

Supplementary Material

Supplementary Table S1 - List of symptomatically similar diagnoses (SSDs) used to identify potential diagnostic opportunities

| Category | ICD-9-CM | ICD-10-CM |
|---|---|--|
| Symptom-based diagnoses | 780.6, 780.60, 780.79, 783.21, 780.8, 784.0, 786.05, 786.07, 786.2, 786.3, 786.30, 786.50, 786.52, 786.59, 787.02, 787.91, 789.00, 789.01, 789.06, 789.07 | R04.2, R05, R06.00, R06.02, R06.09, R06.2, R06.3, R06.83, R06.89, R07.1, R07.81, R07.82, R07.89, R07.9, R10.11, R10.13, R10.84, R10.9, R11.0, R19.7, R50.9, R51, R53.1, R53.81, R53.83, R61, R63.4 |
| Alternative infectious disease-based diagnoses | 010, 011, 012, 013, 014, 015, 016, 017, 018, 079.99, 461.9, 462, 465.8, 465.9, 466.0, 473.9, 482.9, 486, 490, 491.9, 513.0, 599.0, 790.8 | A15, A17, A18, A19, B34.9, B97.89, G93.3, J01.90, J02.9, J06.9, J15.9, J18.2, J18.9, J20.9, J32.9, J40, J85.1, J85.2, N39.0, R50.2 |
| Alternative cardiopulmonary-based diagnoses | 135, 162.3, 162.5, 162.9, 212.3, 235.7, 239.1, 423.9, 428.0, 491.20, 491.21, 492.0, 492.8, 493.20, 493.22, 493.90, 496, 511.0, 511.1, 511.89, 514, 515, 516.9, 518.51, 518.53, 518.81, 518.84, 518.89, 786.09 | C34.10, C34.11, C34.30, C34.90, D14.30, D38.1, D49.1, D64.9, D86.0, D86.9, I31.9, I50.9, I88.9, J42, J43.9, J44.1, J44.9, J45.909, J45.998, J81.1, J82, J84.10, J84.89, J84.9, J85.0, J86.9, J91.8, J93.83, J94.1, J94.8, J94.9, J96.00, J96.01, J96.21, J96.90, J98.19, J98.4, R04.9, R09.1 |
| Alternative gastrointestinal-based diagnosis | 530.81, 560.9 | K21.9, K50.90, K56.60, K80.20 |
| Testing Imaging or Physical Examination-based diagnoses | 276.1, 284.19, 285.9, 287.5, 288.60, 289.3, 429.3, 511.9, 512.8, 512.89, 518.0, 518.3, 555.9, 574.20, 729.81, 782.2, 783.21, 784.2, 785.6, 786.6, 789.2, 790.4, 793.1, 793.11, 793.19, 799.02, V74.1 | D61.818, D69.6, D72.829, E87.1, I51.7, J90, J93.9, J98.11, R09.02, R16.1, R22.0, R22.1, R22.2, R59.0, R59.1, R59.9, R63.4, R74.0, R91.1, R91.8, Z11.1 |

Supplementary Table S2 - Count of specific symptomatically similar diagnoses (SSDs)

| ICD Code | ICD Version | ICD Description | Entire Study Period (1-365 Days Prior to histoplasmosis diagnosis) | | Delay Opportunity Window (1-97 Days Prior to histoplasmosis diagnosis) | |
|--|-------------|--|--|---|--|---|
| | | | Total Visits with SSD (% of all visits in window) | Total Patients with SSD (% of all patients) | Total Visits with SSD (% of all visits in window) | Total Patients with SSD (% of all patients) |
| <i>Alternative Cardio-pulmonary Based Diagnoses</i> | | | | | | |
| 518.89 | 9 | Other diseases of lung, not elsewhere classified | 3452 (7.7%) | 1281 (46.1%) | 2567 (9.2%) | 1139 (41.0%) |
| 496 | 9 | Chronic airway obstruction, not elsewhere classified | 1395 (3.1%) | 300 (10.8%) | 604 (2.2%) | 230 (8.3%) |
| 786.09 | 9 | Other respiratory abnormalities | 856 (1.9%) | 512 (18.4%) | 501 (1.8%) | 354 (12.7%) |
| 493.9 | 9 | Asthma, unspecified type, unspecified | 632 (1.4%) | 266 (9.6%) | 302 (1.1%) | 170 (6.1%) |
| 515 | 9 | Postinflammatory pulmonary fibrosis | 623 (1.4%) | 401 (14.4%) | 452 (1.6%) | 329 (11.8%) |
| 162.9 | 9 | Malignant neoplasm of bronchus and lung, unspecified | 591 (1.3%) | 184 (6.6%) | 380 (1.4%) | 158 (5.7%) |
| 428 | 9 | Congestive heart failure, unspecified | 379 (0.8%) | 114 (4.1%) | 148 (0.5%) | 69 (2.5%) |
| 491.21 | 9 | Obstructive chronic bronchitis with (acute) exacerbation | 314 (0.7%) | 101 (3.6%) | 141 (0.5%) | 64 (2.3%) |

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| 135 | 9 | Sarcoidosis | 289 (0.6%) | 90 (3.2%) | 182 (0.7%) | 77 (2.8%) |
| 492.8 | 9 | Other emphysema | 264 (0.6%) | 110 (4.0%) | 143 (0.5%) | 82 (3.0%) |
| 518.81 | 9 | Acute respiratory failure | 233 (0.5%) | 102 (3.7%) | 141 (0.5%) | 76 (2.7%) |
| 518.84 | 9 | Acute and chronic respiratory failure | 184 (0.4%) | 20 (0.7%) | 42 (0.2%) | 12 (0.4%) |
| 162.3 | 9 | Malignant neoplasm of upper lobe, bronchus or lung | 179 (0.4%) | 47 (1.7%) | 98 (0.4%) | 41 (1.5%) |
| 235.7 | 9 | Neoplasm of uncertain behavior of trachea, bronchus, and lung | 142 (0.3%) | 97 (3.5%) | 127 (0.5%) | 90 (3.2%) |
| 423.9 | 9 | Unspecified disease of pericardium | 125 (0.3%) | 58 (2.1%) | 96 (0.3%) | 48 (1.7%) |
| 511 | 9 | Pleurisy without mention of effusion or current tuberculosis | 120 (0.3%) | 94 (3.4%) | 78 (0.3%) | 60 (2.2%) |
| 212.3 | 9 | Benign neoplasm of bronchus and lung | 116 (0.3%) | 104 (3.7%) | 93 (0.3%) | 86 (3.1%) |
| 239.1 | 9 | Neoplasm of unspecified nature of respiratory system | 112 (0.3%) | 86 (3.1%) | 95 (0.3%) | 73 (2.6%) |
| 162.5 | 9 | Malignant neoplasm of lower lobe, bronchus or lung | 73 (0.2%) | 31 (1.1%) | 55 (0.2%) | 28 (1.0%) |
| 491.2 | 9 | Obstructive chronic bronchitis without exacerbation | 68 (0.2%) | 42 (1.5%) | 31 (0.1%) | 25 (0.9%) |
| 493.2 | 9 | Chronic obstructive asthma, unspecified | 62 (0.1%) | 38 (1.4%) | 24 (0.1%) | 21 (0.8%) |
| 514 | 9 | Pulmonary congestion and hypostasis | 55 (0.1%) | 48 (1.7%) | 37 (0.1%) | 36 (1.3%) |

