Brainteaser

iDPP

Intelligent Disease Progression Prediction Challenge

CLEF 2023, Thessaloniki, Greece

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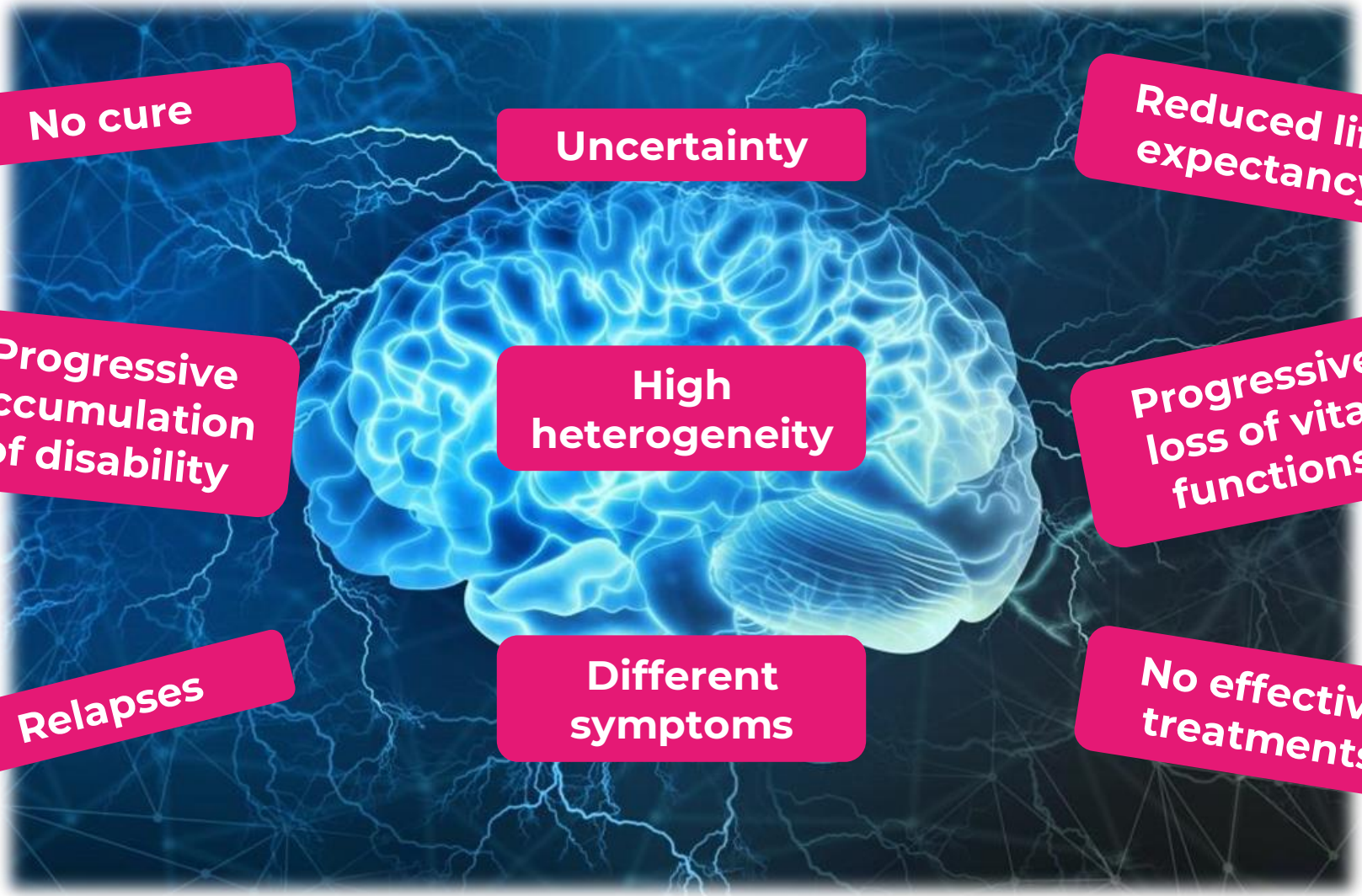
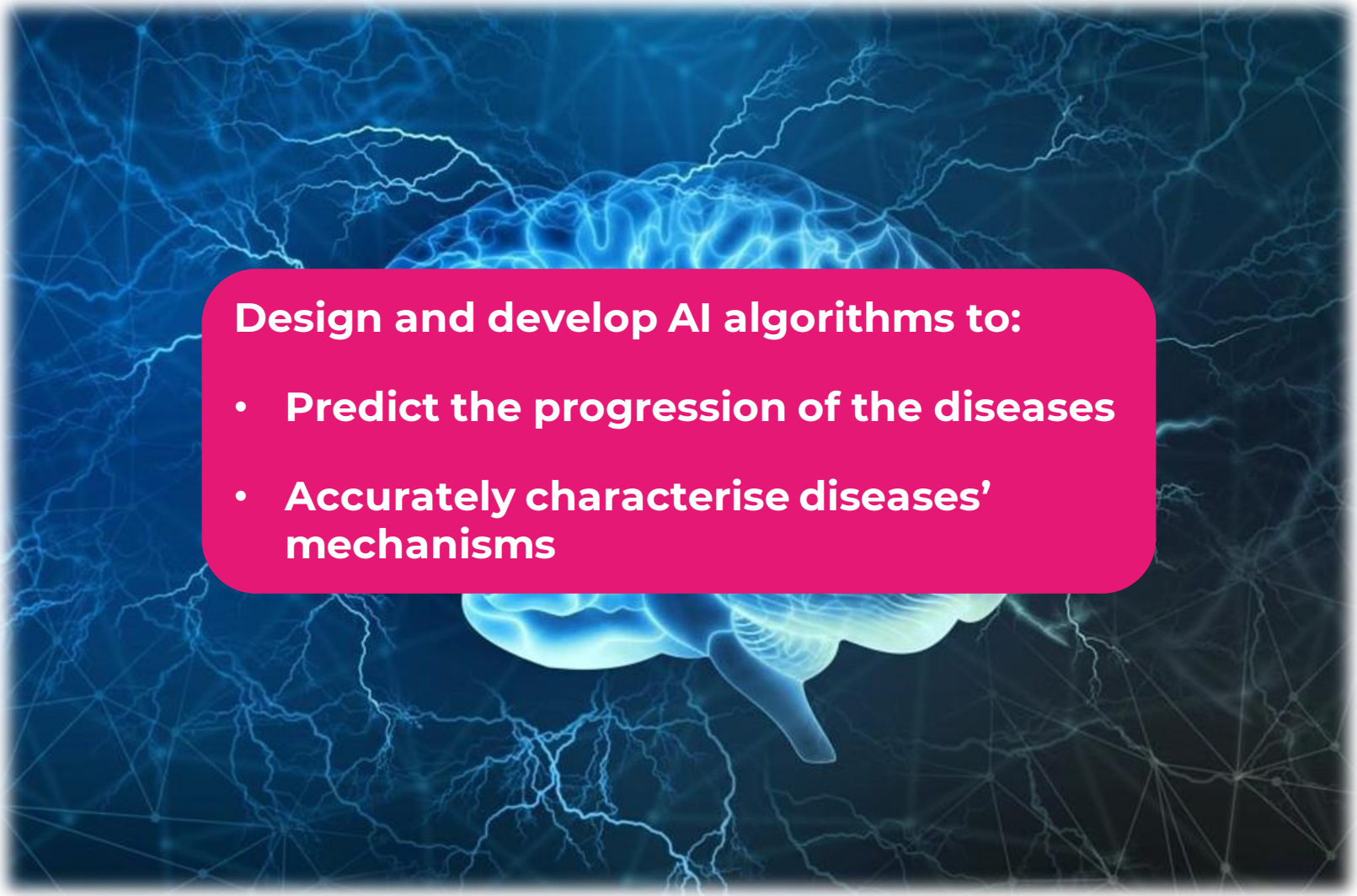
ALS and MS unmet needs



