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Phenome-wide association study of genetically predicted B vitamins and homocysteine biomarkers with multiple health and disease outcomes: analysis of the UK Biobank. [Dataset]

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2023

This dataset consists of the supplementary material for an article that has been published online:
<https://doi.org/10.1016/j.ajcnut.2023.01.005>

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Supplementary Materials

Supplementary Tables

Supplementary Table 1. SNPs used for the generation of weighted genetic risk score.

Biomarker	SNP	Chr	Position (GRCh37)	Effect allele/ other allele	EAF	Beta ¹	SE	P-value	Variance (%)	F-statistics	Gene	Reference
Folate	rs1801133	1	11856378	G/A	0.67	0.096	0.009	9.50E-53	0.408	153.0	<i>MTHFR</i>	Grarup et al.(1)
	rs652197	11	71849741	C/T	0.18	0.069	0.011	1.40E-12	0.141	52.7	<i>FOLR3</i>	
Vitamin B6	rs1256335	1	21890386	A/G	0.79	0.140	0.020	1.40E-15	0.650	31.2	<i>ALPL</i>	Hazra et al.(2)
Vitamin B12	rs2336573	19	8367709	T/C	0.03	0.320	0.007	8.40E-59	0.596	273.3	<i>CD320</i>	Grarup et al.(1)
	rs1131603	22	31018975	C/T	0.06	0.190	0.017	4.90E-49	0.407	186.3	<i>TCN2</i>	
	rs3742801	14	74759006	T/C	0.29	0.045	0.009	1.70E-13	0.083	37.9	<i>ABCD4</i>	
	rs2270655	4	146576418	G/C	0.94	0.066	0.018	2.20E-13	0.049	22.3	<i>MMAA</i>	
	rs12272669	11	71392610	A/G	0.01	0.510	0.007	3.00E-09	0.515	235.9	<i>MMACHC</i>	
	rs34324219	11	59623378	C/A	0.88	0.210	0.007	1.10E-111	0.931	428.3	<i>TCN1</i>	
	rs34528912	11	59631535	T/C	0.04	0.170	0.021	2.10E-15	0.222	101.4	<i>TCN1</i>	
	rs117456053	11	59616831	G/A	0.98	0.160	0.026	1.90E-09	0.100	45.6	<i>TCN1</i>	
	rs7788053	7	86773722	A/G	0.25	0.046	0.007	1.70E-10	0.079	36.0	<i>FUT6</i>	
	rs602662	19	49206985	A/G	0.60	0.160	0.007	2.40E-139	1.229	567.1	<i>FUT2</i>	van Meurs JB et al.(3)
	rs1801222	10	17156151	G/A	0.59	0.110	0.007	3.30E-75	0.585	268.2	<i>CUBN</i>	

Homocysteine	rs56077122	10	17207015	A/C	0.34	0.087	0.009	4.80E-21	0.340	155.5	<i>TRDMT1</i>
	rs41281112	13	100518634	C/T	0.95	0.170	0.020	8.90E-35	0.275	125.7	<i>CLYBL</i>
	rs1141321	6	49412433	C/T	0.63	0.061	0.007	3.60E-26	0.173	79.0	<i>MMUT</i>
	rs1801133	1	11856378	A/G	0.34	0.158	0.007	4.30E-104	1.120	500.0	<i>MTHFR</i>
	rs2275565	1	237048676	G/T	0.79	0.054	0.009	2.00E-10	0.097	42.9	<i>MTR</i>
	rs1047891	2	211540507	A/C	0.33	0.086	0.008	4.60E-27	0.327	144.8	<i>CPS1</i>
	rs9369898	6	49382193	A/G	0.62	0.045	0.007	2.20E-10	0.095	42.0	<i>MUT</i>
	rs7130284	11	89148372	C/T	0.93	0.124	0.013	1.90E-20	0.200	88.5	<i>NOX4</i>
	rs154657	16	89708096	A/G	0.47	0.096	0.007	1.70E-43	0.459	203.6	<i>DPEP1</i>
	rs234709	21	44486964	C/T	0.55	0.072	0.007	3.90E-24	0.257	113.8	<i>CBS</i>
	rs4660306	1	45978675	T/C	0.33	0.043	0.007	2.30E-09	0.082	36.2	<i>PRDX1</i>
	rs548987	6	25869371	C/G	0.13	0.060	0.010	1.10E-08	0.081	35.8	<i>SLC17A3</i>
	rs42648	7	89977760	G/A	0.60	0.039	0.007	2.00E-08	0.073	32.3	<i>GTPBP10</i>
	rs1801222	10	17156151	A/G	0.34	0.045	0.007	8.40E-10	0.091	40.2	<i>CUBN</i>
	rs2251468	12	121405126	C/A	0.35	0.051	0.007	1.30E-12	0.118	52.2	<i>HNFI1A-AS1</i>
	rs838133	19	49259529	A/G	0.45	0.042	0.007	7.50E-09	0.087	38.4	<i>FUT1</i>
	rs12780845	10	17223244	A/G	0.65	0.053	0.009	7.80E-10	0.128	56.6	<i>TRDMT1</i>

EAF: effect allele frequency, SE: standard error.

¹ Weight for each SNP when calculating the wGRS.

Supplementary Table 2. Phenotypes tested in the PheWAS analysis.

Phecode	Description	Category	Cases	Participants
008	Intestinal infection	infectious diseases	5414	385917
008.5	Bacterial enteritis	infectious diseases	3635	384138
008.52	Intestinal infection due to <i>C. difficile</i>	infectious diseases	1087	381590
008.6	Viral Enteritis	infectious diseases	1204	381707
038	Septicemia	infectious diseases	9820	374526
038.1	Gram negative septicemia	infectious diseases	483	365189
038.2	Gram positive septicemia	infectious diseases	910	365616
041	Bacterial infection NOS	infectious diseases	14255	378961
041.1	Staphylococcus infections	infectious diseases	4710	369416
041.11	Methicillin sensitive <i>Staphylococcus aureus</i>	infectious diseases	3351	368057
041.2	Streptococcus infection	infectious diseases	2841	367547
041.4	<i>E. coli</i>	infectious diseases	5585	370291
053	Herpes zoster	infectious diseases	732	379361
054	Herpes simplex	infectious diseases	300	378929
070	Viral hepatitis	infectious diseases	841	379470
070.2	Viral hepatitis B	infectious diseases	246	378875
070.3	Viral hepatitis C	infectious diseases	371	379000
070.4	Chronic hepatitis	infectious diseases	390	379019
070.9	Hepatitis NOS	infectious diseases	396	379025
078	Viral warts & HPV	infectious diseases	1595	380224
079	Viral infection	infectious diseases	3274	381903
079.9	Viremia, NOS	infectious diseases	2370	380999
080	Postoperative infection	infectious diseases	6056	382880

081	Infection/inflammation of internal prosthetic device; implant; and graft	infectious diseases	3539	380363
110	Dermatophytosis / Dermatomycosis	infectious diseases	547	382375
110.1	Dermatophytosis	infectious diseases	456	382284
110.12	Althete's foot	infectious diseases	219	382047
112	Candidiasis	infectious diseases	3154	384982
117	Mycoses	infectious diseases	472	382300
117.4	Aspergillosis	infectious diseases	283	382111
134	Helminthiases	infectious diseases	206	385476
145	Cancer of mouth	neoplasms	1127	383834
145.2	Cancer of tongue	neoplasms	508	383215
145.3	Cancer of major salivary glands	neoplasms	218	382925
149	Cancer of larynx, pharynx, nasal cavities	neoplasms	1090	383797
149.1	Cancer of oropharynx	neoplasms	448	383155
149.4	Cancer of larynx	neoplasms	432	383139
150	Cancer of esophagus	neoplasms	1365	362295
151	Cancer of stomach	neoplasms	1038	361968
153	Colorectal cancer	neoplasms	7981	351262
153.2	Colon cancer	neoplasms	5507	348788
153.3	Malignant neoplasm of rectum, rectosigmoid junction, and anus	neoplasms	3741	347022
155	Cancer of liver and intrahepatic bile duct	neoplasms	831	361761
155.1	Malignant neoplasm of liver, primary	neoplasms	386	361316
157	Pancreatic cancer	neoplasms	1390	362320
158	Neoplasm of unspecified nature of digestive system	neoplasms	1540	362470
159	Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	neoplasms	1184	362114

159.2	Malignant neoplasm of small intestine, including duodenum	neoplasms	353	361283
159.3	Malignant neoplasm of gallbladder and extrahepatic bile ducts	neoplasms	417	361347
159.4	Malignant neoplasm of retroperitoneum and peritoneum	neoplasms	374	361304
165	Cancer within the respiratory system	neoplasms	5345	385851
165.1	Cancer of bronchus; lung	neoplasms	4356	384862
170	Cancer of bone and connective tissue	neoplasms	829	385917
170.1	Bone cancer	neoplasms	225	385313
170.2	Cancer of connective tissue	neoplasms	637	385725
172	Skin cancer	neoplasms	23206	385727
172.1	Melanomas of skin, dx or hx	neoplasms	5329	367850
172.11	Melanomas of skin	neoplasms	5329	367850
172.2	Other non-epithelial cancer of skin	neoplasms	17539	380060
172.3	Carcinoma in situ of skin	neoplasms	2282	364803
173	Neoplasm of uncertain behavior of skin	neoplasms	288	362809
174	Breast cancer	neoplasms	12869	366834
174.1	Breast cancer [female]	neoplasms	12777	366742
174.11	Malignant neoplasm of female breast	neoplasms	11222	365187
175	Acquired absence of breast	neoplasms	4891	357785
180	Cervical cancer and dysplasia	neoplasms	14210	361317
180.1	Cervical cancer	neoplasms	8618	355725
180.3	Cervical intraepithelial neoplasia [CIN] [Cervical dysplasia]	neoplasms	6089	353196
182	Malignant neoplasm of uterus	neoplasms	2201	349368
184	Cancer of other female genital organs	neoplasms	9732	364715
184.1	Malignant neoplasm of ovary and other uterine adnexa	neoplasms	9120	364103
184.11	Malignant neoplasm of ovary	neoplasms	9050	364033

184.2	Cancer of other female genital organs	neoplasms	650	355633
185	Cancer of prostate	neoplasms	15187	367385
187	Cancer of other male genital organs	neoplasms	8497	378583
187.1	Malignant neoplasm of unspecified male genital organ	neoplasms	8046	378132
187.2	Malignant neoplasm of testis	neoplasms	8315	378401
189	Cancer of urinary organs (incl. kidney and bladder)	neoplasms	5761	385917
189.1	Cancer of kidney and renal pelvis	neoplasms	1961	382117
189.11	Malignant neoplasm of kidney, except pelvis	neoplasms	1898	382054
189.2	Cancer of bladder	neoplasms	3870	384026
189.21	Malignant neoplasm of bladder	neoplasms	3390	383546
189.4	Malignant neoplasm of other urinary organs	neoplasms	306	380462
190	Cancer of eye	neoplasms	540	383045
191	Malignant and unknown neoplasms of brain and nervous system	neoplasms	1270	383775
191.1	Cancer of brain and nervous system	neoplasms	1019	383524
191.11	Cancer of brain	neoplasms	928	383433
193	Thyroid cancer	neoplasms	745	383953
195	Cancer, suspected or other	neoplasms	10605	365471
195.1	Malignant neoplasm, other	neoplasms	10517	365383
196	Radiotherapy	neoplasms	2626	357492
197	Chemotherapy	neoplasms	11364	366230
198	Secondary malignant neoplasm	neoplasms	16743	371609
198.1	Secondary malignancy of lymph nodes	neoplasms	9025	363891
198.2	Secondary malignancy of respiratory organs	neoplasms	4633	359499
198.3	Secondary malignant neoplasm of digestive systems	neoplasms	2871	357737
198.4	Secondary malignant neoplasm of liver	neoplasms	5314	360180

198.6	Secondary malignancy of bone	neoplasms	4446	359312
198.7	Secondary malignant neoplasm of skin	neoplasms	363	355229
199	Neoplasm of uncertain behavior	neoplasms	2002	356868
200	Myeloproliferative disease	neoplasms	1780	380424
200.1	Polycythemia vera	neoplasms	596	373710
201	Hodgkin's disease	neoplasms	524	379168
202	Cancer of other lymphoid, histiocytic tissue	neoplasms	2957	381601
202.2	Non-Hodgkins lymphoma	neoplasms	2947	381591
202.21	Nodular lymphoma	neoplasms	570	379214
202.24	Large cell lymphoma	neoplasms	1126	379770
204	Leukemia	neoplasms	3019	381663
204.1	Lymphoid leukemia	neoplasms	1051	379695
204.12	Lymphoid leukemia, chronic	neoplasms	926	379570
204.2	Myeloid leukemia	neoplasms	810	379454
204.21	Myeloid leukemia, acute	neoplasms	598	379242
204.4	Multiple myeloma	neoplasms	1071	379715
208	Benign neoplasm of colon	neoplasms	33993	381542
210	Benign neoplasm of lip, oral cavity, and pharynx	neoplasms	1246	383953
211	Benign neoplasm of other parts of digestive system	neoplasms	9692	373514
212	Benign neoplasm of respiratory and intrathoracic organs	neoplasms	496	385917
213	Benign neoplasm of bone and articular cartilage	neoplasms	387	341853
214	Lipoma	neoplasms	7535	385214
214.1	Lipoma of skin and subcutaneous tissue	neoplasms	5039	382718
215	Other benign neoplasm of connective and other soft tissue	neoplasms	734	378413
216	Benign neoplasm of skin	neoplasms	7657	385039

