

## Supplementary Material

**Table S1:** Set of hyperparameters for each algorithm.

| Algorithm     | Hyperparameters  |
|---------------|--|
| Random Forest | number of trees = {1, 2, 3, ..., 50}<br>depth of estimators = {1, 2, 3, ..., 20}   |
| SVM           | kernel = {rbf, linear}<br>C = {0.001, 0.01, 0.05, 0.1, 0.5, 1, 10}   |
| XGBoost       | number of trees = {1, 2, 3, ..., 50}<br>learning rate = {0.01, 0.05, 0.1};<br>max depth of estimators = {1, 2, 3, ..., 19} |

*SVM: Support Vector Machine*

**Table S2** – Routine laboratory variables measured at baseline in cognitive/functional decliners and non-decliners.

| Variable                    | Cognitive decliners (n=70) | Non-cognitive decliners (n=62) | P value | Functional decliners (n=48) | Non-functional decliners (n=84) | P value       |
|-----------------------------|----------------------------|--------------------------------|---------|-----------------------------|---------------------------------|---------------|
| RBC / mm <sup>3</sup>       | 4890285.71±<br>464508.37   | 4944193.54±<br>421712.15       | 0.488   | 4872195.12±<br>477663.64    | 4924383.56±<br>427089.58        | 0.549         |
| Hemoglobin g/dL             | 14.14±1.18                 | 14.50±1.19                     | 0.079   | 14.22±1.27                  | 14.25±1.14                      | 0.874         |
| Hematocrit %                | 43.56±3.34                 | 44.51±3.52                     | 0.111   | 43.88±3.50                  | 43.89±3.40                      | 0.990         |
| Leukocytes /mm <sup>3</sup> | 5762.85±1447.85            | 5954.83±1282.75                | 0.424   | 5551.21±1466.99             | 6110.95±1409.15                 | <b>0.047*</b> |
| Neutrophils %               | 57.34±8.50                 | 58.50±9.40                     | 0.461   | 55.68±7.92                  | 58.69±8.14                      | 0.057         |
| Eosinophils %               | 3.45±3.70                  | 3.83±3.56                      | 0.548   | 3.56±3.36                   | 3.39±3.63                       | 0.812         |
| Basophils %                 | 0.62±0.56                  | 0.67±0.47                      | 0.594   | 0.58±0.63                   | 0.73±0.44                       | 0.170         |
| Monocytes %                 | 6.61±2.10                  | 6.54±2.10                      | 0.857   | 6.58±2.20                   | 6.80±1.94                       | 0.577         |
| Lymphocytes %               | 31.88±7.58                 | 30.27±8.28                     | 0.245   | 33.46±7.64                  | 30.31±7.57                      | <b>0.036*</b> |
| Platelets /mm <sup>3</sup>  | 221800.00±<br>50808.99     | 219516.12±<br>46816.60         | 0.789   | 208804.87±<br>51607.27      | 237356.16±<br>46282.75          | <b>0.003*</b> |
| RDW %                       | 15.26±1.32                 | 15.04±0.88                     | 0.273   | 15.09±1.23                  | 15.19±1.21                      | 0.670         |
| NLR                         | 170.24±98.74               | 195.54±136.14                  | 0.220   | 150.53±89.04                | 181.24±138.95                   | 0.205         |
| PLR                         | 7463.28±2883.09            | 8300.21±5018.97                | 0.235   | 6678.25±2633.13             | 8528.11±3637.56                 | <b>0.005*</b> |
| Fasting glucose mg/dL       | 112.32±31.49               | 114.54±30.09                   | 0.680   | 113.17±38.78                | 116.32±36.88                    | 0.667         |
| Triglycerides mg/dL         | 139.37±57.07               | 118.90±68.77                   | 0.064   | 125.58±55.72                | 142.21±71.17                    | 0.199         |
| HDL-c mg/dL                 | 52.67±11.22                | 55.33±12.77                    | 0.204   | 54.95±12.38                 | 54.45±11.79                     | 0.831         |

|                   |               |               |       |               |               |               |
|-------------------|---------------|---------------|-------|---------------|---------------|---------------|
| LDL-c mg/dL       | 139.41±39.30  | 133.70±28.13  | 0.335 | 134.85±37.02  | 142.84±30.95  | 0.220         |
| TSH mU/L          | 2.81±4.34     | 2.38±2.01     | 0.295 | 2.92±3.08     | 2.10±1.75     | 0.132         |
| AST U/L           | 23.64±11.88   | 22.37±5.95    | 0.447 | 25.90±15.24   | 22.02±4.79    | 0.132         |
| ALT U/L           | 14.52±6.32    | 14.51±6.58    | 0.991 | 16.70±8.86    | 13.45±4.83    | <b>0.034*</b> |
| GGT U/L           | 35.98±25.58   | 37.85±32.77   | 0.713 | 37.09±29.32   | 36.80±30.91   | 0.960         |
| Creatinine mg/dL  | 0.98±0.30     | 0.92±0.24     | 0.093 | 0.92±0.26     | 0.94±0.30     | 0.718         |
| Albumin g/dL      | 4.18±0.20     | 4.13±0.27     | 0.220 | 4.15±0.30     | 4.16±0.21     | 0.799         |
| Globulin g/dL     | 3.13±0.30     | 3.23±0.36     | 0.081 | 3.10±0.36     | 3.21±0.34     | 0.116         |
| B12 vitamin pg/mL | 492.78±442.02 | 409.25±248.79 | 0.177 | 472.07±372.20 | 415.27±276.55 | 0.356         |
| Cortisol µg/dL    | 13.15±4.59    | 13.49±4.83    | 0.678 | 12.99±4.94    | 13.18±4.40    | 0.832         |

*RBC: red blood cell; RDW: red blood cell distribution width; NLR Neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; AST: aspartate transaminase; ALT: alanine transaminase; GGT: gamma-glutamyl transferase; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; TSH: thyroid-stimulating hormone. Mean + standard deviation. \*Significant:  $p<0.05$ .*

**Table S3.** Performance of Machine Learning models applied in the study.

| Model                     | Sensitivity | Specificity | Accuracy    |
|---------------------------|-------------|-------------|-------------|
| <i>Cognitive decline</i>  |             |             |             |
| Randon Forest             | 0.81        | 0.79        | <i>0.79</i> |
| XGBoost                   | 0.81        | 0.79        | <i>0.79</i> |
| SVM                       | 0.51        | 0.71        | <i>0.71</i> |
| <i>Functional decline</i> |             |             |             |
| Randon Forest             | 0.92        | 0.83        | <i>0.92</i> |
| XGBoost                   | 0.83        | 0.83        | <i>0.83</i> |
| SVM                       | 0.51        | 0.71        | <i>0.71</i> |

*Sensitivity and specificity: weight average. SVM: Support vector machine.*