Unmet needs: proposed approach



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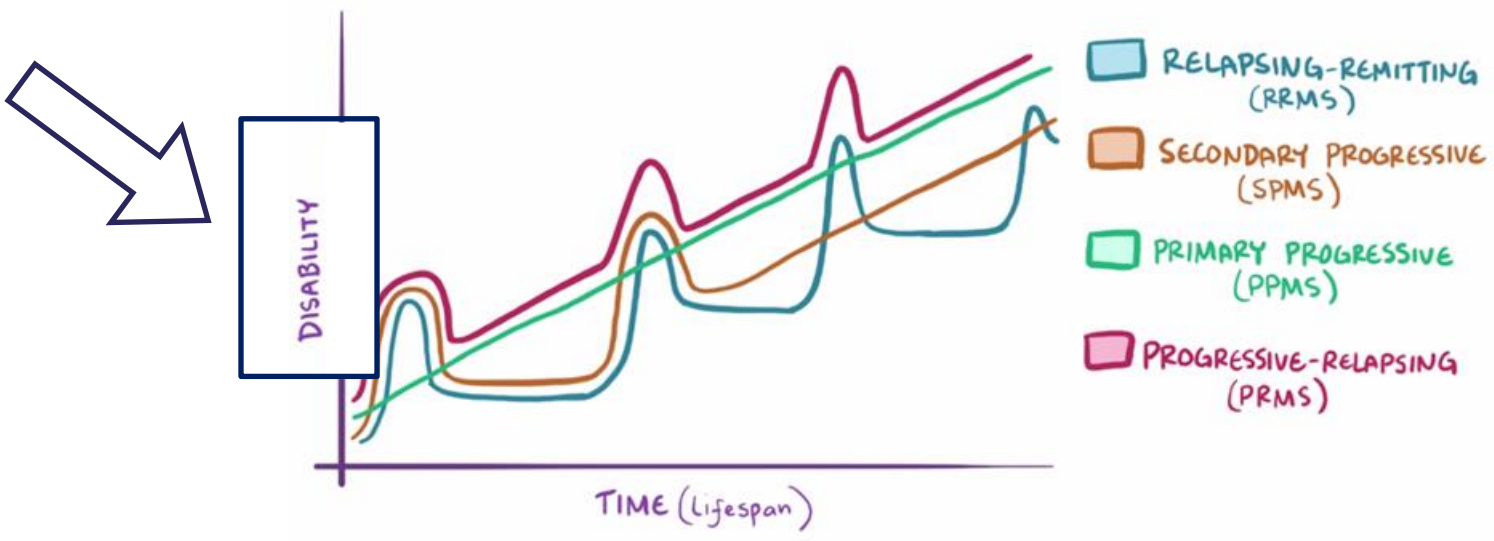
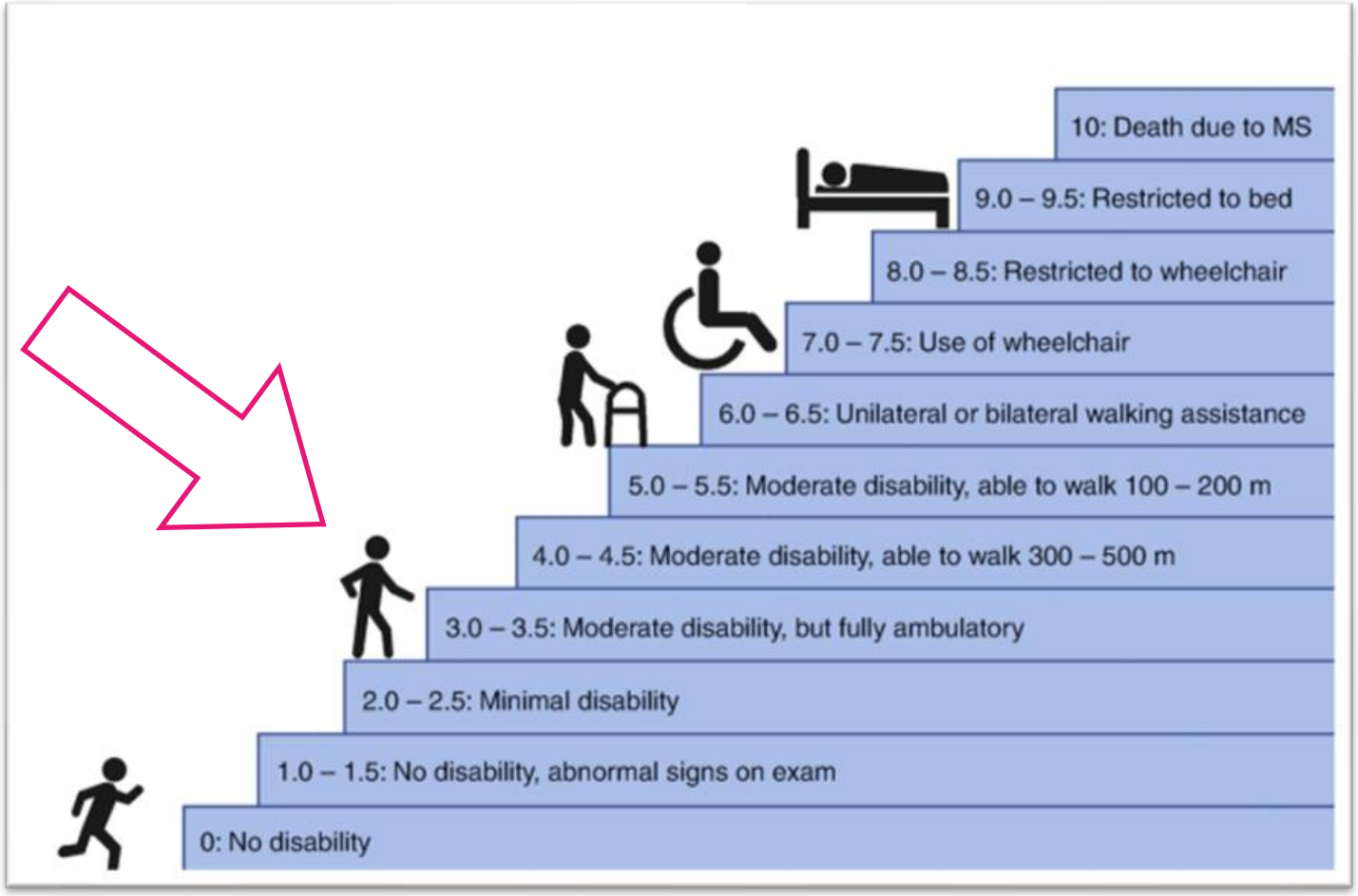
Task 1 and task 2

