

# Recruitment procedure to maximise inclusion of progressors in OA clinical studies using subjects from existing cohorts

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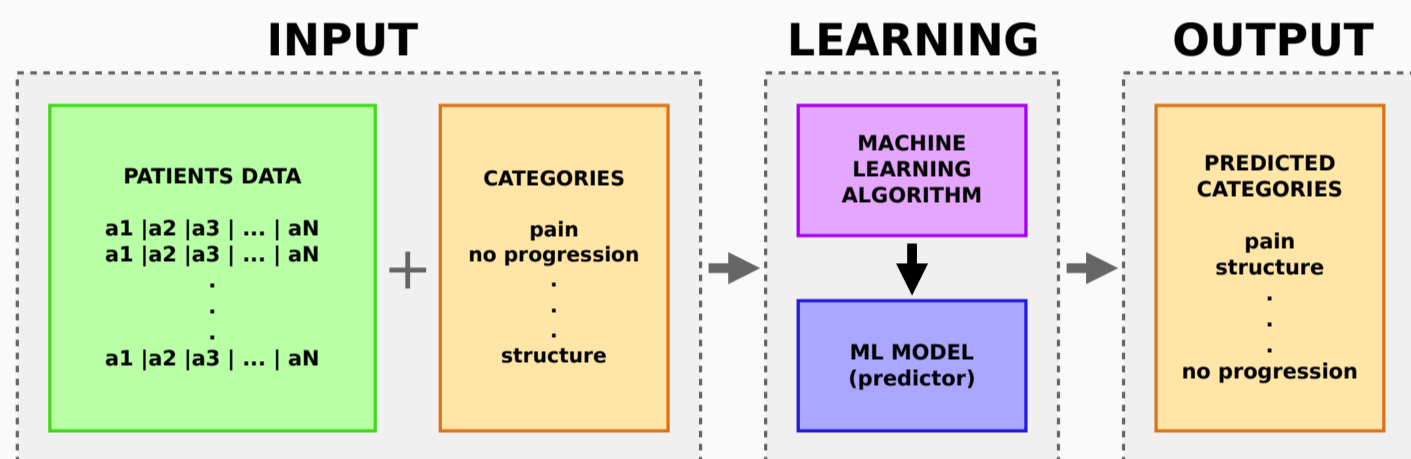
## APPROACH cohort

- new longitudinal cohort focused on **fast** knee OA progressors
- recruited from **5 existing** European OA cohorts using **machine learning** models trained to estimate **progression probability**

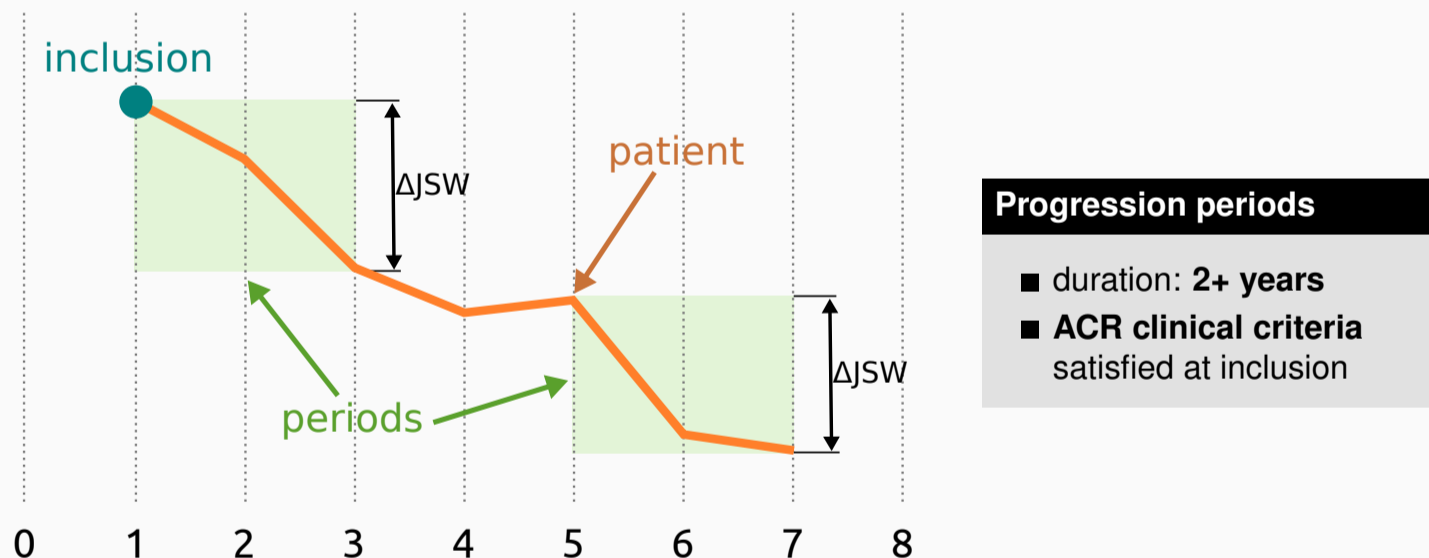
	KL grade	JSN grade	JSW	follow-up	active years
CHECK	✓	✓	✓	1–10 years	2006–2016
MUST	✓	✓		—	2010–2013
HOSTAS				2–4 years	2009–2017
DIGICOD				1 year	2013–2017
PROCOAC	✓			2–9 years	1991–2016

