

# Associations of dietary patterns with brain health from behavioral, neuroimaging, biochemical and genetic analyses

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## **This supplementary material includes as follows:**

### **Part 1: Supplementary Methods**

Method S1. Blood biochemistry processing in the UK Biobank

Method S2. NMR biomarker processing in the UK Biobank

Method S3. Quality control for Structural and Diffusion MRI in the UK Biobank

### **Part 2: Supplementary Figures**

Fig. S1 Guideline of the study.

Fig. S2 The optimal number of food-liking subtypes.

Fig. S3 Sensitivity analyses for identifying food-liking subtypes.

Fig. S4 Distinctive blood and metabolic biomarker profiles across the four subtypes.

Fig. S5 Correlation analysis of polygenic risk scores (PRSs) of dietary patterns and brain MRI data.

Fig. S6 Correlation analysis of PRSs for dietary patterns and mental health symptoms.

### **Part 3: Supplementary Tables**

Table S1 The individual items of each food category

Table S2 Demographic characteristics of the respondents and non-respondents to the food-liking questionnaire

Table S3 Demographic characteristics of the four food-liking subtypes

Table S4 The items used for the assessment of mental health symptoms

Table S5 Summary information for cognitive function tests

Table S6 ANCOVA results (F-tests) of blood and metabolic biomarkers

Table S7 Post hoc analysis results (two-tailed t-tests) of blood and metabolic biomarkers

Table S8 ANCOVA results (F-tests) of gray matter volumes in brain regions (n=32,715)

Table S9 Post hoc analysis results (two-tailed t-tests) of gray matter volumes in brain regions

Table S10 ANCOVA results (F-tests) of mean FA in white matter tracts (n=31,195)

Table S11 Post hoc analysis results (two-tailed t-tests) of mean FA in white matter tracts

Table S12 ANCOVA results (F-tests) of mean MD in white matter tracts (n=31,195)

Table S13 Post hoc analysis results (two-tailed t-tests) of mean MD in white matter tracts

Table S14 The loadings of the latent variables in SEM models (Wald tests, two-sided P values)

## Methods

### Method S1. Blood biochemistry processing in the UK Biobank

Blood biochemistry data (Category 17518) was collected from approximately 480,000 participants during their recruitment visits between 2006 and 2010. Detailed procedures for quality control of blood biomarker can be found in the open-source document ([https://biobank.ndph.ox.ac.uk/showcase/ukb/docs/biomarker\\_issues.pdf](https://biobank.ndph.ox.ac.uk/showcase/ukb/docs/biomarker_issues.pdf)). This document describes the approach that UK Biobank has taken to minimise and mitigate the effects of error (both systematic bias and random error) in order to provide high-quality biomarker data. This includes sample collection and processing, sample retrieval, and monitoring of assay data in order to minimise drift, bias and measurement error. Below, we provide an overview of the essential quality control procedures:

**Sample collection and processing:** The samples were minimally processed at the assessment centres, with most of the processing conducted at the central laboratory using more efficient and reliable automated systems. The use of automation at the central laboratory ensured that all of the samples were processed quickly and allowed for a carefully controlled data trail linking each aliquot correctly to the participant from whom they derived.

**Assays performed immediately:** Standard haematological tests were performed on fresh whole blood within 24 hours of blood collection for all of the participants.

**Sample retrieval for the biochemistry assays:** In order to avoid biases in epidemiological comparisons, the UK Biobank developed algorithms designed to select aliquots that avoided clustering of samples by geography, collection dates or time of day. Simulations of the performance of this picking strategy demonstrated its effectiveness and efficiency for the different sample types and ensured that participant samples were analysed in an effectively random manner during the project (please see Appendix 3 of the serum biochemistry companion document for further details: <http://ace.cts.ox.ac.uk/showcase/refer.cgi?id=1227>). This enabled to better assess the variation caused by lab/assay drift (as the mean biomarker concentration across batches and analysers should effectively be the same).

**Internal and external quality control procedures:** Each assay was registered with an external quality assurance (EQA) scheme and assay performance was externally verified via the results returned from participation in these schemes. The UK Biobank also followed a rigorous internal quality control (QC) protocol to assess precision (using different concentrations of QC samples over multiple batches and analysers) and accuracy and bias (using EQA or other commercially validated material). They verified that the assays were linear over the observed reportable range (using commercial linearity standards and low concentration samples) and that there were no carryover effects (using low and high concentration samples analysed consecutively in a standardised sequence). The UK Biobank also assessed potential assay interferences on each sample that could cause falsely high or low results. Please refer to our online companion document on QC metrics for further details (<https://biobank.ndph.ox.ac.uk/showcase/refer.cgi?id=1227>).

**Identification of issues during internal quality control checks:** All of the participant and QC data generated were reviewed both during the project (to identify and address any issues in real time) and to allow retrospective adjustments to be made, where required. Further details can be observed in open-source document ([https://biobank.ndph.ox.ac.uk/showcase/ukb/docs/biomarker\\_issues.pdf](https://biobank.ndph.ox.ac.uk/showcase/ukb/docs/biomarker_issues.pdf)).

### Method S2. NMR biomarker processing in the UK Biobank

Metabolic biomarkers were measured using a high-throughput NMR-based metabolic biomarker profiling platform from randomly selected EDTA plasma samples collected during the first assessment, which included ~120,000 participants. Nightingale Health Plc. conducted the biomarker profiling for baseline plasma samples from all UK Biobank participants. Additional information on the processing of metabolic biomarkers can be found in a publication by Julkunen et al. <sup>1</sup> (Appendix 1). Below, we provide an overview of the essential quality control procedures:

**Plasma sample preparation:** EDTA plasma samples from aliquot 3 were prepared in 96-well plates by UK Biobank laboratory (Stockport, UK). The plasma samples were shipped Nightingale Health's laboratories in Finland.

**Quantified biomarkers:** The plasma samples were measured in six NMR spectrometers. The biomarkers were quantified using Nightingale Health's proprietary software (quantification library 2020). This simultaneously quantifies 249 metabolic measures per EDTA plasma sample, comprising 168 in absolute levels and 81 ratio measures.

**Quality control protocol:** Two internal control samples provided by Nightingale Health were included in each 96-well plate for tracking the consistency across multiple spectrometers during the project. Four sets of internal control samples with different biomarker concentration span were used across the 1,352 96-well plates measured. These were interleaved between the NMR instruments for extended periods of the project duration.

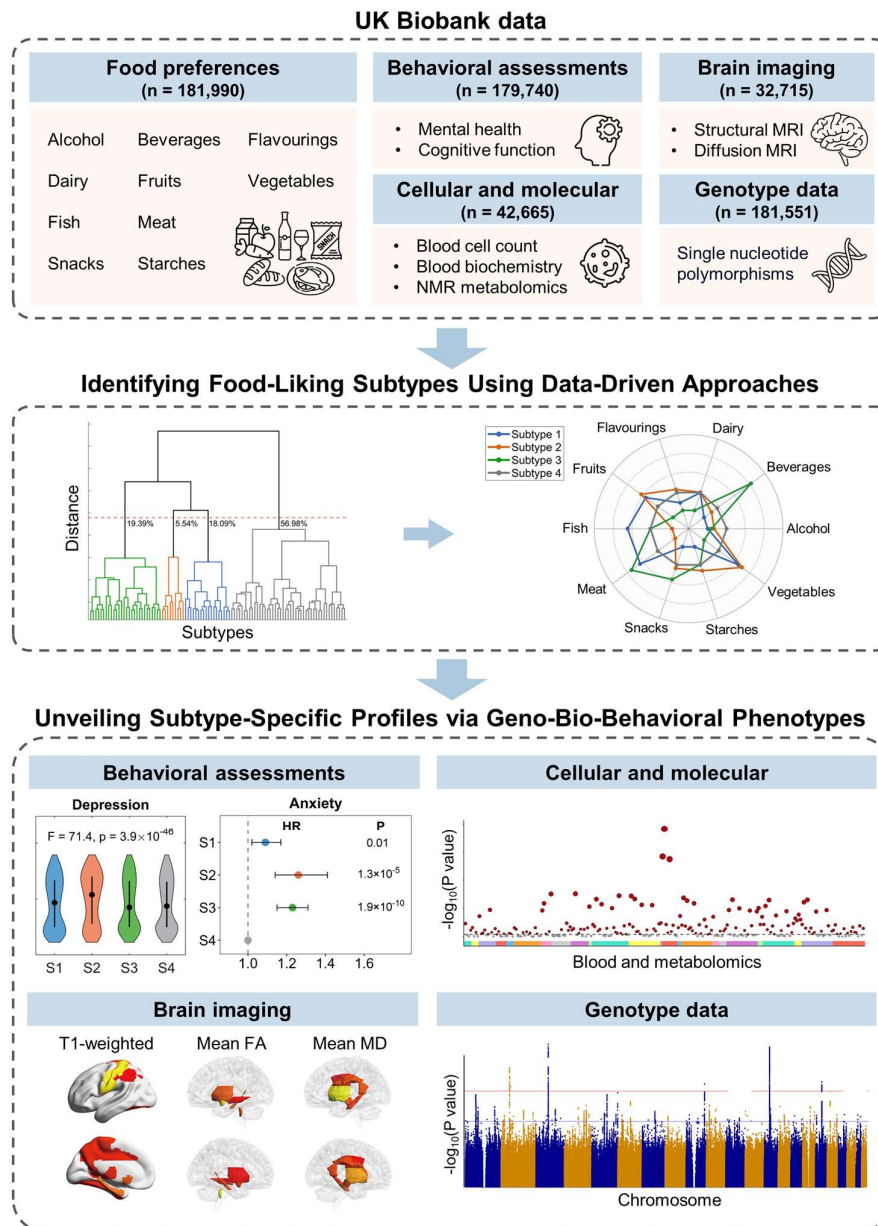
**Technical and biological repeatability** Two blind duplicate samples provided by UK Biobank were included on each 96-well plate. The position information of these blind duplicates was unlocked only after interim results delivery to UK Biobank.

The technical consistency of measurements over consecutive shipment batches and in different NMR spectrometers are illustrated for all the NMR biomarkers in the UK Biobank data resource (<https://biobank.ndph.ox.ac.uk/showcase/label.cgi?id=220>). This resource also shows the correlation for blinded duplicate samples for each biomarker, as well as the biological consistency in repeat-visit samples drawn from the same individuals four years apart.

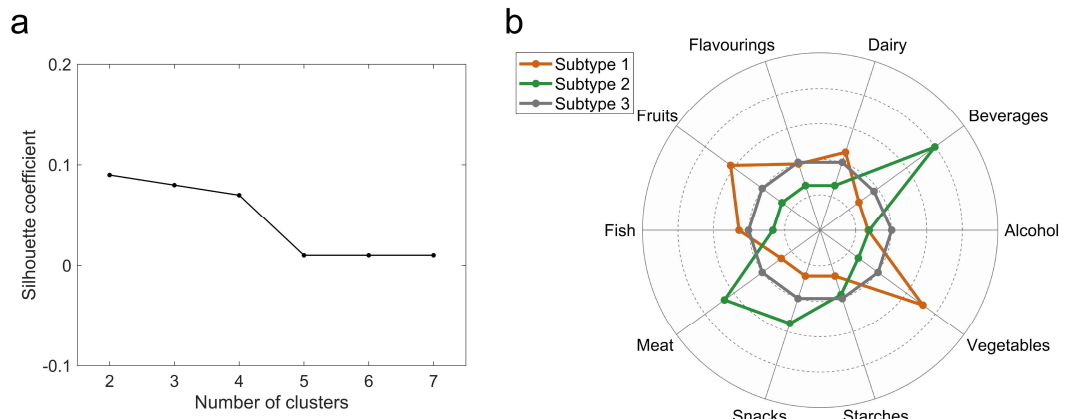
### **Method S3. Quality control for Structural and Diffusion MRI in the UK Biobank**

At the acquisition stage, a set of manual classification categories, specific to each modality, were assigned to every image. These manual categories are described in a publication by Alfaro-Almagro et al. <sup>2</sup>. Following manual quality checks across all modalities, approximately 6% of the final dataset was considered unusable. Subsequently, a basic Quality Control tool was employed to check to verify the correct dimensions of raw data in each modality. Any raw data with incorrect dimensions, corruption, missing components, or deemed unusable for other reasons were excluded from further analysis. Notably, the assessment of structural T1 data includes a semi-automated QC review, which was a trained automated classifier scores all datasets. T1 data that approached the threshold for 'bad data' underwent a thorough manual review. Finally, all datasets flagged for making unusable have a final quick (not comprehensive) manual review. Additional information on the quality control procedures can be found in Alfaro-Almagro et al. (2018) <sup>2</sup>.

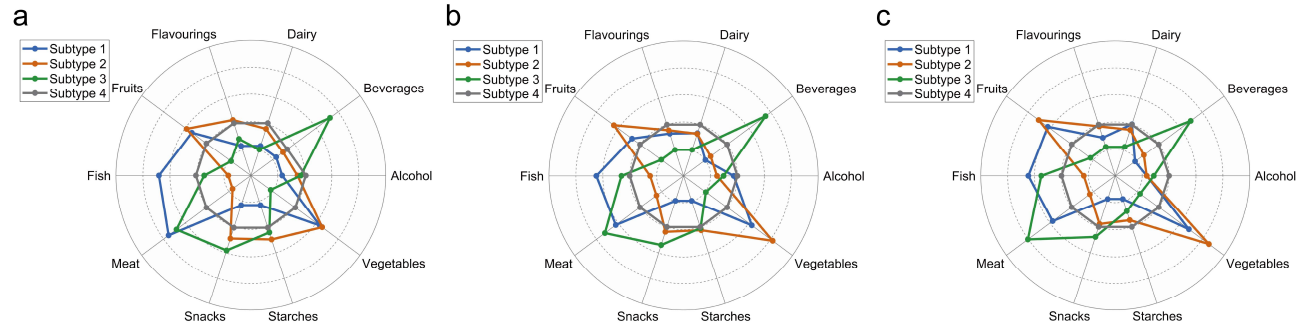
## Figures



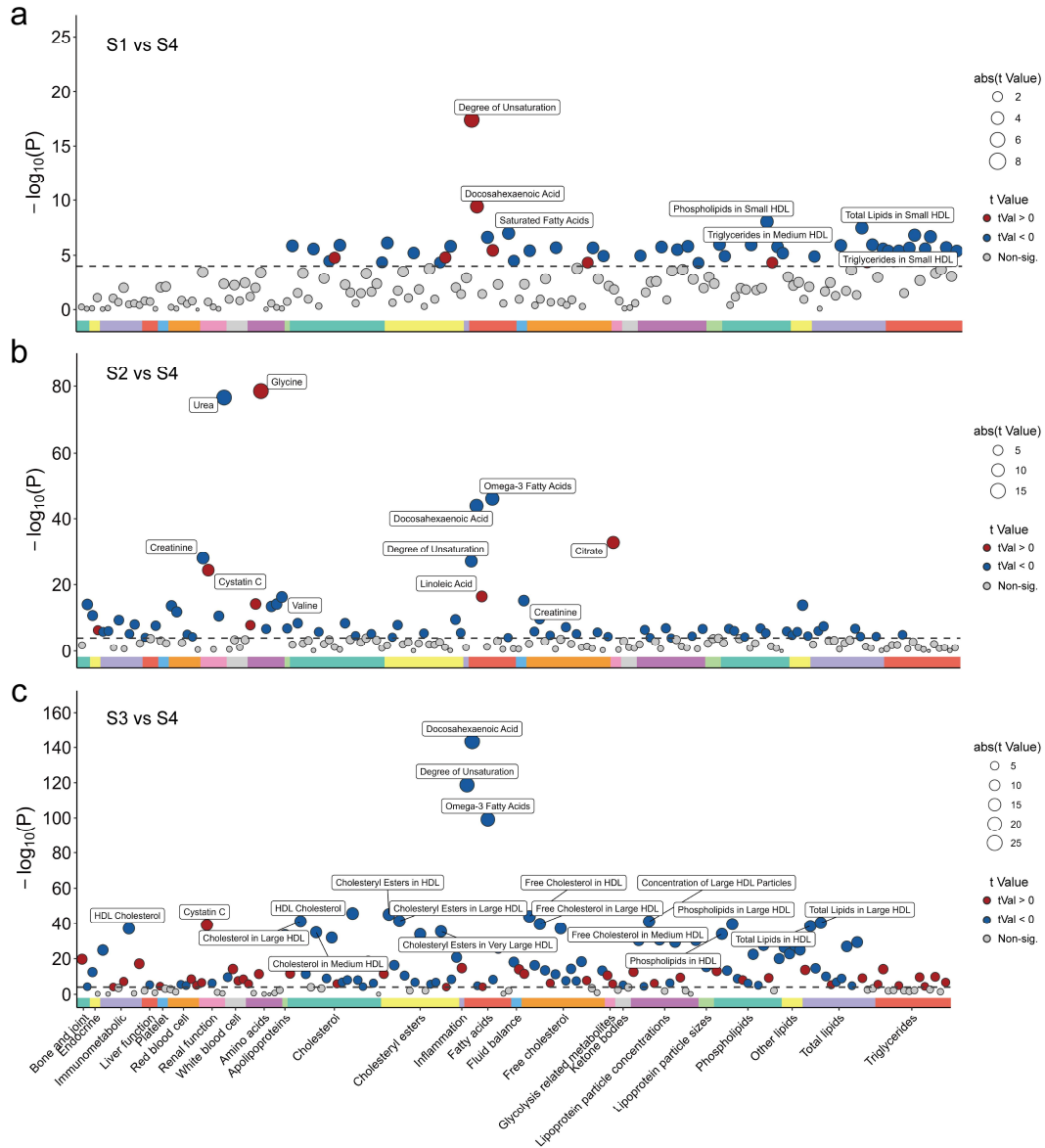
**Fig. S1 | Guideline of the study.** The **top** panel displays the comprehensive UK Biobank datasets used in the study, encompassing food preferences, mental health, cognitive function, blood and metabolic biomarkers, brain imaging, and genomics. The **middle** panel shows that four distinct food-liking subtypes were identified using data-driven approaches (Subtype 1, characterized by a “Starch-free or reduced-starch dietary pattern”; Subtype 2, characterized by a “Vegetarian dietary pattern”; Subtype 3, characterized by a “High protein and low fibre dietary pattern”; Subtype 4, characterized by a “Balanced dietary pattern”). The **bottom** panel presents the significant variations among the four subtypes in terms of mental health, cognitive function, blood and metabolic biomarkers, as well as brain imaging. Additionally, the case-control GWAS analysis identified genetic distinctions between the subtypes.



