Supporting Information

Perkins et al. 10.1073/pnas.1706096114

SI Materials and Methods

Selected data were collected regarding personal medical and family history, risk factors, and medical symptoms before or during study participant visit. Validated questions from the US NHANES were used to collect selected aspects of personal medical and family history and risk factors (Table S4) to facilitate comparison of our study participants with an age- and sex-adjusted US population-based cohort (Table 1). Participants were instructed to stop taking supplements for 72 h and to fast after dinner the night before their morning appointment. On the day of the visit, blood was obtained for WGS (Human Longevity, Inc.) (9), global metabolomics (12, 20, 21) and a new blood test for prediabetes (Quantose IR; Metabolon) (22), and routine clinical laboratory tests (Laboratory Corporation of America) (Table S5). The new blood test for prediabetes (Quantose IR, with its unique biomarkers and algorithm) was discovered and developed based on the correlation with the hyperinsulinemic–euglycemic clamp values, and it is a more accurate test for insulin resistance (22, 57–60). Two-week cardiac rhythm monitoring (Zio XT Patch; iRhythm Technologies, Inc.) kits were applied during study visit or provided with instructions for home application. Height, weight, and sitting blood pressure (61) were obtained.

Genomic variants were annotated using integrated public and proprietary annotation sources in the HLI database, including ClinVar (62) and HGMD Professional (Qiagen). Monogenic rare variants were classified as pathogenic, likely pathogenic, and variant of uncertain significance. The HLI database integrates allele frequencies for variants derived from the HLI database of >12,000 sequences and provides a platform for query of these variants with annotation data.

To identify potentially medically significant rare monogenic variants, we used an internal version of Open Search (release 0.27) (9) in a two-step process: the first step focused on allele frequency <1% in the HLI cohort with annotation using ClinVar and HGMD Professional as well as predicted loss of function variants; the second step focused on participant-specific phenotype-driven queries using an allele frequency of <1% based on family and individual medical history as well as abnormal clinical testing results.

Global metabolic profiling was performed using ultrahigh-performance liquid-phase chromatography separation coupled with tandem MS to assess the metabolic penetrance of the variants in these subject (12, 20, 21). *Z* scores were calculated for all metabolites in each subject against a reference cohort consisting of 42 fasted subjects of normal health, and metabolites with *Z* scores below the 2.5th percentile or above the 97.5th percentile of the reference cohort were indicative of metabolic abnormalities that warranted further investigation. The process of cross-referencing the genomics data and metabolomics data was like that in our previous publications (12, 20). We used sequence interpretation by variant features and databases to determine metabolic genes with potential impairment. Biochemical pathway analysis of the metabolomics data was used to interpret the functionality. Each case was manually curated using this methodology by our experts in clinical genomic medicine.

Study participants underwent noncontrast whole-body MRI (Discovery MR750w 3.0T) in research mode (GE Healthcare) using protocols and postprocessing for volumetric brain imaging (Neuroquant; CorTechs Labs), cancer detection (using restriction spectrum imaging), neurovascular and cardiovascular visualization, liver-specific fat and iron estimation, and quantitative body compartment-specific fat and muscle estimation (Advanced MR Analytics AB) (19); other postprocessing was done by Multimodality Imaging Services (author A.M.D.). DXA was conducted using Lunar iDXA with Pro Package (GE Healthcare) and was used for skeletal and metabolic health assessment. MRI and DXA images were interpreted by author D.S.K. A Vivid* E95 Ultrasound System (GE Healthcare) was used for ECHO. ECHO, ECG, and 2-wk cardiac rhythm monitoring were interpreted by author A.M.K. Out of normal range signals were evaluated by modality for routine clinical laboratories, whole-body MRI, DXA, ECHO, ECG, and 2-wk cardiac rhythm monitoring. These findings are summarized for participants with likely clinical correlations with genomic findings (Table 2 and Table S2) to apply case definitions for five diseases or conditions, including diabetes and diabetes risk, atherosclerosis or atherosclerosis risk, metabolic syndrome, NAFLD, and NASH (Fig. 2) and those with previously unrecognized age-related chronic disease risk requiring prompt (<30 d) medical attention (Table S3). The proportion of study participants who received a recommendation for follow-up imaging is reported.

