Supplementary Materials

Study Population

In the phase I analysis, we drew participants with available plasma metabolomic data previously generated in previous sub-studies, including the cross-sectional Mind-Body Study (NHSII: n=216, number of metabolites=470) and nested case-control studies of chronic stress (NHSII: n=222, number of metabolites=470), ovarian cancer (NHS: n=464, number of metabolites=473; NHSII: n=99, number of metabolites=470), and rheumatoid arthritis (NHS: n=457, number of metabolites=484; NHSII: n=248, number of metabolites=485). All of the sub-studies used three chromatographic methods, i.e. Hydrophilic interaction liquid chromatography (HILIC)-positive, C8-positive, and C18-negative columns, to achieve maximum coverage of metabolites. To balance the sample size between discovery and validation sets, minimize the influence of batch effect, and ensure that all the metabolites identified in the discovery set can be validated, we used the Mind-Body Study and case-control studies of chronic stress and ovarian cancer as the discovery set, and the case-control study of rheumatoid arthritis as the validation set. The difference in numbers of known metabolite across the sub-studies using the same profiling methods was primarily due to the evolving nature of the metabolite profiling and identification methods.

In the phase II analysis, we designed two nested case-control studies for diabetes: participants in the first study were selected from those in the phase I study and another three case-control studies using HILIC-positive and C8-positive methods in the NHS/NHSII, i.e., amyotrophic lateral sclerosis (NHS: n=111, number of metabolites=342), Parkinson's disease (NHS: n=318, number of metabolites=342), and breast cancer (NHSII: n=2089, number of metabolites=345); and participants in the second case-control study were drawn from three case-control studies using C8-positive method in the NHS, i.e., stroke (n=1035, number of metabolites=276), breast cancer (n=1120, metabolites=304), and colorectal cancer (n=817, number of metabolites=300).

Metabolomics Profiling

HILIC-positive analyses of polar metabolites were conducted using a liquid chromatography tandem mass spectrometry (LC-MS) system comprised of a Shimadzu Nexera X2 U-HPLC (Shimadzu Corp.; Marlborough, MA) coupled to a Q Exactive mass spectrometer (Thermo Fisher Scientific; Waltham, MA). Plasma samples (10 µL) were prepared via protein precipitation using 90 µL of acetonitrile/methanol/formic acid (74.9:24.9:0.2 v/v/v) containing stable isotope-labeled internal standards (valine-d8, Sigma-Aldrich; St. Louis, MO; and phenylalanine-d8, Cambridge Isotope Laboratories; Andover, MA). After centrifugation (9,000 x g,10 min, 4°C), the supernatants were injected directly onto a 150 x 2 mm, 3 µm Atlantis HILIC column (Waters; Milford, MA). The column was eluted isocratically at a flow rate of 250 µL/min with 5% mobile phase A (10 mM ammonium formate and 0.1% formic acid in water) for 0.5 minute followed by a linear gradient to

40% mobile phase B (acetonitrile with 0.1% formic acid) over 10 minutes. MS analyses were carried out using electrospray ionization in the positive ion mode using full scan analysis over 70-800 m/z at 70,000 resolution and 3 Hz data acquisition rate. Other MS settings were: sheath gas 40, sweep gas 2, spray voltage 3.5 kV, capillary temperature 350°C, S-lens RF 40, heater temperature 300°C, microscans 1, automatic gain control target 1e6, and maximum ion time 250 ms.

Plasma lipids were profiled using a LC-MS system comprised of a Shimadzu Nexera X2 U-HPLC (Shimadzu Corp.; Marlborough, MA) coupled to a Exactive Plus orbitrap mass spectrometer (Thermo Fisher Scientific; Waltham, MA). Lipids were extracted from plasma (10 µL) using 190 µL of isopropanol containing 1,2-didodecanoyl-sn-glycero-3-phosphocholine (Avanti Polar Lipids; Alabaster, AL). After centrifugation, supernatants were injected directly onto a 100 x 2.1 mm, 1.7 µm ACQUITY BEH C8 column (Waters; Milford, MA). The column was eluted isocratically with 80% mobile phase A (95:5:0.1 vol/vol/vol 10mM ammonium acetate/methanol/formic acid) for 1 minute followed by a linear gradient to 80% mobile-phase B (99.9:0.1 vol/vol methanol/formic acid) over 2 minutes, a linear gradient to 100% mobile phase B over 7 minutes, then 3 minutes at 100% mobile-phase B. MS analyses were carried out using electrospray ionization in the positive ion mode using full scan analysis over 200–1100 m/z at 70,000 resolution and 3 Hz data acquisition rate. Other MS settings were: sheath gas 50, in source CID 5 eV, sweep gas 5, spray voltage 3 kV, capillary temperature 300°C, S-lens RF 60, heater temperature 300°C, microscans 1, automatic gain control target 1e6, and maximum ion time 100 ms. Lipid identities were denoted by total acyl carbon number and total double bond number.

Metabolites of intermediate polarity were profiled using a Nexera X2 U-HPLC (Shimadzu Corp.; Marlborough, MA) coupled to a Q Exactive mass spectrometer (Thermo Fisher Scientific; Waltham, MA). Plasma samples (30 µL) were extracted using 90 µL of methanol containing PGE2-d4 as an internal standard (Cayman Chemical Co.; Ann Arbor, MI) and centrifuged (9,000 x g, 10 min, 4°C). The supernatants (10 µL) were injected onto a 150 x 2.1 mm ACQUITY BEH C18 column (Waters; Milford, MA). The column was eluted isocratically at a flow rate of 450 µL/min with 20% mobile phase A (0.01% formic acid in water) for 3 minutes followed by a linear gradient to 100% mobile phase B (0.01% acetic acid in acetonitril) over 12 minutes. MS analyses were carried out using electrospray ionization in the negative ion mode using full scan analysis over 70-850 m/z. Additional MS settings were: sheath gas 45, spray voltage -3.5 kV, capillary temperature 320°C, heater temperature 300 °C, auxiliary gas 10, and S-lens RF level 60.

Covariate assessment

In the biennial follow-up questionnaires, we collected information on lifestyle factors and medical history, including age, body weight, smoking status, physical activity, regular aspirin/ nonsteroidal anti-inflammatory drug use, menopausal status, menopausal hormone therapy, and history of chronic diseases. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Participants who smoked ≥1 cigarette/d for >6 months were defined as smokers. Physical activity was calculated as the product sum of the metabolic equivalent (MET) values of each specific

recreational activity and hours spent on that activity per week. For non-dietary covariates in this analysis, we used data from the questionnaires administered closest in time to blood draw.

Ascertainment of type 2 diabetes

Incident diabetes cases were identified by self-reports on the biennial questionnaires and confirmed by a supplementary questionnaire inquiring diagnosis date, symptoms, blood glucose levels, and medication use. Before 1998, confirmation of diabetes required at least one of the following criteria from the National Diabetes Data Group (1): 1) classic symptoms such as excessive thirst, polyuria, weight loss, and hunger, plus elevated fasting glucose levels ≥ 7.8 mmol/L (140 mg/dL) or non-fasting glucose ≥ 11.1 mmol/L (200 mg/dL); 2) asymptomatic but elevated glucose levels (by the above criteria) in two separate occasions or abnormal glucose tolerance test results; or 3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). After 1998, a fasting glucose level ≥ 7 mmol/L (126 mg/dL) was adopted according to the new diagnostic criteria of the American Diabetes Association. This supplementary questionnaire has been validated in previous studies with ≥97% questionnaire-confirmed cases reconfirmed through medical record review by a blinded study physician (2,3).

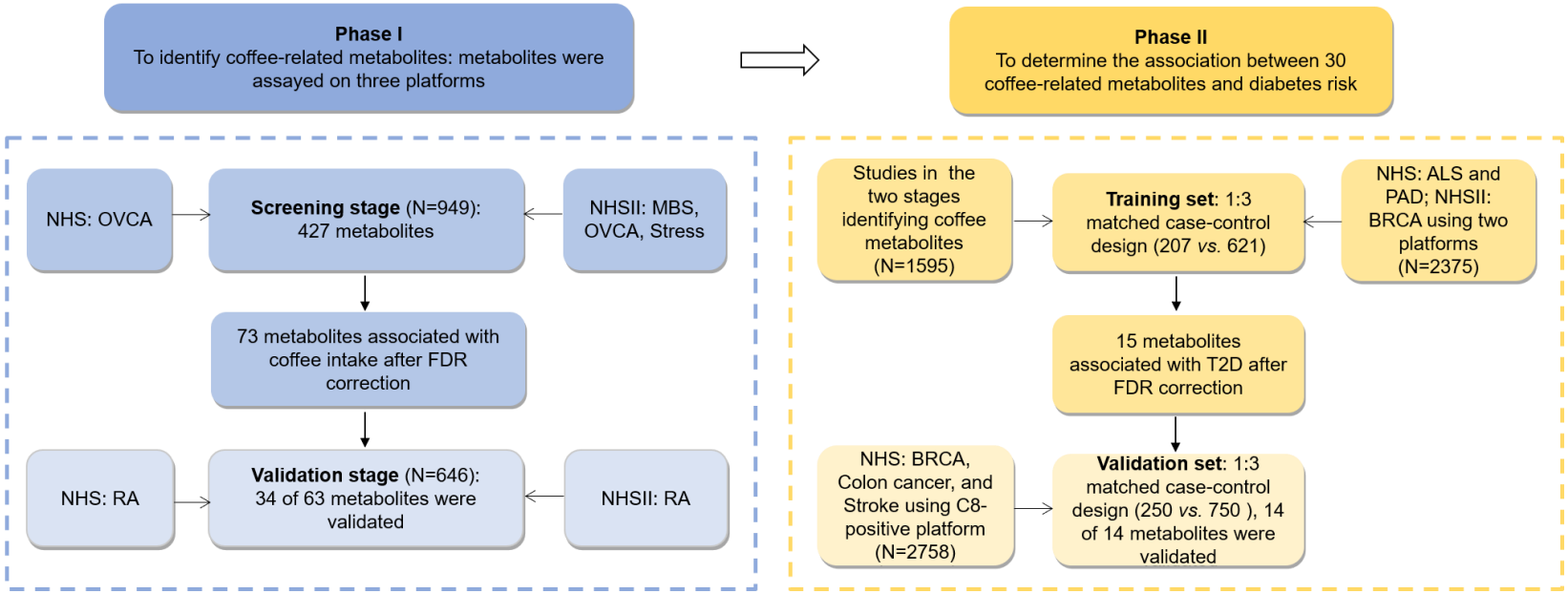
Reference

1. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. National Diabetes Data Group. Diabetes 1979;28:1039-1057

