Parent-of-Origin inference and its role in the genetic architecture of complex traits: evidence from ~265,000 individuals

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This document contains supplementary figures and supplementary tables only.

Supplementary tables can also be visualized online and downloaded via this link in excel format.

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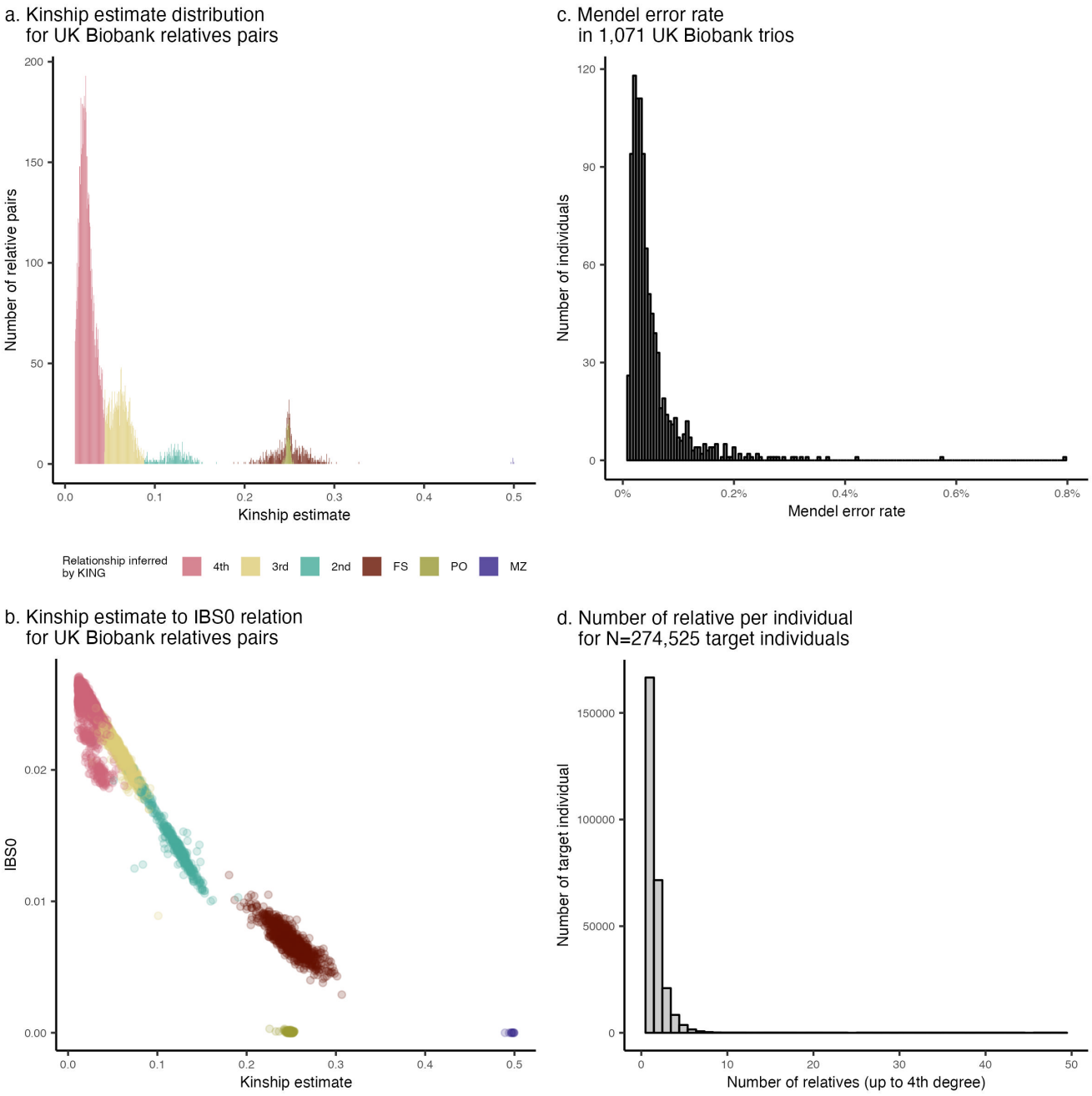
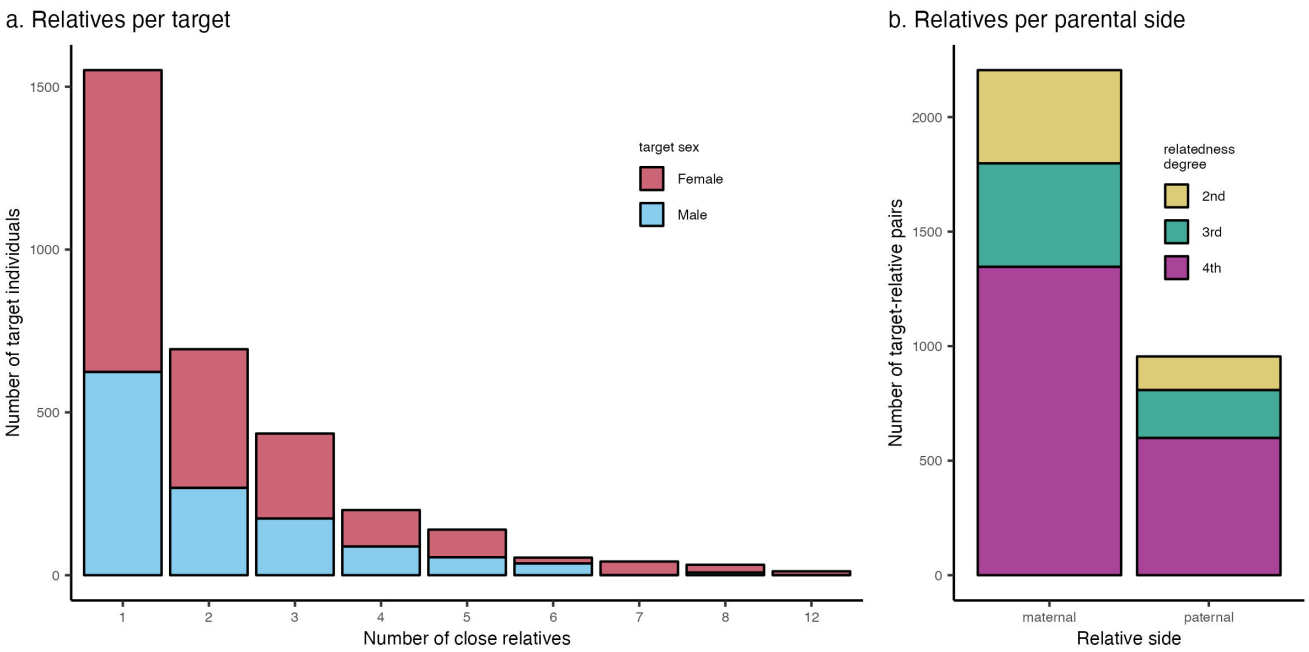
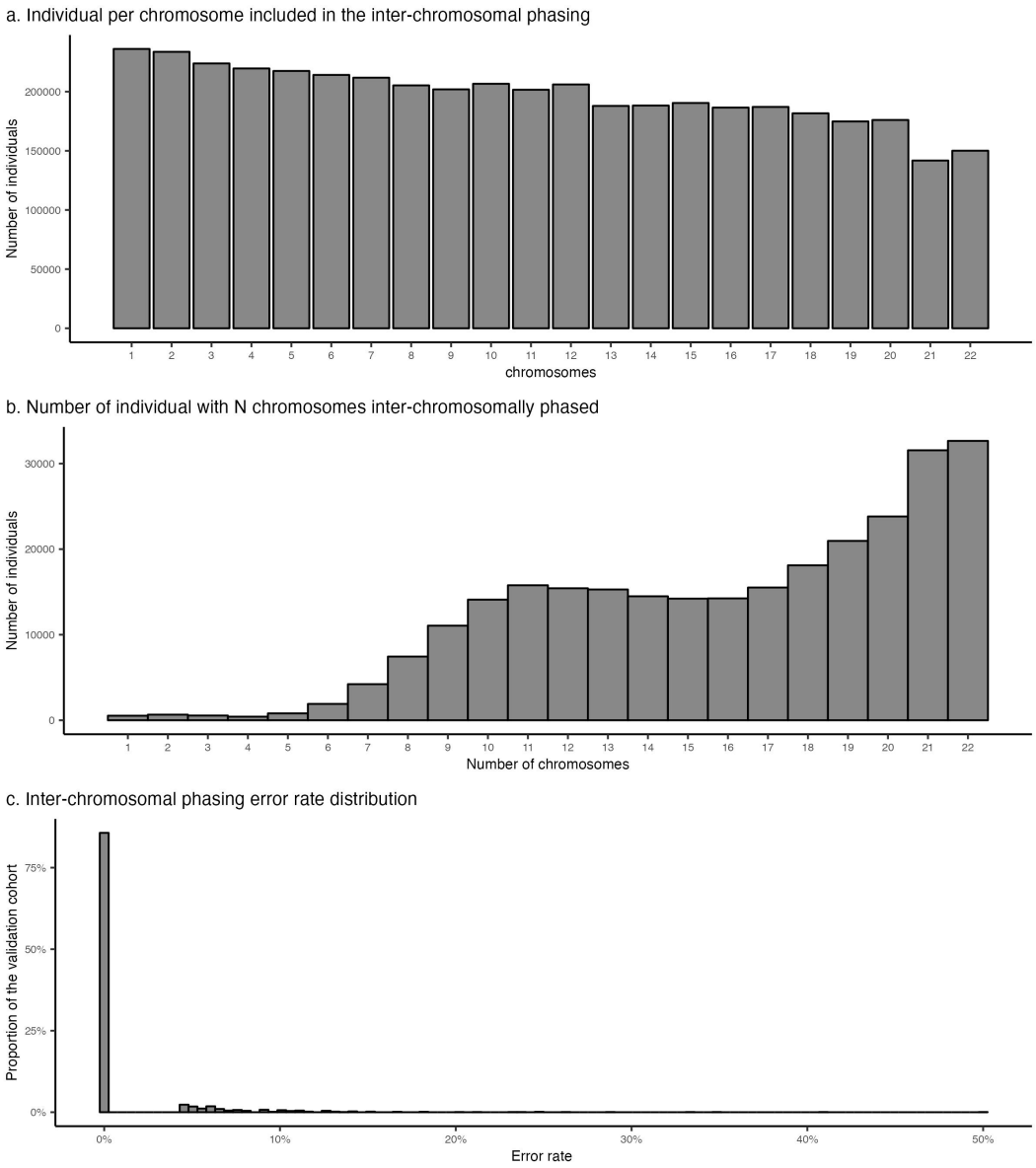
Supplementary Figures