## Machine learning from historical data

- builds computational **models** from **sample inputs**, and uses them to **predict outputs**



## Input data



## Output categories

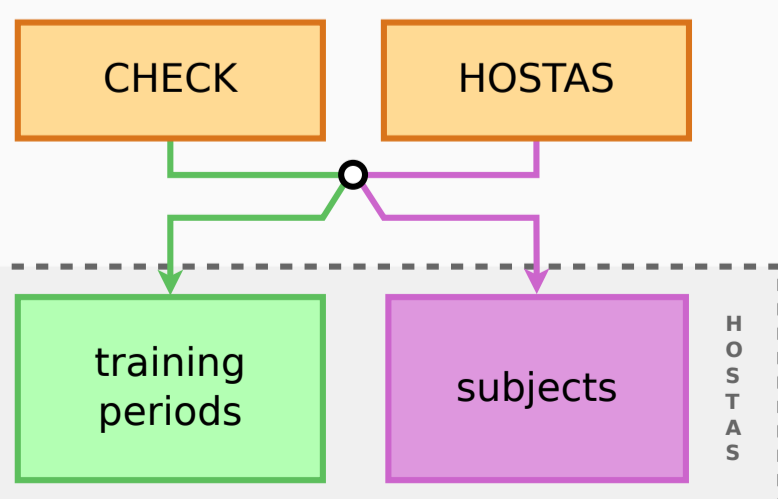
### Structure periods

- minimum total JSW, must **decrease** by at least **0.3mm** per year

### Pain periods

- must experience **progressive** or intense **sustained** pain
- pain **increase** must be at least **5 WOMAC points** per year
- pain at the **follow-up** must be **significant** ( $\geq 40$  WOMAC points)
- special exception**: rapid pain progression ( $\geq 10$  points per year)

## Data harmonisation

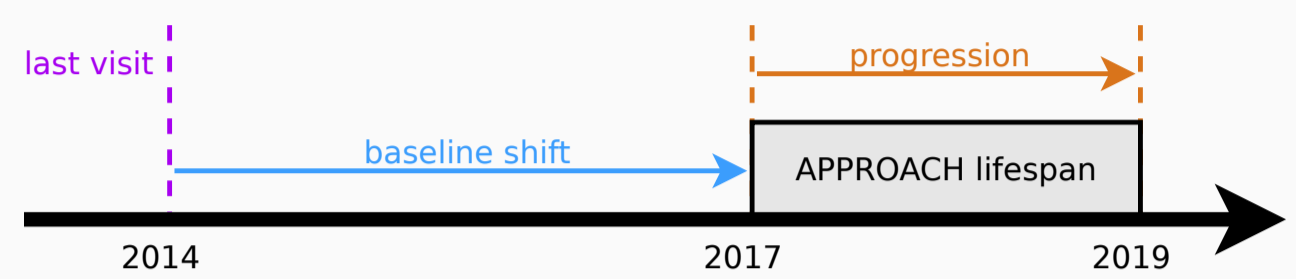


### Procedure

- transformation of CHECK data (common subset of attributes)
- attributes mapping to CHECK

	subjects	attributes	mapped
MUST	630	886	77–84
HOSTAS	538	130	45–50
DIGICOD	377	425	52–61
PROCOAC	983	288	40–57

## Multi-model prediction



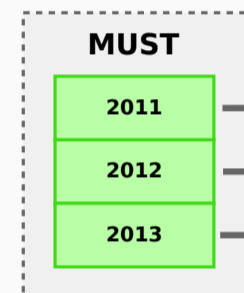
### Model training

- using harmonised CHECK periods
- baseline shift of 0, 2, 3 and 5 years

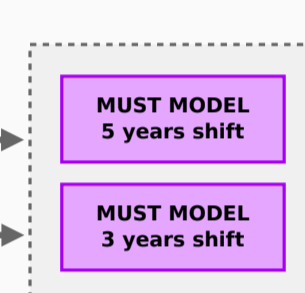
year	3	4	5	6	7	8	9	10	11
MUST	—	91	260	254	25	—	—	—	—
HOSTAS	7	5	37	21	85	79	132	135	37
DIGICOD	—	—	—	—	4	79	144	126	24
PROCOAC	36	44	47	41	53	132	298	220	—
shift	—	—	5y	5y	3y	3y	2y	2y	0y