Multiple Sclerosis (MS)

- **Chronic neurodegenerative disease**
- Attacks **myelin sheath**
- Prevents the appropriate **conduction of nerve stimuli**
- **Incidence** of 6.8/100 000 people/year in Europe
- Usually diagnosed between the **ages of 20 and 50**
- There is no cure, but **disease-modifying treatments**



Expanded Disability Status Scale (EDSS)



MS outcome: “worsening” definition

Two possible definitions of worsening in MS

- The patient crosses the **threshold EDSS ≥ 3** at least twice within a one-year interval
- Worsening definition **based on the baseline EDSS** value:
  - if the baseline is EDSS < 1, then the worsening event occurs when an increase of EDSS by 1.5 points is first observed;
  - if the baseline is 1 ≤ EDSS < 5.5, then the worsening event occurs when an increase of EDSS by 1 point is first observed;
  - if the baseline is EDSS ≥ 5.5, then worsening event occurs when an increase of EDSS by 0.5 points is first observed.

iDPP challenge, tasks 1 and 2 (MS)

Task 1 - Predicting Risk of Disease Worsening (Multiple Sclerosis)

- Goal: rank subjects based on the risk of worsening (survival framework)

Task 2 - Predicting Cumulative Probability of Worsening (Multiple Sclerosis)

- Goal: assign the cumulative probability of worsening at different time windows.

- **Two subtasks**, to account for two different definitions of worsening, based on a specific score to evaluate MS progression.
- To address the challenge: datasets containing **2.5 years of visits**, with several variables.
- Evaluation metric: **C-index** (task 1), **AUROC**, **O/E ratio** (task 2)

Evaluation metrics – C-index

- The C-index is used to summarize **how well a predicted risk score describes an observed sequence of events**.

$$\widehat{C} = \frac{\sum_{i=1}^{N} \Delta_i \sum_{j=i+1}^{N} I\left(T_i^{obs} < T_j^{obs}\right) I(M_i > M_j)}{\sum_{i=1}^{N} \Delta_i \sum_{j=i+1}^{N} I\left(T_i^{obs} < T_j^{obs}\right)}$$

