**Supplementary Materials**

**Characterization of Symptoms and Symptom Clusters for Type 2 Diabetes Mellitus Using a Large Nationwide EHR Database (4948/5000 words – not including 50 references and abstract)**

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**Statistical methods:**

First we formulated the 2x2 contingency table for each of the 59 symptoms and the T2DM status of patients, and then the hypergeometric test (the Fisher exact test) [65] can be used to test the statistical significance whether the symptom is over or under represented among T2DM patients:

|  |  |  |  |
| --- | --- | --- | --- |
|  | T2DM  ND =1,136,301 | Non-T2DM  NND =38,102,627 | Total in Cerner  N=39,238,928 |
| Symptom | N11 | N12 | NS=N11+N12 |
| No Symptom | N21 | N22 | NNS=N21+N22 |
|  | ND=N11+N21 | NND=N12+N22 |  |

From the table above, we could calculate the risk ratio (RR) and the hypergeometric test statistics from the observed data as follows:

1. N11=the number of patients with a symptom among the T2DM cohort, and then % of prevalence of the symptom among the T2DM cohort is N11/ND
2. N12= the number of patients with a symptom in non-T2DM patients, and then % of prevalence of the symptom in non-T2DM patients is N12/NND, where N12=NS - N11 and NND = N - ND.
3. The Risk Ratio (RR) is calculated as RR =
4. Perform the hypergeometric test [65] to obtain the p-value

Similarly, a 2x2 contingency table can be constructed for two symptoms and the hypergeometric test can be performed to identify significant co-occurred symptom pairs.

For testing the significance of co-occurred symptoms with size more than 2 (say, size m>2), we need to construct a mxn contingency table and the Chi-square test could be used to the overall association of the co-occurring symptoms with the size more than 2 [66]. For example, a contingency table for the size 3 co-occurring symptoms is as follows:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Symptom 2 | | | | Total |
|  |  | Yes | | No | |  |
| Symptom 3 |  | Yes | No | Yes | No |  |
| Symptom 1 | Yes | n111 | n110 | n101 | n100 |  |
| No | n011 | n010 | n001 | n000 |  |
| Total |  |  | |  | | N |

N=the total number of occurrences with at least one diagnosis code at the admission time or discharge time of all the encounters from all T2DM patients.