**Fig. S2 | The optimal number of food-liking subtypes.** Panel **a** shows the silhouette coefficients for cluster numbers ranging from two to seven, with the optimal choices being no more than four subtypes. Panel **b** displays a radar chart depicting three food-liking subtypes: one subtype combines two of the four subtypes in Fig. 1b, while the other two subtypes closely resemble two of the four subtypes in Fig. 1b.

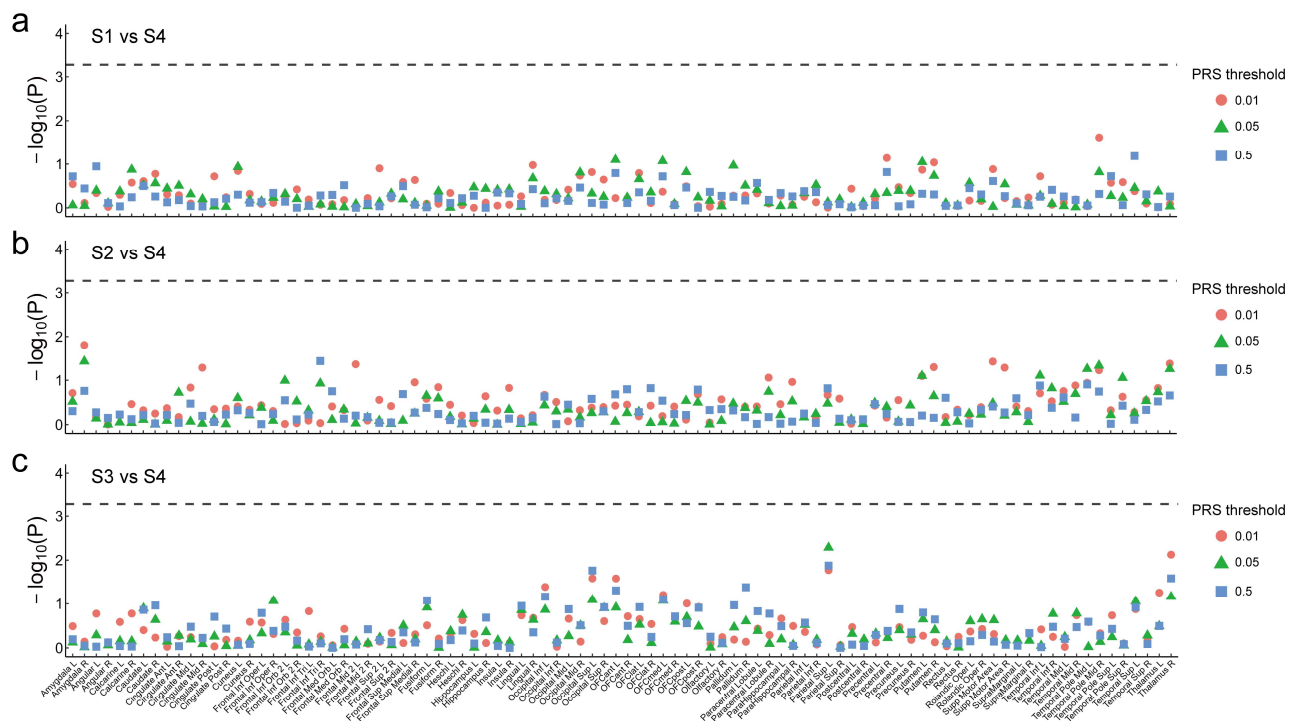


**Fig. S3 | Sensitivity analyses for identifying food-liking subtypes.** Panel **a** shows radar charts of food-liking profiles for four subtypes using non-imputed data from 72,419 participants. Panels **b** and **c** show radar charts for the same four subtypes, utilizing PCA results with explained variance ratios set at 70% and 90% from the imputed dataset of 181,990 participants. These charts closely resemble the subtypes identified from imputed data of 181,990 participants with an 80% PCA explained variance ratio, demonstrating the robustness of our findings with data imputation and validating the reliability of hierarchical clustering results based on PCA components.

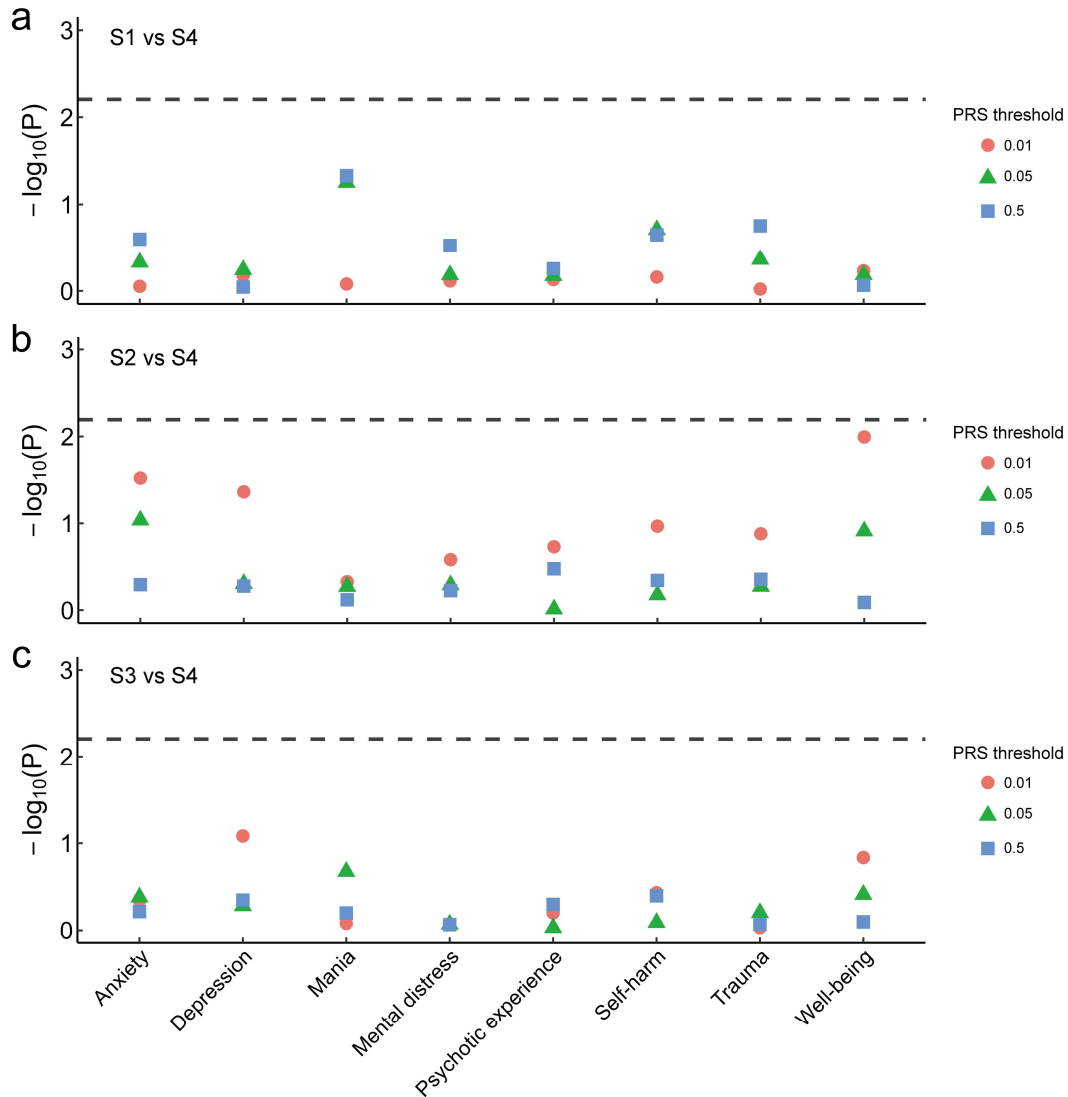


**Fig. S4 | Distinctive blood and metabolic biomarker profiles across the four subtypes.** Panel a, b, and c display Manhattan plots illustrating the results of post hoc tests (two-tailed t-tests) comparing Subtype 1 ("Starch-free or reduced-starch dietary pattern"), Subtype 2 ("Vegetarian dietary pattern"), and Subtype 3 ("High protein and low fibre dietary pattern") against Subtype 4 ("Balanced dietary pattern"), based on the analysis of 167 biomarkers from 24 categories of blood and metabolic biomarkers exhibiting significant differences in the ANCOVAs, as depicted in Fig. 3a. The height of each point represents the negative logarithm of the P value of the t-tests, with the colour bar indicating the different biomarker categories. The black dashed line indicates the Bonferroni threshold for multiple comparisons ( $\alpha = 0.05$ ), and text annotations mark the top 15% of biomarkers exhibiting significant differences after Bonferroni correction ( $P < 0.05/(167 \times 3)$ ). The analysis was adjusted for covariates including age, BMI, education qualifications, and Townsend deprivation index.





**Fig. S5 | Correlation analysis of polygenic risk scores (PRSs) of dietary patterns and brain MRI data.** Panel **a** displays a Manhattan plot illustrating the correlation relationship ( $r$  values) between gray matter volumes of the 94 brain regions in AAL2 atlas and PRSs of the dietary pattern for the comparison between S1 and S4 (calculated at P-value thresholds of 0.01, 0.05, and 0.5). The height of each data point represents the negative logarithm of the P value for the two-tailed test obtained from correlation analyses. The black dashed line denotes the Bonferroni threshold for multiple comparisons ( $\alpha = 0.05$ ). Panels **b** and **c** depict the correlation relationship ( $r$  values) between gray matter volumes and PRSs of the dietary pattern for the comparisons between S2 and S4, as well as S3 and S4, respectively. All three panels (**a**, **b**, and **c**) indicate the absence of significant correlations between brain MRI data and PRSs.



**Fig. S6 | Correlation analysis of PRSs for dietary patterns and mental health symptoms.** Panel **a** displays a Manhattan plot visualizing the correlation relationship ( $r$  values) between eight mental health symptoms and PRSs of the dietary pattern for the comparison between S1 and S4 (calculated at P-value thresholds of 0.01, 0.05, and 0.5). The height of each data point reflects the negative logarithm of the P value for the two-tailed test obtained from correlation analyses. The black dashed line represents the Bonferroni threshold for multiple comparisons ( $\alpha = 0.05$ ). Panels **b** and **c** show the correlation relationship between the eight mental health symptoms and PRSs for dietary patterns for the comparisons of S2 vs S4 and S3 vs S4, respectively. All three panels (**a**, **b**, and **c**) indicate no significant correlations between the eight mental health symptoms and PRSs.

## Tables

Table S1 The individual items of each food category

| Food category | Food items                                                                                                                                                                                                                                                                                                                                      |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alcohol       | bitter/ale, lager, red wine, spirits, whisky, white wine                                                                                                                                                                                                                                                                                        |
| Dairy         | blue cheese, butter on bread, cream, dairy products, eggs, goat's cheese, hard cheese, plain yogurt, skimmed milk, soft cheese, soya milk, whole milk                                                                                                                                                                                           |
| Beverages     | apple juice, coffee with sugar, coffee without sugar, diet fizzy drinks, orange juice, regular (non-diet) fizzy drinks, sweet coffee house drinks, tea with sugar, tea without sugar                                                                                                                                                            |
| Flavourings   | adding salt to foods, aniseed, bitter foods, black pepper, bolognese sauce, burn of spicy foods, coriander, curry, extra virgin olive oil, fatty foods, garlic, honey, horseradish/wasabi, jam, mayonnaise, salad dressing, salty foods, soy sauce, spicy foods, sweet foods, tomato ketchup, vinegar                                           |
| Fruits        | apples, bananas, cherries, dried fruit, fruit, grapefruit, kiwi fruit, lemons, melon, oranges, pears, plums, strawberries                                                                                                                                                                                                                       |
| Fish          | baked/steamed fish, cod, fried/battered fish, haddock, herring, mackerel, pollock, prawns, salmon, sardines, shellfish (other than prawns), smoked fish, tinned tuna                                                                                                                                                                            |
| Meat          | bacon, barbequed or grilled meat, beef steak, burgers (meat), ham, lamb, liver, pork chop, red meat, salami, sausages (meat), chicken, fried chicken, roast chicken                                                                                                                                                                             |
| Snacks        | biscuits, cake, cheesecake, cake icing, cereal/granola bar, chips/french fries, dark chocolate, ice cream, marzipan, milk chocolate, potato crisps, salty pretzels, savoury biscuits                                                                                                                                                            |
| Starches      | brown rice, corn flakes, croissant, pasta, pizza, porridge, potatoes, white bread, white rice, whole grain breakfast cereal, wholemeal bread                                                                                                                                                                                                    |
| Vegetables    | asparagus, aubergine, avocados, beetroot, bell pepper, black olives, broad beans, broccoli, brussel sprouts, butternut squash, cabbage, capers, cauliflower, chilli pepper, cucumber, fresh tomatoes, gherkins, globe artichoke, green olives, lentils/beans, mushrooms, onions, raw carrots, salad leaves, spinach, turnip (white), vegetables |

Table S2 Demographic characteristics of the respondents and non-respondents to the food-liking questionnaire

| Characteristics                    | With food questionnaire |                     | Without food questionnaire |                     |         |                         |
|------------------------------------|-------------------------|---------------------|----------------------------|---------------------|---------|-------------------------|
|                                    | Mean (SD)               | No. of participants | Mean (SD)                  | No. of participants | t Value | p Value                 |
| Age, years                         | 70.7 (7.7)              | 181,990             | 56.9 (8.3)                 | 320,495             | 579.9   | $< 1.0 \times 10^{-15}$ |
| Female                             | —                       | 103,876 (57.1%)     | —                          | 169,526 (52.9%)     | —       | —                       |
| BMI, kg/m <sup>2</sup>             | 26.8 (4.6)              | 181,551             | 27.8 (4.9)                 | 317,881             | -76.2   | $< 1.0 \times 10^{-15}$ |
| Townsend deprivation index, points | -1.7 (2.8)              | 181,770             | -1.1 (3.2)                 | 320,144             | -72.5   | $< 1.0 \times 10^{-15}$ |
| Education qualifications           | 2.6 (1.9)               | 181,990             | 3.8 (2.3)                  | 320,547             | -186.4  | $< 1.0 \times 10^{-15}$ |

Table S3 Demographic characteristics of the four food-liking subtypes

| Characteristics                                                  | No. (%)                 |                         |                         |                          |
|------------------------------------------------------------------|-------------------------|-------------------------|-------------------------|--------------------------|
|                                                                  | Subtype 1<br>(n=32,927) | Subtype 2<br>(n=10,087) | Subtype 3<br>(n=35,280) | Subtype 4<br>(n=103,696) |
| Age, mean (SD), years                                            | 71.5 (7.4)              | 68.1 (7.6)              | 70.8 (7.9)              | 70.6 (7.6)               |
| Female                                                           | 23556 (71.54%)          | 7328 (72.65%)           | 16937 (48.01%)          | 56055 (54.06%)           |
| BMI, mean (SD), kg/m <sup>2</sup>                                | 26.0 (4.4)              | 25.1 (4.3)              | 27.6 (4.9)              | 26.9 (4.4)               |
| Townsend deprivation index, mean (SD), points                    | -1.7 (2.8)              | -1.1 (3.0)              | -1.6 (2.9)              | -1.8 (2.8)               |
| Education Qualifications                                         |                         |                         |                         |                          |
| <i>College or University degree</i>                              | 16525 (50.19%)          | 5906 (58.55%)           | 12056 (34.17%)          | 46904 (45.23%)           |
| <i>A levels/AS levels or equivalent</i>                          | 4406 (13.38%)           | 1287 (12.76%)           | 4757 (13.48%)           | 13919 (13.42%)           |
| <i>O levels/GCSEs or equivalent</i>                              | 5829 (17.70%)           | 1469 (14.56%)           | 8227 (23.32%)           | 20638 (19.90%)           |
| <i>CSEs or equivalent</i>                                        | 921 (2.80%)             | 248 (2.46%)             | 1865 (5.29%)            | 3996 (3.85%)             |
| <i>NVQ or HND or HNC or equivalent</i>                           | 1288 (3.91%)            | 270 (2.68%)             | 2318 (6.57%)            | 5389 (5.20%)             |
| <i>Other professional qualifications e.g.: nursing, teaching</i> | 1792 (5.44%)            | 455 (4.51%)             | 1773 (5.03%)            | 5082 (4.90%)             |
| <i>None of the above</i>                                         | 2166 (6.58%)            | 452 (4.48%)             | 4284 (12.14%)           | 7768 (7.49%)             |

