**Supplementary Table S1 Medications for BD and their corresponding drug targets**

**Supplementary Table S2 Information of QTL and GWAS datasets**

**Supplementary Table S3 783 disease traits analyzed in the phenome-wide MR analysis**

**Supplementary Table S4 Current medications targeting potential causal proteins**

**Supplementary Table S1 Medications for BD and their corresponding drug targets**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Medication** | **Target** | **Gene Name** | **Uniprot ID** | **Drug Group** | **Action** | **Main Side Effects** |
| **Treatment of mania and mixed episodes** | | | | | | |
| Lithium | Inositol monophosphatase 2 | IMPA2 | O14732 | Approved | N/A | • Weight gain  • Polyuria  • Tremor  • Hypothyroidism (~20%)  • Hyperparathyroidism  • Chronic kidney disease with long term use |
| Inositol monophosphatase 1 | IMPA1 | P29218 | N/A |
| Glycogen synthase kinase-3 beta | GSK3B | P49841 | N/A |
| Glutamate receptor 3 | GRIA3 | P42263 | N/A |
| Carbama-  zepine | Voltage-gated sodium channel alpha subunit (Protein Group) | Sodium channel protein type 1 subunit alpha  Sodium channel protein type 10 subunit alpha  Sodium channel protein type 11 subunit alpha  Sodium channel protein type 2 subunit alpha  Sodium channel protein type 3 subunit alpha  Sodium channel protein type 4 subunit alpha  Sodium channel protein type 5 subunit alpha  Sodium channel protein type 7 subunit alpha  Sodium channel protein type 8 subunit alpha  Sodium channel protein type 9 subunit alpha | P35498  Q9Y5Y9  Q9UI33  Q99250  Q9NY46  P35499  Q14524  Q01118  Q9UQD0  Q15858 | Approved  Investigational | Inhibitor | • Dizziness, ataxia  • Syndrome of inappropriate antidiuretic hormone  secretion (<5%)  • Transient hematological abnormalities  • Severe rash/Stevens-Johnson syndrome (~0.01%; higher risk in people of Asian descent)  • Teratogenic (avoid in women of childbearing age) |
| Neuronal acetylcholine receptor subunit alpha-4 | CHRNA4 | P43681 | N/A |
| Nuclear receptor subfamily 1 group I member 2 | NR1I2 | O75469 | Activator |
| Chlorpro-  mazine | Dopamine D2 receptor | DRD2 | P14416 | Approved  Investigational  Vet approved | Antagonist | • Extrapyramidal symptoms  • Sedation  • Weight gain  • Non-specific electrocardiogram changes  • Increased risk cerebrovascular accidents in elderly |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Potassium voltage-gated channel subfamily H member 2 | KCNH2 | Q12809 | Inhibitor |
| D(1) dopamine receptor (Protein Group) | D(1A) dopamine receptor  D(1B) dopamine receptor | P21728  P21918 | Inhibitor |
| Dopamine D3 receptor | DRD3 | P35462 | Inhibitor |
| Dopamine D4 receptor | DRD4 | P21917 | Binder |
| Dopamine D5 receptor | DRD5 | P21918 | Inhibitor |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Binder |
| 5-hydroxytryptamine 2 receptor (Protein Group) | 5-hydroxytryptamine receptor 2A  5-hydroxytryptamine receptor 2B  5-hydroxytryptamine receptor 2C | P28223  P41595  P28335 | Binder |
| Alpha-1 adrenergic receptors (Protein Group) | Alpha-1A adrenergic receptor  Alpha-1B adrenergic receptor  Alpha-1D adrenergic receptor | P35348  P35368  P25100 | Inhibitor |
| Alpha-2 adrenergic receptors (Protein Group) | Alpha-2A adrenergic receptor  Alpha-2B adrenergic receptor  Alpha-2C adrenergic receptor | P08913  P18089  P18825 | Inhibitor |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Sphingomyelin phosphodiesterase | SMPD1 | P17405 | Inhibitor |
| Calmodulin | CALM1 | P0DP23 | Inhibitor |
| alpha1-acid glycoprotein  (Protein Group) | Alpha-1-acid glycoprotein 1  Alpha-1-acid glycoprotein 2 | P02763  P19652 | Binder |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Binder |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Binder |
| Histamine H4 receptor | HRH4 | Q9H3N8 | Binder |
| Risperidone | 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Approved  Investigational | Antagonist | • Extrapyramidal symptoms  • Weight gain  • Hyperprolactinemia  • Orthostatic hypotension |
| Dopamine D2 receptor | DRD2 | P14416 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist |
| D(2L) dopamine receptor | N/A | N/A | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Olanzapine | 5-hydroxytryptamine receptor 2A | HTR2A | [P28223](http://www.uniprot.org/uniprot/P28223) | Approved  Investigational | Antagonist | • Sedation  • Prominent weight gain  • Hyperglycemia  • Metabolic syndrome |
| Dopamine D2 receptor | DRD2 | [P14416](http://www.uniprot.org/uniprot/P14416) | Antagonist |
| Dopamine D1 receptor | DRD1 | [P21728](http://www.uniprot.org/uniprot/P21728) | Antagonist |
| Dopamine D5 receptor | DRD5 | [P21918](http://www.uniprot.org/uniprot/P21918) | Antagonist |
| Dopamine D3 receptor | DRD3 | [P35462](http://www.uniprot.org/uniprot/P35462) | Antagonist |
| Dopamine D4 receptor | DRD4 | [P21917](http://www.uniprot.org/uniprot/P21917) | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | [P28335](http://www.uniprot.org/uniprot/P28335) | Antagonist |
| 5-hydroxytryptamine receptor 3A | HTR3A | [P46098](http://www.uniprot.org/uniprot/P46098) | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | [P50406](http://www.uniprot.org/uniprot/P50406) | Antagonist |
| Histamine H1 receptor | HRH1 | [P35367](http://www.uniprot.org/uniprot/P35367) | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | [P35348](http://www.uniprot.org/uniprot/P35348) | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | [P35368](http://www.uniprot.org/uniprot/P35368) | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | [P11229](http://www.uniprot.org/uniprot/P11229) | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | [P08172](http://www.uniprot.org/uniprot/P08172) | Antagonist |
| Muscarinic acetylcholine receptor M3 | CHRM3 | [P20309](http://www.uniprot.org/uniprot/P20309) | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | [P08173](http://www.uniprot.org/uniprot/P08173) | Antagonist |
| D(1) dopamine receptor  (Protein Group) | D(1A) dopamine receptor  D(1B) dopamine receptor | P21728  P21918 | Antagonist |
| Beta adrenergic receptor  (Protein Group) | Beta-1 adrenergic receptor  Beta-2 adrenergic receptor  Beta-3 adrenergic receptor | P08588  P07550  P13945 | Inhibitor |
| 5-hydroxytryptamine receptor 1 (Protein Group) | 5-hydroxytryptamine receptor 1A  5-hydroxytryptamine receptor 1B  5-hydroxytryptamine receptor 1D  5-hydroxytryptamine receptor 1E  5-hydroxytryptamine receptor 1F | P08908  P28222  P28221  P28566  P30939 | Inhibitor |
| GABA(A) Receptor Benzodiazepine Binding Site (Protein Group) | Gamma-aminobutyric acid receptor subunit alpha-1  Gamma-aminobutyric acid receptor subunit alpha-2  Gamma-aminobutyric acid receptor subunit alpha-3  Gamma-aminobutyric acid receptor subunit alpha-5  Gamma-aminobutyric acid receptor subunit gamma-1  Gamma-aminobutyric acid receptor subunit gamma-2  Gamma-aminobutyric acid receptor subunit gamma-3 | P14867  P47869  P34903  P31644  Q8N1C3  P18507  Q99928 | Inhibitor |
| Quetiapine | 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Approved | Antagonist | • Somnolence  • Dizziness  • Weight gain  • Hyperglycemia  • Metabolic syndrome |
| Dopamine D2 receptor | DRD2 | P14416 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Ligand |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Ligand |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Ligand |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Ligand |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Ligand |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Ligand |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Ligand |
| Dopamine D3 receptor | DRD3 | P35462 | Ligand |
| Dopamine D4 receptor | DRD4 | P21917 | Ligand |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Alpha-1 adrenergic receptors  (Protein Group) | Alpha-1A adrenergic receptor  Alpha-1B adrenergic receptor  Alpha-1D adrenergic receptor | P35348  P35368  P25100 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Ligand |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Ligand |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Ligand |
| Ziprasidone | Dopamine D2 receptor | DRD2 | P14416 | Approved | Antagonist | • QT interval prolongation  • Mild akathisia |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Agonist |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Antagonist |
| Dopamine D3 receptor | DRD3 | P35462 | Antagonist |
| Dopamine D4 receptor | DRD4 | P21917 | Antagonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Antagonist |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Antagonist |
| .5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Antagonist |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Antagonist |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Antagonist |
| 5-hydroxytryptamine 3 receptor (Protein Group) | 5-hydroxytryptamine receptor 3A  5-hydroxytryptamine receptor 3B  5-hydroxytryptamine receptor 3C  5-hydroxytryptamine receptor 3D  5-hydroxytryptamine receptor 3E | P46098  O95264  Q8WXA8  Q70Z44  A5X5Y0 | Antagonist |
| 5-hydroxytryptamine receptor 5A | HTR5A | P47898 | Antagonist |
| Aripiprazole | Dopamine D2 receptor | DRD2 | P14416 | Approved  Investigational | Antagonist  Partial agonist | • Akathisia  • Anxiety |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Partial agonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Dopamine D3 receptor | DRD3 | P35462 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Antagonist  Ligand |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist  Partial agonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist  Other/unkn-own |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Antagonist  Ligand |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist  Partial agonist  Ligand |
| Dopamine D4 receptor | DRD4 | P21917 | Antagonist  Partial agonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Antagonist  Partial agonist  Ligand |
| 5-hydroxytryptamine receptor 2B | HTR2B | P41595 | Inverse agonist |
| 5-hydroxytryptamine receptor 5A | HTR5A | P47898 | Ligand |
| Beta-1 adrenergic receptor | ADRB1 | P08588 | Ligand |
| Beta-2 adrenergic receptor | ADRB2 | P07550 | Ligand |
| Histamine H2 receptor | HRH2 | P25021 | Ligand |
| Histamine H3 receptor | HRH3 | Q9Y5N1 | Ligand |
| Histamine H4 receptor | HRH4 | Q9H3N8 | Ligand |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Ligand |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Ligand |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Ligand |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Ligand |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Ligand |
| Kappa-type opioid receptor | OPRK1 | P41145 | Ligand |
| Mu-type opioid receptor | OPRM1 | P35372 | Ligand |
| Delta-type opioid receptor | OPRD1 | P41143 | Ligand |
| Glutamate (NMDA) receptor (Protein Group) | Glutamate receptor ionotropic, NMDA 1  Glutamate receptor ionotropic, NMDA 2A  Glutamate receptor ionotropic, NMDA 2B  Glutamate receptor ionotropic, NMDA 2C  Glutamate receptor ionotropic, NMDA 2D  Glutamate receptor ionotropic, NMDA 3A  Glutamate receptor ionotropic, NMDA 3B | Q05586  Q12879  Q13224  Q14957  O15399  Q8TCU5  O60391 | Ligand |
| Sodium-dependent dopamine transporter | SLC6A3 | Q01959 | Modulator |
| Sodium-dependent serotonin transporter | SLC6A4 | P31645 | Modulator |
| Asenapine | 5-hydroxytryptamine receptor 2A | HTR2A | [P28223](http://www.uniprot.org/uniprot/P28223) | Approved | Antagonist | • Sedation  • Mild weight gain |
| Dopamine D2 receptor | DRD2 | [P14416](http://www.uniprot.org/uniprot/P14416) | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | [P08908](http://www.uniprot.org/uniprot/P08908) | Antagonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | [P28222](http://www.uniprot.org/uniprot/P28222) | Antagonist |
| 5-hydroxytryptamine receptor 2B | HTR2B | [P41595](http://www.uniprot.org/uniprot/P41595) | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | [P28335](http://www.uniprot.org/uniprot/P28335) | Antagonist |
| 5-hydroxytryptamine receptor 5A | HTR5A | [P47898](http://www.uniprot.org/uniprot/P47898) | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | [P50406](http://www.uniprot.org/uniprot/P50406) | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | [P34969](http://www.uniprot.org/uniprot/P34969) | Antagonist |
| Dopamine D3 receptor | DRD3 | [P35462](http://www.uniprot.org/uniprot/P35462) | Antagonist |
| Dopamine D4 receptor | DRD4 | [P21917](http://www.uniprot.org/uniprot/P21917) | Antagonist |
| Dopamine D1 receptor | DRD1 | [P21728](http://www.uniprot.org/uniprot/P21728) | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | [P35348](http://www.uniprot.org/uniprot/P35348) | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | [P08913](http://www.uniprot.org/uniprot/P08913) | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | [P18089](http://www.uniprot.org/uniprot/P18089) | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | [P18825](http://www.uniprot.org/uniprot/P18825) | Antagonist |
| Histamine H1 receptor | HRH1 | [P35367](http://www.uniprot.org/uniprot/P35367) | Antagonist |
| Histamine H2 receptor | HRH2 | [P25021](http://www.uniprot.org/uniprot/P25021) | Antagonist |
| Beta-1 adrenergic receptor | ADRB1 | [P08588](http://www.uniprot.org/uniprot/P08588) | Antagonist |
| Beta-2 adrenergic receptor | ADRB2 | [P07550](http://www.uniprot.org/uniprot/P07550) | Antagonist |
| **Treatment of bipolar depression** | | | | | | |
| Olanzapine | 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Approved  Investigational | Antagonist | • Weight gain  • Metabolic syndrome |
| Dopamine D2 receptor | DRD2 | P14416 | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Antagonist |
| Dopamine D3 receptor | DRD3 | P35462 | Antagonist |
| Dopamine D4 receptor | DRD4 | P21917 | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Antagonist |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Antagonist |
| D(1) dopamine receptor (Protein Group) | D(1A) dopamine receptor  D(1B) dopamine receptor | P21728  P21918 | Antagonist |