217	Vascular hamartomas and non-neoplastic nevi	neoplasms	921	378303
217.1	Nevus, non-neoplastic	neoplasms	859	378241
218	Benign neoplasm of uterus	neoplasms	11521	367667
218.1	Uterine leiomyoma	neoplasms	11228	367374
218.2	Other benign neoplasm of uterus	neoplasms	410	356556
220	Benign neoplasm of ovary	neoplasms	1817	347066
221	Benign neoplasm of other female genital organs	neoplasms	252	345074
222	Benign neoplasm of male genital organs	neoplasms	212	370298
223	Benign neoplasm of kidney and other urinary organs	neoplasms	293	341759
224	Benign neoplasm of eye	neoplasms	240	382745
225	Benign neoplasm of brain and other parts of nervous system	neoplasms	1541	384046
225.1	Benign neoplasm of brain, cranial nerves, meninges	neoplasms	1430	383935
226	Benign neoplasm of thyroid glands	neoplasms	354	383562
227	Benign neoplasm of other endocrine glands and related structures	neoplasms	1557	384765
227.1	Benign neoplasm of adrenal gland	neoplasms	375	383583
227.2	Benign neoplasm of parathyroid gland	neoplasms	628	383836
227.3	Benign neoplasm of pituitary gland and craniopharyngeal duct (pouch)	neoplasms	551	383759
228	Hemangioma and lymphangioma, any site	neoplasms	2189	385917
229	Benign neoplasm of unspecified sites	neoplasms	284	385917
241	Nontoxic nodular goiter	endocrine/metabolic	2354	362583
241.1	Nontoxic uninodular goiter	endocrine/metabolic	822	361051
241.2	Nontoxic multinodular goiter	endocrine/metabolic	929	361158
242	Thyrotoxicosis with or without goiter	endocrine/metabolic	2910	363139
242.1	Graves' disease	endocrine/metabolic	680	360909
244	Hypothyroidism	endocrine/metabolic	22218	382447

244.1	Secondary hypothyroidism	endocrine/metabolic	1980	362209
244.2	Acquired hypothyroidism	endocrine/metabolic	262	360491
244.4	Hypothyroidism NOS	endocrine/metabolic	21141	381370
245	Thyroiditis	endocrine/metabolic	444	360673
245.2	Chronic thyroiditis	endocrine/metabolic	343	360572
245.21	Chronic lymphocytic thyroiditis	endocrine/metabolic	326	360555
246	Other disorders of thyroid	endocrine/metabolic	691	360920
250	Diabetes mellitus	endocrine/metabolic	28375	384683
250.1	Type 1 diabetes	endocrine/metabolic	3299	359607
250.11	Type 1 diabetes with ketoacidosis	endocrine/metabolic	352	356660
250.2	Type 2 diabetes	endocrine/metabolic	27436	383744
250.23	Type 2 diabetes with ophthalmic manifestations	endocrine/metabolic	2220	358528
250.4	Abnormal glucose	endocrine/metabolic	1856	358164
250.42	Other abnormal glucose	endocrine/metabolic	691	356999
251.1	Hypoglycemia	endocrine/metabolic	2157	354514
252	Disorders of parathyroid gland	endocrine/metabolic	1697	381157
252.1	Hyperparathyroidism	endocrine/metabolic	1500	380960
252.2	Hypoparathyroidism	endocrine/metabolic	355	379815
253	Disorders of the pituitary gland and its hypothalamic control	endocrine/metabolic	1155	380615
253.1	Pituitary hyperfunction	endocrine/metabolic	240	379700
253.2	Pituitary hypofunction	endocrine/metabolic	373	379833
253.7	Other disorders of neurohypophysis	endocrine/metabolic	414	379874
255	Disorders of adrenal glands	endocrine/metabolic	948	380408
255.1	Adrenal hyperfunction	endocrine/metabolic	259	379719
255.2	Adrenal hypofunction	endocrine/metabolic	389	379849

255.21	Glucocorticoid deficiency	endocrine/metabolic	389	379849
256	Ovarian dysfunction	endocrine/metabolic	300	379760
256.4	Polycystic ovaries	endocrine/metabolic	292	379752
257	Testicular dysfunction	endocrine/metabolic	264	379724
257.1	Testicular hypofunction	endocrine/metabolic	254	379714
259	Other endocrine disorders	endocrine/metabolic	219	379679
260	Protein-calorie malnutrition	endocrine/metabolic	536	378645
260.6	Anorexia	endocrine/metabolic	1709	379818
261	Vitamin deficiency	endocrine/metabolic	5055	383164
261.2	Vitamin B-complex deficiencies	endocrine/metabolic	2246	380355
261.4	Vitamin D deficiency	endocrine/metabolic	3010	381119
262	Mineral deficiency NEC	endocrine/metabolic	754	378863
269	Proteinuria	endocrine/metabolic	431	384729
270	Disorders of protein plasma/amino-acid transport and metabolism	endocrine/metabolic	938	385236
270.3	Disorders of plasma protein metabolism	endocrine/metabolic	874	385172
270.32	Paraproteinemia	endocrine/metabolic	757	385055
270.33	Amyloidosis	endocrine/metabolic	305	384603
271	Disorders of carbohydrate transport and metabolism	endocrine/metabolic	257	385917
271.3	Intestinal disaccharidase deficiencies and disaccharide malabsorption	endocrine/metabolic	224	385884
272	Disorders of lipid metabolism	endocrine/metabolic	54333	385917
272.1	Hyperlipidemia	endocrine/metabolic	54099	385683
272.11	Hypercholesterolemia	endocrine/metabolic	50143	381727
272.13	Mixed hyperlipidemia	endocrine/metabolic	284	331868
272.9	Unspecified disorder of lipid metabolism	endocrine/metabolic	641	332225
274	Gout and other crystal arthropathies	endocrine/metabolic	5737	385917

274.1	Gout	endocrine/metabolic	5153	385333
274.11	Gouty arthropathy	endocrine/metabolic	234	380414
274.2	Crystal arthropathies	endocrine/metabolic	664	380844
274.21	Chondrocalcinosis	endocrine/metabolic	525	380705
275	Disorders of mineral metabolism	endocrine/metabolic	5073	385917
275.1	Disorders of iron metabolism	hematopoietic	1055	381899
275.3	Disorders of magnesium metabolism	endocrine/metabolic	1723	382567
275.5	Disorders of calcium/phosphorus metabolism	endocrine/metabolic	2742	383586
276	Disorders of fluid, electrolyte, and acid-base balance	endocrine/metabolic	17810	384307
276.1	Electrolyte imbalance	endocrine/metabolic	12186	378683
276.11	Hyperosmolality and/or hypernatremia	endocrine/metabolic	889	367386
276.12	Hyposmolality and/or hyponatremia	endocrine/metabolic	5738	372235
276.13	Hyperpotassemia	endocrine/metabolic	2541	369038
276.14	Hypopotassemia	endocrine/metabolic	4641	371138
276.4	Acid-base balance disorder	endocrine/metabolic	3198	369695
276.41	Acidosis	endocrine/metabolic	2787	369284
276.42	Alkalosis	endocrine/metabolic	458	366955
276.5	Hypovolemia	endocrine/metabolic	7155	373652
276.6	Fluid overload	endocrine/metabolic	1935	368432
277	Other disorders of metabolism	endocrine/metabolic	1790	385057
277.4	Disorders of bilirubin excretion	endocrine/metabolic	681	383948
278	Overweight, obesity and other hyperalimentation	endocrine/metabolic	24611	385917
278.1	Obesity	endocrine/metabolic	24439	385745
279	Disorders involving the immune mechanism	endocrine/metabolic	472	385586
279.1	Immunity deficiency	endocrine/metabolic	387	385501

279.11	Deficiency of humoral immunity	endocrine/metabolic	274	385388
279.7	Other immunological findings	endocrine/metabolic	342	385456
280	Iron deficiency anemias	hematopoietic	14813	368801
280.1	Iron deficiency anemias, unspecified or not due to blood loss	hematopoietic	14317	368305
280.2	Iron deficiency anemia secondary to blood loss (chronic)	hematopoietic	683	354671
281	Other deficiency anemia	hematopoietic	1972	355960
281.1	Megaloblastic anemia	hematopoietic	1862	355850
281.11	Pernicious anemia	hematopoietic	1144	355132
281.12	Other vitamin B12 deficiency anemia	hematopoietic	297	354285
281.13	Folate-deficiency anemia	hematopoietic	487	354475
282	Hereditary hemolytic anemias	hematopoietic	352	354340
283	Acquired hemolytic anemias	hematopoietic	234	354222
284	Aplastic anemia	hematopoietic	927	354915
285	Other anemias	hematopoietic	20529	374517
285.1	Acute posthemorrhagic anemia	hematopoietic	332	354320
285.2	Anemia of chronic disease	hematopoietic	1206	355194
285.22	Anemia in neoplastic disease	hematopoietic	655	354643
286	Coagulation defects	hematopoietic	1444	382486
286.1	Congenital coagulation defects	hematopoietic	599	381641
286.12	Congenital deficiency of other clotting factors (including factor VII)	hematopoietic	375	381417
286.7	Other and unspecified coagulation defects	hematopoietic	551	381593
286.8	Hypercoagulable state	hematopoietic	312	381354
286.81	Primary hypercoagulable state	hematopoietic	312	381354
287	Purpura and other hemorrhagic conditions	hematopoietic	3371	384413
287.1	Spontaneous ecchymoses	hematopoietic	225	381267

287.3	Thrombocytopenia	hematopoietic	3103	384145
287.31	Primary thrombocytopenia	hematopoietic	641	381683
288	Diseases of white blood cells	hematopoietic	877	374545
288.1	Decreased white blood cell count	hematopoietic	5176	378844
288.11	Neutropenia	hematopoietic	5176	378844
289	Other diseases of blood and blood-forming organs	hematopoietic	1628	375296
289.3	Personal history of diseases of blood and blood-forming organs	hematopoietic	684	374352
289.4	Lymphadenitis	hematopoietic	4277	377945
289.5	Diseases of spleen	hematopoietic	930	374598
289.8	Polycythemia vera, secondary	hematopoietic	549	373254
290	Delirium dementia and amnestic and other cognitive disorders	mental disorders	5597	378536
290.1	Dementias	mental disorders	4002	376941
290.11	Alzheimer's disease	mental disorders	2126	375065
290.13	Senile dementia	mental disorders	2683	375622
291	Other specified nonpsychotic and/or transient mental disorders	mental disorders	833	373772
291.8	Alteration of consciousness	mental disorders	789	373728
292	Neurological disorders	mental disorders	8228	381167
292.1	Aphasia/speech disturbance	mental disorders	1850	374789
292.3	Memory loss	mental disorders	1356	374295
292.4	Altered mental status	mental disorders	5271	378210
292.6	Hallucinations	mental disorders	694	373633
293	Symptoms involving head and neck	mental disorders	2249	384630
293.1	Swelling, mass, or lump in head and neck [Space-occupying lesion, intracranial NOS]	mental disorders	1296	383677
295	Schizophrenia and other psychotic disorders	mental disorders	1052	354230

295.1	Schizophrenia	mental disorders	788	353966
295.3	Psychosis	mental disorders	332	353510
296	Mood disorders	mental disorders	22221	375399
296.1	Bipolar	mental disorders	1393	354571
296.2	Depression	mental disorders	21502	374680
296.22	Major depressive disorder	mental disorders	21431	374609
297	Suicidal ideation or attempt	mental disorders	611	353789
297.2	Suicide or self-inflicted injury	mental disorders	573	353751
300	Anxiety, phobic and dissociative disorders	mental disorders	15361	368539
300.1	Anxiety disorder	mental disorders	14456	367634
300.11	Generalized anxiety disorder	mental disorders	285	353463
300.12	Agoraphobia, social phobia, and panic disorder	mental disorders	1522	354700
300.13	Phobia	mental disorders	1425	354603
300.3	Obsessive-compulsive disorders	mental disorders	230	353408
300.9	Posttraumatic stress disorder	mental disorders	352	353530
301	Personality disorders	mental disorders	478	353656
303	Psychogenic and somatoform disorders	mental disorders	614	353792
303.3	Psychogenic disorder	mental disorders	434	353612
304	Adjustment reaction	mental disorders	367	353545
306	Other mental disorder	mental disorders	541	353719
306.9	Tension headache	mental disorders	481	353659
313	Pervasive developmental disorders	mental disorders	217	384832
315	Develomental delays and disorders	mental disorders	1064	385679
315.1	Learning disorder	mental disorders	245	384860
316	Substance addiction and disorders	mental disorders	572	368689

316.1	Polyneuropathy due to drugs	mental disorders	203	368320
317	Alcohol-related disorders	mental disorders	7544	375661
317.1	Alcoholism	mental disorders	5713	373830
317.11	Alcoholic liver damage	mental disorders	1313	369430
318	Tobacco use disorder	mental disorders	11179	379296
320	Meningitis	neurological	524	384958
323	Encephalitis	neurological	491	384925
324	Other CNS infection and poliomyelitis	neurological	486	384920
327	Sleep disorders	neurological	1841	379380
327.3	Sleep apnea	neurological	7188	384727
327.4	Insomnia	neurological	417	377956
331	Other cerebral degenerations	neurological	1940	368449
331.1	Hydrocephalus	neurological	814	367323
331.9	Cerebral degeneration, unspecified	neurological	1060	367569
332	Parkinson's disease	neurological	2631	369140
333	Extrapyramidal disease and abnormal movement disorders	neurological	1603	368112
333.1	Essential tremor	neurological	709	367218
333.4	Torsion dystonia	neurological	417	366926
333.8	Other degenerative diseases of the basal ganglia	neurological	246	366755
334	Degenerative disease of the spinal cord	neurological	2719	369228
334.1	Spinocerebellar disease	neurological	229	366738
334.2	Anterior horn cell disease	neurological	488	366997
335	Multiple sclerosis	neurological	1610	368119
337	Disorders of the autonomic nervous system	neurological	558	367067
337.1	Peripheral autonomic neuropathy	neurological	302	366811