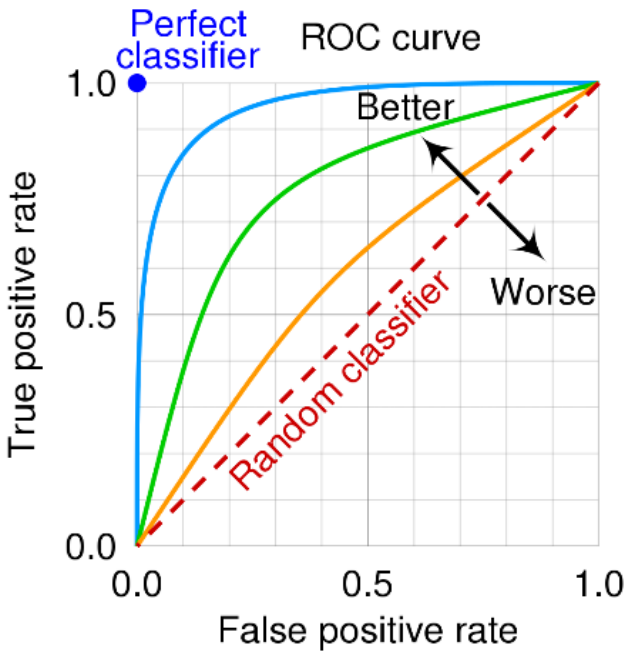
With:

- Δ_i, binary variable, 1 if the subject i experienced the event at some point and 0 if censored
- M predicted risk score of a subject
- T censoring or event times

- The C-index **ranges from 0 to 1**, with 1 representing perfect concordance
- A C-index of 0.5 is the performance of a random prediction

Evaluation metrics – AUROC

- The Receiver Operating Characteristic (ROC) curve is a graphical representation of the **model's true positive rate** (sensitivity) **against the false positive rate** (1 - specificity) at different classification thresholds.
- The AUROC is the area under the ROC.



- The AUROC **ranges from 0 to 1**, a higher value is associated to a better discrimination performance
- A reference value is 0.5, that is the performance of a classifier that assigns labels randomly

Evaluation metrics – O/E ratio

- The O/E ratio is used to assess whether **the observed event rates match the expected event rates** at each considered time interval.

- The O/E ratio does not fit into a limited interval, but an O/E ratio close to 1 indicates good performance. A ratio significantly above 1 suggests an overestimation of the number of worsening events, while a ratio below 1 indicates an underestimation.

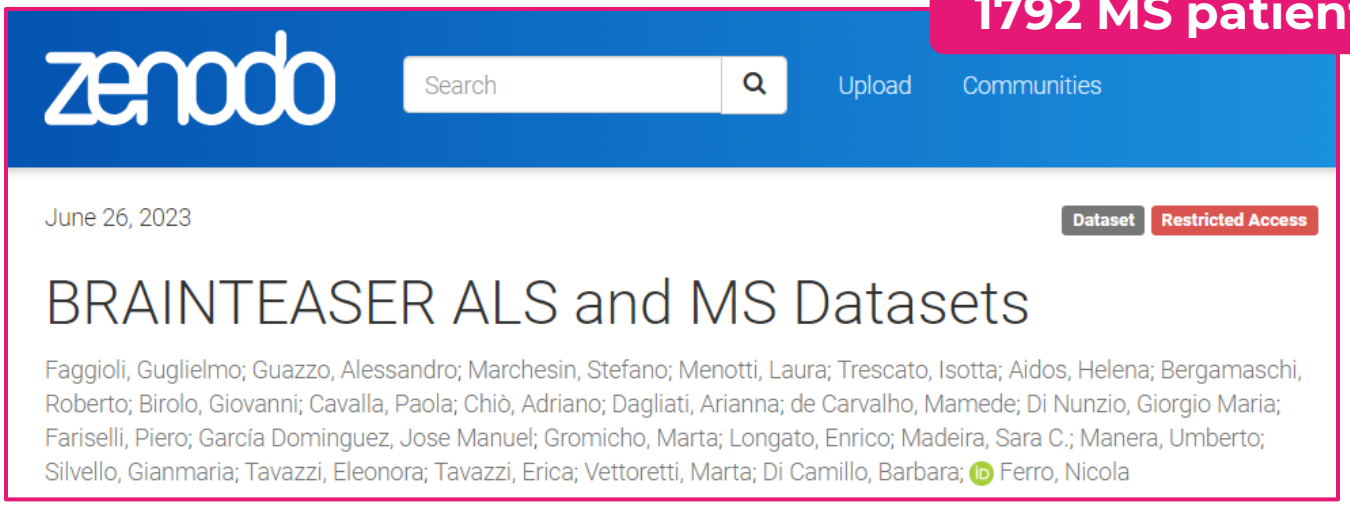
MS data

Section	Sub-Section	Variables
Baseline	Patient	Sex, Date of Birth, ethnicity
	MS Onset	Date, Symptoms
	Diagnosis	MS course, MS in paediatric age, Diagnostic delay, Diagnosis criteria
Follow-up	Progression scores	Total EDSS, EDSS subscores
	Relapses	Occurrence, Length, Symptoms, Need for hospitalization, Need for treatment
	Evoked potentials	Exam date, Altered potential, Location
	Magnetic Resonance Imaging	Exam date, Area observed, Type of lesions, Number of lesions
	Other	MS course (if changed)
Environmental	Environmental	Type of residence area

MS data

	Training set	Test set
Subtask a	441 subjects	111 subjects
Subtask b	511 subjects	129 subjects

