cases in 2011 in France according to French National Cancer Institute
- Slow-progressing cancer and possible development of resistance and / or metastases
- Introduction of new therapeutic strategies in 1st-line treatment for metastatic castration-resistant prostate cancer (mCRPC):
  - Abiraterone acetate in association with prednisone/prednisolone in 2012
  - Enzalutamide in 2014

➢ **CAMERRA study**
- Aims to identify mCRPC patients to assess the therapeutic strategic changes for mCRPC between 2012 and 2014 using the French National Healthcare System database (SNDS)
- No direct indicator is available to identify mCRPC in the SNDS database
- Need to develop an algorithm
  - Built from the permanent 1/97th random sample of SNDS, the "*Echantillon Généraliste des Bénéficiaires*" (EGB)
  - Executed in the SNDS

Objectives

➢ **To assess and validate the algorithm for mCRPC identification using the wealth of data available in the SNDS**

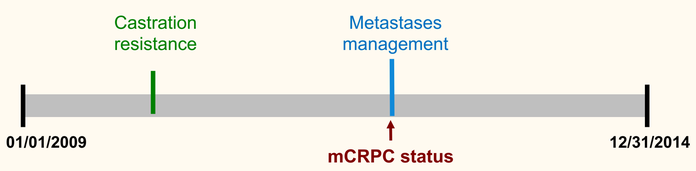
Methods

➢ **Data source:** extraction of SNDS data from 01/01/2009 to 12/31/2016 (2014 cohort of CAMERRA study)

➢ **General approach**

① Execution of the algorithm for cases identification
② Assessment of randomly selected cases by a committee of experts
③ Calculation of positive (PPV) and negative (NPV) predictive values of the algorithm

➢ **CAMERRA algorithm, identification of patients in 4 steps**
- Prostate cancer
- Metastases management
- Castration resistance
- **mCRPC status**



A patient is considered **mCRPC** as soon as a 1st metastases management date and a castration resistance date are identified in his medical history **(Figure 1)**

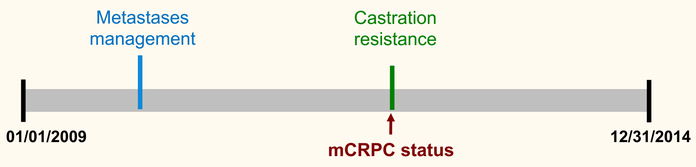


Figure 1. Chronology between date of first metastases management, date of castration-resistance and mCRPC status

➢ **Validation Committee organisation (Figure 2)**
- Random selection of 100 mCRPC cases and 100 non-mCRPC prostate cancer cases following the algorithm execution
- Constitution of 2 experts pairs (1 urologist + 1 oncologist)
- Blind review of the 200 cases using reconstituted pseudonymised medical history: 50 random mCRPC cases + 50 random non-mCRPC cases, per expert pair (**Figures 3 & 4**)
- In case of disagreement within a pair of experts: the case was discussed by the 4 experts to reach consensus
- Calculation of PPV and NPV of the algorithm based on committee conclusions and algorithm results