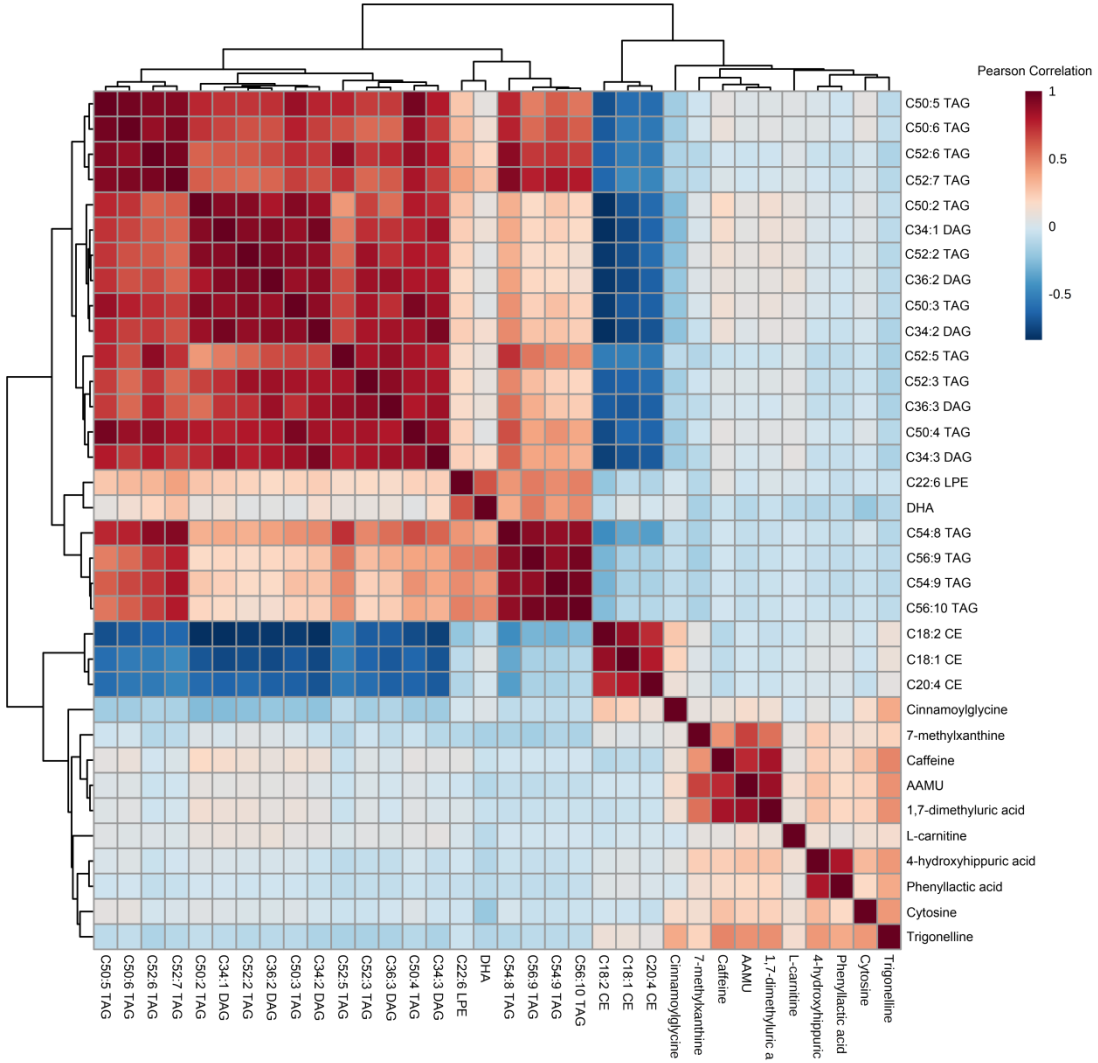
2. Hu FB, Leitzmann MF, Stampfer MJ, Colditz GA, Willett WC, Rimm EB. Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. Arch Intern Med 2001;161:1542-1548

3. Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. Lancet 1991;338:774-778

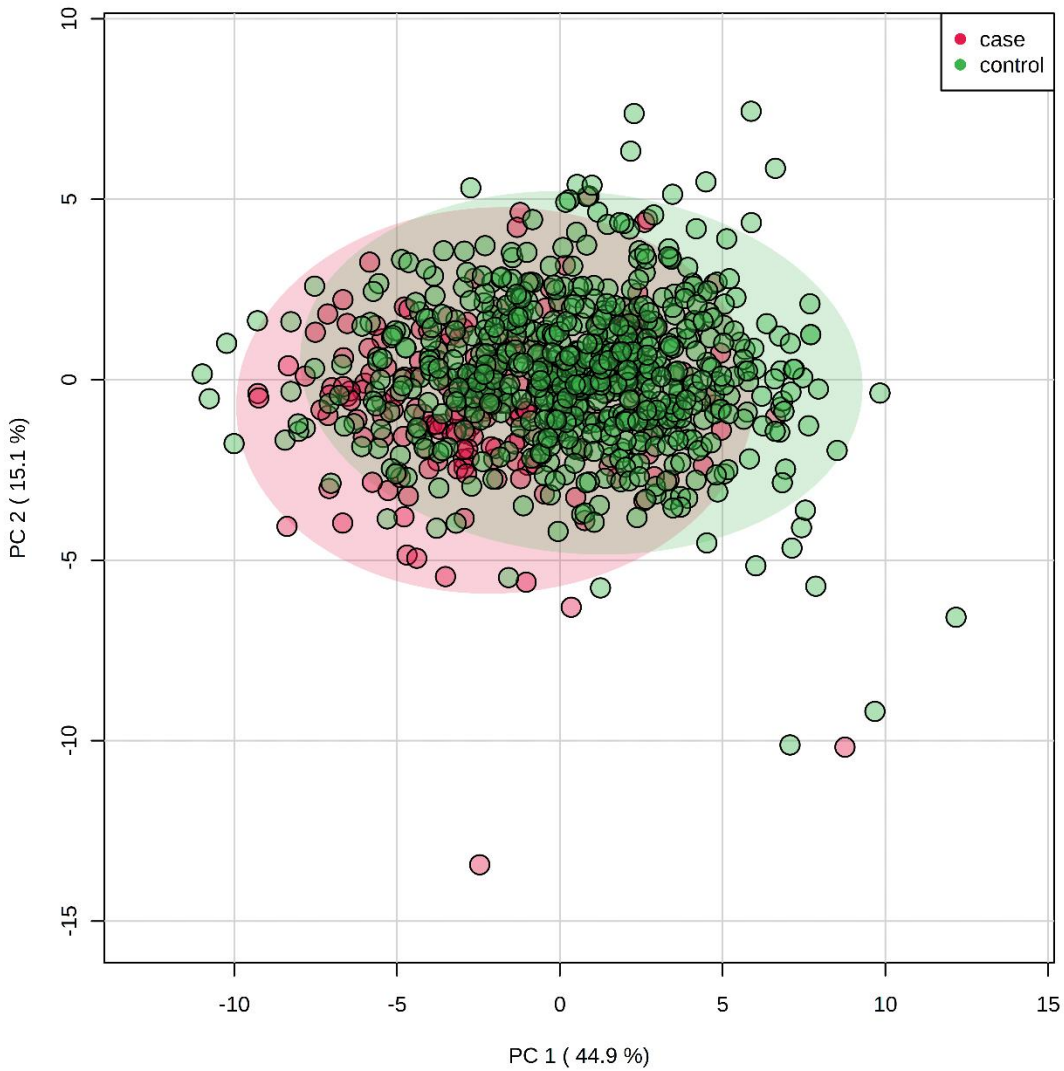
Supplementary Figures and Tables



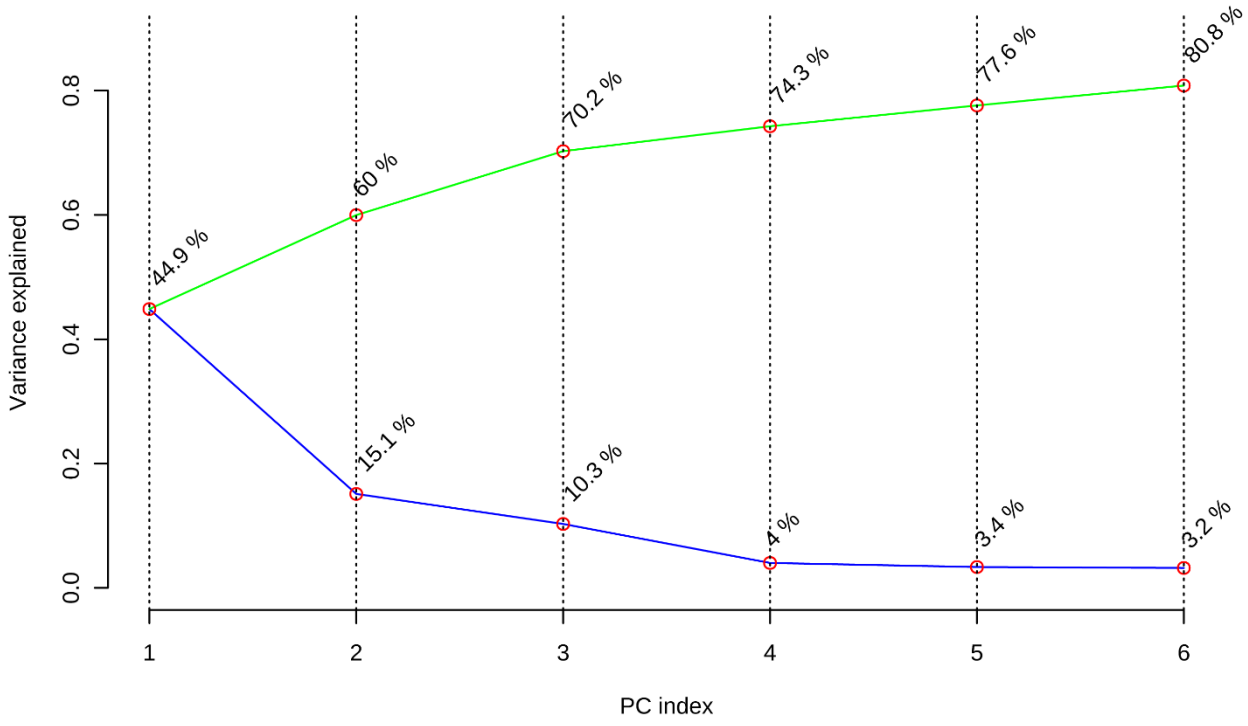
Supplementary Figure 1 Flowchart of study participant selection. Abbreviation: NHS, Nurses' Health Study; OVCA, ovarian cancer; MBS, Mind-Body Study; FDR, false discovery rate; RA, rheumatoid arthritis; ALS, amyotrophic lateral sclerosis; PAD, Parkinson's disease; BRCA, breast cancer.