339	Other headache syndromes	neurological	10719	381836
340	Migraine	neurological	5026	376143
340.1	Migrain with aura	neurological	385	371502
341	Other demyelinating diseases of central nervous system	neurological	302	366811
342	Hemiplegia	neurological	2914	369423
344	Other paralytic syndromes	neurological	965	367474
345	Epilepsy, recurrent seizures, convulsions	neurological	4910	371419
345.1	Epilepsy	neurological	850	367359
345.11	Generalized convulsive epilepsy	neurological	651	367160
346.1	Nonspecific abnormal findings on radiological and other examination of skull and head	neurological	262	366771
348	Other conditions of brain	neurological	1189	367698
348.2	Cerebral edema and compression of brain	neurological	570	367079
348.4	Cerebral cysts	neurological	226	366735
348.7	Coma	neurological	618	367127
348.9	Other conditions of brain, NOS	neurological	366	366875
349	Other and unspecified disorders of the nervous system	neurological	438	366947
350	Abnormal movement	neurological	2595	385771
350.1	Abnormal involuntary movements	neurological	1818	384994
350.3	Lack of coordination	neurological	654	383830
351	Other peripheral nerve disorders	neurological	15046	382986
352	Disorders of other cranial nerves	neurological	2158	370098
352.1	Trigeminal nerve disorders [CN5]	neurological	787	368727
352.2	Facial nerve disorders [CN7]	neurological	1307	369247
353	Nerve root and plexus disorders	neurological	886	368826

355	Complex regional/central pain syndrome	neurological	343	368283
356	Hereditary and idiopathic peripheral neuropathy	neurological	258	382635
357	Inflammatory and toxic neuropathy	neurological	2697	385074
358	Myoneural disorders	neurological	309	382686
358.1	Myasthenia gravis	neurological	267	382644
359	Muscular dystrophies and other myopathies	neurological	439	382816
359.2	Myopathy	neurological	288	382665
360	Disorders of the globe	sense organs	505	368061
360.2	Progressive myopia	sense organs	375	367931
361	Retinal detachments and defects	sense organs	1574	369130
362	Other retinal disorders	sense organs	8067	375617
362.2	Degeneration of macula and posterior pole of retina	sense organs	5949	373499
362.29	Macular degeneration (senile) of retina NOS	sense organs	5946	373496
362.3	Other nondiabetic retinopathy	sense organs	1561	369111
362.31	Separation of retinal layers	sense organs	1484	369034
362.4	Retinal vascular changes and abnormalities	sense organs	329	367879
362.6	Peripheral retinal degenerations	sense organs	265	367815
363	Chorioretinal inflammations, scars, and other disorders of choroid	sense organs	384	367940
364	Corneal opacity and other disorders of cornea	sense organs	1928	369484
364.4	Corneal degenerations	sense organs	1163	368719
364.5	Corneal dystrophy	sense organs	540	368096
365	Glaucoma	sense organs	9255	376811
365.1	Open-angle glaucoma	sense organs	2425	369981
365.2	Primary angle-closure glaucoma	sense organs	1258	368814
366	Cataract	sense organs	38349	385917

366.2	Senile cataract	sense organs	15072	362640
367	Disorders of refraction and accommodation; blindness and low vision	sense organs	7101	385917
367.1	Myopia	sense organs	2733	381549
367.2	Astigmatism	sense organs	2540	381356
367.8	Hypermetropia	sense organs	554	379370
367.9	Blindness and low vision	sense organs	1251	380067
368	Visual disturbances	sense organs	5537	385241
368.1	Amblyopia	sense organs	1196	380900
368.2	Diplopia and disorders of binocular vision	sense organs	1250	380954
368.3	Anisometropia	sense organs	428	380132
368.4	Visual field defects	sense organs	740	380444
368.9	Subjective visual disturbances	sense organs	1138	380842
368.91	Psychophysical visual disturbances	sense organs	472	380176
369	Infection of the eye	sense organs	895	376321
369.5	Conjunctivitis, infectious	sense organs	442	375868
370	Keratitis	sense organs	387	375813
370.1	Corneal ulcer	sense organs	224	375650
371	Inflammation of the eye	sense organs	3655	379081
371.1	Uveitis, noninfectious or NOS	sense organs	563	375989
371.3	Inflammation of eyelids	sense organs	2898	378324
372	Disorders of conjunctiva	sense organs	765	376191
374	Other disorders of eyelids	sense organs	5554	380980
374.1	Ectropion or entropion	sense organs	1841	377267
374.3	Ptosis of eyelid	sense organs	2625	378051
375	Disorders of lacrimal system	sense organs	3402	380202

375.2	Epiphora	sense organs	1221	378021
377	Disorders of optic nerve and visual pathways	sense organs	646	377446
377.3	Optic neuritis/neuropathy	sense organs	264	377064
378	Strabismus and other disorders of binocular eye movements	sense organs	2104	378904
378.1	Strabismus (not specified as paralytic)	sense organs	908	377708
378.2	Nystagmus and other irregular eye movements	sense organs	416	377216
378.5	Paralytic strabismus	sense organs	484	377284
379	Other disorders of eye	sense organs	3088	379888
379.2	Disorders of vitreous body	sense organs	1445	378245
379.3	Aphakia and other disorders of lens	sense organs	455	377255
379.4	Anomalies of pupillary function	sense organs	235	377035
379.5	Disorders of iris and ciliary body	sense organs	565	377365
379.9	Pain, swelling or discharge of eye	sense organs	272	377072
380	Disorders of external ear	sense organs	729	384849
380.1	Otitis externa	sense organs	707	384827
380.4	Impacted cerumen	sense organs	464	384584
381	Otitis media and Eustachian tube disorders	sense organs	2448	383936
381.1	Otitis media	sense organs	1956	383444
381.11	Suppurative and unspecified otitis media	sense organs	975	382463
381.2	Eustachian tube disorders	sense organs	271	381759
381.9	Otorrhea	sense organs	297	381785
382	Otalgia	sense organs	418	381906
383	Otosclerosis	sense organs	357	381845
384	Other disorders of tympanic membrane	sense organs	1344	382832
384.4	Perforation of tympanic membrane	sense organs	1015	382503

385	Other disorders of middle ear and mastoid	sense organs	888	382376
385.3	Cholesteatoma	sense organs	641	382129
385.5	Tympanosclerosis and middle ear disease related to otitis media	sense organs	257	381745
386	Vertiginous syndromes and other disorders of vestibular system	sense organs	3062	378158
386.1	Meniere's disease	sense organs	929	376025
386.2	Peripheral or central vertigo	sense organs	1074	376170
386.3	Labyrinthitis	sense organs	1053	376149
386.9	Dizziness and giddiness (Light-headedness and vertigo)	sense organs	8302	383398
389	Hearing loss	sense organs	10276	385874
389.1	Sensorineural hearing loss	sense organs	1238	376836
389.2	Conductive hearing loss	sense organs	582	376180
389.3	Degenerative and vascular disorders of ear	sense organs	317	375915
389.4	Tinnitus	sense organs	1124	376722
394	Rheumatic disease of the heart valves	circulatory system	6196	375889
394.1	Mitral valve stenosis and aortic valve stenosis	circulatory system	1645	371338
394.2	Mitral valve disease	circulatory system	574	370267
394.7	Disease of tricuspid valve	circulatory system	954	370647
395	Heart valve disorders	circulatory system	10682	380375
395.1	Nonrheumatic mitral valve disorders	circulatory system	4723	374416
395.2	Nonrheumatic aortic valve disorders	circulatory system	5469	375162
395.3	Nonrheumatic tricuspid valve disorders	circulatory system	338	370031
395.4	Nonrheumatic pulmonary valve disorders	circulatory system	445	370138
395.6	Heart valve replaced	circulatory system	2663	372356
396	Abnormal heart sounds	circulatory system	2639	372332
401	Hypertension	circulatory system	109545	385917

401.1	Essential hypertension	circulatory system	109289	385661
401.2	Hypertensive heart and/or renal disease	circulatory system	2172	278544
401.21	Hypertensive heart disease	circulatory system	615	276987
401.22	Hypertensive chronic kidney disease	circulatory system	1552	277924
411	Ischemic Heart Disease	circulatory system	42936	384255
411.1	Unstable angina (intermediate coronary syndrome)	circulatory system	5848	347167
411.2	Myocardial infarction	circulatory system	15134	356453
411.3	Angina pectoris	circulatory system	21291	362610
411.4	Coronary atherosclerosis	circulatory system	28433	369752
411.41	Aneurysm and dissection of heart	circulatory system	316	341635
411.8	Other chronic ischemic heart disease, unspecified	circulatory system	23318	364637
411.9	Other acute and subacute forms of ischemic heart disease	circulatory system	2664	343983
414	Other forms of chronic heart disease	circulatory system	5615	346934
415	Pulmonary heart disease	circulatory system	1974	379892
415.2	Chronic pulmonary heart disease	circulatory system	1863	379781
415.21	Primary pulmonary hypertension	circulatory system	578	378496
416	Cardiomegaly	circulatory system	6621	384539
418	Nonspecific chest pain	circulatory system	455	379864
418.1	Precordial pain	circulatory system	6075	385484
420	Carditis	circulatory system	3637	383807
420.1	Myocarditis	circulatory system	230	380400
420.2	Pericarditis	circulatory system	2465	382635
420.21	Acute pericarditis	circulatory system	280	380450
420.22	Chronic pericarditis	circulatory system	274	380444
420.3	Endocarditis	circulatory system	1058	381228

425	Cardiomyopathy	circulatory system	2303	382473
425.1	Primary/intrinsic cardiomyopathies	circulatory system	2249	382419
425.11	Hypertrophic obstructive cardiomyopathy	circulatory system	237	380407
425.12	Other hypertrophic cardiomyopathy	circulatory system	337	380507
426	Cardiac conduction disorders	circulatory system	11996	356423
426.2	Atrioventricular [AV] block	circulatory system	5127	349554
426.21	First degree AV block	circulatory system	2758	347185
426.23	Second degree AV block	circulatory system	1044	345471
426.24	Atrioventricular block, complete	circulatory system	1355	345782
426.25	Other heart block	circulatory system	235	344662
426.3	Bundle branch block	circulatory system	4409	348836
426.32	Left bundle branch block	circulatory system	3876	348303
426.4	Anomalous atrioventricular excitation	circulatory system	268	344695
426.9	Cardiac pacemaker/device in situ	circulatory system	5149	349576
426.91	Cardiac pacemaker in situ	circulatory system	4833	349260
427	Cardiac dysrhythmias	circulatory system	35983	380410
427.1	Paroxysmal tachycardia, unspecified	circulatory system	5073	349500
427.11	Paroxysmal supraventricular tachycardia	circulatory system	3647	348074
427.12	Paroxysmal ventricular tachycardia	circulatory system	1596	346023
427.2	Atrial fibrillation and flutter	circulatory system	19630	364057
427.21	Atrial fibrillation	circulatory system	4949	349376
427.22	Atrial flutter	circulatory system	1081	345508
427.3	Other specified cardiac dysrhythmias	circulatory system	5898	350325
427.4	Cardiac arrest and ventricular fibrillation	circulatory system	1522	345949
427.41	Ventricular fibrillation and flutter	circulatory system	638	345065

427.42	Cardiac arrest	circulatory system	966	345393
427.5	Arrhythmia (cardiac) NOS	circulatory system	1738	346165
427.6	Premature beats	circulatory system	1264	345691
427.61	Supraventricular premature beats	circulatory system	258	344685
427.7	Tachycardia NOS	circulatory system	4368	348795
427.8	Sinoatrial node dysfunction (Bradycardia)	circulatory system	931	345358
427.9	Palpitations	circulatory system	5710	350137
428	Congestive heart failure; nonhypertensive	circulatory system	9612	385016
428.1	Congestive heart failure (CHF) NOS	circulatory system	4645	380049
428.2	Heart failure NOS	circulatory system	6530	381934
429	Ill-defined descriptions and complications of heart disease	circulatory system	997	376401
429.2	Abnormal function study of cardiovascular system	circulatory system	983	376387
430	Intracranial hemorrhage	circulatory system	2660	372808
430.1	Subarachnoid hemorrhage	circulatory system	1163	371311
430.2	Intracerebral hemorrhage	circulatory system	1515	371663
433	Cerebrovascular disease	circulatory system	14058	384206
433.1	Occlusion and stenosis of precerebral arteries	circulatory system	2337	372485
433.12	Cerebral atherosclerosis	circulatory system	564	370712
433.2	Occlusion of cerebral arteries	circulatory system	5302	375450
433.21	Cerebral artery occlusion, with cerebral infarction	circulatory system	5202	375350
433.3	Cerebral ischemia	circulatory system	6132	376280
433.31	Transient cerebral ischemia	circulatory system	3299	373447
433.5	Cerebral aneurysm	circulatory system	613	370761
440	Atherosclerosis	circulatory system	1790	373521
440.2	Atherosclerosis of the extremities	circulatory system	1384	373115

440.9	Atherosclerosis of aorta	circulatory system	247	371978
441	Vascular insufficiency of intestine	circulatory system	1292	373023
441.1	Acute vascular insufficiency of intestine	circulatory system	576	372307
442	Other aneurysm	circulatory system	3812	375543
442.1	Aortic aneurysm	circulatory system	3076	374807
442.11	Abdominal aortic aneurysm	circulatory system	1893	373624
442.2	Aneurysm of iliac artery	circulatory system	219	371950
442.3	Aneurysm of artery of lower extremity	circulatory system	292	372023
442.8	Aneurysm of other specified artery	circulatory system	409	372140
443	Peripheral vascular disease	circulatory system	6591	378322
443.1	Raynaud's syndrome	circulatory system	2164	373895
443.9	Peripheral vascular disease, unspecified	circulatory system	4529	376260
444	Arterial embolism and thrombosis	circulatory system	1386	373117
444.1	Arterial embolism and thrombosis of lower extremity artery	circulatory system	878	372609
446	Polyarteritis nodosa and allied conditions	circulatory system	1454	373185
446.4	Wegener's granulomatosis	circulatory system	238	371969
446.5	Giant cell arteritis	circulatory system	781	372512
446.9	Arteritis NOS	circulatory system	477	372208
447	Other disorders of arteries and arterioles	circulatory system	2097	373828
447.1	Stricture of artery	circulatory system	1313	373044
450	Noninfectious disorders of lymphatic channels	circulatory system	1684	385917
451	Phlebitis and thrombophlebitis	circulatory system	1986	354812
451.2	Phlebitis and thrombophlebitis of lower extremities	circulatory system	1442	354268
452	Other venous embolism and thrombosis	circulatory system	428	353254
454	Varicose veins	circulatory system	14121	366947

