Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.
eFigure 1. Strategy for SHC and Duke Cohort Assembly

(a) SHC cohort

Contrast-enhanced chest CT (1996 – 2016)

Random selection PE-CT

Stratified random sampling

- 1967 PE positive
- 1247 PE negative

100 outpatient consecutive samples

- 29 PE positive
- 71 PE negative

(b) Duke cohort

Contrast-enhanced chest CT (2009 – 2017)

Random selection PE-CT

Random sampling

101 outpatient consecutive samples

- 38 PE positive
- 202 PE negative
- 23 PE positive
- 78 PE negative
eFigure 2. Performance in Setting 4: 10-Fold Cross Validation Performance of ElasticNet (A) and PE Neural Model (B) on Feature Set of Integrated EMR
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eFigure 4. Patient-Level Feature Importance: Attention Derived By the PE Neural Model Along With the Predicted Probability of PE Presence

(a) case 1

(b) case 2

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eAppendix. Detailed Methods and Findings

1. Methodology for Temporal Feature engineering

Demographics - As demographics, we considered four static features: gender (male/female), race/ethnicity (white/black/asian/native american/others/unknown), age at time of observation, smoking habit (yes/no) and coded them as categorical variables (age binned into 10 groups). In case of change in smoking status, we only considered the current observation and coded as ‘Smoking’/‘Non-smoking’.

Vitals - We considered only the primary vital signs of the patient which includes systolic and diastolic blood pressure, height, weight, body mass index (BMI), temperature, respiration rate, pulse oximetry (spO2), and heart rate. For both internal and external datasets, the primary vitals are recorded using the LOINC standard coding system. In order to capture temporality, we measured the sensitivity to change in primary vitals within a 30 day window by computing derivatives of each vital sign along the temporal axis where first value is the normal range of the targeted vital. The derivative of a vital can be represented as $\frac{dy}{dt}$ where $Y = f(X), X = x_N, x_1, x_2, \ldots, x_t$ is a measure of the $x$ vital over time $t$ and $x_N$ is normal range of the targeted vital. Given that majority of the targeted population are adults (with mean age: Stanford 60.53 and Duke 70.2), as normal range $x_N$ we considered vital signs against normal values if prior baseline vitals were not available.

Inpatient and Outpatient medication - The inpatient and outpatient drug formulary and vocabularies were mapped to a 2016 version of RxNorm. Prescription orders were distilled to the Pharmacologic class labels which active moieties that share scientifically documented properties is defined on the basis of any combination of three attributes: Mechanism of Action (MOA), Physiologic Effect (PE), and Chemical Structure (CS), that the FDA has determined to be scientifically valid and clinically meaningful. For drug feature engineering, we considered a 12 month window and identified 641 unique Pharmacologic class of drugs given to the training set SHC patients (inpatient and outpatient). Afterwards, we coded the medication usage as two numeric representations as: (1) presence/absence of the medication which is a binary value that captures if medication from a particular Pharmacologic class given to the patient within the 12 month window; (2) frequency of the medication as a numeric value to captures how many times the particular medication was repeated within 12 months.

Diagnosis code - Diagnosis codes considered were ICD-9 format (codes with less than 1% occurrences in the training set were excluded). In order to limit the learning space, the diagnosis codes were collapsed to the top diagnosis categories using the the International Classification of Diseases, Version 9. Expansion to subcategories was performed with review of ICD9 taxonomy such that in total 141 unique diagnosis groupings (see Supplement Table 1) were generated for each group as a binary variable representing the presence/absence of a particular diagnosis within the 12 month window. For ensuring no data leakage, we dropped all ICD-9 codes recorded from the same encounter (hospitalization and ED visit) as of the CT exam from our analysis.

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1. [https://www.hl7.org/fhir/observation-vitalsigns.html](https://www.hl7.org/fhir/observation-vitalsigns.html)
2. [https://www.nlm.nih.gov/research/umls/rxnorm/](https://www.nlm.nih.gov/research/umls/rxnorm/)

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Laboratory tests – All available laboratory tests were categorized into 22 unique test categories (Supplement Table 2). Laboratory tests are coded in binary presence/absence as well as we captured the latest value of each test. Missing lab data is coded as ‘0’ value.

2. Cross-validation performance of the models on SHC patient data
eFigure 1 summarize the 10-fold cross-validation results of the SHC cases. The ElasticNet model performance mean AUC was 0.90±0.01 and the Neural model was (0.83±0.01) with both models showing low variations (±0.01) between the folds which represents high generalizability.

3. D-Dimer missing cases from SHC and Duke consecutive out-patient
eTable 1. D-Dimer Missed Cases From SHC and DUKE Consecutive Out-Patient – D-Dimer Score, Models’ Predicted Probability for PE and Clinical Scorings

| Patient | D-Dimer value | PE Presence | ElasticNet | Neural network | Wells | PERC | rGeneva |
|---------|---------------|-------------|------------|----------------|-------|------|---------|
| SHC patients with negative D-Dimer (< 500) - Among 100 patients 29 had D-Dimer and 2 negatives |
| 1       | negative      | Yes         | 0.56       | 0.16           | 0     | 1    | 3       |
| 2       | negative      | No          | 0.4        | 0.015          | 3     | 0    | 3       |
| Duke patients with negative D-Dimer (<500) – Among 101 patients 32 patients had D-Dimer and 4 negatives |
| 1       | negative      | Yes         | 0.76       | 0.6            | 1     | 2    | 3       |
| 2       | negative      | Yes         | 0.82       | 0.84           | 9     | 2    | 8       |
| 3       | negative      | No          | 0.11       | 0.056          | 3     | 0    | 3       |
| 4       | negative      | No          | 0.13       | 0.03           | 1.5   | 3    | 5       |

(D-Dimer <500 normal)

4. Models interpretability

**ElasticNet model** - eFigure 2 shows the trends of the 22 most relevant features for the prediction PE pre-test risk. Looking at the graph we can clearly see that presence of pulmonary embolism and infraction, and neoplasm (cancer) influenced the PE prediction the most. Interesting true value of the D-dimer lab test is also listed as the top features than just the presence of the D-dimer test. Thus we can assume that these features are relevant in order to assess if a new patient has the PE or not.