Table S4 The items used for the assessment of mental health symptoms

|                             |                                                                |
|-----------------------------|----------------------------------------------------------------|
| <b>Anxiety</b>              | <b>Sample size: 118,616</b>                                    |
| <b>Field ID</b>             | <b>Description</b>                                             |
| 20506                       | Feeling nervous, anxious or on edge                            |
| 20509                       | Not being able to stop or control worrying                     |
| 20520                       | Worrying too much about different things                       |
| 20515                       | Trouble relaxing                                               |
| 20516                       | Being so restless that it is hard to sit still                 |
| 20505                       | Becoming easily annoyed or irritable                           |
| 20512                       | Feeling afraid as if something awful might happen              |
| <b>Depression</b>           | <b>Sample size: 118,616</b>                                    |
| <b>Field ID</b>             | <b>Description</b>                                             |
| 20514                       | Little interest or pleasure in doing things                    |
| 20510                       | Feeling down, depressed, or hopeless                           |
| 20517                       | Trouble falling or staying asleep, or sleeping too much        |
| 20519                       | Feeling tired or having little energy                          |
| 20511                       | Poor appetite or overeating                                    |
| 20507                       | Feeling of inadequacy                                          |
| 20508                       | Trouble concentrating on things                                |
| 20518                       | Changes in speed/amount of moving or speaking                  |
| 20513                       | Thoughts of suicide or self-harm                               |
| 20446                       | Ever had prolonged feelings of sadness or depression           |
| 20441                       | Ever had prolonged loss of interest in normal activities       |
| 20532                       | Did your sleep change?                                         |
| 20435                       | Difficulty concentrating during worst depression               |
| 20438                       | Duration of worst depression                                   |
| 20449                       | Feelings of tiredness during worst episode of depression       |
| 20450                       | Feelings of worthlessness during worst period of depression    |
| 20436                       | Fraction of day affected during worst episode of depression    |
| 20439                       | Frequency of depressed days during worst episode of depression |
| 20440                       | Impact on normal roles during worst period of depression       |
| 20437                       | Thoughts of death during worst depression                      |
| 20536                       | Weight change during worst episode of depression               |
| <b>Mania</b>                | <b>Sample size: 118,616</b>                                    |
| <b>Field ID</b>             | <b>Description</b>                                             |
| 20501                       | Ever had period of mania / excitability                        |
| 20502                       | Ever had period extreme irritability                           |
| 20548                       | Manifestations of mania or irritability                        |
| 20492                       | Longest period of mania or irritability                        |
| 20493                       | Severity of problems due to mania or irritability              |
| <b>Mental distress</b>      | <b>Sample size: 118,616</b>                                    |
| <b>Field ID</b>             | <b>Description</b>                                             |
| 20499                       | Ever sought or received professional help for mental distress  |
| 20500                       | Ever suffered mental distress preventing usual activities      |
| 20544                       | Mental health problems ever diagnosed by a professional        |
| <b>Psychotic experience</b> | <b>Sample size: 118,616</b>                                    |

| <b>Field ID</b>   | <b>Description</b>                                                                      |
|-------------------|-----------------------------------------------------------------------------------------|
| 20471             | Ever seen an un-real vision                                                             |
| 20463             | Ever heard an un-real voice                                                             |
| 20474             | Ever believed in un-real communications or signs                                        |
| 20468             | Ever believed in an un-real conspiracy against self                                     |
| 20467             | Frequency of unusual or psychotic experiences in past year                              |
| 20462             | Distress caused by unusual or psychotic experiences                                     |
| <b>Self-harm</b>  | <b>Sample size: 118,616</b>                                                             |
| <b>Field ID</b>   | <b>Description</b>                                                                      |
| 20479             | Ever thought that life not worth living                                                 |
| 20485             | Ever contemplated self-harm                                                             |
| 20480             | Ever self-harmed                                                                        |
| 20482             | Number of times self-harmed                                                             |
| 20553             | Methods of self-harm used                                                               |
| 20483             | Ever attempted suicide                                                                  |
| <b>Trauma</b>     | <b>Sample size: 118,616</b>                                                             |
| <b>Field ID</b>   | <b>Description</b>                                                                      |
| 20489             | Felt loved as a child                                                                   |
| 20488             | Physically abused by family as a child                                                  |
| 20487             | Felt hated by family member as a child                                                  |
| 20490             | Sexually molested as a child                                                            |
| 20491             | Someone to take to doctor when needed as a child                                        |
| 20522             | Been in a confiding relationship as an adult                                            |
| 20523             | Physical violence by partner or ex-partner as an adult                                  |
| 20521             | Belittlement by partner or ex-partner as an adult                                       |
| 20524             | Sexual interference by partner or ex-partner without consent as an adult                |
| 20525             | Able to pay rent/mortgage as an adult                                                   |
| 20531             | Victim of sexual assault                                                                |
| 20529             | Victim of physically violent crime                                                      |
| 20526             | Been in serious accident believed to be life-threatening                                |
| 20530             | Witnessed sudden violent death                                                          |
| 20528             | Diagnosed with life-threatening illness                                                 |
| 20527             | Been involved in combat or exposed to war-zone                                          |
| 20497             | Repeated disturbing thoughts of stressful experience in past month                      |
| 20498             | Felt very upset when reminded of stressful experience in past month                     |
| 20495             | Avoided activities or situations because of previous stressful experience in past month |
| 20496             | Felt distant from other people in past month                                            |
| 20494             | Felt irritable or had angry outbursts in past month                                     |
| <b>Well-being</b> | <b>Sample size: 118,616</b>                                                             |
| <b>Field ID</b>   | <b>Description</b>                                                                      |
| 20458             | In general, how happy you are?                                                          |
| 20459             | In general, how happy you are with your health?                                         |
| 20460             | To what extent do you feel your life to be meaningful?                                  |

Table S5 Summary information for cognitive function tests

| <b>Cognitive function</b> | <b>Field ID</b> | <b>Description</b>                            | <b>Sample size</b> |
|---------------------------|-----------------|-----------------------------------------------|--------------------|
| Fluid intelligence        | 20191           | Fluid intelligence score                      | 96,742             |
| Numeric memory            | 20240           | Maximum digits remembered correctly           | 88,192             |
| Pairs matching            | 20131           | Number of correct matches in round            | 93,394             |
| Symbol-digit substitution | 20159           | Number of symbol digit matches made correctly | 93,325             |
| Trail making              | 20156           | Duration to complete numeric path (trail #1)  | 82,375             |
| Reaction time             | 20023           | Mean time to correctly identify matches       | 179,740            |



Table S6 ANCOVA results (F-tests) of blood and metabolic biomarkers

| Field ID | Description                                     | Category         | S1     | S2     | S3     | S4     | F value | P value  | Sample size |
|----------|-------------------------------------------------|------------------|--------|--------|--------|--------|---------|----------|-------------|
| 30610    | Alkaline phosphatase                            | Bone and joint   | 23.36  | 24.73  | 26.36  | 23.53  | 32.13   | 9.88E-21 | 39926       |
| 30890    | Vitamin D                                       | Bone and joint   | 52.33  | 48.86  | 51.30  | 52.39  | 23.70   | 2.55E-15 | 38302       |
| 30770    | IGF-1                                           | Endocrine        | 38.08  | 37.31  | 37.59  | 38.10  | 30.02   | 2.25E-19 | 39716       |
| 30830    | SHBG                                            | Endocrine        | 111.69 | 113.92 | 110.89 | 111.11 | 9.75    | 1.99E-06 | 36101       |
| 30760    | HDL cholesterol                                 | Immunometabolic  | 2.05   | 2.02   | 1.99   | 2.05   | 62.12   | 4.70E-40 | 36443       |
| 30630    | Apolipoprotein A                                | Immunometabolic  | 1.73   | 1.71   | 1.70   | 1.73   | 41.80   | 5.91E-27 | 36245       |
| 30870    | Triglycerides                                   | Immunometabolic  | -0.72  | -0.66  | -0.61  | -0.71  | 30.69   | 8.29E-20 | 39890       |
| 30690    | Cholesterol                                     | Immunometabolic  | 4.76   | 4.63   | 4.72   | 4.78   | 15.33   | 5.74E-10 | 39915       |
| 30780    | LDL direct                                      | Immunometabolic  | 2.64   | 2.54   | 2.64   | 2.65   | 10.93   | 3.58E-07 | 39848       |
| 30750    | Glycated haemoglobin (HbA1c)                    | Immunometabolic  | 18.39  | 18.36  | 18.60  | 18.22  | 10.65   | 5.41E-07 | 39640       |
| 30710    | C-reactive protein                              | Immunometabolic  | -5.08  | -5.13  | -4.80  | -4.99  | 9.23    | 4.22E-06 | 39831       |
| 30640    | Apolipoprotein B                                | Immunometabolic  | 0.68   | 0.65   | 0.68   | 0.68   | 8.09    | 2.19E-05 | 39744       |
| 30600    | Albumin                                         | Liver function   | 50.20  | 49.93  | 50.00  | 50.16  | 13.04   | 1.64E-08 | 36462       |
| 30730    | Gamma glutamyltransferase                       | Liver function   | -15.92 | -20.04 | -15.33 | -16.01 | 11.55   | 1.44E-07 | 39901       |
| 30620    | Alanine aminotransferase                        | Liver function   | 3.10   | 1.78   | 3.30   | 2.87   | 9.35    | 3.54E-06 | 39909       |
| 30080    | Platelet count                                  | Platelet         | 266.81 | 272.85 | 271.74 | 268.70 | 13.89   | 4.73E-09 | 40748       |
| 30090    | Platelet crit                                   | Platelet         | 0.25   | 0.26   | 0.25   | 0.25   | 10.55   | 6.27E-07 | 40747       |
| 30030    | Haematocrit percentage                          | Red blood cell   | 36.01  | 35.53  | 36.11  | 35.99  | 25.71   | 1.32E-16 | 40748       |
| 30010    | Red blood cell (erythrocyte) count              | Red blood cell   | 4.00   | 3.97   | 4.02   | 4.00   | 19.99   | 6.10E-13 | 40748       |
| 30020    | Haemoglobin concentration                       | Red blood cell   | 12.41  | 12.27  | 12.44  | 12.41  | 19.99   | 6.13E-13 | 40747       |
| 30040    | Mean corpuscular volume                         | Red blood cell   | 90.29  | 89.93  | 90.10  | 90.34  | 11.18   | 2.50E-07 | 40747       |
| 30050    | Mean corpuscular haemoglobin                    | Red blood cell   | 31.12  | 31.04  | 31.04  | 31.15  | 8.78    | 8.15E-06 | 40747       |
| 30070    | Red blood cell (erythrocyte) distribution width | Red blood cell   | 12.89  | 12.91  | 12.94  | 12.89  | 7.00    | 1.06E-04 | 40747       |
| 30670    | Urea                                            | Renal function   | 1.82   | 1.36   | 1.84   | 1.86   | 114.78  | 5.19E-74 | 39903       |
| 30720    | Cystatin C                                      | Renal function   | 0.25   | 0.28   | 0.28   | 0.26   | 91.78   | 3.46E-59 | 39915       |
| 30700    | Creatinine                                      | Renal function   | 52.24  | 49.61  | 53.75  | 52.86  | 65.56   | 2.78E-42 | 39907       |
| 30880    | Urate                                           | Renal function   | 67.24  | 58.43  | 65.96  | 67.40  | 15.38   | 5.33E-10 | 39873       |
| 30810    | Phosphate                                       | Renal function   | 1.21   | 1.21   | 1.20   | 1.21   | 8.72    | 8.86E-06 | 36380       |
| 30140    | Neutrophil count                                | White blood cell | 3.13   | 3.08   | 3.31   | 3.18   | 34.19   | 4.62E-22 | 40668       |
| 30000    | White blood cell (leukocyte) count              | White blood cell | 4.80   | 4.72   | 5.01   | 4.87   | 24.68   | 6.03E-16 | 40747       |
| 30180    | Lymphocyte percentage                           | White blood cell | 29.20  | 29.21  | 28.44  | 29.05  | 17.61   | 2.01E-11 | 40669       |

|       |                                                                                   |                  |       |       |       |       |        |          |       |
|-------|-----------------------------------------------------------------------------------|------------------|-------|-------|-------|-------|--------|----------|-------|
| 30200 | Neutrophill percentage                                                            | White blood cell | 62.31 | 62.14 | 63.08 | 62.47 | 14.88  | 1.11E-09 | 40669 |
| 23462 | Glycine                                                                           | Amino acids      | 0.27  | 0.29  | 0.27  | 0.27  | 122.07 | 9.96E-79 | 42622 |
| 23467 | Valine                                                                            | Amino acids      | 0.12  | 0.11  | 0.12  | 0.12  | 24.55  | 7.25E-16 | 42656 |
| 23461 | Glutamine                                                                         | Amino acids      | 0.56  | 0.57  | 0.55  | 0.55  | 20.84  | 1.73E-13 | 42556 |
| 23464 | Total Concentration of Branched-Chain Amino Acids (Leucine + Isoleucine + Valine) | Amino acids      | 0.21  | 0.20  | 0.21  | 0.21  | 19.90  | 7.00E-13 | 42656 |
| 23466 | Leucine                                                                           | Amino acids      | 0.06  | 0.06  | 0.06  | 0.06  | 19.08  | 2.33E-12 | 42664 |
| 23460 | Alanine                                                                           | Amino acids      | 0.24  | 0.25  | 0.24  | 0.24  | 15.93  | 2.40E-10 | 42664 |
| 23465 | Isoleucine                                                                        | Amino acids      | 0.03  | 0.02  | 0.03  | 0.03  | 9.53   | 2.74E-06 | 42664 |
| 23440 | Apolipoprotein A1                                                                 | Apolipoproteins  | 1.61  | 1.59  | 1.58  | 1.62  | 53.31  | 2.19E-34 | 42665 |
| 23561 | Cholesterol in Large HDL                                                          | Cholesterol      | 0.66  | 0.65  | 0.63  | 0.66  | 75.53  | 1.01E-48 | 42665 |
| 23406 | HDL Cholesterol                                                                   | Cholesterol      | 1.83  | 1.80  | 1.78  | 1.82  | 75.42  | 1.20E-48 | 42665 |
| 23554 | Cholesterol in Very Large HDL                                                     | Cholesterol      | 0.16  | 0.15  | 0.15  | 0.16  | 63.34  | 7.44E-41 | 42665 |
| 23568 | Cholesterol in Medium HDL                                                         | Cholesterol      | 0.62  | 0.61  | 0.60  | 0.62  | 55.73  | 6.02E-36 | 42665 |
| 23484 | Cholesterol in Chylomicrons and Extremely Large VLDL                              | Cholesterol      | -0.04 | -0.04 | -0.03 | -0.04 | 33.60  | 1.12E-21 | 42665 |
| 23526 | Cholesterol in IDL                                                                | Cholesterol      | 0.80  | 0.78  | 0.78  | 0.80  | 31.27  | 3.52E-20 | 42665 |
| 23400 | Total Cholesterol                                                                 | Cholesterol      | 4.25  | 4.19  | 4.18  | 4.28  | 30.59  | 9.54E-20 | 42665 |
| 23491 | Cholesterol in Very Large VLDL                                                    | Cholesterol      | -0.01 | -0.01 | -0.01 | -0.01 | 21.04  | 1.29E-13 | 42665 |
| 23519 | Cholesterol in Very Small VLDL                                                    | Cholesterol      | 0.14  | 0.14  | 0.14  | 0.14  | 18.36  | 6.73E-12 | 42665 |
| 23533 | Cholesterol in Large LDL                                                          | Cholesterol      | 0.98  | 0.96  | 0.96  | 0.98  | 18.08  | 1.02E-11 | 42665 |
| 23575 | Cholesterol in Small HDL                                                          | Cholesterol      | 0.39  | 0.39  | 0.39  | 0.39  | 16.67  | 8.01E-11 | 42665 |
| 23498 | Cholesterol in Large VLDL                                                         | Cholesterol      | -0.02 | -0.01 | -0.01 | -0.01 | 16.37  | 1.26E-10 | 42665 |
| 23404 | Clinical LDL Cholesterol                                                          | Cholesterol      | 2.06  | 2.03  | 2.03  | 2.08  | 13.72  | 6.15E-09 | 42665 |
| 23405 | LDL Cholesterol                                                                   | Cholesterol      | 1.37  | 1.36  | 1.35  | 1.39  | 12.73  | 2.62E-08 | 42665 |
| 23401 | Total Cholesterol Minus HDL-C                                                     | Cholesterol      | 2.42  | 2.39  | 2.40  | 2.45  | 11.59  | 1.37E-07 | 42665 |
| 23402 | Remnant Cholesterol (Non-HDL, Non-LDL -Cholesterol)                               | Cholesterol      | 1.05  | 1.03  | 1.05  | 1.07  | 10.74  | 4.71E-07 | 42665 |
| 23540 | Cholesterol in Medium LDL                                                         | Cholesterol      | 0.27  | 0.27  | 0.27  | 0.27  | 7.23   | 7.54E-05 | 42665 |
| 23403 | VLDL Cholesterol                                                                  | Cholesterol      | 0.25  | 0.25  | 0.26  | 0.26  | 6.54   | 2.04E-04 | 42665 |