**Table S1. Complete list of all 59 symptoms with the corresponding ICD9 codes**

|  |  |  |
| --- | --- | --- |
|  | Symptom category | ICD9 codes |
| 1 | pain | 307.8, 307.80, 307.89, 338, 338.0, 338.1, 338.19, 338.2, 338.29, 338.4, 388.7, 388.72, 413.9, 608.9, 625.9, 719.4, 719.40, 719.41, 719.42, 719.43, 719.44, 719.45, 719.46, 719.47, 719.48, 719.49, 723.1, 724.2, 729.5, 780.96, 784.51, 784.92, 786.5, 786.50, 786.51, 786.52, 786.59, 789, 789.0, 789.00, 789.01, 789.02, 789.03, 789.04, 789.05, 789.06, 789.07, 789.09, 789.6, 789.60, 789.61, 789.62, 789.63, 789.64, 789.65, 789.66, 789.67, 789.69, H92.0, M25.51, M25.52, M25.56, M25.57, M25.59, M54.14, M54.3, M54.5, M54.6, M54.8, M54.9, M79.60, R07.1, R07.4, R10.12, R10.30, R10.39, 786.50, 789.0, 789.00, 789.60, 350.2, 338.11, 338.12, 338.18, 338.21, 338.22, 338.28, 353.6, 368.13, 379.91, 569.42, 608.89, 625, 724.1, 909.3, 996.71, 996.72, 996.73, 996.74, 996.75, 996.76, 996.77, 996.78, 996.79, V58.89 |
| 2 | heartburn | 530.81, 536.8, 787.1, K30, 530.11 |
| 3 | shortness of breath | 786, 786.0, 786.01, 786.04, 786.05, 786.09, 786.0, 327.22, 994.7, E91.38, E96.3, E98.38, V57.0 |
| 4 | fatigue | 780.7, 780.71, 780.79, 799.3, R53, 646.81, 646.83, 992.6 |
| 5 | swelling | 457.1, 568.82, 782.2, 782.3, 784.2, 785.6, 786.6, 789.3, 789.3, 789.30, 789.31, 789.32, 789.33, 789.34, 789.35, 789.36, 789.37, 789.39, 789.5, 789.51, 789.59, R18, 782.2, 789.30, 374.82, 376.33, 379.92, 457.0, 478.25, 478.6, 607.83, 608.86, 646.10, 646.11, 646.12, 646.13, 646.14, 729.81 |
| 6 | change in bowel patterns | 564.0, 564.00, 564.5, 787.3, 787.62, 787.7, 787.91, 787.3, 787.62, 787.7, 787.91, 564, 564.01, 564.02, 564.09, K59.0, 787.63, 787.61, 006.2, 009.0, 009.1, 009.2, 009.3, 558, 558.1, 558.2, 558.42, 560.89 |
| 7 | disturbed sleep | 307.40, 307.45, 307.46, 307.47, 307.48, 307.49, 327.2, 780.5, 780.50, 780.51, 780.52, 780.53, 780.55, 780.56, 780.57, 780.58, 780.59, 786.03, 780.50, 307.41, 307.42, 327.23, 327.52, 327.59, E02.99, V69.4 |
| 8 | skin changes | 692.9, 782,782.1, R21, 692, 692.0, 692.1, 692.2, 692.3, 692.4, 692.5, 692.6, 692.7, 692.70, 692.71, 692.72, 692.73, 692.74, 692.75, 692.76, 692.77, 692.79, 692.8, 692.81, 692.82, 692.83, 692.84, 692.89, 698.4, 698.8, 704.2, 704.3, 782.0, 782, 782.8, 782.9, 782.0, 949.2, 006.6, 054.19, 057.8, 057.9, 059.8, 078.4, 112.3, 333.82, 333.85, 530.5, 691.0, 693.0, 707, 707.10, 707.11, 707.12, 707.13, 707.14, 707.15, 707.19, 707.8, 906.2, 910.2, 910.3, 911.2, 911.3, 912.2, 912.3, 913.2, 913.3, 914.2, 914.3, 915.2, 915.3, 916.2, 916.3, 917.2, 917.3, 919.2, 919.3, 941.2, 941.20, 941.21, 941.22, 941.23, 941.24, 941.25, 941.26, 941.27, 941.28, 941.29, 941.30, 941.31, 941.33, 941.34, 941.35, 941.36, 941.37, 941.38, 941.39, 942.20, 942.21, 942.22, 942.23, 942.24, 942.25, 942.29, 942.30, 942.31, 942.32, 942.33, 942.34, 942.35, 942.39, 943.20, 943.21, 943.22, 943.23, 943.24, 943.25, 943.26, 943.29, 943.30, 943.31, 943.32, 943.33, 943.34, 943.35, 943.39, 944.2, 944.20, 944.21, 944.22, 944.23, 944.24, 944.25, 944.26, 944.27, 944.28, 944.30, 944.31, 944.32, 944.33, 944.34, 944.35, 944.36, 944.37, 944.38, 945.20, 945.21, 945.22, 945.23, 945.24, 945.25, 945.26, 945.29, 945.3, 945.30, 945.31, 945.32, 945.33, 945.34, 945.35, 945.36, 945.39, 946.2, 946.3, 949.3, L98.4 |
| 9 | depression | 296.2, 296.20, 296.21, 296.22, 296.23, 296.24, 296.25, 296.26, 296.3, 296.30, 296.31, 296.32, 296.33, 296.34, 296.35, 296.36, 296.5, 296.50, 296.51, 296.52, 296.53, 296.54, 296.55, 296.56, 296.82, 311, 780.95, 799.24, 799.25, 296.99, 298.0, 301.12, 309.0, 309.1, F31.5 |
| 10 | dizziness | 386.0, 386.1, 386.11, 386.19, 386.3, 386.32, 386.4, 386.40, 386.5, 386.50, 386.51, 386.52, 386.53, 386.54, 386.56, 386.58, 386.8, 386.9, 780.2, 780.4, 786.02, R55 |
| 11 | anxiety | 300.89, 293.84, 300, 300.0, 300.02, 300.09, 300.10, 300.2, 300.21, 300.22, 300.23, 300.81, 300.82, F41.9, 799.21, 799.22, 799.23, 291.89, 292.89, 300.00, 300.01, 300.1, 300.11, 300.12, 300.13, 300.14, 300.15, 300.16, 300.20, 300.29, 300.3, 300.7, 304.60, 308, 308.3, 308.4, 308.9, 309.21, 309.24, 309.9, V61.8, V62.1, V62.8, V62.89 |
| 12 | nausea/vomiting | 307.54, 787, 787.0, 787.01, 787.02, 787.03, 787.04, 994.6, E90.3, 787.0, 536.2, 564.3, 569.87, 643 |
| 13 | cough | 519.11, 786.2, 786.8, R05, 033, 493.82 |
| 14 | headache | 307.81, 339, 339.0, 339.00, 339.01, 339.02, 339.1, 339.10, 339.11, 339.12, 339.3, 339.4, 339.42, 339.43, 339.44, 339.83, 339.84, 339.85, 339.89, 346, 346.0, 346.00, 346.01, 346.02, 346.03, 346.1, 346.10, 346.11, 346.12, 346.13, 346.2, 346.20, 346.21, 346.22, 346.23, 346.3, 346.30, 346.31, 346.32, 346.33, 346.4, 346.40, 346.41, 346.42, 346.43, 346.50, 346.51, 346.52, 346.53, 346.60, 346.61, 346.62, 346.63, 346.7, 346.70, 346.71, 346.72, 346.73, 346.8, 346.80, 346.81, 346.82, 346.83, 346.9, 346.90, 346.91, 346.92, 346.93, 668.84, 784, 784.0, R51, 784.0, 339.2, 339.20, 339.21, 339.22, 339.82, G43.9 |
| 15 | feeling confused | 293.0, 293.1, 293, 780.02, 780.97, 799.5, 799.59, 780.1, R44.0, 298.2 |
| 16 | fever | 672, 672.0, 672.00, 672.02, 672.04, 780.6, 780.6, 780.60, 780.61, 780.62, 780.63, E94.79, 780.60, 078.2, 087.9 |
| 17 | racing heartbeat | 785, 785.0, 785.1, 786.06, R00.2, 785.0 |
| 18 | other musculoskeletal symptoms | 719.5, 719.50, 719.51, 719.52, 719.53, 719.54, 719.55, 719.56, 719.57, 719.58, 719.59, 719.6, 719.60, 719.61, 719.62, 719.63, 719.64, 719.65, 719.66, 719.67, 719.68, 719.69, 723.9, 728.85, 781, 781.9, 781.99, 781, 781.0, 781.4, 781.9, 781.99 |
| 19 | difficulty swallowing | 787.2, 787.20, 787.21, 787.22, 787.23, 787.24, 787.29, 787.20, V41.6 |
| 20 | difficulty walking | 719.7, 719.70, 719.75, 719.76, 719.77, 719.78, 719.79, 781.2, 781.2 |
| 21 | dysuria | 788.1, 788.65, R30.0, 306.53 |
| 22 | urinary frequency | 788.36, 788.4, 788.41, 788.42, 788.43, 788.63 |
| 23 | urinary retention | 788.62, 788.64, 788.2, 788.20, 788.21, 788.29, 788.5, 788.20 |
| 24 | incontinence | 787.6, 787.60, 787.60, 307.6, 307.7, 788.30, 788.30, 788.33, 788.3, 788.31, 788.32, 788.34, 788.35, 788.37, 788.38, 788.39, 788.91, 625.6 |
| 25 | weakness | 728.87, 781.94, 781.94, 438.83 |
| 26 | change in weight | 783.1, 783.2, 783.21 |
| 27 | change in vision | 368, 368.1, 368.10, 368.11, 368.12, 368.16, 368.2, 368.4, 368.44, 368.8, 368.9, 781.93, H53.2, 366.53, 368.55, 368.59, 369, 369.0, 369.01, 369.02, 369.03, 369.04, 369.05, 369.06, 369.08, 369.10, 369.11, 369.12, 369.14, 369.15, 369.16, 369.20, 369.21, 369.22, 369.23, 369.24, 369.25, 369.6, 369.60, 369.61, 369.62, 369.63, 369.64, 369.65, 369.66, 369.67, 369.68, 369.69, 369.7, 369.70, 369.71, 369.72, 369.73, 369.74, 369.75, 369.76, 369.8 |
| 28 | seizures | 780.3, 780.31, 780.32, 780.33, 780.39, 345, 345.4, 345.40, 345.41, 345.5, 345.50, 345.51, 345.70, 345.71, 345.8, 345.80, 345.81 |
| 29 | hearing loss | 388.02, 388.12, 388.2, 388.40, 389, 389.0, 389.00, 389.01, 389.02, 389.03, 389.04, 389.05, 389.06, 389.08, 389.1, 389.10, 389.11, 389.12, 389.13, 389.14, 389.15, 389.16, 389.17, 389.18, 389.2, 389.20, 389.21, 389.22, 389.7, 389.8, 389.9, 388.11, H91.9, V41.2 |
| 30 | difficulty speaking | 784.41, 784.43, 784.44, 784.5, 784.3, 784.59, V40.1 |
| 31 | change in menstruation | 626, 626.0, 626.1, 626.2, 626.3, 626.4, 626.5, 626.6, 626.7, 626.8, 626.9, 625.4, 625.5, 625.8, 629, 629.1, 629.89, 629.9, V25.3 |
| 32 | itching | 698, 698.0, 698.1, 698.2, 698.3, 698.9, 708, 708.0, 708.1, 708.2, 708.3, 708.4, 708.5, 708.8, 708.9 |
| 33 | wheezing | 786.07, 786.1, R06.2 |
| 34 | other cardiovascular symptoms | 785, 785.9, 785.9 |
| 35 | trouble remembering | 780.93, 438.0 |
| 36 | other urinary symptoms | 788, 788.0, 788.6, 788.61, 788.69, 788.8, 788.9, 788.99, 788.0, 788.8 |
| 37 | other general symptoms | 780, 780.9, 780.99, 780, 780.9, 780.99, 783, 783.9, 799.2, 799.29 |
| 38 | other respiratory symptoms | 784.91, 786, 786.00, 786.9, 786.00 |
| 39 | nosebleeds | 784.7, R04.0 |
| 40 | feeling thirsty | 780.8, 783.5, 783.5, 527.7, E904 |
| 41 | change in appetite | 307.1, 307.59, 780.94, 783, 783.6, 783.0, 783.6 |
| 42 | trouble with coordination | 781.3, 315.4 |
| 43 | change in hair | 704.0, 704.00, 704.01, 704.02, 704.09, 704.1, 704.4, 704.41, 704.42, 704.8, 704.9, 704 |
| 44 | sore throat | 472, 472.1, 472.2, 476, 784.1, 034.0 |
| 45 | hemoptysis | 786.3, 786.30, 786.39, 786.30 |
| 46 | other gastrointestinal symptoms | 787.99, 787.99 |
| 47 | change in voice | 784.40, 784.49, 784.4, 784.42, 784.40, 784.49, 464, 464.0, 464.00, 464.01, 464.21, 464.4, 476.0, V41.4 |
| 48 | other head and neck symptoms | 784.9, 784.99 |
| 48 | chills | 780.64, 780.65 |
| 50 | tinnitus | 388.3, 388.30, 388.31, 388.32, H93.1 |
| 51 | drowsiness/sleepiness | 307.43, 307.44, 327.1, 780.54 |
| 52 | bruising | 782.7, 767.19 |
| 53 | other abdominal symptoms | 789, 789.9 |
| 54 | change in sexual interest or activity | 799.81, V27.5, V41.7 |
| 55 | flushing | 782.62 |
| 56 | change in taste or smell | 781.1, 781.1, V41.5 |
| 57 | pallor | 782.6, 782.61, 782.6 |
| 58 | urethral discharge | 788.7 |
| 59 | other GI symptoms | 787, 787.9 |