**PE neural model** - We used a method called sensitivity analysis for computing the relevance of each EMR feature. Sensitivity analysis takes the partial derivative of the loss function of the trained neural recurrence model with respect to each input feature to derive the importance for the targeted prediction task. eFigure 3 represent results of sensitivity analysis of input for two cases where the importance scores are plotted as bar and predicted probability value and ground truth labels are also shown in the figure.

5. EMR grouping criteria: diagnosis code and laboratory exams

In Section 2.2, we described the proposed feature engineering pipeline that can parse EMR while maintaining the significant temporal properties where the pipeline used pre-defined
grouping criteria for diagnosis codes and laboratory test. eTable 2 listed the diagnosis grouping based on ICD9 standard and eTable 3 listed laboratory test grouping which was generated based on discussion with domain experts from both Stanford and Duke sides.

**eTable 2.** Strategy for Grouping the ICD9 Diagnosis Code for PE Risk Assessment

| GROUP                                               | DX SUBGROUP                                                                 | ICD start | ICD end  |
|-----------------------------------------------------|------------------------------------------------------------------------------|-----------|----------|
| CERTAIN CONDITIONS ORIGINATING IN THE PERINATAL PERIOD | MATERNAL CAUSES OF PERINATAL MORBIDITY AND MORTALITY                         | 660       | 669.99   |
|                                                     | OTHER CONDITIONS ORIGINATING IN THE PERINATAL PERIOD                          | 649.99    |          |
| COMPLICATIONS MAINLY RELATED TO PREGNANCY            | COMPLICATIONS OF THE PUERPERIUM                                              | 633.99    |          |
| COMPLICATIONS OCCURRING MAINLY IN THE COURSE OF LABOR AND DELIVERY | ECTOPIC AND MOLAR PREGNANCY                                                 | 630       | 633.99   |
| COMPLICATIONS OF PREGNANCY, CHILDBIRTH, AND THE PUERPERIUM | NORMAL DELIVERY, AND OTHER INDICATIONS FOR CARE IN PREGNANCY, LABOR, AND DELIVERY | 650       | 659.99   |
| OTHER MATERNAL AND FETAL COMPLICATIONS               | OTHER PREGNANCY WITH ABORTIVE OUTCOME                                        | 639.99    |          |
|                                                      | Anencephalus and similar anomalies                                           | 740       | 740      |
| Anomalies of respiratory system, congenital          | Cleft palate and cleft lip                                                   | 749       | 749      |
| Bulbus cordis anomalies and anomalies of cardiac septal closure | Congenital anomalies of ear, face, and neck                                  | 744       | 744      |
| Certain congenital musculoskeletal deformities       | Congenital anomalies of eye                                                  | 743       | 743      |
| Chromosomal anomalies                                | Congenital anomalies of genital organs                                       | 752       | 752      |
| CONGENITAL ANOMALIES                                 | Congenital anomalies of the integument                                       | 757       | 757      |
| Diagnosis                                                                 | Code 1 | Code 2 |
|--------------------------------------------------------------------------|--------|--------|
| Congenital anomalies of urinary system                                  | 753    | 753    |
| Other and unspecified congenital anomalies                              | 759    | 759    |
| Other congenital anomalies of circulatory system                        | 747    | 747    |
| Other congenital anomalies of digestive system                          | 751    | 751    |
| Other congenital anomalies of heart                                     | 746    | 746    |
| Other congenital anomalies of limbs                                     | 755    | 755    |
| Other congenital anomalies of nervous system                            | 742    | 742    |
| Other congenital anomalies of upper alimentary tract                    | 750    | 750    |
| Other congenital musculoskeletal anomalies                              | 756    | 756    |
| Spina bifida                                                            | 741    | 741    |
| Acquired hemolytic anemias                                              | 283    | 283    |
| **DISEASES OF THE BLOOD AND BLOOD-FORMING ORGANS**                      |        |        |
| Aplastic anemia and other bone marrow failure syndromes                 | 284    | 284    |
| Coagulation defects                                                     | 286    | 286    |
| Diseases of white blood cells                                           | 288    | 288    |
| Hereditary hemolytic anemias                                            | 282    | 282    |
| Iron deficiency anemias                                                 | 280    | 280    |
| Other and unspecified anemias                                           | 285    | 285    |
| Other deficiency anemias                                               | 281    | 281    |
| Other diseases of blood and blood-forming organs                        | 289    | 289    |
| Purpura and other hemorrhagic conditions                                | 287    | 287    |
| **ACUTE RHEUMATIC FEVER**                                               | 390    | 392.99 |
| **DISEASES OF THE CIRCULATORY SYSTEM**                                  |        |        |
| CEREBROVASCULAR DISEASE                                                 | 430    | 438.99 |
| CHRONIC RHEUMATIC HEART DISEASE                                         | 393    | 398.99 |
| **DISEASES OF ARTERIES, ARTERIOLES, AND CAPILLARIES**                   | 440    | 449.99 |
| **DISEASES OF PULMONARY CIRCULATION**                                   | 415    | 417.99 |
| **DISEASES OF VEINS AND LYMPHATICS, AND OTHER DISEASES OF CIRCULATORY**| 451    | 459.99 |
| SYSTEM                                                                   |        |        |
| HYPERTENSIVE DISEASE                                                    | 401    | 405.99 |