|       |                                                             |                    |       |       |       |       |        |           |       |
|-------|-------------------------------------------------------------|--------------------|-------|-------|-------|-------|--------|-----------|-------|
| 23562 | Cholesteryl Esters in Large HDL                             | Cholesteryl esters | 0.52  | 0.51  | 0.50  | 0.52  | 76.13  | 4.15E-49  | 42665 |
| 23418 | Cholesteryl Esters in HDL                                   | Cholesteryl esters | 1.45  | 1.43  | 1.41  | 1.45  | 74.53  | 4.51E-48  | 42665 |
| 23555 | Cholesteryl Esters in Very Large HDL                        | Cholesteryl esters | 0.12  | 0.12  | 0.11  | 0.12  | 69.24  | 1.16E-44  | 42665 |
| 23569 | Cholesteryl Esters in Medium HDL                            | Cholesteryl esters | 0.51  | 0.51  | 0.50  | 0.51  | 53.97  | 8.26E-35  | 42665 |
| 23415 | Total Esterified Cholesterol                                | Cholesteryl esters | 3.18  | 3.13  | 3.12  | 3.19  | 34.08  | 5.48E-22  | 42665 |
| 23485 | Cholesteryl Esters in Chylomicrons and Extremely Large VLDL | Cholesteryl esters | -0.02 | -0.02 | -0.02 | -0.02 | 33.62  | 1.08E-21  | 42665 |
| 23527 | Cholesteryl Esters in IDL                                   | Cholesteryl esters | 0.59  | 0.58  | 0.58  | 0.60  | 30.30  | 1.48E-19  | 42665 |
| 23520 | Cholesteryl Esters in Very Small VLDL                       | Cholesteryl esters | 0.11  | 0.10  | 0.10  | 0.11  | 21.60  | 5.68E-14  | 42665 |
| 23492 | Cholesteryl Esters in Very Large VLDL                       | Cholesteryl esters | 0.00  | 0.00  | 0.00  | 0.00  | 17.05  | 4.59E-11  | 42665 |
| 23534 | Cholesteryl Esters in Large LDL                             | Cholesteryl esters | 0.69  | 0.68  | 0.68  | 0.69  | 16.21  | 1.58E-10  | 42665 |
| 23576 | Cholesteryl Esters in Small HDL                             | Cholesteryl esters | 0.30  | 0.30  | 0.30  | 0.30  | 13.11  | 1.48E-08  | 42665 |
| 23499 | Cholesteryl Esters in Large VLDL                            | Cholesteryl esters | 0.00  | 0.00  | 0.00  | 0.00  | 11.74  | 1.09E-07  | 42665 |
| 23417 | Cholesteryl Esters in LDL                                   | Cholesteryl esters | 0.94  | 0.93  | 0.93  | 0.95  | 10.83  | 4.15E-07  | 42665 |
| 23506 | Cholesteryl Esters in Medium VLDL                           | Cholesteryl esters | 0.08  | 0.08  | 0.08  | 0.08  | 8.64   | 1.00E-05  | 42665 |
| 23541 | Cholesteryl Esters in Medium LDL                            | Cholesteryl esters | 0.17  | 0.17  | 0.17  | 0.17  | 6.89   | 1.23E-04  | 42665 |
| 23450 | Docosahexaenoic Acid                                        | Fatty acids        | 0.16  | 0.13  | 0.13  | 0.16  | 312.46 | 1.09E-200 | 42634 |
| 23443 | Degree of Unsaturation                                      | Fatty acids        | 1.44  | 1.41  | 1.41  | 1.43  | 279.28 | 1.55E-179 | 42634 |
| 23444 | Omega-3 Fatty Acids                                         | Fatty acids        | 0.10  | 0.02  | 0.03  | 0.08  | 232.42 | 1.37E-149 | 42634 |
| 23446 | Polyunsaturated Fatty Acids                                 | Fatty acids        | 3.96  | 3.95  | 3.87  | 3.97  | 38.83  | 4.79E-25  | 42634 |
| 23449 | Linoleic Acid                                               | Fatty acids        | 3.15  | 3.29  | 3.14  | 3.17  | 35.49  | 6.78E-23  | 42634 |
| 23447 | Monounsaturated Fatty Acids                                 | Fatty acids        | 0.77  | 0.85  | 0.86  | 0.82  | 20.12  | 5.03E-13  | 42634 |
| 23445 | Omega-6 Fatty Acids                                         | Fatty acids        | 3.86  | 3.94  | 3.84  | 3.89  | 18.42  | 6.14E-12  | 42634 |
| 23448 | Saturated Fatty Acids                                       | Fatty acids        | 1.90  | 1.89  | 1.96  | 1.96  | 13.00  | 1.74E-08  | 42634 |
| 23442 | Total Fatty Acids                                           | Fatty acids        | 6.63  | 6.69  | 6.68  | 6.76  | 6.66   | 1.73E-04  | 42634 |
| 23478 | Creatinine                                                  | Fluid balance      | 0.04  | 0.04  | 0.04  | 0.04  | 51.83  | 1.99E-33  | 40763 |
| 23479 | Albumin                                                     | Fluid balance      | 44.41 | 44.26 | 43.98 | 44.34 | 31.05  | 4.82E-20  | 42657 |
| 23422 | Free Cholesterol in HDL                                     | Free cholesterol   | 0.38  | 0.37  | 0.37  | 0.38  | 72.92  | 4.93E-47  | 42665 |

|       |                                                           |                                     |       |       |       |       |       |          |       |
|-------|-----------------------------------------------------------|-------------------------------------|-------|-------|-------|-------|-------|----------|-------|
| 23563 | Free Cholesterol in Large HDL                             | Free Cholesterol                    | 0.14  | 0.14  | 0.13  | 0.14  | 72.05 | 1.78E-46 | 42665 |
| 23570 | Free Cholesterol in Medium HDL                            | Free Cholesterol                    | 0.10  | 0.10  | 0.10  | 0.10  | 60.11 | 8.99E-39 | 42665 |
| 23556 | Free Cholesterol in Very Large HDL                        | Free Cholesterol                    | 0.04  | 0.04  | 0.04  | 0.04  | 39.88 | 9.97E-26 | 42665 |
| 23528 | Free Cholesterol in IDL                                   | Free Cholesterol                    | 0.20  | 0.20  | 0.20  | 0.20  | 32.81 | 3.56E-21 | 42665 |
| 23486 | Free Cholesterol in Chylomicrons and Extremely Large VLDL | Free Cholesterol                    | -0.02 | -0.02 | -0.02 | -0.02 | 32.74 | 3.98E-21 | 42665 |
| 23577 | Free Cholesterol in Small HDL                             | Free Cholesterol                    | 0.10  | 0.09  | 0.09  | 0.10  | 24.96 | 3.94E-16 | 42665 |
| 23493 | Free Cholesterol in Very Large VLDL                       | Free Cholesterol                    | -0.01 | -0.01 | -0.01 | -0.01 | 24.52 | 7.58E-16 | 42665 |
| 23535 | Free Cholesterol in Large LDL                             | Free Cholesterol                    | 0.29  | 0.28  | 0.28  | 0.29  | 22.98 | 7.34E-15 | 42665 |
| 23419 | Total Free Cholesterol                                    | Free cholesterol                    | 1.07  | 1.06  | 1.06  | 1.08  | 22.11 | 2.67E-14 | 42665 |
| 23500 | Free Cholesterol in Large VLDL                            | Free Cholesterol                    | -0.02 | -0.01 | -0.01 | -0.01 | 21.40 | 7.65E-14 | 42665 |
| 23421 | Free Cholesterol in LDL                                   | Free cholesterol                    | 0.43  | 0.43  | 0.42  | 0.43  | 18.45 | 5.88E-12 | 42665 |
| 23542 | Free Cholesterol in Medium LDL                            | Free Cholesterol                    | 0.10  | 0.10  | 0.10  | 0.10  | 11.61 | 1.33E-07 | 42665 |
| 23521 | Free Cholesterol in Very Small VLDL                       | Free Cholesterol                    | 0.04  | 0.03  | 0.04  | 0.04  | 11.50 | 1.57E-07 | 42665 |
| 23549 | Free Cholesterol in Small LDL                             | Free Cholesterol                    | 0.05  | 0.05  | 0.05  | 0.05  | 10.86 | 4.00E-07 | 42665 |
| 23420 | Free Cholesterol in VLDL                                  | Free cholesterol                    | 0.05  | 0.06  | 0.06  | 0.06  | 8.89  | 6.95E-06 | 42665 |
| 23473 | Citrate                                                   | Glycolysis related metabolites      | 0.05  | 0.05  | 0.05  | 0.05  | 56.15 | 3.24E-36 | 42660 |
| 23471 | Lactate                                                   | Glycolysis related metabolites      | 3.48  | 3.52  | 3.57  | 3.50  | 10.14 | 1.13E-06 | 42565 |
| 23480 | Glycoprotein Acetyls                                      | Inflammation                        | 0.44  | 0.44  | 0.45  | 0.44  | 30.99 | 5.26E-20 | 42665 |
| 23476 | Acetoacetate                                              | Ketone bodies                       | 0.00  | 0.00  | 0.00  | 0.00  | 8.31  | 1.61E-05 | 42664 |
| 23474 | 3-Hydroxybutyrate                                         | Ketone bodies                       | 0.04  | 0.04  | 0.04  | 0.04  | 7.43  | 5.72E-05 | 42207 |
| 23477 | Acetone                                                   | Ketone bodies                       | 0.01  | 0.01  | 0.01  | 0.01  | 7.01  | 1.04E-04 | 42664 |
| 23558 | Concentration of Large HDL Particles                      | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 73.51 | 2.03E-47 | 42665 |
| 23551 | Concentration of Very Large HDL Particles                 | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 56.19 | 3.03E-36 | 42665 |
| 23565 | Concentration of Medium HDL Particles                     | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 49.54 | 5.94E-32 | 42665 |

|       |                                                                  |                                     |       |       |       |       |       |          |       |
|-------|------------------------------------------------------------------|-------------------------------------|-------|-------|-------|-------|-------|----------|-------|
| 23427 | Total Concentration of Lipoprotein Particles                     | Lipoprotein particle concentrations | 0.02  | 0.02  | 0.02  | 0.02  | 48.36 | 3.44E-31 | 42665 |
| 23430 | Concentration of HDL Particles                                   | Lipoprotein particle concentrations | 0.02  | 0.02  | 0.02  | 0.02  | 48.04 | 5.51E-31 | 42665 |
| 23481 | Concentration of Chylomicrons and Extremely Large VLDL Particles | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 33.68 | 9.89E-22 | 42665 |
| 23488 | Concentration of Very Large VLDL Particles                       | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 28.16 | 3.51E-18 | 42665 |
| 23495 | Concentration of Large VLDL Particles                            | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 21.49 | 6.68E-14 | 42665 |
| 23572 | Concentration of Small HDL Particles                             | Lipoprotein particle concentrations | 0.01  | 0.01  | 0.01  | 0.01  | 14.71 | 1.43E-09 | 42665 |
| 23523 | Concentration of IDL Particles                                   | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 10.41 | 7.61E-07 | 42665 |
| 23537 | Concentration of Medium LDL Particles                            | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 8.76  | 8.34E-06 | 42665 |
| 23516 | Concentration of Very Small VLDL Particles                       | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 8.71  | 8.95E-06 | 42665 |
| 23428 | Concentration of VLDL Particles                                  | Lipoprotein particle concentrations | 0.00  | 0.00  | 0.00  | 0.00  | 6.56  | 1.99E-04 | 42665 |
| 23433 | Average Diameter for HDL Particles                               | Lipoprotein particle sizes          | 10.09 | 10.07 | 10.05 | 10.08 | 63.12 | 1.02E-40 | 42665 |
| 23431 | Average Diameter for VLDL Particles                              | Lipoprotein particle sizes          | 35.52 | 35.68 | 35.71 | 35.59 | 45.87 | 1.39E-29 | 42665 |
| 23432 | Average Diameter for LDL Particles                               | Lipoprotein particle sizes          | 24.08 | 24.08 | 24.06 | 24.07 | 37.74 | 2.41E-24 | 42665 |
| 23438 | Sphingomyelins                                                   | Other lipids                        | 0.44  | 0.43  | 0.43  | 0.44  | 53.67 | 1.29E-34 | 42634 |
| 23437 | Phosphatidylcholines                                             | Other lipids                        | 1.93  | 1.91  | 1.89  | 1.94  | 40.72 | 2.86E-26 | 42634 |
| 23436 | Total Cholines                                                   | Other lipids                        | 2.37  | 2.35  | 2.34  | 2.39  | 38.60 | 6.70E-25 | 42634 |
| 23434 | Phosphoglycerides                                                | Other lipids                        | 1.96  | 1.94  | 1.93  | 1.98  | 36.85 | 8.97E-24 | 42634 |
| 23560 | Phospholipids in Large HDL                                       | Phospholipids                       | 0.59  | 0.58  | 0.57  | 0.59  | 70.08 | 3.36E-45 | 42665 |
| 23553 | Phospholipids in Very Large HDL                                  | Phospholipids                       | 0.17  | 0.17  | 0.16  | 0.17  | 55.23 | 1.26E-35 | 42665 |
| 23414 | Phospholipids in HDL                                             | Phospholipids                       | 1.78  | 1.76  | 1.74  | 1.79  | 54.80 | 2.40E-35 | 42665 |
| 23567 | Phospholipids in Medium HDL                                      | Phospholipids                       | 0.50  | 0.49  | 0.49  | 0.50  | 37.13 | 5.92E-24 | 42665 |
| 23483 | Phospholipids in Chylomicrons and                                | Phospholipids                       | -0.04 | -0.03 | -0.03 | -0.03 | 34.93 | 1.55E-22 | 42665 |

|       |                                                        |               |       |       |       |       |       |          |       |
|-------|--------------------------------------------------------|---------------|-------|-------|-------|-------|-------|----------|-------|
|       | Extremely Large VLDL                                   |               |       |       |       |       |       |          |       |
| 23411 | Total Phospholipids in Lipoprotein Particles           | Phospholipids | 2.57  | 2.54  | 2.53  | 2.58  | 33.29 | 1.75E-21 | 42665 |
| 23490 | Phospholipids in Very Large VLDL                       | Phospholipids | -0.03 | -0.02 | -0.02 | -0.02 | 27.57 | 8.42E-18 | 42665 |
| 23497 | Phospholipids in Large VLDL                            | Phospholipids | -0.03 | -0.03 | -0.03 | -0.03 | 25.70 | 1.32E-16 | 42665 |
| 23525 | Phospholipids in IDL                                   | Phospholipids | 0.26  | 0.26  | 0.26  | 0.26  | 23.99 | 1.67E-15 | 42665 |
| 23574 | Phospholipids in Small HDL                             | Phospholipids | 0.52  | 0.52  | 0.52  | 0.53  | 18.42 | 6.12E-12 | 42665 |
| 23532 | Phospholipids in Large LDL                             | Phospholipids | 0.30  | 0.29  | 0.29  | 0.30  | 15.70 | 3.33E-10 | 42665 |
| 23412 | Phospholipids in VLDL                                  | Phospholipids | 0.05  | 0.06  | 0.07  | 0.06  | 11.76 | 1.06E-07 | 42665 |
| 23413 | Phospholipids in LDL                                   | Phospholipids | 0.47  | 0.47  | 0.47  | 0.48  | 10.07 | 1.25E-06 | 42665 |
| 23559 | Total Lipids in Large HDL                              | Total lipids  | 1.27  | 1.24  | 1.22  | 1.26  | 72.17 | 1.50E-46 | 42665 |
| 23426 | Total Lipids in HDL                                    | Total lipids  | 3.65  | 3.59  | 3.56  | 3.65  | 62.10 | 4.73E-40 | 42665 |
| 23552 | Total Lipids in Very Large HDL                         | Total lipids  | 0.33  | 0.32  | 0.32  | 0.33  | 57.98 | 2.13E-37 | 42665 |
| 23566 | Total Lipids in Medium HDL                             | Total lipids  | 1.13  | 1.11  | 1.10  | 1.13  | 43.52 | 4.51E-28 | 42665 |
| 23482 | Total Lipids in Chylomicrons and Extremely Large VLDL  | Total lipids  | -0.22 | -0.20 | -0.19 | -0.21 | 35.51 | 6.53E-23 | 42665 |
| 23489 | Total Lipids in Very Large VLDL                        | Total lipids  | -0.13 | -0.12 | -0.11 | -0.12 | 27.79 | 6.07E-18 | 42665 |
| 23524 | Total Lipids in IDL                                    | Total lipids  | 1.09  | 1.07  | 1.07  | 1.10  | 27.34 | 1.17E-17 | 42665 |
| 23496 | Total Lipids in Large VLDL                             | Total lipids  | -0.09 | -0.08 | -0.08 | -0.09 | 20.26 | 4.07E-13 | 42665 |
| 23573 | Total Lipids in Small HDL                              | Total lipids  | 0.92  | 0.91  | 0.92  | 0.93  | 16.36 | 1.27E-10 | 42665 |
| 23531 | Total Lipids in Large LDL                              | Total lipids  | 1.30  | 1.29  | 1.28  | 1.31  | 16.13 | 1.78E-10 | 42665 |
| 23423 | Total Lipids in Lipoprotein Particles                  | Total lipids  | 6.66  | 6.62  | 6.62  | 6.74  | 15.96 | 2.30E-10 | 42665 |
| 23424 | Total Lipids in VLDL                                   | Total lipids  | 0.04  | 0.09  | 0.12  | 0.08  | 15.10 | 8.06E-10 | 42665 |
| 23425 | Total Lipids in LDL                                    | Total lipids  | 1.89  | 1.87  | 1.86  | 1.90  | 10.92 | 3.61E-07 | 42665 |
| 23517 | Total Lipids in Very Small VLDL                        | Total lipids  | 0.21  | 0.21  | 0.21  | 0.21  | 9.27  | 3.98E-06 | 42665 |
| 23487 | Triglycerides in Chylomicrons and Extremely Large VLDL | Triglycerides | -0.14 | -0.13 | -0.12 | -0.13 | 35.28 | 9.16E-23 | 42665 |
| 23578 | Triglycerides in Small HDL                             | Triglycerides | 0.00  | 0.00  | 0.01  | 0.00  | 29.44 | 5.25E-19 | 42665 |

|       |                                  |               |       |       |       |       |       |          |       |
|-------|----------------------------------|---------------|-------|-------|-------|-------|-------|----------|-------|
| 23494 | Triglycerides in Very Large VLDL | Triglycerides | -0.09 | -0.08 | -0.08 | -0.08 | 28.95 | 1.08E-18 | 42665 |
| 23408 | Triglycerides in VLDL            | Triglycerides | -0.26 | -0.22 | -0.21 | -0.24 | 22.26 | 2.15E-14 | 42665 |
| 23407 | Total Triglycerides              | Triglycerides | -0.15 | -0.11 | -0.09 | -0.12 | 19.66 | 9.91E-13 | 42665 |
| 23501 | Triglycerides in Large VLDL      | Triglycerides | -0.05 | -0.04 | -0.04 | -0.04 | 18.99 | 2.64E-12 | 42665 |
| 23571 | Triglycerides in Medium HDL      | Triglycerides | 0.01  | 0.01  | 0.01  | 0.01  | 17.44 | 2.61E-11 | 42665 |
| 23550 | Triglycerides in Small LDL       | Triglycerides | 0.00  | 0.00  | 0.00  | 0.00  | 15.18 | 7.15E-10 | 42665 |
| 23410 | Triglycerides in HDL             | Triglycerides | 0.04  | 0.04  | 0.04  | 0.04  | 13.57 | 7.55E-09 | 42665 |
| 23508 | Triglycerides in Medium VLDL     | Triglycerides | 0.00  | 0.01  | 0.01  | 0.01  | 13.33 | 1.08E-08 | 42665 |
| 23515 | Triglycerides in Small VLDL      | Triglycerides | 0.00  | 0.00  | 0.00  | 0.00  | 11.08 | 2.87E-07 | 42665 |
| 23564 | Triglycerides in Large HDL       | Triglycerides | 0.02  | 0.02  | 0.02  | 0.02  | 8.39  | 1.43E-05 | 42665 |
| 23543 | Triglycerides in Medium LDL      | Triglycerides | 0.01  | 0.01  | 0.01  | 0.01  | 7.54  | 4.89E-05 | 42665 |
| 23522 | Triglycerides in Very Small VLDL | Triglycerides | 0.01  | 0.01  | 0.01  | 0.01  | 6.76  | 1.48E-04 | 42665 |

