

# High Density Lipoprotein Subclasses and Non-Cardiovascular, Non-Cancer Chronic Inflammatory-Related Events versus Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis

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## SUPPLEMENTAL MATERIAL

**Table S1. Numbers of ICD-10 Codes Mentioned in Any Death That Had Any ICD Qualifying for ChrIRD Death. There Were 131 Unique Codes, Among Which Were 557 Code Occurrences in 319 Deaths.**

ICD 10 code	Rubric	Number of code occurrences
A04.7	Other bacterial intestinal infections: Enterocolitis due to Clostridium difficile	2
A04.8	Other bacterial intestinal infections: Other specified bacterial intestinal infections	1
A31.0	Infection due to other mycobacteria: Pulmonary mycobacterial infection	1
A41.0	Other septicemia: Septicemia due to Staphylococcus aureus	1
A41.2	Other septicemia: Septicemia due to unspecified staphylococcus	1
A41.9	Other septicemia: Septicemia, unspecified	54
A48.1	Other bacterial diseases, not elsewhere classified: Legionnaires' disease	1
A49.0	Bacterial infection of unspecified site: Staphylococcal infection, unspecified	1
A52.1	Late syphilis: Symptomatic neurosyphilis	1
B16.9	Acute hepatitis B: Acute hepatitis B without delta-agent and without hepatic coma	2
B17.1	Other acute viral hepatitis: Acute hepatitis C	1
B18.2	Chronic viral hepatitis: Chronic viral hepatitis C	5
B19.9	Unspecified viral hepatitis: Unspecified viral hepatitis without coma	1

B23.8	Human immunodeficiency virus [HIV] disease resulting in other conditions: HIV disease resulting in other specified conditions	1
B24.	Unspecified human immunodeficiency virus [HIV] disease	5
B99.	Other and unspecified infectious diseases	1
D32.9	Benign neoplasm of meninges: Meninges, unspecified	1
D38.1	Neoplasm of uncertain or unknown behavior of middle ear and respiratory and intrathoracic organs: Trachea, bronchus, and lung	1
D43.2	Neoplasm of uncertain or unknown behavior of brain and central nervous system: Brain, unspecified	1
D45.	Polycythemia vera	2
D46.9	Myelodysplastic syndromes: Myelodysplastic syndrome, unspecified	2
D47.1	Other neoplasms of uncertain or unknown behavior of lymphoid, hematopoietic, and related tissue: Chronic myeloproliferative disease	1
D48.1	Neoplasm of uncertain or unknown behavior of other and unspecified sites: Connective and other soft tissue	1
D51.0	Vitamin B12 deficiency anemia: Vitamin B12 deficiency anemia due to intrinsic factor deficiency	1
D64.9	Other anemias: Anemia, unspecified	10
D65.	Disseminated intravascular coagulation [defibrination syndrome]	1
D70.	Agranulocytosis	1
D72.8	Other disorders of white blood cells: Other specified disorders of white blood cells	1
D73.1	Diseases of spleen: Hypersplenism	2
D76.2	Certain diseases involving lymphoreticular tissue and reticulohistiocytic system: Hemophagocytic syndrome, infection-associated	1
D86.9	Sarcoidosis: Sarcoidosis, unspecified	1
E03.9	Other hypothyroidism: Hypothyroidism, unspecified	6
E27.1	Other disorders of adrenal gland: Primary adrenocortical insufficiency	1
E27.4	Other disorders of adrenal gland: Other and unspecified adrenocortical insufficiency	1
E41.	Nutritional marasmus	1
E85.9	Amyloidosis: Amyloidosis, unspecified	2
G20.	Parkinson's disease	10
G30.0	Alzheimer's disease: Alzheimer's disease with early onset	1
G30.9	Alzheimer's disease: Alzheimer's disease, unspecified	16

