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Supplemental Data

The Contribution of Neanderthals to Phenotypic Variation in Modern Humans

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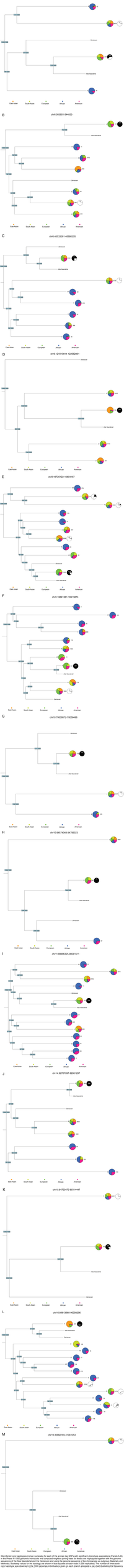
Figure S1.Divergence of the core haplotypes inferred for each of the archaic tag SNPs with significant phenotype associations.



We inferred core haplotypes (roman numerals) for each of the archaic tag SNPs with significant phenotype associations (Panels A-M) at the Phase III 1000 genomes introgressed and ancestral neighbor joining trees for these core haplotypes together with the genome wide maximum parsimony trees for the Denisovan, Alle Neandertal, and the ancestral human haplotype (Methods). Bootstrap values for the topology are shown in blue accurate at each node (1,000 replicates). The number of times each core haplotype was observed in the Phase III 1000 genomes is shown in the pie charts at the tips of the trees, with the relative frequency of the core haplotype in each of the five continental super-populations. Core haplotype clusters in which haplotype carrying the tag allele for the archaic tag SNP are assigned are displayed with an additional pie chart showing the proportion of haplotypes in the cluster that are carriers of the tag SNP. Branch lengths are proportional to the number of haplotypes in the core haplotype cluster. Core haplotypes with fewer than 10 haplotypes assigned are not shown.

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Alcohol drinker status	Alcohol	categorical	112338	
Alcohol intake frequency.	Alcohol	categorical	112338	
Absence of notch position in the pulse waveform	Arterial stiffness		36580	
Arterial pulse-wave stiffness device ID	Arterial stiffness		2014	
Arterial stiffness device ID	Arterial stiffness		36982	
Position of pulse wave notch	Arterial stiffness		36580	
Position of the pulse wave peak	Arterial stiffness		36580	
Position of the shoulder on the pulse waveform	Arterial stiffness		36580	
Pulse rate	Arterial stiffness		36580	
Pulse wave Arterial Stiffness index	Arterial stiffness		36491	
Pulse wave peak to peak time	Arterial stiffness		36563	
Pulse wave pressure versus time response curve	Arterial stiffness		36580	
Pulse wave reflection index	Arterial stiffness		36580	
Pulse wave velocity (manual entry)	Arterial stiffness		39	
Reason for skipping arterial stiffness	Arterial stiffness		185	
Stiffness method	Arterial stiffness		36982	
Auto-refraction method (right)	Autorefraction		24042	
Reason for skipping refractometry (left)	Autorefraction		304	
Reason for skipping refractometry (right)	Autorefraction		263	
Age at recruitment	Baseline characteristics		112338	
Month of birth	Baseline characteristics		112338	
Sex	Baseline characteristics		112338	
Townsend deprivation index at recruitment	Baseline characteristics		112192	
Year of birth	Baseline characteristics		112338	
Blood pressure device ID	Blood pressure		112242	
Blood pressure manual sphygmomanometer device ID	Blood pressure		2119	
Diastolic blood pressure, automated reading	Blood pressure	continuous	104611	
Diastolic blood pressure, manual reading	Blood pressure			X
Method of measuring blood pressure	Blood pressure			X
Pulse rate (during blood-pressure measurement)	Blood pressure			X
Pulse rate, automated reading	Blood pressure	continuous	104611	
Systolic blood pressure, automated reading	Blood pressure	continuous	104611	
Systolic blood pressure, manual reading	Blood pressure			X
Time since interview start at which blood pressure screen(s) shown	Blood pressure			X
Arm fat mass (left)	Body composition by DXA/Impedance measures	continuous	110379	
Arm fat mass (right)	Body composition by DXA/Impedance measures	continuous	110407	
Leg fat mass (left)	Body composition by DXA/Impedance measures	continuous	110420	
Leg fat mass (right)	Body composition by DXA/Impedance measures	continuous	110426	
Trunk fat mass	Body composition by DXA/Impedance measures	continuous	110362	
Hip circumference	Body size measures	continuous	112173	
Reason for skipping hip measurement	Body size measures		92	
Reason for skipping sitting height	Body size measures		119	
Reason for skipping standing height	Body size measures		118	
Reason for skipping waist	Body size measures		84	
Reason for skipping weight	Body size measures		198	
Sitting height	Body size measures	continuous	112063	
Standing height	Body size measures	continuous	112147	
Waist circumference	Body size measures	continuous	112181	
Weight method	Body size measures		112265	
Weight, manual entry	Body size measures		1630	
Body mass index (BMI)	Body size measures/Impedance measures	continuous	112027	
Weight	Body size measures/Impedance measures	continuous	112065	

