# Supplementary materials

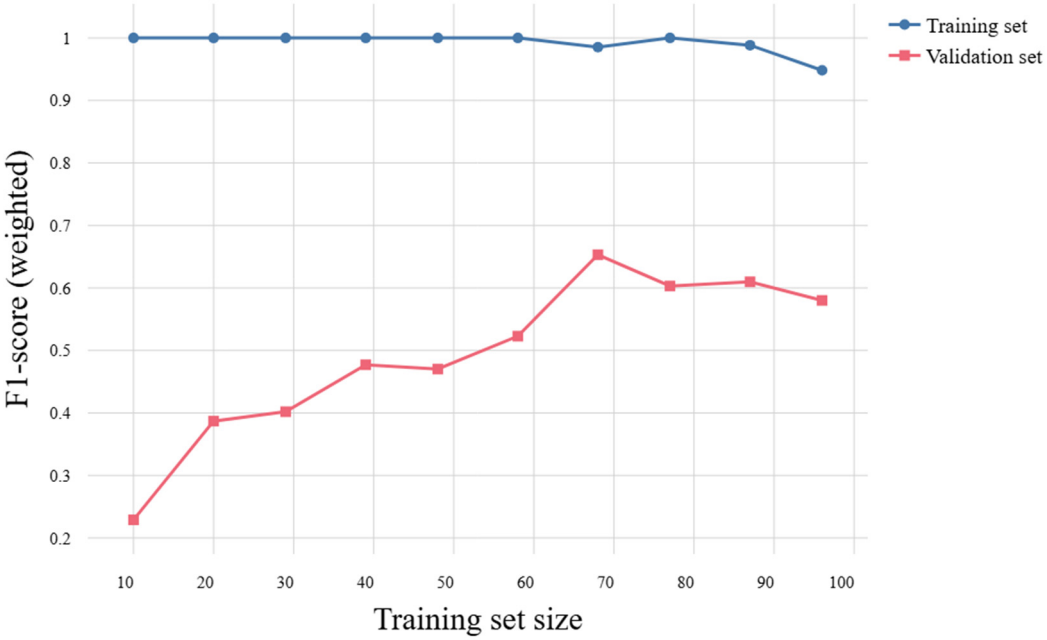



**Figure S1.** Learning Curves for the Gradient Boosting Classifier.

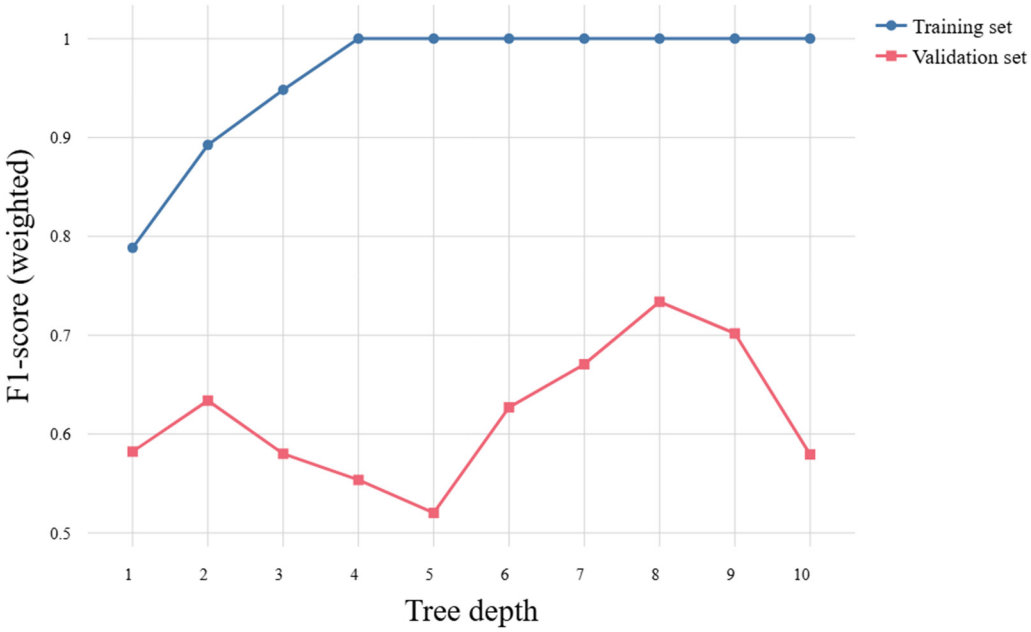



**Figure S2.** Sensitivity Analysis of Model Performance to Tree Depth.

**Supplementary Table S1**. Quantitative comparison of ANOVA variants demonstrates heteroscedasticity-induced inference distortion and Welch ANOVA consensus with robust alternatives (Kruskal–Wallis, Brown–Forsythe, HC3).

| Feature name | ANOVA, p | Welch's ANOVA, p | Levene test, p | Brown-Forsythe, p | HC3, p | Kruskal–Wallis, p |
|---|---|---|---|---|---|---|
| RBC | 8,5051E-04 | 6,6999E-04 | 4,5700E-02 | 4,5615E-02 | 8,3009E-04 | 1,1782E-03 |
| MCV | 3,5927E-02 | 1,2066E-01 | 7,1900E-02 | 8,3296E-02 | 3,8011E-02 | 1,0253E-01 |
| RDW% | 9,0747E-04 | 1,2655E-06 | 1,3000E-03 | 4,8300E-03 | 7,0234E-04 | 3,8529E-03 |
| RDWa | 7,9190E-01 | 5,2503E-03 | 5,8950E-01 | 5,7400E-04 | 1,0486E-04 | 2,8844E-04 |
| HCT | 3,3307E-03 | 4,0513E-03 | 3,3000E-02 | 3,3975E-02 | 3,4884E-03 | 4,2483E-03 |
| PLT | 7,1862E-02 | 1,0372E-01 | 6,6810E-01 | 6,5571E-01 | 7,2827E-02 | 5,8879E-02 |
| MPV | 6,1366E-01 | 4,5304E-01 | 2,2710E-01 | 1,8561E-01 | 5,7608E-01 | 7,3303E-01 |
| PDW | 6,3642E-02 | 4,2905E-03 | 5,2800E-02 | 1,0399E-01 | 1,5952E-02 | 2,2325E-02 |
| PCT | 3,8762E-01 | 4,1714E-01 | 8,9590E-01 | 8,8894E-01 | 3,6580E-01 | 1,2145E-01 |
| LPCR | 4,2821E-01 | 2,0688E-01 | 4,0600E-01 | 4,2290E-01 | 2,3266E-01 | 1,3500E-01 |
| WBC | 1,0513E-01 | 2,0955E-02 | 8,6900E-02 | 1,0459E-01 | 1,0754E-01 | 6,9213E-02 |
| HGB | 2,1103E-03 | 3,4636E-03 | 4,7000E-02 | 4,5351E-02 | 1,1401E-03 | 1,0254E-03 |