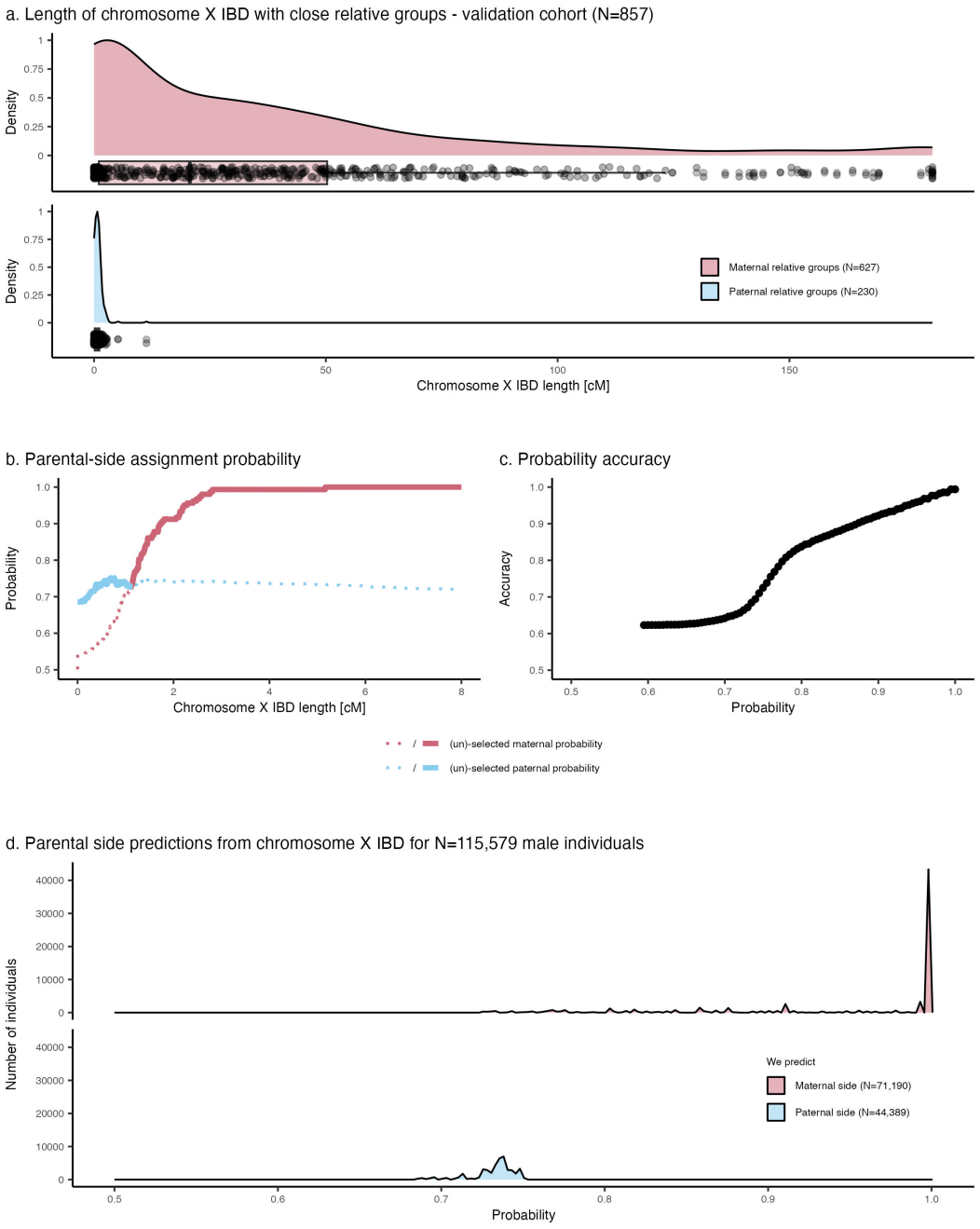
Supplementary Fig. 1 | Relatedness inference and close relative clustering in the UK Biobank. **a**) Kinship estimates distribution and **b**) Kinship estimates versus IBS0 estimates across all UK Biobank monozygotic twins (MZ), first siblings (FS), parent-offspring (PO), second-, third-, and fourth-degree relative pairs. **c**) Mendel error rate distribution across 1,071 UK Biobank parent-offspring trios. None of the trios exhibited a high error rate that would necessitate exclusion. **d**) Distribution of