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| DISEASES OF THE DIGESTIVE SYSTEM | ISCHEMIC HEART DISEASE | 410 | 414.99 |
| - | OTHER FORMS OF HEART DISEASE | 420 | 429.99 |
| - | APPENDICITIS | 540 | 543.99 |
| - | DISEASES OF ESOPHAGUS, STOMACH, AND DUODENUM | 530 | 539.99 |
| - | DISEASES OF ORAL CAVITY, SALIVARY GLANDS, AND JAWS | 520 | 529.99 |
| - | Gastrointestinal mucositis (ulcerative) | 538 | 538 |
| - | HERNIA OF ABDOMINAL CAVITY | 550 | 553.99 |
| - | NONINFECTIONOUS ENTERITIS AND COLITIS | 555 | 558.99 |
| - | OTHER DISEASES OF DIGESTIVE SYSTEM | 570 | 579.99 |
| - | OTHER DISEASES OF INTESTINES AND PERITONEUM | 560 | 569.99 |

| DISEASES OF THE GENITOURINARY SYSTEM | DISEASES OF MALE GENITAL ORGANS | 600 | 608.99 |
| - | DISORDERS OF BREAST | 610 | 612.99 |
| - | INFLAMMATORY DISEASE OF FEMALE PELVIC ORGANS | 614 | 616.99 |
| - | NEPHRITIS, NEPHROTIC SYNDROME, AND NEPHROSIS | 580 | 589.99 |
| - | OTHER DISEASES OF URINARY SYSTEM | 590 | 599.99 |
| - | OTHER DISORDERS OF FEMALE GENITAL TRACT | 617 | 629.99 |

| DISEASES OF THE MUSCULOSKELETAL SYSTEM AND CONNECTIVE TISSUE | ARTHROPATHIES AND RELATED DISORDERS | 710 | 719.99 |
| - | DORSOPATHIES | 720 | 724.99 |
| - | OSTEOPATHIES, CHONDROPATHIES, AND ACQUIRED MUSCULOSKELETAL DEFORMITIES | 730 | 739.99 |
| - | RHEUMATISM, EXCLUDING THE BACK | 725 | 729.99 |