**Table S2. Summary of the occurrences for all 59 symptoms**

Unique Patients: the number of patients with at least one symptom occurrence; % among T2DM Patients: the percentage of patients among all the 1,136,301 T2DM patients; Occurrences: number of occurrences for the symptoms; Average # of occurrences per patient: the ratio of Occurrences over Unique Patients.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Symptom category** | **Unique patients** | **% among T2DM Patients** | **Occurrences** | **Average # of occurrences per patient** |
| pain | 681453 | 59.97% | 5852082 | 8.6 |
| heartburn | 287649 | 25.31% | 2068549 | 7.2 |
| shortness of breath | 272033 | 23.94% | 1551141 | 5.7 |
| fatigue | 263633 | 23.20% | 746994 | 2.8 |
| swelling | 243227 | 21.41% | 938008 | 3.9 |
| change in bowel patterns | 229048 | 20.16% | 610547 | 2.7 |
| disturbed sleep | 205653 | 18.10% | 1289701 | 6.3 |
| skin changes | 199848 | 17.59% | 1071183 | 5.4 |
| depression | 192015 | 16.90% | 1456498 | 7.6 |
| dizziness | 187476 | 16.50% | 563754 | 3 |
| anxiety | 170474 | 15.00% | 891975 | 5.2 |
| nausea/vomiting | 168059 | 14.79% | 496848 | 3 |
| cough | 158571 | 13.96% | 601311 | 3.8 |
| headache | 137240 | 12.08% | 434469 | 3.2 |
| feeling confused | 102742 | 9.04% | 378187 | 3.7 |
| fever | 93625 | 8.24% | 181823 | 1.9 |
| racing heartbeat | 90220 | 7.94% | 290642 | 3.2 |
| difficulty swallowing | 70151 | 6.17% | 163708 | 2.3 |
| other musculoskeletal symptoms | 68589 | 6.04% | 169194 | 2.5 |
| difficulty walking | 63759 | 5.61% | 218658 | 3.4 |
| dysuria | 62989 | 5.54% | 230987 | 3.7 |
| urinary frequency | 58367 | 5.14% | 212369 | 3.6 |
| urinary retention | 58256 | 5.13% | 143475 | 2.5 |
| incontinence | 52724 | 4.64% | 200879 | 3.8 |
| weakness | 49214 | 4.33% | 92708 | 1.9 |
| change in weight | 48401 | 4.26% | 106325 | 2.2 |
| change in vision | 38505 | 3.39% | 93659 | 2.4 |
| seizures | 35912 | 3.16% | 207516 | 5.8 |
| hearing loss | 33920 | 2.99% | 120657 | 3.6 |
| difficulty speaking | 31158 | 2.74% | 95999 | 3.1 |
| change in menstruation | 30014 | 2.64% | 168677 | 5.6 |
| itching | 26164 | 2.30% | 54661 | 2.1 |
| wheezing | 23482 | 2.07% | 63053 | 2.7 |
| other cardiovascular symptoms | 23115 | 2.03% | 58613 | 2.5 |
| trouble remembering | 22834 | 2.01% | 85212 | 3.7 |
| other urinary symptoms | 21005 | 1.85% | 61401 | 2.9 |
| other general symptoms | 19803 | 1.74% | 31949 | 1.6 |
| other respiratory symptoms | 19392 | 1.71% | 38636 | 2 |
| nosebleeds | 18279 | 1.61% | 50788 | 2.8 |
| feeling thirsty | 17571 | 1.55% | 28627 | 1.6 |
| change in appetite | 17495 | 1.54% | 27346 | 1.6 |
| trouble with coordination | 14943 | 1.32% | 41362 | 2.8 |
| change in hair | 13569 | 1.19% | 49074 | 3.6 |
| sore throat | 13114 | 1.15% | 22363 | 1.7 |
| hemoptysis | 11316 | 1.00% | 36677 | 3.2 |
| other gastrointestinal symptoms | 10813 | 0.95% | 17318 | 1.6 |
| change in voice | 10160 | 0.89% | 31729 | 3.1 |
| other head and neck symptoms | 9429 | 0.83% | 12703 | 1.3 |
| chills | 8612 | 0.76% | 11258 | 1.3 |
| tinnitus | 7563 | 0.67% | 34168 | 4.5 |
| drowsiness/sleepiness | 6973 | 0.61% | 20392 | 2.9 |
| bruising | 3643 | 0.32% | 5100 | 1.4 |
| other abdominal symptoms | 2752 | 0.24% | 4171 | 1.5 |
| change in sexual interest or activity | 1914 | 0.17% | 5310 | 2.8 |
| flushing | 1885 | 0.17% | 3177 | 1.7 |
| change in taste or smell | 1190 | 0.10% | 2405 | 2 |
| pallor | 1070 | 0.09% | 1716 | 1.6 |
| urethral discharge | 787 | 0.07% | 2062 | 2.6 |
| other GI symptoms | 15 | 0.00% | 16 | 1.1 |