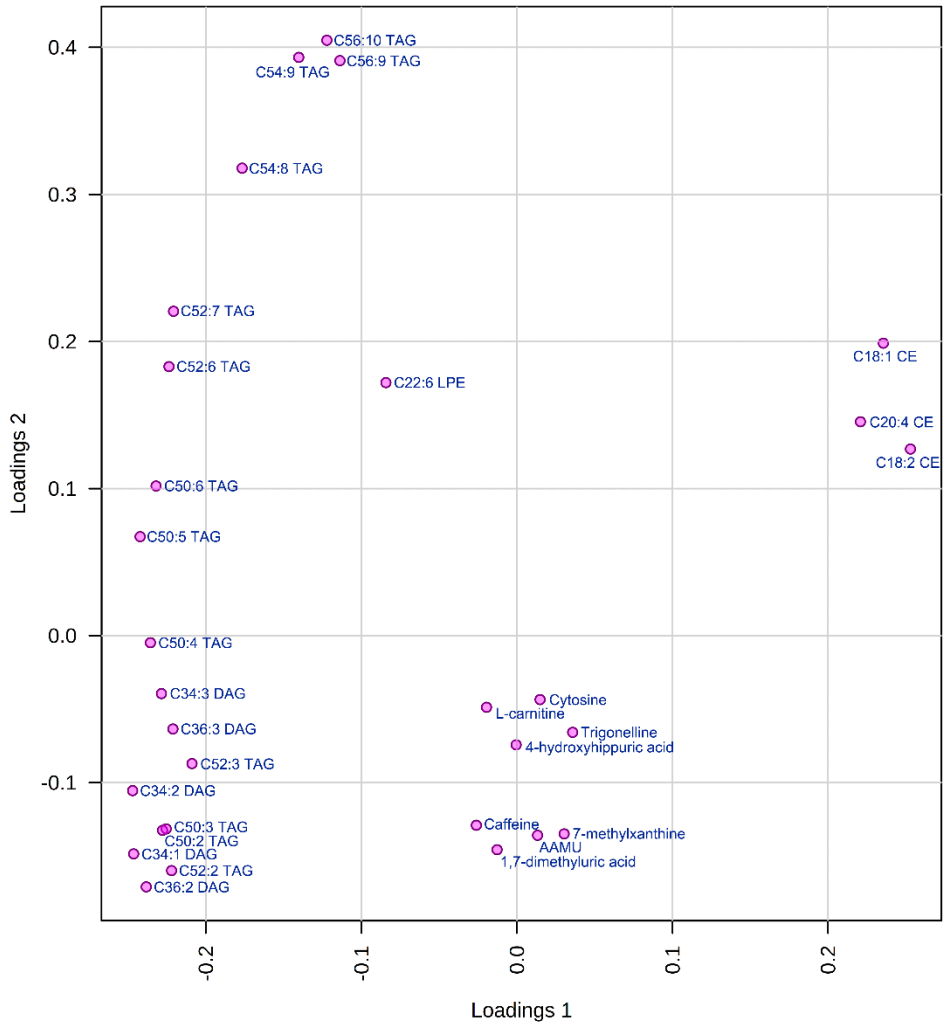
Supplementary Figure 2 Pairwise Pearson correlation matrix of 34 plasma metabolites that were identified to be associated with coffee consumption.



Supplementary Figure 3 Principal component analysis (PCA) score plot of the first two PCs for 30 coffee-related metabolites in a nested case-control study for type 2 diabetes (207 cases and 621 controls)



Supplementary Figure 3 Principal component analysis (PCA) scree plot for 30 coffee-related metabolites in a nested case-control study for type 2 diabetes (207 cases and 621 controls)



Supplementary Figure 3 Principal component analysis (PCA) loading plot for 30 coffee-related metabolites in a nested case-control study for type 2 diabetes (207 cases and 621 controls)

Supplementary Table 1 Metabolites analyzed in the current study

HMDB ID	Method	Metabolite name	Super class	Available in the coffee validation
HMDB00026	HILIC-pos	N-carbamoyl-beta-alanine	Organic acids and derivatives	Yes
HMDB00043	HILIC-pos	betaine	Organic acids and derivatives	Yes
HMDB00050	HILIC-pos	adenosine	Nucleosides, nucleotides, and analogues	Yes
HMDB00054	HILIC-pos	bilirubin	Organoheterocyclic compounds	Yes
HMDB00056	HILIC-pos	beta-alanine	Organic acids and derivatives	Yes
HMDB00062	HILIC-pos	L-carnitine	Organic nitrogen compounds	Yes
HMDB00063	HILIC-pos	cortisol	Lipids and lipid-like moleculesolecules	Yes
HMDB00064	HILIC-pos	creatine	Organic acids and derivatives	Yes
HMDB00086	HILIC-pos	alpha-glycerophosphocholine	Lipids and lipid-like moleculesolecules	Yes
HMDB00092	HILIC-pos	dimethylglycine	Organic acids and derivatives	Yes
HMDB00097	HILIC-pos	choline	Organic nitrogen compounds	Yes
HMDB00112	HILIC-pos	GABA	Organic acids and derivatives	Yes
HMDB00123	HILIC-pos	glycine	Organic acids and derivatives	Yes
HMDB00128	HILIC-pos	guanidoacetic acid	Organic acids and derivatives	Yes
HMDB00132	HILIC-pos	guanine	Organoheterocyclic compounds	Yes
HMDB00138	C18-neg	glycocholate	Lipids and lipid-like moleculesolecules	Yes
HMDB00148	HILIC-pos	glutamate	Organic acids and derivatives	Yes
HMDB00157	HILIC-pos	hypoxanthine	Organoheterocyclic compounds	Yes
HMDB00158	HILIC-pos	tyrosine	Organic acids and derivatives	Yes
HMDB00159	HILIC-pos	phenylalanine	Organic acids and derivatives	Yes
HMDB00161	HILIC-pos	alanine	Organic acids and derivatives	Yes
HMDB00162	HILIC-pos	proline	Organic acids and derivatives	Yes
HMDB00167	HILIC-pos	threonine	Organic acids and derivatives	Yes
HMDB00168	HILIC-pos	asparagine	Organic acids and derivatives	Yes
HMDB00172	HILIC-pos	isoleucine	Organic acids and derivatives	Yes
HMDB00177	HILIC-pos	histidine	Organic acids and derivatives	Yes
HMDB00182	HILIC-pos	lysine	Organic acids and derivatives	Yes
HMDB00187	HILIC-pos	serine	Organic acids and derivatives	Yes
HMDB00195	HILIC-pos	inosine	Nucleosides, nucleotides, and analogues	Yes

HMDB00201	HILIC-pos	C2 carnitine	Lipids and lipid-like molecules	Yes
HMDB00206	HILIC-pos	N6-acetyl-L-lysine	Organic acids and derivatives	Yes
HMDB00207	C18-neg	oleate	Lipids and lipid-like molecules	Yes
HMDB00214	HILIC-pos	ornithine	Organic acids and derivatives	Yes
HMDB00220	C18-neg	palmitate	Lipids and lipid-like molecules	Yes
HMDB00222	HILIC-pos	C16 carnitine	Lipids and lipid-like molecules	Yes
HMDB00235	HILIC-pos	thiamine	Organoheterocyclic compounds	Yes
HMDB00248	HILIC-pos	thyroxine	Organic acids and derivatives	Yes
HMDB00251	HILIC-pos	taurine	Organic acids and derivatives	Yes
HMDB00252	C8-pos	sphingosine	Organic nitrogen compounds	Yes
HMDB00269	HILIC-pos	sphinganine	Organic nitrogen compounds	Yes
HMDB00277	C18-neg	sphingosine 1-phosphate	Lipids and lipid-like molecules	Yes
HMDB00289	HILIC-pos	urate	Organoheterocyclic compounds	Yes
HMDB00292	HILIC-pos	xanthine	Organoheterocyclic compounds	Yes
HMDB00299	HILIC-pos	xanthosine	Nucleosides, nucleotides, and analogues	Yes
HMDB00462	HILIC-pos	allantoin	Organoheterocyclic compounds	Yes
HMDB00472	HILIC-pos	5-hydroxytryptophan	Organoheterocyclic compounds	Yes
HMDB00479	HILIC-pos	3-methylhistidine	Organic acids and derivatives	Yes
HMDB00511	C18-neg	caprate	Lipids and lipid-like molecules	Yes
HMDB00517	C8-pos	C52:7 TAG	Lipids and lipid-like molecules	Yes
HMDB00529	C18-neg	5-dodecenoate	Lipids and lipid-like molecules	Yes
HMDB00562	HILIC-pos	creatinine	Organic acids and derivatives	Yes
HMDB00610	C8-pos	C18:2 CE	Lipids and lipid-like molecules	Yes
HMDB00619	C18-neg	cholate	Lipids and lipid-like molecules	Yes
HMDB00623	C18-neg	dodecanedioate	Lipids and lipid-like molecules	Yes
HMDB00626	C18-neg	deoxycholate	Lipids and lipid-like molecules	Yes
HMDB00630	HILIC-pos	cytosine	Organoheterocyclic compounds	Yes
HMDB00630_1	HILIC-pos	cytosine_isomer	Organoheterocyclic compounds	Yes
HMDB00631	C18-neg	glycodeoxycholate	Lipids and lipid-like molecules	Yes
HMDB00637	C18-neg	glycochenodeoxycholate	Lipids and lipid-like molecules	Yes
HMDB00638	C18-neg	dodecanoate	Lipids and lipid-like molecules	Yes
HMDB00641	HILIC-pos	glutamine	Organic acids and derivatives	Yes
HMDB00651	HILIC-pos	C10 carnitine	Lipids and lipid-like molecules	Yes

HMDB00658	C8-pos	C16:1 CE	Lipids and lipid-like molecules	Yes
HMDB00670	HILIC-pos	homoarginine	Organic acids and derivatives	Yes
HMDB00672	C18-neg	hexadecanedioate	Lipids and lipid-like molecules	Yes
HMDB00673	C18-neg	linoleate	Lipids and lipid-like molecules	Yes
HMDB00687	HILIC-pos	leucine	Organic acids and derivatives	Yes
HMDB00688	HILIC-pos	C5 carnitine	Lipids and lipid-like molecules	Yes
HMDB00696	HILIC-pos	methionine	Organic acids and derivatives	Yes
HMDB00699	HILIC-pos	1-methylnicotinamide	Organoheterocyclic compounds	Yes
HMDB00705	HILIC-pos	C6 carnitine	Lipids and lipid-like molecules	Yes
HMDB00708	C18-neg	glycoursodeoxycholate	Lipids and lipid-like molecules	Yes
HMDB00716	HILIC-pos	pipecolic acid	Organic acids and derivatives	Yes
HMDB00725	HILIC-pos	hydroxyproline	Organic acids and derivatives	Yes
HMDB00767	HILIC-pos	pseudouridine	Nucleosides, nucleotides, and analogues	Yes
HMDB00772	C18-neg	nonadecanoate	Lipids and lipid-like molecules	Yes
HMDB00774	C18-neg	pregnenolone sulfate	Lipids and lipid-like molecules	Yes
HMDB00779	C18-neg	phenyllactic acid	Phenylpropanoids and polyketides	Yes
HMDB00791	HILIC-pos	C8 carnitine	Lipids and lipid-like molecules	Yes
HMDB00792	C18-neg	sebacate	Lipids and lipid-like molecules	Yes
HMDB00801	C18-neg	phytanate	Lipids and lipid-like molecules	Yes
HMDB00806	C18-neg	myristate	Lipids and lipid-like molecules	Yes
HMDB00812	HILIC-pos	N-acetylaspartic acid	Organic acids and derivatives	Yes
HMDB00824	HILIC-pos	C3 carnitine	Lipids and lipid-like molecules	Yes
HMDB00826	C18-neg	pentadecanoate	Lipids and lipid-like molecules	Yes
HMDB00827	C18-neg	stearate	Lipids and lipid-like molecules	Yes
HMDB00848	HILIC-pos	C18 carnitine	Lipids and lipid-like molecules	Yes
HMDB00870	HILIC-pos	histamine	Organic nitrogen compounds	Yes
HMDB00872	C18-neg	tetradecanedioate	Lipids and lipid-like molecules	Yes
HMDB00874	C18-neg	tauroursodeoxycholate	Lipids and lipid-like molecules	Yes
HMDB00875	HILIC-pos	trigonelline	Alkaloids and derivatives	Yes
HMDB00883	HILIC-pos	valine	Organic acids and derivatives	Yes
HMDB00884	HILIC-pos	ribothymidine	Nucleosides, nucleotides, and analogues	Yes
HMDB00885	C8-pos	C16:0 CE	Lipids and lipid-like molecules	Yes
HMDB00895	HILIC-pos	acetylcholine	Organic nitrogen compounds	Yes