1792 MS patients



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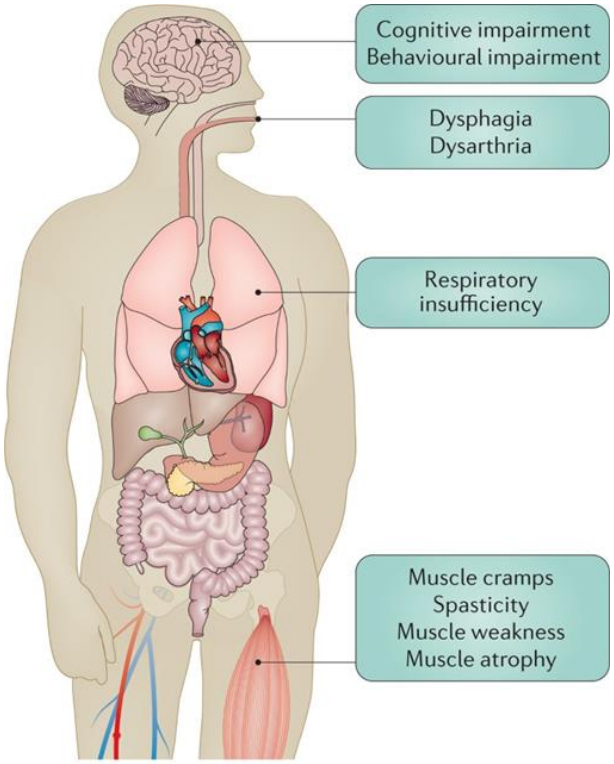
Task 3

Amyotrophic Lateral Sclerosis (ALS)

- **Fatal neurodegenerative disease**
- Attacks **motor neurons**
- Symptoms reflect the progressive **loss of muscles control**
- **Incidence** of 2.3/100 000 people/year in Europe
- Usually diagnosed between the **ages of 40 and 70**
- Average **life expectancy 2-5 years**
- There is **no cure**

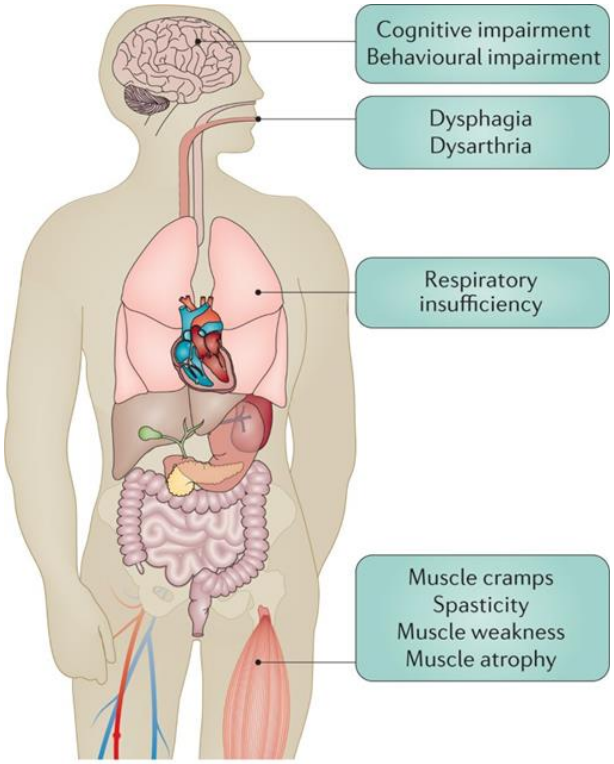


Nature Reviews | Disease Primers

ALS outcomes definition

Common issues in ALS prognosis

- Difficulties in breathing, that lead to **Non-Invasive Ventilation** (NIV)
- Difficulties in swallowing, that lead to **Percutaneous Endoscopic Gastrostomy** (PEG)
- Failure of respiratory muscles: life can be supported with **tracheostomy** or the **death** of the subject may occur



Nature Reviews | Disease Primers

Task 3: a step forward from iDPP 2022

iDPP 2022

- Focused on **ALS data**
- Three clinically relevant outcomes
- Task 1: **Ranking Risk** of Impairment
- Task 2: **Predicting Time** of Impairment
- Task 3: position **papers** on **explainability** of AI algorithms

iDPP 2023, task 3

- **ALS data enriched with environmental data**

iDPP challenge, task 3 (ALS)

Task 3 - Position Papers on Impact of Exposition to Pollutants (Amyotrophic Lateral Sclerosis)

- Goal: submit proposals of different approaches to assess if exposure to different pollutants is a useful variable to predict time to clinically relevant outcomes.

- ▷ Three subtasks for three clinically relevant outcomes (Non-Invasive Ventilation, Percutaneous Endoscopic Gastrostomy, death)
- ▷ To address the challenge: datasets shared for iDPP 2022, enhanced with environmental data, containing 6 months of visits, with several variables.
- ▷ Evaluation metrics: ROC and O/E ratio

ALS data

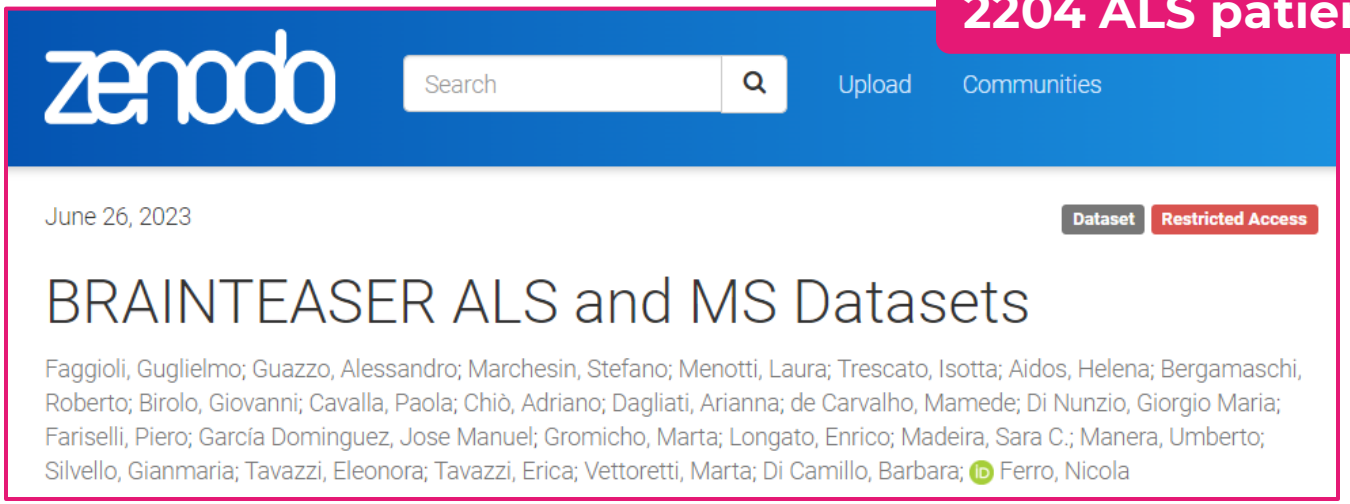
Section	Sub-Section	Variables
Baseline	Patient	Sex, Date of Birth
	ALS Onset	Date, Site
	Diagnosis	Date, Regions affected, Diagnostic Delay, FVC, BMI at diagnosis
Follow-up	Progression scores	ALSFRS-R, MiTos and King's (computable where not available), Rate of disease progression
	Other	Regions affected, Upper and lower motor neuron signs, Cognitive and neurophysiological changes
Clinical Events	History	BMI premorbid, Family history, Comorbidities, Previous surgery and trauma
	Interventions	Date of NIV, Date of PEG, Date of Tracheostomy
	Survival	Date of death
Lifestyle and Environmental	Lifestyle	Working activity, Physical activity, History of smoking, Marital status, Education level
	Environmental	Exposure to: water pollutants, air pollutants, electromagnetic fields, contaminated sites, pesticides, Location of high voltage power lines and telecommunication infrastructures