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Ankle spacing width	Bone-densitometry of heel		64971	
Ankle spacing width (left)	Bone-densitometry of heel		35265	
Ankle spacing width (right)	Bone-densitometry of heel		35266	
Foot measured for bone density	Bone-densitometry of heel		74584	
Fractured heel	Bone-densitometry of heel		74584	
Fractured heel (left)	Bone-densitometry of heel		35565	
Fractured heel (right)	Bone-densitometry of heel		35580	
Heel bone mineral density (BMD)	Bone-densitometry of heel		64940	
Heel bone mineral density (BMD) (left)	Bone-densitometry of heel		35247	
Heel bone mineral density (BMD) (right)	Bone-densitometry of heel		35248	
Heel bone mineral density (BMD) T-score, automated	Bone-densitometry of heel		64971	
Heel bone mineral density (BMD) T-score, automated (left)	Bone-densitometry of heel		35265	
Heel bone mineral density (BMD) T-score, automated (right)	Bone-densitometry of heel		35266	
Heel bone mineral density (BMD) T-score, manual entry (left)	Bone-densitometry of heel		299	
Heel bone mineral density (BMD) T-score, manual entry (right)	Bone-densitometry of heel		313	
Heel bone mineral density (BMD), manual entry	Bone-densitometry of heel		9607	
Heel bone mineral density (BMD), manual entry (left)	Bone-densitometry of heel		299	
Heel bone mineral density (BMD), manual entry (right)	Bone-densitometry of heel		313	
Heel bone ultrasound T-score, manual entry	Bone-densitometry of heel		9607	
Heel Broadband ultrasound attenuation (BUA), manual entry	Bone-densitometry of heel		9607	
Heel broadband ultrasound attenuation (BUA), manual entry (left)	Bone-densitometry of heel		299	
Heel broadband ultrasound attenuation (BUA), manual entry (right)	Bone-densitometry of heel		313	
Heel broadband ultrasound attenuation (left)	Bone-densitometry of heel		35259	
Heel broadband ultrasound attenuation (right)	Bone-densitometry of heel		35265	
Heel Broadband ultrasound attenuation, direct entry	Bone-densitometry of heel		64971	
Heel quantitative ultrasound index (QUI), direct entry	Bone-densitometry of heel		64971	
Heel quantitative ultrasound index (QUI), direct entry (left)	Bone-densitometry of heel		35265	
Heel quantitative ultrasound index (QUI), direct entry (right)	Bone-densitometry of heel		35266	
Heel quantitative ultrasound index (QUI), manual entry	Bone-densitometry of heel		9607	
Heel quantitative ultrasound index (QUI), manual entry (left)	Bone-densitometry of heel		299	
Heel quantitative ultrasound index (QUI), manual entry (right)	Bone-densitometry of heel		313	
Heel ultrasound method	Bone-densitometry of heel		75236	
Heel ultrasound method (left)	Bone-densitometry of heel		36946	
Heel ultrasound method (right)	Bone-densitometry of heel		36946	
Shortness of breath walking on level ground	Breathing		36987	
Wheeze or whistling in the chest in last year	Breathing	continuous	112337	
Age at cancer diagnosis	Cancer register		14915	
Behaviour of cancer tumour	Cancer register		14707	
Date of cancer diagnosis	Cancer register		14915	
Histology of cancer tumour	Cancer register		14558	
Reported occurrences of cancer	Cancer register		14915	
Type of cancer: ICD10	Cancer register		12595	
Type of cancer: ICD9	Cancer register		2320	
Ever had bowel cancer screening	Cancer screening		112336	
Ever had prostate specific antigen (PSA) test	Cancer screening		53326	
Most recent bowel cancer screening	Cancer screening		35401	
Time since last prostate specific antigen (PSA) test	Cancer screening		15773	
Chest pain due to walking ceases when standing still	Chest pain		7166	
Chest pain or discomfort	Chest pain	continuous	112336	
Chest pain or discomfort walking normally	Chest pain		17962	
Chest pain or discomfort when walking uphill or hurrying	Chest pain		14633	
Leg pain in calf/calves	Claudication and peripheral artery disease		8286	
Leg pain on walking	Claudication and peripheral artery disease		36987	

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Leg pain on walking : action taken	Claudication and peripheral artery disease		8286	
Leg pain on walking : effect of standing still	Claudication and peripheral artery disease		8286	
Leg pain when standing still or sitting	Claudication and peripheral artery disease		8286	
Leg pain when walking ever disappears while walking	Claudication and peripheral artery disease		4682	
Leg pain when walking normally	Claudication and peripheral artery disease		8286	
Leg pain when walking uphill or hurrying	Claudication and peripheral artery disease		8286	
Surgery on leg arteries (other than for varicose veins)	Claudication and peripheral artery disease		8286	
Surgery/amputation of toe or leg	Claudication and peripheral artery disease		8286	
Age at death	Death register		2049	
Contributory (secondary) causes of death: ICD10	Death register			X
Date of death	Death register		2049	
Description of cause of death	Death register		1733	
Underlying (primary) cause of death: ICD10	Death register		2048	
Age when last ate meat	Diet		3954	
Bread intake	Diet	continuous	112254	
Bread type	Diet	categorical	108831	
Bread type/intake (pilot)	Diet		83	
Cereal intake	Diet	continuous	112337	
Cereal type	Diet	categorical	93149	
Cheese intake	Diet	categorical	109960	
Coffee intake	Diet	continuous	112338	
Coffee type	Diet	categorical	88164	
Cooked vegetable intake	Diet	continuous	112338	
Fresh fruit intake	Diet	continuous	112338	
Hot drink temperature	Diet	categorical	112338	
Lamb/mutton intake	Diet	categorical	112338	
Major dietary changes in the last 5 years	Diet	categorical	112338	
Milk type used	Diet	categorical	112336	
Never eat eggs, dairy, wheat, sugar	Diet			X
Never eat eggs, dairy, wheat, sugar (pilot)	Diet			X
Non-butter spread type details	Diet		59603	
Non-oily fish intake	Diet	categorical	112338	
Processed meat intake	Diet	categorical	112338	
Salad / raw vegetable intake	Diet	continuous	112338	
Salt added to food	Diet	categorical	112338	
Spread type	Diet	categorical	112254	
Spread type (pilot)	Diet		84	
Tea intake	Diet	continuous	112338	
Variation in diet	Diet	categorical	112254	
Water intake	Diet	continuous	112338	
Dried fruit intake	Diet/Fruit/vegetables yesterday	continuous	112338	
Beef intake	Diet/Meat/fish yesterday	categorical	112338	
Oily fish intake	Diet/Meat/fish yesterday	categorical	112338	
Pork intake	Diet/Meat/fish yesterday	categorical	112338	
Poultry intake	Diet/Meat/fish yesterday	categorical	112338	
Comparative body size at age 10	Early life factors	categorical	112338	
Comparative height size at age 10	Early life factors	categorical	112338	
Handedness (chirality/laterality)	Early life factors	categorical	112338	
Part of a multiple birth	Early life factors	categorical	110757	
Able to walk or cycle unaided for 10 minutes	ECG during exercise		16527	
Chest pain felt during physical activity	ECG during exercise		16527	