454.1	Varicose veins of lower extremity	circulatory system	13457	366283
454.11	Varicose veins of lower extremity, symptomatic	circulatory system	1292	354118
455	Hemorrhoids	circulatory system	16311	369137
456	Chronic venous insufficiency [CVI]	circulatory system	538	353364
458	Hypotension	circulatory system	13850	361032
458.1	Orthostatic hypotension	circulatory system	3916	351098
458.2	Iatrogenic hypotension	circulatory system	469	347651
458.9	Hypotension NOS	circulatory system	8491	355673
459	Other disorders of circulatory system	circulatory system	28851	376033
459.1	Hemorrhage NOS	circulatory system	215	347397
459.9	Circulatory disease NEC	circulatory system	28533	375715
464	Acute sinusitis	respiratory	250	382699
465	Acute upper respiratory infections of multiple or unspecified sites	respiratory	3238	385687
465.2	Acute pharyngitis	respiratory	1238	383687
465.4	Acute laryngitis and tracheitis	respiratory	219	382668
470	Septal Deviations/Turbinate Hypertrophy	respiratory	4987	368244
471	Nasal polyps	respiratory	3719	366976
472	Chronic pharyngitis and nasopharyngitis	respiratory	1345	364602
473	Diseases of the larynx and vocal cords	respiratory	3466	366723
473.3	Paralysis/spasm of vocal cords or larynx	respiratory	467	363724
473.4	Voice disturbance	respiratory	1373	364630
474	Acute and chronic tonsillitis	respiratory	2218	365475
474.1	Acute tonsillitis	respiratory	654	363911
474.2	Chronic tonsillitis and adenoiditis	respiratory	1260	364517
475	Chronic sinusitis	respiratory	3412	366669

476	Allergic rhinitis	respiratory	2620	365877
477	Epistaxis or throat hemorrhage	respiratory	3694	366951
478	Throat pain	respiratory	467	363724
479	Other upper respiratory disease	respiratory	1866	365123
480	Pneumonia	respiratory	21080	385044
480.1	Bacterial pneumonia	respiratory	13568	377532
480.11	Pneumococcal pneumonia	respiratory	12818	376782
480.2	Viral pneumonia	respiratory	215	364179
480.3	Pneumonia due to fungus (mycoses)	respiratory	219	364183
480.5	Bronchopneumonia and lung abscess	respiratory	1564	365528
481	Influenza	respiratory	953	364917
483	Acute bronchitis and bronchiolitis	respiratory	386	364350
496	Chronic airway obstruction	respiratory	19238	385246
496.1	Emphysema	respiratory	3557	369565
496.2	Chronic bronchitis	respiratory	6076	372084
496.21	Obstructive chronic bronchitis	respiratory	5666	371674
496.3	Bronchiectasis	respiratory	4072	370080
497	Bronchitis	respiratory	954	366962
500	Lung disease due to external agents	respiratory	820	362515
500.2	Pneumoconiosis	respiratory	495	362190
501	Pneumonitis due to inhalation of food or vomitus	respiratory	2208	363903
502	Postinflammatory pulmonary fibrosis	respiratory	2139	363834
504	Other alveolar and parietoalveolar pneumonopathy	respiratory	865	362560
506	Empyema and pneumothorax	respiratory	1964	363659
507	Pleurisy; pleural effusion	respiratory	12918	374613

508	Pulmonary collapse; interstitial and compensatory emphysema	respiratory	5776	367471
509	Respiratory failure, insufficiency, arrest	respiratory	6556	368251
509.1	Respiratory failure	respiratory	5332	367027
509.2	Respiratory insufficiency	respiratory	2453	364148
509.5	Respiratory arrest	respiratory	248	361943
509.8	Dependence on respirator [Ventilator] or supplemental oxygen	respiratory	1150	362845
510	Other diseases of lung	respiratory	2378	385869
512	Other symptoms of respiratory system	respiratory	14817	385917
512.1	Wheezing	respiratory	459	371559
512.2	Painful respiration	respiratory	343	371443
512.7	Shortness of breath	respiratory	10577	381677
512.8	Cough	respiratory	5302	376402
513	Respiratory abnormalities	respiratory	938	385917
513.3	Hypoventilation	respiratory	227	385206
513.4	Hyperventilation	respiratory	315	385294
513.8	Disorders of diaphragm	respiratory	304	385283
514	Abnormal findings examination of lungs	respiratory	4711	385864
516	Abnormal sputum	respiratory	2952	385917
516.1	Hemoptysis	respiratory	2814	385779
519	Other diseases of respiratory system, not elsewhere classified	respiratory	16703	385826
519.8	Other diseases of respiratory system, NEC	respiratory	16218	385341
519.9	Symptoms involving respiratory system and other chest symptoms	respiratory	417	369540
520	Disorders of tooth development	digestive	2603	376330
520.2	Disturbances in tooth eruption	digestive	2504	376231
521	Diseases of hard tissues of teeth	digestive	4172	377899

521.1	Dental caries	digestive	4082	377809
522	Diseases of pulp and periapical tissues	digestive	2272	375999
522.5	Periapical abscess	digestive	1581	375308
523	Gingival and periodontal diseases	digestive	2247	375974
523.3	Periodontitis (acute or chronic)	digestive	1516	375243
523.32	Chronic periodontitis	digestive	1339	375066
525	Other diseases of the teeth and supporting structures	digestive	3368	377095
526	Diseases of the jaws	digestive	261	373988
526.1	Cysts of the jaws	digestive	247	373974
527	Diseases of the salivary glands	digestive	991	381711
527.2	Sialoadenitis	digestive	508	381228
528	Diseases of the oral soft tissues, excluding lesions specific for gingiva and tongue	digestive	2698	383418
528.1	Stomatitis and mucositis	digestive	783	381503
528.11	Stomatitis and mucositis (ulcerative)	digestive	687	381407
528.3	Cellulitis and abscess of oral soft tissues	digestive	263	380983
528.5	Diseases of lips	digestive	940	381660
528.7	Sialolithiasis	digestive	367	381087
529	Diseases and other conditions of the tongue	digestive	1765	382485
529.1	Glossitis	digestive	428	381148
530	Diseases of esophagus	digestive	52779	384456
530.1	Esophagitis, GERD and related diseases	digestive	49975	381652
530.11	GERD	digestive	28649	360326
530.12	Ulcer of esophagus	digestive	6108	337785
530.13	Barrett's esophagus	digestive	5177	336854

530.14	Reflux esophagitis	digestive	14401	346078
530.2	Esophageal bleeding (varices/hemorrhage)	digestive	2091	333768
530.3	Stricture and stenosis of esophagus	digestive	3117	334794
530.5	Disorders of esophageal motility	digestive	1056	332733
530.6	Diverticulum of esophagus, acquired	digestive	275	331952
530.7	Gastroesophageal laceration-hemorrhage syndrome	digestive	427	332104
530.9	Heartburn	digestive	2888	334565
531	Peptic ulcer (excl. esophageal)	digestive	10394	385917
531.1	Hemorrhage from gastrointestinal ulcer	digestive	970	376493
531.2	Gastric ulcer	digestive	6066	381589
531.3	Duodenal ulcer	digestive	3912	379435
531.4	Peptic ulcer, site unspecified	digestive	598	376121
535	Gastritis and duodenitis	digestive	40063	374530
535.1	Acute gastritis	digestive	564	335031
535.2	Atrophic gastritis	digestive	645	335112
535.6	Duodenitis	digestive	10335	344802
535.8	Other specified gastritis	digestive	13674	348141
535.9	Gastritis and duodenitis, NOS	digestive	974	335441
536	Disorders of function of stomach	digestive	13479	347946
536.8	Dyspepsia and other specified disorders of function of stomach	digestive	13465	347932
537	Other disorders of stomach and duodenum	digestive	5493	339960
540	Appendiceal conditions	digestive	1808	385917
540.1	Appendicitis	digestive	1489	385598
540.11	Acute appendicitis	digestive	884	384993
550	Abdominal hernia	digestive	47760	385917

550.1	Inguinal hernia	digestive	424	338581
550.2	Diaphragmatic hernia	digestive	38892	377049
550.3	Femoral hernia	digestive	766	338923
550.4	Umbilical hernia	digestive	5226	343383
550.5	Ventral hernia	digestive	4606	342763
550.6	Incisional hernia	digestive	904	339061
555	Inflammatory bowel disease and other gastroenteritis and colitis	digestive	5577	318473
555.1	Regional enteritis	digestive	2166	315062
555.2	Ulcerative colitis	digestive	3976	316872
555.21	Ulcerative colitis (chronic)	digestive	858	313754
556	Ulceration of the lower GI tract	digestive	1726	314622
556.1	Ulceration of intestine	digestive	1150	314046
557	Intestinal malabsorption (non-celiac)	digestive	435	313331
557.1	Celiac disease	digestive	2470	315366
558	Noninfectious gastroenteritis	digestive	17793	330689
559	Ileostomy status	digestive	2300	315196
560	Intestinal obstruction without mention of hernia	digestive	6930	319826
560.1	Paralytic ileus	digestive	1169	314065
560.2	Impaction of intestine	digestive	572	313468
560.3	Peritoneal or intestinal adhesions	digestive	1481	314377
560.4	Other intestinal obstruction	digestive	4557	317453
561	Symptoms involving digestive system	digestive	21722	334618
564	Functional digestive disorders	digestive	37462	350358
564.1	Irritable Bowel Syndrome	digestive	9289	322185
564.9	Personal history of diseases of digestive system	digestive	27072	339968

565	Anal and rectal conditions	digestive	21158	374652
565.1	Anal and rectal polyp	digestive	11633	365127
567	Peritonitis and retroperitoneal infections	digestive	1507	355001
568	Other disorders of peritoneum	digestive	6237	359731
568.1	Peritoneal adhesions (postoperative) (postinfection)	digestive	5861	359355
569	Other disorders of intestine	digestive	7084	360578
569.1	Toxic gastroenteritis and colitis	digestive	575	354069
569.2	Gastrointestinal complications	digestive	804	354298
571	Chronic liver disease and cirrhosis	digestive	7990	376570
571.5	Other chronic nonalcoholic liver disease	digestive	6276	374856
571.51	Cirrhosis of liver without mention of alcohol	digestive	236	368816
571.6	Primary biliary cirrhosis	digestive	357	368937
571.8	Liver abscess and sequelae of chronic liver disease	digestive	1909	370489
571.81	Portal hypertension	digestive	1023	369603
572	Ascites (non malignant)	digestive	2851	371431
573	Other disorders of liver	digestive	3420	372000
573.3	Hepatomegaly	digestive	505	369085
573.5	Jaundice (not of newborn)	digestive	1398	369978
573.7	Abnormal results of function study of liver	digestive	6627	375207
573.9	Abnormal serum enzyme levels	digestive	414	368994
574	Cholelithiasis and cholecystitis	digestive	20567	383100
574.1	Cholelithiasis	digestive	18324	380857
574.11	Cholelithiasis with acute cholecystitis	digestive	2414	364947
574.12	Cholelithiasis with other cholecystitis	digestive	7335	369868
574.2	Calculus of bile duct	digestive	528	363061

574.3	Cholecystitis without cholelithiasis	digestive	3744	366277
575	Other biliary tract disease	digestive	6602	369135
575.1	Cholangitis	digestive	1186	363719
575.2	Obstruction of bile duct	digestive	1437	363970
575.6	Cholesterolosis of gallbladder	digestive	626	363159
575.7	Other disorders of gallbladder	digestive	2173	364706
575.8	Other disorders of biliary tract	digestive	1929	364462
575.9	Nonspecific abnormal findings on radiological and other examination of biliary tract	digestive	628	363161
577	Diseases of pancreas	digestive	4492	385917
577.1	Acute pancreatitis	digestive	2892	384317
577.2	Chronic pancreatitis	digestive	767	382192
577.3	Cyst and pseudocyst of pancreas	digestive	727	382152
578	Gastrointestinal hemorrhage	digestive	28342	381067
578.1	Hematemesis	digestive	2822	355547
578.2	Blood in stool	digestive	3826	356551
578.8	Hemorrhage of rectum and anus	digestive	14511	367236
578.9	Hemorrhage of gastrointestinal tract	digestive	10702	363427
579	Other symptoms involving abdomen and pelvis	digestive	2395	355120
579.2	Splenomegaly	digestive	808	353533
579.8	Nonspecific abnormal findings in stool contents	digestive	3727	356452
580	Nephritis; nephrosis; renal sclerosis	genitourinary	2339	357468
580.1	Glomerulonephritis	genitourinary	1121	356250
580.14	Chronic glomerulonephritis, NOS	genitourinary	832	355961
580.2	Nephrotic syndrome without mention of glomerulonephritis	genitourinary	1057	356186

580.3	Nephritis and nephropathy without mention of glomerulonephritis	genitourinary	468	355597
580.32	Nephritis and nephropathy with pathological lesion	genitourinary	442	355571
585	Renal failure	genitourinary	24469	379598
585.1	Acute renal failure	genitourinary	14846	369975
585.2	Renal failure NOS	genitourinary	2031	357160
585.3	Chronic renal failure [CKD]	genitourinary	12777	367906
585.31	Renal dialysis	genitourinary	740	355869
585.32	End stage renal disease	genitourinary	876	356005
585.33	Chronic Kidney Disease, Stage III	genitourinary	7753	362882
585.34	Chronic Kidney Disease, Stage IV	genitourinary	1103	356232
585.4	Chronic kidney disease, Stage I or II	genitourinary	1143	356272
586	Other disorders of the kidney and ureters	genitourinary	6546	361675
586.1	Anatomical abnormalities of kidney and ureters	genitourinary	404	355533
586.11	Small kidney	genitourinary	363	355492
586.2	Cyst of kidney, acquired	genitourinary	3096	358225
586.4	Stricture/obstruction of ureter	genitourinary	1524	356653
587	Kidney replaced by transplant	genitourinary	483	355612
589	Abnormal results of function study of kidney	genitourinary	275	355404
590	Pyelonephritis	genitourinary	2340	349751
591	Urinary tract infection	genitourinary	20529	367940
592	Cystitis and urethritis	genitourinary	4133	351544
592.1	Cystitis	genitourinary	3978	351389
592.12	Chronic cystitis	genitourinary	1203	348614
592.13	Chronic interstitial cystitis	genitourinary	333	347744
593	Hematuria	genitourinary	18476	365887