| Beta adrenergic receptor (Protein Group) | Beta-1 adrenergic receptor  Beta-2 adrenergic receptor  Beta-3 adrenergic receptor | P08588  P07550  P13945 | Inhibitor |
| 5-hydroxytryptamine receptor 1 (Protein Group) | 5-hydroxytryptamine receptor 1A  5-hydroxytryptamine receptor 1B  5-hydroxytryptamine receptor 1D  5-hydroxytryptamine receptor 1E  5-hydroxytryptamine receptor 1F | P08908  P28222  P28221  P28566  P30939 | Inhibitor |
| GABA(A) Receptor Benzodiazepine Binding Site (Protein Group) | Gamma-aminobutyric acid receptor subunit alpha-1  Gamma-aminobutyric acid receptor subunit alpha-2  Gamma-aminobutyric acid receptor subunit alpha-3  Gamma-aminobutyric acid receptor subunit alpha-5  Gamma-aminobutyric acid receptor subunit gamma-1  Gamma-aminobutyric acid receptor subunit gamma-2  Gamma-aminobutyric acid receptor subunit gamma-3 | P14867  P47869  P34903  P31644  Q8N1C3  P18507  Q99928 | Inhibitor |
| Fluoxetine | Sodium-dependent serotonin transporter | SLC6A4 | P31645 | Approved  Vet approved | Inhibitor |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist |
| Neuronal acetylcholine receptor subunit alpha-2 | CHRNA2 | Q15822 | Antagonist |
| Neuronal acetylcholine receptor subunit alpha-3 | CHRNA3 | P32297 | Antagonist |
| Neuronal acetylcholine receptor subunit beta-4 | CHRNB4 | P30926 | Antagonist |
| Cyclin-dependent kinases regulatory subunit 1 | CKS1B | P61024 | N/A |
| Potassium voltage-gated channel subfamily H member 2 | KCNH2 | Q12809 | Inhibitor |
| Quetiapine | 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Approved | Antagonist | • Somnolence  • Dizziness  • Weight gain  • Metabolic syndrome  • Rare (cataracts) |
| Dopamine D2 receptor | DRD2 | P14416 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Ligand |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Ligand |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Ligand |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Ligand |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Ligand |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Ligand |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Ligand |
| Dopamine D3 receptor | DRD3 | P35462 | Ligand |
| Dopamine D4 receptor | DRD4 | P21917 | Ligand |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Alpha-1 adrenergic receptors (Protein Group) | Alpha-1A adrenergic receptor  Alpha-1B adrenergic receptor  Alpha-1D adrenergic receptor | P35348  P35368  P25100 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Ligand |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Ligand |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Ligand |
| Lurasidone | Dopamine D2 receptor | DRD2 | P14416 | Approved  Investigational | Antagonist | • Mild sedation  • Akathisia |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | N/A |
| Cariprazine | Dopamine D3 receptor | DRD3 | [P35462](http://www.uniprot.org/uniprot/P35462) | Approved  Investigational | Partial agonist | • Extrapyramidal symptoms  • Akathisia |
| Dopamine D2 receptor | DRD2 | [P14416](http://www.uniprot.org/uniprot/P14416) | Partial agonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | [P08908](http://www.uniprot.org/uniprot/P08908) | Partial agonist |
| 5-hydroxytryptamine receptor 2B | HTR2B | [P41595](http://www.uniprot.org/uniprot/P41595) | Antagonist |
| 5-hydroxytryptamine receptor 2A | HTR2A | [P28223](http://www.uniprot.org/uniprot/P28223) | Antagonist |
| Histamine H1 receptor | HRH1 | [P35367](http://www.uniprot.org/uniprot/P35367) | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | [P28335](http://www.uniprot.org/uniprot/P28335) | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | [P35348](http://www.uniprot.org/uniprot/P35348) | Antagonist |
| Lumatepe-rone | Sodium-dependent serotonin transporter | SLC6A4 | P31645 | Approved  Investigational | Inhibitor | • Mild sedation, somnolence |
| Glutamate receptor ionotropic, NMDA 2B | GRIN2B | Q13224 | N/A |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| Dopamine D2 receptor | DRD2 | P14416 | Partial agonist |
| Dopamine D1 receptor | DRD1 | P21728 | N/A |
| **Treatment for bipolar disorder prevention (maintenance)** | | | | | | |
| Lithium | Inositol monophosphatase 2 | IMPA2 | O14732 | Approved | N/A | • Common: weight gain  • Mild tremor  • Hypothyroidism  • Hypoparathyroidism  • Diabetes insipidus  • Chronic renal insufficiency |
| Inositol monophosphatase 1 | IMPA1 | P29218 | N/A |
| Glycogen synthase kinase-3 beta | GSK3B | P49841 | N/A |
| Glutamate receptor 3 | GRIA3 | P42263 | N/A |
| Lamotrigine | Voltage-dependent R-type calcium channel subunit alpha-1E (CACNA1E) | CACNA1E | Q15878 | Approved  Investigational | Inhibitor | • Rash (5-10%)  • Severe rash/Stevens-Johnson syndrome (0.1-0.01%)  • Slower titration schedule and dose if administered with  divalproate, an inhibitor of CYP3A  • Might require higher doses when administered with  carbamazepine, an activator of CYP3A activator |
| Voltage-gated sodium channel alpha subunit (Protein Group) | Sodium channel protein type 1 subunit alpha  Sodium channel protein type 10 subunit alpha  Sodium channel protein type 11 subunit alpha  Sodium channel protein type 2 subunit alpha  Sodium channel protein type 3 subunit alpha  Sodium channel protein type 4 subunit alpha  Sodium channel protein type 5 subunit alpha  Sodium channel protein type 7 subunit alpha  Sodium channel protein type 8 subunit alpha  Sodium channel protein type 9 subunit alpha | P35498  Q9Y5Y9  Q9UI33  Q99250  Q9NY46  P35499  Q14524  Q01118  Q9UQD0  Q15858 | Inhibitor |
| Adenosine receptor A1 | ADORA1 | P30542 | Inhibitor |
| Adenosine receptor A2a | ADORA2A | P29274 | Inhibitor |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Inhibitor |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Inhibitor |
| Beta-1 adrenergic receptor | ADRB1 | P08588 | Inhibitor |
| D(1) dopamine receptor  (Protein Group) | D(1A) dopamine receptor  D(1B) dopamine receptor | P21728  P21918 | Inhibitor |
| Dopamine D2 receptor | DRD2 | P14416 | Agonist  Inhibitor |
| GABA(A) Receptor  (Protein Group) | Gamma-aminobutyric acid receptor subunit alpha-1  Gamma-aminobutyric acid receptor subunit alpha-2  Gamma-aminobutyric acid receptor subunit alpha-3  Gamma-aminobutyric acid receptor subunit alpha-4  Gamma-aminobutyric acid receptor subunit alpha-5  Gamma-aminobutyric acid receptor subunit alpha-6  Gamma-aminobutyric acid receptor subunit beta-1  Gamma-aminobutyric acid receptor subunit beta-2  Gamma-aminobutyric acid receptor subunit beta-3  Gamma-aminobutyric acid receptor subunit delta  Gamma-aminobutyric acid receptor subunit epsilon  Gamma-aminobutyric acid receptor subunit gamma-1  Gamma-aminobutyric acid receptor subunit gamma-2  Gamma-aminobutyric acid receptor subunit gamma-3  Gamma-aminobutyric acid receptor subunit pi  Gamma-aminobutyric acid receptor subunit theta | P14867  P47869  P34903  P48169  P31644  Q16445  P18505  P47870  P28472  O14764  P78334  Q8N1C3  P18507  Q99928  O00591  Q9UN88 | Antagonist  Inducer |
| GABA(A) Receptor Benzodiazepine Binding Site (Protein Group) | Gamma-aminobutyric acid receptor subunit alpha-1  Gamma-aminobutyric acid receptor subunit alpha-2  Gamma-aminobutyric acid receptor subunit alpha-3  Gamma-aminobutyric acid receptor subunit alpha-5  Gamma-aminobutyric acid receptor subunit gamma-1  Gamma-aminobutyric acid receptor subunit gamma-2  Gamma-aminobutyric acid receptor subunit gamma-3 | P14867  P47869  P34903  P31644  Q8N1C3  P18507  Q99928 | Inhibitor |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Kappa-type opioid receptor | OPRK1 | P41145 | Inhibitor |
| Acetylcholine receptor subunit alpha | CHRNA1 | P02708 | Inhibitor |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Inhibitor |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Inhibitor |
| Glutamate receptor 1 | GRIA1 | P42261 | Inhibitor |
| Quetiapine | 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Approved | Antagonist | • Somnolence  • Dizziness  • Weight gain  • Metabolic syndrome  • Rare (cataracts) |
| Dopamine D2 receptor | DRD2 | P14416 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Ligand |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Ligand |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Ligand |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Ligand |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Ligand |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Ligand |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Ligand |
| Dopamine D3 receptor | DRD3 | P35462 | Ligand |
| Dopamine D4 receptor | DRD4 | P21917 | Ligand |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Alpha-1 adrenergic receptors (Protein Group) | Alpha-1A adrenergic receptor  Alpha-1B adrenergic receptor  Alpha-1D adrenergic receptor | P35348  P35368  P25100 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Ligand |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Ligand |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Ligand |
| Ziprasidone | Dopamine D2 receptor | DRD2 | P14416 | Approved | Antagonist | • QT interval prolongation |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Agonist |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Dopamine D5 receptor | DRD5 | P21918 | Antagonist |
| Dopamine D3 receptor | DRD3 | P35462 | Antagonist |
| Dopamine D4 receptor | DRD4 | P21917 | Antagonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Antagonist |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Antagonist |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Antagonist |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Antagonist |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Antagonist |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Antagonist |
| 5-hydroxytryptamine 3 receptor (Protein Group) | 5-hydroxytryptamine receptor 3A  5-hydroxytryptamine receptor 3B  5-hydroxytryptamine receptor 3C  5-hydroxytryptamine receptor 3D  5-hydroxytryptamine receptor 3E | P46098  O95264  Q8WXA8  Q70Z44  A5X5Y0 | Antagonist |
| 5-hydroxytryptamine receptor 5A | HTR5A | P47898 | Antagonist |
| Aripiprazole | Dopamine D2 receptor | DRD2 | P14416 | Approved  Investigational | Antagonist  Partial agonist | • Akathisia  • Extrapyramidal symptoms |
| 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Partial agonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-1B adrenergic receptor | ADRA1B | P35368 | Antagonist |
| Dopamine D3 receptor | DRD3 | P35462 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 1D | HTR1D | P28221 | Antagonist  Ligand |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist  Partial agonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist  Other/unkn-own |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Antagonist  Ligand |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist  Partial agonist |
| 5-hydroxytryptamine receptor 3A | HTR3A | P46098 | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist  Partial agonist  Ligand |
| Dopamine D4 receptor | DRD4 | P21917 | Antagonist  Partial agonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist  Ligand |
| 5-hydroxytryptamine receptor 1E | HTR1E | P28566 | Antagonist  Ligand |
| Dopamine D5 receptor | DRD5 | P21918 | Antagonist  Partial agonist  Ligand |
| 5-hydroxytryptamine receptor 2B | HTR2B | P41595 | Inverse agonist |
| 5-hydroxytryptamine receptor 5A | HTR5A | P47898 | Ligand |
| Beta-1 adrenergic receptor | ADRB1 | P08588 | Ligand |
| Beta-2 adrenergic receptor | ADRB2 | P07550 | Ligand |
| Histamine H2 receptor | HRH2 | P25021 | Ligand |
| Histamine H3 receptor | HRH3 | Q9Y5N1 | Ligand |
| Histamine H4 receptor | HRH4 | Q9H3N8 | Ligand |
| Muscarinic acetylcholine receptor M1 | CHRM1 | P11229 | Ligand |
| Muscarinic acetylcholine receptor M2 | CHRM2 | P08172 | Ligand |
| Muscarinic acetylcholine receptor M3 | CHRM3 | P20309 | Ligand |
| Muscarinic acetylcholine receptor M4 | CHRM4 | P08173 | Ligand |
| Muscarinic acetylcholine receptor M5 | CHRM5 | P08912 | Ligand |
| Kappa-type opioid receptor | OPRK1 | P41145 | Ligand |
| Mu-type opioid receptor | OPRM1 | P35372 | Ligand |
| Delta-type opioid receptor | OPRD1 | P41143 | Ligand |
| Glutamate (NMDA) receptor (Protein Group) | Glutamate receptor ionotropic, NMDA 1  Glutamate receptor ionotropic, NMDA 2A  Glutamate receptor ionotropic, NMDA 2B  Glutamate receptor ionotropic, NMDA 2C  Glutamate receptor ionotropic, NMDA 2D  Glutamate receptor ionotropic, NMDA 3A  Glutamate receptor ionotropic, NMDA 3B | Q05586  Q12879  Q13224  Q14957  O15399  Q8TCU5  O60391 | Ligand |
| Sodium-dependent dopamine transporter | SLC6A3 | Q01959 | Modulator |
| Sodium-dependent serotonin transporter | SLC6A4 | P31645 | Modulator |
| Asenapine | 5-hydroxytryptamine receptor 2A | HTR2A | P28223 | Approved | Antagonist | • Sedation  • Weight gain |
| Dopamine D2 receptor | DRD2 | P14416 | Antagonist |
| 5-hydroxytryptamine receptor 1A | HTR1A | P08908 | Antagonist |
| 5-hydroxytryptamine receptor 1B | HTR1B | P28222 | Antagonist |
| 5-hydroxytryptamine receptor 2B | HTR2B | P41595 | Antagonist |
| 5-hydroxytryptamine receptor 2C | HTR2C | P28335 | Antagonist |
| 5-hydroxytryptamine receptor 5A | HTR5A | P47898 | Antagonist |
| 5-hydroxytryptamine receptor 6 | HTR6 | P50406 | Antagonist |
| 5-hydroxytryptamine receptor 7 | HTR7 | P34969 | Antagonist |
| Dopamine D3 receptor | DRD3 | P35462 | Antagonist |
| Dopamine D4 receptor | DRD4 | P21917 | Antagonist |
| Dopamine D1 receptor | DRD1 | P21728 | Antagonist |
| Alpha-1A adrenergic receptor | ADRA1A | P35348 | Antagonist |
| Alpha-2A adrenergic receptor | ADRA2A | P08913 | Antagonist |
| Alpha-2B adrenergic receptor | ADRA2B | P18089 | Antagonist |
| Alpha-2C adrenergic receptor | ADRA2C | P18825 | Antagonist |
| Histamine H1 receptor | HRH1 | P35367 | Antagonist |
| Histamine H2 receptor | HRH2 | P25021 | Antagonist |
| Beta-1 adrenergic receptor | ADRB1 | P08588 | Antagonist |
| Beta-2 adrenergic receptor | ADRB2 | P07550 | Antagonist |

More details can refer to summary of FDA approved medications for BD and the DRUGBANK database (https://go.drugbank.com/).