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Chest pain felt outside physical activity	ECG during exercise		16527	
Completion status of test	ECG during exercise		16259	
Doctor restricts physical activity due to heart condition	ECG during exercise		16527	
Duration of fitness test	ECG during exercise		16254	
ECG, heart rate	ECG during exercise			X
ECG, load	ECG during exercise			X
ECG, number of stages in a phase	ECG during exercise			X
ECG, phase duration	ECG during exercise			X
ECG, phase name	ECG during exercise			X
ECG, phase time	ECG during exercise			X
ECG, stage duration	ECG during exercise		0	
ECG, stage name	ECG during exercise			X
ECG, trend phase name	ECG during exercise			X
ECG/bike method for fitness test	ECG during exercise		16475	
Maximum heart rate during fitness test	ECG during exercise		16249	
Maximum workload during fitness test	ECG during exercise		16254	
Number of trend entries	ECG during exercise		16254	
Program category	ECG during exercise		16527	
Reason at-rest ECG performed without bicycle	ECG during exercise		191	
Reason ECG not completed	ECG during exercise		44	
Reason for skipping ECG	ECG during exercise		79	
Target heart rate achieved	ECG during exercise		16254	
Qualifications	Education			X
Length of mobile phone use	Electronic device use		112338	
Ethnic background	Ethnicity		112338	
Both eyes present	Eye surgery/complications		24334	
Current eye infection	Eye surgery/complications		24333	
Ever had cataract surgery	Eye surgery/complications		1714	
Ever had corneal graft surgery	Eye surgery/complications		1714	
Ever had eye surgery	Eye surgery/complications		24334	
Ever had laser treatment for glaucoma or high eye pressure	Eye surgery/complications		1714	
Ever had refractive laser eye surgery	Eye surgery/complications		1714	
Ever had surgery for glaucoma or high eye pressure	Eye surgery/complications		1714	
Age at first live birth	Female-specific factors		40126	
Age of primiparous women at birth of child	Female-specific factors		7907	
Ever had stillbirth, spontaneous miscarriage or termination	Female-specific factors		59010	
Ever taken oral contraceptive pill	Female-specific factors		59010	
Length of menstrual cycle	Female-specific factors		12883	
Number of live births	Female-specific factors		59010	
Number of spontaneous miscarriages	Female-specific factors		18626	
Number of stillbirths	Female-specific factors		18626	
Attempted fluid intelligence (FI) test.	Fluid intelligence test		36539	
FI1 : numeric addition test	Fluid intelligence test/Fluid intelligence test		36093	
FI10 : arithmetic sequence recognition	Fluid intelligence test/Fluid intelligence test		7577	
FI11 : antonym	Fluid intelligence test/Fluid intelligence test		3921	
FI12 : square sequence recognition	Fluid intelligence test/Fluid intelligence test		2732	
FI13 : subset inclusion logic	Fluid intelligence test/Fluid intelligence test		981	
FI2 : identify largest number	Fluid intelligence test/Fluid intelligence test		36029	
FI3 : word interpolation	Fluid intelligence test/Fluid intelligence test		36013	
FI4 : positional arithmetic	Fluid intelligence test/Fluid intelligence test		35982	
FI5 : family relationship calculation	Fluid intelligence test/Fluid intelligence test		35339	

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
FI6 : conditional arithmetic	Fluid intelligence test/Fluid intelligence test		31902	
FI7 : synonym	Fluid intelligence test/Fluid intelligence test		26207	
FI8 : chained arithmetic	Fluid intelligence test/Fluid intelligence test		23796	
FI9 : concept interpolation	Fluid intelligence test/Fluid intelligence test		11078	
Fluid intelligence score	Fluid intelligence test/Fluid intelligence test		36093	
Falls in the last year	General health	categorical	112337	
Long-standing illness, disability or infirmity	General health	categorical	112337	
Overall health rating	General health	categorical	112337	
Weight change compared with 1 year ago	General health	categorical	112337	
Hand grip strength (left)	Hand grip strength	continuous	111875	
Hand grip strength (right)	Hand grip strength	continuous	111876	
Reason for skipping grip strength (left)	Hand grip strength		390	
Reason for skipping grip strength (right)	Hand grip strength		389	
Speech-reception-threshold (SRT) estimate (left)	Hearing test		35290	
Speech-reception-threshold (SRT) estimate (right)	Hearing test		35279	
Arm fat percentage (left)	Impedance measures	continuous	110394	
Arm fat percentage (right)	Impedance measures	continuous	110413	
Arm fat-free mass (left)	Impedance measures	continuous	110380	
Arm fat-free mass (right)	Impedance measures	continuous	110398	
Arm predicted mass (left)	Impedance measures	continuous	110378	
Arm predicted mass (right)	Impedance measures	continuous	110397	
Basal metabolic rate	Impedance measures	continuous	110432	
Body fat percentage	Impedance measures	continuous	110365	
Impedance of arm (left)	Impedance measures	continuous	110426	
Impedance of arm (right)	Impedance measures	continuous	110422	
Impedance of leg (left)	Impedance measures	continuous	110428	
Impedance of leg (right)	Impedance measures	continuous	110429	
Impedance of whole body	Impedance measures	continuous	110426	
Leg fat percentage (left)	Impedance measures	continuous	110421	
Leg fat percentage (right)	Impedance measures	continuous	110428	
Leg fat-free mass (left)	Impedance measures	continuous	110416	
Leg fat-free mass (right)	Impedance measures	continuous	110424	
Leg predicted mass (left)	Impedance measures	continuous	110414	
Leg predicted mass (right)	Impedance measures	continuous	110424	
Trunk fat percentage	Impedance measures	continuous	110368	
Trunk fat-free mass	Impedance measures	continuous	110343	
Trunk predicted mass	Impedance measures	continuous	110327	
Whole body fat mass	Impedance measures	continuous	110243	
Whole body fat-free mass	Impedance measures	continuous	110423	
Whole body water mass	Impedance measures	continuous	110434	
Applanation curve (left)	Intraocular pressure		23181	
Applanation curve (right)	Intraocular pressure		23240	
Corneal hysteresis (left)	Intraocular pressure		23181	
Corneal hysteresis (right)	Intraocular pressure		23240	
Corneal resistance factor (left)	Intraocular pressure		23181	
Corneal resistance factor (right)	Intraocular pressure		23240	
Intra-ocular pressure (IOP) method (left)	Intraocular pressure		24040	
Intra-ocular pressure (IOP) method (right)	Intraocular pressure		24042	
Intra-ocular pressure, corneal-compensated (left)	Intraocular pressure		23181	
Intra-ocular pressure, corneal-compensated (right)	Intraocular pressure		23240	
Intra-ocular pressure, Goldmann-correlated (left)	Intraocular pressure		23181	
Intra-ocular pressure, Goldmann-correlated (right)	Intraocular pressure		23240	