**Table S3. The risk ratios of symptoms among T2DM versus patients without T2DM in the database for all 59 symptoms**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Symptom Category | Rank by risk ratio | Freq in T2DM (prevalence in %) | Freq in non-T2DM (prevalence in %) | Risk ratio | P value |
| difficulty speaking | 1 | 31158 (2.742) | 243468 (0.639) | 4.29 | 0 |
| feeling confused | 2 | 102742 (9.042) | 843558 (2.214) | 4.08 | 0 |
| trouble remembering | 3 | 22834 (2.01) | 192746 (0.506) | 3.97 | 0 |
| weakness | 4 | 49214 (4.331) | 491100 (1.289) | 3.36 | 0 |
| drowsiness/sleepiness | 5 | 6973 (0.614) | 71245 (0.187) | 3.28 | 0 |
| heartburn | 6 | 287649 (25.315) | 3066940 (8.049) | 3.14 | 0 |
| chills | 7 | 8612 (0.758) | 92055 (0.242) | 3.14 | 0 |
| change in vision | 8 | 38505 (3.389) | 449179 (1.179) | 2.87 | 0 |
| trouble with coordination | 9 | 14943 (1.315) | 177719 (0.466) | 2.82 | 0 |
| feeling thirsty | 10 | 17571 (1.546) | 210252 (0.552) | 2.80 | 0 |
| fatigue | 11 | 263633 (23.201) | 3226020 (8.467) | 2.74 | 0 |
| change in appetite | 12 | 17495 (1.54) | 214156 (0.562) | 2.74 | 0 |
| shortness of breath | 13 | 272038 (23.941) | 3352931 (8.8) | 2.72 | 0 |
| pallor | 14 | 1070 (0.094) | 13272 (0.035) | 2.70 | 9.63E-165 |
| other respiratory symptoms | 15 | 19392 (1.707) | 248513 (0.652) | 2.62 | 0 |
| other GI symptoms | 16 | 73 (0.006) | 942 (0.002) | 2.60 | 3.65E-12 |
| urinary frequency | 17 | 58367 (5.137) | 773193 (2.029) | 2.53 | 0 |
| disturbed sleep | 18 | 205653 (18.098) | 2732175 (7.171) | 2.52 | 0 |
| change in weight | 19 | 48401 (4.26) | 652075 (1.711) | 2.49 | 0 |
| nosebleeds | 20 | 18279 (1.609) | 249690 (0.655) | 2.45 | 0 |
| flushing | 21 | 1885 (0.166) | 26530 (0.07) | 2.38 | 5.06E-229 |
| dizziness | 22 | 187476 (16.499) | 2643079 (6.937) | 2.38 | 0 |
| urinary retention | 23 | 58256 (5.127) | 859444 (2.256) | 2.27 | 0 |
| other musculoskeletal symptoms | 24 | 79276 (6.977) | 1219450 (3.2) | 2.18 | 0 |
| other abdominal symptoms | 25 | 2752 (0.242) | 42564 (0.112) | 2.17 | 3.74E-273 |
| difficulty walking | 26 | 63759 (5.611) | 1017541 (2.671) | 2.10 | 0 |
| other head and neck symptoms | 27 | 9429 (0.83) | 150985 (0.396) | 2.09 | 0 |
| dysuria | 28 | 62989 (5.543) | 1012540 (2.657) | 2.09 | 0 |
| hemoptysis | 29 | 11316 (0.996) | 190457 (0.5) | 1.99 | 0 |
| change in sexual interest or activity | 30 | 1914 (0.168) | 33276 (0.087) | 1.93 | 5.22E-143 |
| depression | 31 | 192015 (16.898) | 3386343 (8.887) | 1.90 | 0 |
| swelling | 32 | 243227 (21.405) | 4321448 (11.342) | 1.89 | 0 |
| anxiety | 33 | 170476 (15.003) | 3046280 (7.995) | 1.88 | 0 |
| other urinary symptoms | 34 | 21005 (1.849) | 380192 (0.998) | 1.85 | 0 |
| incontinence | 35 | 52724 (4.64) | 1002894 (2.632) | 1.76 | 0 |
| difficulty swallowing | 36 | 70151 (6.174) | 1348135 (3.538) | 1.74 | 0 |
| cough | 37 | 158571 (13.955) | 3231811 (8.482) | 1.65 | 0 |
| other cardiovascular symptoms | 38 | 23115 (2.034) | 472252 (1.239) | 1.64 | 0 |
| change in hair | 39 | 13569 (1.194) | 277808 (0.729) | 1.64 | 0 |
| wheezing | 40 | 23482 (2.067) | 493298 (1.295) | 1.60 | 0 |
| racing heartbeat | 41 | 90222 (7.94) | 1910780 (5.015) | 1.58 | 0 |
| seizures | 42 | 35912 (3.16) | 840232 (2.205) | 1.43 | 0 |
| itching | 43 | 26179 (2.304) | 634781 (1.666) | 1.38 | 0 |
| change in bowel patterns | 44 | 229048 (20.157) | 5692234 (14.939) | 1.35 | 0 |
| skin changes | 45 | 199848 (17.588) | 5041622 (13.232) | 1.33 | 0 |
| tinnitus | 46 | 7563 (0.666) | 191378 (0.502) | 1.33 | 4.57E-118 |
| bruising | 47 | 3643 (0.321) | 96512 (0.253) | 1.27 | 9.97E-42 |
| hearing loss | 48 | 33920 (2.985) | 913614 (2.398) | 1.24 | 0 |
| other general symptoms | 49 | 19804 (1.743) | 534982 (1.404) | 1.24 | 1.01E-186 |
| other gastrointestinal symptoms | 50 | 10813 (0.952) | 301071 (0.79) | 1.20 | 5.42E-77 |
| nausea/vomiting | 51 | 168059 (14.79) | 4686387 (12.299) | 1.20 | 0 |
| change in taste or smell | 52 | 1190 (0.105) | 34909 (0.092) | 1.14 | 4.60E-06 |
| sore throat | 53 | 13114 (1.154) | 819741 (2.151) | 0.54 | 0 |
| urethral discharge | 54 | 787 (0.069) | 32208 (0.085) | 0.82 | 6.68E-09 |
| headache | 55 | 137240 (12.078) | 6064562 (15.916) | 0.76 | 0 |
| change in voice | 56 | 10160 (0.894) | 500471 (1.313) | 0.68 | 0 |
| change in menstruation | 57 | 30014 (2.641) | 1601526 (4.203) | 0.63 | 0 |
| pain | 58 | 681455 (59.971) | 38513305 (101.078) | 0.59 | 0 |
| fever | 59 | 93625 (8.239) | 5585192 (14.658) | 0.56 | 0 |