**Supplementary Table S2** **Information of QTL and GWAS datasets**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Type of dataset** | **Data subtype** | **Resource** | **Sample size** | **Population** | **Reference** | **Download site** |
| pQTL | brain | Wingo et al., 2021 | NpQTLs= 616;  Nprotein= 608 | Wingo et al., 2021: Northern American | Wingo, A. P., Liu, Y., Gerasimov, E. S., Gockley, J., Logsdon, B. A., Duong, D. M., Dammer, E. B., Robins, C., Beach, T. G., Reiman, E. M., Epstein, M. P., De Jager, P. L., Lah, J. J., Bennett, D. A., Seyfried, N. T., Levey, A. I. & Wingo, T. S. (2021). Integrating human brain proteomes with genome-wide association data implicates new proteins in Alzheimer's disease pathogenesis. Nat Genet 53, 143-146. | https://doi.org/10.7303/syn23627957 |
| CSF | Yang et al., 2021 | NpQTLs= 233;  Nprotein= 214 | Yang et al., 2021: non-Hispanic white from North American (95%) and African American (5%) | Yang, C., Farias, F. H. G., Ibanez, L., Suhy, A., Sadler, B., Fernandez, M. V., Wang, F., Bradley, J. L., Eiffert, B., Bahena, J. A., Budde, J. P., Li, Z., Dube, U., Sung, Y. J., Mihindukulasuriya, K. A., Morris, J. C., Fagan, A. M., Perrin, R. J., Benitez, B. A., Rhinn, H., Harari, O. & Cruchaga, C. (2021). Genomic atlas of the proteome from brain, CSF and plasma prioritizes proteins implicated in neurological disorders. Nat Neurosci 24, 1302-1312. | niagads@pennmedicine.upenn.edu |
| plasma | Zheng et al., 2020 | NpQTLs= 616;  Nprotein= 612 | Zheng et al., 2020: generated from a pooled analysis of 5 preliminary studies.  1) Emilsson et al., 2018: Icelander.  2) Yao et al., 2018: American (99.7% white).  3) Folkersen et al., 2017: European (from Finland, France, Italy, the Netherlands and Sweden).  4) Suhre et al., 2017: southern German.  5) Sun et al., 2018: 90.8% white, 2.4% Asian, and other races. | [1] Zheng, J., Haberland, V., Baird, D., Walker, V., Haycock, P. C., Hurle, M. R., Gutteridge, A., Erola, P., Liu, Y., Luo, S., Robinson, J., Richardson, T. G., Staley, J. R., Elsworth, B., Burgess, S., Sun, B. B., Danesh, J., Runz, H., Maranville, J. C., Martin, H. M., Yarmolinsky, J., Laurin, C., Holmes, M. V., Liu, J. Z., Estrada, K., Santos, R., McCarthy, L., Waterworth, D., Nelson, M. R., Smith, G. D., Butterworth, A. S., Hemani, G., Scott, R. A. & Gaunt, T. R. (2020). Phenome-wide Mendelian randomization mapping the influence of the plasma proteome on complex diseases. Nat Genet 52, 1122-1131.  [2] Emilsson, V., Ilkov, M., Lamb, J. R., Finkel, N., Gudmundsson, E. F., Pitts, R., Hoover, H., Gudmundsdottir, V., Horman, S. R., Aspelund, T., Shu, L., Trifonov, V., Sigurdsson, S., Manolescu, A., Zhu, J., Olafsson, Ö., Jakobsdottir, J., Lesley, S. A., To, J., Zhang, J., Harris, T. B., Launer, L. J., Zhang, B., Eiriksdottir, G., Yang, X., Orth, A. P., Jennings, L. L. & Gudnason, V. (2018). Co-regulatory networks of human serum proteins link genetics to disease. Science 361, 769-773.  [3] Yao, C., Chen, G., Song, C., Keefe, J., Mendelson, M., Huan, T., Sun, B. B., Laser, A., Maranville, J. C., Wu, H., Ho, J. E., Courchesne, P., Lyass, A., Larson, M. G., Gieger, C., Graumann, J., Johnson, A. D., Danesh, J., Runz, H., Hwang, S. J., Liu, C., Butterworth, A. S., Suhre, K. & Levy, D. (2018). Genome-wide mapping of plasma protein QTLs identifies putatively causal genes and pathways for cardiovascular disease. Nat Commun 9, 3268.  [4] Folkersen, L., Fauman, E., Sabater-Lleal, M., Strawbridge, R. J., Frånberg, M., Sennblad, B., Baldassarre, D., Veglia, F., Humphries, S. E., Rauramaa, R., de Faire, U., Smit, A. J., Giral, P., Kurl, S., Mannarino, E., Enroth, S., Johansson, Å., Enroth, S. B., Gustafsson, S., Lind, L., Lindgren, C., Morris, A. P., Giedraitis, V., Silveira, A., Franco-Cereceda, A., Tremoli, E., Gyllensten, U., Ingelsson, E., Brunak, S., Eriksson, P., Ziemek, D., Hamsten, A. & Mälarstig, A. (2017). Mapping of 79 loci for 83 plasma protein biomarkers in cardiovascular disease. PLoS Genet 13, e1006706.  [5] Suhre, K., Arnold, M., Bhagwat, A. M., Cotton, R. J., Engelke, R., Raffler, J., Sarwath, H., Thareja, G., Wahl, A., DeLisle, R. K., Gold, L., Pezer, M., Lauc, G., El-Din Selim, M. A., Mook-Kanamori, D. O., Al-Dous, E. K., Mohamoud, Y. A., Malek, J., Strauch, K., Grallert, H., Peters, A., Kastenmüller, G., Gieger, C. & Graumann, J. (2017). Connecting genetic risk to disease end points through the human blood plasma proteome. Nat Commun 8, 14357.  [6] Sun, B. B., Maranville, J. C., Peters, J. E., Stacey, D., Staley, J. R., Blackshaw, J., Burgess, S., Jiang, T., Paige, E., Surendran, P., Oliver-Williams, C., Kamat, M. A., Prins, B. P., Wilcox, S. K., Zimmerman, E. S., Chi, A., Bansal, N., Spain, S. L., Wood, A. M., Morrell, N. W., Bradley, J. R., Janjic, N., Roberts, D. J., Ouwehand, W. H., Todd, J. A., Soranzo, N., Suhre, K., Paul, D. S., Fox, C. S., Plenge, R. M., Danesh, J., Runz, H. & Butterworth, A. S. (2018). Genomic atlas of the human plasma proteome. Nature 558, 73-79. | http://www.epigraphdb.org/pqtl/ |
| GWAS | primary | Mullins et al., 2020 | NCase = 41,917 | Australian, Northern American, European | Mullins N, Forstner AJ, O'Connell KS, et al. Genome-wide association study of more than 40,000 bipolar disorder cases provides new insights into the underlying biology. Nature genetics 2021;53(6):817-29. doi: 10.1038/s41588-021-00857-4 | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8192451/# |
| NControl = 371,549 |
| validation | UK Biobank | NCase = 1,064 | European | Zhou, W., Nielsen, J. B., Fritsche, L. G., et al. Efficiently controlling for case-control imbalance and sample relatedness in large-scale genetic association studies. Nat Genet 2018; 50(9):1335-1341. doi:10.1038/s41588-018-0184-y | http://ukbiobank.ac.uk/ |
| NControl = 365,476 |
| validation | FinnGen | NCase = 7,006 | European | Kurki MI, Karjalainen J, Palta P, et al. FinnGen provides genetic insights from a well-phenotyped isolated population. Nature 2023;613(7944):508-18. doi: 10.1038/s41586-022-05473-8 | https://  finngen.gitbook.io/documentation/ |
| NControl = 329,192 |

**Supplementary Table S3 783 disease traits analyzed in the phenome-wide MR analysis**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **PheCode** | **Number of cases** | **Number of controls** | **Number of excluded controls** | **Phenotype Description** | **Phenotype Category** |
| 008 | 8991 | 399970 | 0 | Intestinal infection | infectious diseases |
| 008.5 | 2737 | 399970 | 6254 | Bacterial enteritis | infectious diseases |
| 008.52 | 650 | 399970 | 8341 | Intestinal infection due to C. difficile | infectious diseases |
| 008.6 | 862 | 399970 | 8129 | Viral Enteritis | infectious diseases |
| 038 | 4005 | 393897 | 11059 | Septicemia | infectious diseases |
| 038.1 | 832 | 393897 | 14232 | Gram negative septicemia | infectious diseases |
| 041 | 12187 | 393897 | 2877 | Bacterial infection NOS | infectious diseases |
| 041.1 | 3149 | 393897 | 11915 | Staphylococcus infections | infectious diseases |
| 041.2 | 1644 | 393897 | 13420 | Streptococcus infection | infectious diseases |
| 041.4 | 2744 | 393897 | 12320 | E. coli | infectious diseases |
| 070 | 1215 | 403316 | 4430 | Viral hepatitis | infectious diseases |
| 078 | 1007 | 403316 | 4638 | Viral warts & HPV | infectious diseases |
| 079 | 2806 | 403316 | 2839 | Viral infection | infectious diseases |
| 080 | 4489 | 402343 | 2129 | Postoperative infection | infectious diseases |
| 081 | 2485 | 402343 | 4133 | Infection/inflammation of internal prosthetic device; implant; and graft | infectious diseases |
| 1000 | 579 | 408382 | 0 | Burns | injuries & poisonings |
| 1001 | 1210 | 407751 | 0 | Foreign body injury | injuries & poisonings |
| 1002 | 5512 | 403449 | 0 | Symptoms concerning nutrition, metabolism, and development | symptoms |
| 1005 | 1222 | 407739 | 0 | Other symptoms | symptoms |
| 1008 | 1007 | 407954 | 0 | Crushing or internal injury to organs | injuries & poisonings |
| 1009 | 8440 | 400521 | 0 | Injury, NOS | injuries & poisonings |
| 1010 | 5972 | 402989 | 0 | Other tests | symptoms |
| 1011 | 9140 | 399821 | 0 | Complications of surgical and medical procedures | injuries & poisonings |
| 1015 | 4230 | 404731 | 0 | Effects of other external causes | symptoms |
| 1019 | 16398 | 392563 | 0 | Other ill-defined and unknown causes of morbidity and mortality | symptoms |
| 112 | 2134 | 406301 | 526 | Candidiasis | infectious diseases |
| 145 | 643 | 406821 | 1497 | Cancer of mouth | neoplasms |
| 149 | 628 | 406821 | 1512 | Cancer of larynx, pharynx, nasal cavities | neoplasms |
| 150 | 720 | 393372 | 14869 | Cancer of esophagus | neoplasms |
| 151 | 554 | 393372 | 15035 | Cancer of stomach | neoplasms |
| 153 | 4562 | 382756 | 21643 | Colorectal cancer | neoplasms |
| 153.2 | 3051 | 382756 | 23154 | Colon cancer | neoplasms |
| 153.3 | 2095 | 382756 | 24110 | Malignant neoplasm of rectum, rectosigmoid junction, and anus | neoplasms |
| 157 | 589 | 393372 | 15000 | Pancreatic cancer | neoplasms |
| 158 | 1056 | 393372 | 14533 | Neoplasm of unspecified nature of digestive system | neoplasms |
| 159 | 5584 | 393372 | 10005 | Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum | neoplasms |
| 165 | 2700 | 406226 | 35 | Cancer within the respiratory system | neoplasms |
| 165.1 | 2101 | 406226 | 634 | Cancer of bronchus; lung | neoplasms |
| 172 | 13752 | 395071 | 138 | Skin cancer | neoplasms |
| 172.1 | 2691 | 395071 | 11199 | Melanomas of skin, dx or hx | neoplasms |
| 172.11 | 2691 | 395071 | 11199 | Melanomas of skin | neoplasms |
| 172.2 | 11149 | 395071 | 2741 | Other non-epithelial cancer of skin | neoplasms |
| 172.3 | 667 | 395071 | 13223 | Carcinoma in situ of skin | neoplasms |
| 174 | 12898 | 388549 | 7514 | Breast cancer | neoplasms |
| 174.1 | 12671 | 388549 | 7741 | Breast cancer [female] | neoplasms |
| 174.11 | 11874 | 388549 | 8538 | Malignant neoplasm of female breast | neoplasms |
| 175 | 2415 | 387566 | 18980 | Acquired absence of breast | neoplasms |
| 180 | 3653 | 381902 | 23406 | Cervical cancer and dysplasia | neoplasms |
| 180.1 | 1659 | 381902 | 25400 | Cervical cancer | neoplasms |
| 180.3 | 2090 | 381902 | 24969 | Cervical intraepithelial neoplasia [CIN] [Cervical dysplasia] | neoplasms |
| 182 | 1284 | 381967 | 25710 | Malignant neoplasm of uterus | neoplasms |
| 184 | 2463 | 389695 | 16803 | Cancer of other female genital organs | neoplasms |
| 184.1 | 2127 | 389695 | 17139 | Malignant neoplasm of ovary and other uterine adnexa | neoplasms |
| 184.11 | 2103 | 389695 | 17163 | Malignant neoplasm of ovary | neoplasms |
| 187.2 | 2981 | 401788 | 4192 | Malignant neoplasm of testis | neoplasms |
| 189 | 4165 | 404796 | 0 | Cancer of urinary organs (incl. kidney and bladder) | neoplasms |
| 189.1 | 1045 | 404796 | 3120 | Cancer of kidney and renal pelvis | neoplasms |
| 189.11 | 1002 | 404796 | 3163 | Malignant neoplasm of kidney, except pelvis | neoplasms |
| 189.2 | 2427 | 404796 | 1738 | Cancer of bladder | neoplasms |
| 189.21 | 2146 | 404796 | 2019 | Malignant neoplasm of bladder | neoplasms |
| 191 | 655 | 407239 | 1067 | Manlignant and unknown neoplasms of brain and nervous system | neoplasms |
| 191.1 | 531 | 407239 | 1191 | Cancer of brain and nervous system | neoplasms |
| 195 | 16725 | 370604 | 21632 | Cancer, suspected or other | neoplasms |
| 195.1 | 15979 | 370604 | 22378 | Malignant neoplasm, other | neoplasms |
| 197 | 21798 | 370604 | 16559 | Chemotherapy | neoplasms |
| 198 | 9483 | 370604 | 28874 | Secondary malignant neoplasm | neoplasms |
| 198.1 | 5379 | 370604 | 32978 | Secondary malignancy of lymph nodes | neoplasms |
| 198.2 | 2211 | 370604 | 36146 | Secondary malignancy of respiratory organs | neoplasms |
| 198.3 | 1519 | 370604 | 36838 | Secondary malignant neoplasm of digestive systems | neoplasms |
| 198.4 | 2638 | 370604 | 35719 | Secondary malignant neoplasm of liver | neoplasms |
| 198.5 | 806 | 370604 | 37551 | Secondary malignancy of brain/spine | neoplasms |
| 198.6 | 2151 | 370604 | 36206 | Secondary malignancy of bone | neoplasms |
| 199 | 1412 | 370604 | 36945 | Neoplasm of uncertain behavior | neoplasms |
| 200 | 995 | 404466 | 3500 | Myeloproliferative disease | neoplasms |
| 202 | 2270 | 404466 | 2225 | Cancer of other lymphoid, histiocytic tissue | neoplasms |
| 202.2 | 1793 | 404466 | 2702 | Non-Hodgkins lymphoma | neoplasms |
| 202.24 | 573 | 404466 | 3922 | Large cell lymphoma | neoplasms |
| 204 | 1661 | 404466 | 2834 | Leukemia | neoplasms |
| 204.1 | 578 | 404466 | 3917 | Lymphoid leukemia | neoplasms |