| DISEASES OF THE NERVOUS SYSTEM AND SENSE ORGANS | DISEASES OF THE EAR AND MASTOID PROCESS | 380 | 389.99 |
| - | DISORDERS OF THE EYE AND ADNEXA | 360 | 379.99 |
| - | DISORDERS OF THE PERIPHERAL NERVOUS SYSTEM | 350 | 359.99 |
| Diagnosis                                                                 | ICD-9 Codes | ICD-10 Codes |
|---------------------------------------------------------------------------|-------------|--------------|
| HEREDITARY AND DEGENERATIVE DISEASES OF THE CENTRAL NERVOUS SYSTEM       |             |              |
| INFLAMMATORY DISEASES OF THE CENTRAL NERVOUS SYSTEM                       | 320         | 326.99       |
| ORGANIC SLEEP DISORDERS                                                  | 327         | 327.99       |
| OTHER DISORDERS OF THE CENTRAL NERVOUS SYSTEM                             | 340         | 349.99       |
| OTHER HEADACHE SYNDROMES                                                 | 339         | 339.99       |
| PAIN                                                                      | 338         | 338.99       |
| ACUTE RESPIRATORY INFECTIONS                                             | 460         | 466.99       |
| DISEASES OF THE RESPIRATORY SYSTEM                                        |             |              |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ALLIED CONDITIONS               | 490         | 496.99       |
| OTHER DISEASES OF RESPIRATORY SYSTEM                                      | 510         | 519          |
| OTHER DISEASES OF THE UPPER RESPIRATORY TRACT                            | 470         | 478.99       |
| PNEUMOCONIOSES AND OTHER LUNG DISEASES DUE TO EXTERNAL AGENTS            | 500         | 508.99       |
| PNEUMONIA AND INFLUENZA INFECTIONS OF SKIN AND SUBCUTANEOUS TISSUE       | 480         | 488.99       |
| DISEASES OF THE SKIN AND SUBCUTANEOUS TISSUE                             | 680         | 686.99       |
| OTHER INFLAMMATORY CONDITIONS OF SKIN AND SUBCUTANEOUS TISSUE            |             |              |
| ENDOCRINE, NUTRITIONAL AND METABOLIC DISEASES, AND IMMUNITY DISORDERS    |             |              |
| DISEASES OF OTHER ENDOCRINE GLANDS                                        | 249         | 259.99       |
| DISORDERS OF THYROID GLAND                                               | 240         | 246.99       |
| NUTRITIONAL DEFICIENCIES                                                 | 260         | 269.99       |
| OTHER METABOLIC AND IMMUNITY DISORDERS                                   | 270         | 279.99       |
| INFECTIOUS AND PARASITIC DISEASES                                         |             |              |
| ARTHROPOD-BORNE VIRAL DISEASES                                            | 60          | 66.99        |
| HELMINTHIASES                                                            | 120         | 129.99       |
| Code | Description | 2019 | 2019 |
|------|-------------|------|------|
| 42   | Human Immunodeficiency Virus [HIV] Infection Intestinal Infectious Diseases | 42.99 | 9.99 |
| 137  | Late Effects of Infectious and Parasitic Diseases Mycoses | 139.99 | 118.99 |
| 30   | Other Bacterial Diseases Other Diseases Due to Viruses and Chlamydiae | 41.99 | 79.99 |
| 130  | Other Infectious and Parasitic Diseases Other Spirochetal Diseases | 136.99 | |
| 45   | Poliomyelitis and Other Non-Arthropod-Borne Viral Diseases and Prion Diseases of Central Nervous System Rickettsioses and Other Arthropod-Borne Diseases | 49.99 | |
| 90   | Syphilis and Other Venereal Diseases Tuberculosis | 99.99 | |
| 50   | Viral Diseases Generally Accompanied by Exanthem Zoonotic Bacterial Diseases | 59.99 | |
| 940  | Burns Certain Traumatic Complications and Unspecified Injuries | 949.99 | 959.99 |
| 996  | Complications of Surgical and Medical Care, Not Elsewhere Classified Contusion with Intact Skin Surface | 999.99 | 924.99 |
| 925  | Crushing Injury Dislocation | 929.99 | 839.99 |
| 930  | Effects of Foreign Body Entering Through Orifice Fractures | 939.99 | 829 |
| 900  | Injury to Blood Vessels Injury to Nerves and Spinal Cord | 904.99 | 957.99 |
| Code | Description |
|------|-------------|
| 860  | INTERNAL INJURY OF THORAX, ABDOMEN, AND PELVIS |
| 869.99 | INTRACRANIAL INJURY, EXCLUDING THOSE WITH SKULL FRACTURE |
| 850  | LATE EFFECTS OF INJURIES, POISONINGS, TOXIC EFFECTS, AND OTHER EXTERNAL CAUSES |
| 854.99 | OPEN WOUNDS |
| 905  | OTHER AND UNSPECIFIED EFFECTS OF EXTERNAL CAUSES |
| 909.99 | POISONING BY DRUGS, MEDICINAL AND BIOLOGICAL SUBSTANCES |
| 870  | SPRAINS AND STRAINS OF JOINTS AND ADJACENT MUSCLES |
| 897.99 | SUPERFICIAL INJURY |
| 980  | TOXIC EFFECTS OF SUBSTANCES CHIEFLY NONMEDICINAL AS TO SOURCE |
| 989.99 | INTELLECTUAL DISABILITIES |
| 990  | LATE EFFECTS OF INJURIES, POISONINGS, TOXIC EFFECTS, AND OTHER EXTERNAL CAUSES |
| 995.99 | OPEN WOUNDS |
| 999  | OTHER AND UNSPECIFIED EFFECTS OF EXTERNAL CAUSES |
| 317  | MENTAL, BEHAVIORAL AND NEURODEVELOPMENTAL DISORDERS |
| 319.99 | NEUROTIC DISORDERS, PERSONALITY DISORDERS, AND OTHER NONPSYCHOTIC MENTAL DISORDERS |
| 290  | PSYCHOSES |
| 299.99 | NEOPLASMS |
| 140  | ILL-DEFINED AND UNKNOWN CAUSES OF MORBIDITY AND MORTALITY |
| 797  | NONSPECIFIC ABNORMAL FINDINGS |
| 799.99 | General symptoms |
| 780  | Other symptoms involving abdomen and pelvis |
| 789  | Symptoms concerning nutrition, metabolism, and development |
| 781  | Symptoms involving cardiovascular system |
| 784  | Symptoms involving digestive system |
| 784  | Symptoms involving head and neck |
| 781  | Symptoms involving nervous and musculoskeletal systems |

| Code | Description |
|------|-------------|
| 780  | General symptoms |
| 783  | Other symptoms involving abdomen and pelvis |
| 783  | Symptoms concerning nutrition, metabolism, and development |
| 787  | Symptoms involving cardiovascular system |
| 787  | Symptoms involving digestive system |
| 781  | Symptoms involving head and neck |
| 781  | Symptoms involving nervous and musculoskeletal systems |

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| SUPPLEMENTARY CLASSIFICATION OF EXTERNAL CAUSES OF INJURY AND POISONING | Symptoms involving respiratory system and other chest symptoms | 786 | 786 |
| SUPPLEMENTARY CLASSIFICATION OF EXTERNAL CAUSES OF INJURY AND POISONING | Symptoms involving skin and other integumentary tissue | 782 | 782 |
| SUPPLEMENTARY CLASSIFICATION OF EXTERNAL CAUSES OF INJURY AND POISONING | Symptoms involving urinary system | 788 | 788 |
| | SUPPLEMENTARY CLASSIFICATION OF EXTERNAL CAUSES OF INJURY AND POISONING | E000 | E999.99 |
| SUPPLEMENTARY CLASSIFICATION OF FACTORS INFLUENCING HEALTH STATUS AND CONTACT WITH HEALTH SERVICES | SUPPLEMENTARY CLASSIFICATION OF FACTORS INFLUENCING HEALTH STATUS AND CONTACT WITH HEALTH SERVICES | V01 | V91.99 |
**eTable 3. Strategy for Grouping the Common Laboratory Tests for PE Risk Assessment**