Table S7 Post hoc analysis results (two-tailed t-tests) of blood and metabolic biomarkers

| <b>Subtype 1 vs Subtype 4</b> |                                                             |                                     |           |           |                |                |                       |                       |
|-------------------------------|-------------------------------------------------------------|-------------------------------------|-----------|-----------|----------------|----------------|-----------------------|-----------------------|
| <b>Field ID</b>               | <b>Description</b>                                          | <b>Category</b>                     | <b>S1</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>S1 sample size</b> | <b>S4 sample size</b> |
| 23491                         | Cholesterol in Very Large VLDL                              | Cholesterol                         | -0.01     | -0.01     | -4.85          | 1.22E-06       | 7657                  | 24456                 |
| 23484                         | Cholesterol in Chylomicrons and Extremely Large VLDL        | Cholesterol                         | -0.04     | -0.04     | -4.83          | 1.40E-06       | 7657                  | 24456                 |
| 23498                         | Cholesterol in Large VLDL                                   | Cholesterol                         | -0.02     | -0.01     | -4.69          | 2.69E-06       | 7657                  | 24456                 |
| 23554                         | Cholesterol in Very Large HDL                               | Cholesterol                         | 0.16      | 0.16      | 4.30           | 1.69E-05       | 7657                  | 24456                 |
| 23575                         | Cholesterol in Small HDL                                    | Cholesterol                         | 0.39      | 0.39      | -4.15          | 3.35E-05       | 7657                  | 24456                 |
| 23403                         | VLDL Cholesterol                                            | Cholesterol                         | 0.25      | 0.26      | -4.09          | 4.34E-05       | 7657                  | 24456                 |
| 23485                         | Cholesteryl Esters in Chylomicrons and Extremely Large VLDL | Cholesteryl esters                  | -0.02     | -0.02     | -4.94          | 7.67E-07       | 7657                  | 24456                 |
| 23492                         | Cholesteryl Esters in Very Large VLDL                       | Cholesteryl esters                  | 0.00      | 0.00      | -4.81          | 1.51E-06       | 7657                  | 24456                 |
| 23499                         | Cholesteryl Esters in Large VLDL                            | Cholesteryl esters                  | 0.00      | 0.00      | -4.52          | 6.17E-06       | 7657                  | 24456                 |
| 23555                         | Cholesteryl Esters in Very Large HDL                        | Cholesteryl esters                  | 0.12      | 0.12      | 4.32           | 1.58E-05       | 7657                  | 24456                 |
| 23576                         | Cholesteryl Esters in Small HDL                             | Cholesteryl esters                  | 0.30      | 0.30      | -4.08          | 4.58E-05       | 7657                  | 24456                 |
| 23443                         | Degree of Unsaturation                                      | Fatty acids                         | 1.44      | 1.43      | 8.68           | 3.97E-18       | 7651                  | 24440                 |
| 23450                         | Docosahexaenoic Acid                                        | Fatty acids                         | 0.16      | 0.16      | 6.26           | 3.78E-10       | 7651                  | 24440                 |
| 23448                         | Saturated Fatty Acids                                       | Fatty acids                         | 1.90      | 1.96      | -5.33          | 9.89E-08       | 7651                  | 24440                 |
| 23447                         | Monounsaturated Fatty Acids                                 | Fatty acids                         | 0.77      | 0.82      | -5.17          | 2.36E-07       | 7651                  | 24440                 |
| 23444                         | Omega-3 Fatty Acids                                         | Fatty acids                         | 0.10      | 0.08      | 4.64           | 3.58E-06       | 7651                  | 24440                 |
| 23442                         | Total Fatty Acids                                           | Fatty acids                         | 6.63      | 6.76      | -4.16          | 3.16E-05       | 7651                  | 24440                 |
| 23500                         | Free Cholesterol in Large VLDL                              | Free Cholesterol                    | -0.02     | -0.01     | -4.75          | 2.06E-06       | 7657                  | 24456                 |
| 23493                         | Free Cholesterol in Very Large VLDL                         | Free Cholesterol                    | -0.01     | -0.01     | -4.74          | 2.12E-06       | 7657                  | 24456                 |
| 23486                         | Free Cholesterol in Chylomicrons and Extremely Large VLDL   | Free Cholesterol                    | -0.02     | -0.02     | -4.62          | 3.86E-06       | 7657                  | 24456                 |
| 23420                         | Free Cholesterol in VLDL                                    | Free cholesterol                    | 0.05      | 0.06      | -4.38          | 1.17E-05       | 7657                  | 24456                 |
| 23556                         | Free Cholesterol in Very Large HDL                          | Free Cholesterol                    | 0.04      | 0.04      | 4.07           | 4.68E-05       | 7657                  | 24456                 |
| 23488                         | Concentration of Very Large VLDL Particles                  | Lipoprotein particle concentrations | 0.00      | 0.00      | -4.81          | 1.54E-06       | 7657                  | 24456                 |
| 23495                         | Concentration of Large VLDL Particles                       | Lipoprotein particle concentrations | 0.00      | 0.00      | -4.78          | 1.78E-06       | 7657                  | 24456                 |



|       |                                                                  |                                     |       |       |       |          |      |       |
|-------|------------------------------------------------------------------|-------------------------------------|-------|-------|-------|----------|------|-------|
| 23572 | Concentration of Small HDL Particles                             | Lipoprotein particle concentrations | 0.01  | 0.01  | -4.67 | 3.07E-06 | 7657 | 24456 |
| 23481 | Concentration of Chylomicrons and Extremely Large VLDL Particles | Lipoprotein particle concentrations | 0.00  | 0.00  | -4.40 | 1.10E-05 | 7657 | 24456 |
| 23431 | Average Diameter for VLDL Particles                              | Lipoprotein particle sizes          | 35.52 | 35.59 | -4.88 | 1.04E-06 | 7657 | 24456 |
| 23574 | Phospholipids in Small HDL                                       | Phospholipids                       | 0.52  | 0.53  | -5.75 | 8.92E-09 | 7657 | 24456 |
| 23497 | Phospholipids in Large VLDL                                      | Phospholipids                       | -0.03 | -0.03 | -4.87 | 1.14E-06 | 7657 | 24456 |
| 23490 | Phospholipids in Very Large VLDL                                 | Phospholipids                       | -0.03 | -0.02 | -4.78 | 1.72E-06 | 7657 | 24456 |
| 23412 | Phospholipids in VLDL                                            | Phospholipids                       | 0.05  | 0.06  | -4.51 | 6.42E-06 | 7657 | 24456 |
| 23483 | Phospholipids in Chylomicrons and Extremely Large VLDL           | Phospholipids                       | -0.04 | -0.03 | -4.38 | 1.20E-05 | 7657 | 24456 |
| 23553 | Phospholipids in Very Large HDL                                  | Phospholipids                       | 0.17  | 0.17  | 4.07  | 4.69E-05 | 7657 | 24456 |
| 23573 | Total Lipids in Small HDL                                        | Total lipids                        | 0.92  | 0.93  | -5.53 | 3.24E-08 | 7657 | 24456 |
| 23489 | Total Lipids in Very Large VLDL                                  | Total lipids                        | -0.13 | -0.12 | -4.87 | 1.12E-06 | 7657 | 24456 |
| 23496 | Total Lipids in Large VLDL                                       | Total lipids                        | -0.09 | -0.09 | -4.84 | 1.28E-06 | 7657 | 24456 |
| 23424 | Total Lipids in VLDL                                             | Total lipids                        | 0.04  | 0.08  | -4.70 | 2.63E-06 | 7657 | 24456 |
| 23482 | Total Lipids in Chylomicrons and Extremely Large VLDL            | Total lipids                        | -0.22 | -0.21 | -4.36 | 1.29E-05 | 7657 | 24456 |
| 23503 | Total Lipids in Medium VLDL                                      | Total lipids                        | 0.16  | 0.17  | -4.22 | 2.42E-05 | 7657 | 24456 |
| 23552 | Total Lipids in Very Large HDL                                   | Total lipids                        | 0.33  | 0.33  | 4.09  | 4.37E-05 | 7657 | 24456 |
| 23571 | Triglycerides in Medium HDL                                      | Triglycerides                       | 0.01  | 0.01  | -5.25 | 1.50E-07 | 7657 | 24456 |
| 23578 | Triglycerides in Small HDL                                       | Triglycerides                       | 0.00  | 0.00  | -5.19 | 2.06E-07 | 7657 | 24456 |
| 23494 | Triglycerides in Very Large VLDL                                 | Triglycerides                       | -0.09 | -0.08 | -4.76 | 1.97E-06 | 7657 | 24456 |
| 23501 | Triglycerides in Large VLDL                                      | Triglycerides                       | -0.05 | -0.04 | -4.74 | 2.16E-06 | 7657 | 24456 |
| 23508 | Triglycerides in Medium VLDL                                     | Triglycerides                       | 0.00  | 0.01  | -4.70 | 2.56E-06 | 7657 | 24456 |
| 23410 | Triglycerides in HDL                                             | Triglycerides                       | 0.04  | 0.04  | -4.61 | 3.95E-06 | 7657 | 24456 |
| 23407 | Total Triglycerides                                              | Triglycerides                       | -0.15 | -0.12 | -4.61 | 4.09E-06 | 7657 | 24456 |
| 23408 | Triglycerides in VLDL                                            | Triglycerides                       | -0.26 | -0.24 | -4.61 | 4.09E-06 | 7657 | 24456 |
| 23487 | Triglycerides in Chylomicrons and Extremely Large VLDL           | Triglycerides                       | -0.14 | -0.13 | -4.14 | 3.50E-05 | 7657 | 24456 |

| Subtype 2 vs Subtype 4 |                                                                                   |                    |        |        |         |          |                |                |
|------------------------|-----------------------------------------------------------------------------------|--------------------|--------|--------|---------|----------|----------------|----------------|
| Field ID               | Description                                                                       | Category           | S2     | S4     | t Value | P value  | S2 sample size | S4 sample size |
| 30890                  | Vitamin D                                                                         | Bone and joint     | 48.86  | 52.39  | -7.77   | 8.44E-15 | 2149           | 21864          |
| 30770                  | IGF-1                                                                             | Endocrine          | 37.31  | 38.10  | -6.73   | 1.69E-11 | 2207           | 22646          |
| 30830                  | SHBG                                                                              | Endocrine          | 113.92 | 111.11 | 5.07    | 4.04E-07 | 1984           | 20615          |
| 30690                  | Cholesterol                                                                       | Immunometabolic    | 4.63   | 4.78   | -6.26   | 3.97E-10 | 2219           | 22751          |
| 30780                  | LDL direct                                                                        | Immunometabolic    | 2.54   | 2.65   | -5.78   | 7.56E-09 | 2215           | 22716          |
| 30640                  | Apolipoprotein B                                                                  | Immunometabolic    | 0.65   | 0.68   | -4.96   | 7.21E-07 | 2211           | 22664          |
| 30630                  | Apolipoprotein A                                                                  | Immunometabolic    | 1.71   | 1.73   | -4.85   | 1.27E-06 | 1987           | 20708          |
| 30760                  | HDL cholesterol                                                                   | Immunometabolic    | 2.02   | 2.05   | -4.56   | 5.03E-06 | 2004           | 20816          |
| 30730                  | Gamma glutamyltransferase                                                         | Liver function     | -20.04 | -16.01 | -5.63   | 1.81E-08 | 2217           | 22747          |
| 30620                  | Alanine aminotransferase                                                          | Liver function     | 1.78   | 2.87   | -4.02   | 5.82E-05 | 2216           | 22752          |
| 30030                  | Haematocrit percentage                                                            | Red blood cell     | 35.53  | 35.99  | -7.64   | 2.20E-14 | 2268           | 23240          |
| 30020                  | Haemoglobin concentration                                                         | Red blood cell     | 12.27  | 12.41  | -7.09   | 1.35E-12 | 2268           | 23239          |
| 30040                  | Mean corpuscular volume                                                           | Red blood cell     | 89.93  | 90.34  | -4.48   | 7.47E-06 | 2268           | 23239          |
| 30010                  | Red blood cell (erythrocyte) count                                                | Red blood cell     | 3.97   | 4.00   | -4.10   | 4.13E-05 | 2268           | 23240          |
| 30670                  | Urea                                                                              | Renal function     | 1.36   | 1.86   | -18.68  | 2.55E-77 | 2215           | 22747          |
| 30700                  | Creatinine                                                                        | Renal function     | 49.61  | 52.86  | -11.13  | 1.07E-28 | 2215           | 22751          |
| 30720                  | Cystatin C                                                                        | Renal function     | 0.28   | 0.26   | 10.34   | 4.98E-25 | 2215           | 22754          |
| 30880                  | Urate                                                                             | Renal function     | 58.43  | 67.40  | -6.68   | 2.41E-11 | 2215           | 22726          |
| 23462                  | Glycine                                                                           | Amino acids        | 0.29   | 0.27   | 18.91   | 3.09E-79 | 2321           | 24431          |
| 23467                  | Valine                                                                            | Amino acids        | 0.11   | 0.12   | -8.39   | 5.00E-17 | 2322           | 24449          |
| 23461                  | Glutamine                                                                         | Amino acids        | 0.57   | 0.55   | 7.80    | 6.19E-15 | 2320           | 24392          |
| 23464                  | Total Concentration of Branched-Chain Amino Acids (Leucine + Isoleucine + Valine) | Amino acids        | 0.20   | 0.21   | -7.79   | 6.75E-15 | 2322           | 24449          |
| 23466                  | Leucine                                                                           | Amino acids        | 0.06   | 0.06   | -7.59   | 3.35E-14 | 2323           | 24455          |
| 23460                  | Alanine                                                                           | Amino acids        | 0.25   | 0.24   | 5.69    | 1.26E-08 | 2323           | 24455          |
| 23465                  | Isoleucine                                                                        | Amino acids        | 0.02   | 0.03   | -5.24   | 1.66E-07 | 2323           | 24455          |
| 23440                  | Apolipoprotein A1                                                                 | Apolipoproteins    | 1.59   | 1.62   | -5.30   | 1.17E-07 | 2323           | 24456          |
| 23526                  | Cholesterol in IDL                                                                | Cholesterol        | 0.78   | 0.80   | -5.92   | 3.18E-09 | 2323           | 24456          |
| 23519                  | Cholesterol in Very Small VLDL                                                    | Cholesterol        | 0.14   | 0.14   | -5.92   | 3.22E-09 | 2323           | 24456          |
| 23568                  | Cholesterol in Medium HDL                                                         | Cholesterol        | 0.61   | 0.62   | -4.84   | 1.32E-06 | 2323           | 24456          |
| 23400                  | Total Cholesterol                                                                 | Cholesterol        | 4.19   | 4.28   | -4.58   | 4.77E-06 | 2323           | 24456          |
| 23406                  | HDL Cholesterol                                                                   | Cholesterol        | 1.80   | 1.82   | -4.27   | 1.97E-05 | 2323           | 24456          |
| 23520                  | Cholesteryl Esters in Very Small VLDL                                             | Cholesteryl esters | 0.10   | 0.11   | -6.32   | 2.63E-10 | 2323           | 24456          |