| 204.12 | 506 | 404466 | 3989 | Lymphoid leukemia, chronic | neoplasms |
| 204.4 | 552 | 404466 | 3943 | Multiple myeloma | neoplasms |
| 208 | 20204 | 386011 | 2746 | Benign neoplasm of colon | neoplasms |
| 210 | 984 | 406821 | 1156 | Benign neoplasm of lip, oral cavity, and pharynx | neoplasms |
| 211 | 5280 | 395301 | 8380 | Benign neoplasm of other parts of digestive system | neoplasms |
| 214 | 6271 | 401613 | 1077 | Lipoma | neoplasms |
| 214.1 | 4611 | 401613 | 2737 | Lipoma of skin and subcutaneous tissue | neoplasms |
| 215 | 1110 | 401613 | 6238 | Other benign neoplasm of connective and other soft tissue | neoplasms |
| 216 | 7722 | 400618 | 621 | Benign neoplasm of skin | neoplasms |
| 217 | 649 | 400618 | 7694 | Vascular hamartomas and non-neoplastic nevi | neoplasms |
| 217.1 | 597 | 400618 | 7746 | Nevus, non-neoplastic | neoplasms |
| 218 | 10610 | 391653 | 6698 | Benign neoplasm of uterus | neoplasms |
| 218.1 | 10345 | 391653 | 6963 | Uterine leiomyoma | neoplasms |
| 220 | 1482 | 380325 | 27154 | Benign neoplasm of ovary | neoplasms |
| 225 | 828 | 407239 | 894 | Benign neoplasm of brain and other parts of nervous system | neoplasms |
| 225.1 | 774 | 407239 | 948 | Benign neoplasm of brain, cranial nerves, meninges | neoplasms |
| 227 | 876 | 407399 | 686 | Benign neoplasm of other endocrine glands and related structures | neoplasms |
| 228 | 1603 | 407358 | 0 | Hemangioma and lymphangioma, any site | neoplasms |
| 229 | 2402 | 406559 | 0 | Benign neoplasm of unspecified sites | neoplasms |
| 240 | 602 | 391429 | 16930 | Simple and unspecified goiter | endocrine/metabolic |
| 241 | 1143 | 391429 | 16389 | Nontoxic nodular goiter | endocrine/metabolic |
| 241.2 | 680 | 391429 | 16852 | Nontoxic multinodular goiter | endocrine/metabolic |
| 242 | 1860 | 391429 | 15672 | Thyrotoxicosis with or without goiter | endocrine/metabolic |
| 244 | 14871 | 391429 | 2661 | Hypothyroidism | endocrine/metabolic |
| 244.1 | 1117 | 391429 | 16415 | Secondary hypothyroidism | endocrine/metabolic |
| 244.4 | 14171 | 391429 | 3361 | Hypothyroidism NOS | endocrine/metabolic |
| 250 | 20203 | 388756 | 2 | Diabetes mellitus | endocrine/metabolic |
| 250.1 | 2660 | 388756 | 17545 | Type 1 diabetes | endocrine/metabolic |
| 250.2 | 18945 | 388756 | 1260 | Type 2 diabetes | endocrine/metabolic |
| 250.23 | 1298 | 388756 | 18907 | Type 2 diabetes with ophthalmic manifestations | endocrine/metabolic |
| 250.24 | 575 | 388756 | 19630 | Type 2 diabetes with neurological manifestations | endocrine/metabolic |
| 250.4 | 685 | 388756 | 19520 | Abnormal glucose | endocrine/metabolic |
| 250.7 | 1339 | 396859 | 10763 | Diabetic retinopathy | endocrine/metabolic |
| 251 | 943 | 405386 | 2632 | Other disorders of pancreatic internal secretion | endocrine/metabolic |
| 251.1 | 939 | 386319 | 21703 | Hypoglycemia | endocrine/metabolic |
| 252 | 877 | 405386 | 2698 | Disorders of parathyroid gland | endocrine/metabolic |
| 252.1 | 781 | 405386 | 2794 | Hyperparathyroidism | endocrine/metabolic |
| 253 | 693 | 405386 | 2882 | Disorders of the pituitary gland and its hypothalamic control | endocrine/metabolic |
| 255 | 642 | 405386 | 2933 | Disorders of adrenal glands | endocrine/metabolic |
| 260 | 1057 | 406492 | 1412 | Protein-calorie malnutrition | endocrine/metabolic |
| 260.6 | 835 | 406492 | 1634 | Anorexia | endocrine/metabolic |
| 261 | 1208 | 406492 | 1261 | Vitamin deficiency | endocrine/metabolic |
| 261.2 | 754 | 406492 | 1715 | Vitamin B-complex deficiencies | endocrine/metabolic |
| 272 | 35927 | 373034 | 0 | Disorders of lipoid metabolism | endocrine/metabolic |
| 272.1 | 35844 | 373034 | 83 | Hyperlipidemia | endocrine/metabolic |
| 272.11 | 33242 | 373034 | 2685 | Hypercholesterolemia | endocrine/metabolic |
| 274 | 3763 | 405198 | 0 | Gout and other crystal arthropathies | endocrine/metabolic |
| 274.1 | 3195 | 405198 | 568 | Gout | endocrine/metabolic |
| 274.2 | 616 | 405198 | 3147 | Crystal arthropathies | endocrine/metabolic |
| 274.21 | 560 | 405198 | 3203 | Chondrocalcinosis | endocrine/metabolic |
| 275 | 2127 | 406834 | 0 | Disorders of mineral metabolism | endocrine/metabolic |
| 275.1 | 669 | 406834 | 1458 | Disorders of iron metabolism | hematopoietic |
| 275.5 | 1204 | 406834 | 923 | Disorders of calcium/phosphorus metabolism | endocrine/metabolic |
| 276 | 7455 | 401506 | 0 | Disorders of fluid, electrolyte, and acid-base balance | endocrine/metabolic |
| 276.1 | 4123 | 401506 | 3332 | Electrolyte imbalance | endocrine/metabolic |
| 276.12 | 1826 | 401506 | 5629 | Hyposmolality and/or hyponatremia | endocrine/metabolic |
| 276.13 | 975 | 401506 | 6480 | Hyperpotassemia | endocrine/metabolic |
| 276.14 | 1430 | 401506 | 6025 | Hypopotassemia | endocrine/metabolic |
| 276.4 | 1161 | 401506 | 6294 | Acid-base balance disorder | endocrine/metabolic |
| 276.41 | 1055 | 401506 | 6400 | Acidosis | endocrine/metabolic |
| 276.5 | 2834 | 401506 | 4621 | Hypovolemia | endocrine/metabolic |
| 277 | 1424 | 407537 | 0 | Other disorders of metabolism | endocrine/metabolic |
| 278 | 10968 | 397993 | 0 | Overweight, obesity and other hyperalimentation | endocrine/metabolic |
| 278.1 | 10799 | 397993 | 169 | Obesity | endocrine/metabolic |
| 280 | 7787 | 390026 | 11148 | Iron deficiency anemias | hematopoietic |
| 280.1 | 7414 | 390026 | 11521 | Iron deficiency anemias, unspecified or not due to blood loss | hematopoietic |
| 281 | 1133 | 390026 | 17802 | Other deficiency anemia | hematopoietic |
| 281.1 | 1076 | 390026 | 17859 | Megaloblastic anemia | hematopoietic |
| 281.11 | 754 | 390026 | 18181 | Pernicious anemia | hematopoietic |
| 285 | 12256 | 390026 | 6679 | Other anemias | hematopoietic |
| 285.2 | 702 | 390026 | 18233 | Anemia of chronic disease | hematopoietic |
| 286 | 941 | 406281 | 1739 | Coagulation defects | hematopoietic |
| 287 | 1791 | 406281 | 889 | Purpura and other hemorrhagic conditions | hematopoietic |
| 287.3 | 1563 | 406281 | 1117 | Thrombocytopenia | hematopoietic |
| 288 | 3788 | 401375 | 3798 | Diseases of white blood cells | hematopoietic |
| 288.1 | 3184 | 401375 | 4402 | Decreased white blood cell count | hematopoietic |
| 288.11 | 3184 | 401375 | 4402 | Neutropenia | hematopoietic |
| 289 | 4177 | 401375 | 3409 | Other diseases of blood and blood-forming organs | hematopoietic |
| 289.4 | 2622 | 401375 | 4964 | Lymphadenitis | hematopoietic |
| 289.5 | 515 | 401375 | 7071 | Diseases of spleen | hematopoietic |
| 290 | 1970 | 402383 | 4608 | Delirium dementia and amnestic and other cognitive disorders | mental disorders |
| 290.1 | 956 | 402383 | 5622 | Dementias | mental disorders |
| 290.2 | 654 | 402383 | 5924 | Delirium due to conditions classified elsewhere | mental disorders |
| 291 | 641 | 402383 | 5937 | Other specified nonpsychotic and/or transient mental disorders | mental disorders |
| 292 | 4655 | 402383 | 1923 | Neurological disorders | mental disorders |
| 292.1 | 1514 | 402383 | 5064 | Aphasia/speech disturbance | mental disorders |
| 292.3 | 700 | 402383 | 5878 | Memory loss | mental disorders |
| 292.4 | 2189 | 402383 | 4389 | Altered mental status | mental disorders |
| 293 | 2986 | 405975 | 0 | Symptoms involving head and neck | mental disorders |
| 293.1 | 907 | 405975 | 2079 | Swelling, mass, or lump in head and neck [Space-occupying lesion, intracranial NOS] | mental disorders |
| 295 | 850 | 365476 | 42635 | Schizophrenia and other psychotic disorders | mental disorders |
| 295.1 | 571 | 365476 | 42914 | Schizophrenia | mental disorders |
| 296 | 12560 | 365476 | 30925 | Mood disorders | mental disorders |
| 296.1 | 1064 | 365476 | 42421 | Bipolar | mental disorders |
| 296.2 | 11901 | 365476 | 31584 | Depression | mental disorders |
| 300 | 6939 | 365476 | 36546 | Anxiety disorders | mental disorders |
| 300.1 | 6375 | 365476 | 37110 | Anxiety disorder | mental disorders |
| 300.12 | 709 | 365476 | 42776 | Agorophobia, social phobia, and panic disorder | mental disorders |
| 300.13 | 503 | 365476 | 42982 | Phobia | mental disorders |
| 303 | 529 | 365476 | 42956 | Psychogenic and somatoform disorders | mental disorders |
| 306 | 28791 | 365476 | 14694 | Other mental disorder | mental disorders |
| 317 | 12922 | 379355 | 16684 | Alcohol-related disorders | mental disorders |
| 317.1 | 8968 | 379355 | 20638 | Alcoholism | mental disorders |
| 317.11 | 802 | 379355 | 28804 | Alcoholic liver damage | mental disorders |
| 318 | 19780 | 379355 | 9826 | Tobacco use disorder | mental disorders |
| 327 | 5238 | 403723 | 0 | Sleep disorders | neurological |
| 327.3 | 4471 | 403723 | 767 | Sleep apnea | neurological |
| 331 | 1112 | 395209 | 12640 | Other cerebral degenerations | neurological |
| 332 | 1127 | 395209 | 12625 | Parkinson's disease | neurological |
| 333 | 891 | 395209 | 12861 | Extrapyramidal disease and abnormal movement disorders | neurological |
| 334 | 1789 | 395209 | 11963 | Degenerative disease of the spinal cord | neurological |
| 335 | 1356 | 395209 | 12396 | Multiple sclerosis | neurological |
| 338 | 771 | 408190 | 0 | Pain | symptoms |
| 339 | 7891 | 398780 | 2290 | Other headache syndromes | neurological |
| 340 | 2870 | 398780 | 7311 | Migraine | neurological |
| 342 | 1500 | 395209 | 12252 | Hemiplegia | neurological |
| 344 | 660 | 395209 | 13092 | Other paralytic syndromes | neurological |
| 345 | 5087 | 395209 | 8665 | Epilepsy, recurrent seizures, convulsions | neurological |
| 345.1 | 901 | 395209 | 12851 | Epilepsy | neurological |
| 345.3 | 2232 | 395209 | 11520 | Convulsions | neurological |
| 348 | 1426 | 395209 | 12326 | Other conditions of brain | neurological |
| 350 | 2744 | 406217 | 0 | Abnormal movement | neurological |
| 350.1 | 888 | 406217 | 1856 | Abnormal involuntary movements | neurological |
| 350.2 | 1601 | 406217 | 1143 | Abnormality of gait | neurological |
| 351 | 12592 | 394067 | 2302 | Other peripheral nerve disorders | neurological |
| 352 | 1393 | 394067 | 13501 | Disorders of other cranial nerves | neurological |
| 352.2 | 880 | 394067 | 14014 | Facial nerve disorders [CN7] | neurological |
| 353 | 1139 | 394067 | 13755 | Nerve root and plexus disorders | neurological |
| 357 | 1368 | 406852 | 741 | Inflammatory and toxic neuropathy | neurological |
| 361 | 3263 | 397761 | 7937 | Retinal detachments and defects | sense organs |
| 361.1 | 1392 | 397761 | 9808 | Retinal detachment with retinal defect | sense organs |
| 362 | 3867 | 396859 | 8235 | Other retinal disorders | sense organs |
| 362.2 | 2191 | 396859 | 9911 | Degeneration of macula and posterior pole of retina | sense organs |
| 362.29 | 2188 | 396859 | 9914 | Macular degeneration (senile) of retina NOS | sense organs |
| 362.4 | 849 | 396859 | 11253 | Retinal vascular changes and abnomalities | sense organs |
| 364 | 732 | 397761 | 10468 | Corneal opacity and other disorders of cornea | sense organs |
| 365 | 4462 | 397761 | 6738 | Glaucoma | sense organs |
| 365.1 | 1043 | 397761 | 10157 | Open-angle glaucoma | sense organs |
| 365.11 | 1037 | 397761 | 10163 | Primary open angle glaucoma | sense organs |
| 365.2 | 705 | 397761 | 10495 | Primary angle-closure glaucoma | sense organs |
| 366 | 20352 | 388609 | 0 | Cataract | sense organs |
| 366.2 | 8369 | 388609 | 11983 | Senile cataract | sense organs |
| 367 | 2431 | 406530 | 0 | Disorders of refraction and accommodation; blindness and low vision | sense organs |
| 367.1 | 1257 | 406530 | 1174 | Myopia | sense organs |
| 367.9 | 723 | 406530 | 1708 | Blindness and low vision | sense organs |
| 368 | 3307 | 405654 | 0 | Visual disturbances | sense organs |
| 368.1 | 538 | 405654 | 2769 | Amblyopia | sense organs |
| 368.2 | 732 | 405654 | 2575 | Diplopia and disorders of binocular vision | sense organs |
| 368.9 | 615 | 405654 | 2692 | Subjective visual disturbances | sense organs |
| 369 | 560 | 399306 | 9095 | Infection of the eye | sense organs |
| 371 | 3174 | 399306 | 6481 | Inflammation of the eye | sense organs |
| 371.3 | 2396 | 399306 | 7259 | Inflammation of eyelids | sense organs |
| 372 | 765 | 399306 | 8890 | Disorders of conjunctiva | sense organs |
| 374 | 5726 | 399306 | 3929 | Other disorders of eyelids | sense organs |
| 374.1 | 1068 | 399306 | 8587 | Ectropion or entropion | sense organs |
| 374.3 | 1834 | 399306 | 7821 | Ptosis of eyelid | sense organs |
| 375 | 2218 | 401245 | 5498 | Disorders of lacrimal system | sense organs |
| 375.2 | 899 | 401245 | 6817 | Epiphora | sense organs |
| 378 | 1442 | 401245 | 6274 | Strabismus and other disorders of binocular eye movements | sense organs |
| 378.1 | 918 | 401245 | 6798 | Strabismus (not specified as paralytic) | sense organs |