594	Urinary calculus	genitourinary	8724	385126
594.1	Calculus of kidney	genitourinary	4748	381150
594.2	Calculus of lower urinary tract	genitourinary	1257	377659
594.3	Calculus of ureter	genitourinary	3106	379508
594.8	Renal colic	genitourinary	2207	378609
595	Hydronephrosis	genitourinary	1682	378084
596	Other disorders of bladder	genitourinary	13488	381066
596.1	Bladder neck obstruction	genitourinary	2461	370039
596.5	Functional disorders of bladder	genitourinary	1804	369382
597	Other disorders of urethra and urinary tract	genitourinary	5196	372774
597.1	Urethral stricture (not specified as infectious)	genitourinary	4468	372046
598	Abnormal findings on examination of urine	genitourinary	354	385917
599	Other symptoms/disorders of the urinary system	genitourinary	15603	375460
599.1	Urinary obstruction	genitourinary	264	360121
599.2	Retention of urine	genitourinary	13605	373462
599.3	Dysuria	genitourinary	1575	361432
599.4	Urinary incontinence	genitourinary	4864	364721
599.5	Frequency of urination and polyuria	genitourinary	4828	364685
599.6	Oliguria and anuria	genitourinary	218	360075
600	Hyperplasia of prostate	genitourinary	19046	371244
601	Inflammatory diseases of prostate	genitourinary	3051	355249
601.1	Prostatitis	genitourinary	2198	354396
601.11	Acute prostatitis	genitourinary	381	352579
601.12	Chronic prostatitis	genitourinary	1259	353457
601.4	Balanoposthitis	genitourinary	425	352623

601.8	Other inflammatory disorders of male genital organs	genitourinary	424	352622
602	Other disorders of prostate	genitourinary	1710	353908
603	Other disorders of testis	genitourinary	1911	361329
603.1	Hydrocele	genitourinary	1784	361202
604	Disorders of penis	genitourinary	2058	361476
604.3	Peyronie's disease	genitourinary	927	360345
608	Other disorders of male genital organs	genitourinary	3463	362881
609	Male infertility and abnormal spermatozoa	genitourinary	230	359648
610	Benign mammary dysplasias	genitourinary	3001	381041
610.1	Cystic mastopathy	genitourinary	1003	379043
610.2	Fibroadenosis of breast	genitourinary	342	378382
610.3	Fibrosclerosis of breast	genitourinary	342	378382
610.4	Benign neoplasm of breast	genitourinary	1590	379630
610.8	Other specified benign mammary dysplasias	genitourinary	824	378864
611	Abnormal findings on mammogram or breast exam	genitourinary	1750	379790
611.3	Lump or mass in breast	genitourinary	1747	379787
612	Breast conditions, congenital or relating to hormones	genitourinary	968	379008
612.2	Hypertrophy of breast (Gynecomastia)	genitourinary	885	378925
613	Other nonmalignant breast conditions	genitourinary	2281	385917
613.1	Inflammatory disease of breast	genitourinary	814	384450
613.7	Other signs and symptoms in breast	genitourinary	792	384428
613.8	Other specified disorders of breast	genitourinary	442	384078
613.9	Breast disorder NOS	genitourinary	217	383853
614	Inflammatory diseases of female pelvic organs	genitourinary	7043	382841
614.1	Pelvic peritoneal adhesions, female (postoperative) (postinfection)	genitourinary	2976	378774

614.3	Pelvic inflammatory disease (PID)	genitourinary	1021	376819
614.32	Chronic inflammatory pelvic disease	genitourinary	453	376251
614.33	Pelvic inflammatory disease, NOS	genitourinary	377	376175
614.4	Inflammatory diseases of uterus, except cervix	genitourinary	321	376119
614.5	Inflammatory disease of cervix, vagina, and vulva	genitourinary	3191	378989
614.51	Cervicitis and endocervicitis	genitourinary	1295	377093
614.52	Vaginitis and vulvovaginitis	genitourinary	825	376623
614.53	Cyst or abscess of Bartholin's gland	genitourinary	790	376588
614.54	Abscess or ulceration of vulva	genitourinary	325	376123
615	Endometriosis	genitourinary	4230	380028
618	Genital prolapse	genitourinary	13443	385917
618.1	Prolapse of vaginal walls	genitourinary	8639	381113
618.2	Uterine/Uterovaginal prolapse	genitourinary	6186	378660
618.5	Prolapse of vaginal vault after hysterectomy	genitourinary	536	373010
618.6	Vaginal enterocele, congenital or acquired	genitourinary	797	373271
619	Noninflammatory female genital disorders	genitourinary	10470	385917
619.1	Noninflammatory disorders of ovary, fallopian tube, and broad ligament	genitourinary	859	376306
619.2	Disorders of uterus, NEC	genitourinary	3901	379348
619.3	Noninflammatory disorders of cervix	genitourinary	3127	378574
619.4	Noninflammatory disorders of vagina	genitourinary	1952	377399
619.5	Noninflammatory disorders of vulva and perineum	genitourinary	1553	377000
621	Endometrial hyperplasia	genitourinary	1061	373412
622	Polyp of female genital organs	genitourinary	11910	384261
622.1	Polyp of corpus uteri	genitourinary	8874	381225
622.2	Mucous polyp of cervix	genitourinary	3611	375962

623	Hypertrophy of female genital organs	genitourinary	1321	373672
624	Symptoms involving female genital tract	genitourinary	1212	377589
624.1	Dystrophy of female genital tract	genitourinary	454	376831
624.2	Atrophy of female genital tract	genitourinary	647	377024
624.9	stress incontinence, female	genitourinary	6351	382728
625	Pain and other symptoms associated with female genital organs	genitourinary	2291	378668
625.1	Dyspareunia	genitourinary	1149	377526
626	Disorders of menstruation and other abnormal bleeding from female genital tract	genitourinary	18230	372024
626.1	Irregular menstrual cycle/bleeding	genitourinary	15413	369207
626.12	Excessive or frequent menstruation	genitourinary	9559	363353
626.13	Irregular menstrual cycle	genitourinary	1917	355711
626.14	Irregular menstrual bleeding	genitourinary	3787	357581
626.2	Dysmenorrhea	genitourinary	1683	355477
626.8	Infertility, female	genitourinary	1339	355133
627	Menopausal and postmenopausal disorders	genitourinary	11897	365691
627.1	Postmenopausal bleeding	genitourinary	10086	363880
627.2	Symptomatic menopause	genitourinary	212	354006
627.3	Postmenopausal atrophic vaginitis	genitourinary	1550	355344
627.4	Premenopausal menorrhagia	genitourinary	325	354119
628	Ovarian cyst	genitourinary	5424	359218
634	Miscarriage; stillbirth	pregnancy complications	2877	382776
634.1	Missed abortion/Hydatidiform mole	pregnancy complications	1176	381075
634.3	Ectopic pregnancy	pregnancy complications	319	380218
635	Hemorrhage during pregnancy; childbirth and postpartum	pregnancy complications	1978	381877

635.2	Antepartum hemorrhage, abruptio placentae, and placenta previa	pregnancy complications	855	380754
635.3	Placenta previa and abruptio placenta	pregnancy complications	1255	381154
636	Early or threatened labor; hemorrhage in early pregnancy	pregnancy complications	2457	382356
636.3	Hemorrhage in early pregnancy	pregnancy complications	1012	380911
642	Hypertension complicating pregnancy, childbirth, and the puerperium	pregnancy complications	1112	385917
642.1	Preeclampsia and eclampsia	pregnancy complications	321	385126
643	Excessive vomiting in pregnancy	pregnancy complications	222	385917
646	Other complications of pregnancy NEC	pregnancy complications	731	385917
653	Problems associated with amniotic cavity and membranes	pregnancy complications	258	385710
655	Known or suspected fetal abnormality affecting management of mother	pregnancy complications	845	385917
669	Complications of labor and delivery NEC	pregnancy complications	490	385917
681	Superficial cellulitis and abscess	dermatologic	1293	382940
681.1	Cellulitis and abscess of fingers/toes	dermatologic	879	382526
681.2	Cellulitis and abscess of face/neck	dermatologic	244	381891
686	Other local infections of skin and subcutaneous tissue	dermatologic	2407	384054
686.4	Pyogenic granuloma	dermatologic	451	382098
687	Symptoms affecting skin	dermatologic	1919	378926
687.1	Rash and other nonspecific skin eruption	dermatologic	3113	380120
687.4	Disturbance of skin sensation	dermatologic	4175	381182
689	Disorder of skin and subcutaneous tissue NOS	dermatologic	9563	385917
690	Erythematousquamous dermatosis	dermatologic	4732	376094
690.1	Seborrheic dermatitis	dermatologic	4707	376069
694	Dyschromia and Vitiligo	dermatologic	1558	372920
694.2	Other dyschromia	dermatologic	1212	372574
695	Erythematous conditions	dermatologic	3946	375308

695.2	Bullous dermatoses	dermatologic	263	371625
695.3	Rosacea	dermatologic	598	371960
695.4	Lupus (localized and systemic)	dermatologic	594	370443
695.41	Cutaneous lupus erythematosus	dermatologic	213	370062
695.42	Systemic lupus erythematosus	dermatologic	484	370333
695.7	Prurigo and Lichen	dermatologic	1174	372536
695.8	Other specified erythematous conditions	dermatologic	367	371729
695.9	Unspecified erythematous condition	dermatologic	878	372240
696	Psoriasis and related disorders	dermatologic	4044	370652
696.4	Psoriasis	dermatologic	3949	370557
696.41	Psoriasis vulgaris	dermatologic	3149	369757
696.42	Psoriatic arthropathy	dermatologic	1082	367690
697	Sarcoidosis	dermatologic	783	372145
698	Pruritus and related conditions	dermatologic	1152	385917
700	Corns and callosities	dermatologic	414	379172
701	Other hypertrophic and atrophic conditions of skin	dermatologic	6759	385517
701.2	Scar conditions and fibrosis of skin	dermatologic	2931	381689
701.3	Circumscribed scleroderma	dermatologic	728	379486
701.4	Keloid scar	dermatologic	266	379024
701.5	Abnormal granulation tissue	dermatologic	628	379386
702	Degenerative skin conditions and other dermatoses	dermatologic	8268	379458
702.1	Actinic keratosis	dermatologic	4123	381772
702.2	Seborrheic keratosis	dermatologic	4580	382229
703	Diseases of nail, NOS	dermatologic	501	384250
703.1	Ingrowing nail	dermatologic	1088	384837

704	Diseases of hair and hair follicles	dermatologic	589	384338
704.1	Alopecia	dermatologic	253	384002
705	Disorders of sweat glands	dermatologic	263	375872
706	Diseases of sebaceous glands	dermatologic	10091	385700
706.2	Sebaceous cyst	dermatologic	9985	385594
707	Chronic ulcer of skin	dermatologic	5226	385917
707.1	Decubitus ulcer	dermatologic	3211	383902
707.2	Chronic ulcer of leg or foot	dermatologic	2336	383027
709	Diffuse diseases of connective tissue	dermatologic	1361	371625
709.2	Sicca syndrome	dermatologic	835	371099
709.3	Systemic sclerosis	dermatologic	230	370494
709.7	Unspecified diffuse connective tissue disease	dermatologic	254	370518
710	Osteomyelitis, periostitis, and other infections involving bone	musculoskeletal	502	376925
710.1	Osteomyelitis	musculoskeletal	440	376863
710.19	Unspecified osteomyelitis	musculoskeletal	247	376670
711	Arthropathy associated with infections	musculoskeletal	289	376712
714	Rheumatoid arthritis and other inflammatory polyarthropathies	musculoskeletal	5461	379202
714.1	Rheumatoid arthritis	musculoskeletal	4820	378561
715	Other inflammatory spondylopathies	musculoskeletal	2905	376646
715.2	Ankylosing spondylitis	musculoskeletal	643	374384
716	Other arthropathies	musculoskeletal	603	377026
716.9	Arthropathy NOS	musculoskeletal	210	376633
717	Polymyalgia Rheumatica	musculoskeletal	2803	385917
720	Spinal stenosis	musculoskeletal	6823	381210
720.1	Spinal stenosis of lumbar region	musculoskeletal	4913	379300

721	Spondylosis and allied disorders	musculoskeletal	4036	378423
721.1	Spondylosis without myelopathy	musculoskeletal	3224	377611
721.2	Spondylosis with myelopathy	musculoskeletal	335	374722
721.8	Other allied disorders of spine	musculoskeletal	611	374998
722	Intervertebral disc disorders	musculoskeletal	1574	375961
722.9	Other and unspecified disc disorder	musculoskeletal	1227	375614
723	Other disorders of cervical region	musculoskeletal	209	374596
724	Other and unspecified disorders of back	musculoskeletal	593	374980
724.1	Disorders of sacrum	musculoskeletal	461	374848
724.2	Disorders of coccyx	musculoskeletal	407	374794
726	Peripheral enthesopathies and allied syndromes	musculoskeletal	18190	375002
726.1	Enthesopathy	musculoskeletal	11943	368755
726.2	Synoviopathy	musculoskeletal	782	357594
726.3	Bursitis	musculoskeletal	864	357676
726.4	Calcaneal spur; Exostosis NOS	musculoskeletal	955	357767
727	Other disorders of synovium, tendon, and bursa	musculoskeletal	11748	368560
727.1	Synovitis and tenosynovitis	musculoskeletal	2083	358895
727.4	Ganglion and cyst of synovium, tendon, and bursa	musculoskeletal	3716	360528
727.5	Rupture of synovium	musculoskeletal	698	357510
727.6	Rupture of tendon, nontraumatic	musculoskeletal	5350	362162
728	Disorders of muscle, ligament, and fascia	musculoskeletal	468	357280
728.2	Laxity of ligament or hypermobility syndrome	musculoskeletal	596	357408
728.7	Fasciitis	musculoskeletal	4218	361030
728.71	Contracture of palmar fascia [Dupuytren's disease]	musculoskeletal	3844	360656
729	Other disorders of soft tissues	musculoskeletal	677	357489