|       |                                              |                                     |      |      |        |          |      |       |
|-------|----------------------------------------------|-------------------------------------|------|------|--------|----------|------|-------|
| 23527 | Cholesteryl Esters in IDL                    | Cholesteryl esters                  | 0.58 | 0.60 | -5.71  | 1.13E-08 | 2323 | 24456 |
| 23415 | Total Esterified Cholesterol                 | Cholesteryl esters                  | 3.13 | 3.19 | -4.72  | 2.41E-06 | 2323 | 24456 |
| 23569 | Cholesteryl Esters in Medium HDL             | Cholesteryl esters                  | 0.51 | 0.51 | -4.65  | 3.29E-06 | 2323 | 24456 |
| 23418 | Cholesteryl Esters in HDL                    | Cholesteryl esters                  | 1.43 | 1.45 | -4.04  | 5.36E-05 | 2323 | 24456 |
| 23444 | Omega-3 Fatty Acids                          | Fatty acids                         | 0.02 | 0.08 | -14.39 | 8.74E-47 | 2321 | 24440 |
| 23450 | Docosaheptaenoic Acid                        | Fatty acids                         | 0.13 | 0.16 | -14.04 | 1.29E-44 | 2321 | 24440 |
| 23443 | Degree of Unsaturation                       | Fatty acids                         | 1.41 | 1.43 | -10.93 | 9.90E-28 | 2321 | 24440 |
| 23449 | Linoleic Acid                                | Fatty acids                         | 3.29 | 3.17 | 8.44   | 3.44E-17 | 2321 | 24440 |
| 23448 | Saturated Fatty Acids                        | Fatty acids                         | 1.89 | 1.96 | -3.98  | 6.96E-05 | 2321 | 24440 |
| 23478 | Creatinine                                   | Fluid balance                       | 0.04 | 0.04 | -8.10  | 5.98E-16 | 2211 | 23353 |
| 23528 | Free Cholesterol in IDL                      | Free Cholesterol                    | 0.20 | 0.20 | -6.38  | 1.77E-10 | 2323 | 24456 |
| 23570 | Free Cholesterol in Medium HDL               | Free Cholesterol                    | 0.10 | 0.10 | -5.45  | 4.96E-08 | 2323 | 24456 |
| 23422 | Free Cholesterol in HDL                      | Free cholesterol                    | 0.37 | 0.38 | -4.89  | 9.95E-07 | 2323 | 24456 |
| 23521 | Free Cholesterol in Very Small VLDL          | Free Cholesterol                    | 0.03 | 0.04 | -4.78  | 1.79E-06 | 2323 | 24456 |
| 23577 | Free Cholesterol in Small HDL                | Free Cholesterol                    | 0.09 | 0.10 | -4.55  | 5.36E-06 | 2323 | 24456 |
| 23535 | Free Cholesterol in Large LDL                | Free Cholesterol                    | 0.28 | 0.29 | -4.34  | 1.43E-05 | 2323 | 24456 |
| 23419 | Total Free Cholesterol                       | Free cholesterol                    | 1.06 | 1.08 | -4.14  | 3.48E-05 | 2323 | 24456 |
| 23473 | Citrate                                      | Glycolysis related metabolites      | 0.05 | 0.05 | 12.09  | 1.44E-33 | 2323 | 24453 |
| 23565 | Concentration of Medium HDL Particles        | Lipoprotein particle concentrations | 0.00 | 0.00 | -5.32  | 1.03E-07 | 2323 | 24456 |
| 23427 | Total Concentration of Lipoprotein Particles | Lipoprotein particle concentrations | 0.02 | 0.02 | -5.24  | 1.65E-07 | 2323 | 24456 |
| 23430 | Concentration of HDL Particles               | Lipoprotein particle concentrations | 0.02 | 0.02 | -5.11  | 3.17E-07 | 2323 | 24456 |
| 23516 | Concentration of Very Small VLDL Particles   | Lipoprotein particle concentrations | 0.00 | 0.00 | -4.21  | 2.62E-05 | 2323 | 24456 |
| 23523 | Concentration of IDL Particles               | Lipoprotein particle concentrations | 0.00 | 0.00 | -3.97  | 7.22E-05 | 2323 | 24456 |
| 23537 | Concentration of Medium LDL Particles        | Lipoprotein particle concentrations | 0.00 | 0.00 | -3.90  | 9.81E-05 | 2323 | 24456 |
| 23438 | Sphingomyelins                               | Other lipids                        | 0.43 | 0.44 | -7.70  | 1.39E-14 | 2321 | 24440 |
| 23434 | Phosphoglycerides                            | Other lipids                        | 1.94 | 1.98 | -4.85  | 1.25E-06 | 2321 | 24440 |
| 23437 | Phosphatidylcholines                         | Other lipids                        | 1.91 | 1.94 | -4.35  | 1.34E-05 | 2321 | 24440 |
| 23436 | Total Cholines                               | Other lipids                        | 2.35 | 2.39 | -4.23  | 2.36E-05 | 2321 | 24440 |
| 23567 | Phospholipids in Medium HDL                  | Phospholipids                       | 0.49 | 0.50 | -5.30  | 1.17E-07 | 2323 | 24456 |
| 23414 | Phospholipids in HDL                         | Phospholipids                       | 1.76 | 1.79 | -5.25  | 1.50E-07 | 2323 | 24456 |
| 23525 | Phospholipids in IDL                         | Phospholipids                       | 0.26 | 0.26 | -4.98  | 6.43E-07 | 2323 | 24456 |

| 23411                         | Total Phospholipids in Lipoprotein Particles    | Phospholipids    | 2.54   | 2.58   | -4.92   | 8.88E-07 | 2323           | 24456          |
|-------------------------------|-------------------------------------------------|------------------|--------|--------|---------|----------|----------------|----------------|
| 23574                         | Phospholipids in Small HDL                      | Phospholipids    | 0.52   | 0.53   | -4.68   | 2.94E-06 | 2323           | 24456          |
| 23532                         | Phospholipids in Large LDL                      | Phospholipids    | 0.29   | 0.30   | -4.08   | 4.50E-05 | 2323           | 24456          |
| 23524                         | Total Lipids in IDL                             | Total lipids     | 1.07   | 1.10   | -5.55   | 2.84E-08 | 2323           | 24456          |
| 23566                         | Total Lipids in Medium HDL                      | Total lipids     | 1.11   | 1.13   | -5.26   | 1.43E-07 | 2323           | 24456          |
| 23426                         | Total Lipids in HDL                             | Total lipids     | 3.59   | 3.65   | -4.97   | 6.70E-07 | 2323           | 24456          |
| 23517                         | Total Lipids in Very Small VLDL                 | Total lipids     | 0.21   | 0.21   | -4.15   | 3.32E-05 | 2323           | 24456          |
| 23573                         | Total Lipids in Small HDL                       | Total lipids     | 0.91   | 0.93   | -4.15   | 3.38E-05 | 2323           | 24456          |
| 23564                         | Triglycerides in Large HDL                      | Triglycerides    | 0.02   | 0.02   | -4.43   | 9.48E-06 | 2323           | 24456          |
| <b>Subtype 3 vs Subtype 4</b> |                                                 |                  |        |        |         |          |                |                |
| Field ID                      | Description                                     | Category         | S3     | S4     | t Value | P value  | S3 sample size | S4 sample size |
| 30610                         | Alkaline phosphatase                            | Bone and joint   | 26.36  | 23.53  | 9.27    | 1.96E-20 | 7653           | 22760          |
| 30890                         | Vitamin D                                       | Bone and joint   | 51.30  | 52.39  | -4.04   | 5.39E-05 | 7324           | 21864          |
| 30770                         | IGF-1                                           | Endocrine        | 37.59  | 38.10  | -7.27   | 3.73E-13 | 7610           | 22646          |
| 30760                         | HDL cholesterol                                 | Immunometabolic  | 1.99   | 2.05   | -12.87  | 8.47E-38 | 6993           | 20816          |
| 30630                         | Apolipoprotein A                                | Immunometabolic  | 1.70   | 1.73   | -10.47  | 1.39E-25 | 6967           | 20708          |
| 30870                         | Triglycerides                                   | Immunometabolic  | -0.61  | -0.71  | 8.62    | 6.81E-18 | 7645           | 22737          |
| 30750                         | Glycated haemoglobin (HbA1c)                    | Immunometabolic  | 18.60  | 18.22  | 5.39    | 7.19E-08 | 7565           | 22625          |
| 30710                         | C-reactive protein                              | Immunometabolic  | -4.80  | -4.99  | 3.95    | 7.89E-05 | 7634           | 22714          |
| 30600                         | Albumin                                         | Liver function   | 50.00  | 50.16  | -4.58   | 4.76E-06 | 6997           | 20827          |
| 30080                         | Platelet count                                  | Platelet         | 271.74 | 268.70 | 4.18    | 2.95E-05 | 7783           | 23240          |
| 30010                         | Red blood cell (erythrocyte) count              | Red blood cell   | 4.02   | 4.00   | 5.91    | 3.35E-09 | 7783           | 23240          |
| 30050                         | Mean corpuscular haemoglobin                    | Red blood cell   | 31.04  | 31.15  | -4.67   | 2.99E-06 | 7783           | 23239          |
| 30070                         | Red blood cell (erythrocyte) distribution width | Red blood cell   | 12.94  | 12.89  | 4.45    | 8.67E-06 | 7783           | 23239          |
| 30040                         | Mean corpuscular volume                         | Red blood cell   | 90.10  | 90.34  | -4.39   | 1.14E-05 | 7783           | 23239          |
| 30720                         | Cystatin C                                      | Renal function   | 0.28   | 0.26   | 13.24   | 7.10E-40 | 7655           | 22754          |
| 30700                         | Creatinine                                      | Renal function   | 53.75  | 52.86  | 5.13    | 2.95E-07 | 7650           | 22751          |
| 30810                         | Phosphate                                       | Renal function   | 1.20   | 1.21   | -5.01   | 5.43E-07 | 6982           | 20776          |
| 30140                         | Neutrophil count                                | White blood cell | 3.31   | 3.18   | 7.79    | 6.75E-15 | 7769           | 23190          |
| 30180                         | Lymphocyte percentage                           | White blood cell | 28.44  | 29.05  | -6.32   | 2.68E-10 | 7769           | 23191          |
| 30000                         | White blood cell (leukocyte) count              | White blood cell | 5.01   | 4.87   | 5.89    | 3.96E-09 | 7783           | 23239          |
| 30200                         | Neutrophil percentage                           | White blood cell | 63.08  | 62.47  | 5.56    | 2.72E-08 | 7769           | 23191          |

|       |                                                             |                    |       |       |        |          |      |       |
|-------|-------------------------------------------------------------|--------------------|-------|-------|--------|----------|------|-------|
| 23462 | Glycine                                                     | Amino acids        | 0.27  | 0.27  | 6.93   | 4.33E-12 | 8217 | 24431 |
| 23460 | Alanine                                                     | Amino acids        | 0.24  | 0.24  | 4.82   | 1.43E-06 | 8229 | 24455 |
| 23440 | Apolipoprotein A1                                           | Apolipoproteins    | 1.58  | 1.62  | -12.17 | 5.30E-34 | 8229 | 24456 |
| 23406 | HDL Cholesterol                                             | Cholesterol        | 1.78  | 1.82  | -14.34 | 1.70E-46 | 8229 | 24456 |
| 23561 | Cholesterol in Large HDL                                    | Cholesterol        | 0.63  | 0.66  | -13.58 | 6.70E-42 | 8229 | 24456 |
| 23568 | Cholesterol in Medium HDL                                   | Cholesterol        | 0.60  | 0.62  | -12.46 | 1.41E-35 | 8229 | 24456 |
| 23554 | Cholesterol in Very Large HDL                               | Cholesterol        | 0.15  | 0.16  | -11.90 | 1.36E-32 | 8229 | 24456 |
| 23400 | Total Cholesterol                                           | Cholesterol        | 4.18  | 4.28  | -9.00  | 2.32E-19 | 8229 | 24456 |
| 23526 | Cholesterol in IDL                                          | Cholesterol        | 0.78  | 0.80  | -8.44  | 3.18E-17 | 8229 | 24456 |
| 23484 | Cholesterol in Chylomicrons and Extremely Large VLDL        | Cholesterol        | -0.03 | -0.04 | 7.00   | 2.67E-12 | 8229 | 24456 |
| 23533 | Cholesterol in Large LDL                                    | Cholesterol        | 0.96  | 0.98  | -6.93  | 4.32E-12 | 8229 | 24456 |
| 23575 | Cholesterol in Small HDL                                    | Cholesterol        | 0.39  | 0.39  | -6.07  | 1.28E-09 | 8229 | 24456 |
| 23404 | Clinical LDL Cholesterol                                    | Cholesterol        | 2.03  | 2.08  | -5.74  | 9.75E-09 | 8229 | 24456 |
| 23405 | LDL Cholesterol                                             | Cholesterol        | 1.35  | 1.39  | -5.72  | 1.10E-08 | 8229 | 24456 |
| 23519 | Cholesterol in Very Small VLDL                              | Cholesterol        | 0.14  | 0.14  | -5.23  | 1.66E-07 | 8229 | 24456 |
| 23401 | Total Cholesterol Minus HDL-C                               | Cholesterol        | 2.40  | 2.45  | -4.99  | 6.05E-07 | 8229 | 24456 |
| 23491 | Cholesterol in Very Large VLDL                              | Cholesterol        | -0.01 | -0.01 | 4.84   | 1.33E-06 | 8229 | 24456 |
| 23402 | Remnant Cholesterol (Non-HDL, Non-LDL - Cholesterol)        | Cholesterol        | 1.05  | 1.07  | -4.05  | 5.14E-05 | 8229 | 24456 |
| 23418 | Cholesteryl Esters in HDL                                   | Cholesteryl esters | 1.41  | 1.45  | -14.25 | 6.20E-46 | 8229 | 24456 |
| 23562 | Cholesteryl Esters in Large HDL                             | Cholesteryl esters | 0.50  | 0.52  | -13.61 | 4.53E-42 | 8229 | 24456 |
| 23555 | Cholesteryl Esters in Very Large HDL                        | Cholesteryl esters | 0.11  | 0.12  | -12.57 | 3.94E-36 | 8229 | 24456 |
| 23569 | Cholesteryl Esters in Medium HDL                            | Cholesteryl esters | 0.50  | 0.51  | -12.28 | 1.41E-34 | 8229 | 24456 |
| 23415 | Total Esterified Cholesterol                                | Cholesteryl esters | 3.12  | 3.19  | -9.53  | 1.62E-21 | 8229 | 24456 |
| 23527 | Cholesteryl Esters in IDL                                   | Cholesteryl esters | 0.58  | 0.60  | -8.40  | 4.82E-17 | 8229 | 24456 |
| 23485 | Cholesteryl Esters in Chylomicrons and Extremely Large VLDL | Cholesteryl esters | -0.02 | -0.02 | 6.95   | 3.70E-12 | 8229 | 24456 |
| 23534 | Cholesteryl Esters in Large LDL                             | Cholesteryl esters | 0.68  | 0.69  | -6.63  | 3.37E-11 | 8229 | 24456 |
| 23520 | Cholesteryl Esters in Very Small VLDL                       | Cholesteryl esters | 0.10  | 0.11  | -5.87  | 4.33E-09 | 8229 | 24456 |

|       |                                                           |                                |       |       |        |           |      |       |
|-------|-----------------------------------------------------------|--------------------------------|-------|-------|--------|-----------|------|-------|
| 23417 | Cholesteryl Esters in LDL                                 | Cholesteryl esters             | 0.93  | 0.95  | -5.21  | 1.89E-07  | 8229 | 24456 |
| 23576 | Cholesteryl Esters in Small HDL                           | Cholesteryl esters             | 0.30  | 0.30  | -5.20  | 2.02E-07  | 8229 | 24456 |
| 23506 | Cholesteryl Esters in Medium VLDL                         | Cholesteryl esters             | 0.08  | 0.08  | -4.73  | 2.26E-06  | 8229 | 24456 |
| 23450 | Docosahexaenoic Acid                                      | Fatty acids                    | 0.13  | 0.16  | -25.69 | 3.71E-144 | 8222 | 24440 |
| 23443 | Degree of Unsaturation                                    | Fatty acids                    | 1.41  | 1.43  | -23.34 | 1.77E-119 | 8222 | 24440 |
| 23444 | Omega-3 Fatty Acids                                       | Fatty acids                    | 0.03  | 0.08  | -21.29 | 6.37E-100 | 8222 | 24440 |
| 23446 | Polyunsaturated Fatty Acids                               | Fatty acids                    | 3.87  | 3.97  | -10.72 | 9.44E-27  | 8222 | 24440 |
| 23445 | Omega-6 Fatty Acids                                       | Fatty acids                    | 3.84  | 3.89  | -5.82  | 5.88E-09  | 8222 | 24440 |
| 23449 | Linoleic Acid                                             | Fatty acids                    | 3.14  | 3.17  | -4.31  | 1.65E-05  | 8222 | 24440 |
| 23447 | Monounsaturated Fatty Acids                               | Fatty acids                    | 0.86  | 0.82  | 4.00   | 6.37E-05  | 8222 | 24440 |
| 23479 | Albumin                                                   | Fluid balance                  | 43.98 | 44.34 | -8.86  | 8.04E-19  | 8229 | 24450 |
| 23478 | Creatinine                                                | Fluid balance                  | 0.04  | 0.04  | 7.74   | 1.02E-14  | 7906 | 23353 |
| 23422 | Free Cholesterol in HDL                                   | Free cholesterol               | 0.37  | 0.38  | -14.07 | 7.58E-45  | 8229 | 24456 |
| 23563 | Free Cholesterol in Large HDL                             | Free Cholesterol               | 0.13  | 0.14  | -13.33 | 2.11E-40  | 8229 | 24456 |
| 23570 | Free Cholesterol in Medium HDL                            | Free Cholesterol               | 0.10  | 0.10  | -12.87 | 7.75E-38  | 8229 | 24456 |
| 23556 | Free Cholesterol in Very Large HDL                        | Free Cholesterol               | 0.04  | 0.04  | -8.93  | 4.59E-19  | 8229 | 24456 |
| 23528 | Free Cholesterol in IDL                                   | Free Cholesterol               | 0.20  | 0.20  | -8.38  | 5.45E-17  | 8229 | 24456 |
| 23577 | Free Cholesterol in Small HDL                             | Free Cholesterol               | 0.09  | 0.10  | -7.82  | 5.42E-15  | 8229 | 24456 |
| 23535 | Free Cholesterol in Large LDL                             | Free Cholesterol               | 0.28  | 0.29  | -7.57  | 3.87E-14  | 8229 | 24456 |
| 23419 | Total Free Cholesterol                                    | Free cholesterol               | 1.06  | 1.08  | -7.52  | 5.43E-14  | 8229 | 24456 |
| 23486 | Free Cholesterol in Chylomicrons and Extremely Large VLDL | Free Cholesterol               | -0.02 | -0.02 | 6.96   | 3.42E-12  | 8229 | 24456 |
| 23421 | Free Cholesterol in LDL                                   | Free cholesterol               | 0.42  | 0.43  | -6.88  | 5.98E-12  | 8229 | 24456 |
| 23493 | Free Cholesterol in Very Large VLDL                       | Free Cholesterol               | -0.01 | -0.01 | 5.62   | 1.87E-08  | 8229 | 24456 |
| 23542 | Free Cholesterol in Medium LDL                            | Free Cholesterol               | 0.10  | 0.10  | -5.57  | 2.62E-08  | 8229 | 24456 |
| 23549 | Free Cholesterol in Small LDL                             | Free Cholesterol               | 0.05  | 0.05  | -5.52  | 3.42E-08  | 8229 | 24456 |
| 23500 | Free Cholesterol in Large VLDL                            | Free Cholesterol               | -0.01 | -0.01 | 4.99   | 6.17E-07  | 8229 | 24456 |
| 23473 | Citrate                                                   | Glycolysis related metabolites | 0.05  | 0.05  | 6.67   | 2.63E-11  | 8227 | 24453 |
| 23471 | Lactate                                                   | Glycolysis related metabolites | 3.57  | 3.50  | 4.80   | 1.57E-06  | 8203 | 24406 |