| NAME                                      | GROUP     |
|-------------------------------------------|-----------|
| Albumin                                   | Albumin   |
| Albumin (Serum/Plasma)                    |           |
| Albumin, Ser/Plas                         |           |
| Albumin, Serum                            |           |
| Albumin, Serum/Plas                       |           |
| ALK PTASE Total, Serum (Manual Entry) See EMR for details | ALK       |
| Alk PTASE, Total                          |           |
| Alk PTASE, Total, Ser/Plas                |           |
| Alkaline Phosphatase                      |           |
| Alkaline Phosphatase (Serum/Plasma)       |           |
| Alkaline Phosphatase Bone                 |           |
| Alkaline Phosphatase Iso                  |           |
| Alkaline Phosphatase Total                |           |
| Alkaline Phosphatase, Total, Ser/Plas     |           |
| ALT                                       | AST       |
| ALT (Manual Entry) See EMR for details     |           |
| ALT (SGPT) OSL                            |           |
| ALT (SGPT), Ser/Plas                      |           |
| Anion Gap                                 | ANION     |
| ANION GAP                                 |           |
| Anion Gap (Serum/Plasma)                  |           |
| Anion Gap, ISTAT                          |           |
| AST                                       | AST       |
| AST (Manual Entry) See EMR for details     |           |
| AST (SGOT), Ser/Plas                      |           |
| BUN                                       | BUN       |
| BUN (Manual Entry) See EMR for details     |           |
| BUN, Arterial                             |           |
| BUN, ISTAT                                |           |
| BUN, Peripheral                           |           |
| BUN, Ser/Plas                             |           |
| BUN, Venous                               |           |
| BUN/ Creatinine Ratio                     | BUN/CREATININE |
| Bun/Creat Ratio                           |           |
| BUN/Creatinine                            |           |
| Bun/Creatinine Ratio                      |           |
| BUN/Creatinine Ratio OSL                  |           |
| Calcium                                   | Calcium   |
| Test Description                                                                 | Test Abbreviation  |
|----------------------------------------------------------------------------------|--------------------|
| Calcium (Serum/Plasma)                                                           | Calcium            |
| Creatinine                                                                       | Creatinine         |
| Creatinine (Serum)                                                               | Creatinine         |
| Creatinine (Serum/Plasma)                                                        | Creatinine         |
| Creatinine, Fluid                                                                | Creatinine         |
| Creatinine, ISTAT                                                                | Creatinine         |
| Creatinine, SER                                                                  | Creatinine         |
| Creatinine, Ser/Plas                                                             | Creatinine         |
| Creatinine, Serum                                                                | Creatinine         |
| Creatinine, ISTAT                                                                | Creatinine         |
| D-Dimer                                                                          | D-Dimer            |
| D-DIMER (MANUAL ENTRY) See EMR for details                                        | D-Dimer            |
| D-Dimer (Plasma/Whole Blood)                                                     | D-Dimer            |
| D-Dimer OSL                                                                      | D-Dimer            |
| D-Dimer, ELISA                                                                   | D-Dimer            |
| D-Dimer, Elisa                                                                   | D-Dimer            |
| D-Dimer, Quantitative                                                            | D-Dimer            |
| Glucose                                                                          | Glucose            |
| GLUCOSE                                                                          | Glucose            |
| Glucose - 1 hour                                                                 | Glucose            |
| Glucose - 2 hour                                                                 | Glucose            |
| Glucose - 3 hour                                                                 | Glucose            |
| Glucose - Fasting                                                                | Glucose            |
| Glucose (Serum/Plasma)                                                           | Glucose            |
| Glucose (Whole Blood)                                                            | Glucose            |
| Glucose , GDM Screen (Serum/Plasma)                                              | Glucose            |
| Glucose Non Fasting OSL                                                          | Glucose            |
| Glucose, ISTAT                                                                   | Glucose            |
| Glucose, Nonfasting                                                              | Glucose            |
| Glucose, Non-fasting                                                             | Glucose            |
| Glucose, Nonfasting (Serum/Plasma)                                               | Glucose            |
| Glucose, Plasma                                                                  | Glucose            |
| Glucose, Ser/Plas                                                                | Glucose            |
| Glucose, Serum                                                                   | Glucose            |
| Glucose, WB                                                                      | Glucose            |
| Glucose, Whole Blood                                                             | Glucose            |
| Glucose, ISTAT                                                                   | Glucose            |
| Hemoglobin                                                                       | Hemoglobin         |
| Hemoglobin (calc mv), ISTAT                                                       | Hemoglobin         |
| Hemoglobin (calc), ISTAT                                                          | Hemoglobin         |
| Hemoglobin (circ), ISTAT                                                          | Hemoglobin         |
| Test                        | Abbreviation    |
|-----------------------------|-----------------|
| Hemoglobin (HGB)            | Hemoglobin      |
| Hemoglobin (Manual Entry)   | Hemoglobin      |
| Hemoglobin (PBG)            | Hemoglobin      |
| Hemoglobin (xcalc), ISTAT   | Hemoglobin      |
| Hemoglobin, Plasma          | Hemoglobin      |
| Hemoglobin A1c              | Hemoglobin A1c  |
| Hemoglobin A1C              | Hemoglobin A1c  |
| Hemoglobin A1c (Manual Entry) | Hemoglobin A1c  |
| Hemoglobin A1c (Whole Blood) | Hemoglobin A1c  |
| Hemoglobin A1c (Whole Blood), POC | Hemoglobin A1c  |
| Hemoglobin A1C, POC         | Hemoglobin A1C  |
| Hgb                          | Hgb             |
| Hgb (calc mv), ISTAT        | Hgb             |
| Hgb (CIRC), ISTAT           | Hgb             |
| Hgb (circ), ISTAT           | Hgb             |
| HGB (Manual Entry) See EMR for details | HGB             |
| Hgb (post-oxy calc), ISTAT  | Hgb             |
| Hgb (xcalc), ISTAT          | Hgb             |
| INR                         | INR             |
| INR (Manual Entry) See EMR for details | INR             |
| INR (Manual)                | INR             |
| INR OSL                     | INR             |
| INR, ACLTOP Method          | INR             |
| INR, Fingerstick            | INR             |
| INR, Fingerstick {Menlo}    | INR             |
| INR, ISTAT                  | INR             |
| INR, Manual                 | INR             |
| INR, POCT                   | INR             |
| Lactate (circ), ISTAT       | Lactate         |
| Lactate (mv), ISTAT         | Lactate         |
| Lactate (post-oxy), ISTAT   | Lactate         |
| Lactate Dehyd(LD), S        | Lactate         |
| Lactate Dehydrogenase (LDH) | Lactate         |
| Lactate Dehydrogenase, Total (Serum/Plasma) | Lactate         |
| Lactate(mv), ISTAT          | Lactate         |
| Lactate(x), ISTAT           | Lactate         |
| Lactate, ISTAT              | Lactate         |
| Lactate, Whole Bld          | Lactate         |
| Lactic Acid                 | Lactic Acid     |
| Lactic Acid (Plasma)        | Lactic Acid     |
| Lactic Acid OSL             | Lactic Acid     |
| **Test**              | **Description**                        |
|----------------------|----------------------------------------|
| **Platelet**         |                                        |
| **Platelet count**   |                                        |
| **Platelet Count**   |                                        |
| **Platelet Count (Manual Entry) See EMR for details** | |
| **Platelet Count (PLT)** |                                    |
| **Platelet Ct, Manual** |                                    |
| **Platelets**        |                                        |
| **Potassium**        |                                        |
| **Potassium (circ), ISTAT** |                                |
| **Potassium (CIRC), ISTAT** |                                |
| **Potassium (Whole Blood)** |              |
| **Prothrombin Time** | **PTT**                                |
| **PROTHROMBIN TIME** |                                        |
| **Prothrombin Time (Manual Entry) See EMR for details** | |
| **Prothrombin Time, Manual** |                                |
| **PTT**              |                                        |
| **PTT (Manual)**     |                                        |
| **Sodium**           | **Sodium**                             |
| **Sodium (circ), ISTAT** |                                |
| **Sodium (CIRC), ISTAT** |                                |
| **Sodium (Manual Entry) See EMR for details** | |
| **Sodium (Serum/Plasma)** |                                |
| **Sodium (Whole Blood)** |                                |
| **Sodium (x), ISTAT** |                                        |
| **Total Alkaline Phosphatase** | **AST** |
| **Total Alkaline Phosphatase** | **ALK** |
| **Total bile acids** |                                        |
| **Total Bilirubin**  | **Bilirubin**                          |
| **Total Bilirubin (Manual Entry) See EMR for details** | |
| **Total Bilirubin, Ser/Plas** |                                |
| **Urea Nitrogen (Bun)** | **BUN**                               |
| **Urea Nitrogen (Serum/Plasma)** |                            |
| **Urea Nitrogen, Ser/Plas** |                                |
| **Urea Nitrogen,Ser/Plas** |                                |
| **Urea Nitrogen/Creatinine (Serum/Plasma)** | |
6. **Comparison between multiple machine learning models**