| 379 | 3910 | 401245 | 3806 | Other disorders of eye | sense organs |
| 379.2 | 1372 | 401245 | 6344 | Disorders of vitreous body | sense organs |
| 379.3 | 1825 | 401245 | 5891 | Aphakia and other disorders of lens | sense organs |
| 380 | 1451 | 407510 | 0 | Disorders of external ear | sense organs |
| 380.1 | 524 | 407510 | 927 | Otitis externa | sense organs |
| 381 | 2259 | 404888 | 1814 | Otitis media and Eustachian tube disorders | sense organs |
| 381.1 | 1824 | 404888 | 2249 | Otitis media | sense organs |
| 381.11 | 856 | 404888 | 3217 | Suppurative and unspecified otitis media | sense organs |
| 384 | 1364 | 404888 | 2709 | Other disorders of tympanic membrane | sense organs |
| 384.4 | 1044 | 404888 | 3029 | Perforation of tympanic membrane | sense organs |
| 385 | 828 | 404888 | 3245 | Other disorders of middle ear and mastoid | sense organs |
| 385.3 | 608 | 404888 | 3465 | Cholesteatoma | sense organs |
| 386 | 6134 | 402827 | 0 | Vertiginous syndromes and other disorders of vestibular system | sense organs |
| 386.1 | 578 | 402827 | 5556 | Meniere's disease | sense organs |
| 386.3 | 767 | 402827 | 5367 | Labyrinthitis | sense organs |
| 386.9 | 4611 | 402827 | 1523 | Dizziness and giddiness (Light-headedness and vertigo) | sense organs |
| 389 | 4256 | 404562 | 143 | Hearing loss | sense organs |
| 389.4 | 515 | 404562 | 3884 | Tinnitus | sense organs |
| 394 | 4895 | 402421 | 1645 | Rheumatic disease of the heart valves | circulatory system |
| 394.2 | 2985 | 402421 | 3555 | Mitral valve disease | circulatory system |
| 394.3 | 1260 | 402421 | 5280 | Aortic valve disease | circulatory system |
| 394.7 | 1058 | 402421 | 5482 | Disease of tricuspid valve | circulatory system |
| 395 | 4239 | 402421 | 2301 | Heart valve disorders | circulatory system |
| 395.1 | 2892 | 402421 | 3648 | Nonrheumatic mitral valve disorders | circulatory system |
| 395.6 | 1499 | 402421 | 5041 | Heart valve replaced | circulatory system |
| 396 | 1049 | 402421 | 5491 | Abnormal heart sounds | circulatory system |
| 401 | 77977 | 330366 | 618 | Hypertension | circulatory system |
| 401.1 | 77723 | 330366 | 872 | Essential hypertension | circulatory system |
| 401.2 | 1719 | 330366 | 76876 | Hypertensive heart and/or renal disease | circulatory system |
| 401.22 | 1548 | 330366 | 77047 | Hypertensive chronic kidney disease | circulatory system |
| 402 | 1487 | 330366 | 77108 | Elevated blood pressure reading without diagnosis of hypertension | circulatory system |
| 411 | 31355 | 377103 | 503 | Ischemic Heart Disease | circulatory system |
| 411.1 | 5181 | 377103 | 26677 | Unstable angina (intermediate coronary syndrome) | circulatory system |
| 411.2 | 11703 | 377103 | 20155 | Myocardial infarction | circulatory system |
| 411.3 | 16175 | 377103 | 15683 | Angina pectoris | circulatory system |
| 411.4 | 20023 | 377103 | 11835 | Coronary atherosclerosis | circulatory system |
| 411.41 | 698 | 377103 | 31160 | Aneurysm and dissection of heart | circulatory system |
| 411.8 | 14921 | 377103 | 16937 | Other chronic ischemic heart disease, unspecified | circulatory system |
| 411.9 | 1169 | 377103 | 30689 | Other acute and subacute forms of ischemic heart disease | circulatory system |
| 414 | 1796 | 377103 | 30062 | Other forms of chronic heart disease | circulatory system |
| 415 | 4257 | 402375 | 2329 | Pulmonary heart disease | circulatory system |
| 415.2 | 590 | 402375 | 5996 | Chronic pulmonary heart disease | circulatory system |
| 416 | 2573 | 402375 | 4013 | Cardiomegaly | circulatory system |
| 418 | 31429 | 377532 | 0 | Nonspecific chest pain | circulatory system |
| 418.1 | 3582 | 377532 | 27847 | Precordial pain | circulatory system |
| 420 | 2020 | 405779 | 1162 | Carditis | circulatory system |
| 420.2 | 1273 | 405779 | 1909 | Pericarditis | circulatory system |
| 420.3 | 686 | 405779 | 2496 | Endocarditis | circulatory system |
| 425 | 1247 | 405779 | 1935 | Cardiomyopathy | circulatory system |
| 425.1 | 1208 | 405779 | 1974 | Primary/intrinsic cardiomyopathies | circulatory system |
| 426 | 6959 | 380919 | 21083 | Cardiac conduction disorders | circulatory system |
| 426.2 | 2125 | 380919 | 25917 | Atrioventricular [AV] block | circulatory system |
| 426.21 | 988 | 380919 | 27054 | First degree AV block | circulatory system |
| 426.24 | 587 | 380919 | 27455 | Atrioventricular block, complete | circulatory system |
| 426.3 | 3353 | 380919 | 24689 | Bundle branch block | circulatory system |
| 426.31 | 1498 | 380919 | 26544 | Right bundle branch block | circulatory system |
| 426.32 | 1757 | 380919 | 26285 | Left bundle branch block | circulatory system |
| 426.9 | 2487 | 380919 | 25555 | Cardiac pacemaker/device in situ | circulatory system |
| 426.91 | 2283 | 380919 | 25759 | Cardiac pacemaker in situ | circulatory system |
| 427 | 24681 | 380919 | 3361 | Cardiac dysrhythmias | circulatory system |
| 427.1 | 3225 | 380919 | 24817 | Paroxysmal tachycardia, unspecified | circulatory system |
| 427.11 | 2359 | 380919 | 25683 | Paroxysmal supraventricular tachycardia | circulatory system |
| 427.12 | 938 | 380919 | 27104 | Paroxysmal ventricular tachycardia | circulatory system |
| 427.2 | 14820 | 380919 | 13222 | Atrial fibrillation and flutter | circulatory system |
| 427.3 | 3236 | 380919 | 24806 | Other specified cardiac dysrhythmias | circulatory system |
| 427.4 | 1137 | 380919 | 26905 | Cardiac arrest and ventricular fibrillation | circulatory system |
| 427.42 | 927 | 380919 | 27115 | Cardiac arrest | circulatory system |
| 427.5 | 922 | 380919 | 27120 | Arrhythmia (cardiac) NOS | circulatory system |
| 427.6 | 536 | 380919 | 27506 | Premature beats | circulatory system |
| 427.7 | 2193 | 380919 | 25849 | Tachycardia NOS | circulatory system |
| 427.9 | 3832 | 380919 | 24210 | Palpitations | circulatory system |
| 428 | 5415 | 402834 | 712 | Congestive heart failure; nonhypertensive | circulatory system |
| 428.1 | 2031 | 402834 | 4096 | Congestive heart failure (CHF) NOS | circulatory system |
| 428.2 | 4269 | 402834 | 1858 | Heart failure NOS | circulatory system |
| 429 | 796 | 402834 | 5331 | Ill-defined descriptions and complications of heart disease | circulatory system |
| 429.2 | 524 | 402834 | 5603 | Abnormal function study of cardiovascular system | circulatory system |
| 430 | 1796 | 399017 | 8148 | Intracranial hemorrhage | circulatory system |
| 430.1 | 812 | 399017 | 9132 | Subarachnoid hemorrhage | circulatory system |
| 430.2 | 700 | 399017 | 9244 | Intracerebral hemorrhage | circulatory system |
| 433 | 8742 | 399017 | 1202 | Cerebrovascular disease | circulatory system |
| 433.1 | 1185 | 399017 | 8759 | Occlusion and stenosis of precerebral arteries | circulatory system |
| 433.2 | 4134 | 399017 | 5810 | Occlusion of cerebral arteries | circulatory system |
| 433.21 | 1501 | 399017 | 8443 | Cerebral artery occlusion, with cerebral infarction | circulatory system |
| 433.3 | 2920 | 399017 | 7024 | Cerebral ischemia | circulatory system |
| 433.31 | 2146 | 399017 | 7798 | Transient cerebral ischemia | circulatory system |
| 433.8 | 1263 | 399017 | 8681 | Late effects of cerebrovascular disease | circulatory system |
| 440 | 1324 | 400595 | 7042 | Atherosclerosis | circulatory system |
| 440.2 | 811 | 400595 | 7555 | Atherosclerosis of the extremities | circulatory system |
| 441 | 576 | 400595 | 7790 | Vascular insufficiency of intestine | circulatory system |
| 442 | 1808 | 400595 | 6558 | Other aneurysm | circulatory system |
| 442.1 | 1374 | 400595 | 6992 | Aortic aneurysm | circulatory system |
| 442.11 | 903 | 400595 | 7463 | Abdominal aortic aneurysm | circulatory system |
| 443 | 3927 | 400595 | 4439 | Peripheral vascular disease | circulatory system |
| 443.1 | 1148 | 400595 | 7218 | Raynaud's syndrome | circulatory system |
| 443.9 | 2566 | 400595 | 5800 | Peripheral vascular disease, unspecified | circulatory system |
| 444 | 921 | 400595 | 7445 | Arterial embolism and thrombosis | circulatory system |
| 444.1 | 557 | 400595 | 7809 | Arterial embolism and thrombosis of lower extremity artery | circulatory system |
| 446 | 828 | 400595 | 7538 | Polyarteritis nodosa and allied conditions | circulatory system |
| 447 | 1333 | 400595 | 7033 | Other disorders of arteries and arterioles | circulatory system |
| 447.1 | 873 | 400595 | 7493 | Stricture of artery | circulatory system |
| 450 | 705 | 408256 | 0 | Noninfectious disorders of lymphatic channels | circulatory system |
| 451 | 3900 | 369592 | 35469 | Phlebitis and thrombophlebitis | circulatory system |
| 451.2 | 3587 | 369592 | 35782 | Phlebitis and thrombophlebitis of lower extremities | circulatory system |
| 452 | 558 | 369592 | 38811 | Other venous embolism and thrombosis | circulatory system |
| 454 | 12172 | 369592 | 27197 | Varicose veins | circulatory system |
| 454.1 | 11697 | 369592 | 27672 | Varicose veins of lower extremity | circulatory system |
| 454.11 | 633 | 369592 | 38736 | Varicose veins of lower extremity, symptomtic | circulatory system |
| 455 | 23896 | 369592 | 15473 | Hemorrhoids | circulatory system |
| 458 | 5827 | 387905 | 15229 | Hypotension | circulatory system |
| 458.1 | 1347 | 387905 | 19709 | Orthostatic hypotension | circulatory system |
| 458.9 | 3518 | 387905 | 17538 | Hypotension NOS | circulatory system |
| 459 | 16544 | 387905 | 4512 | Other disorders of circulatory system | circulatory system |
| 459.9 | 16366 | 387905 | 4690 | Circulatory disease NEC | circulatory system |
| 465 | 2335 | 406447 | 179 | Acute upper respiratory infections of multiple or unspecified sites | respiratory |
| 465.2 | 870 | 406447 | 1644 | Acute pharyngitis | respiratory |
| 470 | 4939 | 390045 | 13977 | Septal Deviations/Turbinate Hypertrophy | respiratory |
| 471 | 3311 | 390045 | 15605 | Nasal polyps | respiratory |
| 472 | 966 | 390045 | 17950 | Chronic pharyngitis and nasopharyngitis | respiratory |
| 473 | 2630 | 390045 | 16286 | Diseases of the larynx and vocal cords | respiratory |
| 473.4 | 1086 | 390045 | 17830 | Voice disturbance | respiratory |
| 474 | 2013 | 390045 | 16903 | Acute and chronic tonsillitis | respiratory |
| 474.1 | 614 | 390045 | 18302 | Acute tonsillitis | respiratory |
| 474.2 | 1126 | 390045 | 17790 | Chronic tonsillitis and adenoiditis | respiratory |
| 475 | 2602 | 390045 | 16314 | Chronic sinusitis | respiratory |
| 476 | 1060 | 390045 | 17856 | Allergic rhinitis | respiratory |
| 477 | 2456 | 390045 | 16460 | Epistaxis or throat hemorrhage | respiratory |
| 479 | 4101 | 390045 | 14815 | Other upper respiratory disease | respiratory |
| 480 | 10059 | 398538 | 364 | Pneumonia | respiratory |
| 480.1 | 6710 | 398538 | 3713 | Bacterial pneumonia | respiratory |
| 480.11 | 5951 | 398538 | 4472 | Pneumococcal pneumonia | respiratory |
| 495 | 26332 | 375505 | 7124 | Asthma | respiratory |
| 496 | 10502 | 375505 | 22954 | Chronic airway obstruction | respiratory |
| 496.1 | 1727 | 375505 | 31729 | Emphysema | respiratory |
| 496.2 | 2934 | 375505 | 30522 | Chronic bronchitis | respiratory |
| 496.21 | 2698 | 375505 | 30758 | Obstructive chronic bronchitis | respiratory |
| 496.3 | 1882 | 375505 | 31574 | Bronchiectasis | respiratory |
| 497 | 631 | 375505 | 32825 | Bronchitis | respiratory |
| 501 | 586 | 397411 | 10964 | Pneumonitis due to inhalation of food or vomitus | respiratory |
| 502 | 887 | 397411 | 10663 | Postinflammatory pulmonary fibrosis | respiratory |
| 506 | 1174 | 397411 | 10376 | Empyema and pneumothorax | respiratory |
| 507 | 6448 | 397411 | 5102 | Pleurisy; pleural effusion | respiratory |
| 508 | 2005 | 397411 | 9545 | Pulmonary collapse; interstitial and compensatory emphysema | respiratory |
| 509 | 2565 | 397411 | 8985 | Respiratory failure, insufficiency, arrest | respiratory |
| 509.1 | 2018 | 397411 | 9532 | Respiratory failure | respiratory |
| 509.2 | 1749 | 397411 | 9801 | Respiratory insufficiency | respiratory |
| 510 | 781 | 408180 | 0 | Other diseases of lung | respiratory |
| 512 | 9128 | 399833 | 0 | Other symptoms of respiratory system | respiratory |
| 512.7 | 5884 | 399833 | 3244 | Shortness of breath | respiratory |
| 512.8 | 2884 | 399833 | 6244 | Cough | respiratory |
| 512.9 | 912 | 399833 | 8216 | Other dyspnea | respiratory |
| 513 | 611 | 408350 | 0 | Respiratory abnormalities | respiratory |
| 514 | 2500 | 406461 | 0 | Abnormal findings examination of lungs | respiratory |
| 516 | 2167 | 406794 | 0 | Abnormal sputum | respiratory |
| 516.1 | 2073 | 406794 | 94 | Hemoptysis | respiratory |
| 519 | 9436 | 399525 | 0 | Other diseases of respiratory system, not elsewhere classified | respiratory |