G31.8	Other degenerative diseases of nervous system, not elsewhere classified: Other specified degenerative diseases of nervous system	1
G47.3	Sleep disorders: Sleep apnea	2
G62.8	Other polyneuropathies: Other specified polyneuropathies	2
G62.9	Other polyneuropathies: Polyneuropathy, unspecified	1
G70.0	Myasthenia gravis and other myoneural disorders: Myasthenia gravis	1
G93.4	Other disorders of brain: Encephalopathy, unspecified	1
J06.9	Acute upper respiratory infections of multiple and unspecified sites: Acute upper respiratory infection, unspecified	1
J15.1	Bacterial pneumonia, not elsewhere classified: Pneumonia due to Pseudomonas	1
J18.0	Pneumonia, organism unspecified: Bronchopneumonia, unspecified	1
J18.1	Pneumonia, organism unspecified: Lobar pneumonia, unspecified	3
J18.9	Pneumonia, organism unspecified: Pneumonia, unspecified	50
J20.9	Acute bronchitis: Acute bronchitis, unspecified	1
J40.	Bronchitis, not specified as acute or chronic	1
J42.	Unspecified chronic bronchitis	1
J43.9	Emphysema: Emphysema, unspecified	8
J44.0	Other chronic obstructive pulmonary disease: Chronic obstructive pulmonary disease with acute lower respiratory infection	3
J44.9	Other chronic obstructive pulmonary disease: Chronic obstructive pulmonary disease, unspecified	41
J45.9	Asthma: Asthma, unspecified	9
J47.	Bronchiectasis	1
J61.	Pneumoconiosis due to asbestos and other mineral fibers	3
J62.8	Pneumoconiosis due to dust containing silica: Pneumoconiosis due to other dust containing silica	1
J69.0	Pneumonitis due to solids and liquids: Pneumonitis due to food and vomit	6
J80.	Adult respiratory distress syndrome	1
J84.1	Other interstitial pulmonary diseases: Other interstitial pulmonary diseases with fibrosis	17
J90.	Pleural effusion, not elsewhere classified	3
J96.0	Respiratory failure, not elsewhere classified: Acute respiratory failure	4
J96.1	Respiratory failure, not elsewhere classified: Chronic respiratory failure	2

J96.9	Respiratory failure, not elsewhere classified: Respiratory failure, unspecified	38
J98.4	Other respiratory disorders: Other disorders of lung	2
K25.9	Gastric ulcer: Unspecified as acute or chronic, without hemorrhage or perforation	1
K27.9	Peptic ulcer, site unspecified: Unspecified as acute or chronic, without hemorrhage or perforation	1
K55.9	Vascular disorders of intestine: Vascular disorder of intestine, unspecified	10
K56.7	Paralytic ileus and intestinal obstruction without hernia: Ileus, unspecified	1
K59.3	Other functional intestinal disorders: Megacolon, not elsewhere classified	1
K63.1	Other diseases of intestine: Perforation of intestine (nontraumatic)	2
K65.9	Peritonitis: Peritonitis, unspecified	2
K70.3	Alcoholic liver disease: Alcoholic cirrhosis of liver	1
K70.9	Alcoholic liver disease: Alcoholic liver disease, unspecified	1
K72.9	Hepatic failure, not elsewhere classified: Hepatic failure, unspecified	4
K74.6	Fibrosis and cirrhosis of liver: Other and unspecified cirrhosis of liver	11
K75.4	Other inflammatory liver diseases: Autoimmune hepatitis	1
K75.9	Other inflammatory liver diseases: Inflammatory liver disease, unspecified	2
K76.0	Other diseases of liver: Fatty (change of) liver, not elsewhere classified	1
K76.7	Other diseases of liver: Hepatorenal syndrome	1
K81.0	Cholecystitis: Acute cholecystitis	1
K82.2	Other diseases of gallbladder: Perforation of gallbladder	1
K86.9	Other diseases of pancreas: Disease of pancreas, unspecified	2
L03.9	Cellulitis: Cellulitis, unspecified	1
L04.9	Acute lymphadenitis: Acute lymphadenitis, unspecified	1
L93.0	Lupus erythematosus: Discoid lupus erythematosus	1
M00.9	Pyogenic arthritis: Pyogenic arthritis, unspecified	1
M06.9	Other rheumatoid arthritis: Rheumatoid arthritis, unspecified	4
M10.9	Gout: Gout, unspecified	1
M13.9	Other arthritis: Arthritis, unspecified	1
M19.9	Other arthrosis: Arthrosis, unspecified	3
M31.0	Other necrotizing vasculopathies: Hypersensitivity angiitis	1
M35.0	Other systemic involvement of connective tissue: Sicca syndrome [Sjögren]	1