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Pressure curve (left)	Intraocular pressure		23181	
Pressure curve (right)	Intraocular pressure		23240	
Reason for skipping IOP (left)	Intraocular pressure		496	
Reason for skipping IOP (right)	Intraocular pressure		457	
Hair/balding pattern	Male-specific factors		53283	
Number of children fathered	Male-specific factors		53283	
Relative age of first facial hair	Male-specific factors		53283	
Relative age voice broke	Male-specific factors		53283	
Cancer code, self-reported	Medical conditions			X
Cancer year/age first occurred	Medical conditions			X
Interpolated Age of participant when cancer first diagnosed	Medical conditions	continuous	84969	
Interpolated Age of participant when non-cancer illness first diagnosed	Medical conditions	continuous	84969	
Interpolated Year when cancer first diagnosed	Medical conditions			X
Interpolated Year when non-cancer illness first diagnosed	Medical conditions			X
Method of recording time when cancer first diagnosed	Medical conditions			X
Method of recording time when non-cancer illness first diagnosed	Medical conditions			X
Non-cancer illness code, self-reported	Medical conditions			X
Non-cancer illness year/age first occurred	Medical conditions	continuous	84969	
Number of self-reported cancers	Medical conditions	continuous	112327	
Number of self-reported non-cancer illnesses	Medical conditions	continuous	112327	
Pregnant	Medical conditions		58968	
Bipolar and major depression status	Mental health		26838	
Bipolar disorder status	Mental health		333	
Ever depressed for a whole week	Mental health		36987	
Ever highly irritable/argumentative for 2 days	Mental health		36987	
Ever manic/hyper for 2 days	Mental health		36987	
Ever unenthusiastic/disinterested for a whole week	Mental health		36987	
Family relationship satisfaction	Mental health		36987	
Fed-up feelings	Mental health	categorical	112337	
Financial situation satisfaction	Mental health		36987	
Frequency of depressed mood in last 2 weeks	Mental health	categorical	112337	
Frequency of tenseness / restlessness in last 2 weeks	Mental health	categorical	112337	
Frequency of tiredness / lethargy in last 2 weeks	Mental health	categorical	112337	
Frequency of unenthusiasm / disinterest in last 2 weeks	Mental health	categorical	112337	
Friendships satisfaction	Mental health		36987	
Guilty feelings	Mental health	categorical	112337	
Happiness	Mental health		36987	
Health satisfaction	Mental health		36987	
Illness, injury, bereavement, stress in last 2 years	Mental health	categorical	112253	
Illness, injury, bereavement, stress in last 2 years (pilot)	Mental health			X
Irritability	Mental health	categorical	112337	
Length of longest manic/irritable episode	Mental health		7593	
Loneliness, isolation	Mental health	categorical	112337	
Longest period of depression	Mental health		19426	
Longest period of unenthusiasm / disinterest	Mental health		13101	
Manic/hyper symptoms	Mental health			X
Miserableness	Mental health	categorical	112337	
Mood swings	Mental health	categorical	112337	
Nervous feelings	Mental health	categorical	112337	
Neuroticism score	Mental health	continuous	91620	
Number of depression episodes	Mental health		19426	
Number of unenthusiastic/disinterested episodes	Mental health		13101	
Probable recurrent major depression (moderate)	Mental health		3432	
Probable recurrent major depression (severe)	Mental health		2040	