| 519.8 | 8844 | 399525 | 592 | Other diseases of respiratory system, NEC | respiratory |
| 520 | 2449 | 398136 | 8376 | Disorders of tooth development | digestive |
| 520.2 | 2364 | 398136 | 8461 | Disturbances in tooth eruption | digestive |
| 521 | 3091 | 398136 | 7734 | Diseases of hard tissues of teeth | digestive |
| 521.1 | 3051 | 398136 | 7774 | Dental caries | digestive |
| 522 | 1795 | 398136 | 9030 | Diseases of pulp and periapical tissues | digestive |
| 522.5 | 1177 | 398136 | 9648 | Periapical abscess | digestive |
| 523 | 1742 | 398136 | 9083 | Gingival and periodontal diseases | digestive |
| 523.3 | 1222 | 398136 | 9603 | Periodontitis (acute or chronic) | digestive |
| 523.31 | 668 | 398136 | 10157 | Acute periodontitis | digestive |
| 523.32 | 561 | 398136 | 10264 | Chronic periodontitis | digestive |
| 525 | 2689 | 398136 | 8136 | Other diseases of the teeth and supporting structures | digestive |
| 526 | 960 | 398136 | 9865 | Diseases of the jaws | digestive |
| 527 | 710 | 403323 | 4928 | Diseases of the salivary glands | digestive |
| 528 | 3939 | 403323 | 1699 | Diseases of the oral soft tissues, excluding lesions specific for gingiva and tongue | digestive |
| 528.5 | 684 | 403323 | 4954 | Diseases of lips | digestive |
| 529 | 1236 | 403323 | 4402 | Diseases and other conditions of the tongue | digestive |
| 530 | 35852 | 369275 | 3834 | Diseases of esophagus | digestive |
| 530.1 | 32108 | 369275 | 7578 | Esophagitis, GERD and related diseases | digestive |
| 530.11 | 14223 | 369275 | 25463 | GERD | digestive |
| 530.12 | 5243 | 369275 | 34443 | Ulcer of esophagus | digestive |
| 530.14 | 10551 | 369275 | 29135 | Reflux esophagitis | digestive |
| 530.2 | 1672 | 369275 | 38014 | Esophageal bleeding (varices/hemorrhage) | digestive |
| 530.3 | 1874 | 369275 | 37812 | Stricture and stenosis of esophagus | digestive |
| 530.5 | 639 | 369275 | 39047 | Disorders of esophageal motility | digestive |
| 530.9 | 2100 | 369275 | 37586 | Heartburn | digestive |
| 531 | 7436 | 401525 | 0 | Peptic ulcer (excl. esophageal) | digestive |
| 531.1 | 617 | 401525 | 6819 | Hemorrhage from gastrointestinal ulcer | digestive |
| 531.2 | 4109 | 401525 | 3327 | Gastric ulcer | digestive |
| 531.3 | 3002 | 401525 | 4434 | Duodenal ulcer | digestive |
| 532 | 6482 | 369275 | 33204 | Dysphagia | digestive |
| 535 | 28941 | 378124 | 1896 | Gastritis and duodenitis | digestive |
| 535.1 | 1184 | 378124 | 29653 | Acute gastritis | digestive |
| 535.6 | 7655 | 378124 | 23182 | Duodenitis | digestive |
| 535.8 | 8147 | 378124 | 22690 | Other specified gastritis | digestive |
| 537 | 3404 | 378124 | 27433 | Other disorders of stomach and duodenum | digestive |
| 540 | 3409 | 405552 | 0 | Appendiceal conditions | digestive |
| 540.1 | 3217 | 405552 | 192 | Appendicitis | digestive |
| 540.11 | 2608 | 405552 | 801 | Acute appendicitis | digestive |
| 550 | 47344 | 361617 | 0 | Abdominal hernia | digestive |
| 550.1 | 15995 | 361617 | 31349 | Inguinal hernia | digestive |
| 550.2 | 27126 | 361617 | 20218 | Diaphragmatic hernia | digestive |
| 550.3 | 651 | 361617 | 46693 | Femoral hernia | digestive |
| 550.4 | 3727 | 361617 | 43617 | Umbilical hernia | digestive |
| 550.5 | 3448 | 361617 | 43896 | Ventral hernia | digestive |
| 555 | 4528 | 334783 | 69650 | Inflammatory bowel disease and other gastroenteritis and colitis | digestive |
| 555.1 | 1743 | 334783 | 72435 | Regional enteritis | digestive |
| 555.2 | 3195 | 334783 | 70983 | Ulcerative colitis | digestive |
| 555.21 | 539 | 334783 | 73639 | Ulcerative colitis (chronic) | digestive |
| 556 | 1063 | 334783 | 73115 | Ulceration of the lower GI tract | digestive |
| 556.1 | 674 | 334783 | 73504 | Ulceration of intestine | digestive |
| 557 | 2103 | 334783 | 72075 | Intestinal malabsorption (non-celiac) | digestive |
| 557.1 | 1855 | 334783 | 72323 | Celiac disease | digestive |
| 558 | 15747 | 334783 | 58431 | Noninfectious gastroenteritis | digestive |
| 559 | 1660 | 334783 | 72518 | Ileostomy status | digestive |
| 560 | 3994 | 334783 | 70184 | Intestinal obstruction without mention of hernia | digestive |
| 560.1 | 522 | 334783 | 73656 | Paralytic ileus | digestive |
| 560.3 | 832 | 334783 | 73346 | Peritoneal or intestinal adhesions | digestive |
| 560.4 | 3346 | 334783 | 70832 | Other intestinal obstruction | digestive |
| 561 | 15977 | 334783 | 58201 | Symptoms involving digestive system | digestive |
| 561.2 | 1689 | 334783 | 72489 | Flatulence | digestive |
| 562 | 27311 | 334783 | 46867 | Diverticulosis and diverticulitis | digestive |
| 562.1 | 27268 | 334783 | 46910 | Diverticulosis | digestive |
| 563 | 10442 | 334783 | 63736 | Constipation | digestive |
| 564 | 22138 | 334783 | 52040 | Functional digestive disorders | digestive |
| 564.1 | 5548 | 334783 | 68630 | Irritable Bowel Syndrome | digestive |
| 564.8 | 1650 | 334783 | 72528 | Abnormal findings on exam of gastrointestinal tract/ abdominal area | digestive |
| 564.9 | 15392 | 334783 | 58786 | Personal history of diseases of digestive system | digestive |
| 565 | 14997 | 387338 | 6626 | Anal and rectal conditions | digestive |
| 565.1 | 7408 | 387338 | 14215 | Anal and rectal polyp | digestive |
| 567 | 887 | 387338 | 20736 | Peritonitis and retroperitoneal infections | digestive |
| 568 | 3308 | 387338 | 18315 | Other disorders of peritoneum | digestive |
| 568.1 | 3108 | 387338 | 18515 | Peritoneal adhesions (postoperative) (postinfection) | digestive |
| 569 | 4200 | 387338 | 17423 | Other disorders of intestine | digestive |
| 571 | 2895 | 400055 | 6011 | Chronic liver disease and cirrhosis | digestive |
| 571.5 | 1664 | 400055 | 7242 | Other chronic nonalcoholic liver disease | digestive |
| 571.8 | 942 | 400055 | 7964 | Liver abscess and sequelae of chronic liver disease | digestive |
| 571.81 | 529 | 400055 | 8377 | Portal hypertension | digestive |
| 572 | 1547 | 400055 | 7359 | Ascites (non malignant) | digestive |
| 573 | 5847 | 400055 | 3059 | Other disorders of liver | digestive |
| 573.5 | 897 | 400055 | 8009 | Jaundice (not of newborn) | digestive |
| 573.7 | 3479 | 400055 | 5427 | Abnormal results of function study of liver | digestive |
| 574 | 16225 | 391307 | 1429 | Cholelithiasis and cholecystitis | digestive |
| 574.1 | 13777 | 391307 | 3877 | Cholelithiasis | digestive |
| 574.11 | 1513 | 391307 | 16141 | Cholelithiasis with acute cholecystitis | digestive |
| 574.12 | 5472 | 391307 | 12182 | Cholelithiasis with other cholecystitis | digestive |
| 574.2 | 2634 | 391307 | 15020 | Calculus of bile duct | digestive |
| 574.3 | 2761 | 391307 | 14893 | Cholecystitis without cholelithiasis | digestive |
| 575 | 3892 | 391307 | 13762 | Other biliary tract disease | digestive |
| 575.2 | 777 | 391307 | 16877 | Obstruction of bile duct | digestive |
| 575.7 | 1412 | 391307 | 16242 | Other disorders of gallbladder | digestive |
| 575.8 | 1040 | 391307 | 16614 | Other disorders of biliary tract | digestive |
| 577 | 2690 | 406271 | 0 | Diseases of pancreas | digestive |
| 577.1 | 1986 | 406271 | 704 | Acute pancreatitis | digestive |
| 577.2 | 514 | 406271 | 2176 | Chronic pancreatitis | digestive |
| 578 | 21137 | 385157 | 2667 | Gastrointestinal hemorrhage | digestive |
| 578.1 | 1961 | 385157 | 21843 | Hematemesis | digestive |
| 578.2 | 2639 | 385157 | 21165 | Blood in stool | digestive |
| 578.8 | 13222 | 385157 | 10582 | Hemorrhage of rectum and anus | digestive |
| 578.9 | 5229 | 385157 | 18575 | Hemorrhage of gastrointestinal tract | digestive |
| 579 | 3195 | 385157 | 20609 | Other symptoms involving abdomen and pelvis | digestive |
| 579.8 | 1659 | 385157 | 22145 | Nonspecific abnormal findings in stool contents | digestive |
| 580 | 1522 | 397602 | 9837 | Nephritis; nephrosis; renal sclerosis | genitourinary |
| 580.1 | 1033 | 397602 | 10326 | Glomerulonephritis | genitourinary |
| 580.14 | 845 | 397602 | 10514 | Chronic glomerulonephritis, NOS | genitourinary |
| 585 | 6985 | 397602 | 4374 | Renal failure | genitourinary |
| 585.1 | 4521 | 397602 | 6838 | Acute renal failure | genitourinary |
| 585.2 | 1412 | 397602 | 9947 | Renal failure NOS | genitourinary |
| 585.3 | 2629 | 397602 | 8730 | Chronic renal failure [CKD] | genitourinary |
| 586 | 3362 | 397602 | 7997 | Other disorders of the kidney and ureters | genitourinary |
| 586.2 | 1260 | 397602 | 10099 | Cyst of kidney, acquired | genitourinary |
| 586.4 | 913 | 397602 | 10446 | Stricture/obstruction of ureter | genitourinary |
| 590 | 1324 | 379936 | 27701 | Pyelonephritis | genitourinary |
| 591 | 12491 | 379936 | 16534 | Urinary tract infection | genitourinary |
| 592 | 3088 | 379936 | 25937 | Cystitis and urethritis | genitourinary |
| 592.1 | 2948 | 379936 | 26077 | Cystitis | genitourinary |
| 592.12 | 892 | 379936 | 28133 | Chronic cystitis | genitourinary |
| 593 | 16409 | 379936 | 12616 | Hematuria | genitourinary |
| 594 | 6643 | 401005 | 1313 | Urinary calculus | genitourinary |
| 594.1 | 3191 | 401005 | 4765 | Calculus of kidney | genitourinary |
| 594.2 | 778 | 401005 | 7178 | Calculus of lower urinary tract | genitourinary |
| 594.3 | 2417 | 401005 | 5539 | Calculus of ureter | genitourinary |
| 594.8 | 2055 | 401005 | 5901 | Renal colic | genitourinary |
| 595 | 1951 | 401005 | 6005 | Hydronephrosis | genitourinary |
| 596 | 9933 | 394699 | 4329 | Other disorders of bladder | genitourinary |
| 596.1 | 1980 | 394699 | 12282 | Bladder neck obstruction | genitourinary |
| 596.5 | 1664 | 394699 | 12598 | Functional disorders of bladder | genitourinary |
| 597 | 4069 | 394699 | 10193 | Other disorders of urethra and urinary tract | genitourinary |
| 597.1 | 3331 | 394699 | 10931 | Urethral stricture (not specified as infectious) | genitourinary |
| 598 | 3547 | 405414 | 0 | Abnormal findings on examination of urine | genitourinary |
| 599 | 24031 | 384930 | 0 | Other symptoms/disorders or the urinary system | genitourinary |
| 599.2 | 6755 | 384930 | 17276 | Retention of urine | genitourinary |
| 599.3 | 1199 | 384930 | 22832 | Dysuria | genitourinary |
| 599.4 | 8856 | 384930 | 15175 | Urinary incontinence | genitourinary |
| 599.5 | 4037 | 384930 | 19994 | Frequency of urination and polyuria | genitourinary |
| 599.9 | 1926 | 384930 | 22105 | Other abnormality of urination | genitourinary |
| 608 | 2833 | 389094 | 17034 | Other disorders of male genital organs | genitourinary |
| 610 | 3379 | 401746 | 3836 | Benign mammary dysplasias | genitourinary |
| 610.1 | 928 | 401746 | 6287 | Cystic mastopathy | genitourinary |
| 610.4 | 1553 | 401746 | 5662 | Benign neoplasm of breast | genitourinary |
| 610.8 | 696 | 401746 | 6519 | Other specified benign mammary dysplasias | genitourinary |
| 611 | 1580 | 401746 | 5635 | Abnormal findings on mammogram or breast exam | genitourinary |
| 611.3 | 1525 | 401746 | 5690 | Lump or mass in breast | genitourinary |
| 612 | 942 | 401746 | 6273 | Breast conditions, congenital or relating to hormones | genitourinary |
| 612.2 | 854 | 401746 | 6361 | Hypertrophy of breast (Gynecomastia) | genitourinary |
| 613 | 1983 | 406978 | 0 | Other nonmalignant breast conditions | genitourinary |
| 613.1 | 723 | 406978 | 1260 | Inflammatory disease of breast | genitourinary |
| 613.7 | 704 | 406978 | 1279 | Other signs and symptoms in breast | genitourinary |
| 614 | 6204 | 399757 | 3000 | Inflammatory diseases of female pelvic organs | genitourinary |
| 614.1 | 2546 | 399757 | 6658 | Pelvic peritoneal adhesions, female (postoperative) (postinfection) | genitourinary |
| 614.3 | 936 | 399757 | 8268 | Pelvic inflammatory disease (PID) | genitourinary |
| 614.5 | 2864 | 399757 | 6340 | Inflammatory disease of cervix, vagina, and vulva | genitourinary |
| 614.51 | 1323 | 399757 | 7881 | Cervicitis and endocervicitis | genitourinary |
| 614.53 | 758 | 399757 | 8446 | Cyst or abscess of Bartholin's gland | genitourinary |
| 615 | 4053 | 399757 | 5151 | Endometriosis | genitourinary |
| 618 | 11966 | 396730 | 265 | Genital prolapse | genitourinary |
| 618.1 | 7462 | 396730 | 4769 | Prolapse of vaginal walls | genitourinary |
| 618.2 | 5428 | 396730 | 6803 | Uterine/Uterovaginal prolapse | genitourinary |
| 618.5 | 513 | 396730 | 11718 | Prolapse of vaginal vault after hysterectomy | genitourinary |
| 618.6 | 681 | 396730 | 11550 | Vaginal enterocele, congenital or acquired | genitourinary |
| 619 | 9332 | 399629 | 0 | Noninflammatory female genital disorders | genitourinary |
| 619.1 | 730 | 399629 | 8602 | Noninflammatory disorders of ovary, fallopian tube, and broad ligament | genitourinary |