M35.3	Other systemic involvement of connective tissue: Polymyalgia rheumatica	1
M48.0	Other spondylopathies: Spinal stenosis	2
M81.9	Osteoporosis without pathological fracture: Osteoporosis, unspecified	3
M86.9	Osteomyelitis: Osteomyelitis, unspecified	4
M89.8	Other disorders of bone: Other specified disorders of bone	2
N03.9	Chronic nephritic syndrome: Unspecified	3
N04.	Nephrotic syndrome	1
N17.	Acute renal failure	1
N17.9	Acute renal failure: Acute renal failure, unspecified	20
N18.0	Chronic renal failure: End-stage renal disease	12
N18.9	Chronic renal failure: Chronic renal failure, unspecified	9
N19.	Unspecified renal failure	24
N28.8	Other disorders of kidney and ureter, not elsewhere classified: Other specified disorders of kidney and ureter	2
N28.9	Other disorders of kidney and ureter, not elsewhere classified: Disorder of kidney and ureter, unspecified	1
N39.0	Other disorders of urinary system: Urinary tract infection, site not specified	10
R04.8	Hemorrhage from respiratory passages: Hemorrhage from other sites in respiratory passages	1
R06.0	Abnormalities of breathing: Dyspnea	2
R09.0	Other symptoms and signs involving the circulatory and respiratory systems: Asphyxia	1
R09.2	Other symptoms and signs involving the circulatory and respiratory systems: Respiratory arrest	9
R09.8	Other symptoms and signs involving the circulatory and respiratory systems: Other specified symptoms and signs involving the circulatory and respiratory systems	1
R13.	Dysphagia	3
R16.0	Hepatomegaly and splenomegaly, not elsewhere classified: Hepatomegaly, not elsewhere classified	1
R31.	Unspecified hematuria	1
R53.	Malaise and fatigue	3
R54.	Senility	4
R57.0	Shock, not elsewhere classified: Cardiogenic shock	3
R57.9	Shock, not elsewhere classified: Shock, unspecified	3
R62.8	Lack of expected normal physiological development: Other lack of expected normal physiological development	8
R63.4	Symptoms and signs concerning food and fluid intake: Abnormal weight loss	2

R63.8	Symptoms and signs concerning food and fluid intake: Other symptoms and signs concerning food and fluid intake	1
R64.	Cachexia	1
R68.8	Other general symptoms and signs: Other specified general symptoms and signs	4
R91.	Abnormal findings on diagnostic imaging of lung	1
R96.0	Other sudden death, cause unknown: Instantaneous death	1
R99.	Other ill-defined and unspecified causes of mortality	3

**Table S2. Numbers of ICD-9 Codes Mentioned in Any Hospitalization That Had Any ICD Qualifying for ChrIRD Hospitalization. There Were 159 Unique Codes, Among Which Were 2392 Code Occurrences Across 983 Hospitalizations.**