the number of close relatives (up to the fourth degree) per individual across 274,252 UK Biobank individuals with available surrogate parent cluster(s). We found on average 1.65 relatives per individual.



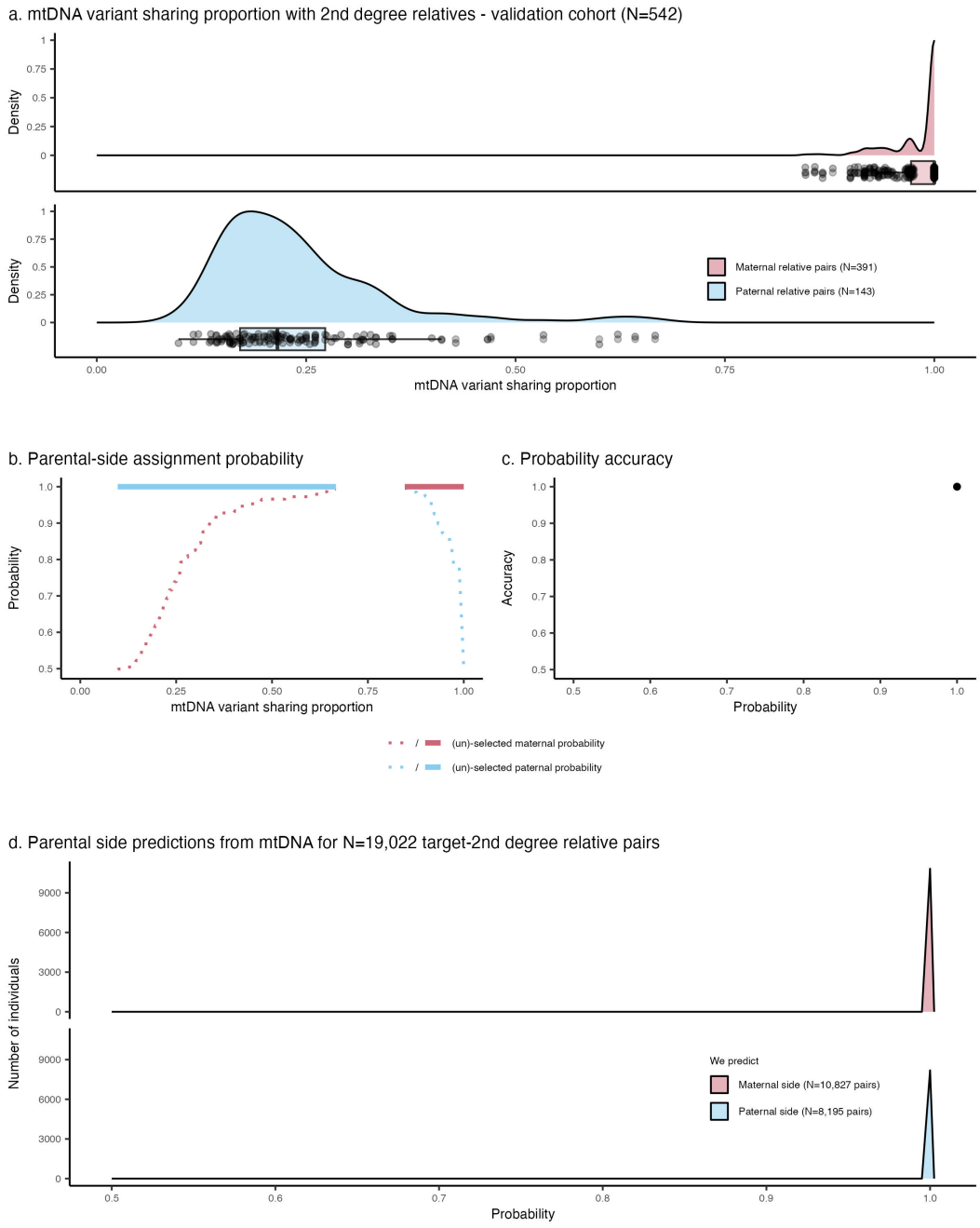
Supplementary Fig. 2 | Validation cohort structure. **a**) Distribution of the number of close relatives (up to the fourth degree) per individual across 2,141 UK Biobank individuals with both available surrogate parent cluster(s) and available parental genomes. Most target individuals are females (60.3%) and have a single surrogate parent (49%). **b**) Distribution of surrogate mother and surrogate father stratified by relatedness degree for 3,160 target-relative pairs. Approximately 70% of surrogate parents in the validation cohort are on the maternal side (i.e., surrogate mothers), and the majority are fourth-degree relatives pairs (61.5%).



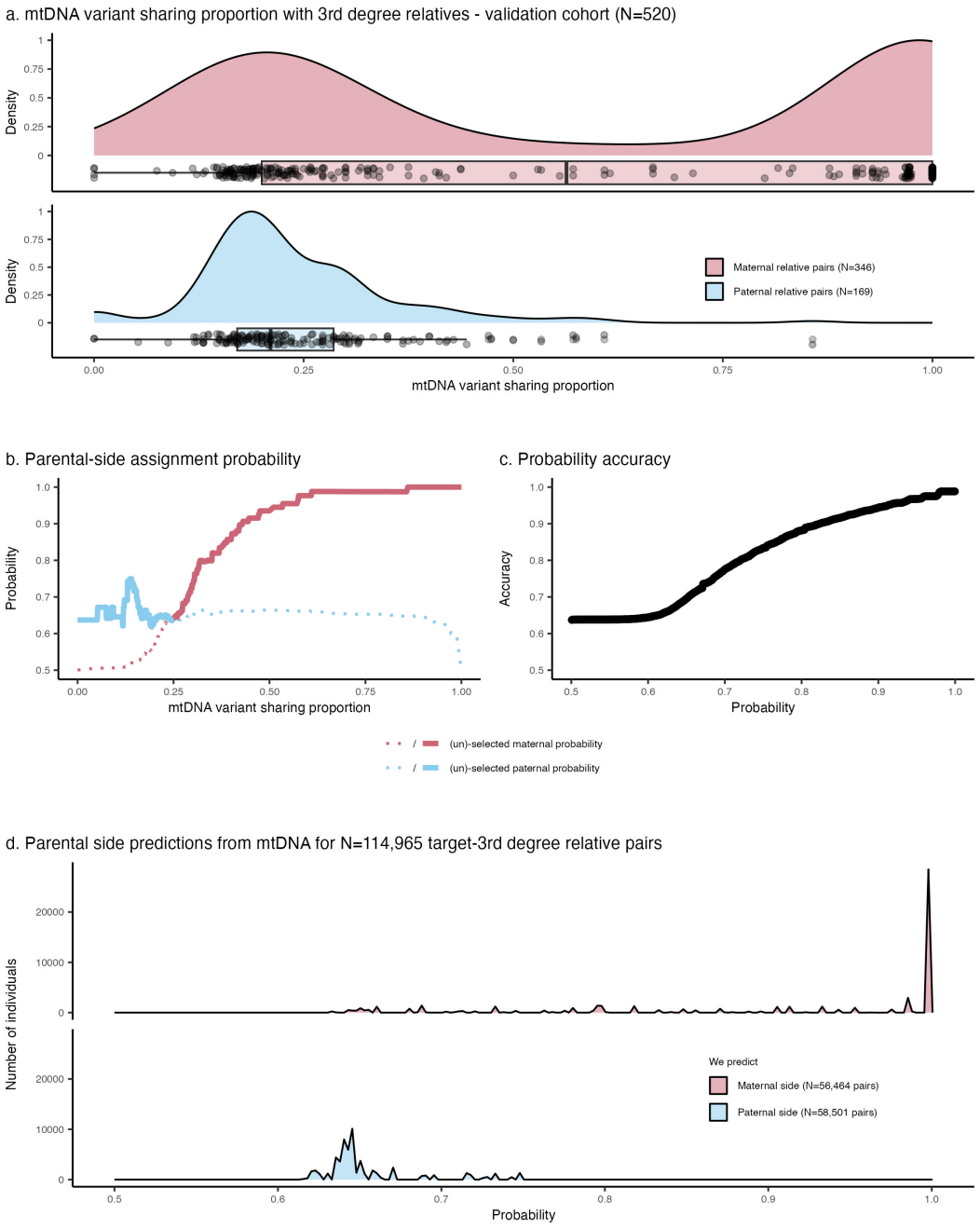
Supplementary Fig. 3 | Inter-chromosomal phasing from close relative groups. **a**) Distribution of the number of individuals with a given chromosome included in the inter-chromosomal phasing. The sample sizes vary across chromosomes, as inter-chromosomal phasing requires at least one IBD segment shared with a surrogate parent on the chromosome. Larger chromosomes are more frequently included, likely due to a higher likelihood of containing at least one IBD segment. **b**) Distribution of the number of individuals with N chromosomes (x-axis) successfully included in the inter-chromosomal phasing. Only 12% of individuals (32,651) had all 22 autosomes phased inter-chromosomally. On average, individuals had 16 chromosomes included in inter-chromosomal phasing. **c**) Distribution of inter-chromosomal phasing error rates across individuals in the validation cohort. Error rates were calculated by comparing phasing results based on surrogate parents to the ground truth obtained from available parental genomes. Most individuals (85.6%) were perfectly phased, with an average error rate of only 1.06% for flipped haplotypes, underscoring the robustness and reliability of the inter-chromosomal phasing method in accurately resolving parental haplotype sets.