729.1	Rheumatism, unspecified and fibrositis	musculoskeletal	377	357189
732	Osteochondropathies	musculoskeletal	616	365943
732.1	Juvenile osteochondrosis	musculoskeletal	258	365585
733	Other disorders of bone and cartilage	musculoskeletal	2142	367469
733.2	Cyst of bone	musculoskeletal	451	365778
733.4	Aseptic necrosis of bone	musculoskeletal	300	365627
733.6	Costochondritis	musculoskeletal	297	365624
735	Acquired foot deformities	musculoskeletal	12116	380511
735.1	Flat foot	musculoskeletal	265	368660
735.2	Acquired toe deformities	musculoskeletal	6330	374725
735.21	Hammer toe (acquired)	musculoskeletal	2568	370963
735.23	Hallux rigidus	musculoskeletal	1842	370237
735.3	Hallux valgus (Bunion)	musculoskeletal	7816	376211
736	Other acquired deformities of limbs	musculoskeletal	1692	370087
736.2	Acquired deformities of finger	musculoskeletal	306	368701
736.4	Genu valgum or varum (acquired)	musculoskeletal	833	369228
736.5	Acquired deformities of knee	musculoskeletal	531	368926
737	Curvature of spine	musculoskeletal	1322	369717
737.3	Kyphoscoliosis and scoliosis	musculoskeletal	1169	369564
738	Other acquired musculoskeletal deformity	musculoskeletal	2902	371297
738.4	Acquired spondylolisthesis	musculoskeletal	2382	370777
739	Contracture of joint	musculoskeletal	388	368783
740	Osteoarthritis	musculoskeletal	62035	385917
740.1	Osteoarthritis; localized	musculoskeletal	49340	373222
740.11	Osteoarthritis, localized, primary	musculoskeletal	15129	339011

740.12	Osteoarthritis, localized, secondary	musculoskeletal	1974	325856
740.2	Osteoarthritis, generalized	musculoskeletal	10835	334717
740.9	Osteoarthritis NOS	musculoskeletal	23040	346922
741	Symptoms and disorders of the joints	musculoskeletal	5061	383924
741.2	Stiffness of joint	musculoskeletal	612	379475
741.3	Difficulty in walking	musculoskeletal	617	379480
741.4	Joint effusions	musculoskeletal	2235	381098
741.5	Hemarthrosis	musculoskeletal	201	379064
742	Derangement of joint, non-traumatic	musculoskeletal	2253	381116
742.1	Loose body in joint	musculoskeletal	383	379246
742.2	Pathological, developmental or recurrent dislocation	musculoskeletal	599	379462
742.8	Articular cartilage disorder	musculoskeletal	492	379355
742.9	Other derangement of joint	musculoskeletal	850	379713
743	Osteoporosis, osteopenia and pathological fracture	musculoskeletal	1871	385917
743.2	Pathologic fracture	musculoskeletal	1292	385338
743.21	Pathologic fracture of vertebrae	musculoskeletal	804	384850
743.9	Osteopenia or other disorder of bone and cartilage	musculoskeletal	343	384389
745	Pain in joint	musculoskeletal	10325	385917
747	Cardiac and circulatory congenital anomalies	congenital anomalies	1843	385917
747.1	Cardiac congenital anomalies	congenital anomalies	1580	385654
747.11	Cardiac shunt/ heart septal defect	congenital anomalies	788	384862
747.12	Valvular heart disease/ heart chambers	congenital anomalies	456	384530
747.2	Congenital anomalies of peripheral vascular system	congenital anomalies	248	384322
749	Congenital anomalies of face and neck	congenital anomalies	359	385832
750	Digestive congenital anomalies	congenital anomalies	1140	384163

750.1	Upper gastrointestinal congenital anomalies	congenital anomalies	575	383598
750.13	Congenital anomalies of mouth/tongue	congenital anomalies	314	383337
750.2	Lower gastrointestinal congenital anomalies	congenital anomalies	560	383583
750.21	Congenital anomalies of intestine	congenital anomalies	356	383379
751	Genitourinary congenital anomalies	congenital anomalies	1842	384865
751.1	Congenital anomalies of genital organs	congenital anomalies	681	383704
751.11	Congenital anomalies of female genital organs	congenital anomalies	452	383475
751.12	Congenital anomalies of male genital organs	congenital anomalies	204	383227
751.2	Congenital anomalies of urinary system	congenital anomalies	1141	384164
751.21	Cystic kidney disease	congenital anomalies	547	383570
751.22	Other specified congenital anomalies of kidney	congenital anomalies	545	383568
752	Nervous system congenital anomalies	congenital anomalies	803	385684
752.1	Neural tube defects	congenital anomalies	688	385569
752.11	Spina bifida	congenital anomalies	258	385139
754	Congenital musculoskeletal deformities of spine	congenital anomalies	410	384327
755	Congenital anomalies of limbs	congenital anomalies	603	384520
755.1	Congenital deformities of feet	congenital anomalies	298	384215
755.6	Other congenital anomalies of lower limb, including pelvic girdle	congenital anomalies	225	384142
756	Other congenital musculoskeletal anomalies	congenital anomalies	1028	384945
756.3	Congenital anomalies of muscle, tendon, fascia, and connective tissue	congenital anomalies	636	384553
756.5	Congenital osteodystrophies	congenital anomalies	770	384687
758	Chromosomal anomalies and genetic disorders	congenital anomalies	209	384612
759	Other and unspecified congenital anomalies	congenital anomalies	266	384669
760	Back pain	symptoms	10669	385917
761	Cervicalgia	symptoms	1664	385917

763	Thoracic or lumbosacral neuritis or radiculitis, unspecified	symptoms	822	382431
764	Sciatica	symptoms	2732	384341
765	Cervical radiculitis	symptoms	271	381880
766	Neuralgia, neuritis, and radiculitis NOS	symptoms	724	382333
770	Myalgia and myositis unspecified	symptoms	2332	385917
771	Musculoskeletal symptoms referable to limbs	symptoms	1060	385698
771.1	Swelling of limb	symptoms	219	384857
780	Hypothermia/Chills	symptoms	484	385917
781	Symptoms involving nervous and musculoskeletal systems	symptoms	7921	385914
782.3	Edema	symptoms	4308	385608
782.6	Pallor and flushing	symptoms	332	381632
783	Fever of unknown origin	symptoms	6358	385917
785	Abdominal pain	symptoms	24892	385917
788	Syncope and collapse	symptoms	14378	385917
789	Nausea and vomiting	symptoms	18157	385917
790	Nonspecific findings on examination of blood	symptoms	498	384964
790.6	Other abnormal blood chemistry	symptoms	864	385330
797	Shock	symptoms	373	385917
797.1	Cardiogenic shock	symptoms	240	385784
798	Malaise and fatigue	symptoms	6713	385917
798.1	Chronic fatigue syndrome	symptoms	959	380163
800	Fracture of lower limb	injuries & poisonings	6260	369990
800.1	Fracture of neck of femur	injuries & poisonings	3633	367363
800.2	Fracture of unspecified part of femur	injuries & poisonings	487	364217
800.3	Fracture of tibia and fibula	injuries & poisonings	1727	365457

800.4	Fracture of patella	injuries & poisonings	646	364376
801	Fracture of ankle and foot	injuries & poisonings	2022	365752
801.1	Fracture of foot	injuries & poisonings	897	364627
802	Fracture of pelvis	injuries & poisonings	1319	365049
803	Fracture of upper limb	injuries & poisonings	11687	375417
803.1	Fracture of humerus	injuries & poisonings	2539	366269
803.2	Fracture of radius and ulna	injuries & poisonings	8065	371795
803.3	Fracture of clavicle or scapula	injuries & poisonings	1572	365302
804	Fracture of hand or wrist	injuries & poisonings	2609	366339
805	Fracture of vertebral column without mention of spinal cord injury	injuries & poisonings	334	364064
807	Fracture of ribs	injuries & poisonings	415	364145
809	Fracture of unspecified bones	injuries & poisonings	488	364218
819	Skull and face fracture and other intercranial injury	injuries & poisonings	1416	385813
830	Dislocation	injuries & poisonings	802	370119
835	Internal derangement of knee	injuries & poisonings	15840	385157
840	Sprains and strains	injuries & poisonings	789	385737
840.3	Joint/ligament sprain	injuries & poisonings	394	385342
851	Complications of transplants and reattached limbs	injuries & poisonings	280	380565
857	Mechanical complication of unspecified genitourinary device, implant, and graft	injuries & poisonings	1892	382177
858	Complication of internal orthopedic device	injuries & poisonings	2896	383181
859	Complication due to other implant and internal device	injuries & poisonings	434	380719
870	Open wounds of head; neck; and trunk	injuries & poisonings	1246	384157
870.2	Open wound of ear	injuries & poisonings	279	383190
870.3	Other open wound of head and face	injuries & poisonings	616	383527

871	Open wounds of extremities	injuries & poisonings	1208	384119
871.3	Open wound of foot except toe(s) alone	injuries & poisonings	235	383146
872	Traumatic amputation	injuries & poisonings	492	383403
907	Injuries to the nervous system	injuries & poisonings	1081	385917
916	Contusion	injuries & poisonings	2585	385917
930	Allergic reaction to food	injuries & poisonings	253	379498
938	Dermatitis due to solar radiation	injuries & poisonings	576	379821
938.2	Chronic dermatitis due to solar radiation	injuries & poisonings	391	379636
939	Atopic/contact dermatitis due to other or unspecified	dermatologic	4279	383524
941	Adverse reaction to serum or vaccine	injuries & poisonings	426	379671
946	Anaphylactic shock NOS	injuries & poisonings	741	379986
947	Urticaria	injuries & poisonings	596	379841
958	Certain early complications of trauma or procedure	injuries & poisonings	433	385917
960	Poisoning by antibiotics	injuries & poisonings	29143	370385
960.2	Allergy/adverse effect of penicillin	injuries & poisonings	24450	365692
961	Poisoning by other anti-infectives	injuries & poisonings	648	341890
961.1	Poisoning/allergy of sulfonamides	injuries & poisonings	1277	342519
965	Poisoning by analgesics, antipyretics, and antirheumatics	injuries & poisonings	8331	349573
965.1	Opiates and related narcotics causing adverse effects in therapeutic use	injuries & poisonings	3501	344743
967	Adverse effects of sedatives or other central nervous system depressants and anesthetics	injuries & poisonings	623	341865
977	Personal history of allergy to medicinal agents	injuries & poisonings	12921	354163
979	Adverse drug events and drug allergies	injuries & poisonings	476	341718
981	Toxic effect of (non-ethyl) alcohol and petroleum and other solvents	injuries & poisonings	214	385589
990	Effects radiation NOS	injuries & poisonings	8314	377787

994	Sepsis and SIRS	injuries & poisonings	9328	385917
994.2	Sepsis	injuries & poisonings	9328	385917

Supplementary Table 3. Significant PheWAS associations in different subgroups stratified by sex.

Phenotype	Sex	Cases	Participants	OR (95%CI)	FDR adjusted p-value	Heterogeneity p-value	I ² (%)
Vitamin B6							
Urinary calculus	Female	2617	207292	0.59 (0.37, 0.94)	0.996	0.512	0
	Male	6018	176544	0.49 (0.36, 0.67)	5.59E-03		
Calculus of kidney	Female	1571	206246	0.66 (0.36, 1.19)	0.996	0.187	43
	Male	3130	173656	0.40 (0.26, 0.61)	8.11E-03		
Vitamin B12							
Vitamin deficiency	Female	3000	206142	0.82 (0.72, 0.93)	0.180	0.022	81
	Male	2015	175751	0.64 (0.55, 0.76)	2.72E-05		
Neoplasm of unspecified nature of digestive system	Female	737	195812	1.66 (1.30, 2.11)	8.95E-03	0.282	13
	Male	799	165455	1.38 (1.09, 1.74)	0.476		

Supplementary Table 4. Replication of MR effect estimates for all associations identified by PheWAS.