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| 493.22 | 9 | Chronic obstructive asthma with (acute) exacerbation | 37 (0.1%) | 16 (0.6%) | 13 (0.0%) | 7 (0.3%) |
| 492 | 9 | Emphysematous bleb | 22 (0.0%) | 18 (0.6%) | 11 (0.0%) | 9 (0.3%) |
| 511.89 | 9 | Other specified forms of effusion, except tuberculous | 11 (0.0%) | 8 (0.3%) | 7 (0.0%) | 7 (0.3%) |
| 516.9 | 9 | Unspecified alveolar and parietoalveolar pneumonopathy | 8 (0.0%) | 8 (0.3%) | 5 (0.0%) | 5 (0.2%) |
| 518.51 | 9 | Acute respiratory failure following trauma and surgery | 7 (0.0%) | 7 (0.3%) | 3 (0.0%) | 3 (0.1%) |
| 511.1 | 9 | Pleurisy with effusion, with mention of a bacterial cause other than tuberculosis | 5 (0.0%) | 5 (0.2%) | 4 (0.0%) | 4 (0.1%) |
| J44.9 | 10 | Chronic obstructive pulmonary disease, unspecified | 129 (0.3%) | 25 (0.9%) | 53 (0.2%) | 20 (0.7%) |
| J98.4 | 10 | Other disorders of lung | 98 (0.2%) | 50 (1.8%) | 77 (0.3%) | 42 (1.5%) |
| J84.10 | 10 | Pulmonary fibrosis, unspecified | 44 (0.1%) | 23 (0.8%) | 27 (0.1%) | 17 (0.6%) |
| C34.90 | 10 | Malignant neoplasm of unspecified part of unspecified bronchus or lung | 38 (0.1%) | 9 (0.3%) | 19 (0.1%) | 8 (0.3%) |
| J84.9 | 10 | Interstitial pulmonary disease, unspecified | 37 (0.1%) | 8 (0.3%) | 27 (0.1%) | 7 (0.3%) |
| D64.9 | 10 | Anemia, unspecified | 35 (0.1%) | 18 (0.6%) | 23 (0.1%) | 14 (0.5%) |
| J45.909 | 10 | Unspecified asthma, uncomplicated | 35 (0.1%) | 16 (0.6%) | 18 (0.1%) | 11 (0.4%) |

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| J44.1 | 10 | Chronic obstructive pulmonary disease with (acute) exacerbation | 32 (0.1%) | 8 (0.3%) | 10 (0.0%) | 5 (0.2%) |
| D86.9 | 10 | Sarcoidosis, unspecified | 23 (0.1%) | 6 (0.2%) | 13 (0.0%) | 5 (0.2%) |
| J96.01 | 10 | Acute respiratory failure with hypoxia | 22 (0.0%) | 10 (0.4%) | 20 (0.1%) | 8 (0.3%) |
| J96.21 | 10 | Acute and chronic respiratory failure with hypoxia | 19 (0.0%) | 6 (0.2%) | 13 (0.0%) | 4 (0.1%) |
| I50.9 | 10 | Heart failure, unspecified | 17 (0.0%) | 4 (0.1%) | 8 (0.0%) | 3 (0.1%) |
| J43.9 | 10 | Emphysema, unspecified | 16 (0.0%) | 10 (0.4%) | 9 (0.0%) | 6 (0.2%) |
| C34.11 | 10 | Malignant neoplasm of upper lobe, right bronchus or lung | 12 (0.0%) | 4 (0.1%) | 12 (0.0%) | 4 (0.1%) |
| D86.0 | 10 | Sarcoidosis of lung | 8 (0.0%) | 7 (0.3%) | 5 (0.0%) | 4 (0.1%) |
| J85.0 | 10 | Gangrene and necrosis of lung | 7 (0.0%) | 6 (0.2%) | 7 (0.0%) | 6 (0.2%) |
| R09.1 | 10 | Pleurisy | 7 (0.0%) | 5 (0.2%) | 6 (0.0%) | 5 (0.2%) |
| J91.8 | 10 | Pleural effusion in other conditions classified elsewhere | 6 (0.0%) | 4 (0.1%) | 5 (0.0%) | 3 (0.1%) |
| J96.00 | 10 | Acute respiratory failure, unspecified whether with hypoxia or hypercapnia | 6 (0.0%) | 6 (0.2%) | 6 (0.0%) | 6 (0.2%) |
| J84.89 | 10 | Other specified interstitial pulmonary diseases | 5 (0.0%) | 5 (0.2%) | 5 (0.0%) | 5 (0.2%) |
| J96.90 | 10 | Respiratory failure, unspecified, unspecified whether with hypoxia or hypercapnia | 5 (0.0%) | 4 (0.1%) | 4 (0.0%) | 3 (0.1%) |
| D38.1 | 10 | Neoplasm of uncertain behavior of trachea, bronchus and lung | 4 (0.0%) | 4 (0.1%) | 3 (0.0%) | 3 (0.1%) |