Baseline characteristics, including reported past medical history for major categories of age-related chronic diseases by study participants, were compared with responses from the NHANES, a US population-based cohort, adjusted for age and sex distributions (Table 1 and Table S4).

Participants with likely clinical correlations with genomic findings were identified by expert review to identify convergent genomic and clinical (or phenotype) data relationships including at least three generations of pedigree- and metabolite-level correlation based on pathway mapping (Table 2). Clinical data were collected before and independent of genomic findings. Clinical data were used in WGS variant interpretation as supporting evidence for pathogenicity (e.g., "PP1: Cosegregation with disease in multiple affected family members in a gene definitively known to cause the disease, and PP5: Patient's phenotype or family history is highly specific for a single genetic etiology") (26, 27).

Participants with evidence of age-related chronic disease or disease risk factors were identified as having (*i*) type 2 diabetes (34), prediabetes (34), and insulin resistance (Quantose IR) (22); (*ii*) likely atherosclerotic disease or at-risk; (*iii*) metabolic syndrome (35); or (*iv*) NAFLD or NASH based on clinical guidelines or other recent literature. Measured fasting blood glucose, hemoglobin A1c, personal medical history for diabetes, or Quantose IR was used to identify participants as having diabetes, prediabetes, or insulin resistance. The presence of any of the following was considered to be evidence of likely atherosclerotic disease or risk ["yes" in response to any of the following questions: (*i*) ever told you had coronary artery disease, (*ii*) ever told you had a heart attack, (*iii*) ever told you had congestive heart failure, (*iv*) taking prescription for hypertension, and (*v*) taking prescription for cholesterol] or if sitting blood pressure > normal, LDL cholesterol > normal, or lipoprotein-associated phospholipase A_2 > normal. The presence of any three of the following five criteria was considered to be evidence of metabolic syndrome: (*i*) visceral adipose tissue measured by MRI (postprocessing by Advanced MR Analytics) ≥2 SD above normal (19) or android/gynoid fat measured by DXA > normal, (*ii*) triglycerides ≥ 150 mg/dL, (*iii*) HDL cholesterol <40 mg/dL in men and <50 mg/dL in women or the participant is currently taking prescribed medicine for high cholesterol, (*iv*) blood pressure ≥130/85 mmHg or the participant is currently taking prescription for hypertension, or (*v*) measured fasting glucose or hemoglobin A1c indicates prediabetes (35) or "borderline" in response to the question of if a doctor told you that you have diabetes. The presence of NAFLD or NASH was considered likely if, for NAFLD, MRI-based estimated liver fat was <4% and did not have alcohol dependence, and for these

individuals, we used a formula including other demographic and laboratory data to identify likely NASH (36).

Study participants with previously unrecognized age-related chronic disease risk requiring prompt (<30 d) medical attention were defined as having a new genomic and/or other clinical findings, which based on current medical practice, indicated the need for medical attention to avoid potentially life-threatening consequences immediately or within 30 d from their visit.

Table S1. Variant annotation

	SNVs		Indels	
Variant type	All sites	High confidence region only	All sites	High confidence region only (9)
Total	21,761,709	18,616,803	5,721,120	3,799,425
Annotation				
Intergenic_region	10,286,095	8,599,254	2,659,418	1,659,136
Intron_variant	10,885,401	9,657,406	2,965,523	1,891,268
Non_coding_exon_variant	510,613	420,384	70,849	48,362
3_Prime_UTR_variant	258,778	232,706	62,933	43,533
5_Prime_UTR_variant	74,794	64,541	13,056	7,855
Upstream_gene_variant	3,087,718	2,582,160	853,663	508,199
Downstream_gene_variant	3,175,525	2,651,038	877,657	526,415
TF_binding_site_variant	10,130	7,684	4,916	1,774
Variant effect				
Splice_acceptor_variant	1,304	1,030	878	522
Splice_donor_variant	1,967	1,657	373	260
Missense_variant	106,221	91,887	NA	NA
Synonymous_variant	80,234	71,240	NA	NA
Start_lost	303	270	52	42
Stop_gained	1,851	1,567	63	50
Stop_lost	166	131	44	31
Frameshift_variant	NA	NA	2,845	2,233

NA, not applicable.