| MCH | 8,5162E-02 | 1,6679E-01 | 9,8200E-02 | 7,8596E-02 | 6,8396E-02 | 2,0015E-02 |
| MCHC | 2,7073E-02 | 9,6814E-04 | 5,0020E-01 | 4,9520E-01 | 2,2732E-02 | 1,7891E-03 |
| LYM | 5,2710E-01 | 6,6189E-01 | 1,8310E-01 | 2,1358E-01 | 5,2914E-01 | 8,6178E-01 |
| GRAN | 2,5800E-03 | 1,9648E-03 | 1,1250E-01 | 2,5231E-02 | 7,6518E-04 | 1,8860E-04 |
| MID/Mon | 9,6808E-01 | 9,2593E-01 | 2,9040E-01 | 2,6839E-01 | 9,7172E-01 | 7,3656E-01 |
| LYM% | 2,0219E-03 | 9,2005E-03 | 4,9790E-01 | 5,6903E-01 | 2,1835E-03 | 9,8892E-03 |
| GRA% | 9,4053E-04 | 6,4821E-03 | 1,8130E-01 | 8,1910E-03 | 9,4064E-05 | 5,6383E-04 |
| MID%/Mon% | 7,7077E-01 | 5,7091E-01 | 6,4140E-01 | 7,0677E-01 | 6,2504E-01 | 4,0509E-01 |
| BChE | 6,9030E-05 | 8,6869E-05 | 1,6600E-02 | 1,2641E-02 | 4,6110E-05 | 9,2393E-05 |
| PON1 | 1,2470E-01 | 1,7453E-01 | 3,3940E-01 | 3,3442E-01 | 1,0913E-01 | 1,9118E-01 |
| ALT | 3,9147E-01 | 7,0025E-01 | 6,2230E-01 | 6,4448E-01 | 4,8824E-01 | 3,6785E-01 |
| AST | 1,1519E-01 | 1,4500E-01 | 8,4200E-02 | 8,9263E-02 | 1,1324E-01 | 7,2283E-02 |
| ALB | 2,7941E-10 | 4,8232E-04 | 1,0000E-04 | 1,6100E-04 | 4,0000E-10 | 1,4822E-05 |
| Glu | 1,4298E-06 | 1,4424E-04 | 4,0290E-01 | 3,3060E-01 | 5,0090E-07 | 4,8000E-09 |
| GGT | 1,2528E-01 | 3,2373E-01 | 3,0450E-01 | 3,0402E-01 | 1,2868E-01 | 5,1474E-02 |
| Tot.Prot | 1,4225E-02 | 2,0200E-02 | 7,6390E-01 | 8,1158E-01 | 9,4529E-03 | 4,8213E-03 |
| PHOS | 9,5336E-01 | 9,5530E-01 | 6,0610E-01 | 6,5200E-01 | 9,5567E-01 | 9,4775E-01 |
| UREA | 5,2244E-01 | 4,3262E-01 | 1,5700E-02 | 1,9434E-02 | 4,1219E-01 | 2,3446E-01 |
| TRIGS | 5,4092E-01 | 2,7576E-01 | 4,6360E-01 | 4,4415E-01 | 4,4995E-01 | 3,1072E-01 |

