Identification of treatment intent from the actual time-to-treatment distribution in prostate cancer patients

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PROBLEM

- Conservative management aims to reduce over-treatment of patients with prostate cancer.
- At time of diagnosis a decision must be made: conservative management or immediate treatment.
- It is an important task of clinical research to inform this decision.
- Observational research could provide such research.
- Unfortunately, the decision is rarely captured in observational data.
- It might be feasible to infer what the decision might have been by checking whether or not there was immediate treatment.
- However, there is no obvious or generally accepted cut-off time after which a treatment can be designated "deferred".
- A data driven approach might help distinguish between patients with the two choice.

OBJECTIVE

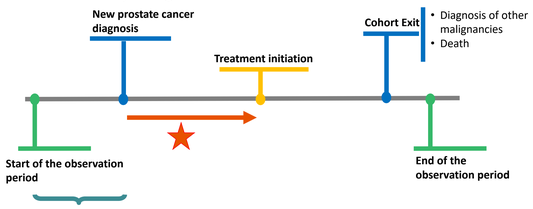
- To empirically identify the two distinct populations immediate from deferred from the data, and to determine the optimal cut-off, minimizing misclassification of the patients and potential selection bias.

METHODS

Data

1. IQVIA Ambulatory EMR (EHR)
2. IQVIA Hospital Charge Data Master (charge data)
3. IQVIA Oncology EMR (EHR)
4. IQVIA Open Claims (unadjudicated claims)
5. IQVIA PharMetrics Plus (adjudicated claims)

Schematic Study Design



- Fitting time to treatment initiation data to finite mixture models via EM
- Bayesian information criterion (BIC) to select the best model
- Maximum likelihood estimation (MLE) used to estimate parameters of the selected distribution

Inclusion criteria:

- >18 years old
- Male
- No history of PCa or PCa-related condition one year prior
- Prostate biopsy +/- 30 days of the first PCa diagnosis
- No ADT or other hormone therapies one year prior

Table 1. Median days (IQR) Time to treatment initiation and follow-up in the participating databases

	N. Patients	Time to Treatment initiation	Follow-up time
IQVIA Ambulatory EMR	9791	31 (30, 33)	980 (957, 1001)
IQVIA Hospital CDM	7476	73 (71, 75)	753 (727, 773)
IQVIA Oncology EMR	219	14 (10, 18)	359 (295, 457)
IQVIA Open Claims	692286	55 (55, 55)	1899 (1895, 1904)
IQVIA PharMetrics Plus	203017	61 (60, 61)	950 (944, 955)

Identification of treatment intent from observational data is context-dependent and challenging. Potential for substantial degree of patient misclassification

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RESULTS

- 912,789 newly diagnosed prostate cancer patients across a network of claims and EHR data were included in the study (Table 1)
- A bimodal two-parameter Weibull distribution fitted the data better than a unimodal one (Figure 2)
- The distribution of the two populations shows substantial overlap across the participating databases (Figure 2)

Figure 1. Fitted unimodal (green) and bimodal (blue) Weibull distributions together with the observed data red).

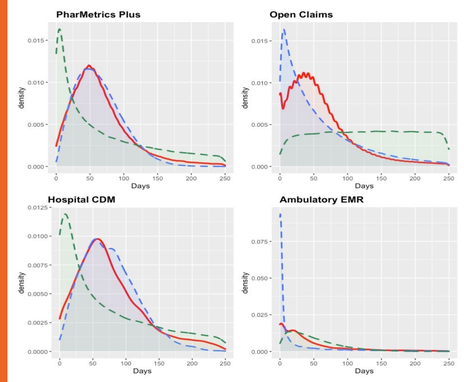
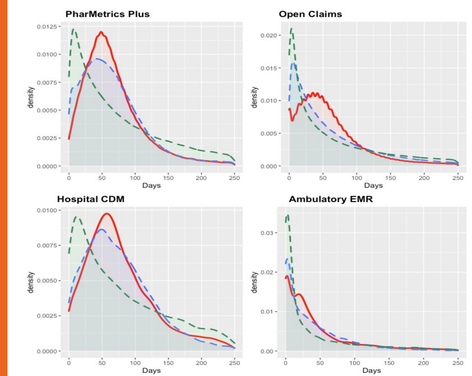


Figure 2. Empirical depiction of the two patient populations. Green and blue density plots represent the two distinct putative patient populations.



- Prostate cancer patients seem to be composed of two populations with different time to treatment characteristics, as expected from the treatment guidelines.
- The parameters of the optimal fitted models are in line with expectations:
  - 49-76 days for the putative "immediate" group
  - 295-1067 days for the "deferred" group,
  - a proportion with a dominant "immediate" group in the claims versus a 50/50 distribution in the ambulatory setting.

Table 2. EM estimated parameters for the TTT distribution.

		Component 1	Component 2
PharMetrics Plus	**Proportions**	0.8	0.2
	Mean	63	30
	Shape	1.9	0.6
	Scale	71	189
Open Claims	**Proportions**	0.9	0.1
	Mean	68	1068
	Shape	0.9	1.1
	Scale	64	1111
Ambulatory EMR	**Proportions**	0.5	0.5
	Mean	1025	49
	Shape	0.2	1.3
	Scale	29	53
Hospital CDM	**Proportions**	0.7	0.3
	Mean	77	336
	Shape	1.9	0.6
	Scale	86	200

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