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Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Risk taking	Mental health	categorical	112337	
Seen a psychiatrist for nerves, anxiety, tension or depression	Mental health	categorical	112337	
Seen doctor (GP) for nerves, anxiety, tension or depression	Mental health	categorical	112337	
Sensitivity / hurt feelings	Mental health	categorical	112337	
Severity of manic/irritable episodes	Mental health		7593	
Single episode of probable major depression	Mental health		2250	
Suffer from 'nerves'	Mental health	categorical	112337	
Tense / 'highly strung'	Mental health	categorical	112337	
Work/job satisfaction	Mental health		36987	
Worrier / anxious feelings	Mental health	categorical	112337	
Worry too long after embarrassment	Mental health	categorical	112337	
Mouth/teeth dental problems	Mouth	categorical	112253	
Mouth/teeth dental problems (pilot)	Mouth			X
Back pain for 3+ months	Pain		28709	
Facial pains for 3+ months	Pain		2023	
General pain for 3+ months	Pain		1769	
Headaches for 3+ months	Pain		22091	
Hip pain for 3+ months	Pain		12995	
Knee pain for 3+ months	Pain		24373	
Neck/shoulder pain for 3+ months	Pain		25998	
Pain type(s) experienced in last month	Pain	categorical	112336	
Stomach/abdominal pain for 3+ months	Pain		9556	
Number of incorrect matches in round	Pairs matching test/Pairs matching test			X
Frequency of heavy DIY in last 4 weeks	Physical activity		48818	
Frequency of light DIY in last 4 weeks	Physical activity		57730	
Frequency of other exercises in last 4 weeks	Physical activity		53000	
Frequency of stair climbing in last 4 weeks	Physical activity	categorical	111878	
Frequency of strenuous sports in last 4 weeks	Physical activity		11008	
Frequency of walking for pleasure in last 4 weeks	Physical activity	categorical	79141	
Number of days/week walked 10+ minutes	Physical activity	categorical	112338	
Types of physical activity in last 4 weeks	Physical activity	categorical	111935	
Usual walking pace	Physical activity	categorical	111962	
Duration screen displayed	Prospective memory test		36850	
Final attempt correct	Prospective memory test		36850	
History of attempts	Prospective memory test		36850	
Number of attempts	Prospective memory test		36850	
PM: final answer	Prospective memory test		36850	
PM: initial answer	Prospective memory test		36850	
Prospective memory result	Prospective memory test		36850	
Test completion status	Prospective memory test		36850	
Time screen exited	Prospective memory test		36850	
Time to answer	Prospective memory test		36850	
Time when initial screen shown	Prospective memory test		36850	
Age when attended assessment centre	Reception		112338	
Date of attending assessment centre	Reception		112338	
UK Biobank assessment centre	Reception		112338	
OCT measured (left)	Retinal optical coherence tomography		16533	
OCT measured (right)	Retinal optical coherence tomography		16531	
Reason for skipping OCT (left)	Retinal optical coherence tomography		716	
Reason for skipping OCT (right)	Retinal optical coherence tomography		675	
Age first had sexual intercourse	Sexual factors	continuous	103379	
Answered sexual history questions	Sexual factors		112337	
Ever had same-sex intercourse	Sexual factors	categorical	102415	
Lifetime number of same-sex sexual partners	Sexual factors		3374	

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Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Lifetime number of sexual partners	Sexual factors	continuous	102415	
Daytime dozing / sleeping (narcolepsy)	Sleep	categorical	112338	
Getting up in morning	Sleep	categorical	112254	
Morning/evening person (chronotype)	Sleep	categorical	112254	
Nap during day	Sleep	categorical	112338	
Sleep duration	Sleep	continuous	112338	
Sleeplessness / insomnia	Sleep	categorical	112338	
Snoring	Sleep	categorical	112338	
Smoking status	Smoking	categorical	112338	
Episodes containing "Diagnoses - main ICD10 - addendum" data	Spell and Episode Data (diagnoses)		458	
Episodes containing "Diagnoses - main ICD10" data	Spell and Episode Data (diagnoses)		79357	
Episodes containing "Diagnoses - secondary ICD10 addendum" data	Spell and Episode Data (diagnoses)		550	
Episodes containing "Diagnoses - secondary ICD10" data	Spell and Episode Data (diagnoses)		59042	
Episodes containing "External cause - ICD10 addendum" data	Spell and Episode Data (diagnoses)		56	
Episodes containing "External cause - ICD10" data	Spell and Episode Data (diagnoses)		10661	
Acceptability of each blow result (text)	Spirometry			X
Acceptability of each blow result (text) (pilot)	Spirometry			X
Caffeine drink within last hour	Spirometry	categorical	105523	
Contra-indications for spirometry	Spirometry	categorical	112265	
Data points for blow	Spirometry			X
Data points for blow (pilot)	Spirometry			X
Forced expiratory volume in 1-second (FEV1)	Spirometry			X
Forced expiratory volume in 1-second (FEV1) (pilot)	Spirometry			X
Forced expiratory volume in 1-second (FEV1), Best measure	Spirometry	continuous	91907	
Forced expiratory volume in 1-second (FEV1), predicted	Spirometry		56611	
Forced expiratory volume in 1-second (FEV1), predicted percentage	Spirometry		56611	
Forced vital capacity (FVC)	Spirometry			X
Forced vital capacity (FVC) (pilot)	Spirometry			X
Forced vital capacity (FVC), Best measure	Spirometry	continuous	91907	
Number of measurements made	Spirometry		104956	
Ordering of blows	Spirometry			X
Peak expiratory flow (PEF)	Spirometry			X
Peak expiratory flow (PEF) (pilot)	Spirometry			X
Reason for skipping spirometry	Spirometry		339	
Reproduciblity of spirometry measurement using ERS/ATS criteria	Spirometry		91907	
Result ranking	Spirometry			X
Result ranking (pilot)	Spirometry			X
Smoked cigarette or pipe within last hour	Spirometry		12758	
Spirometry method	Spirometry		105444	
Spirometry method (pilot)	Spirometry		79	
Used an inhaler for chest within last hour	Spirometry		105523	
Diagnoses - main ICD10	Summary Information (diagnoses)			X
Diagnoses - secondary ICD10	Summary Information (diagnoses)			X
External causes	Summary Information (diagnoses)			X
History of psychiatric care on admission	Summary Information (psychiatric)			X
Mental categories	Summary Information (psychiatric)			X
Childhood sunburn occasions	Sun exposure	continuous	112254	
Ease of skin tanning	Sun exposure	categorical	112254	
Facial ageing	Sun exposure	categorical	112253	
Hair colour (natural, before greying)	Sun exposure	categorical	112338	
Skin colour	Sun exposure	categorical	112338	
Time spend outdoors in summer	Sun exposure	continuous	112254	
Time spent outdoors in winter	Sun exposure	continuous	112254	
Glasses worn/required (left)	Visual acuity		16640	

Table S1: Table of phenotypes from the UK biobank.