| 619.2 | 3336 | 399629 | 5996 | Disorders of uterus, NEC | genitourinary |
| 619.3 | 2884 | 399629 | 6448 | Noninflammatory disorders of cervix | genitourinary |
| 619.4 | 1776 | 399629 | 7556 | Noninflammatory disorders of vagina | genitourinary |
| 619.5 | 1355 | 399629 | 7977 | Noninflammatory disorders of vulva and perineum | genitourinary |
| 621 | 1133 | 396384 | 11444 | Endometrial hyperplasia | genitourinary |
| 622 | 10881 | 396384 | 1696 | Polyp of female genital organs | genitourinary |
| 622.1 | 7910 | 396384 | 4667 | Polyp of corpus uteri | genitourinary |
| 622.2 | 3450 | 396384 | 9127 | Mucous polyp of cervix | genitourinary |
| 623 | 1275 | 396384 | 11302 | Hypertrophy of female genital organs | genitourinary |
| 624 | 6688 | 399509 | 2764 | Symptoms involving female genital tract | genitourinary |
| 624.9 | 5924 | 399509 | 3528 | stress incontinence, female | genitourinary |
| 625 | 3003 | 399509 | 6449 | Pain and other symptoms associated with female genital organs | genitourinary |
| 625.1 | 1192 | 399509 | 8260 | Dyspareunia | genitourinary |
| 626 | 18580 | 377857 | 12524 | Disorders of menstruation and other abnormal bleeding from female genital tract | genitourinary |
| 626.1 | 15880 | 377857 | 15224 | Irregular menstrual cycle/bleeding | genitourinary |
| 626.12 | 9820 | 377857 | 21284 | Excessive or frequent menstruation | genitourinary |
| 626.13 | 1989 | 377857 | 29115 | Irregular menstrual cycle | genitourinary |
| 626.14 | 3817 | 377857 | 27287 | Irregular menstrual bleeding | genitourinary |
| 626.2 | 1787 | 377857 | 29317 | Dysmenorrhea | genitourinary |
| 626.8 | 1370 | 377857 | 29734 | Infertility, female | genitourinary |
| 627 | 10699 | 377857 | 20405 | Menopausal and postmenopausal disorders | genitourinary |
| 627.1 | 9109 | 377857 | 21995 | Postmenopausal bleeding | genitourinary |
| 627.3 | 1115 | 377857 | 29989 | Postmenopausal atrophic vaginitis | genitourinary |
| 628 | 4777 | 377857 | 26327 | Ovarian cyst | genitourinary |
| 634 | 5463 | 400946 | 2552 | Miscarriage; stillbirth | pregnancy complications |
| 634.1 | 1251 | 400946 | 6764 | Missed abortion/Hydatidiform mole | pregnancy complications |
| 635 | 2005 | 400946 | 6010 | Hemorrhage during pregnancy; childbirth and postpartum | pregnancy complications |
| 635.2 | 866 | 400946 | 7149 | Antepartum hemorrhage, abruptio placentae, and placenta previa | pregnancy complications |
| 635.3 | 1274 | 400946 | 6741 | Placenta previa and abruptio placenta | pregnancy complications |
| 636 | 2558 | 400946 | 5457 | Early or threatened labor; hemorrhage in early pregnancy | pregnancy complications |
| 636.2 | 617 | 400946 | 7398 | Early onset of delivery | pregnancy complications |
| 636.3 | 1083 | 400946 | 6932 | Hemorrhage in early pregnancy | pregnancy complications |
| 642 | 1114 | 407847 | 0 | Hypertension complicating pregnancy, childbirth, and the puerperium | pregnancy complications |
| 645 | 1256 | 407705 | 0 | Late pregnancy and failed induction | pregnancy complications |
| 646 | 2235 | 406726 | 0 | Other complications of pregnancy NEC | pregnancy complications |
| 650 | 1928 | 407033 | 0 | Normal delivery | pregnancy complications |
| 652 | 1720 | 405994 | 1247 | Malposition and malpresentation of fetus or obstruction | digestive |
| 653 | 1404 | 405994 | 1563 | Problems associated with amniotic cavity and membranes | pregnancy complications |
| 655 | 4325 | 404636 | 0 | Known or suspected fetal abnormality affecting management of mother | pregnancy complications |
| 661 | 2272 | 401037 | 5652 | Fetal distress and abnormal forces of labor | pregnancy complications |
| 663 | 533 | 401037 | 7391 | Umbilical cord complications during labor and delivery | pregnancy complications |
| 665 | 5335 | 401037 | 2589 | Obstetrical/birth trauma | pregnancy complications |
| 669 | 2559 | 401037 | 5365 | Complications of labor and delivery NEC | pregnancy complications |
| 681 | 7451 | 397635 | 3875 | Superficial cellulitis and abscess | dermatologic |
| 681.1 | 566 | 397635 | 10760 | Cellulitis and abscess of fingers/toes | dermatologic |
| 681.2 | 524 | 397635 | 10802 | Cellulitis and abscess of face/neck | dermatologic |
| 681.3 | 5539 | 397635 | 5787 | Cellulitis and abscess of arm/hand | dermatologic |
| 681.5 | 5547 | 397635 | 5779 | Cellulitis and abscess of leg, except foot | dermatologic |
| 681.6 | 5502 | 397635 | 5824 | Cellulitis and abscess of foot, toe | dermatologic |
| 681.7 | 602 | 397635 | 10724 | Cellulitis and abscess of trunk | dermatologic |
| 686 | 4520 | 397635 | 6806 | Other local infections of skin and subcutaneous tissue | dermatologic |
| 686.1 | 2302 | 397635 | 9024 | Carbuncle and furuncle | dermatologic |
| 686.3 | 587 | 397635 | 10739 | Pilonidal cyst | dermatologic |
| 687 | 5554 | 403407 | 0 | Symptoms affecting skin | dermatologic |
| 687.1 | 2157 | 403407 | 3397 | Rash and other nonspecific skin eruption | dermatologic |
| 687.4 | 2900 | 403407 | 2654 | Disturbance of skin sensation | dermatologic |
| 689 | 5782 | 403179 | 0 | Disorder of skin and subcutaneous tissue NOS | dermatologic |
| 694 | 987 | 402672 | 5302 | Dyschromia and Vitiligo | dermatologic |
| 694.2 | 783 | 402672 | 5506 | Other dyschromia | dermatologic |
| 695 | 2420 | 402672 | 3869 | Erythematous conditions | dermatologic |
| 695.7 | 779 | 402672 | 5510 | Prurigo and Lichen | dermatologic |
| 696 | 2293 | 398199 | 8469 | Psoriasis and related disorders | dermatologic |
| 696.4 | 2237 | 398199 | 8525 | Psoriasis | dermatologic |
| 696.41 | 1684 | 398199 | 9078 | Psoriasis vulgaris | dermatologic |
| 696.42 | 708 | 398199 | 10054 | Psoriatic arthropathy | dermatologic |
| 697 | 548 | 402672 | 5741 | Sarcoidosis | dermatologic |
| 698 | 783 | 408178 | 0 | Pruritus and related conditions | dermatologic |
| 701 | 4804 | 403875 | 282 | Other hypertrophic and atrophic conditions of skin | dermatologic |
| 701.2 | 2356 | 403875 | 2730 | Scar conditions and fibrosis of skin | dermatologic |
| 702 | 5522 | 398746 | 4693 | Degenerative skin conditions and other dermatoses | dermatologic |
| 702.1 | 2594 | 403439 | 2928 | Actinic keratosis | dermatologic |
| 702.2 | 3092 | 403439 | 2430 | Seborrheic keratosis | dermatologic |
| 703 | 1287 | 402357 | 5317 | Diseases of nail, NOS | dermatologic |
| 703.1 | 970 | 402357 | 5634 | Ingrowing nail | dermatologic |
| 704 | 5344 | 402357 | 1260 | Diseases of hair and hair follicles | dermatologic |
| 705 | 817 | 399255 | 8889 | Disorders of sweat glands | dermatologic |
| 705.8 | 592 | 399255 | 9114 | Hyperhidrosis | dermatologic |
| 706 | 8948 | 399255 | 758 | Diseases of sebaceous glands | dermatologic |
| 706.2 | 8876 | 399255 | 830 | Sebaceous cyst | dermatologic |
| 707 | 1988 | 406973 | 0 | Chronic ulcer of skin | dermatologic |
| 707.1 | 913 | 406973 | 1075 | Decubitus ulcer | dermatologic |
| 709 | 3463 | 399404 | 6094 | Diffuse diseases of connective tissue | dermatologic |
| 709.2 | 513 | 399404 | 9044 | Sicca syndrome | dermatologic |
| 709.7 | 2720 | 399404 | 6837 | Unspecified diffuse connective tissue disease | dermatologic |
| 710 | 612 | 365819 | 42530 | Osteomyelitis, periostitis, and other infections involving bone | musculoskeletal |
| 710.1 | 565 | 365819 | 42577 | Osteomyelitis | musculoskeletal |
| 714 | 4879 | 365085 | 38997 | Rheumatoid arthritis and other inflammatory polyarthropathies | musculoskeletal |
| 714.1 | 4412 | 365085 | 39464 | Rheumatoid arthritis | musculoskeletal |
| 715 | 1671 | 365085 | 42205 | Other inflammatory spondylopathies | musculoskeletal |
| 715.2 | 620 | 365085 | 43256 | Ankylosing spondylitis | musculoskeletal |
| 716 | 38715 | 365819 | 4427 | Other arthropathies | musculoskeletal |
| 716.1 | 3535 | 365819 | 39607 | Unspecified polyarthropathy or polyarthritis | musculoskeletal |
| 716.2 | 15790 | 365819 | 27352 | Unspecified monoarthritis | musculoskeletal |
| 716.9 | 37043 | 365819 | 6099 | Arthropathy NOS | musculoskeletal |
| 717 | 1152 | 407809 | 0 | Polymyalgia Rheumatica | musculoskeletal |
| 720 | 3733 | 391917 | 13311 | Spinal stenosis | musculoskeletal |
| 721 | 7930 | 391917 | 9114 | Spondylosis and allied disorders | musculoskeletal |
| 721.1 | 5077 | 391917 | 11967 | Spondylosis without myelopathy | musculoskeletal |
| 722 | 9241 | 391917 | 7803 | Intervertebral disc disorders | musculoskeletal |
| 722.1 | 513 | 391917 | 16531 | Displacement of intervertebral disc | musculoskeletal |
| 722.6 | 2846 | 391917 | 14198 | Degeneration of intervertebral disc | musculoskeletal |
| 722.9 | 4434 | 391917 | 12610 | Other and unspecified disc disorder | musculoskeletal |
| 723 | 521 | 391917 | 16523 | Other disorders of cervical region | musculoskeletal |
| 724 | 2077 | 391917 | 14967 | Other and unspecified disorders of back | musculoskeletal |
| 724.9 | 1617 | 391917 | 15427 | Other unspecified back disorders | musculoskeletal |
| 726 | 14983 | 378711 | 15267 | Peripheral enthesopathies and allied syndromes | musculoskeletal |
| 726.1 | 9668 | 378711 | 20582 | Enthesopathy | musculoskeletal |
| 726.3 | 858 | 378711 | 29392 | Bursitis | musculoskeletal |
| 727 | 7629 | 378711 | 22621 | Other disorders of synovium, tendon, and bursa | musculoskeletal |
| 727.1 | 2754 | 378711 | 27496 | Synovitis and tenosynovitis | musculoskeletal |
| 727.4 | 3185 | 378711 | 27065 | Ganglion and cyst of synovium, tendon, and bursa | musculoskeletal |
| 727.5 | 593 | 378711 | 29657 | Rupture of synovium | musculoskeletal |
| 728 | 4488 | 378711 | 25762 | Disorders of muscle, ligament, and fascia | musculoskeletal |
| 728.7 | 3843 | 378711 | 26407 | Fasciitis | musculoskeletal |
| 728.71 | 3503 | 378711 | 26747 | Contracture of palmar fascia [Dupuytren's disease] | musculoskeletal |
| 729 | 6170 | 378711 | 24080 | Other disorders of soft tissues | musculoskeletal |
| 729.1 | 1010 | 378711 | 29240 | Rheumatism, unspecified and fibrositis | musculoskeletal |
| 733 | 3773 | 391041 | 14147 | Other disorders of bone and cartilage | musculoskeletal |
| 733.4 | 542 | 391041 | 17378 | Aseptic necrosis of bone | musculoskeletal |
| 733.8 | 1268 | 391041 | 16652 | Malunion and nonunion of fracture | musculoskeletal |
| 735 | 9865 | 394914 | 4182 | Acquired foot deformities | musculoskeletal |
| 735.2 | 5144 | 394914 | 8903 | Acquired toe deformities | musculoskeletal |
| 735.21 | 1939 | 394914 | 12108 | Hammer toe (acquired) | musculoskeletal |
| 735.23 | 1561 | 394914 | 12486 | Hallux rigidus | musculoskeletal |
| 735.3 | 6699 | 394914 | 7348 | Hallux valgus (Bunion) | musculoskeletal |
| 736 | 1649 | 394914 | 12398 | Other acquired deformities of limbs | musculoskeletal |
| 737 | 1134 | 394914 | 12913 | Curvature of spine | musculoskeletal |
| 737.3 | 1063 | 394914 | 12984 | Kyphoscoliosis and scoliosis | musculoskeletal |
| 738 | 1921 | 394914 | 12126 | Other acquired musculoskeletal deformity | musculoskeletal |
| 738.4 | 1521 | 394914 | 12526 | Acquired spondylolisthesis | musculoskeletal |
| 740 | 28439 | 380522 | 0 | Osteoarthrosis | musculoskeletal |
| 740.1 | 17691 | 380522 | 10748 | Osteoarthritis; localized | musculoskeletal |
| 740.11 | 9069 | 380522 | 19370 | Osteoarthrosis, localized, primary | musculoskeletal |
| 740.2 | 599 | 380522 | 27840 | Osteoarthrosis, generalized | musculoskeletal |
| 740.9 | 12436 | 380522 | 16003 | Osteoarthrosis NOS | musculoskeletal |
| 741 | 3634 | 402633 | 2694 | Symptoms and disorders of the joints | musculoskeletal |
| 741.2 | 615 | 402633 | 5713 | Stiffness of joint | musculoskeletal |
| 741.4 | 1425 | 402633 | 4903 | Joint effusions | musculoskeletal |
| 742 | 2913 | 402633 | 3415 | Derangement of joint, non-traumatic | musculoskeletal |
| 742.9 | 2000 | 402633 | 4328 | Other derangement of joint | musculoskeletal |
| 743 | 7682 | 401279 | 0 | Osteoporosis, osteopenia and pathological fracture | musculoskeletal |
| 743.1 | 6484 | 401279 | 1198 | Osteoporosis | musculoskeletal |
| 743.11 | 5622 | 401279 | 2060 | Osteoporosis NOS | musculoskeletal |
| 743.13 | 532 | 401279 | 7150 | Other specified osteoporosis | musculoskeletal |
| 743.2 | 514 | 401279 | 7168 | Pathologic fracture | musculoskeletal |
| 743.9 | 820 | 401279 | 6862 | Osteopenia or other disorder of bone and cartilage | musculoskeletal |
| 745 | 8037 | 400924 | 0 | Pain in joint | musculoskeletal |
| 747 | 2796 | 406165 | 0 | Cardiac and circulatory congenital anomalies | congenital anomalies |
| 747.1 | 2618 | 406165 | 178 | Cardiac congenital anomalies | congenital anomalies |
| 747.11 | 586 | 406165 | 2210 | Cardiac shunt/ heart septal defect | congenital anomalies |
| 747.13 | 1799 | 406165 | 997 | Congenital anomalies of great vessels | congenital anomalies |