**Table S4. Summary statistics for all sizes of the co-occurring symptoms**

# of unique clusters: the number of unique combination of co-occurred symptoms for each size; # of patients: the number of patients with the co-occurred symptoms for each size; % among T2DM patients: percentage of patients among all T2DM patients; # of encounters: the number of encounters for the corresponding patients; # of occurrence: the number of occurrence of the co-occurred symptoms for each size; Average # of occurrence per patient: the ratio of number of occurrences over the number of patients for each co-occurring symptom size.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Cluster size | # of unique clusters | # of patients | % among T2DM patients | # of encounters | # of occurrence | Average # of occurrence per patient |
| 2 | 1516 | 547016 | 48.14% | 1501191 | 1594999 | 2.92 |
| 3 | 11202 | 279878 | 24.63% | 526113 | 543584 | 1.94 |
| 4 | 25839 | 129211 | 11.37% | 199673 | 203393 | 1.57 |
| 5 | 28148 | 57864 | 5.09% | 79025 | 80054 | 1.38 |
| 6 | 19077 | 24833 | 2.19% | 30666 | 30944 | 1.25 |
| 7 | 9866 | 10328 | 0.91% | 11868 | 11954 | 1.16 |
| 8 | 4506 | 4333 | 0.38% | 4807 | 4844 | 1.12 |
| 9 | 1933 | 1862 | 0.16% | 2001 | 2023 | 1.09 |
| 10 | 788 | 754 | 0.07% | 819 | 830 | 1.1 |
| 11 | 346 | 340 | 0.03% | 358 | 362 | 1.06 |
| 12 | 168 | 166 | 0.01% | 170 | 175 | 1.05 |
| 13 | 85 | 82 | 0.01% | 94 | 100 | 1.22 |
| 14 | 43 | 43 | 0.00% | 43 | 44 | 1.02 |
| 15 | 18 | 18 | 0.00% | 18 | 18 | 1 |
| 16 | 6 | 6 | 0.00% | 6 | 6 | 1 |
| 17 | 5 | 5 | 0.00% | 5 | 6 | 1.2 |
| 18 | 3 | 3 | 0.00% | 3 | 3 | 1 |
| 19 | 2 | 2 | 0.00% | 2 | 3 | 1.5 |
| 27 | 1 | 1 | 0.00% | 1 | 1 | 1 |

**Table S5. Top 20 significant co-occurring symptoms for size 2 (ranked by the number of co-occurrences)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Symptom 1** | **Symptom 2** | **# of Occurrence for all sizes** | **# of Occurrence for symptom 1** | **# of Occurrence for symptom 2** | **RR** | **Adjusted p value** |
| change in bowel patterns | pain | 149284 | 610547 | 5852082 | 1.76 | 0 |
| nausea/vomiting | pain | 148115 | 496848 | 5852082 | 2.30 | 0 |
| anxiety | pain | 141938 | 891975 | 5852082 | 1.03 | 1.89E-17 |
| anxiety | depression | 137124 | 891975 | 1456498 | 4.51 | 0 |
| disturbed sleep | heartburn | 124401 | 1289701 | 2068549 | 1.83 | 0 |
| depression | heartburn | 116558 | 1456498 | 2068549 | 1.49 | 0 |
| anxiety | heartburn | 96322 | 891975 | 2068549 | 2.08 | 0 |
| depression | disturbed sleep | 87144 | 1456498 | 1289701 | 1.80 | 0 |
| headache | pain | 78995 | 434469 | 5852082 | 1.21 | 0 |
| change in bowel patterns | heartburn | 67388 | 610547 | 2068549 | 2.13 | 0 |
| anxiety | disturbed sleep | 67214 | 891975 | 1289701 | 2.29 | 0 |
| change in bowel patterns | nausea/vomiting | 63158 | 610547 | 496848 | 8.82 | 0 |
| disturbed sleep | shortness of breath | 61726 | 1289701 | 1551141 | 1.17 | 0 |
| shortness of breath | swelling | 44791 | 1551141 | 938008 | 1.17 | 9.3E-213 |
| skin changes | swelling | 43699 | 1071183 | 938008 | 1.67 | 0 |
| cough | shortness of breath | 42175 | 601311 | 1551141 | 1.75 | 0 |
| fatigue | shortness of breath | 41005 | 746994 | 1551141 | 1.35 | 0 |
| heartburn | nausea/vomiting | 37681 | 2068549 | 496848 | 1.41 | 0 |
| change in bowel patterns | depression | 37323 | 610547 | 1456498 | 1.62 | 0 |
| other musculoskeletal symptoms | pain | 36876 | 169194 | 5852082 | 1.51 | 0 |

**Table S6. Top 20 most frequently co-occurred symptoms for size 2 (ranked by the number of patients)**

Occurrence (N): the number of occurrences of the co-occurring symptoms of size 2; # of patients: the number of patients with at least one co-occurred symptoms; N per patient: average number of occurrences per patient.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Occurrence (N)** | **# of patient** | **N per patient** | **Symptom 1** | **Symptom 2** |
| 86277 | 58431 | 1.48 | pain | heartburn |
| 71256 | 53765 | 1.33 | pain | swelling |
| 63963 | 48109 | 1.33 | pain | shortness of breath |
| 61661 | 41728 | 1.48 | pain | nausea/vomiting |
| 53507 | 41031 | 1.30 | pain | change in bowel patterns |
| 43844 | 29626 | 1.48 | pain | disturbed sleep |
| 38705 | 29034 | 1.33 | pain | skin changes |
| 37560 | 19057 | 1.97 | depression | anxiety |
| 35439 | 23813 | 1.49 | pain | depression |
| 33919 | 23035 | 1.47 | pain | anxiety |
| 32643 | 20363 | 1.60 | heartburn | disturbed sleep |
| 30744 | 24905 | 1.23 | pain | fatigue |
| 28060 | 20878 | 1.34 | pain | headache |
| 22988 | 10537 | 2.18 | skin changes | swelling |
| 22689 | 18781 | 1.21 | pain | dizziness |
| 21279 | 16110 | 1.32 | shortness of breath | disturbed sleep |
| 21131 | 14733 | 1.43 | depression | heartburn |
| 18607 | 15833 | 1.18 | shortness of breath | cough |
| 17150 | 13615 | 1.26 | shortness of breath | swelling |
| 17067 | 10880 | 1.57 | depression | disturbed sleep |

**Table S7. Top 20 mostly frequently co-occurred symptoms for size 3 (ranked by the number of patients)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| N | # of patient | N per patient | Symptom 1 | Symptom 2 | Symptom 3 |
| 16266 | 13232 | 1.23 | change in bowel patterns | nausea/vomiting | pain |
| 12021 | 8738 | 1.38 | disturbed sleep | heartburn | pain |
| 11437 | 8318 | 1.37 | anxiety | depression | pain |
| 8799 | 6821 | 1.29 | depression | heartburn | pain |
| 8276 | 6508 | 1.27 | anxiety | heartburn | pain |
| 7121 | 5524 | 1.29 | anxiety | depression | heartburn |
| 6924 | 6057 | 1.14 | change in bowel patterns | heartburn | pain |
| 5709 | 3643 | 1.57 | anxiety | depression | disturbed sleep |
| 5514 | 4758 | 1.16 | heartburn | nausea/vomiting | pain |
| 5448 | 3892 | 1.40 | depression | disturbed sleep | heartburn |
| 5302 | 3976 | 1.33 | depression | disturbed sleep | pain |
| 5037 | 4526 | 1.11 | heartburn | pain | shortness of breath |
| 4476 | 3912 | 1.14 | pain | shortness of breath | swelling |
| 4293 | 3699 | 1.16 | disturbed sleep | pain | shortness of breath |
| 4019 | 3093 | 1.30 | anxiety | disturbed sleep | pain |
| 3813 | 3487 | 1.09 | cough | pain | shortness of breath |
| 3413 | 3137 | 1.09 | fatigue | pain | shortness of breath |
| 3322 | 2798 | 1.19 | pain | skin changes | swelling |
| 3218 | 2853 | 1.13 | nausea/vomiting | pain | shortness of breath |
| 3175 | 2606 | 1.22 | headache | nausea/vomiting | pain |