Phenotype	Meta phenotype	Data type	Number of individuals	Complex phenotype
Glasses worn/required (right)	Visual acuity		16656	
logMAR, final (left)	Visual acuity		23991	
logMAR, final (right)	Visual acuity		24002	
Reason for skipping visual acuity (left)	Visual acuity		96	
Reason for skipping visual acuity (right)	Visual acuity		78	
Visual acuity measured (left)	Visual acuity		24290	
Visual acuity measured (right)	Visual acuity		24292	

Table includes all UK Biobank phenotypes to which we had access (column 1, with meta phenotype provided by UK biobank in column 2). The 136 phenotypes included in this study are highlighted in bold. Column 3 provides format in which the 136 phenotype we included are represented and column 4 the number of individuals selected for this study because both genotype and phenotype information were available (Material and Methods). In Column 5 phenotypes with complex measurements (i.e. phenotypes that do not have one single measurement) are marked with an ‘X’.

Table S3: Significantly associated phenotypes that show an over- or under-representation of Neandertal alleles.

phenotype	P-value	FDR	maximum enrichment	OR	direction
Pork intake	<0.001	0.023	2	0.222	under-representation
Ease of skin tanning	<0.001	0.023	5	0.364	under-representation
Smoking status	<0.001	0.023	5	4.629	over-representation
Morning/evening person (chronotype)	<0.001	0.023	3	22.22	over-representation
Loneliness, isolation	<0.001	0.023	2	487.388	over-representation
Frequency of unenthusiasm / disinterest in last 2 weeks	0.002	0.039	3	14.164	over-representation
Pain type(s) experienced in last month	0.004	0.052	4	0.399	under-representation
Number of days/week walked 10+ minutes	0.004	0.052	5	5.39	over-representation
Alcohol intake frequency.	0.004	0.052	4	7.162	over-representation
Water intake	0.008	0.077	3	13.83	over-representation
Body mass index (BMI)	0.01	0.077	13	2.268	over-representation
Handedness (chirality/laterality)	0.01	0.077	5	4.516	over-representation
Salad / raw vegetable intake	0.01	0.077	5	4.616	over-representation
Non-cancer illness year/age first occurred	0.01	0.077	4	5.814	over-representation
Frequency of tiredness / lethargy in last 2 weeks	0.01	0.077	4	6.008	over-representation
Non-oily fish intake	0.012	0.082	1	0.28	under-representation
Coffee intake	0.012	0.082	1	163.265	over-representation
Bread intake	0.014	0.09	2	13.976	over-representation
Tea intake	0.016	0.095	1	122.401	over-representation
Processed meat intake	0.018	0.095	1	0.279	under-representation
Ever had same-sex intercourse	0.018	0.095	2	0.316	under-representation
Pulse rate, automated reading	0.018	0.095	10	2.339	over-representation
Alcohol drinker status	0.02	0.097	2	0.354	under-representation
Coffee type	0.02	0.097	3	6.111	over-representation
Daytime dozing / sleeping (narcolepsy)	0.022	0.102	3	6.412	over-representation
Caffeine drink within last hour	0.024	0.103	7	2.778	over-representation
Miserableness	0.024	0.103	1	81.376	over-representation
Seen a psychiatrist for nerves, anxiety, tension or depression	0.028	0.112	4	4.367	over-representation
Frequency of depressed mood in last 2 weeks	0.028	0.112	1	69.875	over-representation
Whole body fat-free mass	0.032	0.12	1	0.306	under-representation
Basal metabolic rate	0.032	0.12	2	0.376	under-representation
Trunk fat-free mass	0.036	0.13	1	0.292	under-representation
Trunk predicted mass	0.042	0.148	2	0.374	under-representation
Lifetime number of sexual partners	0.046	0.157	1	42.462	over-representation
Hand grip strength (left)	0.048	0.159	2	7.322	over-representation
Major dietary changes in the last 5 years	0.066	0.213	2	6.474	over-representation
Interpolated Year when non-cancer illness first diagnosed	0.074	0.232	1	25.718	over-representation
Standing height	0.076	0.232	1	0.324	under-representation
Childhood sunburn occasions	0.092	0.274	4	0.545	under-representation
Mouth/teeth dental problems	0.096	0.278	3	3.906	over-representation
Cheese intake	0.112	0.315	2	5.652	over-representation
Nap during day	0.114	0.315	3	3.568	over-representation

Table S3: Significantly associated phenotypes that show an over- or under-representation of Neandertal alleles.

