## Detailed Description

### Blood Ions

<table>
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<th>Trait</th>
<th>Detailed Description</th>
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<tbody>
<tr>
<td>SONA</td>
<td>Abbreviations are as follows: SONA, sodium; potassium; CHL, chloride. Most of the sodium in the body (about 85%) is found in blood and lymph fluid. Sodium is both an electrolyte and mineral. It helps keep the water and electrolyte balance of the body. Other electrolytes, such as potassium and chloride, were checked in the subjects at the same time as a blood test for sodium. The level of potassium is inversely related to the sodium level. Potassium is also both</td>
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<tr>
<td>POTA</td>
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<td>CHL</td>
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### BMD

Bone density is a proxy measurement for bone strength, which is the resistance to fracture, widely used to screen for osteoporosis. Bone density was estimated by T-score by dividing the difference of measured SOS (speed of sound) from mean SOS in healthy young adult population by the standard deviation of SOS in young adult population. Bone SOS was measured by quantitative ultrasound at distal radius or mid-shaft tibia in the subjects of the KARE GWAS [1].

### Blood Pressure

Blood pressure refers to the force exerted by circulating blood on the walls of blood vessels and constitutes one of the principal vital signs. Typical values for a resting, healthy adult human are approximately 120 mmHg systolic and 80 mmHg diastolic although there is substantial individual variation. In this study, diastolic and systolic BP values analyzed were the averages of three recumbent measurements. Genetic factors are thought to play a prominent role in the development of essential hypertension, though few, if any, robust associations have been found [1]. Both diastolic and systolic BP values were measured in sitting (SBP0, DBP0) and lying positions (SBP, DBP).

### Blood Cell Count

The hematopoietic system has various functions including oxygen transport, immunity, blood wall surveillance, homeostasis, and wound curing. Hematological parameters include the number of white blood cells (WBC; 10^3/L), red blood cells (RBC; 10^6/L), platelets (PLAT; 10^5/L), and hematocrit (HCT; %) [11] from the whole blood. The number of WBC was natural log transformed to approximate a normal distribution.

### Blood Glucose and Insulin Index

The level of potassium is inversely related to the sodium level. Potassium is also both

### Lipids

Abbreviations are as follows: HDL, high-density lipoprotein cholesterol; TCHL, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein cholesterol. TCHL, HDL, and TG were extracted from human blood. LDL was calculated by Fredewald formula when TG level was under 400 mg/dl. Otherwise, LDL was considered to be missing, because it could not be calculated from formula [5]. The Fredewald formula is \( \text{LDL} = \text{TCHL} - \left( \frac{\text{TG}}{5} \right) \). [6] Before modeling, HDL and TG traits were natural log transformed to approximate a normal distribution. NONHDL is HDL subtracted from TG. Finally, TDHL is the natural logarithmic transformed measure of TG divided by HDL.

### Obesity

BMI, weight in kilograms divided by height in meters squared, is a widely used index of obesity. Obesity itself is one of the major risk factors for common complex diseases such as T2DM, heart disease, metabolic syndrome, hypertension, stroke, and some forms of cancer [1].

### Waist

Waist was measured in cm scale.

### Hip

Hip circumference was measured in cm scale.

### WHR

WHR is the ratio of the waist to hip circumferences and is a commonly used measure of the central accumulation of fat [1].

### Weight

Weight was measured in kg scale.

### SUB SUP

Subscapular and suprailiac skinfold thickness values are measurements for upper central body fat distribution around the waist. It is measured just below the angle of the left scapula with the fold either in a vertical line or slightly inclined [2]. The suprailiac measure is a diagonal fold taken midway between the hip joint and the bottom of the rib cage. Natural logarithmic transformation and square root transformation were applied to the subscapular and suprailiac measures respectively [3].

### Pulse

Pulse rate, also called heart rate, is the frequency of the heart beat (beats per minute, BPM) [1]. A normal pulse rate for a healthy adult, while resting, ranges from 60 to 80 BPM [4]. Changes in pulse rate may be caused by heart disease or problems in heart [1].

### BMD

Bone density is a proxy measurement for bone strength, which is the resistance to fracture, widely used to screen for osteoporosis. Bone density was estimated by T-score by dividing the difference of measured SOS (speed of sound) from mean SOS in healthy young adult population by the standard deviation of SOS in young adult population. Bone SOS was measured by quantitative ultrasound at distal radius or mid-shaft tibia in the subjects of the KARE GWAS [1].