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| I31.9 | 10 | Disease of pericardium, unspecified | 4 (0.0%) | 2 (0.1%) | 4 (0.0%) | 2 (0.1%) |
| I88.9 | 10 | Nonspecific lymphadenitis, unspecified | 4 (0.0%) | 4 (0.1%) | 3 (0.0%) | 3 (0.1%) |
| D49.1 | 10 | Neoplasm of unspecified behavior of respiratory system | 2 (0.0%) | 1 (0.0%) | 2 (0.0%) | 1 (0.0%) |
| J42 | 10 | Unspecified chronic bronchitis | 2 (0.0%) | 2 (0.1%) | 1 (0.0%) | 1 (0.0%) |
| J81.1 | 10 | Chronic pulmonary edema | 2 (0.0%) | 2 (0.1%) | 2 (0.0%) | 2 (0.1%) |
| 518.89 | 10 | Other diseases of lung, not elsewhere classified | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) |
| C34.30 | 10 | Malignant neoplasm of lower lobe, unspecified bronchus or lung | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) |
| D14.30 | 10 | Benign neoplasm of unspecified bronchus and lung | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) | 1 (0.0%) |
| <i>Alternative Gastrointestinal Based Diagnoses</i> | | | | | | |
| 530.81 | 9 | Esophageal reflux | 709 (1.6%) | 379 (13.6%) | 324 (1.2%) | 219 (7.9%) |
| 560.9 | 9 | Unspecified intestinal obstruction | 48 (0.1%) | 25 (0.9%) | 20 (0.1%) | 12 (0.4%) |
| K21.9 | 10 | Gastro-esophageal reflux disease without esophagitis | 60 (0.1%) | 34 (1.2%) | 36 (0.1%) | 24 (0.9%) |
| K50.90 | 10 | Crohn's disease, unspecified, without complications | 55 (0.1%) | 8 (0.3%) | 23 (0.1%) | 7 (0.3%) |
| K80.20 | 10 | Calculus of gallbladder without cholecystitis without obstruction | 2 (0.0%) | 2 (0.1%) | 1 (0.0%) | 1 (0.0%) |
| <i>Alternative Infectious Disease Based Diagnoses</i> | | | | | | |

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| 486 | 9 | Pneumonia, organism unspecified | 2163 (4.8%) | 748 (26.9%) | 1537 (5.5%) | 591 (21.3%) |
| 466 | 9 | Acute bronchitis | 684 (1.5%) | 473 (17.0%) | 309 (1.1%) | 231 (8.3%) |
| 599 | 9 | Urinary tract infection, site not specified | 619 (1.4%) | 293 (10.5%) | 231 (0.8%) | 141 (5.1%) |
| 461.9 | 9 | Acute sinusitis, unspecified | 524 (1.2%) | 383 (13.8%) | 173 (0.6%) | 151 (5.4%) |
| 465.9 | 9 | Acute upper respiratory infections of unspecified site | 381 (0.9%) | 303 (10.9%) | 171 (0.6%) | 144 (5.2%) |
| 473.9 | 9 | Unspecified sinusitis (chronic) | 358 (0.8%) | 200 (7.2%) | 173 (0.6%) | 117 (4.2%) |
| 462 | 9 | Acute pharyngitis | 352 (0.8%) | 276 (9.9%) | 139 (0.5%) | 125 (4.5%) |
| 490 | 9 | Bronchitis, not specified as acute or chronic | 310 (0.7%) | 230 (8.3%) | 155 (0.6%) | 130 (4.7%) |
| 79.99 | 9 | Unspecified viral infection | 184 (0.4%) | 147 (5.3%) | 117 (0.4%) | 95 (3.4%) |
| 482.9 | 9 | Bacterial pneumonia, unspecified | 148 (0.3%) | 63 (2.3%) | 91 (0.3%) | 47 (1.7%) |
| 513 | 9 | Abscess of lung | 148 (0.3%) | 86 (3.1%) | 122 (0.4%) | 75 (2.7%) |
| 491.9 | 9 | Unspecified chronic bronchitis | 53 (0.1%) | 39 (1.4%) | 34 (0.1%) | 29 (1.0%) |
| 465.8 | 9 | Acute upper respiratory infections of other multiple sites | 25 (0.1%) | 20 (0.7%) | 12 (0.0%) | 10 (0.4%) |
| 790.8 | 9 | Viremia, unspecified | 14 (0.0%) | 10 (0.4%) | 11 (0.0%) | 7 (0.3%) |
| J18.9 | 10 | Pneumonia, unspecified organism | 154 (0.3%) | 52 (1.9%) | 126 (0.5%) | 48 (1.7%) |
| N39.0 | 10 | Urinary tract infection, site not specified | 89 (0.2%) | 33 (1.2%) | 42 (0.2%) | 19 (0.7%) |
| J20.9 | 10 | Acute bronchitis, unspecified | 33 (0.1%) | 22 (0.8%) | 19 (0.1%) | 15 (0.5%) |
| J06.9 | 10 | Acute upper respiratory infection, unspecified | 28 (0.1%) | 25 (0.9%) | 17 (0.1%) | 15 (0.5%) |

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| J32.9 | 10 | Chronic sinusitis, unspecified | 27 (0.1%) | 12 (0.4%) | 11 (0.0%) | 6 (0.2%) |
| J01.90 | 10 | Acute sinusitis, unspecified | 24 (0.1%) | 18 (0.6%) | 14 (0.1%) | 10 (0.4%) |
| J02.9 | 10 | Acute pharyngitis, unspecified | 17 (0.0%) | 13 (0.5%) | 11 (0.0%) | 9 (0.3%) |
| J40 | 10 | Bronchitis, not specified as acute or chronic | 14 (0.0%) | 11 (0.4%) | 10 (0.0%) | 8 (0.3%) |
| B34.9 | 10 | Viral infection, unspecified | 12 (0.0%) | 11 (0.4%) | 9 (0.0%) | 8 (0.3%) |
| J15.9 | 10 | Unspecified bacterial pneumonia | 4 (0.0%) | 3 (0.1%) | 3 (0.0%) | 2 (0.1%) |
| B97.89 | 10 | Other viral agents as the cause of diseases classified elsewhere | 3 (0.0%) | 3 (0.1%) | 1 (0.0%) | 1 (0.0%) |
| J85.2 | 10 | Abscess of lung without pneumonia | 3 (0.0%) | 2 (0.1%) | 3 (0.0%) | 2 (0.1%) |
| J85.1 | 10 | Abscess of lung with pneumonia | 2 (0.0%) | 2 (0.1%) | 1 (0.0%) | 1 (0.0%) |
| <i>Symptom Based Diagnoses</i> | | | | | | |
| 786.5 | 9 | Chest pain, unspecified | 1782 (4.0%) | 900 (32.4%) | 1027 (3.7%) | 598 (21.5%) |
| 786.2 | 9 | Cough | 1762 (3.9%) | 940 (33.8%) | 1159 (4.1%) | 684 (24.6%) |
| 786.05 | 9 | Shortness of breath | 1551 (3.5%) | 803 (28.9%) | 946 (3.4%) | 595 (21.4%) |
| 780.6 | 9 | Fever, unspecified | 1147 (2.6%) | 496 (17.8%) | 917 (3.3%) | 416 (15.0%) |
| 780.79 | 9 | Other malaise and fatigue | 1085 (2.4%) | 614 (22.1%) | 562 (2.0%) | 386 (13.9%) |
| 789 | 9 | Abdominal pain, unspecified site | 1013 (2.3%) | 530 (19.1%) | 485 (1.7%) | 301 (10.8%) |
| 784 | 9 | Headache | 693 (1.6%) | 342 (12.3%) | 322 (1.2%) | 202 (7.3%) |
| 780.6 | 9 | Fever and other physiologic disturbances of temperature regulation | 499 (1.1%) | 196 (7.1%) | 362 (1.3%) | 155 (5.6%) |

