#11137 Linking an early access program (EAP) to the National Health Data System (NHDS) in France and assessing its performances and potential biases

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Background:

- Early access programs (EAP) are a unique opportunity to document first use of innovative treatments in real-world settings.
- Requirements from the French HTA body:
  - Mandatory collection of EAP patients' clinical data
  - Anticipation of the linkage EAP data to the National Health Data System (NHDS).
- Prior to drug initiation, the collected data is almost complete contrary to follow-up data.

Objectives:
To propose a methodology to link EAP to the French Cancer cohort (FCC), an extract of the NHDS of over 8 million persons diagnosed for cancer and some people at high risk, and to assess its assets and downsides. To best of our knowledge, no other study described one yet.

Methods:

Two datasets :
- patients informed and treated with durvalumab in unresectable locally advanced NSCLC during the French EAP (Oct 1st, 2017 to Dec 31st, 2018) from 113 hospitals in France
- patients who received durvalumab at the time of the EAP in the FCC

No direct identifiers were available in both data sources: indirect deterministic linkage was used.

Steps of the linkage methodology:
- Pre-process both data sources,
- Define matching, control and study variables,
- Test multiple indirect deterministic linkage algorithms,
- Assess their performances: success rate, consistency and differences between data sources in linked and unlinked patients.

Results:

Table 1. Variables used in tested linkage algorithms.

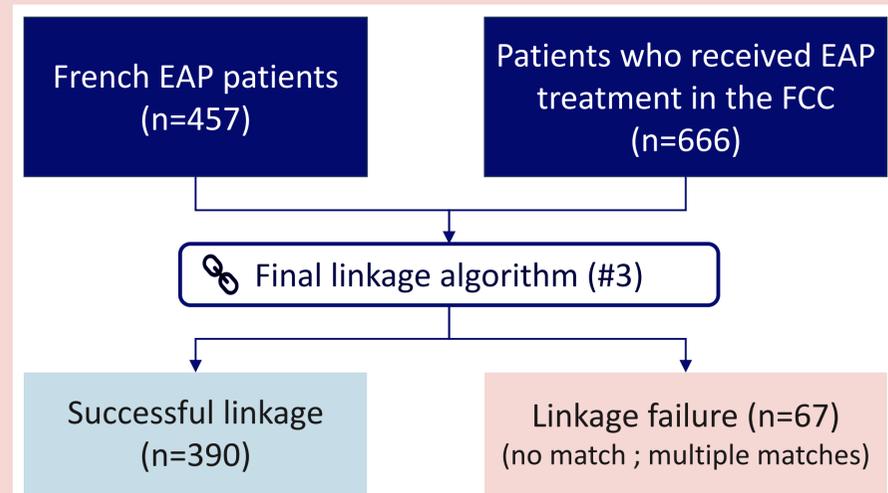| Algorithm	Sex	Birth month	Birth year	Hosp. ID	Hosp. dpt
#1	X	X	X	X	
#2	X	X	X		X
#3*	X*	X*	X		X

Hosp. ID = hospital ID, Hosp. dpt = hospital department
* In algorithm #3, linkage required equality of (sex or birth month) and birth year and hospital department.

Table 2. Success rate of tested linkage algorithms.

Algorithm	Successful linkage	Failures: no match ; multiple matches
#1	80.9% (370/457)	83 ; 4
#2	84.0% (384/457)	69 ; 4
#3	**85.3% (390/457)**	**63 ; 4**

Algorithm #3 yielded the highest linkage success rate and was used for the rest of the work.

Figure 1. Final linkage methodology

French EAP patients (n=457) / Patients who received EAP treatment in the FCC (n=666) → Final linkage algorithm (#3) → Successful linkage (n=390) / Linkage failure (n=67) (no match ; multiple matches)

Consistency between data sources

The consistency of linkage variables was substantial (Cohen's kappa > 0.8) or excellent (ICC > 0.9).

Table 3. Data consistency on control variables in linked patients

Control variable	Median difference (IQR)
1st administration of EAP treatment: foreseen date (EAP) vs effective date (FCC) (days)	-1 (-9 ; 0)
Cancer diagnosis date (EAP) vs date of 1st healthcare use related to cancer (FCC) (days)	0 (-24 ; 8)

Control variable	EAP data	FCC data
Diagnosis of lung cancer	390 (100%)	387 (99%)
Dispensation of EAP treatment	390 (100%)	390 (100%)
History of chemotherapy	389 (100%)	388 (99%)
History of radiation therapy	389 (100%)	260 (67%)

Differences between linked patients and unlinked patients

Linked patients vs unlinked patients (EAP cohort): no statistically significant difference on matching and control variables, except for few cases on history of chemotherapy and of radiation therapy prior to durvalumab. Results were similar for linked patients vs unlinked patients (FCC), except for history of radiation therapy and treating hospital department.

Main limitations

- Differences in data contents refrained from using some variables as linkage or control variables, such as hospital ID (reconstituted in EAP) and comorbidities (different definition in EAP vs FCC).
- Lack of reported diagnosis in out-of-hospital settings in NHDS resulted in lack of related diagnosis of radiation therapy in out-of-hospital settings : could not be used as linkage or control variables.

Conclusions & perspectives:

- Linkage of Early Access Program data to the French NDHS with a success rate > 85% is feasible with indirect deterministic linkage.
- We can leverage on this linkage to follow up EAP patients in real-world setting!

➔ Additional EAP linkages will be required to ensure the validation and reproducibility of such methodology.
➔ Further works in progress will document the adequacy of French NHDS data to address effectiveness.

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