ICD 9 code	Rubric	Number of code occurrences
7.4	Cryptosporidiosis	1
8	Intestinal infection due to e. Coli, unspecified	1
8.45	Intestinal infection due to clostridium difficile	38
8.46	Intestinal infection due to other anaerobes	2
9	Infectious colitis, enteritis, and gastroenteritis	3
9.1	Colitis, enteritis, and gastroenteritis of presumed infectious origin	1
11.9	Unspecified pulmonary tuberculosis	1
11.9	Unspecified pulmonary tuberculosis, confirmation unspecified	1
30.9	Leprosy, unspecified	1
38	Streptococcal septicemia	14
38.1	Staphylococcal septicemia, unspecified	4
38.11	Methicillin susceptible staphylococcus aureus septicemia	12
38.12	Methicillin resistant staphylococcus aureus septicemia	7
38.19	Other staphylococcal septicemia	4
38.2	Pneumococcal septicemia	2
38.3	Septicemia due to anaerobes	4
38.4	Septicemia due to gram-negative organism, unspecified	3
38.42	Septicemia due to escherichia coli (e. Coli)	15
38.43	Septicemia due to pseudomonas	3
38.49	Other septicemia due to gram-negative organisms	11
38.8	Other specified septicemias	6
38.9	Unspecified septicemia	128
39.1	Pulmonary actinomycotic infection	1
70.2	Viral hepatitis b with hepatic coma, acute or unspecified, without mention of hepatitis delta	1
70.6	Unspecified viral hepatitis with hepatic coma	1
70.7	Unspecified viral hepatitis c	1
70.7	Unspecified viral hepatitis c without hepatic coma	18
70.71	Unspecified viral hepatitis c with hepatic coma	1
242	Toxic diffuse goiter without mention of thyrotoxic crisis or storm	10
242.1	Toxic uninodular goiter without mention of thyrotoxic crisis or storm	1
242.3	Toxic nodular goiter, unspecified type	2
242.4	Thyrotoxicosis from ectopic thyroid nodule	1
242.8	Thyrotoxicosis of other specified origin without mention of thyrotoxic crisis or storm	2
242.9	Thyrotoxicosis without mention of goiter or other cause	1

Thyrotoxicosis without mention of goiter or other cause, and without	
242.9 mention of thyrotoxic crisis or storm	20
245.2 Chronic lymphocytic thyroiditis	1
245.8 Other and unspecified chronic thyroiditis	2
253 Acromegaly and gigantism	2
253.2 Panhypopituitarism	1
287.39 Other primary thrombocytopenia	1
289.83 Myelofibrosis	1
320.2 Streptococcal meningitis	1
320.3 Staphylococcal meningitis	1
320.82 Meningitis due to gram-negative bacteria, not elsewhere classified	1
320.9 Meningitis due to unspecified bacterium	1
321 Cryptococcal meningitis	5
322.9 Meningitis, unspecified	1
324 Intracranial abscess	1
480.2 Pneumonia due to parainfluenza virus	1
482 Pneumonia due to klebsiella pneumoniae	3
482.1 Pneumonia due to pseudomonas	12
482.2 Pneumonia due to hemophilus influenzae (h. Influenzae)	2
482.3 Pneumonia due to streptococcus, unspecified	4
482.39 Pneumonia due to other streptococcus	2
482.4 Pneumonia due to staphylococcus, unspecified	4
482.41 Methicillin susceptible pneumonia due to staphylococcus aureus	10
482.42 Methicillin resistant pneumonia due to staphylococcus aureus	5
482.81 Pneumonia due to anaerobes	1
482.82 Pneumonia due to escherichia coli [e.coli]	5
482.83 Pneumonia due to other gram-negative bacteria	5
482.84 Pneumonia due to legionnaires' disease	4
482.9 Bacterial pneumonia, unspecified	8
483 Pneumonia due to mycoplasma pneumoniae	1
483.8 Pneumonia due to other specified organism	1
484.1 Pneumonia in cytomegalic inclusion disease	1
485 Bronchopneumonia, organism unspecified	3
486 Pneumonia, organism unspecified	341
502 Pneumoconiosis due to other silica or silicates	2
510 Empyema with fistula	2
510.9 Empyema without mention of fistula	11
511.81 Malignant pleural effusion	6
518.81 Acute respiratory failure	164
518.84 Acute and chronic respiratory failure	21
530.21 Ulcer of esophagus with bleeding	3
531 Acute gastric ulcer with hemorrhage, without mention of obstruction	6
531.1 Acute gastric ulcer with perforation, without mention of obstruction	1