phenotype	P-value	FDR	maximum enrichment	OR	direction
Types of physical activity in last 4 weeks	0.12	0.324	1	0.447	under-representation
Comparative height size at age 10	0.128	0.337	5	2.261	over-representation
Frequency of walking for pleasure in last 4 weeks	0.134	0.341	2	4.687	over-representation
Frequency of tenseness / restlessness in last 2 weeks	0.136	0.341	3	3.101	over-representation
Impedance of arm (left)	0.144	0.341	1	0.498	under-representation
Diastolic blood pressure, automated reading	0.146	0.341	3	0.568	under-representation
Arm fat percentage (right)	0.146	0.341	4	2.515	over-representation
Contra-indications for spirometry	0.148	0.341	1	0.478	under-representation
Impedance of leg (right)	0.15	0.341	5	0.595	under-representation
Leg predicted mass (right)	0.16	0.356	2	0.507	under-representation
Number of self-reported cancers	0.166	0.356	3	0.601	under-representation
Trunk fat mass	0.17	0.356	1	0.478	under-representation
Fed-up feelings	0.17	0.356	1	11.109	over-representation
Hair colour (natural, before greying)	0.172	0.356	9	0.706	under-representation
Leg fat-free mass (right)	0.178	0.359	2	0.513	under-representation
Time spend outdoors in summer	0.182	0.359	3	2.712	over-representation
Impedance of arm (right)	0.188	0.359	2	0.536	under-representation
Number of self-reported non-cancer illnesses	0.19	0.359	3	2.662	over-representation
Skin colour	0.192	0.359	4	0.662	under-representation
Forced expiratory volume in 1-second (FEV1), Best measure	0.192	0.359	2	3.833	over-representation
Leg fat mass (right)	0.204	0.375	5	1.986	over-representation
Sleeplessness / insomnia	0.208	0.375	2	3.675	over-representation
Interpolated Age of participant when non-cancer illness first diagnosed	0.214	0.375	3	2.366	over-representation
Frequency of stair climbing in last 4 weeks	0.214	0.375	1	8.652	over-representation
Trunk fat percentage	0.218	0.375	3	2.465	over-representation
Leg fat-free mass (left)	0.22	0.375	2	0.561	under-representation
Leg predicted mass (left)	0.224	0.377	2	0.57	under-representation
Arm fat mass (left)	0.232	0.382	9	1.527	over-representation
Milk type used	0.234	0.382	1	0.581	under-representation
Lamb/mutton intake	0.238	0.383	3	0.595	under-representation
Facial ageing	0.244	0.388	5	1.772	over-representation
Poultry intake	0.26	0.402	4	1.951	over-representation
Overall health rating	0.26	0.402	2	3.076	over-representation
Impedance of whole body	0.266	0.406	1	0.736	under-representation
Fresh fruit intake	0.284	0.428	1	6.608	over-representation
Bread type	0.288	0.428	2	2.952	over-representation
Impedance of leg (left)	0.294	0.432	8	0.724	under-representation
Beef intake	0.298	0.432	3	2.231	over-representation
Whole body fat mass	0.304	0.435	2	0.626	under-representation
Arm fat mass (right)	0.32	0.447	6	1.568	over-representation
Never eat eggs, dairy, wheat, sugar	0.324	0.447	1	0.539	under-representation
Cereal intake	0.324	0.447	2	2.604	over-representation

Table S3: Significantly associated phenotypes that show an over- or under-representation of Neandertal alleles.

phenotype	P-value	FDR	maximum enrichment	OR	direction
Hot drink temperature	0.328	0.448	1	5.228	over-representation
Illness, injury, bereavement, stress in last 2 years	0.348	0.469	2	2.643	over-representation
Hip circumference	0.364	0.485	2	0.703	under-representation
Mood swings	0.402	0.529	2	2.276	over-representation
Weight	0.41	0.529	3	0.714	under-representation
Sitting height	0.422	0.529	2	0.7	under-representation
Systolic blood pressure, automated reading	0.422	0.529	2	0.705	under-representation
Snoring	0.422	0.529	1	4.25	over-representation
Sleep duration	0.424	0.529	2	2.305	over-representation
Spread type	0.442	0.545	2	2.23	over-representation
Usual walking pace	0.448	0.547	1	1.012	under-representation
Neuroticism score	0.472	0.564	1	0.7	under-representation
Hand grip strength (right)	0.472	0.564	2	2.174	over-representation
Comparative body size at age 10	0.486	0.575	3	0.737	under-representation
Part of a multiple birth	0.512	0.6	2	1.973	over-representation
Leg fat mass (left)	0.522	0.605	1	0.756	under-representation
Forced vital capacity (FVC), Best measure	0.53	0.605	5	1.394	over-representation
Age first had sexual intercourse	0.532	0.605	1	3.155	over-representation
Waist circumference	0.538	0.605	1	3.292	over-representation
Cereal type	0.544	0.605	2	1.897	over-representation
Sensitivity / hurt feelings	0.548	0.605	1	3.064	over-representation
Arm fat percentage (left)	0.562	0.615	3	1.571	over-representation
Leg fat percentage (right)	0.568	0.616	3	1.612	over-representation
Cooked vegetable intake	0.6	0.641	2	1.865	over-representation
Wheeze or whistling in the chest in last year	0.602	0.641	2	1.814	over-representation
Dried fruit intake	0.642	0.675	2	0.9	under-representation
Salt added to food	0.646	0.675	1	2.42	over-representation
Body fat percentage	0.68	0.704	2	1.596	over-representation
Falls in the last year	0.686	0.704	1	0.905	under-representation
Risk taking	0.702	0.714	2	0.892	under-representation
Leg fat percentage (left)	0.714	0.72	2	1.625	over-representation
Long-standing illness, disability or infirmity	0.734	0.734	1	1.055	under-representation

For each phenotype (column 1) we show the empirical P value (column 2) for the comparison of the cumulative association P-value distribution (for P<10-4) for archaic alleles and 1,000 cumulative non-archaic allele association P-value distributions. The corresponding false discovery rates (column 3), the rank of the sorted set of archaic SNPs (by P value) for which the archaic distribution has the largest distance to the mean non-archaic distributions (column 4) and the corresponding largest odds ratio between the archaic association P-value distributions (column 5) are provided. Column 6 identifies whether the Neandertal alleles are under- or over-represented compared to non-archaic alleles based on the direction of enrichment.

Table S5: Amino acid variants associated with hair color variation at MC1R.