| 750 | 703 | 406730 | 1528 | Digestive congenital anomalies | congenital anomalies |
| 751 | 1596 | 406730 | 635 | Genitourinary congenital anomalies | congenital anomalies |
| 751.1 | 732 | 406730 | 1499 | Congenital anomalies of genital organs | congenital anomalies |
| 751.2 | 855 | 406730 | 1376 | Congenital anomalies of urinary system | congenital anomalies |
| 756 | 594 | 407831 | 536 | Other congenital musculoskeletal anomalies | congenital anomalies |
| 760 | 11274 | 397687 | 0 | Back pain | symptoms |
| 761 | 1796 | 407165 | 0 | Cervicalgia | symptoms |
| 764 | 2383 | 405481 | 1097 | Sciatica | symptoms |
| 766 | 1181 | 405481 | 2299 | Neuralgia, neuritis, and radiculitis NOS | symptoms |
| 770 | 642 | 408319 | 0 | Myalgia and myositis unspecified | symptoms |
| 771 | 5493 | 403468 | 0 | Musculoskeletal symptoms referable to limbs | symptoms |
| 771.1 | 4663 | 403468 | 830 | Swelling of limb | symptoms |
| 772 | 698 | 408263 | 0 | Symptoms of the muscles | symptoms |
| 773 | 6327 | 402634 | 0 | Pain in limb | symptoms |
| 781 | 1886 | 407075 | 0 | Symptoms involving nervous and musculoskeletal systems | symptoms |
| 782 | 1816 | 407145 | 0 | Symptoms involving skin and other integumentary tissue | symptoms |
| 782.3 | 1648 | 407145 | 168 | Edema | symptoms |
| 783 | 3940 | 405021 | 0 | Fever of unknown origin | symptoms |
| 785 | 41316 | 367645 | 0 | Abdominal pain | symptoms |
| 788 | 9163 | 399798 | 0 | Syncope and collapse | symptoms |
| 789 | 11706 | 397255 | 0 | Nausea and vomiting | symptoms |
| 790 | 6619 | 402342 | 0 | Nonspecific findings on examination of blood | symptoms |
| 790.6 | 6413 | 402342 | 206 | Other abnormal blood chemistry | symptoms |
| 791 | 550 | 408411 | 0 | Gangrene | symptoms |
| 793 | 698 | 408263 | 0 | Nonspecific abnormal findings on radiological and other examination of musculoskeletal system | injuries & poisonings |
| 793.2 | 567 | 408263 | 131 | Nonspecific abnormal findings on radiological and other examination of other intrathoracic organs (echocardiogram, etc) | circulatory system |
| 798 | 3429 | 405532 | 0 | Malaise and fatigue | symptoms |
| 798.1 | 593 | 405532 | 2836 | Chronic fatigue syndrome | symptoms |
| 800 | 7251 | 387765 | 13945 | Fracture of lower limb | injuries & poisonings |
| 800.1 | 1814 | 387765 | 19382 | Fracture of neck of femur | injuries & poisonings |
| 800.3 | 2162 | 387765 | 19034 | Fracture of tibia and fibula | injuries & poisonings |
| 800.4 | 768 | 387765 | 20428 | Fracture of patella | injuries & poisonings |
| 801 | 2339 | 387765 | 18857 | Fracture of ankle and foot | injuries & poisonings |
| 801.1 | 1842 | 387765 | 19354 | Fracture of foot | injuries & poisonings |
| 802 | 722 | 387765 | 20474 | Fracture of pelvis | injuries & poisonings |
| 803 | 8521 | 387765 | 12675 | Fracture of upper limb | injuries & poisonings |
| 803.1 | 1692 | 387765 | 19504 | Fracture of humerus | injuries & poisonings |
| 803.2 | 5246 | 387765 | 15950 | Fracture of radius and ulna | injuries & poisonings |
| 803.3 | 1521 | 387765 | 19675 | Fracture of clavicle or scapula | injuries & poisonings |
| 804 | 3357 | 387765 | 17839 | Fracture of hand or wrist | injuries & poisonings |
| 805 | 1352 | 387765 | 19844 | Fracture of vertebral column without mention of spinal cord injury | injuries & poisonings |
| 807 | 775 | 387765 | 20421 | Fracture of ribs | injuries & poisonings |
| 809 | 1304 | 387765 | 19892 | Fracture of unspecified bones | injuries & poisonings |
| 818 | 508 | 405554 | 2899 | Intracranial hemorrhage (injury) | injuries & poisonings |
| 819 | 2957 | 405554 | 450 | Skull and face fracture and other intercranial injury | injuries & poisonings |
| 823 | 1674 | 385157 | 22130 | Torus fracture | injuries & poisonings |
| 830 | 2094 | 391457 | 15410 | Dislocation | injuries & poisonings |
| 835 | 15430 | 391457 | 2074 | Internal derangement of knee | injuries & poisonings |
| 836 | 528 | 391457 | 16976 | Traumatic arthropathy | injuries & poisonings |
| 850 | 5329 | 394929 | 8703 | Hemorrhage or hematoma complicating a procedure | injuries & poisonings |
| 853 | 502 | 394929 | 13530 | Complication of colostomy or enterostomy | injuries & poisonings |
| 854 | 1789 | 394929 | 12243 | Complications of cardiac/vascular device, implant, and graft | injuries & poisonings |
| 857 | 1241 | 394929 | 12791 | Mechanical complication of unspecified genitourinary device, implant, and graft | injuries & poisonings |
| 858 | 3167 | 394929 | 10865 | Complication of internal orthopedic device | injuries & poisonings |
| 859 | 3265 | 394929 | 10767 | Complication due to other implant and internal device | injuries & poisonings |
| 870 | 3837 | 400426 | 4698 | Open wounds of head; neck; and trunk | injuries & poisonings |
| 870.3 | 2919 | 400426 | 5616 | Other open wound of head and face | injuries & poisonings |
| 871 | 4219 | 400426 | 4316 | Open wounds of extremities | injuries & poisonings |
| 907 | 1315 | 407496 | 150 | Injuries to the nervous system | injuries & poisonings |
| 915 | 4289 | 403595 | 1077 | Superficial injury without mention of infection | injuries & poisonings |
| 916 | 1486 | 407475 | 0 | Contusion | injuries & poisonings |
| 939 | 2110 | 404817 | 2034 | Atopic/contact dermatitis due to other or unspecified | dermatologic |
| 946 | 548 | 404817 | 3596 | Anaphylactic shock NOS | injuries & poisonings |
| 960 | 18430 | 381797 | 8734 | Poisoning by antibiotics | injuries & poisonings |
| 960.2 | 16090 | 381797 | 11074 | Allergy/adverse effect of penicillin | injuries & poisonings |
| 961 | 1256 | 381797 | 25908 | Poisoning by other anti-infectives | injuries & poisonings |
| 961.1 | 874 | 381797 | 26290 | Poisoning/allergy of sulfonamides | injuries & poisonings |
| 965 | 6910 | 381797 | 20254 | Poisoning by analgesics, antipyretics, and antirheumatics | injuries & poisonings |
| 965.1 | 1150 | 381797 | 26014 | Opiates and related narcotics causing adverse effects in therapeutic use | injuries & poisonings |
| 966 | 509 | 381797 | 26655 | Poisoning by anticonvulsants and anti-Parkinsonism drugs | injuries & poisonings |
| 967 | 588 | 381797 | 26576 | Adverse effects of sedatives or other central nervous system depressants and anesthetics | injuries & poisonings |
| 969 | 1940 | 381797 | 25224 | Poisoning by psychotropic agents | injuries & poisonings |
| 979 | 695 | 381797 | 26469 | Adverse drug events and drug allergies | injuries & poisonings |
| 990 | 3130 | 403295 | 2536 | Effects radiation NOS | injuries & poisonings |
| 994 | 2811 | 406150 | 0 | Sepsis and SIRS | infectious diseases |
| 994.2 | 2811 | 406150 | 0 | Sepsis | infectious diseases |

**Supplementary Table S4 Current medications targeting potential causal proteins**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Target** | **Gene** | **Medication** | **Indication** | **Drug Group** | **Action** |
| deafness, autosomal dominant 5 | DFNA5 | N/A | N/A | N/A | N/A |
| multiple C2 and transmembrane domain containing 1 | MCTP1 | N/A | N/A | N/A | N/A |
| dynamin 3 | DNM3 | N/A | N/A | N/A | N/A |
| Peptide deformylase | PDF | 2-[(Formyl-Hydroxy-Amino)-Methyl]-Heptanoic Acid [1-(2-Hydroxymethyl-Pyrrolidine-1-Carbonyl)-2-Methyl-Propyl]-Amide | N/A | experimental | N/A |
| ATP-binding cassette sub-family B member 8 | ABCB8 | Doxorubicin | [AIDS-related Kaposi's Sarcoma](https://go.drugbank.com/indications/DBCOND0025353),  [Acute Lymphoblastic Leukemia (ALL)](https://go.drugbank.com/indications/DBCOND0031335),  [Acute Myeloid Leukemia](https://go.drugbank.com/indications/DBCOND0029883),  [Advanced Endometrial Cancer](https://go.drugbank.com/indications/DBCOND0050728),  [Advanced Ovarian Cancer](https://go.drugbank.com/indications/DBCOND0037926),  [Breast Cancer](https://go.drugbank.com/indications/DBCOND0028036),  [Hodgkin's Lymphoma](https://go.drugbank.com/indications/DBCOND0030382),  [Metastatic Bone Sarcomas](https://go.drugbank.com/indications/DBCOND0038791),  [Metastatic Breast Cancer](https://go.drugbank.com/indications/DBCOND0030200),  [Metastatic Soft Tissue Sarcoma](https://go.drugbank.com/indications/DBCOND0055864),  [Metastatic Thyroid Cancer](https://go.drugbank.com/indications/DBCOND0076871),  [Metastatic Urothelial Cancer](https://go.drugbank.com/indications/DBCOND0066157),  [Multiple Myeloma (MM)](https://go.drugbank.com/indications/DBCOND0040908),  [Mycosis Fungoides (MF)](https://go.drugbank.com/indications/DBCOND0057197),  [Non-Hodgkin's Lymphoma (NHL)](https://go.drugbank.com/indications/DBCOND0030854),  [Sezary Syndrome](https://go.drugbank.com/indications/DBCOND0001518),  [Waldenström's Macroglobulinemia (WM)](https://go.drugbank.com/indications/DBCOND0092565),  [Advanced Thymoma](https://go.drugbank.com/indications/DBCOND0021657),  [Advanced uterine sarcoma](https://go.drugbank.com/indications/DBCOND0022592),  [Metastatic Bronchogenic Carcinoma](https://go.drugbank.com/indications/DBCOND0155378),  [Metastatic Gastric carcinoma](https://go.drugbank.com/indications/DBCOND0022589),  [Metastatic Neuroblastoma](https://go.drugbank.com/indications/DBCOND0022582),  [Metastatic Ovarian carcinoma](https://go.drugbank.com/indications/DBCOND0022585),  [Metastatic Wilms' tumor](https://go.drugbank.com/indications/DBCOND0022581), | approved, investigational | substrate |
| Cathepsin F | CTSF | 4-Morpholin-4-Yl-Piperidine-1-Carboxylic Acid [1-(3-Benzenesulfonyl-1-Propyl-Allylcarbamoyl)-2-Phenylethyl]-Amide | N/A | experimental | N/A |
| [1-(1-Methyl-4,5-Dioxo-Pent-2-Enylcarbamoyl)-2-Phenyl-Ethyl]-Carbamic Acid Benzyl Ester | N/A | experimental | N/A |
| HOMOPHENYLALANINYLMETHANE | N/A | experimental | N/A |
| WRR-99 | N/A | experimental | N/A |
| WRR-112 | N/A | experimental | N/A |
| [1-(1-Benzyl-3-Hydroxy-2-Oxo-Propylcarbamoyl)-2-Phenyl-Ethyl]-Carbamic Acid Benzyl Ester | N/A | experimental | N/A |
| Benzyl N-[(2S)-5-(diaminomethylamino)-1-[[(2S)-4-fluoro-3-oxobutan-2-yl]amino]-1-oxopentan-2-yl]carbamate | N/A | experimental | N/A |
| Benzoyl-tyrosine-alanine-fluoro-methyl ketone | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | experimental | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| Agouti-related protein | AGRP | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| Frizzled-related protein | FRZB | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| Low-density lipoprotein receptor-related protein 8 | LRP8 | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| Interleukin-36 alpha | IL36A | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| Tissue inhibitor of metalloproteinases 4 | TIMP4 | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| lectin, mannose binding 2 like | LMAN2L | N/A | N/A | N/A | N/A |
| Inter-alpha-trypsin inhibitor heavy chain H1 | ITIH1 | Zinc | [Candidiasis](https://go.drugbank.com/indications/DBCOND0020645),  [Common Cold](https://go.drugbank.com/indications/DBCOND0000353),  [Diaper Dermatitis](https://go.drugbank.com/indications/DBCOND0078869),  [Diaper Rash](https://go.drugbank.com/indications/DBCOND0005733),  [Eye redness](https://go.drugbank.com/indications/DBCOND0023338),  [Iron Deficiency (ID)](https://go.drugbank.com/indications/DBCOND0132786),  [Ocular Irritation](https://go.drugbank.com/indications/DBCOND0042226),  [Skin Irritation](https://go.drugbank.com/indications/DBCOND0062614),  [Sunburn](https://go.drugbank.com/indications/DBCOND0005372),  [Wilson's Disease](https://go.drugbank.com/indications/DBCOND0032702),  [Zinc Deficiency](https://go.drugbank.com/indications/DBCOND0037140), | approved, investigational | [N/A](https://zhuanlan.zhihu.com/p/495978713) |
| Mersalyl | Elevated blood pressure, edema | experimental | inducer |
| Zinc acetate | Pruritus,  Skin Irritation,  Oozing and weeping,  Pain and itching, | approved, investigational | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| Zinc chloride | Dietary supplementation | approved, investigational | binder |
| Zinc sulfate, unspecified form | Nutritional supplementation,  Dietary supplementation | approved, experimental | binder |
| Phosphatidylinositol 3-kinase catalytic subunit type 3 | PI3 | N-(5-{4-Chloro-3-[(2-hydroxyethyl)sulfamoyl]phenyl}-4-methyl-1,3-thiazol-2-yl)acetamide | N/A | experimental | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| GSK-1059615 | N/A | investigational | inhibitor |
| Neural cell adhesion molecule 1 | NCAM1 | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |
| C-X3-C motif chemokine ligand 1 | CX3CL1 | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) | [N/A](https://www.bing.com/search?q=Bing+AI&showconv=1&FORM=hpcodx) |