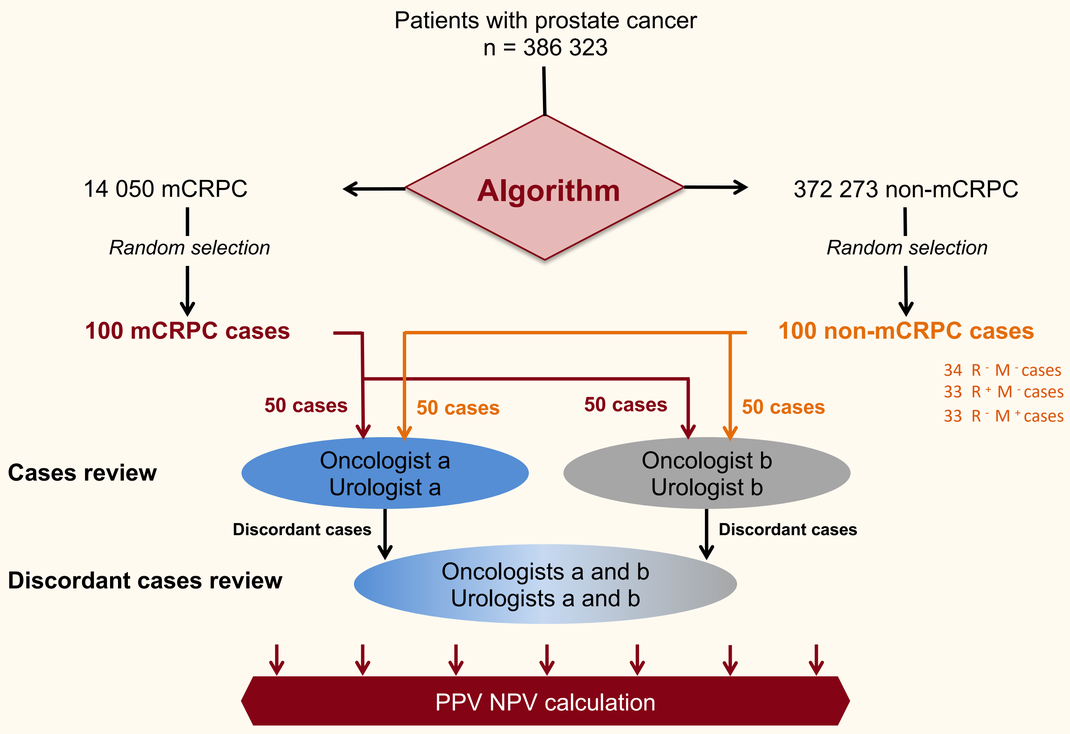


Figure 2. Validation Committee for CAMERRA algorithm

➢ **SNDS data formatting for cases review (Figure 3)**
- For each case, medical chart was reconstructed using data of the 6-year SNDS extraction: Long term disease registration [LTD], hospitalizations, medical procedures (surgery, radiotherapy…), drug dispensings, lab tests, pathology, *etc.*
- Addressing patient re-identification risk:
  - Calculation of relative dates (time from prostate cancer diagnosis date)
  - Deletion of "sensitive" variables (e.g. location, place of care, *etc.*)

Historic - Patient PAT_7

Actes d'interêt	Type de soins	Date de début d'exécution	Date de fin d'exécution	Détail
	ALD	- 11 ans 2 mois 25 jours	+ 4 ans 11 mois 35 jours	ALD 30 - tumeur maligne, affection maligne du tissu lymphatique ou hématopoïétique / CIM C15 - tumeur maligne de l'oesophage
	Délivrance d'un traitement	- 3 mois 19 jours		OMEPRAZOLE DISTRIQUIMICA 20 MG 1 BOITE DE 28, GELU - ATC A02BC01 (OMEPRAZOLE)
	Délivrance d'un traitement	- 3 mois 19 jours		SEROPLEX 10 MG CPR 28 - ATC N06AB10 (ESCITALOPRAM)
	Délivrance d'un traitement	- 1 mois 14 jours		INIPOMP 20 MG CPR 28 - ATC A02BC02 (PANTOPRAZOLE)
	Délivrance d'un traitement	- 1 mois 14 jours		PROPRANOLOL EG 40MG CPR 50 - ATC C07AA05 (PROPRANOLOL)
⇒	1 ALD	Diagnostic	+ 4 ans 11 mois 35 jours	ALD 30 - tumeur maligne, affection maligne du tissu lymphatique ou hématopoïétique / CIM C61 - tumeur maligne de la prostate
	Biologie	+ 11 jours		1104 - hemogramme y compris plaquettes (nfs , nfp)
	Biologie	+ 11 jours		1124 - vitesse de sedimentation (vs)
	⋮			
⇒	1 Biologie	+ 11 jours		7318 - antigene prostatique specifique (psa) : dosage
	⋮			
⇒	1 Acte CCAM	+ 1 mois 16 jours		JGHJ001 - biopsie de la prostate, par voie transrectale avec guidage échographique
	⋮			
	1 Biologie	+ 10 mois 17 jours		7318 - antigene prostatique specifique (psa) : dosage
	Biologie	+ 10 mois 17 jours		9005 - forfait de prise en charge pre-analytique du patient. ce forfait comprend : - le recueil des donne
	Biologie	+ 10 mois 17 jours		9105 - forfait de securite pour le traitement d'un echantillon sanguin dans les conditions prevues par
	Délivrance d'un traitement	+ 1 an 2 jours		CELEBREX 200MG GELULE 30 - ATC M01AH01 (CELECOXIB)
	Délivrance d'un traitement	+ 1 an 2 jours		IXPRIM 37,5MG/325MG CPR 20 - ATC N02AX52 (TRAMADOL EN ASSOCIATION)
⇒	1 Délivrance d'un traitement	+ 1 an 2 jours		LYTOS 520MG CPR 30 - ATC M05BA02 (CLODRONIQUE ACIDE)
	⋮			
	1 Délivrance d'un traitement	+ 1 an 2 mois 31 jours		ZOMETA 4 MG SOL INJ 1/5 ML - ATC M05BA08 (ZOLEDRONIQUE ACIDE)
	Acte CCAM	+ 1 an 3 mois 4 jours		ZZMK014 - préparation à une irradiation externe sans dosimétrie, avec simulation sous l'appareil de traitement
	Acte CCAM	+ 1 an 3 mois 4 jours		ZZML002 - contrôle de la dose d'irradiation externe reâ§ue [dosimétrie in vivo]
	Acte CCAM	+ 1 an 3 mois 4 jours		ZZMP017 - enregistrement numérisé et vérification des paramètres d'un traitement par irradiation externe [système record and verify]
	Biologie	+ 1 an 3 mois 4 jours		1104 - hemogramme y compris plaquettes (nfs , nfp)
	Biologie	+ 1 an 3 mois 4 jours		593 - uree et creatinine pour les actes 0592 et 0593, il est recommande pour le dosage de la creatinine
	1 Biologie	+ 1 an 3 mois 4 jours		7318 - antigene prostatique specifique (psa) : dosage
	Biologie	+ 1 an 3 mois 4 jours		9005 - forfait de prise en charge pre-analytique du patient. ce forfait comprend : - le recueil des donne
	Biologie	+ 1 an 3 mois 4 jours		9105 - forfait de securite pour le traitement d'un echantillon sanguin dans les conditions prevues par
⇒	1 Radiothérapie CCAM	+ 1 an 3 mois 4 jours		ZZMK018 - préparation à une irradiation externe avec repérage par scanographe, dosimétrie tridimensionnelle avec hdv, simulation virtuelle
⇒	1 Hospitalisation	+ 1 an 3 mois 4 jours	+ 1 an 6 mois 18 jours	GHM 28Z08Z - Préparations à une irradiation externe avec une dosimétrie tridimensionnelle / DP Z5100 - séance de préparation à une irradiation / DR C61 - tumeur maligne de la prostate / DAS