| | | | | | | |
|---|---|---|---|---|---|---|
| CREA | 8,2687E-01 | 6,9288E-01 | 7,8670E-01 | 7,4201E-01 | 8,5630E-01 | 3,6023E-01 |
| ALP | 4,6137E-03 | 6,7308E-03 | 4,0000E-04 | 2,9100E-04 | 4,1194E-03 | 2,4783E-03 |
| K-GUV | 2,7468E-01 | 2,3002E-01 | 6,0100E-02 | 6,6990E-03 | 8,0799E-02 | 2,0911E-03 |
| BilAc | 6,5471E-01 | 3,3276E-01 | 6,4300E-02 | 1,9990E-01 | 6,1561E-01 | 1,4517E-01 |
| HDL | 3,0541E-03 | 2,3157E-03 | 1,1870E-01 | 1,0509E-01 | 3,1937E-03 | 4,8701E-03 |
| LDL | 9,7080E-05 | 3,4208E-06 | 3,5000E-03 | 3,9680E-03 | 8,1024E-05 | 1,4952E-04 |
| CK-NAC | 5,1357E-03 | 6,7553E-03 | 5,3160E-01 | 5,5540E-01 | 5,4838E-03 | 1,7477E-03 |
| Chol | 4,2202E-05 | 1,2984E-05 | 9,3600E-02 | 1,4779E-01 | 3,2150E-05 | 7,5430E-05 |
| LDH | 4,3388E-04 | 8,5892E-06 | 6,6000E-03 | 5,7530E-03 | 4,1411E-04 | 1,1932E-03 |
| Ur. Acid | 8,9246E-03 | 4,2259E-03 | 1,0590E-01 | 1,9230E-01 | 1,0577E-02 | 8,1855E-03 |
| LAC | 2,6645E-01 | 2,2781E-01 | 3,8910E-01 | 3,4846E-01 | 2,9935E-01 | 2,6175E-01 |
| NEFA | 1,6336E-03 | 1,1740E-03 | 5,2590E-01 | 4,7766E-01 | 1,8790E-03 | 2,9905E-03 |
| Transf | 1,1429E-10 | 5,5512E-09 | 1,7730E-01 | 1,5974E-01 | 1,0000E-10 | 7,1000E-08 |
| Fe | 6,9375E-04 | 6,3257E-10 | 1,0300E-02 | 1,0332E-02 | 7,8995E-04 | 1,1299E-05 |
| a1-AGP | 1,8778E-02 | 3,9015E-02 | 3,1360E-01 | 3,4780E-01 | 2,3781E-02 | 1,2017E-02 |