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| 786.59 | 9 | Other chest pain | 436 (1.0%) | 287 (10.3%) | 238 (0.9%) | 179 (6.4%) |
| 787.91 | 9 | Diarrhea | 431 (1.0%) | 234 (8.4%) | 200 (0.7%) | 120 (4.3%) |
| 789.07 | 9 | Abdominal pain, generalized | 291 (0.7%) | 173 (6.2%) | 131 (0.5%) | 83 (3.0%) |
| 783.21 | 9 | Loss of weight | 271 (0.6%) | 162 (5.8%) | 185 (0.7%) | 119 (4.3%) |
| 787.02 | 9 | Nausea alone | 242 (0.5%) | 142 (5.1%) | 123 (0.4%) | 83 (3.0%) |
| 789.01 | 9 | Abdominal pain, right upper quadrant | 218 (0.5%) | 120 (4.3%) | 104 (0.4%) | 68 (2.4%) |
| 786.52 | 9 | Painful respiration | 209 (0.5%) | 152 (5.5%) | 143 (0.5%) | 106 (3.8%) |
| 789.06 | 9 | Abdominal pain, epigastric | 202 (0.5%) | 133 (4.8%) | 102 (0.4%) | 71 (2.6%) |
| 786.3 | 9 | Hemoptysis | 107 (0.2%) | 45 (1.6%) | 76 (0.3%) | 30 (1.1%) |
| 786.07 | 9 | Wheezing | 84 (0.2%) | 69 (2.5%) | 40 (0.1%) | 35 (1.3%) |
| 786.3 | 9 | Hemoptysis, unspecified | 81 (0.2%) | 44 (1.6%) | 59 (0.2%) | 34 (1.2%) |
| 780.8 | 9 | Generalized hyperhidrosis | 73 (0.2%) | 53 (1.9%) | 45 (0.2%) | 35 (1.3%) |
| R06.02 | 10 | Shortness of breath | 153 (0.3%) | 54 (1.9%) | 84 (0.3%) | 41 (1.5%) |
| R05 | 10 | Cough | 140 (0.3%) | 77 (2.8%) | 106 (0.4%) | 62 (2.2%) |
| R50.9 | 10 | Fever, unspecified | 112 (0.3%) | 41 (1.5%) | 101 (0.4%) | 37 (1.3%) |
| R07.9 | 10 | Chest pain, unspecified | 98 (0.2%) | 53 (1.9%) | 64 (0.2%) | 39 (1.4%) |
| R06.00 | 10 | Dyspnea, unspecified | 60 (0.1%) | 32 (1.2%) | 32 (0.1%) | 23 (0.8%) |
| R10.9 | 10 | Unspecified abdominal pain | 55 (0.1%) | 36 (1.3%) | 30 (0.1%) | 19 (0.7%) |
| R07.89 | 10 | Other chest pain | 54 (0.1%) | 29 (1.0%) | 28 (0.1%) | 16 (0.6%) |
| R53.83 | 10 | Other fatigue | 40 (0.1%) | 28 (1.0%) | 27 (0.1%) | 21 (0.8%) |
| R51 | 10 | Headache | 27 (0.1%) | 17 (0.6%) | 19 (0.1%) | 13 (0.5%) |
| R04.2 | 10 | Hemoptysis | 26 (0.1%) | 9 (0.3%) | 17 (0.1%) | 8 (0.3%) |
| R63.4 | 10 | Abnormal weight loss | 26 (0.1%) | 13 (0.5%) | 17 (0.1%) | 11 (0.4%) |
| R19.7 | 10 | Diarrhea, unspecified | 20 (0.0%) | 12 (0.4%) | 11 (0.0%) | 6 (0.2%) |
| R06.09 | 10 | Other forms of dyspnea | 18 (0.0%) | 11 (0.4%) | 9 (0.0%) | 7 (0.3%) |
| R07.81 | 10 | Pleurodynia | 18 (0.0%) | 12 (0.4%) | 13 (0.0%) | 8 (0.3%) |