We experimented with multiple linear and non-linear machine learning models using the same temporal feature vector and reported the performance as AUROC and Negative Predictive Value (NPV) in eTable 4. In the manuscript, we only described the ElasticNet model which resulted the superior performance in terms of AUROC and NPV on both SHC and Duke hold-out test set.
Table 4. Comparison Between Linear and Non-Linear Machine Learning Models on the SHC and Duke Hold-Out Test Set

| Model                  | AUROC on SHC data | NPV  | AUROC on Duke data (external testset) | NPV  |
|------------------------|-------------------|------|---------------------------------------|------|
| ElasticNet model       | 0.93              | 0.81 | 0.7                                   | 0.89 |
| Logistic Regression    | 0.88              | 0.79 | 0.69                                  | 0.907|
| RandomForest           | 0.9               | 0.77 | 0.71                                  | 0.9  |
| AdaBoost               | 0.88              | 0.79 | 0.69                                  | 0.9  |

7. **Grid search for hyperparameters tuning**

For choosing the optimal hyper-parameters for the PE neural model, we applied grid-search on 10% training data as validation set and optimized the validation accuracy. The top 50 hyperparameter settings with training (acc) and validation (val acc) accuracy is summarized in eTable 5.
**Table 5.** Grid Search Results for PE Neural Model Hyperparameter Tuning on the SHC Validation Set