**Supplementary Table S2**. Distributional comparison of key biomarkers between the training cohort and the independent cohort for out-of-distribution assessment. Only biomarkers present in both the training cohort and the independent cohort were included; features were selected based on availability in the independent cohort.

| Feature name | Mean ± SD (training cohort, n=20) | Mean ± SD (external cohort, n=28) | Median [Q1-Q3] (training cohort, n=20) | Median [Q1-Q3] (external cohort, n=28) |
|---|---|---|---|---|
| WBC | 7,22 ± 1,47 | 7,62 ± 3,93 | 6,95 [5,98 - 8] | 7,15 [5,88 - 7,75] |
| LYM | 2,13 ± 0,79 | 1,77 ± 0,65 | 2 [1,65 - 2,8] | 1,6 [1,3 - 2,15] |
| MID/Mon | 0,52 ± 0,13 | 0,51 ± 0,15 | 0,5 [0,4 - 0,6] | 0,5 [0,4 - 0,6] |
| GRAN | 4,57 ± 1,48 | 5,34 ± 3,88 | 4,4 [3,2 - 5,63] | 4,75 [3,55 - 5,5] |
| HGB | 118,57 ± 15,98 | 114,96 ± 17,02 | 122 [109 - 128] | 116 [106,5 - 124,25] |
| MCH | 30,27 ± 2,35 | 30,04 ± 1,55 | 30,35 [28,95 - 31,2] | 29,9 [29,18 - 31,05] |
| MCHC | 346,1 ± 8,66 | 336,54 ± 9,17 | 346,5 [340,5 - 351,25] | 337 [334 - 341] |
| RBC | 3,91 ± 0,48 | 3,84 ± 0,6 | 3,96 [3,6 - 4,26] | 3,86 [3,39 - 4,17] |
| MCV | 87,21 ± 6,36 | 89,28 ± 5,08 | 88,45 [82,55 - 90,33] | 88,9 [86,75 - 91,4] |
| RDWa | 66,32 ± 6,8 | 62,02 ± 5,12 | 66,6 [61,25 - 70,43] | 61,1 [58,8 - 64] |
| HCT | 34,33 ± 4,75 | 34,24 ± 5,31 | 34,9 [32,48 - 36,82] | 34,35 [31,1 - 37,15] |
| RDW% | 19,18 ± 1,32 | 17,41 ± 0,87 | 18,9 [18,08 - 19,73] | 17,25 [16,7 - 17,73] |
| PLT | 255 ± 78,76 | 258,71 ± 96,85 | 243,5 [203 - 295,25] | 246,5 [214,75 - 287,5] |
| MPV | 8,61 ± 0,96 | 8,21 ± 0,78 | 8,55 [7,98 - 9,13] | 8,25 [7,78 - 8,7] |
| PDW | 12,45 ± 1,31 | 11,91 ± 1,1 | 12,35 [11,5 - 13,15] | 12,05 [11,2 - 12,45] |
| LPCR | 18,78 ± 5,86 | 16,86 ± 5,22 | 18,8 [14,35 - 22,08] | 16,8 [13 - 19,78] |
| PCT | 0,21 ± 0,06 | 0,21 ± 0,07 | 0,21 [0,18 - 0,25] | 0,19 [0,17 - 0,24] |
| ALT | 25,76 ± 20,65 | 13,35 ± 22,32 | 21,35 [17,35 - 25,7] | 7,35 [4,5 - 10,05] |
| AST | 27,4 ± 12,54 | 25,23 ± 35,63 | 25 [21,75 - 27,25] | 16,1 [12,85 - 20,68] |