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| R10.11 | 10 | Right upper quadrant pain | 18 (0.0%) | 10 (0.4%) | 6 (0.0%) | 5 (0.2%) |
| R10.13 | 10 | Epigastric pain | 15 (0.0%) | 12 (0.4%) | 8 (0.0%) | 7 (0.3%) |
| R06.2 | 10 | Wheezing | 14 (0.0%) | 8 (0.3%) | 10 (0.0%) | 7 (0.3%) |
| R10.84 | 10 | Generalized abdominal pain | 13 (0.0%) | 12 (0.4%) | 7 (0.0%) | 7 (0.3%) |
| R53.81 | 10 | Other malaise | 11 (0.0%) | 7 (0.3%) | 6 (0.0%) | 3 (0.1%) |
| R06.89 | 10 | Other abnormalities of breathing | 10 (0.0%) | 6 (0.2%) | 5 (0.0%) | 4 (0.1%) |
| R61 | 10 | Generalized hyperhidrosis | 10 (0.0%) | 9 (0.3%) | 7 (0.0%) | 6 (0.2%) |
| R53.1 | 10 | Weakness | 9 (0.0%) | 7 (0.3%) | 6 (0.0%) | 4 (0.1%) |
| R11.0 | 10 | Nausea | 7 (0.0%) | 6 (0.2%) | 3 (0.0%) | 3 (0.1%) |
| R07.1 | 10 | Chest pain on breathing | 5 (0.0%) | 4 (0.1%) | 2 (0.0%) | 2 (0.1%) |
| R06.83 | 10 | Snoring | 4 (0.0%) | 2 (0.1%) | 4 (0.0%) | 2 (0.1%) |
| Testing Imaging or Physical Exam Based Diagnoses | | | | | | |
| 786.6 | 9 | Swelling, mass, or lump in chest | 2263 (5.1%) | 862 (31.0%) | 1817 (6.5%) | 767 (27.6%) |
| 785.6 | 9 | Enlargement of lymph nodes | 1915 (4.3%) | 778 (28.0%) | 1531 (5.5%) | 678 (24.4%) |
| 793.1 | 9 | Lung field | 999 (2.2%) | 554 (19.9%) | 731 (2.6%) | 446 (16.0%) |
| 793.19 | 9 | Other nonspecific abnormal finding of lung field | 956 (2.1%) | 440 (15.8%) | 726 (2.6%) | 381 (13.7%) |
| 285.9 | 9 | Anemia, unspecified | 887 (2.0%) | 366 (13.2%) | 429 (1.5%) | 226 (8.1%) |
| 793.11 | 9 | Solitary pulmonary nodule | 777 (1.7%) | 313 (11.3%) | 621 (2.2%) | 282 (10.1%) |
| 555.9 | 9 | Regional enteritis of unspecified site | 698 (1.6%) | 86 (3.1%) | 277 (1.0%) | 71 (2.6%) |
| 511.9 | 9 | Unspecified pleural effusion | 449 (1.0%) | 244 (8.8%) | 328 (1.2%) | 194 (7.0%) |
| 518 | 9 | Pulmonary collapse | 405 (0.9%) | 320 (11.5%) | 310 (1.1%) | 250 (9.0%) |
| 518.3 | 9 | Pulmonary eosinophilia | 359 (0.8%) | 219 (7.9%) | 272 (1.0%) | 179 (6.4%) |

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| 783.21 | 9 | Loss of weight | 271 (0.6%) | 162 (5.8%) | 185 (0.7%) | 119 (4.3%) |
| 287.5 | 9 | Thrombocytopenia, unspecified | 251 (0.6%) | 110 (4.0%) | 150 (0.5%) | 81 (2.9%) |
| 276.1 | 9 | Hyposmolality and/or hyponatremia | 223 (0.5%) | 117 (4.2%) | 144 (0.5%) | 90 (3.2%) |
| 799.02 | 9 | Hypoxemia | 213 (0.5%) | 89 (3.2%) | 108 (0.4%) | 67 (2.4%) |
| 289.3 | 9 | Lymphadenitis, unspecified, except mesenteric | 180 (0.4%) | 137 (4.9%) | 139 (0.5%) | 114 (4.1%) |
| 784.2 | 9 | Swelling, mass, or lump in head and neck | 169 (0.4%) | 90 (3.2%) | 89 (0.3%) | 53 (1.9%) |
| 729.81 | 9 | Swelling of limb | 167 (0.4%) | 134 (4.8%) | 82 (0.3%) | 67 (2.4%) |
| 429.3 | 9 | Cardiomegaly | 145 (0.3%) | 120 (4.3%) | 79 (0.3%) | 70 (2.5%) |
| 512.8 | 9 | Other pneumothorax and air leak | 143 (0.3%) | 87 (3.1%) | 108 (0.4%) | 74 (2.7%) |
| 574.2 | 9 | Calculus of gallbladder without mention of cholecystitis, without mention of obstruction | 142 (0.3%) | 93 (3.3%) | 74 (0.3%) | 51 (1.8%) |
| 789.2 | 9 | Splenomegaly | 141 (0.3%) | 95 (3.4%) | 106 (0.4%) | 76 (2.7%) |
| V74.1 | 9 | Screening examination for pulmonary tuberculosis | 138 (0.3%) | 124 (4.5%) | 73 (0.3%) | 70 (2.5%) |
| 288.6 | 9 | Leukocytosis, unspecified | 113 (0.3%) | 72 (2.6%) | 62 (0.2%) | 45 (1.6%) |
| 284.19 | 9 | Other pancytopenia | 97 (0.2%) | 39 (1.4%) | 65 (0.2%) | 29 (1.0%) |
| 790.4 | 9 | Nonspecific elevation of levels of transaminase or lactic acid dehydrogenase [LDH] | 95 (0.2%) | 62 (2.2%) | 62 (0.2%) | 39 (1.4%) |
| 512.89 | 9 | Other pneumothorax | 89 (0.2%) | 57 (2.1%) | 76 (0.3%) | 49 (1.8%) |

| | | | | | | |
|---------|----|--|------------|-----------|------------|-----------|
| 782.2 | 9 | Localized superficial swelling, mass, or lump | 75 (0.2%) | 62 (2.2%) | 45 (0.2%) | 37 (1.3%) |
| R91.8 | 10 | Other nonspecific abnormal finding of lung field | 315 (0.7%) | 99 (3.6%) | 235 (0.8%) | 92 (3.3%) |
| R91.1 | 10 | Solitary pulmonary nodule | 212 (0.5%) | 69 (2.5%) | 162 (0.6%) | 63 (2.3%) |
| R59.0 | 10 | Localized enlarged lymph nodes | 77 (0.2%) | 41 (1.5%) | 62 (0.2%) | 34 (1.2%) |
| J90 | 10 | Pleural effusion, not elsewhere classified | 57 (0.1%) | 22 (0.8%) | 48 (0.2%) | 19 (0.7%) |
| R22.2 | 10 | Localized swelling, mass and lump, trunk | 38 (0.1%) | 20 (0.7%) | 27 (0.1%) | 17 (0.6%) |
| R59.1 | 10 | Generalized enlarged lymph nodes | 35 (0.1%) | 19 (0.7%) | 29 (0.1%) | 19 (0.7%) |
| R59.9 | 10 | Enlarged lymph nodes, unspecified | 29 (0.1%) | 22 (0.8%) | 24 (0.1%) | 19 (0.7%) |
| J98.11 | 10 | Atelectasis | 26 (0.1%) | 23 (0.8%) | 18 (0.1%) | 17 (0.6%) |
| R63.4 | 10 | Abnormal weight loss | 26 (0.1%) | 13 (0.5%) | 17 (0.1%) | 11 (0.4%) |
| R09.02 | 10 | Hypoxemia | 18 (0.0%) | 8 (0.3%) | 10 (0.0%) | 6 (0.2%) |
| J93.9 | 10 | Pneumothorax, unspecified | 16 (0.0%) | 13 (0.5%) | 13 (0.0%) | 12 (0.4%) |
| D72.829 | 10 | Elevated white blood cell count, unspecified | 15 (0.0%) | 7 (0.3%) | 10 (0.0%) | 6 (0.2%) |
| E871 | 10 | Foreign object left in body during procedure | 13 (0.0%) | 10 (0.4%) | 11 (0.0%) | 9 (0.3%) |
| R16.1 | 10 | Splenomegaly, not elsewhere classified | 13 (0.0%) | 9 (0.3%) | 13 (0.0%) | 9 (0.3%) |
| D61.818 | 10 | Other pancytopenia | 12 (0.0%) | 3 (0.1%) | 6 (0.0%) | 3 (0.1%) |