Figure 3. Reconstructed medical chart of patient using SNDS data

➢ **Summary sheet with experts conclusions (Figure 4)**

Summary sheet - Patient PAT_7

Indicators	
Initial diagnosis of prostate cancer	2009
Age of patient	[60 - 65[years
Vital status and survival	
Charlson score	13
Death	+ 4 years 9 months 4 days
Survival period after initial diagnosis (months)	57
Prostate cancer and other	
Prostate cancer LTD	Diagnostic
Other LTD for cancer	- ** ans 9 months 10 days
ICD-10	C15
At least one radiotherapy session (whatever the target)	Yes
Metastatic specific management	
Denosumab (first dispensing)	+ 3 years 11 months 14 days
Zoledronic acid (first dispensing)	+ 1 year 1 month 28 jdays
Targeted therapy for bone metastases: Sa-153, Str-89 or	NA
Radiofrequency ablation of liver metastases	NA
Castration	
Orchiectomy	NA
Pulpectomy	NA
Analog or LHRH antagonist (first dispensing)	+ 1 month 16 days
Anti-androgen	
Start date	+ 1 year 1 month 28 days
End date	+ 1 year 9 months 33 days
Prostate management	
Prostate biopsy	+ 1 month 16 days
Radical prostatectomy	NA
High-intensity focused ultrasound (HIFU)	NA
Brachytherapy	NA
Cryotherapy	NA
mCPRC specific treatments	
First mCPRC specific treatment dispensed	Docetaxel
Start date (index date)	+ 2 years 2 months 5 days
Age of patient	[60 - 65[years

		If yes, please specify the convincing element(s)
Castration resistance	YES / NO	
Metastases	YES / NO	
mCRPC status	YES / NO	
Comment(s):		

- Summary of the main elements of the case
  - Age class
  - Year of diagnosis and survival duration
  - Charlson score and other cancers
  - Key steps of prostate cancer management
- Key steps for prostate cancer management
  - Surgery
  - Androgen deprivation therapy
  - mCRPC specific treatment
- For each case, expert opinion on:
  - castration resistance
  - Presence of metastases
  - mCRPC status
- Expert decision clarified by free text

Figure 4. Summary sheet

Results

➢ **PPV and NPV calculation (Figure 5)**
- Confirmation of 92 out of 100 mCRPC cases and 93 out of 100 non-mCRPC cases
- PPV = 0.92 and NPV = 0.93

		Experts		
		mCRPC +	**mCRPC -**	**Total**
Algorithm	**mCRPC +**	92	8	100
	mCRPC -	7	93	100
	Total	**99**	**101**	200

Figure 5. PPV and NPV calculation

Conclusion

- **The wealth of data available in the SNDS enables**
  - ✓ The implementation of algorithms to detect complex diseases
  - ✓ The validation of these algorithms *via* the reconstitution of pseudonymized medical charts based on SNDS data
- **Here, the validation study**
  - ✓ Shows **good performances** of the algorithm for mCRPC identification
  - ✓ Allows to adjust some parameters to **optimize the algorithm performances**
  - ✓ Will provide a **validated algorithm** generating **accurate estimation** of the number of **mCRPC cases** in France, as well as a description of their characteristics and therapeutic changes

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