Autoimmune Disease Algorithm   
External Validation Instructions

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The evaluation aims to evaluate the precision of the curated diagnosis codes for selected autoimmune diseases.

**1. Test Patients Selection:**

After running the algorithm for cases (Appendix A), randomly select two patients per sub-phenotype for 51 conditions arriving at a total of 102 patients.

After running the algorithm for controls (Appendix B), randomly select 25 patients.

**2. Validation Session:**

For each patient, use all EHR information for review. For each sub-phenotype, each case must have the autoimmune condition corresponding to the sub-phenotype. Each control must be free of any autoimmune diseases (not limited to the listed 51 conditions), chronic auto-inflammatory condition, or any selected positive serology tests.

As an output following chart review, enter information into the respective template tables and submit the completed tables via PheKB:

* Cases - Validation\_Results\_Template\_Cases.xlsx
* Controls - Validation\_Results\_Template\_Controls.xlsx

**3. Calculating PPV for cases and PPV for controls:**

PPV for cases is calculated by dividing the total number of true cases identified by validators by 102.

PPV for controls is calculated by dividing the total number of true controls identified by validators by 25 (Table 1).

**Table 1.** Validation Results Worksheet

|  |  |
| --- | --- |
|  | Number of Patients |
| True Positive for all subphenotypes |  |
| Total for all subphenotypes | 102 |
| True Positive for Controls |  |
| Total for Controls | 25 |

Appendices

**Appendix A. Autoimmune Disease Case** (AIDalgorithm\_V1\_coding\_cases.csv)

The presence of at least one autoimmune disease qualifies the patient to be a case.

A patient meeting the following condition (*Case Cohort: Condition A*) is defined as having at least one autoimmune disease:

*Case Cohort: Condition A.* Any 3 diagnosis codes on distinct days within the same disease with the second or third diagnosis at least 7 days from the first diagnosis. Of note, we are asking for three ICD codes within the same category (they may be different codes but falling within the same disease grouping).

For patients with diagnosis codes for type 1 diabetes mellitus (T1DM), an additional exclusion criterion of no type 2 diabetes mellitus (T2DM) codes is applied.  Patients meeting the case eligibility criteria will be tagged as belonging to group(s) and disease(s) based on the presence of diagnosis code(s).

Data Types: ICD9CM, ICD10CM, and SNOMED codes given.

**Appendix B. Autoimmune Disease Control** (AIDalgorithm\_V1\_coding\_controls.csv)

The absence of any selected auto-inflammatory condition, autoimmune disease, and positive serology test qualifies a patient to be a control.

A patient not having any auto-inflammatory condition, autoimmune disease, and positive serology test must meet both of the below conditions (*Control Cohort: Condition A* and *Control Cohort: Condition B*):

*Control Cohort: Condition A.* No autoimmune and auto-inflammatory diagnosis codes.

Data Types: ICD9CM, ICD10CM, and SNOMED codes given.

*Control Cohort: Condition B.*No instances of any positive serologies as defined by institutional and assay recommendations from a list of serologies (Appendix Table 1).

Data Types: LOINC codes given. In addition to LOINC codes, use institution-specific lab codes as well.

Note: An index to the coding dictionary sorted by *Conditions* is in Appendix Table 2.

Note: Opening \*.csv in Excel will strips the “.0” in ICD9 codes.

**Appendix Table 1.** Antibody Tests

|  |  |
| --- | --- |
| **#** | **Antibody Tests:** |
| 1 | Anti Nuclear Antibody (ANA) |
| 2 | Anti-Cytoplasmic Neutrophil Antibodies (ANCA)\* |
| 3 | Anti-DNA Antibody (dsDNA) |
| 4 | Cyclic Citrullinated Peptide Antibody (CCP) |
| 5 | Rheumatoid Factor (RF) |
| 6 | Beta 2 Glycoprotein I Antibody (B2 Glycoprotein 1) |
| 7 | RNA Polymerase 3 Antibody (RNA PIII) |
| 8 | Anti-Cardiolipin Antibodies (Cardiolipin)\* |
| 9 | Centromere Antibody IgG |
| 10 | Extractable Nuclear Antibodies (ENA)\* |