| | | | | | | |
|-------|----|---|-----------|----------|----------|----------|
| D69.6 | 10 | Thrombocytopenia, unspecified | 12 (0.0%) | 7 (0.3%) | 9 (0.0%) | 6 (0.2%) |
| Z11.1 | 10 | Encounter for screening for respiratory tuberculosis | 11 (0.0%) | 9 (0.3%) | 3 (0.0%) | 3 (0.1%) |
| I51.7 | 10 | Cardiomegaly | 9 (0.0%) | 6 (0.2%) | 7 (0.0%) | 5 (0.2%) |
| R22.1 | 10 | Localized swelling, mass and lump, neck | 7 (0.0%) | 3 (0.1%) | 6 (0.0%) | 2 (0.1%) |
| R22.0 | 10 | Localized swelling, mass and lump, head | 3 (0.0%) | 3 (0.1%) | 3 (0.0%) | 3 (0.1%) |
| R74.0 | 10 | Nonspecific elevation of levels of transaminase and lactic acid dehydrogenase [LDH] | 2 (0.0%) | 2 (0.1%) | 2 (0.0%) | 2 (0.1%) |

Supplementary Table S3 - List of Respiratory Antibiotics

Levofloxacin, Ciprofloxacin, Azithromycin, Cephalexin, Amoxicillin, Doxycycline, Moxifloxacin, Clindamycin, Vancomycin, Cefuroxime, Clarithromycin, Cefdinir, Penicillin, Ampicillin, Tetracycline, Erythromycin, Minocycline, Linezolid, Cefpodoxime, Cefaclor, Cefprozil, Dicloxacillin, Cefditoren, Cefixime, Ceftibuten, Telithromycin, Cefazolin, Cefonicid, Cefotetan, Cefoxitin, Loracarbef, Cefotaxime, Ceftizoxime, Ceftriaxone, Cefoperazone, Ceftazidime, Cefepime, Ceftaroline, Ceftolozane, Aztreonam, Imipenem, Meropenem, Ertapenem, Doripenem, Tazobactam, Sulfamethoxazole

Supplementary Table S4 – ICD and CPT codes used in risk factor analysis

| Category | Codes (ICD/CPT/CCS) |
|--------------------------|--|
| Asthma | <p><u>ICD-9-CM</u>: 493.00, 493.01, 493.02, 493.10, 493.11, 493.12, 493.20, 493.21, 493.22, 493.81, 493.82, 493.90,493.92</p> <p><u>ICD-10-CM</u>: J45.20, J45.21, J45.22, J45.30, J45.31, J45.32, J45.40, J45.41, J45.42, J45.50, J45.51, J45.52, J45.901, J45.902, J45.909, J45.990, J45.991, J45.998</p> |
| COPD | <p><u>ICD-9-CM</u>: 490, 491.0, 491.1, 491.8, 491.9</p> <p><u>ICD-10-CM</u>: J40, J41.0, J41.1, J42, J44.0, J47.0</p> |
| IPD | <p><u>ICD-9-CM</u>: 516.3, 516.30, 516.31, 516.32, 516.33, 516.34, 516.35, 516.36, 516.37</p> <p><u>ICD-10-CM</u>: J84, J84.0, J84.01, J84.02, J84.03, J84.09, J84.1, J84.10, J84.11, J84.111, J84.112, J84.113, J84.114, J84.115, J84.116, J84.117, J84.17, J84.2, J84.8, J84.81, J84.82, J84.83, J84.84, J84.841, J84.842, J84.843, J84.848, J84.89, J84.9</p> |
| HIV (CCS code) | 5 |
| Chest – CT (CPT codes) | 71260, 71250, 71270 |
| Chest – Xray (CPT codes) | 71010, 71015, 71020, 71021, 71022, 71023, 71030, 71034, 71035, 71101, 71111, 71120,71045, 71046, 71047, 71048 |

Supplementary Table S5 – Regression results for likelihood of experiencing a delay based on various geographic models

| Variable | Effect Estimate | 95% CI | P-value |
|--|-----------------|--------------|---------|
| <i>Using Metropolitan Statistical Area (MSA) Case Counts in Truven</i> | | | |
| Top 5% of MSAs | 0.947 | 0.852, 1.052 | 0.312 |
| Top 10% of MSAs | 0.897 | 0.807, 0.996 | 0.043 |
| Top 15% of MSAs | 0.933 | 0.835, 1.042 | 0.220 |
| Top 20% of MSAs | 0.950 | 0.845, 1.069 | 0.395 |
| Top 1 MSAs | 0.910 | 0.717, 1.153 | 0.434 |
| Top 2 MSAs | 0.850 | 0.715, 1.010 | 0.065 |
| Top 3 MSAs | 0.879 | 0.755, 1.023 | 0.096 |
| Top 4 MSAs | 0.882 | 0.768, 1.013 | 0.075 |
| Top 5 MSAs | 0.931 | 0.818, 1.059 | 0.278 |
| Top 10 MSAs | 0.955 | 0.855, 1.068 | 0.421 |
| Top 20 MSAs | 0.927 | 0.835, 1.029 | 0.155 |
| Top 30 MSAs | 0.899 | 0.810, 0.998 | 0.046 |
| Top 50 MSAs | 0.933 | 0.835, 1.042 | 0.220 |
| Top 100 MSAs | 0.990 | 0.868, 1.129 | 0.877 |
| <i>Using Weighted Annual MSA Incidence in MarketScan Data</i> | | | |
| Top 5% of MSAs | 0.878 | 0.504, 1.528 | 0.645 |
| Top 10% of MSAs | 1.035 | 0.792, 1.354 | 0.799 |
| Top 15% of MSAs | 1.016 | 0.829, 1.245 | 0.877 |
| Top 20% of MSAs | 1.023 | 0.853, 1.225 | 0.809 |
| Top 1 MSAs | 0.878 | 0.190, 4.050 | 0.868 |
| Top 2 MSAs | 0.862 | 0.220, 3.380 | 0.831 |
| Top 3 MSAs | 0.914 | 0.275, 3.042 | 0.884 |
| Top 4 MSAs | 1.012 | 0.343, 2.987 | 0.983 |
| Top 5 MSAs | 1.114 | 0.413, 3.001 | 0.831 |
| Top 10 MSAs | 1.137 | 0.566, 2.285 | 0.718 |
| Top 20 MSAs | 1.025 | 0.627, 1.676 | 0.921 |
| Top 30 MSAs | 0.960 | 0.711, 1.296 | 0.789 |
| Top 50 MSAs | 1.013 | 0.828, 1.240 | 0.901 |
| Top 100 MSAs | 0.990 | 0.871, 1.126 | 0.882 |
| <i>Using Incidence Based on Map from Baddley JW, et al. (Geographic distribution of endemic fungal infections among older persons, United States. Emerg Infect Dis. 2011 Sep;17(9):1664-9.)</i> | | | |
| 0.55 - 0.99 | REF | REF | REF |
| 1.14 - 1.86 | 1.145 | 0.906, 1.449 | 0.258 |
| 2.07 - 3.06 | 1.048 | 0.855, 1.283 | 0.653 |