NEW!

ALS data

	Training set	Test set
Subtask a	1432 subjects	346 subjects
Subtask b	1679 subjects	422 subjects
Subtask c	1716 subjects	486 subjects

2204 ALS patients



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iDPP results

iDPP methods

Task 1a results (C-index)

uwb_T1a_survRFmri
uwb_T1a_AvgEnsemble
uwb_T1a_AvgEnsemble_minVal
uwb_T1a_survRF
uwb_T1a_survGB_minVal
CBMUniTO_T1a_coxnet
fcool_T1a_RandomSurvivalForest
fcool_T1a_FastKernelSurvivalSVM
uwb_T1a_survGB
fcool_T1a_CoxPHSurvivalAnalysis
fcool_T1a_FastSurvivalSVM
HULATUC3M_T1a_survcoxnet
CBMUniTO_T1a_cwgbsa
sisinflab-aibio_T1a_RF2
sisinflab-aibio_T1a_GB2
CBMUniTO_T1a_evilcox
HULATUC3M_T1a_survRF
fcool_T1a_GradientBoostingSurvivalAnalysis
uwb_T1a_CGBSA
sisinflab-aibio_T1a_RF1
uhu-etsi-1_T1a_02
uwb_T1a_SurvTRACE_minVal
uhu-etsi-1_T1a_0305
uhu-etsi-1_T1a_030405
uhu-etsi-1_T1a_04
uhu-etsi-1_T1a_05
sisinflab-aibio_T1a_GB1
uhu-etsi-1_T1a_03
sbb_T1a_Cox
sbb_T1a_SSVM
onto-med_T1a_0.2.1.0e-5.10000.200
onto-med_T1a_0.2.1.0e-5.10000.100
onto-med_T1a_0.2.1.0e-5.5000.200
sbb_T1a_RSF
onto-med_T1a_0.2.1.0e-5.5000.100
stefagroup_T1a_xgb_lcmm
sisinflab-aibio_T1a_GB3
stefagroup_T1a_xgb
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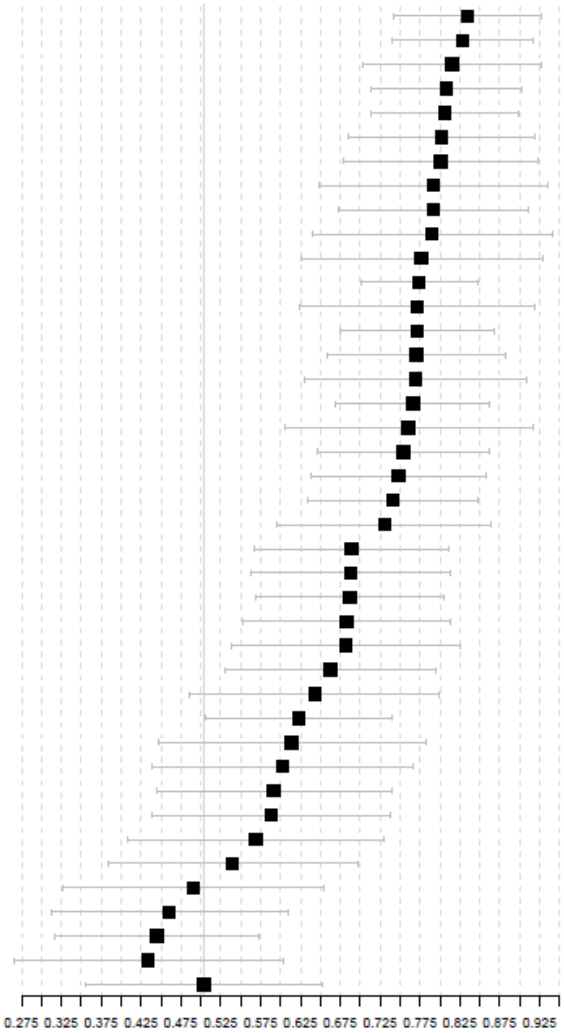
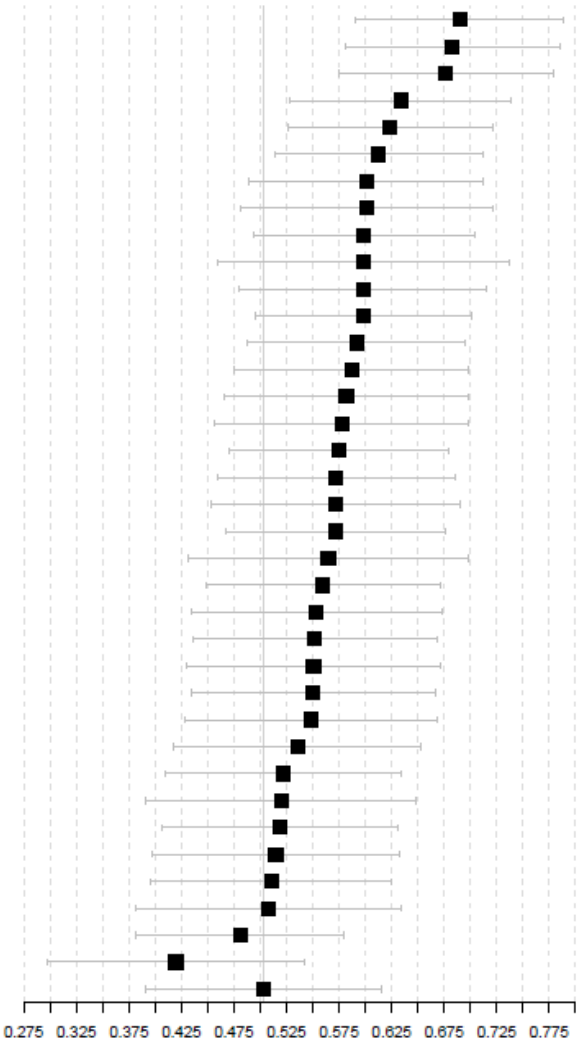
uwb_T1a_SurvTRACE
random_classifier