Table S2. Rare monogenic variants with likely clinical correlates by disease group

Disease group	Gene	Disease associated with gene variant	MOI	c.HGVS	Zygosity	Likely clinical correlates
Pathogenic						
Neoplasm	RAD50	Hereditary cancer-predisposing syndrome	AD	c.326_329delCAGA	Het	Family history: first degree (maternal two cases colon cancer)
Neoplasm	NBN	Hereditary cancer-predisposing syndrome	AD	c.657_661delACAAA	Het	Family history: second degree (paternal sibling brain cancer)
Neoplasm	NBN	Hereditary cancer-predisposing syndrome	AD	c.127C > T	Het	Family history: first and second degree cancer (mother, brother, father, paternal aunt, paternal uncle)
Neoplasm	ALDH2	Aldehyde dehydrogenase deficiency, susceptibility to esophageal cancer	AD	c.1510G > A	Het	Affected (metabolomics); family history: first degree cancer (father, brother)
Neoplasm	ALDH2	Aldehyde dehydrogenase deficiency, susceptibility to esophageal cancer	AD	c.1510G > A	Het	Affected (MRI, metabolomics); family history: second degree (paternal grandfather and siblings, paternal uncle)
Neoplasm	ALDH2	Aldehyde dehydrogenase deficiency, susceptibility to esophageal cancer	AD	c.1510G > A	Het	Affected (MRI, metabolomics); family history: second degree (paternal grandfather and siblings, paternal uncle)
Neoplasm	ATM	Hereditary cancer-predisposing syndrome, ataxia telangiectasia	AD, AR	c.6100C > T	Het	Affected (history colon cancer); family history: first and second degree cancer (father, maternal grandmother, paternal grandmother)
Cardiovascular	PKP2	Arrhythmogenic right ventricular dysplasia 9	AD	c.314delC	Het	Affected (history mitral valve tear); ECHO, ECG, cardiac rhythm monitor; family history: first and second degree myocardial infarction (father, paternal grandfather)
Cardiovascular	APOB	Familial hypercholesterolemia	AD	c.10580G > A	Het	Affected (clinical laboratories, ECHO); family history: first degree and second degree
Cirrhosis	HFE	Hemochromatosis; susceptibility to cirrhosis, diabetes, and liver cancer	AR	c.845G > A	Homo	Affected (MRI, ECHO, ECG, cardiac rhythm monitor, metabolomics); family history: first degree affected
Diabetes	SPINK1	Pancreatitis; susceptibility to fibrocalculous pancreatic diabetes, tropical calcific pancreatitis	AR, AD	c.101A > G	Het	Affected (metabolomics)
Diabetes	SPINK1	Pancreatitis; susceptibility to fibrocalculous pancreatic diabetes, tropical calcific pancreatitis	AR, AD	c.101A > G	Het	Affected (metabolomics)
Diabetes	SPINK1	Pancreatitis; susceptibility to fibrocalculous pancreatic diabetes, tropical calcific pancreatitis	AR, AD	c.101A > G	Het	Affected (clinical laboratories, MRI, metabolomics); family history: first degree (brother)
Diabetes	SPINK1	Pancreatitis; susceptibility to fibrocalculous pancreatic diabetes, tropical calcific pancreatitis	AR, AD	c.101A > G	Het	Affected (clinical laboratories, metabolomics)
Diabetes	FMO3	Trimethylaminuria	AR	c.458C > T	Homo	Affected (metabolomics)
Metabolic	ACADM	MCAD deficiency	AR	c.1084A > G	Het	Affected (metabolomics)
Metabolic	ACADS	Deficiency of butyryl-CoA dehydrogenase	AR	c.319C > T,c.511C > T*	Het	Affected (metabolomics)
Metabolic	ACSF3	Combined malonic and methylmalonic aciduria	AR	c.1672C > T	Het	Affected (metabolomics)
Metabolic	ALDH2	Aldehyde dehydrogenase deficiency, susceptibility to esophageal cancer	AD	c.1510G > A	Het	Affected (metabolomics)
Metabolic	ALDH2	Aldehyde dehydrogenase deficiency, susceptibility to esophageal cancer	AD	c.1510G > A	Het	Affected (metabolomics, MRI)
Metabolic	CTH	Cystathioninuria	AR	c.200C > T	Het	Affected (metabolomics)
Metabolic	PAH	Phenylketonuria	AR	c.814G > T	Het	Affected (metabolomics)
Likely pathogenic						

Table S2. Cont.