|  |
| --- |
| **Anti-Cytoplasmic Neutrophil Antibodies include:** |
| Serum Anti Neutrophil Cytoplasmic Antibody C Test |
| Serum Anti Neutrophil Cytoplasmic Antibody P Test |
|  |
| **Anti-Cardiolipin Antibodies include:** |
| Anti-Cardiolipin IgG Antibody Measurement |
| Anti-Cardiolipin IgM Antibody Measurement |
|  |
| **Extractable Nuclear Antibodies include:** |
| Jo 1 Autoantibody |
| Ribonucleoprotein (U1RNP) Autoantibody |
| Sclerdoma (Scl 70) Autoantibody |
| Smith (Sm) Autoantibodies |
| Sjogren's Syndrome A (SS-A) Antibodies IgG |
| Sjogren's Syndrome B (SS-A) Antibodies IgG |

**Appendix Table 2.** An index to the coding dictionary sorted by each *Condition*

|  |  |
| --- | --- |
| *Condition*, Description of Data | **Filename**, Variable Name |
| *Case Cohort: Condition A,*  Autoimmune diseases | **AIDalgorithm\_V1\_coding\_cases.csv,**  Arthritis: Ankylosing spondylitis  Arthritis: Behcet's disease  Arthritis: Palindromic rheumatism  Arthritis: Polymyalgia rheumatica  Arthritis: Psoriatic arthritis  Arthritis: Reiter's syndrome  Arthritis: Rheumatoid arthritis (RA)  Connective: Lupus erythematosus  Connective: Mixed Connective Tissue Disease (MCTD)  Connective: Sarcoidosis  Connective: Scleroderma  Connective: Sjogren's syndrome  Endocrine: Graves' Disease  Endocrine: Hashimoto's thyroiditis  Endocrine: T1D  GI: Autoimmune hepatitis  GI: Celiac Disease  GI: Crohn's disease  GI: Primary biliary cholangitis (PBC)  GI: Ulcerative colitis (UC)  Heme: Antiphospholipid syndrome (APS)  Heme: Autoimmune hemolytic anemia (AIHA)  Heme: Autoimmune neutropenia  Heme: Evans syndrome  Heme: Thrombocytopenic purpura (TTP)  Muscle: Dermatomyositis + Polymyositis  Muscle: Inflammatory and immune myopathies  Neuro: Guillain-Barre Syndrome  Neuro: Lambert-Eaton syndrome  Neuro: Multiple sclerosis  Neuro: Myasthenia gravis  Neuro: Myelitis transversa  Neuro: Optic neuritis + Optic Papillitis  Neuro: Schilder's disease  Skin: Alopecia areata  Skin: Dermatitis herpetiformis  Skin: Pemphigoid + Ocular cicatricial pemphigoid  Skin: Pemphigus  Skin: Psoriasis  Skin: Pyoderma  Skin: Raynaud  Skin: Vitiligo  Vasculitis: Arteritis + Cerebral Arteritis + Giant Cell Arteritis  Vasculitis: Goodpasture's syndrome  Vasculitis: Granulomatosis  Vasculitis: Takayasu's disease |
| *Case Cohort: Condition A,*  T2DM | **AIDalgorithm\_V1\_coding\_cases.csv,**  Type 2 Diabetes Mellitus (T2DM) |
| *Control Cohort: Condition A,*  Autoimmune diseases and Auto-inflammatory diseases | **AIDalgorithm\_V1\_coding\_controls.csv,**  Auto-inflammatory + Autoimmune (SNOMED) |
| *Control Cohort: Condition B,*  Serologies | **AIDalgorithm\_V1\_coding\_controls.csv,**  Serology: ANA  Serology: ANCA  Serology: dsDNA  Serology: CCP  Serology: RF  Serology: B2 Glycoprotein 1  Serology: RNA PIII  Serology: Cardiolipin  Serology: Centromere IgG  Serology: ENA |