Task 1b results (C-index)

fcool_T1b_FastKernelSurvivalSVM
fcool_T1b_CoxPHSurvivalAnalysis
fcool_T1b_FastSurvivalSVM
CBMUniTO_T1b_coxnet
CBMUniTO_T1b_evilcox
CBMUniTO_T1b_cwgbsa
fcool_T1b_GradientBoostingSurvivalAnalysis
uwb_T1b_SurvTRACE
fcool_T1b_RandomSurvivalForest
sbb_T1b_Cox
uhu-etsi-1_T1b_s02
uwb_T1b_survGB_minVal
uwb_T1b_AvgEnsemble_minVal
sisinflab-aibio_T1b_GB2
uhu-etsi-1_T1b_03s02
sbb_T1b_SSVM
uwb_T1b_AvgEnsemble
uhu-etsi-1_T1b_03
uhu-etsi-1_T1b_03s0205
uwb_T1b_survGB
sisinflab-aibio_T1b_RF2
uwb_T1b_survRFmri
uwb_T1b_CGBSA
uhu-etsi-1_T1b_04
sisinflab-aibio_T1b_RF1
uwb_T1b_survRF
uhu-etsi-1_T1b_05
uhu-etsi-1_T1b_s01
onto-med_T1b_0.2.1.0e-5.5000.200
sisinflab-aibio_T1b_GB1
onto-med_T1b_0.2.1.0e-5.10000.100
onto-med_T1b_0.2.1.0e-5.10000.200
onto-med_T1b_0.2.1.0e-5.5000.100
HULATUC3M_T1b_survRF
sbb_T1b_RSF
uwb_T1b_SurvTRACE_minVal
random_classifier



Task 2a results (2-year time interval)

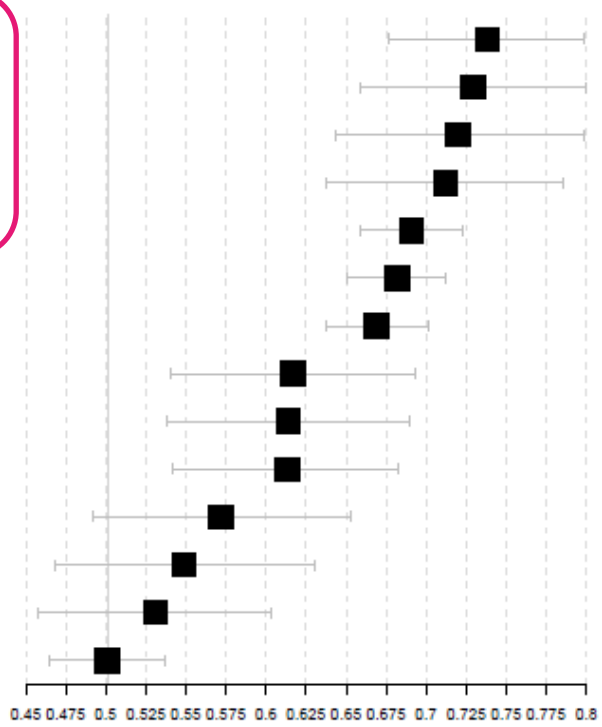
identifier	AUROC	O/E ratio
CBMUniTO_T2a_coxnet	0.890 (0.739, 1.000)	0.443 (-0.018, 0.904)
CBMUniTO_T2a_cwgbsa	0.841 (0.618, 1.000)	0.467 (-0.007, 0.940)
CBMUniTO_T2a_evilcox	0.854 (0.655, 1.000)	0.449 (-0.015, 0.913)
HULATUC3M_T2a_survcoxnet	0.864 (0.770, 0.958)	0.437 (-0.021, 0.895)
HULATUC3M_T2a_survRF	0.840 (0.710, 0.969)	0.451 (-0.014, 0.917)
onto-med_T2a_0.01.1.0e-5.10000.100.adj	0.731 (0.482, 0.980)	0.133 (-0.120, 0.386)
onto-med_T2a_0.2.1.0e-5.10000.100	0.696 (0.440, 0.951)	0.269 (-0.090, 0.628)
onto-med_T2a_0.2.1.0e-5.10000.200	0.716 (0.446, 0.987)	0.234 (-0.101, 0.570)
onto-med_T2a_0.2.1.0e-5.5000.100	0.647 (0.399, 0.896)	0.380 (-0.047, 0.807)
onto-med_T2a_0.2.1.0e-5.5000.200	0.590 (0.337, 0.842)	0.358 (-0.057, 0.772)
sbb_T2a_Cox	0.708 (0.491, 0.926)	0.389 (-0.043, 0.821)
sbb_T2a_RSF	0.604 (0.386, 0.822)	0.385 (-0.045, 0.815)
sbb_T2a_SSVM	0.624 (0.461, 0.787)	0.358 (-0.057, 0.772)
sisinflab-aibio_T2a_GB1	0.677 (0.462, 0.893)	0.000 (0.000, 0.000)
sisinflab-aibio_T2a_GB2	0.782 (0.618, 0.945)	0.000 (0.000, 0.000)
sisinflab-aibio_T2a_GB3	0.481 (0.259, 0.703)	0.000 (-0.002, 0.002)
sisinflab-aibio_T2a_RF1	0.754 (0.537, 0.970)	0.017 (-0.073, 0.107)
sisinflab-aibio_T2a_RF2	0.569 (0.347, 0.791)	0.010 (-0.060, 0.081)
uhu-etsi-1_T2a_03	0.769 (0.621, 0.916)	0.678 (0.107, 1.248)
uhu-etsi-1_T2a_04	0.812 (0.690, 0.933)	0.713 (0.128, 1.298)
uhu-etsi-1_T2a_05	0.774 (0.636, 0.912)	0.697 (0.119, 1.276)
uwb_T2a_CGBSA	0.862 (0.731, 0.993)	3.106 (1.885, 4.327)
uwb_T2a_survGB	0.877 (0.745, 1.000)	0.919 (0.255, 1.583)
uwb_T2a_survGB_minVal	0.894 (0.787, 1.000)	**0.946** (0.272, 1.620)
uwb_T2a_survRF	0.914 (0.784, 1.000)	1.811 (0.879, 2.744)
uwb_T2a_survRFmri	**0.924** (0.800, 1.000)	1.889 (0.937, 2.842)