531.4	Chronic or unspecified gastric ulcer with hemorrhage, without mention of obstruction	29
531.41	Chronic or unspecified gastric ulcer with hemorrhage, with obstruction	1
531.5	Chronic or unspecified gastric ulcer with perforation, without mention of obstruction	3
532	Acute duodenal ulcer with hemorrhage, without mention of obstruction	5
532.1	Acute duodenal ulcer with perforation, without mention of obstruction	1
532.4	Chronic or unspecified duodenal ulcer with hemorrhage, without mention of obstruction	14
532.5	Chronic or unspecified duodenal ulcer with perforation, without mention of obstruction	3
532.7	Chronic duodenal ulcer without mention of hemorrhage or perforation, without mention of obstruction	1
533.4	Chronic or unspecified peptic ulcer of unspecified site with hemorrhage, without mention of obstruction	1
533.6	Chronic or unspecified peptic ulcer of unspecified site with hemorrhage and perforation, without mention of obstruction	2
534.4	Chronic or unspecified gastrojejunal ulcer with hemorrhage, without mention of obstruction	1
535.01	Acute gastritis with hemorrhage	1
535.11	Atrophic gastritis with hemorrhage	2
535.41	Other specified gastritis with hemorrhage	3
535.51	Unspecified gastritis and gastroduodenitis with hemorrhage	4
536.1	Acute dilatation of stomach	2
536.41	Infection of gastrostomy	2
540	Acute appendicitis with generalized peritonitis	10
540.1	Acute appendicitis with peritoneal abscess	2
556.6	Universal ulcerative (chronic) colitis	3
558.41	Eosinophilic gastroenteritis	1
562.02	Diverticulosis of small intestine with hemorrhage	1
562.13	Diverticulitis of colon with hemorrhage	11
567.23	Spontaneous bacterial peritonitis	3
567.29	Other suppurative peritonitis	1
569.5	Abscess of intestine	9
569.83	Perforation of intestine	9
570	Acute and subacute necrosis of liver	17
571.42	Autoimmune hepatitis	1
572	Abscess of liver	8
574.7	Calculus of gallbladder and bile duct with other cholecystitis, without mention of obstruction	1
577	Acute pancreatitis	39
577.1	Chronic pancreatitis	15
580.9	Acute glomerulonephritis with unspecified pathological lesion in kidney	3

	Nephritis and nephropathy, not specified as acute or chronic, in diseases classified elsewhere	44
583.81		
584	Acute renal failure	2
584.5	Acute kidney failure with lesion of tubular necrosis	42
584.8	Acute kidney failure with other specified pathological lesion in kidney	6
584.9	Acute kidney failure, unspecified	343
585.6	End stage renal disease	83
590	Chronic pyelonephritis without lesion of renal medullary necrosis	1
590.1	Acute pyelonephritis	1
590.1	Acute pyelonephritis without lesion of renal medullary necrosis	12
590.2	Renal and perinephric abscess	2
595.1	Chronic interstitial cystitis	1
682.1	Cellulitis and abscess of neck	1
695.13	Stevens-johnson syndrome	1
695.4	Lupus erythematosus	2
696	Psoriatic arthropathy	2
696.1	Other psoriasis and similar disorders	19
707.23	Pressure ulcer, stage iii	5
710	Diffuse diseases of connective tissue	1
710	Systemic lupus erythematosus	22
710.3	Dermatomyositis	1
710.4	Polymyositis	2
711	Pyogenic arthritis	1
711.06	Pyogenic arthritis involving lower leg	8
711.07	Pyogenic arthritis involving ankle and foot	1
714	Rheumatoid arthritis	136
714.1	Felty's syndrome	1
725	Polymyalgia rheumatica	17
728	Infective myositis	1
728.88	Rhabdomyolysis	22
730	Acute osteomyelitis, site unspecified	1
730.07	Acute osteomyelitis involving ankle and foot	7
730.1	Chronic osteomyelitis, site unspecified	1
730.15	Chronic osteomyelitis involving pelvic region and thigh	1
730.17	Chronic osteomyelitis involving ankle and foot	2
730.2	Unspecified osteomyelitis, site unspecified	2
730.21	Unspecified osteomyelitis involving shoulder region	3
730.23	Unspecified osteomyelitis involving forearm	1
730.26	Unspecified osteomyelitis involving lower leg	1
730.27	Unspecified osteomyelitis involving ankle and foot	12
730.28	Unspecified osteomyelitis involving other specified sites	7
780.01	Coma	9
780.2	Syncope and collapse	213

780.3	Convulsions	1
780.39	Other convulsions	87
780.71	Chronic fatigue syndrome	2
785.51	Cardiogenic shock	24
785.52	Septic shock	56
786.03	Apnea	1
789.51	Malignant ascites	2