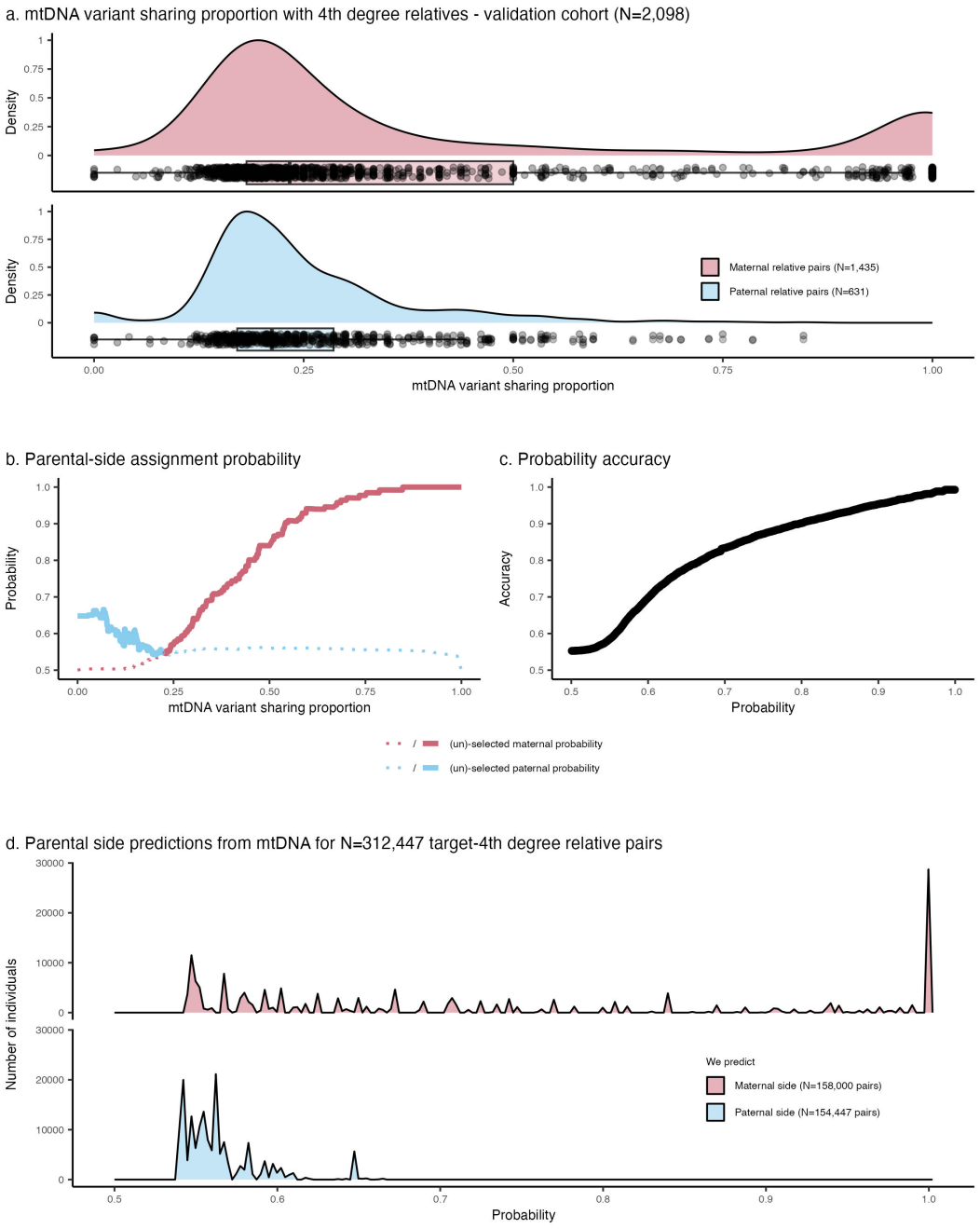
Supplementary Fig. 4 | Parental side assignment from chromosome X IBD analysis in male individuals. **a**) Density distribution of chromosome X IBD segment length in centimorgan (cM) between targets and surrogate father (blue) and targets and surrogate mother (red) across the validation cohort's male individuals. Boxes indicate the interquartile range (IQR), with the bottom and top of the box representing the 25th (Q1) and 75th (Q3) percentiles, respectively. The horizontal line within the box represents the median (50th percentile). Whiskers extend to the smallest and largest values within $Q1-1.5\times IQR$ and $Q3+1.5\times IQR$. Each point represent a target-relative pair. **b**) Parental side probabilities depending on chromosome X IBD segment length derived from the validation cohort. Selected and unselected maternal (red) and paternal (blue) probabilities for a given x-axis value are indicated by solid and dotted lines, respectively. **c**) Accuracy of parental side predictions (y-axis) as a function of the parental side probability (x-axis). **d**) Distribution of maternal (red) and paternal (blue) side assignment probabilities derived chromosome X IBD across 115,579 UK Biobank male individuals.