Task 2b results (2-year time interval)

identifier	AUROC	O/E ratio
CBMUniTO_T2b_coxnet	0.676 (0.514, 0.838)	1.082 (0.467, 1.697)
CBMUniTO_T2b_cwgbsa	0.632 (0.477, 0.787)	1.101 (0.481, 1.721)
HULATUC3M_T2b_survRF	0.560 (0.329, 0.791)	1.019 (0.422, 1.615)
onto-med_T2b_0.2.1.0e-5.10000.100	0.604 (0.432, 0.776)	0.585 (0.133, 1.037)
onto-med_T2b_0.2.1.0e-5.10000.200	0.585 (0.433, 0.736)	0.547 (0.110, 0.985)
onto-med_T2b_0.2.1.0e-5.5000.100	0.569 (0.384, 0.754)	1.065 (0.455, 1.675)
onto-med_T2b_0.2.1.0e-5.5000.200	0.523 (0.329, 0.717)	1.035 (0.434, 1.636)
sbb_T2b_Cox	0.642 (0.397, 0.887)	1.098 (0.449, 1.748)
sbb_T2b_RSF	0.514 (0.281, 0.747)	0.966 (0.357, 1.576)
sbb_T2b_SSVM	0.547 (0.345, 0.750)	0.814 (0.255, 1.373)
sisinflab-aibio_T2b_GB1	0.462 (0.249, 0.675)	0.000 (-0.003, 0.003)
sisinflab-aibio_T2b_GB2	0.614 (0.442, 0.786)	0.000 (0.000, 0.000)
sisinflab-aibio_T2b_RF1	0.469 (0.265, 0.672)	0.018 (-0.062, 0.098)
sisinflab-aibio_T2b_RF2	0.535 (0.324, 0.746)	0.011 (-0.052, 0.075)
uhu-etsi-1_T2b_03	0.652 (0.488, 0.816)	1.475 (0.757, 2.193)
uhu-etsi-1_T2b_05	0.630 (0.450, 0.811)	1.328 (0.647, 2.009)
uhu-etsi-1_T2b_s02	0.644 (0.460, 0.827)	1.483 (0.764, 2.203)
uwb_T2b_CGBSA	0.514 (0.311, 0.717)	1.818 (1.021, 2.615)
uwb_T2b_survGB	0.569 (0.392, 0.747)	1.045 (0.441, 1.649)
uwb_T2b_survGB_minVal	0.606 (0.437, 0.776)	0.920 (0.353, 1.486)
uwb_T2b_survRF	0.590 (0.410, 0.769)	2.292 (1.398, 3.187)
uwb_T2b_survRFmri	0.596 (0.421, 0.770)	2.257 (1.370, 3.145)

Task 3a results

neurotn_T3a_base_ClassifEnsemble
neurotn_T3a_base_survRFOpt
neurotn_T3a_EW6_survRFOpt
neurotn_T3a_EW6_ClassifEnsemble
fcool_T3a_base_GradientBoostingSurvivalAnalysis
fcool_T3a_base_RandomSurvivalForest
fcool_T3a_base_FastSurvivalSVM
fcool_T3a_EWP_CoxPHSurvivalAnalysis
fcool_T3a_EW6_CoxPHSurvivalAnalysis
fcool_T3a_EW6_GradientBoostingSurvivalAnalysis
fcool_T3a_EWP_GradientBoostingSurvivalAnalysis
fcool_T3a_EW6_RandomSurvivalForest
fcool_T3a_EWP_RandomSurvivalForest
random_classifier



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Thank You for your attention

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PhD student

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