- need to train a **separate** model for each **cohort** and each **shift**

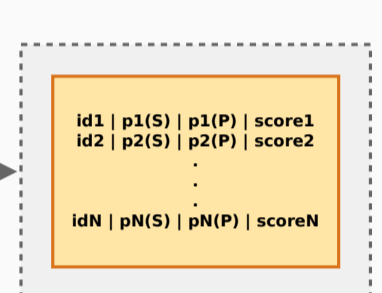
### PATIENTS DATA



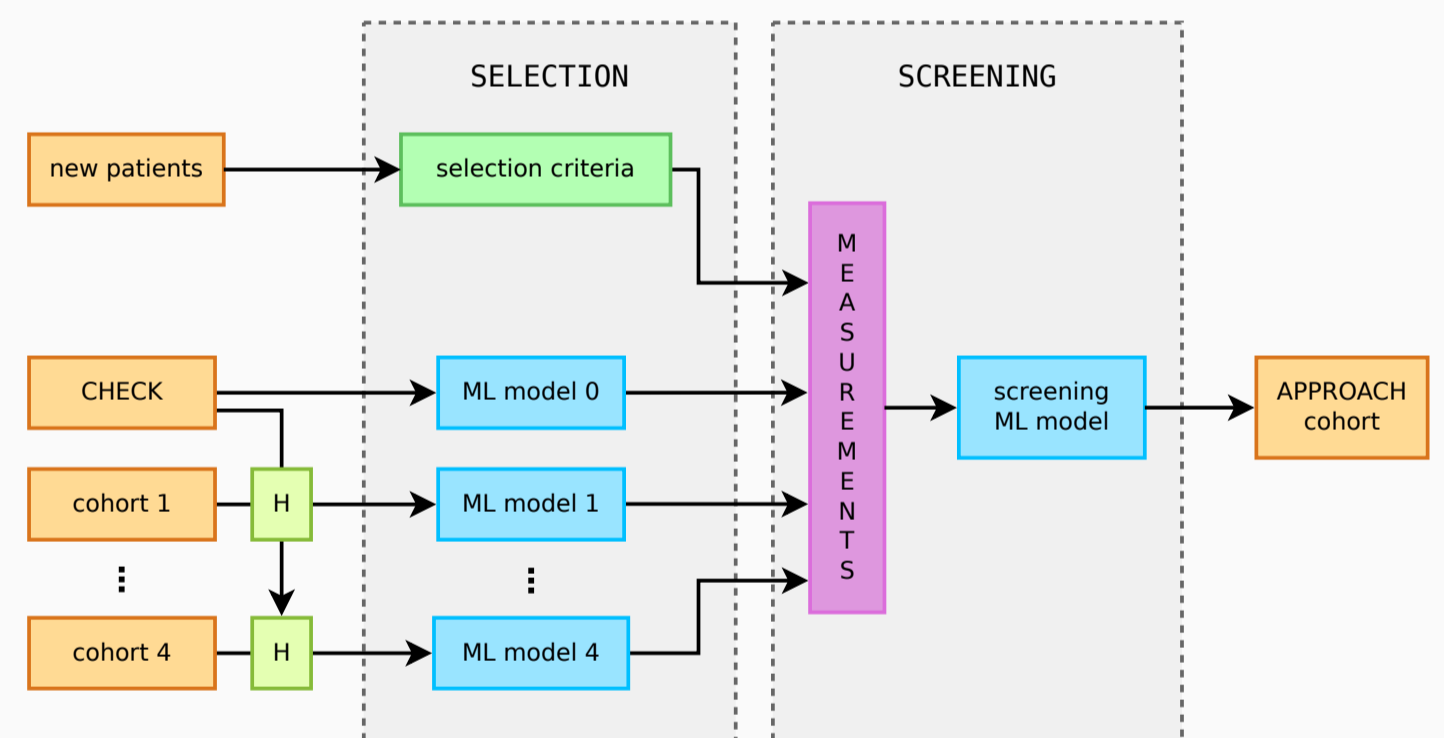
### PREDICTION



### RANKING



## Two-stage recruitment process



- additional screening visit to have **up-to-date** data for all patients
- enrol** 75% of screened patients (the most likely to progress)

### Measured attributes

- basic**: age, sex, BMI
- KIDA**: bone density, eminence height, joint space width, varus angle, osteophyte area
- pain intensity**: KOOS, NRS

## Ranking based on model confidence

- the ML model is composed of two **sub-models**, separately predicting **pain (P)** and **structure (S)** related progression
- the **outcome** of the model is per subject **probability** of becoming an OA progressor
- the probabilities are used to **rank** the subjects
- top subjects** in the ranking are **more likely** to progress

sum			z-score sum		
P	S	score	P	S	score
0.782	0.544	1.326	0.707	0.597	4.6
0.724	0.584	1.308	0.724	0.584	4.555
...	...	...	...	...	...
0.112	0.175	0.287	0.106	0.179	-3.819
0.106	0.179	0.285	0.112	0.175	-3.828