AA variant	chromosomal position (chr 16)	rsID	Vindija 33.19	Altai	ref	alt	publication(s)
Val60Leu	89985844	*rs1805005*	G	G	G	T	1,2,3,4,6,7
Ala64Ser	89985856		G	G	G	T	5
Arg67Gln	89985866	*rs34090186*	G	G	G	A	1,8
Phe76Tyr	89985893		T	T	T	A	5
Ala81Pro	89985907		G	G	G	C	7
Asp84Glu	89985918	*rs1805006*	C	C	C	A	1,2,3,4,5,6,7
Val92Met	89985940	*rs2228479*	G	G	G	A	1,2,3,4,5,6,7
Thr95Met	89985950		C	C	C	T	4,5,7
Val97Ile	89985955		G	G	G	A	5
Ala103Val	89985974		C	C	C	T	5
Gly104Ser	89985976	*rs2229617*	G	G	G	A	7
Leu106Gln	89985983		T	T	T	A	5
Arg142His	89986091	*rs11547464*	G	G	G	A	1,2,3,4,7
Arg151Cys	89986117	*rs1805007*	C	C	C	T	1,2,3,4,6,7
Ile155Thr	89986130	*rs1110400*	T	T	T	C	1,2,3,4,6,7
Arg160Trp	89986144	*rs1805008*	C	C	C	T	1,2,3,4,6,7
Arg163Gln	89986154	*rs885479*	G	G	G	A	1,2,3,4,6,7,8
Val174Ile	89986186		G	G	G	A	7
Pro230Leu	89986355	*rs368714912*	C	C	C	T	7
His260Pro	89986445		A	A	A	A	7
Val265Ile	89986459	*rs587783376*	G	A	G	A	
Lys278Glu	89986498	*rs201171524*	A	A	A	G	7
Asn279Ser	89986502	*rs376692024*	A	A	A	G	7
Ile287Met	89986527	*rs373957223*	C	C	C	G	1,8
Asp294His	89986546	*rs1805009*	G	G	G	C	1,2,3,4,5,6,7
Arg307Gly	89986586		G	G	G		9

Table includes previously reported non-synonymous variants which have been significantly associated with hair color variation and their genotype in two high-coverage Neandertals (columns 4,5).

(1) Box et al., 1997
(2) Sturm et al., 1998
(3) Box et al., 2001b
(4) Flanagan et al., 2000
(5) Valverde et al., 1995
(6) Harding et al., 2000
(7) Bastiaens et al., 2001
(8) Rana et al., 1999
(9) Lalueza-Fox et al. 2010

Table S6: : Frequency of significantly associated Neandertal alleles in the UK biobank cohort and 1,000 Genomes (phase III) populations

	UK biobank	CEU	TSI	FIN	GBR	IBS	CHB	JPT	CHS	CDX	KHV	GIH	PJL	BEB	STU	ITU	YRI	LWK	GWD	MSL	ESN	ASW	ACB	MXL	PUR	CLM	PEL
chr2:239316043	12.4	13.6	8.3	18.2	13.6	10.3	7.8	2.4	5.1	4.5	5	8	5.7	2.3	3.4	3.4	0	0	0	0	0	0.8	1.6	3.7	7.6	4.3	2.3
chr6:121947984	2.9	3	4.2	3.5	3.3	3.3	10.7	9.1	14.4	17.2	16.8	0.9	1	1.7	0.5	0.5	0	1.5	0	0	0	0	0	0.7	2.4	1.1	1.7
chr6:45553288	7.5	7.1	4.6	8.1	7.6	5.1	0.5	0	0	0.5	0.5	1.4	2.1	0.6	1.5	3.9	0	0	0	0	0	0.8	1	4.5	3.3	4.3	1.2
chr6:503851	7	5.6	1.4	8.1	5.4	6.5	1	0	0	0	0	5.2	3.1	3.5	3.4	1.5	0	0	0	0	0	2.3	1	3.7	3.3	2.1	1.2
chr9:16804167	76.5	80.3	69	74.2	75	66.4	0	0	0	0	0	22.6	26	13.4	12.1	14.1	0	1.5	0	0	0	9.8	8.9	29.1	48.6	46.3	12.2
chr9:16904635	19.3	22.7	17.6	17.7	19	17.8	0	0	0	0	0	4.7	6.2	5.2	2.9	4.9	0	0.5	0	0	0	3.8	3.6	9	12.9	9.6	4.1
chr10:70019371	15.9	12.6	13.4	23.7	15.2	15.9	16.5	12	16.7	15.7	10.4	22.6	22.4	27.9	22.8	18.9	0	0	0.9	0	0	3	6.2	23.9	11	21.8	48.8
chr10:94711457	1.7	2	1.9	1	2.2	2.8	0	0	0	0	0	0.9	0.5	2.9	0.5	1.5	0	0	0	0	0	0.8	0.5	2.2	0	2.7	2.3
chr11:89996325	4.1	3.5	1.9	6.1	4.3	2.8	1.5	1.4	1.4	0.5	0.5	4.7	5.7	3.5	3.4	1.5	0	0	0	0	0	0.8	0.5	0.7	3.3	2.1	2.9
chr14:92793206	8.9	12.1	14.8	5.6	8.7	10.7	3.9	4.3	4.2	5.6	4	3.3	6.2	2.9	3.9	4.9	0	0	0.4	0	0	0.8	2.1	9	14.8	8	5.2
chr15:84716986	26.6	28.8	30.1	27.8	24.5	24.8	6.3	2.4	6.5	5.6	6.9	16	25	19.8	17.5	21.8	0	1.5	0.4	0	0	4.5	3.1	16.4	21.4	17.6	15.1
chr16:89947203	9.7	6.6	6	5.6	11.4	5.1	20.4	10.6	32.9	42.9	39.6	2.8	3.6	2.3	0	0.5	0	0	0	0	0	2.3	2.1	5.2	2.9	1.1	1.2
chr19:31033240	16.2	18.7	13	19.7	15.8	17.8	0	0	0	0	0	4.2	1	1.2	6.8	2.4	0	0	0.4	0	0	3.8	2.1	7.5	12.9	12.8	5.2