HMDB00896	C18-neg	taurodeoxycholate	Lipids and lipid-like molecules	Yes
HMDB00897	HILIC-pos	7-methylguanine	Organoheterocyclic compounds	Yes
HMDB00904	HILIC-pos	citrulline	Organic acids and derivatives	Yes
HMDB00918	C8-pos	C18:1 CE	Lipids and lipid-like molecules	Yes
HMDB00925	HILIC-pos	trimethylamine-N-oxide	Organic nitrogen compounds	Yes
HMDB00929	HILIC-pos	tryptophan	Organoheterocyclic compounds	Yes
HMDB00951	C18-neg	taurochenodeoxycholate	Lipids and lipid-like molecules	Yes
HMDB00965	HILIC-pos	hypotaurine	Organic acids and derivatives	Yes
HMDB00991	HILIC-pos	2-aminooctanoate	Organic acids and derivatives	Yes
HMDB01008	HILIC-pos	biliverdin	Organoheterocyclic compounds	Yes
HMDB01043	C18-neg	arachidonate	Lipids and lipid-like molecules	Yes
HMDB01046	HILIC-pos	cotinine	Organoheterocyclic compounds	Yes
HMDB01276	HILIC-pos	N1-acetylspermidine	Organic acids and derivatives	Yes
HMDB01325	HILIC-pos	N6,N6,N6-trimethyllysine	Organic acids and derivatives	Yes
HMDB01348	HILIC-pos	C18:0 SM	Lipids and lipid-like molecules	Yes
HMDB01388	C18-neg	alpha-linolenate	Lipids and lipid-like molecules	Yes
HMDB01390	HILIC-pos	hydroxycotinine	Organoheterocyclic compounds	Yes
HMDB01406	HILIC-pos	niacinamide	Organoheterocyclic compounds	Yes
HMDB01431	HILIC-pos	pyridoxamine	Organoheterocyclic compounds	Yes
HMDB01539	HILIC-pos	ADMA/SDMA	Organic acids and derivatives	Yes
HMDB01563	HILIC-pos	1-methylguanosine	Nucleosides, nucleotides, and analogues	Yes
HMDB01847	HILIC-pos	caffeine	Organoheterocyclic compounds	Yes
HMDB01855	HILIC-pos	5-hydroxytryptophol	Organoheterocyclic compounds	Yes
HMDB01859	HILIC-pos	acetaminophen	Benzenoids	Yes
HMDB01906	HILIC-pos	2-aminoisobutyric acid	Organic acids and derivatives	Yes
HMDB01954	C18-neg	3-hydroxyoctanoate	Organic acids and derivatives	Yes
HMDB01976	C18-neg	docosapentaenoate	Lipids and lipid-like molecules	Yes
HMDB01991	HILIC-pos	7-methylxanthine	Organoheterocyclic compounds	Yes
HMDB01999	C18-neg	eicosapentaenoate	Lipids and lipid-like molecules	Yes
HMDB02000	C18-neg	myristoleate	Lipids and lipid-like molecules	Yes
HMDB02005	HILIC-pos	methionine sulfoxide	Organic acids and derivatives	Yes
HMDB02013	HILIC-pos	C4 carnitine	Lipids and lipid-like molecules	Yes
HMDB02014	HILIC-pos	C14:1 carnitine	Lipids and lipid-like molecules	Yes

HMDB02064	HILIC-pos	N-acetylputrescine	Organic acids and derivatives	Yes
HMDB02068	C18-neg	13-docosenoate	Lipids and lipid-like molecules	Yes
HMDB02172	HILIC-pos	N1,N12-diacetylspermine	Organic acids and derivatives	Yes
HMDB02183	C18-neg	docosahexaenoic acid	Lipids and lipid-like molecules	Yes
HMDB02203	HILIC-pos	3-hydroxydecanoate	Organic acids and derivatives	Yes
HMDB02212	C18-neg	arachidate	Lipids and lipid-like molecules	Yes
HMDB02226	C18-neg	adrenate	Lipids and lipid-like molecules	Yes
HMDB02231	C18-neg	eicosenoate	Lipids and lipid-like molecules	Yes
HMDB02250	HILIC-pos	C12 carnitine	Lipids and lipid-like molecules	Yes
HMDB02259	C18-neg	heptadecanoate	Lipids and lipid-like molecules	Yes
HMDB02271	HILIC-pos	imidazole propionate	Organoheterocyclic compounds	Yes
HMDB02366	HILIC-pos	C5:1 carnitine	Lipids and lipid-like molecules	Yes
HMDB02368	C18-neg	nervonate	Lipids and lipid-like molecules	Yes
HMDB02802	HILIC-pos	cortisone	Lipids and lipid-like molecules	Yes
HMDB02815	C8-pos	C18:1 LPC	Lipids and lipid-like molecules	Yes
HMDB02815_1	C8-pos	C18:1 LPC_B	Lipids and lipid-like molecules	Yes
HMDB02820	HILIC-pos	methylimidazoleacetic acid	Organoheterocyclic compounds	Yes
HMDB02925	C18-neg	eicosatrienoate	Lipids and lipid-like molecules	Yes
HMDB03229	C18-neg	palmitoleate	Lipids and lipid-like molecules	Yes
HMDB03282	HILIC-pos	1-methylguanine	Organoheterocyclic compounds	Yes
HMDB03331	HILIC-pos	1-methyladenosine	Nucleosides, nucleotides, and analogues	Yes
HMDB03333	HILIC-pos	8-hydroxy-deoxyguanosine	Nucleosides, nucleotides, and analogues	Yes
HMDB03334	HILIC-pos	SDMA	Organic acids and derivatives	Yes
HMDB03357	HILIC-pos	N-acetylornithine	Organic acids and derivatives	Yes
HMDB03681	HILIC-pos	4-acetamidobutanoate	Organic acids and derivatives	Yes
HMDB04193	HILIC-pos	N1-methyl-2-pyridone-5-carboxamide	Organoheterocyclic compounds	Yes
HMDB04231	C18-neg	pantothenol	Lipids and lipid-like molecules	Yes
HMDB04400	HILIC-pos	5-acetylamino-6-amino-3-methyluracil	Organic nitrogen compounds	Yes
HMDB04620	HILIC-pos	N-alpha-acetyl-L-arginine	Organic acids and derivatives	Yes
HMDB04824	HILIC-pos	N2,N2-dimethylguanosine	Nucleosides, nucleotides, and analogues	Yes
HMDB04827	HILIC-pos	proline betaine	Organic acids and derivatives	Yes
HMDB04949	C8-pos	C16:0 Ceramide (d18:1)	Lipids and lipid-like molecules	Yes

HMDB04952	C8-pos	C22:0 Ceramide (d18:1)	Lipids and lipid-like molecules	Yes
HMDB04953	C8-pos	C24:1 Ceramide (d18:1)	Lipids and lipid-like molecules	Yes
HMDB04956	C8-pos	C24:0 Ceramide (d18:1)	Lipids and lipid-like molecules	Yes
HMDB05060	C8-pos	eicosadienoate	Lipids and lipid-like molecules	Yes
HMDB05065	HILIC-pos	C18:1 carnitine	Lipids and lipid-like molecules	Yes
HMDB05066	HILIC-pos	C14 carnitine	Lipids and lipid-like molecules	Yes
HMDB05356	C8-pos	C48:0 TAG	Lipids and lipid-like molecules	Yes
HMDB05357	C8-pos	C50:0 TAG	Lipids and lipid-like molecules	Yes
HMDB05359	C8-pos	C48:1 TAG	Lipids and lipid-like molecules	Yes
HMDB05360	C8-pos	C50:1 TAG	Lipids and lipid-like molecules	Yes
HMDB05363	C8-pos	C52:4 TAG	Lipids and lipid-like molecules	Yes
HMDB05365	C8-pos	C52:0 TAG	Lipids and lipid-like molecules	Yes
HMDB05367	C8-pos	C52:1 TAG	Lipids and lipid-like molecules	Yes
HMDB05369	C8-pos	C52:2 TAG	Lipids and lipid-like molecules	Yes
HMDB05370	C8-pos	C54:4 TAG	Lipids and lipid-like molecules	Yes
HMDB05376	C8-pos	C48:2 TAG	Lipids and lipid-like molecules	Yes
HMDB05377	C8-pos	C50:2 TAG	Lipids and lipid-like molecules	Yes
HMDB05380	C8-pos	C52:5 TAG	Lipids and lipid-like molecules	Yes
HMDB05384	C8-pos	C52:3 TAG	Lipids and lipid-like molecules	Yes
HMDB05385	C8-pos	C54:5 TAG	Lipids and lipid-like molecules	Yes
HMDB05391	C8-pos	C54:6 TAG	Lipids and lipid-like molecules	Yes
HMDB05392	C8-pos	C56:8 TAG	Lipids and lipid-like molecules	Yes
HMDB05395	C8-pos	C54:1 TAG	Lipids and lipid-like molecules	Yes
HMDB05396	C8-pos	C56:1 TAG	Lipids and lipid-like molecules	Yes
HMDB05398	C8-pos	C56:4 TAG	Lipids and lipid-like molecules	Yes
HMDB05403	C8-pos	C54:2 TAG	Lipids and lipid-like molecules	Yes
HMDB05404	C8-pos	C56:2 TAG	Lipids and lipid-like molecules	Yes
HMDB05405	C8-pos	C54:3 TAG	Lipids and lipid-like molecules	Yes
HMDB05406	C8-pos	C56:5 TAG	Lipids and lipid-like molecules	Yes
HMDB05410	C8-pos	C56:3 TAG	Lipids and lipid-like molecules	Yes
HMDB05413	C8-pos	C58:8 TAG	Lipids and lipid-like molecules	Yes
HMDB05432	C8-pos	C48:3 TAG	Lipids and lipid-like molecules	Yes
HMDB05433	C8-pos	C50:3 TAG	Lipids and lipid-like molecules	Yes