**Table S8. Top 20 mostly frequently co-occurred symptoms for size 4 (ranked by the number of patients)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| N | # of patient | N per patient | Symptom 1 | Symptom 2 | Symptom 3 | Symptom 4 |
| 1890 | 1490 | 1.27 | anxiety | depression | disturbed sleep | heartburn |
| 609 | 542 | 1.12 | anxiety | change in bowel patterns | depression | heartburn |
| 554 | 114 | 4.86 | change in hair | difficulty walking | other general symptoms | skin changes |
| 455 | 421 | 1.08 | anxiety | depression | heartburn | pain |
| 448 | 365 | 1.23 | anxiety | depression | headache | heartburn |
| 359 | 314 | 1.14 | anxiety | depression | heartburn | nausea/vomiting |
| 301 | 271 | 1.11 | change in bowel patterns | depression | disturbed sleep | heartburn |
| 275 | 237 | 1.16 | anxiety | depression | disturbed sleep | pain |
| 271 | 246 | 1.10 | anxiety | depression | disturbed sleep | heartburn |
| 270 | 241 | 1.12 | anxiety | change in bowel patterns | depression | disturbed sleep |
| 249 | 230 | 1.08 | anxiety | depression | heartburn | pain |
| 236 | 222 | 1.06 | anxiety | change in bowel patterns | depression | nausea/vomiting |
| 236 | 189 | 1.25 | anxiety | depression | disturbed sleep | headache |
| 233 | 213 | 1.09 | anxiety | change in bowel patterns | disturbed sleep | heartburn |
| 232 | 222 | 1.05 | depression | disturbed sleep | heartburn | pain |
| 232 | 71 | 3.27 | change in hair | other general symptoms | pain | skin changes |
| 220 | 199 | 1.11 | anxiety | disturbed sleep | heartburn | pain |
| 211 | 168 | 1.26 | depression | disturbed sleep | headache | heartburn |
| 210 | 186 | 1.13 | anxiety | depression | disturbed sleep | headache |
| 209 | 199 | 1.05 | anxiety | depression | fatigue | heartburn |

**Table S9. Top 20 mostly frequently co-occurred symptoms for size 5 (ranked by the number of patients)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| N | # of patient | N per patient | Symptom 1 | Symptom 2 | Symptom 3 | Symptom 4 | Symptom 5 |
| 1890 | 1490 | 1.27 | anxiety | depression | disturbed sleep | heartburn | pain |
| 609 | 542 | 1.12 | anxiety | change in bowel patterns | depression | heartburn | pain |
| 554 | 114 | 4.86 | change in hair | difficulty walking | other general symptoms | skin changes | swelling |
| 455 | 421 | 1.08 | anxiety | depression | heartburn | pain | shortness of breath |
| 448 | 365 | 1.23 | anxiety | depression | headache | heartburn | pain |
| 359 | 314 | 1.14 | anxiety | depression | heartburn | nausea/vomiting | pain |
| 301 | 271 | 1.11 | change in bowel patterns | depression | disturbed sleep | heartburn | pain |
| 275 | 237 | 1.16 | anxiety | depression | disturbed sleep | pain | shortness of breath |
| 271 | 246 | 1.10 | anxiety | depression | disturbed sleep | heartburn | shortness of breath |
| 270 | 241 | 1.12 | anxiety | change in bowel patterns | depression | disturbed sleep | pain |
| 249 | 230 | 1.08 | anxiety | depression | heartburn | pain | swelling |
| 236 | 222 | 1.06 | anxiety | change in bowel patterns | depression | nausea/vomiting | pain |
| 236 | 189 | 1.25 | anxiety | depression | disturbed sleep | headache | heartburn |
| 233 | 213 | 1.09 | anxiety | change in bowel patterns | disturbed sleep | heartburn | pain |
| 232 | 222 | 1.05 | depression | disturbed sleep | heartburn | pain | shortness of breath |
| 232 | 71 | 3.27 | change in hair | other general symptoms | pain | skin changes | swelling |
| 220 | 199 | 1.11 | anxiety | disturbed sleep | heartburn | pain | shortness of breath |
| 211 | 168 | 1.26 | depression | disturbed sleep | headache | heartburn | pain |
| 210 | 186 | 1.13 | anxiety | depression | disturbed sleep | headache | pain |
| 209 | 199 | 1.05 | anxiety | depression | fatigue | heartburn | pain |

**Table S10. Top 20 mostly frequently co-occurred symptoms for size 6 (ranked by the number of patients)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| N | # of patient | N per patient | Symptom 1 | Symptom 2 | Symptom 3 | Symptom 4 | Symptom 5 | Symptom 6 |
| 252 | 216 | 1.17 | anxiety | depression | disturbed sleep | headache | heartburn | pain |
| 245 | 232 | 1.06 | anxiety | change in bowel patterns | depression | disturbed sleep | heartburn | pain |
| 219 | 199 | 1.10 | anxiety | depression | disturbed sleep | heartburn | pain | shortness of breath |
| 136 | 129 | 1.05 | anxiety | change in bowel patterns | depression | heartburn | nausea/vomiting | pain |
| 118 | 111 | 1.06 | anxiety | depression | disturbed sleep | heartburn | pain | swelling |
| 107 | 104 | 1.03 | anxiety | depression | disturbed sleep | heartburn | pain | skin changes |
| 103 | 37 | 2.78 | change in hair | difficulty walking | other general symptoms | pain | skin changes | swelling |
| 93 | 82 | 1.13 | anxiety | depression | disturbed sleep | dizziness | heartburn | pain |
| 93 | 87 | 1.07 | anxiety | depression | disturbed sleep | heartburn | nausea/vomiting | pain |
| 79 | 75 | 1.05 | anxiety | depression | disturbed sleep | fatigue | heartburn | pain |
| 72 | 69 | 1.04 | anxiety | depression | disturbed sleep | feeling confused | heartburn | pain |
| 71 | 63 | 1.13 | anxiety | depression | disturbed sleep | heartburn | incontinence | pain |
| 69 | 67 | 1.03 | anxiety | change in bowel patterns | depression | headache | heartburn | pain |
| 57 | 56 | 1.02 | anxiety | depression | disturbed sleep | heartburn | pain | racing heartbeat |
| 55 | 25 | 2.20 | depression | disturbed sleep | heartburn | incontinence | shortness of breath | swelling |
| 52 | 49 | 1.06 | change in bowel patterns | depression | disturbed sleep | heartburn | nausea/vomiting | pain |
| 50 | 50 | 1.00 | anxiety | change in bowel patterns | depression | fatigue | heartburn | pain |
| 46 | 44 | 1.05 | anxiety | change in bowel patterns | depression | heartburn | pain | shortness of breath |
| 46 | 45 | 1.02 | anxiety | depression | headache | heartburn | nausea/vomiting | pain |
| 45 | 39 | 1.15 | anxiety | depression | difficulty swallowing | disturbed sleep | heartburn | pain |