Disease group	Gene	Disease associated with gene variant	MOI	c.HGVS	Zygosity	Likely clinical correlates
Neoplasm	EPCAM	Lynch syndrome	AD	c.491+1G > A	Het	Family history: first, second, and third degree cancer (father, two maternal great aunts)
Neoplasm	TP53	Osteosarcoma, Li Fraumeni-like syndrome	AD	c.844C > T	Het	Affected; family history: first degree cancer (three relatives)
Neoplasm	RECQL	Hereditary cancer-predisposing syndrome	AD	c.643C > T	Het	Family history: first and second degree cancer (mother, father, two maternal uncles, two maternal aunts, maternal grandfather)
Cardiovascular	KCNH2	Long QT syndrome	AD	c.2785dupG	Het	Affected; family history: first degree (brother)
Other	TNFRSF13B	Common variable immunodeficiency 2	AR, AD	c.310T > C	Het	Affected (clinical laboratories, MRI, metabolomics)
Metabolic	ASS1	Citrullinemia	AR	c.1030C > T	Het	Affected (metabolomics)
Metabolic	GCDH	Glutaricaciduria	AR	c.1093G > A	Het	Affected (metabolomics)
Metabolic	PKLR	Pyruvate kinase deficiency	AR	c.1456C > T	Het	Affected (metabolomics)
Metabolic	SLC7A9	Cystinuria	AR	c.544G > A	Het	Affected (metabolomics)
Risk factor						
Neurologic	APOE	Alzheimer's disease	AD	c.388T > C	Homo	Affected; family history: first and second degree (father, both paternal grandparents)
VUS						
Neoplasm	PALB2	Familial cancer of breast, hereditary cancer-predisposing syndrome	AD	c.508A > G	Het	Affected
Neoplasm	PMS1	Lynch syndrome	AD	c.1888C > T	Het	Affected; family history: second degree cancer (paternal grandparent)
Neoplasm	CHEK2	Hereditary cancer-predisposing syndrome	AD	c.190G > A	Het	Family history: first and second degree (father, maternal grandmother)
Neoplasm	RAD50	Hereditary cancer-predisposing syndrome	AD	c.2177G > A	Het	Affected; family history: first and second degree (father, sister, paternal aunts)
Cardiovascular	DSP	Arrhythmogenic right ventricular dysplasia	AD	c.8531G > T	Het	Affected (cardiac rhythm monitor); family history: first and second degree (father, mother, paternal grandfather, maternal grandparents, maternal aunt)
Cardiovascular	DSP	Arrhythmogenic right ventricular dysplasia	AD	c.8531G > T	Het	Affected (cardiac rhythm monitor); family history: first and second degree (father, mother, paternal grandfather, maternal grandparents, maternal aunt)
Cardiovascular	DSP	Arrhythmogenic right ventricular dysplasia	AD	c.8531G > T	Het	Affected (ECHO, ECG, cardiac rhythm monitor); family history: first and second degree (father, mother, paternal grandfather, maternal grandparents, maternal aunt)
Cardiovascular	APOB	Familial hypercholesterolemia	AD	c.9452C > T	Het	Affected (clinical laboratories); family history: first degree (mother)
Cardiovascular	APOB	Familial hypercholesterolemia	AD	c.9452C > T	Het	Affected (clinical laboratories); family history: first and second degree (mother, father, paternal grandparents, maternal grandparents)
Cardiovascular	APOB	Familial hypercholesterolemia	AD	c.9452C > T	Het	Affected (clinical laboratories); family history: first and second degree (mother, father, paternal grandparents, maternal grandparents)
Cardiovascular	MYBPC3	Dilated cardiomyopathy, hypertrophic cardiomyopathy	AD	c.1468G > A	Het	Affected (ECHO); family history: first and second degree: father, two brothers, two sisters, maternal grandfather)

Table S2. Cont.