HMDB05435	C8-pos	C50:4 TAG	Lipids and lipid-like molecules	Yes
HMDB05436	C8-pos	C52:6 TAG	Lipids and lipid-like molecules	Yes
HMDB05447	C8-pos	C54:7 TAG	Lipids and lipid-like molecules	Yes
HMDB05448	C8-pos	C56:9 TAG	Lipids and lipid-like molecules	Yes
HMDB05456	C8-pos	C56:6 TAG	Lipids and lipid-like molecules	Yes
HMDB05458	C8-pos	C58:6 TAG	Lipids and lipid-like molecules	Yes
HMDB05462	C8-pos	C56:7 TAG	Lipids and lipid-like molecules	Yes
HMDB05463	C8-pos	C58:9 TAG	Lipids and lipid-like molecules	Yes
HMDB05471	C8-pos	C58:7 TAG	Lipids and lipid-like molecules	Yes
HMDB05476	C8-pos	C58:10 TAG	Lipids and lipid-like molecules	Yes
HMDB05478	C8-pos	C60:12 TAG	Lipids and lipid-like molecules	Yes
HMDB05923	HILIC-pos	N4-acetylcytidine	Nucleosides, nucleotides, and analogues	Yes
HMDB06111	C8-pos	12-HETE	Lipids and lipid-like molecules	Yes
HMDB06344	HILIC-pos	phenylacetylglutamine	Organic acids and derivatives	Yes
HMDB06347	HILIC-pos	C26 carnitine	Lipids and lipid-like molecules	Yes
HMDB06469	HILIC-pos	C18:2 carnitine	Lipids and lipid-like molecules	Yes
HMDB06725	C8-pos	C14:0 CE	Lipids and lipid-like molecules	Yes
HMDB06726	C8-pos	C20:4 CE	Lipids and lipid-like molecules	Yes
HMDB06729	C8-pos	C22:4 CE	Lipids and lipid-like molecules	Yes
HMDB06731	C8-pos	C20:5 CE	Lipids and lipid-like molecules	Yes
HMDB06733	C8-pos	C22:6 CE	Lipids and lipid-like molecules	Yes
HMDB06736	C8-pos	C20:3 CE	Lipids and lipid-like molecules	Yes
HMDB06831	HILIC-pos	butyrobetaine	Lipids and lipid-like molecules	Yes
HMDB07011	C8-pos	C30:0 DAG	Lipids and lipid-like molecules	Yes
HMDB07098	C8-pos	C32:0 DAG	Lipids and lipid-like molecules	Yes
HMDB07099	C8-pos	C32:1 DAG	Lipids and lipid-like molecules	Yes
HMDB07100	C8-pos	C34:0 DAG	Lipids and lipid-like molecules	Yes
HMDB07102	C8-pos	C34:1 DAG	Lipids and lipid-like molecules	Yes
HMDB07103	C8-pos	C34:2 DAG	Lipids and lipid-like molecules	Yes
HMDB07128	C8-pos	C32:2 DAG	Lipids and lipid-like molecules	Yes
HMDB07132	C8-pos	C34:3 DAG	Lipids and lipid-like molecules	Yes
HMDB07158	C8-pos	C36:0 DAG	Lipids and lipid-like molecules	Yes
HMDB07199	C8-pos	C38:5 DAG	Lipids and lipid-like molecules	Yes

HMDB07216	C8-pos	C36:1 DAG	Lipids and lipid-like molecules	Yes
HMDB07218	C8-pos	C36:2 DAG	Lipids and lipid-like molecules	Yes
HMDB07219	C8-pos	C36:3 DAG	Lipids and lipid-like molecules	Yes
HMDB07248	C8-pos	C36:4 DAG	Lipids and lipid-like molecules	Yes
HMDB07869	C8-pos	C30:0 PC	Lipids and lipid-like molecules	Yes
HMDB07870	C8-pos	C30:1 PC	Lipids and lipid-like molecules	Yes
HMDB07871	C8-pos	C32:0 PC	Lipids and lipid-like molecules	Yes
HMDB07873	C8-pos	C32:1 PC	Lipids and lipid-like molecules	Yes
HMDB07874	C8-pos	C32:2 PC	Lipids and lipid-like molecules	Yes
HMDB07883	C8-pos	C34:4 PC	Lipids and lipid-like molecules	Yes
HMDB07970	C8-pos	C34:0 PC	Lipids and lipid-like molecules	Yes
HMDB07972	C8-pos	C34:1 PC	Lipids and lipid-like molecules	Yes
HMDB07973	C8-pos	C34:2 PC	Lipids and lipid-like molecules	Yes
HMDB07983	C8-pos	C36:4 PC	Lipids and lipid-like molecules	Yes
HMDB07991	C8-pos	C38:6 PC	Lipids and lipid-like molecules	Yes
HMDB08006	C8-pos	C34:3 PC	Lipids and lipid-like molecules	Yes
HMDB08036	C8-pos	C36:0 PC	Lipids and lipid-like molecules	Yes
HMDB08038	C8-pos	C36:1 PC	Lipids and lipid-like molecules	Yes
HMDB08039	C8-pos	C36:2 PC	Lipids and lipid-like molecules	Yes
HMDB08039_1	C8-pos	C36:2 PC-B	Lipids and lipid-like molecules	Yes
HMDB08047	C8-pos	C38:3 PC	Lipids and lipid-like molecules	Yes
HMDB08048	C8-pos	C38:4 PC	Lipids and lipid-like molecules	Yes
HMDB08057	C8-pos	C40:6 PC	Lipids and lipid-like molecules	Yes
HMDB08105	C8-pos	C36:3 PC	Lipids and lipid-like molecules	Yes
HMDB08138	C8-pos	C36:4 PC-B	Lipids and lipid-like molecules	Yes
HMDB08270	C8-pos	C38:2 PC	Lipids and lipid-like molecules	Yes
HMDB08511	C8-pos	C40:10 PC	Lipids and lipid-like molecules	Yes
HMDB08731	C8-pos	C40:9 PC	Lipids and lipid-like molecules	Yes
HMDB08923	C8-pos	C32:0 PE	Lipids and lipid-like molecules	Yes
HMDB08925	C8-pos	C34:0 PE	Lipids and lipid-like molecules	Yes
HMDB08928	C8-pos	C34:2 PE	Lipids and lipid-like molecules	Yes
HMDB08937	C8-pos	C36:4 PE	Lipids and lipid-like molecules	Yes
HMDB08942	C8-pos	C38:2 PE	Lipids and lipid-like molecules	Yes

HMDB08952	C8-pos	C34:2 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB08991	C8-pos	C36:0 PE	Lipids and lipid-like molecules	Yes
HMDB08993	C8-pos	C36:1 PE	Lipids and lipid-like molecules	Yes
HMDB08994	C8-pos	C36:2 PE	Lipids and lipid-like molecules	Yes
HMDB09003	C8-pos	C38:4 PE	Lipids and lipid-like molecules	Yes
HMDB09016	C8-pos	C36:1 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB09060	C8-pos	C36:3 PE	Lipids and lipid-like molecules	Yes
HMDB09069	C8-pos	C38:5 PE	Lipids and lipid-like molecules	Yes
HMDB09082	C8-pos	C36:2 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB09102	C8-pos	C38:6 PE	Lipids and lipid-like molecules	Yes
HMDB09805	C8-pos	C34:0 PI	Lipids and lipid-like molecules	Yes
HMDB09815	C8-pos	C38:4 PI	Lipids and lipid-like molecules	Yes
HMDB10167	C8-pos	C40:6 PS	Lipids and lipid-like molecules	Yes
HMDB10169	HILIC-pos	C16:0 SM	Lipids and lipid-like molecules	Yes
HMDB10316	HILIC-pos	acetaminophen glucuronide	Organic oxygen compounds	Yes
HMDB10368	C8-pos	C18:0 CE	Lipids and lipid-like molecules	Yes
HMDB10370	C8-pos	C18:3 CE	Lipids and lipid-like molecules	Yes
HMDB10375	C8-pos	C22:5 CE	Lipids and lipid-like molecules	Yes
HMDB10379	C8-pos	C14:0 LPC	Lipids and lipid-like molecules	Yes
HMDB10382	C8-pos	C16:0 LPC	Lipids and lipid-like molecules	Yes
HMDB10382_1	C8-pos	C16:0 LPC-B	Lipids and lipid-like molecules	Yes
HMDB10383	C8-pos	C16:1 LPC	Lipids and lipid-like molecules	Yes
HMDB10384	C8-pos	C18:0 LPC	Lipids and lipid-like molecules	Yes
HMDB10386	C8-pos	C18:2 LPC	Lipids and lipid-like molecules	Yes
HMDB10395	C8-pos	C20:4 LPC	Lipids and lipid-like molecules	Yes
HMDB10397	C8-pos	C20:5 LPC	Lipids and lipid-like molecules	Yes
HMDB10403	HILIC-pos	C22:5 LPC	Lipids and lipid-like molecules	Yes
HMDB10404	C8-pos	C22:6 LPC	Lipids and lipid-like molecules	Yes
HMDB10407	HILIC-pos	C16:1 LPC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB10411	C8-pos	C46:0 TAG	Lipids and lipid-like molecules	Yes
HMDB10412	C8-pos	C46:1 TAG	Lipids and lipid-like molecules	Yes
HMDB10419	C8-pos	C46:2 TAG	Lipids and lipid-like molecules	Yes
HMDB10471	C8-pos	C50:5 TAG	Lipids and lipid-like molecules	Yes

HMDB10497	C8-pos	C50:6 TAG	Lipids and lipid-like molecules	Yes
HMDB10498	C8-pos	C54:9 TAG	Lipids and lipid-like molecules	Yes
HMDB10513	C8-pos	C56:10 TAG	Lipids and lipid-like molecules	Yes
HMDB10517	C8-pos	C52:7 TAG	Lipids and lipid-like molecules	Yes
HMDB10518	C8-pos	C54:8 TAG	Lipids and lipid-like molecules	Yes
HMDB10531	C8-pos	C58:11 TAG	Lipids and lipid-like molecules	Yes
HMDB11103	HILIC-pos	1,7-dimethyluric acid	Organoheterocyclic compounds	Yes
HMDB11130	C8-pos	C18:0 LPE	Lipids and lipid-like molecules	Yes
HMDB11131	C8-pos	C18:0 MAG	Lipids and lipid-like molecules	Yes
HMDB11208	C8-pos	C34:1 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11210	C8-pos	C34:2 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11211	C8-pos	C34:3 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11212	C8-pos	C34:4 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11214	C8-pos	C34:5 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11220	C8-pos	C36:5 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11221	C8-pos	C36:5 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11229	C8-pos	C38:7 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11239	C8-pos	C34:1 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11241	C8-pos	C36:1 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11243	C8-pos	C36:2 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11244	C8-pos	C36:3 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11252	C8-pos	C38:4 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11294	C8-pos	C40:7 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11310	C8-pos	C36:4 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11319	C8-pos	C38:6 PC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11343	C8-pos	C34:3 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11384	C8-pos	C38:3 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11386	C8-pos	C38:5 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11387	C8-pos	C38:6 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11394	C8-pos	C40:7 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11410	C8-pos	C36:5 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11420	C8-pos	C38:7 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11441	C8-pos	C36:3 PE plasmalogen	Lipids and lipid-like molecules	Yes