| epochs | val loss | loss | acc | val acc | losses | activation | batch size | optimizer | dropout | first neuron | epochs | shape | learning rate | hidden layers |
|--------|----------|------|-----|--------|--------|------------|------------|-----------|---------|--------------|--------|-------|---------------|-------------|
| 200    | 0.14     | 0.05 | 0.95| 0.85   | mean squared error | <elu> | 50         | <class 'Adam'> | 0.4     | 200          | 200    | brick | 0.0505        | 2            |
| 200    | 0.14     | 0.04 | 0.97| 0.85   | mean squared error | <elu> | 50         | <class 'RMSprop'> | 0.3     | 200          | 200    | funnel | 0.0901        | 2            |
| 100    | 0.15     | 0.04 | 0.96| 0.85   | mean squared error | <elu> | 50         | <class 'Nadam'> | 0.4     | 200          | 100    | brick | 0.0703        | 1            |
| 150    | 0.14     | 0.07 | 0.93| 0.85   | mean squared error | <elu> | 50         | <class 'Adam'> | 0.4     | 200          | 150    | funnel | 0.0208        | 2            |
| 150    | 0.15     | 0.04 | 0.96| 0.85   | mean squared error | <relu> | 100        | <class 'RMSprop'> | 0.4     | 200          | 150    | brick | 0.0802        | 2            |
| 200    | 0.15     | 0.02 | 0.98| 0.85   | mean squared error | <relu> | 50         | <class 'RMSprop'> | 0.3     | 200          | 200    | funnel | 0.0604        | 2            |
| 100    | 0.15     | 0.03 | 0.98| 0.85   | mean squared error | <relu> | 50         | <class 'Adam'> | 0.2     | 150          | 100    | funnel | 0.0802        | 2            |
| 200    | 0.15     | 0.04 | 0.95| 0.85   | mean squared error | <relu> | 100        | <class 'Adam'> | 0.4     | 200          | 200    | funnel | 0.0406        | 2            |
| Batch Size | Initial Learning Rate | Dropout Rate | Initial Char Error | Activation Function | Learning Rate Schedule | epochs | Batch Size | Loss Function | Learning Rate | Initial Char Error | Learning Rate | Batch Size | Epochs | Error | Result |
|------------|-----------------------|--------------|--------------------|---------------------|-----------------------|--------|------------|--------------|----------------|------------------|--------------|------------|--------|------|-------|
| 100        | 0.14                  | 0.05         | 0.95               | 0.85                | mean squared error    | <relu> | 50         | <class 'Adam'> | 0.4            | 150              | brick        | 0.0505    | 1      |
| 100        | 0.14                  | 0.05         | 0.95               | 0.85                | mean squared error    | <elu>  | 50         | <class 'RMSprop'> | 0.4            | 200              | funnel       | 0.0901    | 1      |
| 150        | 0.14                  | 0.03         | 0.97               | 0.85                | mean squared error    | <relu> | 50         | <class 'RMSprop'> | 0.3            | 200              | funnel       | 0.0604    | 2      |
| 100        | 0.15                  | 0.04         | 0.96               | 0.84                | mean squared error    | <elu>  | 50         | <class 'Nadam'> | 0.3            | 200              | brick        | 0.0703    | 2      |
| 200        | 0.15                  | 0.05         | 0.95               | 0.84                | mean squared error    | <elu>  | 50         | <class 'RMSprop'> | 0.2            | 200              | brick        | 0.0208    | 1      |
| 200        | 0.50                  | 0.06         | 0.98               | 0.84                | binary crossentropy   | <relu> | 50         | <class 'Adam'> | 0.2            | 100              | brick        | 0.0505    | 2      |
| 100        | 0.48                  | 0.17         | 0.95               | 0.84                | binary crossentropy   | <elu>  | 50         | <class 'RMSprop'> | 0.4            | 200              | funnel       | 0.0901    | 1      |
| 100        | 0.15                  | 0.05         | 0.95               | 0.84                | mean squared error    | <elu>  | 100        | <class 'Nadam'> | 0.4            | 200              | brick        | 0.0505    | 1      |
| 150        | 0.49                  | 0.13         | 0.96               | 0.84                | binary crossentropy   | <elu>  | 50         | <class 'RMSprop'> | 0.4            | 200              | brick        | 0.0505    | 1      |
| 150        | 0.16                  | 0.03         | 0.96               | 0.84                | mean squared error    | <elu>  | 50         | <class 'RMSprop'> | 0.3            | 200              | brick        | 0.0505    | 2      |
| Epochs | Learning Rate | Dropout Rate | Test Accuracy | Test Loss | Loss Function | Activation Function | Batch Size | Optimizer | Loss Function Class | Loss | Weight Decay | model | Time |
|--------|---------------|--------------|---------------|-----------|---------------|---------------------|------------|-----------|--------------------|------|-------------|-------|------|
| 200    | 0.15          | 0.05         | 0.95          | 0.84      | mean squared error | <elu>       | 50         | <class 'RMSprop'> | 0.4  | 100         | 200   | brick | 0.0505 | 1     |
| 150    | 0.15          | 0.06         | 0.94          | 0.84      | mean squared error | <elu>       | 100        | <class 'RMSprop'> | 0.3  | 150         | 150   | brick | 0.0406 | 2     |
| 50     | 0.15          | 0.11         | 0.88          | 0.84      | mean squared error | <elu>       | 50         | <class 'RMSprop'> | 0.4  | 150         | 50    | funnel | 0.0406 | 2     |