Disease group	Gene	Disease associated with gene variant	MOI	c.HGVS	Zygosity	Likely clinical correlates
Cardiovascular	MYL2	Hypertrophic cardiomyopathy	AD	c.401A > C	Het	Affected (ECHO, ECG, cardiac rhythm monitor)
Cardiovascular	RYR2	Ventricular tachycardia, polymorphic	AD	c.1396C > G	Het	Affected (ECHO, ECG); family history: first and second degree (father, brother, paternal uncles, paternal aunts, paternal grandmother)
Cardiovascular	MYH7	Cardiomyopathy	AD	c.29G > C	Het	Affected; family history: first and second degree (father, two maternal uncles, maternal grandparents, paternal uncle, paternal grandfather)
Cardiovascular	LPL	Combined hyperlipidemia, familial; lipoprotein lipase deficiency	AR, AD	c.286G > C	Het	Affected (ECHO, ECG); family history: first and second degree (father, maternal cousin, maternal grandfather)
Cardiovascular	MYBPC3	Hypertrophic cardiomyopathy; dilated cardiomyopathy	AD	c.1000G > A	Het	Affected (ECHO); family history: first degree (mother, father)
Diabetes	PRSS1	Hereditary pancreatitis	AD	c.107C > G	Het	Affected (metabolomics, clinical laboratories); family history: first and second degree (mother, maternal grandmother, maternal aunt)
Diabetes	PRSS1	Hereditary pancreatitis	AD	c.107C > G	Het	Affected (metabolomics); family history: first and second degree (mother, maternal aunt, maternal grandmother)

Het, heterozygosity; Homo, homozygosity; MOI, mode of inheritance; VUS, variant of uncertain significance.
*Next-generation sequencing assay could not determine whether c.319C > T and c.511C > T occur in *cis* or in *trans* (55).

Table S3. Previously unrecognized age-related chronic diseases requiring prompt (<30 d) medical attention

Disease group	Sex	Age, y	Findings and follow-up
Cardiovascular diseases	M	67	Past medical history: no history of cardiovascular disease. Finding: initial bundle branch block/IVCD; atrial fibrillation burden 1%. Follow-up: pending
Cardiovascular diseases	M	47	Finding: right common iliac artery aneurysm measuring 2.6 cm. No involvement of abdominal aorta or internal or external iliac arteries. Recommend CT angiogram for further evaluation and confirmation. Follow-up: pending
Cardiovascular diseases	M	68	Medical history: increased blood pressure, increased cholesterol. Finding: paroxysmal atrial fibrillation; atrial fibrillation burden 3%. Follow-up: individual now taking anticoagulant
Cardiovascular diseases	M	73	Medical history: increased blood pressure. Finding: first degree atrioventricular block; atrial fibrillation burden 7%. Follow-up: individual now taking anticoagulant
Cardiovascular diseases	F	64	Medical history: increased cholesterol, increased blood pressure. Finding: atrial fibrillation burden 2%. Follow-up: pending
Cardiovascular diseases	F	66	Finding: limited noncontrast neck MRA. String of beads appearance to the bilateral cervical internal carotid arteries may represent fibromuscular dysplasia. Motion artifact is considered less likely. Recommend i.v. contrast-enhanced CT or MR angiogram of the carotid arteries for further evaluation. Follow-up: CT with contrast for scans of carotid and renal arteries; nothing to report
Cardiovascular diseases	F	47	Medical history: high cholesterol. Finding: a 5-mm aneurysm originating from the left cavernous ICA just proximal to the opthalmic artery. Recommend neurosurgery evaluation. Consider CT or conventional angiogram. Follow-up: pending
Cardiovascular diseases	F	61	Finding: head: noncontrast brain MRA; 50% loss of signal of the left internal carotid artery at the junction of the cavernous and petrous portions may represent artifact vs. partial narrowing. Recommend CT angiogram of the brain for further evaluation. Chest: 4- × 2-cm lesion in the medial right lower lobe. Suggestion of connection to the pulmonary vessels. Recommend CT chest to rule out pulmonary arteriovenous malformation. Other considerations include mass, sarcoid, sequestration, or atelectasis. Follow-up: pending
Neoplasm	M	63	Medical history: melanoma finding. A 3-cm lobulated contour of the left kidney may represent a benign dromedary hump. However, there is limited evaluation. Recommend renal ultrasound to rule out a mass. Follow-up: surgically resected and found to be high-grade early-stage renal cell carcinoma
Neoplasm	M	56	Finding: 5-cm anterior mediastinal mass with differential including lymphoma, thymoma, or germ cell tumor. The mass is most likely a thymoma, likely stage 1 or 2. There is no obvious vascular invasion and no lymph nodes. Recommend contrast-enhanced CT and thoracic surgery consultation. Follow-up: thymoma
Neoplasm	M	33	Finding: 1.5- × 1.9-cm cystic lesion in the left parotid gland with differential including sialocele, pleomorphic adenoma, lymphatic malformation, or first branchial cleft cyst. Favor a pleomorphic adenoma. Recommend contrast-enhanced MRI or CT for further evaluation along with ENT surgery consultation. Follow-up: pleomorphic adenoma, biopsy pending
Neoplasm	M	65	Finding: two lesions noted, the most concerning of which is a PIRADS 4 lesion in the left posterior peripheral zone. Recommend urology consultation to consider targeted biopsy. The anterior transitional zone lesion is a PIRADS 3 lesion, which may represent a BPH nodule, although neoplasia is within the differential. Follow-up: prostate cancer confirmed
Neoplasm	M	69	Finding: prostate volume of 52 cc (normal range is 15–30 cc). Right lateral peripheral/transitional zone lesion as noted above is stable going back two examinations from 1/4/14 and 1/9/13. The lesion is categorized as PIRADS 3. Favor BPH nodule given stability, but neoplasia is within the differential. Recommend close imaging follow-up. Follow-up: prostate cancer confirmed and surgically resected
Neoplasm risk	M	57	Finding: abdomen: 4.8-cm complex left renal cyst with septations. Although this may represent a complex benign cyst, cystic renal cell carcinoma is not excluded. Recommend renal mass protocol CT or MRI for further evaluation. Follow-up: CT imaging of renal cyst indicated Bosniak stage 2
Neoplasm risk	M	70	Medical history: history of nonmelanoma skin cancer. Finding: a 2.5-cm complex lesion in the lower pole of the left kidney with differential considerations, including hemorrhagic cyst. A solid mass is not entirely excluded. Recommend ultrasound or contrast-enhanced CT for further evaluation. Follow-up: repeat CT for kidney mass repeated. No significant findings reported