|       |                                                                  |                                     |       |       |        |          |      |       |
|-------|------------------------------------------------------------------|-------------------------------------|-------|-------|--------|----------|------|-------|
| 23480 | Glycoprotein Acetyls                                             | Inflammation                        | 0.45  | 0.44  | 7.95   | 2.00E-15 | 8229 | 24456 |
| 23476 | Acetoacetate                                                     | Ketone bodies                       | 0.00  | 0.00  | -4.53  | 5.98E-06 | 8229 | 24455 |
| 23558 | Concentration of Large HDL Particles                             | Lipoprotein particle concentrations | 0.00  | 0.00  | -13.57 | 7.91E-42 | 8229 | 24456 |
| 23565 | Concentration of Medium HDL Particles                            | Lipoprotein particle concentrations | 0.00  | 0.00  | -11.68 | 1.95E-31 | 8229 | 24456 |
| 23427 | Total Concentration of Lipoprotein Particles                     | Lipoprotein particle concentrations | 0.02  | 0.02  | -11.62 | 3.98E-31 | 8229 | 24456 |
| 23430 | Concentration of HDL Particles                                   | Lipoprotein particle concentrations | 0.02  | 0.02  | -11.61 | 4.39E-31 | 8229 | 24456 |
| 23551 | Concentration of Very Large HDL Particles                        | Lipoprotein particle concentrations | 0.00  | 0.00  | -11.41 | 4.25E-30 | 8229 | 24456 |
| 23481 | Concentration of Chylomicrons and Extremely Large VLDL Particles | Lipoprotein particle concentrations | 0.00  | 0.00  | 7.32   | 2.63E-13 | 8229 | 24456 |
| 23488 | Concentration of Very Large VLDL Particles                       | Lipoprotein particle concentrations | 0.00  | 0.00  | 6.24   | 4.34E-10 | 8229 | 24456 |
| 23572 | Concentration of Small HDL Particles                             | Lipoprotein particle concentrations | 0.01  | 0.01  | -5.04  | 4.70E-07 | 8229 | 24456 |
| 23495 | Concentration of Large VLDL Particles                            | Lipoprotein particle concentrations | 0.00  | 0.00  | 4.94   | 7.66E-07 | 8229 | 24456 |
| 23530 | Concentration of Large LDL Particles                             | Lipoprotein particle concentrations | 0.00  | 0.00  | -4.33  | 1.53E-05 | 8229 | 24456 |
| 23523 | Concentration of IDL Particles                                   | Lipoprotein particle concentrations | 0.00  | 0.00  | -4.13  | 3.66E-05 | 8229 | 24456 |
| 23433 | Average Diameter for HDL Particles                               | Lipoprotein particle sizes          | 10.05 | 10.08 | -12.21 | 3.14E-34 | 8229 | 24456 |
| 23431 | Average Diameter for VLDL Particles                              | Lipoprotein particle sizes          | 35.71 | 35.59 | 8.59   | 8.99E-18 | 8229 | 24456 |
| 23432 | Average Diameter for LDL Particles                               | Lipoprotein particle sizes          | 24.06 | 24.07 | -8.13  | 4.27E-16 | 8229 | 24456 |
| 23438 | Sphingomyelins                                                   | Other lipids                        | 0.43  | 0.44  | -11.05 | 2.54E-28 | 8222 | 24440 |
| 23437 | Phosphatidylcholines                                             | Other lipids                        | 1.89  | 1.94  | -10.78 | 4.67E-27 | 8222 | 24440 |
| 23436 | Total Cholines                                                   | Other lipids                        | 2.34  | 2.39  | -10.49 | 1.11E-25 | 8222 | 24440 |
| 23434 | Phosphoglycerides                                                | Other lipids                        | 1.93  | 1.98  | -10.01 | 1.56E-23 | 8222 | 24440 |
| 23560 | Phospholipids in Large HDL                                       | Phospholipids                       | 0.57  | 0.59  | -13.31 | 2.47E-40 | 8229 | 24456 |
| 23414 | Phospholipids in HDL                                             | Phospholipids                       | 1.74  | 1.79  | -12.29 | 1.23E-34 | 8229 | 24456 |
| 23553 | Phospholipids in Very Large HDL                                  | Phospholipids                       | 0.16  | 0.17  | -11.04 | 2.63E-28 | 8229 | 24456 |
| 23567 | Phospholipids in Medium HDL                                      | Phospholipids                       | 0.49  | 0.50  | -9.92  | 3.65E-23 | 8229 | 24456 |
| 23411 | Total Phospholipids in Lipoprotein Particles                     | Phospholipids                       | 2.53  | 2.58  | -9.35  | 9.47E-21 | 8229 | 24456 |
| 23525 | Phospholipids in IDL                                             | Phospholipids                       | 0.26  | 0.26  | -7.53  | 5.06E-14 | 8229 | 24456 |
| 23483 | Phospholipids in Chylomicrons and Extremely Large VLDL           | Phospholipids                       | -0.03 | -0.03 | 7.46   | 8.58E-14 | 8229 | 24456 |

|       |                                                        |               |       |       |        |          |      |       |
|-------|--------------------------------------------------------|---------------|-------|-------|--------|----------|------|-------|
| 23490 | Phospholipids in Very Large VLDL                       | Phospholipids | -0.02 | -0.02 | 6.17   | 6.95E-10 | 8229 | 24456 |
| 23532 | Phospholipids in Large LDL                             | Phospholipids | 0.29  | 0.30  | -6.02  | 1.76E-09 | 8229 | 24456 |
| 23497 | Phospholipids in Large VLDL                            | Phospholipids | -0.03 | -0.03 | 5.73   | 9.94E-09 | 8229 | 24456 |
| 23413 | Phospholipids in LDL                                   | Phospholipids | 0.47  | 0.48  | -4.97  | 6.75E-07 | 8229 | 24456 |
| 23574 | Phospholipids in Small HDL                             | Phospholipids | 0.52  | 0.53  | -4.45  | 8.49E-06 | 8229 | 24456 |
| 23559 | Total Lipids in Large HDL                              | Total lipids  | 1.22  | 1.26  | -13.43 | 4.85E-41 | 8229 | 24456 |
| 23426 | Total Lipids in HDL                                    | Total lipids  | 3.56  | 3.65  | -13.13 | 2.91E-39 | 8229 | 24456 |
| 23552 | Total Lipids in Very Large HDL                         | Total lipids  | 0.32  | 0.33  | -11.39 | 5.38E-30 | 8229 | 24456 |
| 23566 | Total Lipids in Medium HDL                             | Total lipids  | 1.10  | 1.13  | -10.90 | 1.29E-27 | 8229 | 24456 |
| 23524 | Total Lipids in IDL                                    | Total lipids  | 1.07  | 1.10  | -7.91  | 2.70E-15 | 8229 | 24456 |
| 23482 | Total Lipids in Chylomicrons and Extremely Large VLDL  | Total lipids  | -0.19 | -0.21 | 7.64   | 2.24E-14 | 8229 | 24456 |
| 23531 | Total Lipids in Large LDL                              | Total lipids  | 1.28  | 1.31  | -6.47  | 1.01E-10 | 8229 | 24456 |
| 23489 | Total Lipids in Very Large VLDL                        | Total lipids  | -0.11 | -0.12 | 6.13   | 9.08E-10 | 8229 | 24456 |
| 23423 | Total Lipids in Lipoprotein Particles                  | Total lipids  | 6.62  | 6.74  | -6.05  | 1.43E-09 | 8229 | 24456 |
| 23425 | Total Lipids in LDL                                    | Total lipids  | 1.86  | 1.90  | -5.24  | 1.58E-07 | 8229 | 24456 |
| 23496 | Total Lipids in Large VLDL                             | Total lipids  | -0.08 | -0.09 | 4.61   | 3.97E-06 | 8229 | 24456 |
| 23573 | Total Lipids in Small HDL                              | Total lipids  | 0.92  | 0.93  | -4.32  | 1.58E-05 | 8229 | 24456 |
| 23487 | Triglycerides in Chylomicrons and Extremely Large VLDL | Triglycerides | -0.12 | -0.13 | 7.77   | 7.93E-15 | 8229 | 24456 |
| 23494 | Triglycerides in Very Large VLDL                       | Triglycerides | -0.08 | -0.08 | 6.40   | 1.61E-10 | 8229 | 24456 |
| 23578 | Triglycerides in Small HDL                             | Triglycerides | 0.01  | 0.00  | 6.31   | 2.77E-10 | 8229 | 24456 |
| 23408 | Triglycerides in VLDL                                  | Triglycerides | -0.21 | -0.24 | 5.20   | 1.97E-07 | 8229 | 24456 |
| 23407 | Total Triglycerides                                    | Triglycerides | -0.09 | -0.12 | 4.70   | 2.60E-06 | 8229 | 24456 |
| 23501 | Triglycerides in Large VLDL                            | Triglycerides | -0.04 | -0.04 | 4.36   | 1.28E-05 | 8229 | 24456 |
| 23550 | Triglycerides in Small LDL                             | Triglycerides | 0.00  | 0.00  | 4.13   | 3.68E-05 | 8229 | 24456 |



Table S8 ANCOVA results (F-tests) of gray matter volumes in brain regions (n=32,715)

| Brain region         | S1      | S2      | S3      | S4      | F value | P value  | FDR      |
|----------------------|---------|---------|---------|---------|---------|----------|----------|
| Postcentral L        | 1591.48 | 1602.74 | 1578.87 | 1592.44 | 8.54    | 1.15E-05 | 3.61E-04 |
| Caudate R            | 341.60  | 341.34  | 341.67  | 336.26  | 8.76    | 8.43E-06 | 3.61E-04 |
| Putamen L            | 706.53  | 700.99  | 705.39  | 699.58  | 8.72    | 8.89E-06 | 3.61E-04 |
| Putamen R            | 758.29  | 753.79  | 758.05  | 752.63  | 6.86    | 1.29E-04 | 3.04E-03 |
| ParaHippocampal L    | 676.57  | 679.55  | 673.45  | 677.15  | 6.28    | 2.94E-04 | 3.95E-03 |
| Pallidum L           | 80.17   | 78.25   | 79.60   | 78.90   | 6.30    | 2.89E-04 | 3.95E-03 |
| Thalamus R           | 936.16  | 946.55  | 933.18  | 935.33  | 6.44    | 2.37E-04 | 3.95E-03 |
| Paracentral Lobule R | 306.96  | 313.47  | 308.41  | 309.73  | 5.92    | 4.94E-04 | 4.65E-03 |
| Caudate L            | 369.67  | 367.92  | 368.43  | 365.12  | 5.94    | 4.78E-04 | 4.65E-03 |
| Pallidum R           | 110.96  | 109.31  | 110.79  | 109.74  | 5.92    | 4.95E-04 | 4.65E-03 |
| Parietal Inf R       | 640.69  | 645.05  | 635.61  | 640.53  | 4.88    | 2.15E-03 | 0.02     |
| Precuneus L          | 1284.70 | 1300.10 | 1277.55 | 1283.98 | 4.80    | 2.41E-03 | 0.02     |
| Paracentral Lobule L | 388.64  | 396.48  | 387.98  | 391.33  | 4.93    | 2.00E-03 | 0.02     |
| Thalamus L           | 952.41  | 962.76  | 950.73  | 952.28  | 4.81    | 2.38E-03 | 0.02     |
| Cingulate Mid L      | 1118.12 | 1118.10 | 1108.82 | 1114.73 | 4.68    | 2.85E-03 | 0.02     |
| ParaHippocampal R    | 813.90  | 815.82  | 809.37  | 813.34  | 4.58    | 3.30E-03 | 0.02     |
| Fusiform L           | 1629.85 | 1628.74 | 1619.68 | 1627.79 | 4.56    | 3.39E-03 | 0.02     |
| Frontal Inf Tri R    | 706.84  | 709.21  | 699.42  | 703.32  | 4.22    | 5.47E-03 | 0.03     |
| Postcentral R        | 1434.37 | 1439.98 | 1423.19 | 1432.63 | 4.20    | 5.63E-03 | 0.03     |
| Rolandic Oper R      | 559.26  | 559.29  | 552.90  | 557.99  | 4.06    | 6.78E-03 | 0.03     |
| Parietal Inf L       | 1193.76 | 1198.93 | 1185.17 | 1190.65 | 3.95    | 7.93E-03 | 0.03     |
| SupraMarginal R      | 872.48  | 877.85  | 867.79  | 874.30  | 3.96    | 7.86E-03 | 0.03     |
| Temporal Pole Mid L  | 414.40  | 415.16  | 411.19  | 414.08  | 3.94    | 8.03E-03 | 0.03     |

Table S9 Post hoc analysis results (two-tailed t-tests) of gray matter volumes in brain regions

| <b>Subtype 1 (n=5,730) vs Subtype 4 (n=19,128)</b> |           |           |                |                |            |
|----------------------------------------------------|-----------|-----------|----------------|----------------|------------|
| <b>Brain region</b>                                | <b>S1</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| Putamen L                                          | 706.53    | 699.58    | 4.32           | 1.54E-05       | 5.80E-04   |
| Caudate L                                          | 369.67    | 365.12    | 3.70           | 2.13E-04       | 1.84E-03   |
| Caudate R                                          | 341.60    | 336.26    | 3.82           | 1.33E-04       | 1.60E-03   |
| Pallidum L                                         | 80.17     | 78.90     | 3.71           | 2.10E-04       | 1.84E-03   |
| Putamen R                                          | 758.29    | 752.63    | 3.61           | 3.11E-04       | 2.15E-03   |
| Pallidum R                                         | 110.96    | 109.74    | 3.30           | 9.63E-04       | 5.11E-03   |
| Paracentral Lobule R                               | 306.96    | 309.73    | -2.91          | 3.56E-03       | 0.01       |
| <b>Subtype 2 (n=1,813) vs Subtype 4 (n=19,128)</b> |           |           |                |                |            |
| <b>Brain region</b>                                | <b>S2</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| Thalamus R                                         | 946.55    | 935.33    | 3.97           | 7.10E-05       | 1.36E-03   |
| Thalamus L                                         | 962.76    | 952.28    | 3.54           | 4.05E-04       | 2.51E-03   |
| Precuneus L                                        | 1300.10   | 1283.98   | 2.92           | 3.49E-03       | 0.01       |
| Paracentral Lobule R                               | 313.47    | 309.73    | 2.41           | 0.02           | 0.04       |
| <b>Subtype 3 (n=6,044) vs Subtype 4 (n=19,128)</b> |           |           |                |                |            |
| <b>Brain region</b>                                | <b>S3</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| Postcentral L                                      | 1578.87   | 1592.44   | -4.30          | 1.68E-05       | 5.80E-04   |
| Caudate R                                          | 341.67    | 336.26    | 3.95           | 7.91E-05       | 1.36E-03   |
| ParaHippocampal L                                  | 673.45    | 677.15    | -3.81          | 1.39E-04       | 1.60E-03   |
| Putamen L                                          | 705.39    | 699.58    | 3.67           | 2.47E-04       | 1.90E-03   |
| Putamen R                                          | 758.05    | 752.63    | 3.52           | 4.37E-04       | 2.51E-03   |
| Fusiform L                                         | 1619.68   | 1627.79   | -3.27          | 1.09E-03       | 5.35E-03   |
| Rolandic Oper R                                    | 552.90    | 557.99    | -3.06          | 2.20E-03       | 8.00E-03   |
| ParaHippocampal R                                  | 809.37    | 813.34    | -3.14          | 1.70E-03       | 7.83E-03   |
| Parietal Inf R                                     | 635.61    | 640.53    | -3.09          | 2.00E-03       | 8.00E-03   |
| SupraMarginal R                                    | 867.79    | 874.30    | -3.09          | 2.03E-03       | 8.00E-03   |
| Temporal Pole Mid L                                | 411.19    | 414.08    | -3.07          | 2.16E-03       | 8.00E-03   |
| Pallidum R                                         | 110.79    | 109.74    | 2.93           | 3.36E-03       | 0.01       |
| Postcentral R                                      | 1423.19   | 1432.63   | -2.88          | 4.01E-03       | 0.01       |
| Cingulate Mid L                                    | 1108.82   | 1114.73   | -2.76          | 5.82E-03       | 0.02       |
| Caudate L                                          | 368.43    | 365.12    | 2.73           | 6.29E-03       | 0.02       |
| Paracentral Lobule L                               | 387.98    | 391.33    | -2.36          | 0.02           | 0.05       |

Table S10 ANCOVA results (F-tests) of mean FA in white matter tracts (n=31,195)

| Field ID | Description                                            | S1     | S2     | S3     | S4     | F value | P value | FDR      |
|----------|--------------------------------------------------------|--------|--------|--------|--------|---------|---------|----------|
| 25064    | Mean FA in medial lemniscus on FA skeleton (right)     | 0.6323 | 0.6316 | 0.6307 | 0.6325 | 6.26    | 0.00    | 5.93E-03 |
| 25101    | Mean FA in uncinate fasciculus on FA skeleton (left)   | 0.5591 | 0.5621 | 0.5579 | 0.5597 | 6.19    | 0.00    | 5.93E-03 |
| 25089    | Mean FA in external capsule on FA skeleton (left)      | 0.5377 | 0.5385 | 0.5366 | 0.5378 | 4.85    | 0.00    | 0.02     |
| 25065    | Mean FA in medial lemniscus on FA skeleton (left)      | 0.6293 | 0.6287 | 0.6280 | 0.6296 | 4.82    | 0.00    | 0.02     |
| 25092    | Mean FA in cingulum hippocampus on FA skeleton (right) | 0.4810 | 0.4802 | 0.4786 | 0.4793 | 4.76    | 0.00    | 0.02     |
| 25100    | Mean FA in uncinate fasciculus on FA skeleton (right)  | 0.5683 | 0.5709 | 0.5675 | 0.5690 | 4.55    | 0.00    | 0.02     |
| 25087    | Mean FA in sagittal stratum on FA skeleton (left)      | 0.6403 | 0.6417 | 0.6393 | 0.6408 | 4.23    | 0.01    | 0.03     |
| 25088    | Mean FA in external capsule on FA skeleton (right)     | 0.5300 | 0.5310 | 0.5291 | 0.5300 | 4.17    | 0.01    | 0.03     |