### Diabetes Index

Type 2 diabetes (T2D) is a state of chronic hyperglycemia defined as elevated glucose levels measured either when fasting or 2 h after glucose challenge during oral glucose tolerance test (OGTT) [7]. Subject underwent a 75-g OGTT with blood sampling at fasting (GLU0, INS0), and 60 (GLU60, INS60) and 120 min (GLU120, INS120) after the oral glucose load to measure the glucose and insulin levels [8]. All of the blood glucose and insulin levels were natural log transformed to approximate a normal distribution. Homeostasis model assessment for insulin resistance (HOMA-IR) was assessed using the formula: HOMA-IR=fasting serum insulin (mU/ml) × fasting glucose (mmol/L)/22.5. [9] The HOMA-IR was square root transformed to approximate a normal distribution. HBA1C, glycosylated hemoglobin, reflects blood glucose concentrations over the preceding 8 to 12 weeks [10].

### WBC RBC PLAT HCT

The hematopoietic system has various functions including oxygen transport, immunity, blood wall surveillance, homeostasis, and wound curing. Hematological parameters include the number of white blood cells (WBC; 10^3/L), red blood cells (RBC; 10^6/L), platelets (PLAT; 10^5/L), and hematocrit (HCT; %) [11] from the whole blood. The number of WBC was natural log transformed to approximate a normal distribution.
an electrolyte and a mineral. Sodium and potassium levels are known to affect the risk of hypertension[12]. Chloride is one of the most important electrolytes in the blood. C-reactive protein (CRP) is a plasma protein synthesized by the liver and found in the blood, and thus a sensitive and dynamic systemic marker of inflammation [13]. The distribution of CRP concentrations (mg/L) was positively skewed and hence CRP concentration was natural log transformed for all analyses. Hemoglobin (HB) was measured in g/dl scale and extracted from whole blood. Alanine transaminase (ALT) is a crucial enzyme found predominately in the liver. Increased activity of ALT in serum suggests hepatocyte damage [14]. When a cell is damaged, it leaks this enzyme into the blood, where it is measured. Aspartate transaminase (AST) is similar to ALT in that it is another enzyme associated with liver parenchymal cells. It is a less specific indicator of liver inflammation than the AST, as AST level change can be caused by diseases affecting other organs. The value of ALT was transformed to 1/square root (y) while AST was transformed to 1/(y). Gamma-glutamyltranspeptidase (RGTP) is a membrane-bound glycoprotein that transfers gamma-glutamyl functional groups between peptides or amino acids [15]. It is found in many tissues, but the most notable one being the liver, and has significance in medicine as a diagnostic marker [16]. The value of RGTP was transformed to 1/square root (y).

Lung Functions

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<th>SP1</th>
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<th>SP3</th>
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<td>Forced vital capacity (FVC) is the volume of air that can forcibly be blown out after full inspiration, measured in liters. FVC is the most basic maneuver in spirometry tests, and FEV1 is the forced expiratory volume in one second [17]. All values were corrected and expressed as a percentage of those predicted (%pred) for age, sex and height. The predicted values for FVC (FVC_%PRED), FEV1 (FEV1_%PRED), and FEV1/FVC (FEV1/FVC_%PRED) from the cohorts were used, and those values are abbreviated as SP1, SP2, SP3, respectively.</td>
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Kidney Functions

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<th>RENIN</th>
<th>Bun</th>
<th>Creatine</th>
<th>SG</th>
<th>pH</th>
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<td>Abbreviations are as follows: BUN, blood urea nitrogen; SG, specific gravity of urine. Plasma renin activity (PRA) is a measure of the activity of the plasma enzyme renin which plays a crucial role in the body’s regulation of blood pressure and urine output [18]. The PRA was natural log transformed to approximate a normal distribution. The level of blood urea nitrogen (BUN) and creatine show how well kidneys are working. The plasma levels of the BUN and creatine were measured in serum, using mg/dL and the BUN was log transformed before all analyses. Specific gravity of urine (SG) and pH of urine measure the kidney’s ability to concentrate or dilute urine in relation to plasma [19,20].</td>
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References