Table S3. Cont.

Disease group	Sex	Age, y	Findings and follow-up
Other	F	69	Finding: alkaline phosphatase, S 229 (abnormal Flag: H); alanine aminotransferase 77 (abnormal flag: H); aspartate aminotransferase 73 (abnormal flag: H); C-reactive protein, quant 7 (abnormal flag: H); cancer antigen 19–9 101 (abnormal flag: H); cancer antigen 125 58.5 (abnormal flag: H); cholesterol, total 253 (abnormal flag: H); cystatin C 1.05 (abnormal flag: H); ferritin, serum 209 (abnormal flag: H); fibrinogen antigen 366 (abnormal flag: H); GGT 515 (abnormal flag: H); iron, serum 161 (abnormal flag: H); LDL cholesterol calc 152 (abnormal flag: H); Lp-PLA_2 386 (abnormal flag: H); platelets 130 (abnormal flag: L). Follow-up: finding of primary biliary cholangitis based on liver biopsy
Other	M	66	Medical history: history of kidney stones (6). Finding: xanthinuria on metabolome analysis (xanthine kidney stones). Follow-up: pending

The Global Burden of Disease benchmarks for health loss from death or disability was used to categorize our findings based on the leading causes of and/or risks for noncommunicable death. BPH, benign prostatic hyperplasia; CT, computed tomography; ENT, ear, nose, and throat; GGT, gamma-glutamyl transferase; ICA, intracranial aneurysm; IVCD, interventricular conduction delay; F, female; Lp-PLA_2, lipoprotein-associated phospholipase A_2; M, male; MR, magnetic resonance; MRA, magnetic resonance angiogram; PIRADS, prostate imaging reporting and data system.

Table S4. Validated questions from the NHANES

Instrument	Questions	Website
NHANES 2013–2014	ALQ101_had at least 12 alcoholic drinks per 1 y	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	SMQ020_smoked at least 100 cigarettes in life	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	BPQ020_ever told you had high blood pressure	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	BPQ040A_taking prescription for hypertension	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	BPQ080_doctor told you that you have high cholesterol level	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	BPQ090D_told to take prescription for cholesterol	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	BPQ100D_now taking prescribed medicine	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	DIQ010_doctor told you that you have diabetes	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ300C_close relative had diabetes	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2011–2012	KIQ022_ever told you had weak/failing kidneys	https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/MCQ_G.htm
NHANES 2013–2014	MCQ084_difficulties in thinking or remembering	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ160B_ever told you had congestive heart failure	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ160C_ever told you had coronary heart disease	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ180C_age when told that you had coronary heart disease	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ160E_ever told you had heart attack	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ300A_close relative had heart attack	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ160F_ever told you had a stroke	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ160L_ever told you had any liver condition	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ160O_ever told you had COPD	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ220_ever told you had cancer or malignancy	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2013–2014	MCQ230A-D_what kind of cancer	https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/MCQ_H.htm
NHANES 2003–2004	MCQ250B_blood relatives have Alzheimer's	https://wwwn.cdc.gov/Nchs/Nhanes/2003-2004/MCQ_C.htm