**Table S11. Top 20 significant co-occurring symptoms for size 3 (ranked by the Chi-square statistics)**

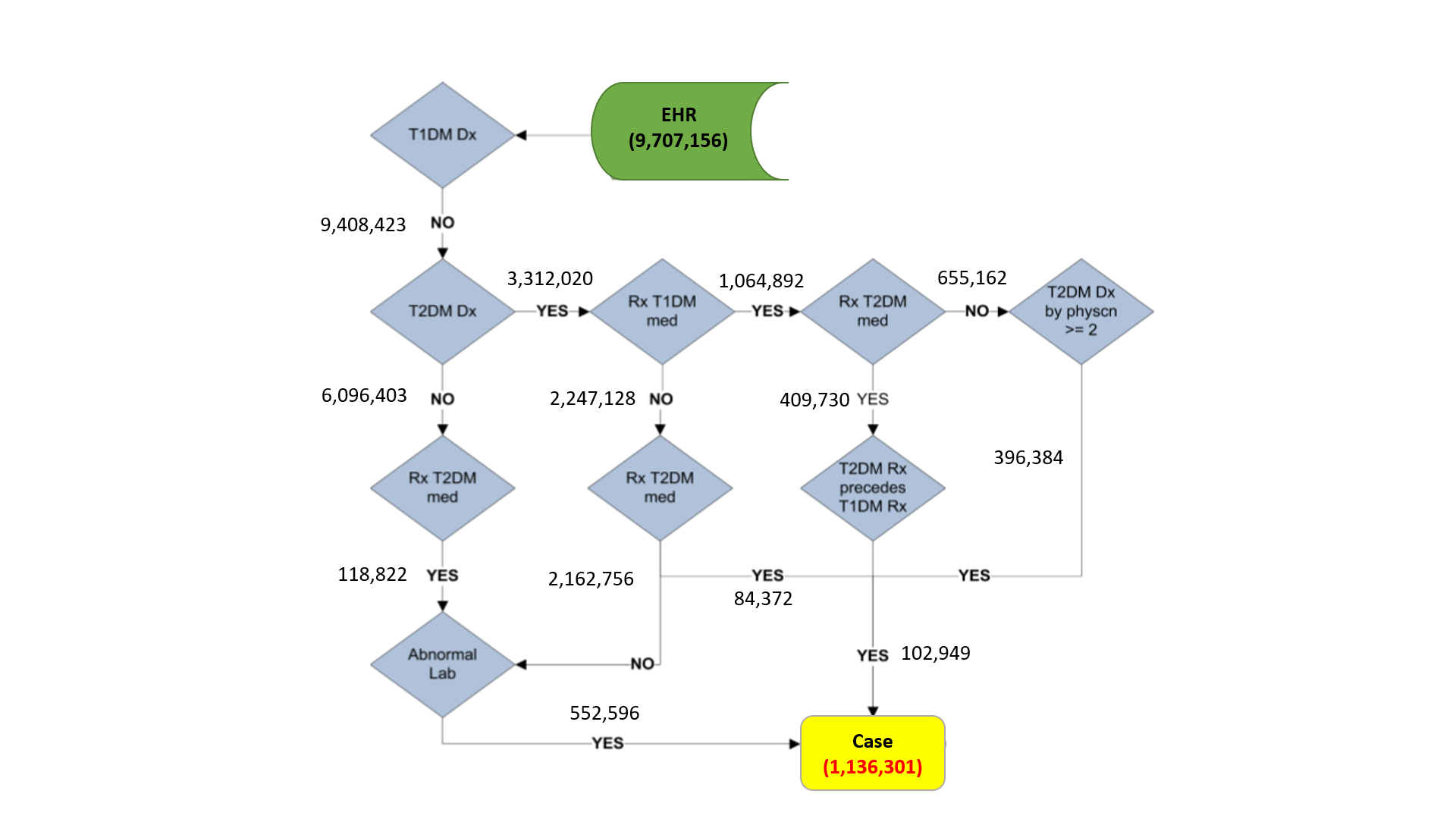
Column 1-3: three co-occurring symptoms; # of Occurrence for all sizes: the number of occurrences for the three symptoms including those with other symptoms; Average RR: the average risk ratio of the three symptoms co-occurred together versus one of the symptom occurred alone; Chi-square value: Chi-square statistics for the overall Chi-square test for the association among the 3 co-occurring symptoms; Adjusted p value: p-value of the Chi-square test after Bonferroni multiple testing adjustment.

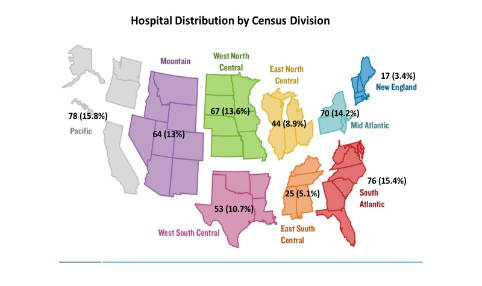
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Symptom 1** | **Symptom 2** | **Symptom 3** | **# of Occurrence for all sizes** | **Average RR** | **Chi-square value** | **Adjusted p value** |
| other head and neck symptoms | other respiratory symptoms | shortness of breath | 7417 | 359.64 | 4424780.57 | 0 |
| other head and neck symptoms | other respiratory symptoms | swelling | 608 | 350.04 | 1762238.93 | 0 |
| change in hair | other general symptoms | skin changes | 2805 | 27.94 | 705308.81 | 0 |
| change in hair | other general symptoms | swelling | 2642 | 27.87 | 657617.25 | 0 |
| anxiety | depression | heartburn | 39452 | 2.64 | 397471.31 | 0 |
| anxiety | depression | disturbed sleep | 28158 | 2.82 | 365555.02 | 0 |
| anxiety | depression | headache | 8876 | 2.71 | 350957.52 | 0 |
| anxiety | change in bowel patterns | depression | 12058 | 2.74 | 347109.49 | 0 |
| anxiety | depression | fatigue | 8413 | 2.30 | 341833.79 | 0 |
| anxiety | depression | feeling confused | 5529 | 2.39 | 341332.89 | 0 |
| anxiety | depression | urinary retention | 2292 | 2.50 | 339593.28 | 0 |
| anxiety | depression | other musculoskeletal symptoms | 2207 | 2.40 | 339552.92 | 0 |
| anxiety | depression | difficulty swallowing | 3055 | 2.73 | 339465.33 | 0 |
| anxiety | depression | incontinence | 3216 | 2.48 | 339350.69 | 0 |
| anxiety | depression | hearing loss | 1619 | 2.34 | 339203.92 | 0 |
| anxiety | change in vision | depression | 1196 | 2.31 | 339047.92 | 0 |
| anxiety | depression | weakness | 1272 | 2.42 | 339026.43 | 0 |
| anxiety | change in weight | depression | 1034 | 2.24 | 338917.68 | 0 |
| anxiety | depression | feeling thirsty | 430 | 2.78 | 338853.48 | 0 |
| anxiety | change in appetite | depression | 835 | 3.48 | 338819.52 | 0 |