HMDB11442	C8-pos	C36:4 PE plasmalogen	Lipids and lipid-like molecules	Yes
HMDB11478	HILIC-pos	C18:3 LPE	Lipids and lipid-like molecules	Yes
HMDB11503	C8-pos	C16:0 LPE	Lipids and lipid-like molecules	Yes
HMDB11506	C8-pos	C18:1 LPE	Lipids and lipid-like molecules	Yes
HMDB11507	C8-pos	C18:2 LPE	Lipids and lipid-like molecules	Yes
HMDB11511	HILIC-pos	C20:0 LPE	Lipids and lipid-like molecules	Yes
HMDB11512	HILIC-pos	C20:1 LPE	Lipids and lipid-like molecules	Yes
HMDB11517	C8-pos	C20:4 LPE	Lipids and lipid-like molecules	Yes
HMDB11526	C8-pos	C22:6 LPE	Lipids and lipid-like molecules	Yes
HMDB11565	C8-pos	C16:1 MAG	Lipids and lipid-like molecules	Yes
HMDB11621	HILIC-pos	cinnamoylglycine	Organic acids and derivatives	Yes
HMDB11697	C8-pos	C24:0 SM	Lipids and lipid-like molecules	Yes
HMDB11705	C8-pos	C49:1 TAG	Lipids and lipid-like molecules	Yes
HMDB11706	C8-pos	C49:2 TAG	Lipids and lipid-like molecules	Yes
HMDB12097	C8-pos	C14:0 SM	Lipids and lipid-like molecules	Yes
HMDB12101	C8-pos	C18:1 SM	Lipids and lipid-like molecules	Yes
HMDB12101_1	C8-pos	C18:1 SM-B	Lipids and lipid-like molecules	Yes
HMDB12102	C8-pos	C20:0 SM	Lipids and lipid-like molecules	Yes
HMDB12103	C8-pos	C22:0 SM	Lipids and lipid-like molecules	Yes
HMDB12104	C8-pos	C22:1 SM	Lipids and lipid-like molecules	Yes
HMDB12107	C8-pos	C24:1 SM	Lipids and lipid-like molecules	Yes
HMDB12252	HILIC-pos	linoleoyl ethanolamide	Organic nitrogen compounds	Yes
HMDB12356	C8-pos	C34:0 PS	Lipids and lipid-like molecules	Yes
HMDB12362	C8-pos	C38:6 PS	Lipids and lipid-like molecules	Yes
HMDB13122	C8-pos	C18:1 LPC plasmalogen	Lipids and lipid-like molecules	Yes
HMDB13122_1	C8-pos	C18:1 LPC plasmalogen-B	Lipids and lipid-like molecules	Yes
HMDB13127	HILIC-pos	C4-OH carnitine	Lipids and lipid-like molecules	Yes
HMDB13130	HILIC-pos	C5-DC carnitine	Lipids and lipid-like molecules	Yes
HMDB13133	HILIC-pos	C3-DC-CH3 carnitine	Lipids and lipid-like molecules	Yes
HMDB13238	HILIC-pos	C7 carnitine	Lipids and lipid-like molecules	Yes
HMDB13287	HILIC-pos	Ne,Ne dimethyllysine	Organic acids and derivatives	Yes
HMDB13288	HILIC-pos	C9 carnitine	Lipids and lipid-like molecules	Yes
HMDB13325	HILIC-pos	C10:2 carnitine	Lipids and lipid-like molecules	Yes

HMDB13326	HILIC-pos	C12:1 carnitine	Lipids and lipid-like molecules	Yes
HMDB13331	HILIC-pos	C14:2 carnitine	Lipids and lipid-like molecules	Yes
HMDB13678	HILIC-pos	4-hydroxyhippuric acid	Benzenoids	Yes
HMDB13713	HILIC-pos	N-acetyltryptophan	Organic acids and derivatives	Yes
HMDB29377	HILIC-pos	piperine	Alkaloids and derivatives	Yes
HMDB29416	HILIC-pos	NMMA	Organic acids and derivatives	Yes
HMDB42063	C8-pos	C44:0 TAG	Lipids and lipid-like molecules	Yes
HMDB42076	C8-pos	C47:2 TAG	Lipids and lipid-like molecules	Yes
HMDB42099	C8-pos	C45:1 TAG	Lipids and lipid-like molecules	Yes
HMDB42100	C8-pos	C47:1 TAG	Lipids and lipid-like molecules	Yes
HMDB42103	C8-pos	C49:3 TAG	Lipids and lipid-like molecules	Yes
HMDB42196	C8-pos	C53:2 TAG	Lipids and lipid-like molecules	Yes
HMDB42226	C8-pos	C55:2 TAG	Lipids and lipid-like molecules	Yes
HMDB42466	C8-pos	C55:3 TAG	Lipids and lipid-like molecules	Yes
HMDB43170	C8-pos	C45:2 TAG	Lipids and lipid-like molecules	Yes
HMDB60038	C18-neg	10-heptadecenoate	Lipids and lipid-like molecules	Yes
HMDB61710	C18-neg	17-methylstearate	Lipids and lipid-like molecules	Yes
HMDB00017	HILIC-pos	4-pyridoxate	Organoheterocyclic compounds	No
HMDB00122	HILIC-pos	glucose	Organic oxygen compounds	No
HMDB00197	HILIC-pos	indoleacetic acid	Organoheterocyclic compounds	No
HMDB00210	HILIC-pos	pantothenate	Organic acids and derivatives	No
HMDB00212	HILIC-pos	N-acetylgalactosamine	Organic oxygen compounds	No
HMDB00267	HILIC-pos	pyroglutamic acid	Organic acids and derivatives	No
HMDB00267_1	HILIC-pos	pyroglutamic acid_isomor	Organic acids and derivatives	No
HMDB00666	C18-neg	heptanoate	Lipids and lipid-like molecules	No
HMDB00679	HILIC-pos	homocitrulline	Organic acids and derivatives	No
HMDB00714	HILIC-pos	hippurate	Benzenoids	No
HMDB00720	C18-neg	levulinate	Organic acids and derivatives	No
HMDB00766	HILIC-pos	N-acetylalanine	Organic acids and derivatives	No
HMDB00786	HILIC-pos	oxypurinol	Organoheterocyclic compounds	No
HMDB01182	HILIC-pos	6,8-dihydroxypurine	Organoheterocyclic compounds	No
HMDB01414	HILIC-pos	putrescine	Organic nitrogen compounds	No
HMDB01488	HILIC-pos	nicotinate	Organoheterocyclic compounds	No

HMDB01545	HILIC-pos	pyridoxal	Organoheterocyclic compounds	No
HMDB01855_1	HILIC-pos	5-hydroxytryptophol_isomer	Organoheterocyclic compounds	No
HMDB01886	HILIC-pos	3-methylxanthine	Organoheterocyclic compounds	No
HMDB02369	C18-neg	9-cis-retinoic acid	Lipids and lipid-like molecules	No
HMDB03073	C18-neg	gamma-linolenic acid	Lipids and lipid-like molecules	No
HMDB03231	C18-neg	transvaccenate	Lipids and lipid-like molecules	No
HMDB03282_1	HILIC-pos	1-methylguanine_isomer	Organoheterocyclic compounds	No
HMDB04158_1	HILIC-pos	urobilinogen_isomer	Organoheterocyclic compounds	No
HMDB04667	C18-neg	13-HODE	Lipids and lipid-like molecules	No
HMDB04827_1	HILIC-pos	proline betaine_isomer	Organic acids and derivatives	No
HMDB04953_1	C8-pos	C24:1 Ceramide (d18:1)-B	Lipids and lipid-like molecules	No
HMDB05362	C8-pos	C51:2 TAG	Lipids and lipid-like molecules	No
HMDB05362_1	C8-pos	C51:2 TAG-B	Lipids and lipid-like molecules	No
HMDB05391_1	C8-pos	C54:6 TAG-B	Lipids and lipid-like molecules	No
HMDB05447_1	C8-pos	C54:7 TAG-B	Lipids and lipid-like molecules	No
HMDB07170	C8-pos	C38:4 DAG	Lipids and lipid-like molecules	No
HMDB09789	C8-pos	C36:4 PI	Lipids and lipid-like molecules	No
HMDB09809	C8-pos	C36:2 PI	Lipids and lipid-like molecules	No
HMDB10387	C8-pos	C18:3 LPC	Lipids and lipid-like molecules	No
HMDB11520	C8-pos	C22:0 LPE	Lipids and lipid-like molecules	No
HMDB11582	C8-pos	C22:1 MAG	Lipids and lipid-like molecules	No
HMDB11701	C8-pos	C51:3 TAG	Lipids and lipid-like molecules	No
HMDB11701_1	C8-pos	C51:3 TAG-B	Lipids and lipid-like molecules	No
HMDB12107_1	C8-pos	C24:1 SM-B	Lipids and lipid-like molecules	No
HMDB13299	HILIC-pos	pentadecanol	Lipids and lipid-like molecules	No
HMDB13733	HILIC-pos	trimethylbenzene	Benzenoids	No
HMDB13733_1	HILIC-pos	trimethylbenzene_isomer	Benzenoids	No
HMDB31106	C8-pos	C51:0 TAG	Lipids and lipid-like molecules	No
HMDB31106_1	C8-pos	C51:0 TAG-B	Lipids and lipid-like molecules	No
HMDB33585	C18-neg	acesulfame	Organic acids and derivatives	No
HMDB42104	C8-pos	C51:1 TAG	Lipids and lipid-like molecules	No
HMDB42104_1	C8-pos	C51:1 TAG-B	Lipids and lipid-like molecules	No
HMDB43058	C8-pos	C53:3 TAG	Lipids and lipid-like molecules	No

HMDB55685	C8-pos	C54:10 TAG	Lipids and lipid-like molecules	No
HMDB62548	C18-neg	2-hydroxyhexadecanoate	Lipids and lipid-like molecules	No
HMDB62658	C18-neg	10-nonadecenoate	Lipids and lipid-like molecules	No

Supplementary Table 2 Percentage differences (95% confidence intervals) in validated metabolites according to coffee consumption among never smokers[1]