| | | | | |
|---|---|---|---|---|
| GGT | 50,5 ± 84,91 | 26,93 ± 33,01 | 27 [21 - 41] | 12,8 [10 - 28,65] |
| Glu | 4,53 ± 1,28 | 4,64 ± 0,94 | 4,3 [3,9 - 4,55] | 4,59 [3,98 - 4,96] |
| ALB | 38,72 ± 4,88 | 33,38 ± 7,2 | 40,3 [35,75 - 42,4] | 33,15 [27,8 - 37,33] |
| Fe | 16,03 ± 4,9 | 12,24 ± 4,43 | 15,05 [13,43 - 17,03] | 12,85 [8,4 - 14,35] |
| CREA 2R | 84,5 ± 12,17 | 94,46 ± 35,59 | 85 [74,75 - 89,25] | 89,5 [70 - 98,5] |
| Ca 2R | 2,62 ± 0,24 | 2,22 ± 0,3 | 2,7 [2,53 - 2,8] | 2,25 [2,04 - 2,39] |
| CK-NAC | 95,85 ± 74,06 | 62,04 ± 55,45 | 72,5 [37,5 - 116,75] | 36,5 [22 - 79,75] |
| LDH L-P | 259,4 ± 77,68 | 266,57 ± 97,93 | 245 [206,25 - 295,25] | 243 [202,5 - 313,75] |
| UREA 1R | 4,98 ± 2,38 | 7,03 ± 4,13 | 4,41 [3,28 - 6,08] | 5,69 [4,08 - 9,39] |
| TP | 76,53 ± 8,99 | 65,85 ± 10,67 | 78,6 [74,05 - 80,88] | 65,3 [56,98 - 72,95] |
| TRIGS | 1,32 ± 0,91 | 1,37 ± 0,54 | 1,08 [0,81 - 1,31] | 1,28 [0,93 - 1,69] |
| PHOS | 1,23 ± 0,29 | 1,26 ± 0,25 | 1,23 [1,1 - 1,4] | 1,21 [1,15 - 1,31] |
| Chol | 4,37 ± 0,92 | 4,16 ± 1,33 | 4,42 [3,87 - 5,21] | 4,07 [3,25 - 4,89] |
| ALP | 196,98 ± 16,53 | 315,21 ± 285,91 | 195,75 [192,13 - 198,25] | 229,5 [187,5 - 300] |
| BChE | 1854,07 ± 815,74 | 5562,96 ± 2093,37 | 1842,16 [1513,27 - 2207,74] | 5087 [4188,75 - 6155,5] |
| HDL R | 1,2 ± 0,24 | 1,09 ± 0,45 | 1,19 [1,06 - 1,43] | 0,99 [0,8 - 1,28] |
| LDL R | 2,7 ± 0,77 | 1,98 ± 0,89 | 2,67 [2,35 - 3,45] | 1,94 [1,5 - 2,64] |

**Supplementary Table S3**. Population Stability Index (PSI) for key biomarkers between the training cohort and the independent cohort (4 bins).

| **Feature name** | **PSI** | **Feature name** | **PSI** | **Feature name** | **PSI** |
|---|---|---|---|---|---|
| WBC | 0.2045 | PLT | 0.1546 | Ca 2R | 4.6216 |
| LYM | 0.5058 | MPV | 0.1199 | CK-NAC | 0.1561 |
| MID/Mon | 0.0276 | PDW | 0.1875 | LDH L-P | 0.0295 |
| GRAN | 0.0715 | LPCR | 0.1270 | UREA 1R | 0.2472 |
| HGB | 0.4493 | PCT | 0.0797 | TP | 4.1882 |
| MCH | 0.0290 | ALT | 2.7170 | TRIGS | 0.2832 |
| MCHC | 0.8825 | AST | 1.2445 | PHOS | 0.2696 |
| RBC | 0.1546 | GGT | 2.6373 | Chol | 0.1905 |
| MCV | 0.4475 | Glu | 0.4511 | ALP | 3.9345 |
| RDWa | 1.0455 | ALB | 0.6789 | BChE | 5.9256 |
| HCT | 0.0583 | Fe | 0.3257 | HDL R | 0.4039 |
| RDW% | 2.5532 | CREA 2R | 0.4706 | LDL R | 0.8380 |