| 200    | 0.51          | 0.07         | 0.98          | 0.84      | binary crossentropy | <elu>       | 50         | <class 'Nadam'>  | 0.4  | 200         | 200   | brick | 0.0802 | 1     |
| 100    | 0.15          | 0.02         | 0.98          | 0.84      | mean squared error | <relu>      | 50         | <class 'Nadam'>  | 0.2  | 150         | 100   | funnel | 0.0802 | 2     |
| 200    | 0.15          | 0.03         | 0.96          | 0.84      | mean squared error | <relu>      | 50         | <class 'RMSprop'> | 0.4  | 200         | 200   | brick | 0.0505 | 0     |
| 200    | 0.15          | 0.02         | 0.98          | 0.84      | mean squared error | <relu>      | 50         | <class 'Adam'>   | 0.2  | 100         | 200   | funnel | 0.0901 | 2     |
| 50     | 0.15          | 0.04         | 0.96          | 0.84      | mean squared error | <elu>       | 50         | <class 'Nadam'>  | 0.2  | 200         | 50    | brick | 0.0802 | 1     |
| 150    | 0.15          | 0.03         | 0.97          | 0.85      | mean squared error | <relu>      | 100        | <class 'Nadam'>  | 0.4  | 200         | 150   | funnel | 0.0406 | 1     |
| N  | p1  | p2  | p3  | p4  | error          | model  | n1  | n2  | n3  | n4  | error          | model  | n1  | n2  | n3  | n4  |
|----|-----|-----|-----|-----|---------------|--------|-----|-----|-----|-----|---------------|--------|-----|-----|-----|-----|
| 200| 0.15| 0.03| 0.97| 0.84| mean squared energy <elu> | 200    | <class 'Nadam'> | 0.3  | 200 | 200 | funnel         | 0.0802 | 1   |
| 50 | 0.15| 0.08| 0.92| 0.84| mean squared energy <elu> | 50     | <class 'RMSprop'> | 0.3  | 100 | 50  | funnel         | 0.0703 | 2   |
| 100| 0.15| 0.04| 0.96| 0.84| mean squared energy <elu> | 50     | <class 'RMSprop'> | 0.1  | 100 | 100 | brick          | 0.0802 | 2   |
| 100| 0.15| 0.03| 0.97| 0.84| mean squared energy <elu> | 50     | <class 'Nadam'>  | 0.3  | 200 | 100 | funnel         | 0.0703 | 2   |
| 100| 0.15| 0.04| 0.96| 0.84| mean squared energy <elu> | 50     | <class 'Adam'>   | 0.3  | 200 | 100 | funnel         | 0.0703 | 1   |
| 100| 0.16| 0.03| 0.97| 0.84| mean squared energy <relu> | 50     | <class 'Adam'>   | 0.2  | 200 | 100 | funnel         | 0.0604 | 2   |
| 200| 0.15| 0.04| 0.96| 0.84| mean squared energy <relu> | 50     | <class 'Adam'>   | 0.4  | 150 | 200 | brick          | 0.0406 | 2   |
| 150| 0.15| 0.02| 0.98| 0.84| mean squared energy <relu> | 100    | <class 'Nadam'>  | 0.2  | 100 | 150 | funnel         | 0.0802 | 1   |
| 150| 0.15| 0.03| 0.96| 0.84| mean squared error     | 100    | <class 'Adam'>   | 0.4  | 200 | 150 | brick          | 0.0703 | 1   |
| Layer  | Input 1 | Input 2 | Input 3 | Input 4 | Loss Function | Activation | Epochs | Learning Rate | Learning Rate 2 | Architecture | Accuracy | MSE | 
|--------|---------|---------|---------|---------|---------------|------------|--------|--------------|----------------|--------------|----------|-----| 
|        | 150     | 0.15    | 0.04    | 0.96    | 0.84          | mean squared error | <elu>   | 50           | <class 'RMSprop'> | 0.2          | 150      | 150  | brick | 0.0703 | 2   | 
|        | 100     | 0.15    | 0.02    | 0.98    | 0.84          | mean squared error | <elu>   | 50           | <class 'RMSprop'> | 0.2          | 200      | 100  | funnel | 0.0802 | 1   | 
|        | 100     | 0.49    | 0.24    | 0.92    | 0.84          | binary crossentropy | <elu>   | 50           | <class 'RMSprop'> | 0.4          | 200      | 100  | funnel | 0.0406 | 2   | 
|        | 100     | 0.15    | 0.04    | 0.96    | 0.84          | mean squared error | <elu>   | 50           | <class 'RMSprop'> | 0.1          | 200      | 100  | brick | 0.0109 | 2   | 
|        | 50      | 0.16    | 0.04    | 0.96    | 0.84          | mean squared error | <elu>   | 100          | <class 'RMSprop'> | 0.3          | 150      | 50   | funnel | 0.0802 | 2   | 
|        | 50      | 0.15    | 0.05    | 0.95    | 0.84          | mean squared error | <elu>   | 50           | <class 'RMSprop'> | 0.3          | 200      | 50   | funnel | 0.0505 | 2   | 
|        | 150     | 0.15    | 0.03    | 0.97    | 0.84          | mean squared error | <elu>   | 50           | <class 'RMSprop'> | 0.3          | 200      | 150  | brick | 0.0901 | 1   | 
|        | 200     | 0.16    | 0.02    | 0.98    | 0.84          | mean squared error | <elu>   | 100          | <class 'RMSprop'> | 0.3          | 150      | 200  | brick | 0.0604 | 0   | 
|        | 150     | 0.15    | 0.03    | 0.97    | 0.84          | mean squared error | <elu>   | 100          | <class 'RMSprop'> | 0.2          | 150      | 150  | brick | 0.0802 | 1   |
| Layer Size | Learning Rate | Weight Decay |  \( R^2 \) | MSE | Activation |  \( \text{param} \) |  \( \text{opt} \) | Metric | Score |
|------------|--------------|-------------|-------|-----|------------|--------|-------|-------|-------|
| 150        | 0.15         | 0.02        | 0.98  | 0.84| mean squared error | 50     | 0.3   | 200   | 150   | funnel | 0.0802 | 1     |
| 50         | 0.15         | 0.10        | 0.89  | 0.84| mean squared error | 50     | 0.4   | 150   | 50    | funnel | 0.0505 | 2     |
| 200        | 0.50         | 0.05        | 0.98  | 0.84| binary crossentropy | 50     | 0.2   | 200   | 200   | funnel | 0.0505 | 1     |
| 100        | 0.15         | 0.04        | 0.96  | 0.84| mean squared error | 50     | 0.2   | 150   | 100   | funnel | 0.0406 | 2     |
| 100        | 0.49         | 0.21        | 0.94  | 0.84| binary crossentropy | 50     | 0.4   | 100   | 100   | brick  | 0.0802 | 2     |