| | | | |
|--|-------|--------------|-------|
| 3.26 - 5.19 | 1.087 | 0.907, 1.303 | 0.366 |
| 5.60 - 7.39 | 0.995 | 0.824, 1.202 | 0.959 |
| 7.84 - 12.30 | 1.019 | 0.855, 1.216 | 0.830 |
| <i>Using Regions Based on US Census Bureau Regions and Divisions by State</i> | | | |
| Midwest | REF | REF | REF |
| Northeast | 1.088 | 0.874, 1.356 | 0.450 |
| South | 0.973 | 0.886, 1.069 | 0.573 |
| West | 0.925 | 0.723, 1.183 | 0.533 |
| <i>Using Weighted Annual State Incidence in Marketscan</i> | | | |
| Incidence > 40/100,000 | 0.962 | 0.880, 1.051 | 0.389 |
| <i>Using CDC Reportable States</i> | | | |
| CDC Reportable States (AR, DE, IL, IN, KS, KY, LA, MI, MN, NE, PA, RI, and WI) | 0.976 | 0.893, 1.067 | 0.598 |

Note: Models were adjusted for all variables in Table 3. MSA = metropolitan statistical area.

Supplementary Table S6 - Count of symptomatically similar diagnoses (SSDs) by category

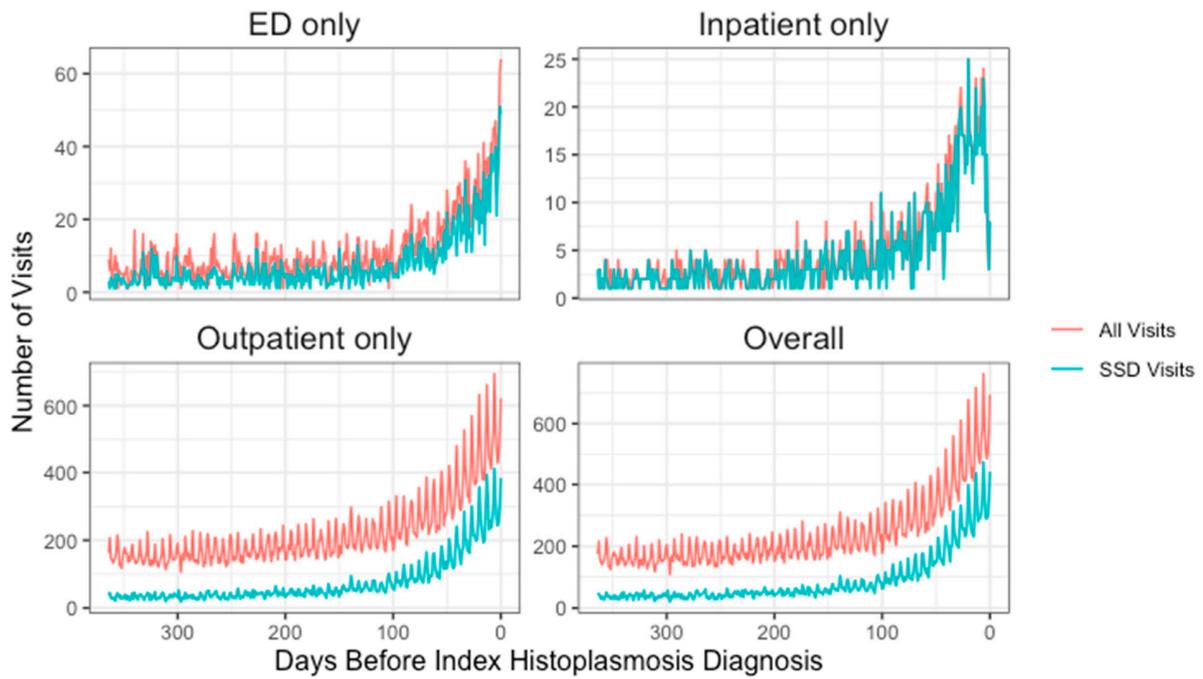
| SSD | Entire Study Period (1-365 Days Prior to histoplasmosis diagnosis) | | Delay Opportunity Window (1-97 Days Prior to histoplasmosis diagnosis) | |
|--|--|---|--|---|
| | Total Patients with SSD (% of all patients) | Total Visits with SSD (% of all visits in window) | Total Patients with SSD (% of all patients) | Total Visits with SSD (% of all visits in window) |
| Alternative-Gastrointestinal-Based Diagnoses | 437 (15.4%) | 929 (1.1%) | 260 (9.1%) | 431 (0.5%) |
| Alternative-Infectious-Disease-Based Diagnoses | 1911 (67.2%) | 6588 (7.6%) | 1349 (47.5%) | 3681 (4.0%) |
| Alternative-Cardiopulmonary-Based Diagnoses | 1916 (67.4%) | 10103 (11.6%) | 1734 (61.0%) | 6184 (6.8%) |
| Testing-, Imaging-, or Physical-Exam-Based | 2188 (77.0%) | 11652 (13.4%) | 1980 (69.7%) | 7991 (8.7%) |
| Symptom-Based Diagnoses | 2385 (83.9%) | 12105 (13.9%) | 1990 (70.0%) | 7119 (7.8%) |
| All SSDS | 2727 (96.0%) | 32140 (36.9%) | 2562 (90.1%) | 18886 (20.7%) |

Note: SSD = Symptomatically Similar Diagnosis.