**Table S3. Non-lipid, Non-lipoprotein Predictors of ChrIRD (non CVD, non-cancer chronic inflammatory-related Hospitalization and Death) in Poisson regression up 10.1 Years**

	Unit or category	Relative risk	Lower limit	Upper limit	P for trend
Age	10 Years	1.80	1.66	1.95	<.0001
Race/ethnicity	White vs Hispanic	1.05	0.88	1.26	0.57
	Chinese vs Hispanic	0.76	0.58	0.98	0.04
	Black vs Hispanic	0.97	0.81	1.18	0.78
Sex	Female	0.74	0.61	0.89	0.002
Height	10 cm	1.07	0.97	1.18	0.17
Heart rate	10 beats/min	1.11	1.04	1.18	0.002
Systolic BP	20 mmHg	1.15	1.06	1.25	0.001
Diastolic BP	10 mmHg	0.94	0.86	1.03	0.21
Antihypertensive Rx	Non user vs user	0.86	0.75	0.98	0.03
BMI	5 kg/m <sup>2</sup>	1.07	1.00	1.14	0.04
Smoking	Former vs Never	1.09	0.95	1.25	0.22
	Current vs Never	1.65	1.37	2.00	<.0001
Diabetes	No vs Yes	0.76	0.64	0.90	0.001
IL- 6	1.22 pg/mL	1.17	1.11	1.23	<.0001
hsCrp	5.2 mg/L	1.03	0.96	1.10	0.4334
D-Dimer	0.77 µg/mL	1.08	1.04	1.11	<.0001

**Table S4. Model Selection Among High Density Lipoprotein (HDL)-related Variables (HS-P, HM-P, HL-P, and HDL-C). HDL-related variables added to base model 1. Base model 1 includes with the set of covariates\*, but no lipid or lipoprotein variables. Values Are -2 log likelihood<sup>†</sup> for the Base Model and Changes from This for Other Models.**

	Added variables		
	HL-P HDL-C	HS-P HM-P	HS-P HM-P HL-P HDL-C
Number of variables added	2	2	4
Chi-square p=0.05 cutpoint	-5.99	-5.99	-9.49
Chronic inflammatory-related disease (ChrIRD)	-9.7	-19.9	-23.8
Any Cardiovascular Disease (CVD)	-5.4	-7.6	-9.7
Coronary Heart Disease (CHD)	-8.8	-10.3	-14.6
Stroke	-6.2	-0.4	-6.4
Heart Failure (HF)	-2.5	-0.9	-2.5

\* The covariates and the variables in the LDL family are listed in the Methods section.

<sup>†</sup> Lower -2 log likelihood represents model improvement. The chi-square cutpoint for improvement which is statistically significant at the p = 0.05 level is given in each subtable.

**Table S5. Model Selection Among High Density Lipoprotein (HDL)-related Variables (HS-P, HM-P, HL-P, and HDL-C). HDL-related variables added to a base model. Base model 2 includes the set of covariates and 8 lipid and lipoprotein variables in the LDL family\*. Values Are -2 log likelihood<sup>†</sup> for the Base Model and Changes from This for Other Models.**

	Added Variables						
	HS-P	HM-P	HL-P	HDL-C	HL-P HDL-C	HS-P HM-P	HS-P HM-P HL-P HDL-C
Number of variables added	1	1	1	1	2	2	4
Chi-square p=0.05 cutpoint	-3.84	-3.84	-3.84	-3.84	-5.99	-5.99	-9.49
ChrIRD	-1.9	-8.0	-2.0	0.0	-3.8	-22.7	-25.8
Any CVD	-0.1	-3.6	-0.1	-2.1	-3.5	-6.7	-7.2
CHD	-0.1	-3.0	-0.2	-2.5	-3.4	-5.7	-6.4
Stroke	-0.1	0.0	-0.9	-0.4	-0.9	-0.2	-1.2
HF	0.0	-1.3	0.0	-1.8	-3.2	-1.7	-3.4

\* The covariates and the variables in the LDL family are listed in the Methods section.

<sup>†</sup> Lower -2 log likelihood represents model improvement. The chi-square cutpoint for improvement which is statistically significant at the p = 0.05 level is given in each subtable.