Exposure	Outcome & data source	MR method	Beta	SE	OR (95%CI)	P-value ¹	Intercept ²	P-value ²	Cases	Participants
Folate	Megaloblastic anemia									
	UKBB	PheWAS	-0.099	0.023	0.91 (0.87, 0.95)	2.50E-05	-	-	1862	355850
	OpenGWAS: finn-D3_ANAEMIA_B12_DEF	IVW	-0.384	0.359	0.68 (0.34, 1.38)	0.284	-	-	1707	212822
	Other deficiency anemia									
	UKBB	PheWAS	-0.093	0.023	0.91 (0.87, 0.95)	4.19E-05	-	-	1972	355960
	OpenGWAS: finn-D3_ANAEMIA_IRONDEF_NAS	IVW	-0.137	0.225	0.87 (0.56, 1.36)	0.542	-	-	4321	215436
	Essential hypertension									
	UKBB	PheWAS	-0.016	0.004	0.98 (0.98, 0.99)	5.01E-05	-	-	109289	385661
	OpenGWAS: finn-I9_HYPTENSESS	IVW	-0.047	0.250	0.95 (0.58, 1.56)	0.852	-	-	42857	205694
	Hypertension									
	UKBB	PheWAS	-0.016	0.004	0.98 (0.98, 0.99)	5.06E-05	-	-	109545	385917
	OpenGWAS: finn-I9_HYPTENS	IVW	-0.032	0.224	0.97 (0.62, 1.50)	0.886	-	-	55917	218754
	Disorders of lipid metabolism									
	UKBB	PheWAS	-0.019	0.005	0.98 (0.97, 0.99)	9.79E-05	-	-	54333	385917
	OpenGWAS: finn-E4_LIPOPROT	IVW	-0.135	0.136	0.87 (0.67, 1.14)	0.318	-	-	14010	211269
	Hypercholesterolemia									
	UKBB	PheWAS	-0.020	0.005	0.98 (0.97, 0.99)	9.92E-05	-	-	50143	381727
	OpenGWAS: finn-E4_HYPERCHOL	IVW	-0.230	0.187	0.79 (0.55, 1.15)	0.220	-	-	6840	167301

	Hyperlipidemia									
	UKBB	PheWAS	-0.019	0.005	0.98 (0.97, 0.99)	1.06E-04	-	-	54099	385683
	OpenGWAS: finn-E4_HYPERLIPNAS	IVW	-0.256	0.339	0.77 (0.40, 1.50)	0.450	-	-	4535	201794
	Eenteritis									
	UKBB	PheWAS	-0.079	0.022	0.92 (0.89, 0.96)	3.02E-04	-	-	2166	315062
	OpenGWAS: finn-K11_ENERCOLNONINF	IVW	0.062	0.166	1.06 (0.77, 1.47)	0.710	-	-	8492	218792
Vitamin B6	Calculus of kidney and ureter									
	UKBB	PheWAS	-0.058	0.014	0.94 (0.92, 0.97)	4.03E-05	-	-	4748	381150
	OpenGWAS: finn-N14_CALCUKIDUR	Wald ratio ³	-0.453	0.213	0.64 (0.42, 0.97)	0.033	-	-	3856	176613
Vitamin B12	Vitamin B-complex deficiencies									
	UKBB	PheWAS	-0.753	0.079	0.47 (0.40, 0.55)	1.36E-21	-	-	2246	380355
	OpenGWAS: finn-E4_VIT_B_DEF	IVW	-0.379	0.306	0.68 (0.38, 1.25)	0.214	-	-	284	209891
		Weighted median ⁴	-0.173	0.240	0.84 (0.53, 1.35)	0.472	-	-		
		MR-Egger ⁴	0.134	0.478	1.14 (0.45, 2.92)	0.785	-0.110	0.199		
		MR-PRESSO ⁴	-0.379	0.306	0.68 (0.38, 1.25)	0.238	-	-		
	Vitamin deficiency									
	UKBB	PheWAS	-0.296	0.051	0.74 (0.67, 0.82)	5.51E-09	-	-	5055	383164
	OpenGWAS: finn-E4_VIT_DEF	IVW	-0.018	0.131	0.98 (0.76, 1.27)	0.892	-	-	632	210239
		Weighted median	-0.006	0.165	0.99 (0.72, 1.37)	0.971	-	-		
MR-Egger		0.151	0.211	1.16 (0.77, 1.76)	0.490	-0.037	0.332			

		MR-PRESSO	-0.018	0.128	0.98 (0.76, 1.26)	0.890	-	-			
	Cholelithiasis										
	UKBB	PheWAS	0.097	0.025	1.10 (1.05, 1.16)	9.36E-05	-	-	20567	383100	
	OpenGWAS: CHOLELITH_BROAD	finn-	IVW	0.045	0.040	1.05 (0.97, 1.13)	0.252	-	-	19883	215027
			Weighted median	0.036	0.035	1.04 (0.97, 1.11)	0.308	-	-		
			MR-Egger	-0.030	0.061	0.97 (0.86, 1.09)	0.634	0.017	0.143		
			MR-PRESSO	0.037	0.031	1.04 (0.98, 1.10)	0.263	-	-		
	Megaloblastic anemia										
	UKBB	PheWAS	-0.316	0.084	0.73 (0.62, 0.86)	1.53E-04	-	-	1862	355850	
	OpenGWAS: D3_ANAEMIA_B12_DEF	finn-	IVW	-0.213	0.169	0.81 (0.58, 1.13)	0.208	-	-	1707	212822
			Weighted median	-0.047	0.108	0.95 (0.77, 1.18)	0.662	-	-		
			MR-Egger	0.137	0.253	1.15 (0.70, 1.88)	0.598	-0.078	0.106		
			MR-PRESSO	-0.409	0.229	0.66 (0.42, 1.04)	0.102	-	-		
Homocystein e	Hyperlipidemia										
	UKBB	PheWAS	0.128	0.027	1.14 (1.08, 1.20)	2.17E-06	-	-	54099	385683	
	OpenGWAS: E4_HYPERLIPNAS	finn-	IVW	0.126	0.102	1.13 (0.93, 1.39)	0.215	-	-	4535	201794
			Weighted median	0.017	0.121	1.02 (0.80, 1.29)	0.887	-	-		
			MR-Egger	-0.139	0.214	0.87 (0.57, 1.32)	0.531	0.022	0.192		
			MR-PRESSO	0.126	0.102	1.13 (0.93, 1.39)	0.239	-	-		
	Disorders of lipid metabolism										
	UKBB	PheWAS	0.127	0.027	1.14 (1.08, 1.20)	2.74E-06	-	-	54333	385917	
	IVW	0.145	0.085	1.16 (0.98, 1.37)	0.089	-	-	14010	211269		

	OpenGWAS: E4_LIPOPROT	finn-	Weighted median	0.103	0.076	1.11 (0.96, 1.29)	0.177	-	-		
			MR-Egger	-0.012	0.187	0.99 (0.68, 1.43)	0.948	0.013	0.364		
			MR-PRESSO	0.107	0.073	1.11 (0.96, 1.28)	0.171	-	-		
	Hypercholesterolemia										
	UKBB		PheWAS	0.122	0.028	1.13 (1.07, 1.19)	1.34E-05	-	-	50143	381727
	OpenGWAS: E4_HYPERCHOL	finn-	IVW	0.245	0.103	1.28 (1.04, 1.56)	0.018	-	-	6840	167301
			Weighted median	0.210	0.106	1.23 (1.00, 1.52)	0.047	-	-		
			MR-Egger	0.093	0.230	1.10 (0.70, 1.72)	0.695	0.013	0.471		
			MR-PRESSO	0.245	0.103	1.28 (1.04, 1.56)	0.035	-	-		
	Spondylosis										
	UKBB		PheWAS	1.186	0.305	3.27 (1.80, 5.95)	9.99E-05	-	-	335	374722
	OpenGWAS: M13_SPONDYLOSIS	finn-	IVW	0.090	0.069	1.09 (0.96, 1.25)	0.192	-	-	9371	174053
			Weighted median	0.109	0.090	1.12 (0.93, 1.33)	0.228	-	-		
			MR-Egger	0.093	0.158	1.10 (0.81, 1.50)	0.570	-0.0002	0.988		
			MR-PRESSO	0.090	0.069	1.09 (0.96, 1.25)	0.216	-	-		
	Chronic kidney disease										
	UKBB		PheWAS	0.252	0.065	1.29 (1.13, 1.46)	1.04E-04	-	-	7753	362882
	OpenGWAS: ebi-GCST008026		IVW	0.276	0.110	1.32 (1.06, 1.63)	0.012	-	-	1533	20920
			Weighted median	0.134	0.149	1.14 (0.85, 1.53)	0.368	-	-		
			MR-Egger	0.070	0.250	1.07 (0.66, 1.75)	0.784	0.017	0.376		
			MR-PRESSO	0.276	0.110	1.32 (1.06, 1.63)	0.026	-	-		

		Cerebrovascular disease								
UKBB		PheWAS	0.188	0.049	1.21 (1.10, 1.33)	1.12E-04	-	-	14058	384206
OpenGWAS: I9_CEREBVASC	finn-	IVW	-0.001	0.083	1.00 (0.85, 1.18)	0.990	-	-	15724	218792
		Weighted median	-0.018	0.078	0.98 (0.84, 1.14)	0.817	-	-		
		MR-Egger	-0.118	0.185	0.89 (0.62, 1.28)	0.536	0.010	0.491		
		MR-PRESSO	0.016	0.059	1.02 (0.91, 1.14)	0.794	-	-		
Vitamin B-complex deficiencies										
UKBB		PheWAS	0.453	0.118	1.57 (1.25, 1.98)	1.33E-04	-	-	2246	380355
OpenGWAS: E4_VIT_B_DEF	finn-	IVW	-0.115	0.479	0.89 (0.35, 2.28)	0.810	-	-	284	209891
		Weighted median	0.029	0.517	1.03 (0.37, 2.84)	0.955	-	-		
		MR-Egger	-1.109	1.039	0.33 (0.04, 2.53)	0.309	0.083	0.305		
		MR-PRESSO	0.283	0.414	1.33 (0.59, 2.99)	0.509	-	-		
Vitamin deficiency										
UKBB		PheWAS	0.296	0.079	1.34 (1.15, 1.57)	1.92E-04	-	-	5055	383164
OpenGWAS: finn-E4_VIT_DEF		IVW	-0.065	0.259	0.94 (0.56, 1.56)	0.803	-	-	632	210239
		Weighted median	-0.065	0.335	0.94 (0.49, 1.81)	0.846	-	-		
		MR-Egger	-0.576	0.565	0.56 (0.19, 1.70)	0.330	0.043	0.330		
		MR-PRESSO	-0.065	0.259	0.94 (0.56, 1.56)	0.807	-	-		
Coronary atherosclerosis										
UKBB		PheWAS	0.133	0.036	1.14 (1.06, 1.22)	2.07E-04	-	-	28433	369752
		IVW	0.030	0.089	1.03 (0.87, 1.23)	0.738	-	-	23363	211203

	OpenGWAS: I9_CORATHER	finn-	Weighted median	0.063	0.074	1.07 (0.92, 1.23)	0.396	-	-		
			MR-Egger	0.031	0.204	1.03 (0.69, 1.54)	0.881	-0.0001	0.995		
			MR-PRESSO	0.127	0.063	1.14 (1.00, 1.28)	0.068	-	-		
	Syncope and collapse										
	UKBB		PheWAS	0.177	0.048	1.19 (1.09, 1.31)	2.17E-04	-	-	14378	385917
	OpenGWAS: R18_SYNCO_COLLAP	finn-	IVW	0.020	0.070	1.02 (0.89, 1.17)	0.770	-	-	8140	181139
			Weighted median	0.075	0.093	1.08 (0.90, 1.29)	0.416	-	-		
			MR-Egger	0.110	0.153	1.12 (0.83, 1.51)	0.486	-0.008	0.522		
			MR-PRESSO	0.020	0.067	1.02 (0.89, 1.16)	0.767	-	-		
	Hypoparathyroidism										
	UKBB		PheWAS	-1.034	0.301	0.36 (0.20, 0.64)	5.89E-04	-	-	355	379815
	OpenGWAS: E4_HYPOPARA	finn-	IVW	0.071	0.272	1.07 (0.63, 1.83)	0.793	-	-	485	211608
			Weighted median	0.160	0.351	1.17 (0.59, 2.33)	0.650	-	-		
			MR-Egger	0.180	0.594	1.20 (0.37, 3.84)	0.768	-0.009	0.841		
			MR-PRESSO	0.071	0.203	1.07 (0.72, 1.60)	0.732	-	-		
	Migraine										
	UKBB		PheWAS	0.274	0.080	1.32 (1.12, 1.54)	5.90E-04	-	-	5026	376143
	OpenGWAS: MIGRAINE_TRIPTAN	finn-	IVW	0.054	0.050	1.06 (0.96, 1.16)	0.279	-	-	19676	218792
			Weighted median	0.047	0.064	1.05 (0.92, 1.19)	0.465	-	-		
			MR-Egger	0.077	0.110	1.08 (0.87, 1.34)	0.495	-0.002	0.817		
			MR-PRESSO	0.054	0.037	1.06 (0.98, 1.13)	0.166	-	-		

¹ The p value of the MR effect estimates from different methods.

² The Egger regression intercept and horizontal pleiotropy p value of MR-Egger analysis.

³ Wald ratio method was applied to examine MR estimates for vitamin B6 as only one SNP was used as instrumental variable for vitamin B6.

⁴ These three sensitivity methods were applied to detect any pleiotropic effect when performing multivariable MR analysis.

Note: The bold text represents that the association was successfully replicated by MR analysis with a p value less than 0.05.

Supplementary Table 5. Mediation effects of homocysteine on the associations between vitamin B12 and the identified outcomes.

Outcome ¹	ACME effect ²	ACME LCI ²	ACME UCI ²	ACME p ²	ADE effect ³	ADE LCI ³	ADE UCI ³	ADE p ³	Total effect	Total LCI	Total UCI	Total p	Prop mediated estimate ⁴	Prop mediated LCI ⁴	Prop mediated UCI ⁴	Prop mediated p ⁴	Sample size	Simulation
261.2	-9.01E-05	-1.40E-04	-4.32E-05	<0.001	-3.94E-03	-4.71E-03	-3.20E-03	<0.001	-3.99E-03	-4.75E-03	-3.26E-03	<0.001	2.18E-02(+)	1.19E-02(+)	3.66E-02(+)	<0.001	379106	100
261	-1.20E-04	-1.74E-04	-5.00E-05	<0.001	-3.52E-03	-4.58E-03	-2.41E-03	<0.001	-3.61E-03	-4.70E-03	-2.51E-03	<0.001	3.41E-02(+)	1.41E-02(+)	5.19E-02(+)	<0.001	381893	100
158	1.22E-05	-1.90E-05	4.58E-05	0.44	1.83E-03	1.08E-03	2.58E-03	<0.001	1.85E-03	1.09E-03	2.61E-03	<0.001	6.27E-03(+)	1.04E-02(-)	2.66E-02(+)	0.44	361267	100
574	-6.17E-06	-1.25E-04	9.20E-05	0.98	5.16E-03	2.09E-03	7.95E-03	<0.001	5.15E-03	2.00E-03	7.91E-03	<0.001	1.90E-04(-)	2.87E-02(-)	2.24E-02(+)	0.98	381818	100
574.1	-2.62E-05	-1.41E-04	8.60E-05	0.66	4.69E-03	2.28E-03	6.97E-03	<0.001	4.66E-03	2.25E-03	6.91E-03	<0.001	6.00E-03(-)	2.96E-02(-)	2.17E-02(+)	0.66	379585	100
281.1	-6.45E-05	-1.10E-04	-1.64E-05	<0.001	-1.51E-03	-2.31E-03	-8.26E-04	<0.001	-1.56E-03	-2.39E-03	-8.85E-04	<0.001	4.22E-02(+)	9.98E-03(+)	7.61E-02(+)	<0.001	354765	100
281.11	-5.19E-05	-8.46E-05	-1.56E-05	0.02	-1.18E-03	-1.74E-03	-5.98E-04	<0.001	-1.22E-03	-1.77E-03	-6.29E-04	<0.001	4.33E-02(+)	1.30E-02(+)	9.08E-02(+)	0.02	354059	100

¹ Phencode of significant outcomes identified by PheWAS;

² Estimates, 95% CI and p value of average causal mediation effects (indirect effect explained by mediator);

³ Estimates, 95% CI and p value of average direct effects (direct effect explained by exposure);

⁴ Estimates, 95% CI and p value of proportion of mediation.