The NHANES information is at https://www.cdc.gov/nchs/nhanes/. COPD, chronic obstructive pulmonary disease.

Table S5. A list of routine clinical laboratory tests

Antimyeloperoxidase Abs	Eos	Insulin
Antinuclear antibodies	Eos (absolute)	LH
Apolipoprotein B/A-1 ratio	Estradiol	Prolactin
Apolipoprotein A-1	Ferritin, serum	Lipase, serum
Apolipoprotein B	FSH	Cholesterol, total
C-reactive protein, quant	Hemoglobin	HDL cholesterol
Calcitonin, serum	Hemoglobin A1c	LDL cholesterol calc
Calcitriol(1,25 di-OH vit D)	Immature grans (Abs)	Triglycerides
CCP antibodies IgG/IgA	Immature granulocytes	VLDL cholesterol cal
AFP, serum, tumor marker	Iron binding capacity	Lipoprotein (a)
Cancer antigen 19–9	Iron saturation	Lp-PLA_2
Cancer antigen 125	Iron, serum	hCG, beta Subunit, Qnt, serum
CEA	Lymphs	Progesterone
Albumin, serum	Lymphs (absolute)	A/G ratio
Alkaline phosphatase, S	MCH	Albumin
Alanine aminotransferase	MCHC	Alpha-1-globulin
Aspartate aminotransferase	MCV	Alpha-2-globulin
Bilirubin, direct	Monocytes	Beta globulin
Bilirubin, total	Monocytes (absolute)	Gamma globulin
BUN	Neutrophils	% Free PSA*
BUN/creatinine ratio	Neutrophils (absolute)	Prostate-specific Ag, serum*
Calcium, serum	Platelets	PSA, free*
Carbon dioxide, total	RBC	PTH, intact
Chloride, serum	RDW	Selenium, serum/plasma
Creatinine, serum	Testosterone, serum	Free thyroxine index
eGFR if African American	TSH	T3 uptake
eGFR if not African American	UIBC	Reverse T3, serum
Globulin, total	Vitamin D, 25-hydroxy	Thyroid peroxidase Ab
Glucose, serum	WBC	Sex horm binding glob, serum
LDH	Fibrinogen antigen	Testost., % free + weakly bound
Magnesium, serum	Folate, hemolysate	Testost., free + weakly bound
Potassium, serum	Folate, RBC	Thyroxine (T4)
Protein, total, serum	Hematocrit	*t*-Transglutaminase IgA
Sodium, serum	GGT	*t*-Transglutaminase IgG
Uric acid, serum	Hep A Ab, total	Vitamin A, serum
Copper, whole blood	Hep B surface Ab, qual	Vitamin B1, whole blood
Cortisol	Hep C virus Ab	Vitamin B12
Creatine kinase, total, serum	Arsenic, blood	Zinc, whole blood
Cystatin C	Cadmium, blood	
DHEA-sulfate	Lead, blood	
Baso (absolute)	Mercury, blood	
Basos	Homocyst(e)ine, plasma	

AFP, alpha-fetoprotein; A/G, albumin/globulin ratio; BUN, blood urea nitrogen; CCP, cyclic citrullinated peptide; CEA, carcinoembryonic antigen; DHEA, dehydroepiandrosterone; eGFR, estimated glomerular filtration rate; FSH, follicle-stimulating hormone; GGT, gamma-glutamyl transferase; hCG, human chorionic gonadotropin; HDL, high-density lipoprotein; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; LH, luteinizing hormone; Lp-PLA_2, lipoprotein-associated phospholipase A_2; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; PSA, prostate specific antigen; PTH, parathyroid hormone; RDW, red cell distribution width; TSH, thyroid stimulating hormone; UIBC, unsaturated iron binding capacity; VLDL, very low-density lipoprotein.
*Obtained for males only.