Table S11 Post hoc analysis results (two-tailed t-tests) of mean FA in white matter tracts

| <b>Subtype 1 (n=5,457) vs Subtype 4 (n=18,251)</b> |                                                        |           |           |                |                |            |
|----------------------------------------------------|--------------------------------------------------------|-----------|-----------|----------------|----------------|------------|
| <b>Field ID</b>                                    | <b>Description</b>                                     | <b>S1</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| 25092                                              | Mean FA in cingulum hippocampus on FA skeleton (right) | 0.4810    | 0.4793    | 3.08           | 2.04E-03       | 8.18E-03   |
| <b>Subtype 2 (n=1,727) vs Subtype 4 (n=18,251)</b> |                                                        |           |           |                |                |            |
| <b>Field ID</b>                                    | <b>Description</b>                                     | <b>S2</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| 25101                                              | Mean FA in uncinate fasciculus on FA skeleton (left)   | 0.5621    | 0.5597    | 2.40           | 0.02           | 0.04       |
| <b>Subtype 3 (n=5,760) vs Subtype 4 (n=18,251)</b> |                                                        |           |           |                |                |            |
| <b>Field ID</b>                                    | <b>Description</b>                                     | <b>S3</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| 25064                                              | Mean FA in medial lemniscus on FA skeleton (right)     | 0.6307    | 0.6325    | -4.21          | 2.56E-05       | 6.13E-04   |
| 25065                                              | Mean FA in medial lemniscus on FA skeleton (left)      | 0.6280    | 0.6296    | -3.72          | 2.02E-04       | 2.43E-03   |
| 25089                                              | Mean FA in external capsule on FA skeleton (left)      | 0.5366    | 0.5378    | -3.41          | 6.62E-04       | 5.29E-03   |
| 25101                                              | Mean FA in uncinate fasciculus on FA skeleton (left)   | 0.5579    | 0.5597    | -3.11          | 1.85E-03       | 8.18E-03   |
| 25087                                              | Mean FA in sagittal stratum on FA skeleton (left)      | 0.6393    | 0.6408    | -3.16          | 1.59E-03       | 8.18E-03   |
| 25088                                              | Mean FA in external capsule on FA skeleton (right)     | 0.5291    | 0.5300    | -2.70          | 6.96E-03       | 0.02       |
| 25100                                              | Mean FA in uncinate fasciculus on FA skeleton (right)  | 0.5675    | 0.5690    | -2.64          | 8.36E-03       | 0.03       |

Table S12 ANCOVA results (F-tests) of mean MD in white matter tracts (n=31,195)

| Field ID | Description                                                            | S1       | S2       | S3       | S4       | F value | P value  | FDR      |
|----------|------------------------------------------------------------------------|----------|----------|----------|----------|---------|----------|----------|
| 25137    | Mean MD in external capsule on FA skeleton (left)                      | 6.18E-04 | 6.19E-04 | 6.20E-04 | 6.17E-04 | 9.74    | 2.03E-06 | 1.95E-04 |
| 25121    | Mean MD in anterior limb of internal capsule on FA skeleton (left)     | 5.86E-04 | 5.86E-04 | 5.88E-04 | 5.85E-04 | 8.75    | 8.52E-06 | 4.09E-04 |
| 25136    | Mean MD in external capsule on FA skeleton (right)                     | 6.32E-04 | 6.33E-04 | 6.34E-04 | 6.31E-04 | 7.63    | 4.26E-05 | 1.36E-03 |
| 25146    | Mean MD in superior fronto-occipital fasciculus on FA skeleton (right) | 4.53E-04 | 4.50E-04 | 4.54E-04 | 4.50E-04 | 6.12    | 3.71E-04 | 5.93E-03 |
| 25120    | Mean MD in anterior limb of internal capsule on FA skeleton (right)    | 5.81E-04 | 5.82E-04 | 5.83E-04 | 5.81E-04 | 5.95    | 4.74E-04 | 6.50E-03 |
| 25145    | Mean MD in superior longitudinal fasciculus on FA skeleton (left)      | 6.23E-04 | 6.23E-04 | 6.25E-04 | 6.23E-04 | 5.84    | 5.50E-04 | 6.60E-03 |
| 25118    | Mean MD in cerebral peduncle on FA skeleton (right)                    | 7.15E-04 | 7.18E-04 | 7.17E-04 | 7.16E-04 | 5.62    | 7.58E-04 | 8.08E-03 |
| 25144    | Mean MD in superior longitudinal fasciculus on FA skeleton (right)     | 6.35E-04 | 6.34E-04 | 6.36E-04 | 6.34E-04 | 5.54    | 8.47E-04 | 8.13E-03 |
| 25141    | Mean MD in cingulum hippocampus on FA skeleton (left)                  | 7.24E-04 | 7.24E-04 | 7.24E-04 | 7.22E-04 | 5.29    | 1.20E-03 | 0.01     |
| 25147    | Mean MD in superior fronto-occipital fasciculus on FA skeleton (left)  | 3.83E-04 | 3.79E-04 | 3.83E-04 | 3.80E-04 | 5.03    | 1.73E-03 | 0.01     |
| 25128    | Mean MD in superior corona radiata on FA skeleton (right)              | 5.99E-04 | 5.98E-04 | 6.00E-04 | 5.98E-04 | 4.18    | 5.78E-03 | 0.03     |

Table S13 Post hoc analysis results (two-tailed t-tests) of mean MD in white matter tracts

| <b>Subtype 1 (n=5,457) vs Subtype 4 (n=18,251)</b> |                                                                        |           |           |                |                |            |
|----------------------------------------------------|------------------------------------------------------------------------|-----------|-----------|----------------|----------------|------------|
| <b>Field ID</b>                                    | <b>Description</b>                                                     | <b>S1</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| 25147                                              | Mean MD in superior fronto-occipital fasciculus on FA skeleton (left)  | 3.83E-04  | 3.80E-04  | 2.78           | 5.36E-03       | 0.01       |
| 25137                                              | Mean MD in external capsule on FA skeleton (left)                      | 6.18E-04  | 6.17E-04  | 2.31           | 0.02           | 0.05       |
| 25121                                              | Mean MD in anterior limb of internal capsule on FA skeleton (left)     | 5.86E-04  | 5.85E-04  | 2.40           | 0.02           | 0.04       |
| <b>Subtype 2 (n=1,727) vs Subtype 4 (n=18,251)</b> |                                                                        |           |           |                |                |            |
| <b>Field ID</b>                                    | <b>Description</b>                                                     | <b>S2</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| 25118                                              | Mean MD in cerebral peduncle on FA skeleton (right)                    | 7.18E-04  | 7.16E-04  | 3.07           | 2.18E-03       | 6.53E-03   |
| <b>Subtype 3 (n=5,760) vs Subtype 4 (n=18,251)</b> |                                                                        |           |           |                |                |            |
| <b>Field ID</b>                                    | <b>Description</b>                                                     | <b>S3</b> | <b>S4</b> | <b>t Value</b> | <b>P value</b> | <b>FDR</b> |
| 25137                                              | Mean MD in external capsule on FA skeleton (left)                      | 6.20E-04  | 6.17E-04  | 5.20           | 1.96E-07       | 6.46E-06   |
| 25121                                              | Mean MD in anterior limb of internal capsule on FA skeleton (left)     | 5.88E-04  | 5.85E-04  | 4.90           | 9.62E-07       | 1.59E-05   |
| 25136                                              | Mean MD in external capsule on FA skeleton (right)                     | 6.34E-04  | 6.31E-04  | 4.69           | 2.76E-06       | 3.04E-05   |
| 25145                                              | Mean MD in superior longitudinal fasciculus on FA skeleton (left)      | 6.25E-04  | 6.23E-04  | 4.13           | 3.67E-05       | 3.03E-04   |
| 25120                                              | Mean MD in anterior limb of internal capsule on FA skeleton (right)    | 5.83E-04  | 5.81E-04  | 4.05           | 5.06E-05       | 3.34E-04   |
| 25146                                              | Mean MD in superior fronto-occipital fasciculus on FA skeleton (right) | 4.54E-04  | 4.50E-04  | 3.97           | 7.13E-05       | 3.36E-04   |
| 25144                                              | Mean MD in superior longitudinal fasciculus on FA skeleton (right)     | 6.36E-04  | 6.34E-04  | 3.98           | 7.05E-05       | 3.36E-04   |
| 25141                                              | Mean MD in cingulum hippocampus on FA skeleton (left)                  | 7.24E-04  | 7.22E-04  | 3.53           | 4.17E-04       | 1.72E-03   |
| 25128                                              | Mean MD in superior corona radiata on FA skeleton (right)              | 6.00E-04  | 5.98E-04  | 3.23           | 1.25E-03       | 4.57E-03   |
| 25147                                              | Mean MD in superior fronto-occipital fasciculus on FA skeleton (left)  | 3.83E-04  | 3.80E-04  | 3.18           | 1.49E-03       | 4.91E-03   |
| 25118                                              | Mean MD in cerebral peduncle on FA skeleton (right)                    | 7.17E-04  | 7.16E-04  | 2.89           | 3.90E-03       | 0.01       |

Table S14 The loadings of the latent variables in SEM models (Wald tests, two-sided P values)

| <b>Subtype 1 vs Subtype 4</b>                                      |                          |                |                   |
|--------------------------------------------------------------------|--------------------------|----------------|-------------------|
| <b>Latent variable</b>                                             | <b>Standard loadings</b> | <b>Z value</b> | <b>P(&gt; z )</b> |
| <b>Mental health</b> =~                                            |                          |                |                   |
| Depressive symptoms                                                | 0.85                     |                |                   |
| Anxiety symptoms                                                   | 0.53                     | 50.45          | <1.0E-15          |
| Self-harm                                                          | 0.51                     | 47.88          | <1.0E-15          |
| Trauma                                                             | 0.47                     | 44.94          | <1.0E-15          |
| Well-being                                                         | -0.47                    | -44.90         | <1.0E-15          |
| Mental distress                                                    | 0.62                     | 57.67          | <1.0E-15          |
| <b>Cognition</b> =~                                                |                          |                |                   |
| Fluid intelligence                                                 | 0.32                     |                |                   |
| Pairs matching                                                     | 0.12                     | 3.21           | 1.00E-03          |
| Reaction time                                                      | -0.25                    | -2.97          | 3.00E-03          |
| <b>Brain</b> =~                                                    |                          |                |                   |
| Putamen L                                                          | 0.94                     |                |                   |
| Caudate L                                                          | 0.58                     | 70.57          | <1.0E-15          |
| Caudate R                                                          | 0.60                     | 72.75          | <1.0E-15          |
| Pallidum L                                                         | 0.80                     | 119.80         | <1.0E-15          |
| Putamen R                                                          | 0.92                     | 172.51         | <1.0E-15          |
| Pallidum R                                                         | 0.86                     | 141.78         | <1.0E-15          |
| Parcntrl Lbl R                                                     | 0.09                     | 9.17           | <1.0E-15          |
| Mean FA in cingulum hippocampus on FA skeleton (right)             | 0.04                     | 4.16           | <1.0E-15          |
| Mean MD in external capsule on FA skeleton (left)                  | 0.18                     | 18.84          | <1.0E-15          |
| Mean MD in anterior limb of internal capsule on FA skeleton (left) | 0.27                     | 28.12          | <1.0E-15          |
| <b>Subtype 2 vs Subtype 4</b>                                      |                          |                |                   |
| <b>Latent variable</b>                                             | <b>Standard loadings</b> | <b>Z value</b> | <b>P(&gt; z )</b> |
| <b>Mental health</b> =~                                            |                          |                |                   |
| Depressive symptoms                                                | 0.84                     |                |                   |
| Anxiety symptoms                                                   | 0.54                     | 47.36          | <1.0E-15          |
| Psychotic experience                                               | 0.22                     | 19.18          | <1.0E-15          |
| Self-harm                                                          | 0.52                     | 45.45          | <1.0E-15          |
| Trauma                                                             | 0.49                     | 42.87          | <1.0E-15          |
| Well-being                                                         | -0.49                    | -42.49         | <1.0E-15          |
| Mental distress                                                    | 0.61                     | 52.85          | <1.0E-15          |
| <b>Cognition</b> =~                                                |                          |                |                   |
| Symbol-digit substitution                                          | 0.66                     |                |                   |
| Reaction time                                                      | -0.18                    | -2.36          | 0.01              |
| <b>Brain</b> =~                                                    |                          |                |                   |
| Thalamus R                                                         | 0.95                     |                |                   |
| Thalamus L                                                         | 0.94                     | 71.17          | <1.0E-15          |
| Precuneus L                                                        | 0.31                     | 29.40          | <1.0E-15          |
| Parcntrl Lbl R                                                     | 0.16                     | 14.53          | <1.0E-15          |
| Mean FA in uncinate fasciculus on FA skeleton (left)               | 0.09                     | 8.17           | <1.0E-15          |
| Mean MD in cerebral peduncle on FA skeleton (right)                | -0.04                    | -3.49          | <1.0E-15          |

| <b>Subtype 3 vs Subtype 4</b>                                          |                          |                |                   |
|------------------------------------------------------------------------|--------------------------|----------------|-------------------|
| <b>Latent variable</b>                                                 | <b>Standard loadings</b> | <b>Z value</b> | <b>P(&gt; z )</b> |
| <b>Mental health =~</b>                                                |                          |                |                   |
| Depressive symptoms                                                    | 0.73                     |                |                   |
| Anxiety symptoms                                                       | 0.63                     | 51.31          | <1.0E-15          |
| Self-harm                                                              | 0.54                     | 45.59          | <1.0E-15          |
| Trauma                                                                 | 0.55                     | 46.52          | <1.0E-15          |
| Well-being                                                             | -0.57                    | -47.89         | <1.0E-15          |
| <b>Cognition =~</b>                                                    |                          |                |                   |
| Symbol-digit substitution                                              | 0.67                     |                |                   |
| Fluid intelligence                                                     | 0.38                     | 9.88           | <1.0E-15          |
| Reaction time                                                          | -0.20                    | -9.29          | <1.0E-15          |
| <b>Brain =~</b>                                                        |                          |                |                   |
| Postcentral L                                                          | 0.22                     |                |                   |
| Caudate R                                                              | -0.21                    | -15.84         | <1.0E-15          |
| ParaHippcmpl L                                                         | 0.17                     | 14.16          | <1.0E-15          |
| Putamen L                                                              | -0.08                    | -7.59          | <1.0E-15          |
| Putamen R                                                              | -0.10                    | -9.12          | <1.0E-15          |
| Fusiform L                                                             | 0.21                     | 16.05          | <1.0E-15          |
| Rolandic Opr R                                                         | 0.16                     | 13.62          | <1.0E-15          |
| ParaHippcmpl R                                                         | 0.16                     | 13.42          | <1.0E-15          |
| Parietal Inf R                                                         | 0.12                     | 11.03          | <1.0E-15          |
| SupraMarginl R                                                         | 0.17                     | 13.95          | <1.0E-15          |
| Mean FA in medial lemniscus on FA skeleton (right)                     | 0.35                     | 19.84          | <1.0E-15          |
| Mean FA in medial lemniscus on FA skeleton (left)                      | 0.35                     | 19.76          | <1.0E-15          |
| Mean FA in external capsule on FA skeleton (left)                      | 0.63                     | 22.37          | <1.0E-15          |
| Mean FA in uncinate fasciculus on FA skeleton (left)                   | 0.40                     | 20.65          | <1.0E-15          |
| Mean FA in sagittal stratum on FA skeleton (left)                      | 0.52                     | 21.76          | <1.0E-15          |
| Mean FA in external capsule on FA skeleton (right)                     | 0.66                     | 22.50          | <1.0E-15          |
| Mean FA in uncinate fasciculus on FA skeleton (right)                  | 0.41                     | 20.68          | <1.0E-15          |
| Mean MD in external capsule on FA skeleton (left)                      | -0.76                    | -22.83         | <1.0E-15          |
| Mean MD in anterior limb of internal capsule on FA skeleton (left)     | -0.72                    | -22.71         | <1.0E-15          |
| Mean MD in external capsule on FA skeleton (right)                     | -0.79                    | -22.92         | <1.0E-15          |
| Mean MD in superior longitudinal fasciculus on FA skeleton (left)      | -0.82                    | -22.98         | <1.0E-15          |
| Mean MD in anterior limb of internal capsule on FA skeleton (right)    | -0.72                    | -22.73         | <1.0E-15          |
| Mean MD in superior fronto-occipital fasciculus on FA skeleton (right) | -0.67                    | -22.56         | <1.0E-15          |
| Mean MD in superior longitudinal fasciculus on FA skeleton (right)     | -0.84                    | -23.01         | <1.0E-15          |
| Mean MD in cingulum hippocampus on FA skeleton (left)                  | -0.38                    | -20.33         | <1.0E-15          |
| Mean MD in superior corona radiata on FA skeleton (right)              | -0.84                    | -23.01         | <1.0E-15          |
| Mean MD in superior fronto-occipital fasciculus on FA skeleton (left)  | -0.61                    | -22.31         | <1.0E-15          |



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