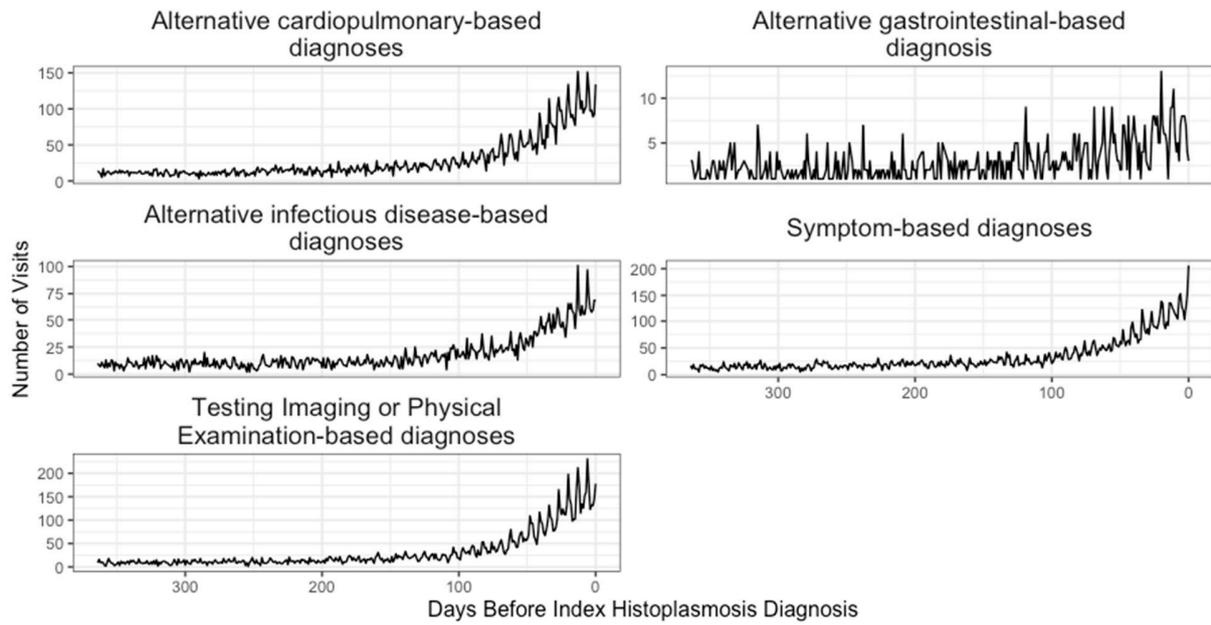
Supplementary Table S7 – Regression model stratified by ICD-9/10 index diagnosis

| Variable | ICD-9-CM Index Diagnosis (n Patients = 2,592) (OR(CI); p-value) | ICD-10-CM Index Diagnosis (n Patients = 250) (OR(CI); p-value) |
|---|--|---|
| Weekend (visits that occurred on a Saturday or Sunday) | 1.829 (1.482, 2.257); <0.001 | 2.118 (0.931, 4.821); 0.074 |
| Female Sex | 0.995 (0.908, 1.09); 0.912 | 0.787 (0.528, 1.173); 0.239 |
| Age | | |
| < 18 | REF | REF |
| 18 - 35 | 1.106 (0.874, 1.398); 0.401 | 0.421 (0.140, 1.268); 0.124 |
| 36 - 45 | 1.171 (0.930, 1.475); 0.180 | 0.382 (0.123, 1.190); 0.097 |
| 46 - 55 | 1.206 (0.966, 1.505); 0.098 | 0.501 (0.161, 1.561); 0.234 |
| 56 - 65 | 1.193 (0.956, 1.489); 0.118 | 0.783 (0.261, 2.346); 0.661 |
| >65 | 1.281 (1.005, 1.633); 0.046 | 0.772 (0.243, 2.454); 0.661 |
| Settings visited | | |
| Outpatient only | REF | REF |
| All three (inpatient, outpatient, and ED) | 0.164 (0.104, 0.257); <0.001 | 0.054 (0.003, 0.860); 0.039 |
| ED only | 11.28 (5.329, 23.878); <0.001 | 1.619 (0.615, 4.262); 0.329 |
| Inpatient only | 0.131 (0.111, 0.153); <0.001 | 0.084 (0.044, 0.164); <0.001 |
| Inpatient and ED | 0.146 (0.107, 0.199); <0.001 | 0.291 (0.056, 1.520); 0.143 |
| Inpatient and outpatient | 0.132 (0.112, 0.156); <0.001 | 0.139 (0.071, 0.271); <0.001 |
| Outpatient and ED | 2.596 (1.625, 4.147); <0.001 | 8.564 (1.117, 65.631); 0.039 |
| Urban vs. not urban | 1.040 (0.936, 1.156); 0.469 | 0.646 (0.412, 1.012); 0.057 |
| Asthma prior to change point | 1.160 (0.977, 1.376); 0.090 | 1.072 (0.490, 2.348); 0.861 |
| COPD prior to change point | 1.316 (1.140, 1.518); <0.001 | 1.119 (0.622, 2.015); 0.707 |
| IPD prior to change point | 1.627 (0.829, 3.194); 0.157 | NA |
| HIV prior to index | 0.845 (0.669, 1.068); 0.159 | 1.014 (0.113, 9.070); 0.990 |
| Chest CT prior to change point | 1.597 (1.447, 1.762); <0.001 | 2.165 (1.437, 3.262); <0.001 |
| Chest X-Ray prior to change point | 2.283 (2.045, 2.548); <0.001 | 3.706 (2.428, 5.655); <0.001 |
| Respiratory antibiotics between change point and 1 days prior to index | 1.278 (1.162, 1.404); <0.001 | 1.441 (0.970, 2.141); 0.07 |

Note: Model was also adjusted for year and month of SSD/index visit. ED = emergency department.



Supplementary Figure S1 – Trend in symptomatic similar diagnosis (SSD) visits and all visits prior to the index histoplasmosis diagnoses broken down by type of healthcare setting. The red lines depict all visits, and the blue line depicts visits with SSD-related conditions



Supplementary Figure S2 – Trend in symptomatically similar diagnosis (SSD) visits prior to diagnosis for the five SSD categories