HMDB ID	Metabolite name	Super class	Pooled never smokers		
			Total coffee per cup increase	Caffeinated coffee per cup increase	Decaffeinated coffee per cup increase
HMDB00875	Trigonelline	Alkaloids and derivatives	50.3(45.1, 55.7)	48.4(42.3, 54.7)	30.6(21.1, 40.8)
HMDB04400	AAMU	Organic nitrogen compounds	26.9(21.3, 32.8)	35.7(29.2, 42.5)	-3.2(-11.0, 5.2)
HMDB11621	Cinnamoylglycine	Organic acids and derivatives	18.2(13.2, 23.5)	15.9(10.4, 21.7)	15.7(7.0, 25.0)
HMDB11103	1,7-dimethyluric acid	Organoheterocyclic compounds	21.4(16.1, 27.1)	32.3(26.0, 38.9)	-9.9(-17.0, -2.2)
HMDB01847	Caffeine	Organoheterocyclic compounds	19.2(14.2, 24.4)	28.4(22.6, 34.5)	-8.6(-15.4, -1.3)
HMDB00779	Phenyllactic acid	Phenylpropanoids and polyketides	12.9(8.2, 17.8)	10.7(5.6, 16.1)	13.8(5.5, 22.7)
HMDB13678	4-hydroxyhippuric acid	Benzenoids	13.9(9.1, 19.0)	13.1(7.8, 18.7)	10.7(2.6, 19.6)
HMDB00630	Cytosine	Organoheterocyclic compounds	10.2(5.3, 15.3)	11.6(6.2, 17.3)	2.1(-5.7, 10.5)
HMDB01991	7-methylxanthine	Organoheterocyclic compounds	10.0(5.0, 15.3)	12.2(6.6, 18.2)	0.6(-7.3, 9.3)
HMDB00062	L-carnitine	Organic nitrogen compounds	6.0(1.4, 10.8)	9.2(3.9, 14.7)	-3.9(-11.1, 3.8)
HMDB06726	C20:4 CE	Lipids and lipid-like molecules	3.2(-1.3, 8.0)	2.8(-2.2, 8.0)	3.3(-4.5, 11.7)
HMDB00918	C18:1 CE	Lipids and lipid-like molecules	4.3(0.01, 8.7)	2.4(-2.3, 7.3)	7.1(-0.5, 15.2)
HMDB00610	C18:2 CE	Lipids and lipid-like molecules	5.3(1.1, 9.7)	3.8(-0.8, 8.6)	7.1(-0.3, 15.0)
HMDB05377	C50:2 TAG	Lipids and lipid-like molecules	-5.8(-9.5, -1.8)	-5.0(-9.3, -0.6)	-5.5(-12.0, 1.6)
HMDB07102	C34:1 DAG	Lipids and lipid-like molecules	-5.6(-9.5, -1.6)	-5.8(-10.0, -1.4)	-3.0(-9.8, 4.3)
HMDB10497	C50:6 TAG	Lipids and lipid-like molecules	-6.2(-10.2, -2.0)	-5.7(-10.2, -1.0)	-4.9(-11.9, 2.7)
HMDB10513	C56:10 TAG	Lipids and lipid-like molecules	-6.9(-11.1, -2.7)	-7.3(-11.8, -2.5)	-3.4(-10.8, 4.6)
HMDB10471	C50:5 TAG	Lipids and lipid-like molecules	-5.6(-9.6, -1.4)	-5.1(-9.6, -0.4)	-4.7(-11.7, 2.9)
HMDB05433	C50:3 TAG	Lipids and lipid-like molecules	-5.6(-9.5, -1.4)	-4.8(-9.2, -0.2)	-5.4(-12.2, 2.0)
HMDB05369	C52:2 TAG	Lipids and lipid-like molecules	-6.3(-10.2, -2.3)	-6.2(-10.5, -1.7)	-4.4(-11.2, 3.0)
HMDB10498	C54:9 TAG	Lipids and lipid-like molecules	-8.3(-12.5, -3.9)	-8.9(-13.5, -4.0)	-3.5(-11.2, 4.9)
HMDB11526	C22:6 LPE	Lipids and lipid-like molecules	-5.9(-10.0, -1.6)	-5.6(-10.1, -0.7)	-4.5(-11.7, 3.3)
HMDB07218	C36:2 DAG	Lipids and lipid-like molecules	-4.5(-8.5, -0.4)	-4.7(-9.0, -0.1)	-2.2(-9.1, 5.3)

HMDB05435	C50:4 TAG	Lipids and lipid-like molecules	-5.2(-9.2, -1.0)	-4.6(-9.1, 0.1)	-4.5(-11.5, 3.0)
HMDB05448	C56:9 TAG	Lipids and lipid-like molecules	-5.7(-9.8, -1.4)	-5.9(-10.4, -1.1)	-3.2(-10.4, 4.7)
HMDB07103	C34:2 DAG	Lipids and lipid-like molecules	-6.8(-10.6, -2.8)	-6.6(-10.8, -2.2)	-4.6(-11.3, 2.6)
HMDB07219	C36:3 DAG	Lipids and lipid-like molecules	-4.9(-9.0, -0.7)	-5.2(-9.6, -0.5)	-2.2(-9.3, 5.5)
HMDB02183	DHA	Lipids and lipid-like molecules	-6.5(-10.3, -2.4)	-7.1(-11.3, -2.6)	-2.4(-9.3, 5.1)
HMDB05384	C52:3 TAG	Lipids and lipid-like molecules	-6.8(-10.8, -2.6)	-6.3(-10.7, -1.6)	-5.6(-12.6, 2.0)
HMDB05380	C52:5 TAG	Lipids and lipid-like molecules	-5.6(-9.7, -1.3)	-5.3(-9.9, -0.5)	-4.3(-11.5, 3.5)
HMDB07132	C34:3 DAG	Lipids and lipid-like molecules	-7.2(-11.1, -3.2)	-6.7(-11.0, -2.1)	-5.8(-12.6, 1.5)
HMDB10517	C52:7 TAG	Lipids and lipid-like molecules	-7.1(-11.1, -3.0)	-7.0(-11.3, -2.4)	-4.7(-11.7, 2.8)
HMDB10518	C54:8 TAG	Lipids and lipid-like molecules	-7.4(-11.5, -3.1)	-7.4(-12.0, -2.6)	-4.5(-11.8, 3.5)
HMDB05436	C52:6 TAG	Lipids and lipid-like molecules	-7.5(-11.4, -3.3)	-7.1(-11.5, -2.5)	-5.4(-12.4, 2.1)

Abbreviation: AAMU, 5-acetylamino-6-amino-3-methyluracil; CE, cholesteryl ester; TAG, triacylglycerol; DAG, diacylglycerol; LPE, lysophoshatidylethanolamine; DHA, docosahexaenoic acid.

[1] Multivariate linear regression analysis was conducted to adjust for age at blood draw (continuous), fasting status (yes, no), race (white, nonwhite), study cohort, case-control status, cumulative average levels of BMI (< 23.0, 23.0-24.9, 25.0-27.4, 27.5-29.9, ≥ 30.0 kg/m^2), physical activity(< 3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 MET-hours/week), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, ≥ 15.0 g/day), whole grains (quintiles), fruits (quintiles), vegetables (quintiles), polyunsaturated fat to saturated fat ratio (quintiles), fish (quintiles), red meat (quintiles), sugar-sweetened beverages (quintiles), total energy intake (quintiles), regular multivitamin use (yes, no), regular aspirin/nonsteroidal anti-inflammatory drug use (yes, no), hypertension (yes, no), hypercholesterolemia (yes, no), menopausal status (premenopausal, postmenopausal, or unknown), and menopausal hormone therapy (never, past, or current use).

Supplementary Table 3 Percentage differences (95% confidence intervals) in validated metabolites according to coffee consumption among controls[1]

HMDB ID	Metabolite name	Super class	Pooled controls		
			Total coffee per cup increase	Caffeinated coffee per cup increase	Decaffeinated coffee per cup increase
HMDB00875	Trigonelline	Alkaloids and derivatives	45.5(41.2, 50.0)	45.2(40.3, 50.2)	15.9(9.4, 22.8)
HMDB04400	AAMU	Organic nitrogen compounds	22.3(17.9, 26.9)	31.7(26.7, 36.8)	-7.5(-12.8, -1.8)
HMDB11621	Cinnamoylglycine	Organic acids and derivatives	18.9(14.7, 23.1)	17.4(12.9, 22.0)	9.7(3.6, 16.1)
HMDB11103	1,7-dimethyluric acid	Organoheterocyclic compounds	19.7(15.5, 24.2)	32.1(27.3, 37.2)	-12.8(-17.8, -7.6)
HMDB01847	Caffeine	Organoheterocyclic compounds	18.2(14.1, 22.5)	29.6(24.8, 34.5)	-12.0(-16.9, -6.8)
HMDB00779	Phenyllactic acid	Phenylpropanoids and polyketides	13.8(9.4, 18.4)	11.7(7.0, 16.6)	9.5(2.9, 16.6)
HMDB13678	4-hydroxyhippuric acid	Benzenoids	14.3(10.0, 18.9)	12.9(8.2, 17.8)	8.3(1.8, 15.2)
HMDB00630	Cytosine	Organoheterocyclic compounds	12.2(8.1, 16.4)	13.4(8.9, 18.0)	2.3(-3.5, 8.5)
HMDB01991	7-methylxanthine	Organoheterocyclic compounds	9.5(5.3, 13.9)	14.5(9.8, 19.5)	-5.5(-11.2, 0.5)
HMDB00062	L-carnitine	Organic nitrogen compounds	4.2(0.1, 8.4)	3.0(-1.4, 7.5)	4.3(-1.9, 11.0)
HMDB06726	C20:4 CE	Lipids and lipid-like molecules	5.9(2.0, 10.0)	3.9(-0.3, 8.3)	6.4(0.2, 12.9)
HMDB00918	C18:1 CE	Lipids and lipid-like molecules	9.3(5.4, 13.2)	6.1(2.0, 10.3)	9.4(3.5, 15.8)
HMDB00610	C18:2 CE	Lipids and lipid-like molecules	10.2(6.4, 14.2)	6.9(2.8, 11.0)	10.3(4.4, 16.5)
HMDB05377	C50:2 TAG	Lipids and lipid-like molecules	-7.5(-10.7, -4.3)	-5.0(-8.5, -1.3)	-8.2(-13.1, -3.0)
HMDB07102	C34:1 DAG	Lipids and lipid-like molecules	-7.4(-10.6, -4.1)	-6.0(-9.5, -2.3)	-5.8(-10.9, -0.4)
HMDB10497	C50:6 TAG	Lipids and lipid-like molecules	-6.6(-10.0, -3.0)	-6.2(-9.9, -2.3)	-3.2(-8.7, 2.7)
HMDB10513	C56:10 TAG	Lipids and lipid-like molecules	-6.2(-9.7, -2.6)	-6.9(-10.7, -3.0)	-0.8(-6.5, 5.3)
HMDB10471	C50:5 TAG	Lipids and lipid-like molecules	-6.4(-9.8, -2.8)	-5.6(-9.4, -1.7)	-3.9(-9.4, 1.9)
HMDB05433	C50:3 TAG	Lipids and lipid-like molecules	-6.4(-9.7, -2.9)	-4.4(-8.1, -0.6)	-6.4(-11.5, -1.0)
HMDB05369	C52:2 TAG	Lipids and lipid-like molecules	-8.2(-11.4, -4.9)	-5.8(-9.4, -2.1)	-8.3(-13.2, -3.0)
HMDB10498	C54:9 TAG	Lipids and lipid-like molecules	-7.0(-10.4, -3.4)	-7.6(-11.4, -3.7)	-1.1(-6.8, 5.0)
HMDB11526	C22:6 LPE	Lipids and lipid-like molecules	-5.3(-8.8, -1.8)	-3.0(-6.9, 1.0)	-7.0(-12.2, -1.4)
HMDB07218	C36:2 DAG	Lipids and lipid-like molecules	-7.2(-10.5, -3.8)	-5.6(-9.3, -1.9)	-5.8(-10.9, -0.3)
HMDB05435	C50:4 TAG	Lipids and lipid-like molecules	-5.9(-9.3, -2.3)	-4.8(-8.5, -0.9)	-4.4(-9.7, 1.3)

HMDB05448	C56:9 TAG	Lipids and lipid-like molecules	-6.3(-9.7, -2.7)	-6.9(-10.6, -3.0)	-1.3(-6.9, 4.7)
HMDB07103	C34:2 DAG	Lipids and lipid-like molecules	-7.5(-10.8, -4.2)	-6.3(-9.9, -2.6)	-5.4(-10.5, 0.1)
HMDB07219	C36:3 DAG	Lipids and lipid-like molecules	-6.0(-9.5, -2.4)	-5.7(-9.4, -1.7)	-2.9(-8.4, 3.0)
HMDB02183	DHA	Lipids and lipid-like molecules	-4.9(-8.2, -1.5)	-5.0(-8.6, -1.3)	-1.9(-7.2, 3.7)
HMDB05384	C52:3 TAG	Lipids and lipid-like molecules	-6.9(-10.3, -3.4)	-5.4(-9.2, -1.6)	-5.7(-11.0, -0.03)
HMDB05380	C52:5 TAG	Lipids and lipid-like molecules	-5.4(-8.9, -1.7)	-5.2(-9.1, -1.3)	-2.3(-8.0, 3.7)
HMDB07132	C34:3 DAG	Lipids and lipid-like molecules	-7.5(-10.8, -4.0)	-6.8(-10.4, -3.0)	-4.4(-9.8, 1.3)
HMDB10517	C52:7 TAG	Lipids and lipid-like molecules	-8.0(-11.4, -4.5)	-7.6(-11.3, -3.8)	-3.8(-9.2, 2.0)
HMDB10518	C54:8 TAG	Lipids and lipid-like molecules	-7.8(-11.3, -4.2)	-8.0(-11.7, -4.1)	-2.7(-8.3, 3.3)
HMDB05436	C52:6 TAG	Lipids and lipid-like molecules	-8.0(-11.4, -4.5)	-7.5(-11.2, -3.7)	-4.1(-9.6, 1.7)

Abbreviation: AAMU, 5-acetylamino-6-amino-3-methyluracil; CE, cholesteryl ester; TAG, triacylglycerol; DAG, diacylglycerol; LPE, lysophoshatidylethanolamine; DHA, docosahexaenoic acid.