**Table 12S. Top 20 significant co-occurring symptoms for size 4 (ranked by Chi-square statistics)**

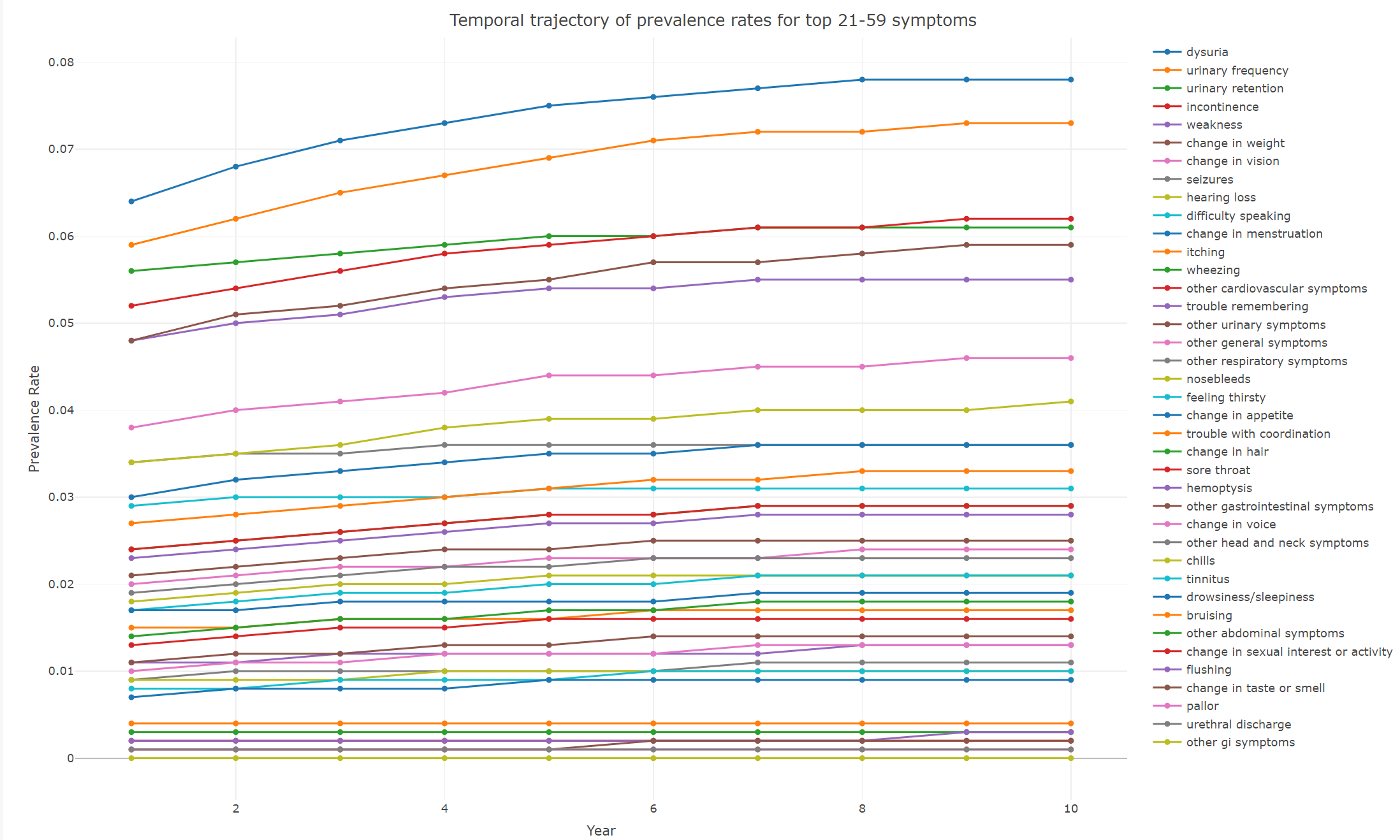
Column 1-4: four co-occurring symptoms; # of Occurrence for all sizes: the number of occurrences for the four symptoms including those with other symptoms; Average RR: the average risk ratio of the four symptoms co-occurred together versus one of the symptom occurred alone; Chi-square value: Chi-square statistics for the overall Chi-square test for the association among the 4 co-occurring symptoms; Adjusted p value: p-value of the Chi-square test after Bonferroni multiple testing adjustment.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Symptom 1** | | **Symptom 2** | | **Symptom 3** | | **Symptom 4** | | **# of Occurrence for all sizes** | | **Average RR** | **Chi-square value** | | **Adjusted p value** |
| cough | other head and neck symptoms | | other respiratory symptoms | | shortness of breath | | 7557 | | 182.01 | | 4527322.87 | 0 | |
| disturbed sleep | other head and neck symptoms | | other respiratory symptoms | | shortness of breath | | 6574 | | 180.81 | | 4489009.09 | 0 | |
| fatigue | other head and neck symptoms | | other respiratory symptoms | | shortness of breath | | 7124 | | 180.76 | | 4437413.45 | 0 | |
| other cardiovascular symptoms | other head and neck symptoms | | other respiratory symptoms | | shortness of breath | | 7312 | | 181.90 | | 4433286.91 | 0 | |
| fever | other head and neck symptoms | | other respiratory symptoms | | shortness of breath | | 7299 | | 181.78 | | 4429406.36 | 0 | |
| change in hair | difficulty walking | | other general symptoms | | swelling | | 2249 | | 16.16 | | 1536220.16 | 0 | |
| change in hair | other general symptoms | | skin changes | | swelling | | 1520 | | 15.65 | | 472331.14 | 0 | |
| anxiety | change in bowel patterns | | depression | | heartburn | | 55381 | | 2.31 | | 428195.71 | 0 | |
| anxiety | change in appetite | | depression | | heartburn | | 40476 | | 2.75 | | 399511.49 | 0 | |
| anxiety | change in weight | | depression | | heartburn | | 40850 | | 1.90 | | 398513.56 | 0 | |
| anxiety | chills | | depression | | heartburn | | 39701 | | 2.16 | | 397651.66 | 0 | |
| anxiety | change in appetite | | change in weight | | depression | | 2037 | | 9.50 | | 387831.30 | 0 | |
| anxiety | change in bowel patterns | | depression | | disturbed sleep | | 42478 | | 2.33 | | 379062.20 | 0 | |
| anxiety | change in vision | | depression | | headache | | 10401 | | 2.94 | | 367161.59 | 0 | |
| anxiety | change in vision | | depression | | disturbed sleep | | 29594 | | 2.03 | | 367052.15 | 0 | |
| anxiety | change in appetite | | depression | | disturbed sleep | | 29127 | | 2.73 | | 366954.74 | 0 | |
| anxiety | chills | | depression | | disturbed sleep | | 28357 | | 2.22 | | 365783.84 | 0 | |
| anxiety | change in bowel patterns | | depression | | headache | | 21412 | | 2.27 | | 361151.92 | 0 | |
| anxiety | change in bowel patterns | | depression | | urinary retention | | 15117 | | 2.77 | | 359289.99 | 0 | |
| anxiety | change in appetite | | change in bowel patterns | | depression | | 13196 | | 4.04 | | 357166.68 | 0 | |

****Figure S1.** Type 2 diabetes mellitus (T2DM) phenotyping flowchart with patient count at each step.

**Figure S2.** Distribution of type 2 diabetes mellitus (T2DM) population among census divisions of USA

**Figure S3.** Temporal trajectory of prevalence rates for other symptoms



**Figure S4.** Temporal trajectory of occurrence per patient for other symptoms