Note: The bold text means that statistically significant mediation effects were detected, with a p value less than 0.05.

Supplementary Table 6. Pathways enrichment results of homocysteine-associated genes and outcome-associated genes.

Outcome	Source	ID	Description	Observed gene count	Background gene count	Strength	FDR
Hyperlipidemia	KEGG	hsa04979	Cholesterol metabolism	7	48	1.99	4.62E-10
		hsa00270	Cysteine and methionine metabolism	5	49	1.84	2.49E-06
		hsa04977	Vitamin digestion and absorption	4	24	2.05	8.65E-06
		hsa01100	Metabolic pathways	11	1447	0.71	3.10E-04
		hsa00670	One carbon pool by folate	3	20	2.01	3.40E-04
		hsa03320	PPAR signaling pathway	4	75	1.56	3.40E-04
		hsa01230	Biosynthesis of amino acids	3	73	1.44	9.10E-03
		hsa01200	Carbon metabolism	3	117	1.24	3.06E-02
		hsa01523	Antifolate resistance	2	31	1.64	4.05E-02
	Reactome	HSA-196854	Metabolism of vitamins and cofactors	13	189	1.67	1.28E-15
		HSA-174824	Plasma lipoprotein assembly, remodeling, and clearance	9	71	1.93	2.02E-12
		HSA-1430728	Metabolism	21	2089	0.83	5.70E-12
		HSA-8963901	Chylomicron remodeling	6	10	2.61	2.60E-11
		HSA-8963899	Plasma lipoprotein remodeling	7	32	2.17	4.60E-11
		HSA-1614635	Sulfur amino acid metabolism	6	27	2.18	2.36E-09
		HSA-8964043	Plasma lipoprotein clearance	6	33	2.09	5.92E-09
		HSA-975634	Retinoid metabolism and transport	6	44	1.96	2.50E-08
		HSA-8964026	Chylomicron clearance	4	5	2.73	1.05E-07
		HSA-196849	Metabolism of water-soluble vitamins and cofactors	7	123	1.58	1.31E-07
		HSA-8963888	Chylomicron assembly	4	10	2.43	6.94E-07
		HSA-3296469	Defects in cobalamin (B12) metabolism	4	14	2.29	1.81E-06
		HSA-196741	Cobalamin (Cbl, vitamin B12) transport and metabolism	4	21	2.11	6.50E-06

		HSA-382551	Transport of small molecules	10	721	0.97	6.60E-06
		HSA-8964058	HDL remodeling	3	10	2.31	9.43E-05
		HSA-71291	Metabolism of amino acids and derivatives	7	365	1.11	9.93E-05
		HSA-156581	Methylation	3	14	2.16	2.00E-04
		HSA-196757	Metabolism of folate and pterines	3	17	2.08	3.20E-04
		HSA-3000480	Scavenging by Class A Receptors	3	18	2.05	3.60E-04
		HSA-8963889	Assembly of active LPL and LIPC lipase complexes	3	19	2.03	4.00E-04
		HSA-3359467	Defective MTRR causes methylmalonic aciduria and homocystinuria type cblE	2	2	2.83	1.10E-03
		HSA-3359469	Defective MTR causes methylmalonic aciduria and homocystinuria type cblG	2	2	2.83	1.10E-03
		HSA-8957275	Post-translational protein phosphorylation	4	107	1.40	1.70E-03
		HSA-5668914	Diseases of metabolism	5	244	1.14	2.20E-03
		HSA-381426	Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)	4	124	1.34	2.60E-03
		HSA-8964011	HDL clearance	2	5	2.43	3.00E-03
		HSA-3000471	Scavenging by Class B Receptors	2	6	2.35	3.90E-03
		HSA-1643685	Disease	9	1548	0.59	1.82E-02
		HSA-211859	Biological oxidations	4	214	1.10	1.82E-02
		HSA-8964038	LDL clearance	2	19	1.85	2.63E-02
Chronic renal failure	KEGG	hsa00270	Cysteine and methionine metabolism	5	49	1.82	5.97E-06
		hsa00670	One carbon pool by folate	3	20	1.99	9.40E-04
		hsa01523	Antifolate resistance	3	31	1.80	2.10E-03
		hsa01100	Metabolic pathways	10	1447	0.65	3.20E-03
		hsa05202	Transcriptional misregulation in cancer	4	171	1.18	9.40E-03

		hsa01230	Biosynthesis of amino acids	3	73	1.43	1.01E-02
		hsa05230	Central carbon metabolism in cancer	3	69	1.45	1.01E-02
		hsa05410	Hypertrophic cardiomyopathy	3	89	1.34	1.56E-02
		hsa01200	Carbon metabolism	3	117	1.22	2.48E-02
		hsa04614	Renin-angiotensin system	2	23	1.75	2.48E-02
		hsa04977	Vitamin digestion and absorption	2	24	1.74	2.48E-02
		hsa00260	Glycine, serine and threonine metabolism	2	38	1.54	4.31E-02
		hsa04218	Cellular senescence	3	150	1.12	4.31E-02
		hsa05216	Thyroid cancer	2	36	1.56	4.31E-02
		hsa05206	MicroRNAs in cancer	3	160	1.09	4.36E-02
	Reactome	HSA-1614635	Sulfur amino acid metabolism	6	27	2.16	1.77E-08
		HSA-196849	Metabolism of water-soluble vitamins and cofactors	7	123	1.57	9.36E-07
		HSA-3296469	Defects in cobalamin (B12) metabolism	4	14	2.27	9.74E-06
		HSA-196741	Cobalamin (Cbl, vitamin B12) transport and metabolism	4	21	2.09	2.40E-05
		HSA-1430728	Metabolism	14	2089	0.64	2.20E-04
		HSA-71291	Metabolism of amino acids and derivatives	7	365	1.10	3.20E-04
		HSA-156581	Methylation	3	14	2.15	5.20E-04
		HSA-196757	Metabolism of folate and pterines	3	17	2.06	7.90E-04
		HSA-3359467	Defective MTRR causes methylmalonic aciduria and homocystinuria type cblE	2	2	2.81	2.70E-03
		HSA-3359469	Defective MTR causes methylmalonic aciduria and homocystinuria type cblG	2	2	2.81	2.70E-03
		HSA-5668914	Diseases of metabolism	5	244	1.13	5.80E-03
		HSA-1643685	Disease	10	1548	0.62	1.04E-02

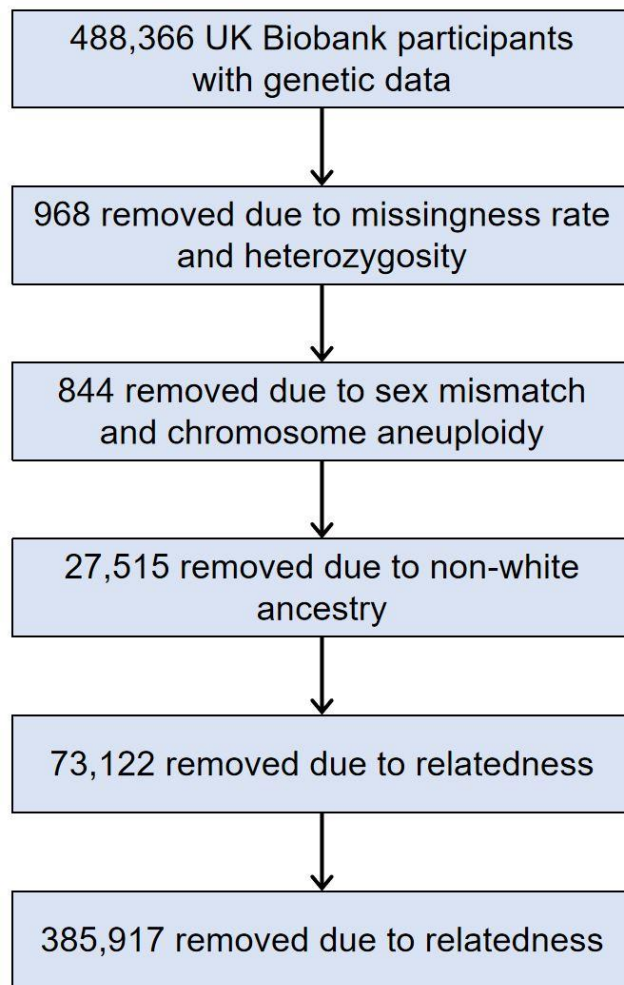
		HSA-6803207	TP53 Regulates Transcription of Caspase Activators and Caspases	2	12	2.04	2.95E-02
		HSA-211859	Biological oxidations	4	214	1.09	4.42E-02
Chronic kidney disease	KEGG	hsa00270	Cysteine and methionine metabolism	5	49	1.82	5.97E-06
		hsa01523	Antifolate resistance	4	31	1.93	3.80E-05
		hsa00670	One carbon pool by folate	3	20	1.99	6.30E-04
		hsa04933	AGE-RAGE signaling pathway in diabetic complications	4	98	1.43	1.40E-03
		hsa05146	Amoebiasis	4	100	1.42	1.40E-03
		hsa05143	African trypanosomiasis	3	36	1.74	1.60E-03
		hsa01100	Metabolic pathways	10	1447	0.65	1.80E-03
		hsa05144	Malaria	3	46	1.63	2.40E-03
		hsa05321	Inflammatory bowel disease	3	60	1.51	4.50E-03
		hsa05140	Leishmaniasis	3	70	1.45	6.30E-03
		hsa01230	Biosynthesis of amino acids	3	73	1.43	6.40E-03
		hsa05133	Pertussis	3	74	1.42	6.40E-03
		hsa04061	Viral protein interaction with cytokine and cytokine receptor	3	96	1.31	1.19E-02
		hsa05142	Chagas disease	3	99	1.30	1.20E-02
		hsa04625	C-type lectin receptor signaling pathway	3	102	1.28	1.22E-02
		hsa04977	Vitamin digestion and absorption	2	24	1.74	1.51E-02
		hsa01200	Carbon metabolism	3	117	1.22	1.59E-02
		hsa05310	Asthma	2	27	1.68	1.67E-02
		hsa05135	Yersinia infection	3	125	1.19	1.72E-02
		hsa05330	Allograft rejection	2	34	1.58	2.32E-02
		hsa05332	Graft-versus-host disease	2	36	1.56	2.46E-02
		hsa00260	Glycine, serine and threonine metabolism	2	38	1.54	2.60E-02

		hsa04216	Ferroptosis	2	41	1.50	2.79E-02
		hsa05161	Hepatitis B	3	159	1.09	2.79E-02
		hsa04672	Intestinal immune network for IgA production	2	43	1.48	2.80E-02
		hsa05010	Alzheimer disease	4	355	0.87	2.80E-02
		hsa05152	Tuberculosis	3	168	1.07	2.80E-02
		hsa04621	NOD-like receptor signaling pathway	3	174	1.05	2.95E-02
		hsa05169	Epstein-Barr virus infection	3	193	1.01	3.80E-02
		hsa05134	Legionellosis	2	55	1.38	3.84E-02
		hsa05166	Human T-cell leukemia virus 1 infection	3	211	0.97	4.55E-02
		hsa05163	Human cytomegalovirus infection	3	218	0.95	4.82E-02
	Reactome	HSA-1614635	Sulfur amino acid metabolism	6	27	2.16	1.77E-08
		HSA-196849	Metabolism of water-soluble vitamins and cofactors	7	123	1.57	9.36E-07
		HSA-3296469	Defects in cobalamin (B12) metabolism	4	14	2.27	9.74E-06
		HSA-196741	Cobalamin (Cbl, vitamin B12) transport and metabolism	4	21	2.09	2.40E-05
		HSA-1430728	Metabolism	14	2089	0.64	2.20E-04
		HSA-71291	Metabolism of amino acids and derivatives	7	365	1.10	3.20E-04
		HSA-156581	Methylation	3	14	2.15	5.20E-04
		HSA-196757	Metabolism of folate and pterines	3	17	2.06	7.90E-04
		HSA-3359467	Defective MTRR causes methylmalonic aciduria and homocystinuria type cbLE	2	2	2.81	2.70E-03
		HSA-3359469	Defective MTR causes methylmalonic aciduria and homocystinuria type cbLG	2	2	2.81	2.70E-03
		HSA-6785807	Interleukin-4 and Interleukin-13 signaling	4	107	1.39	4.00E-03
		HSA-3299685	Detoxification of Reactive Oxygen Species	3	37	1.72	4.80E-03
		HSA-5668914	Diseases of metabolism	5	244	1.13	5.10E-03

		HSA-6783783	Interleukin-10 signaling	3	45	1.64	7.30E-03
		HSA-1643685	Disease	10	1548	0.62	8.60E-03
		HSA-9662834	CD163 mediating an anti-inflammatory response	2	9	2.16	1.49E-02
		HSA-211859	Biological oxidations	4	214	1.09	3.72E-02

Note: Bold fonts represent pathways related to the development and progression of the specific outcome.

Supplementary Figures



Supplementary Figure 1. Sample quality control in the UK Biobank.