[1] Multivariate linear regression analysis was conducted to adjust for age at blood draw (continuous), fasting status (yes, no), race (white, nonwhite), study cohort, cumulative average levels of BMI (< 23.0, 23.0-24.9, 25.0-27.4, 27.5-29.9, ≥ 30.0 kg/m^2), physical activity(< 3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 MET-hours/week), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, ≥ 15.0 g/day), smoking status (never, past < 30, past ≥ 30, current < 30, current ≥ 30 pack-years), whole grains (quintiles), fruits (quintiles), vegetables (quintiles), polyunsaturated fat to saturated fat ratio (quintiles), fish (quintiles), red meat (quintiles), sugar-sweetened beverages (quintiles), total energy intake (quintiles), regular multivitamin use (yes, no), regular aspirin/nonsteroidal anti-inflammatory drug use (yes, no), hypertension (yes, no), hypercholesterolemia (yes, no), menopausal status (premenopausal, postmenopausal, or unknown), and menopausal hormone therapy (never, past, or current use).

Supplementary Table 4 Characteristics of type 2 diabetes cases and 1:3 matched controls at blood draw in the training and validation sets in the NHS and NHSII[1]

	Training set		Validation set	
	Case (n=207)	Controls (n=621)	Case (n=250)	Controls (n=750)
White (%)	95	98	98	99
Blood fasting, n(%)	71	71	72	72
Age at blood draw (year)	49.9(7.7)	49.8(7.7)	57.3(6.7)	57.3(6.8)
Total coffee (cups/d)[2]	1.7(1.6)	1.9 (1.5)	2.2(1.6)	2.4(1.7)
Caffeinated coffee (cups/d)[2]	1.2(1.4)	1.4 (1.4)	1.6(1.5)	1.6(1.6)
Decaffeinated coffee (cups/d)[2]	0.5(0.9)	0.5(0.9)	0.7(1.0)	0.8(1.1)
BMI (kg/m^2) [2]	31.0(6.7)	25.3 (5.0)	28.8(5.4)	25.0(4.2)
Physical activity (MET-h/wk)[2]	14.7(18.4)	19.6 (19.8)	14.0(15.9)	18.4(16.5)
Smoking status				
Never (%)	59	60	44	45
Past (%)	31	31	39	43
Current (%)	10	9	16	12
Alcohol consumption (g/d)[2]	2.9 (5.1)	4.9 (8.0)	4.7(7.8)	6.8(10.1)
Total energy intake (kcal/d)[2]	1841(487)	1805(463)	1786(450)	1801(466)
Hypertension (%)	38	17	33	20
Hypercholesterolemia (%)	49	31	41	40
Family history of diabetes (%)	37	19	44	27
Postmenopausal (%)	41	43	76	74
Current menopausal hormone use (%)[3]	57	59	40	47
Regular multivitamin use (%)	43	51	33	40
Regular aspirin/NSAID use (%)[4]	60	51	66	62

[1] Matching criteria were age at blood draw ± 1 year, study cohort, and fasting status. Mean (SD) is presented for continuous variables and percentage for categorical variables.
[2] Cumulative average assessments most proximate to blood draw were used to derive the values.
[3] Defined in menopausal women only.
[4] Regular users are defined as ≥2 tablets of aspirin (325 mg/tablet) or nonsteroidal anti-inflammatory drugs per week.

Supplementary Table 5 Association between coffee-related metabolites and risk of type 2 diabetes in the validation case-control study[1]

HMDB ID	Metabolite name	Super class	250 cases vs. 750 controls	
			OR per 1-SD (95% CI)	*P*
Positively associated with coffee				
HMDB00610	C18:2 CE	Lipids and lipid-like molecules	0.60(0.50, 0.71)	<.0001
HMDB00918	C18:1 CE	Lipids and lipid-like molecules	0.65(0.56, 0.76)	<.0001
HMDB06726	C20:4 CE	Lipids and lipid-like molecules	0.69(0.59, 0.81)	<.0001
Negatively associated with coffee				
HMDB05377	C50:2 TAG	Lipids and lipid-like molecules	1.59(1.35, 1.89)	<.0001
HMDB07102	C34:1 DAG	Lipids and lipid-like molecules	1.51(1.30, 1.76)	<.0001
HMDB05369	C52:2 TAG	Lipids and lipid-like molecules	1.65(1.37, 1.99)	<.0001
HMDB07132	C34:3 DAG	Lipids and lipid-like molecules	1.43(1.23, 1.66)	<.0001
HMDB07218	C36:2 DAG	Lipids and lipid-like molecules	1.47(1.27, 1.70)	<.0001
HMDB07103	C34:2 DAG	Lipids and lipid-like molecules	1.49(1.28, 1.73)	<.0001
HMDB05433	C50:3 TAG	Lipids and lipid-like molecules	1.44(1.19, 1.75)	<.001
HMDB05384	C52:3 TAG	Lipids and lipid-like molecules	1.50(1.25, 1.81)	<.0001
HMDB10471	C50:5 TAG	Lipids and lipid-like molecules	1.39(1.19, 1.62)	<.0001
HMDB07219	C36:3 DAG	Lipids and lipid-like molecules	1.35(1.16, 1.56)	<.0001
HMDB10497	C50:6 TAG	Lipids and lipid-like molecules	1.33(1.14, 1.53)	<.001

Abbreviation: OR, odds ratio; CI, confidence interval; CE, cholesteryl ester; DAG, diacylglycerol; TAG, triacylglycerol.

[1] Conditional logistic regression analysis was conducted to adjust for age at blood draw (continuous), race (white, nonwhite), cumulative average levels of BMI (< 23.0, 23.0-24.9, 25.0-27.4, 27.5-29.9, ≥ 30.0 kg/m^2), physical activity (< 3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 MET-hours/week), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, ≥ 15.0 g/day), smoking status (never, past < 30, past ≥ 30, current < 30, current ≥ 30 pack-years), whole grains (quintiles), fruits (quintiles), vegetables (quintiles), polyunsaturated fat to saturated fat ratio (quintiles), fish (quintiles), red meat (quintiles), sugar-sweetened beverages (quintiles), total energy intake (quintiles), regular multivitamin use (yes, no), regular aspirin/nonsteroidal anti-inflammatory drug use (yes, no), family history of diabetes (yes, no), menopausal status (premenopausal, postmenopausal, or unknown), and menopausal hormone therapy (never, past, or current use).

Supplementary Table 6 The C-statistic, sensitivity and specificity at the optimal cutoffs for individual metabolites associated with type 2 diabetes[1]

HMDB ID	Metabolite name	207 cases vs. 621 controls			250 cases vs. 750 controls		
		C-statistic (95% CI)	Sensitivity	Specificity	C-statistic (95% CI)	Sensitivity	Specificity
HMDB05377	C50:2 TAG	0.74(0.70, 0.78)	0.72	0.69	0.68(0.63, 0.72)	0.72	0.54
HMDB07102	C34:1 DAG	0.74(0.71, 0.78)	0.69	0.75	0.69(0.65, 0.72)	0.61	0.70
HMDB05369	C52:2 TAG	0.73(0.70, 0.77)	0.78	0.62	0.68(0.64, 0.72)	0.68	0.59
HMDB00610	C18:2 CE	0.73(0.69, 0.77)	0.63	0.73	0.68(0.64, 0.72)	0.60	0.71
HMDB00918	C18:1 CE	0.72(0.68, 0.76)	0.70	0.67	0.68(0.64, 0.72)	0.56	0.72
HMDB07103	C34:2 DAG	0.72(0.68, 0.76)	0.66	0.72	0.67(0.63, 0.71)	0.64	0.65
HMDB07218	C36:2 DAG	0.71(0.68, 0.75)	0.73	0.65	0.66(0.62, 0.70)	0.49	0.76
HMDB07132	C34:3 DAG	0.71(0.67, 0.75)	0.65	0.70	0.68(0.64, 0.71)	0.51	0.75
HMDB05433	C50:3 TAG	0.70(0.66, 0.74)	0.66	0.70	0.64(0.60, 0.68)	0.76	0.49
HMDB06726	C20:4 CE	0.69(0.65, 0.73)	0.72	0.60	0.64(0.60, 0.68)	0.45	0.77
HMDB05384	C52:3 TAG	0.67(0.63, 0.71)	0.69	0.63	0.66(0.62, 0.70)	0.61	0.63
HMDB05435	C50:4 TAG	0.67(0.63, 0.71)	0.59	0.70	NA	NA	NA
HMDB10471	C50:5 TAG	0.67(0.63, 0.71)	0.81	0.47	0.62(0.57, 0.66)	0.76	0.43
HMDB10497	C50:6 TAG	0.66(0.62, 0.70)	0.72	0.54	0.61(0.57, 0.65)	0.65	0.54
HMDB07219	C36:3 DAG	0.65(0.61, 0.69)	0.72	0.53	0.61(0.57, 0.65)	0.51	0.69

Abbreviation: CI, confidence interval; TAG, triacylglycerol; DAG, diacylglycerol; CE, cholesteryl ester; NA, not available.

[1] Derived from univariate ROC curve analysis.

Supplementary Table 7 Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) of the risk prediction models for type 2 diabetes in the NHS and NHSII

	Training set			Validation set		
	Classical factor model[1]	Classical factor and metabolite model[2]		Classical factor model[1]	Classical factor and metabolite model[2]	
	Values (95% CI)	Values (95% CI)	*P*	Values (95% CI)	Values (95% CI)	*P*
NRI						
Category-free NRI (%)	Ref	62.2(47.2, 77.1)	<.0001	Ref	47.7 (33.8, 61.7)	<.0001
% of events correctly reclassified	-	31		-	18	
% of non-events correctly reclassified	-	31		-	29	
IDI	Ref	0.077(0.056, 0.098)	<.0001	Ref	0.055(0.037, 0.072)	<.0001

[1] Classical factor model included age, body mass index, physical activity, smoking, and family history of diabetes.

[2] Classical factor and metabolite model: further included diabetes-associated metabolites in the training set (n=15) and the validation set (n=14).