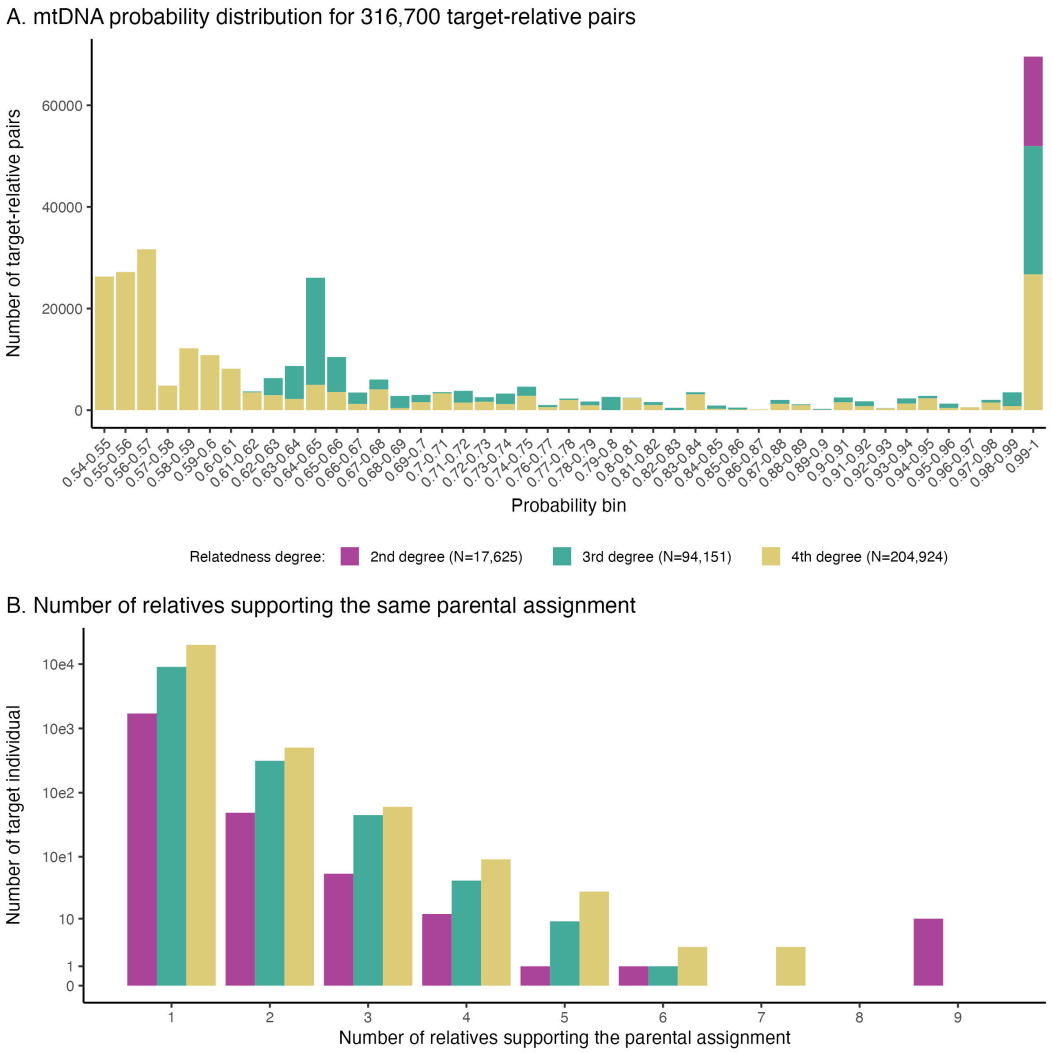
Supplementary Fig. 5 | Parental side assignment from mitochondrial DNA Minor Variant Sharing (MVS) analysis in 2^{nd} degree relative pairs. a) Density distribution of mtDNA Minor Variant Sharing (MVS) between targets and 2^{nd} degree surrogate father (blue) and targets and 2^{nd} degree surrogate mother (red) across the validation cohort's individuals. Boxes indicate the interquartile range (IQR), with the bottom and top of the box representing the 25th (Q1) and 75th (Q3) percentiles, respectively. The horizontal line within the box represents the median (50th percentile). Whiskers extend to the smallest and largest values within $Q1-1.5\times IQR$ and $Q3+1.5\times IQR$. Each point represent a target-relative pair. **b**) Parental side probabilities depending on mtDNA MVS derived from the validation cohort. Selected and unselected maternal (red) and paternal (blue) probabilities for a given x-axis value are indicated by solid and dotted lines, respectively. **c**) Accuracy of parental side predictions (y-axis) as a function of the parental side probability (x-axis). **d**) Distribution of maternal (red) and paternal (blue) side assignment probabilities derived from mtDNA MVS across 19,022 UK Biobank 2^{nd} degree relative pairs.



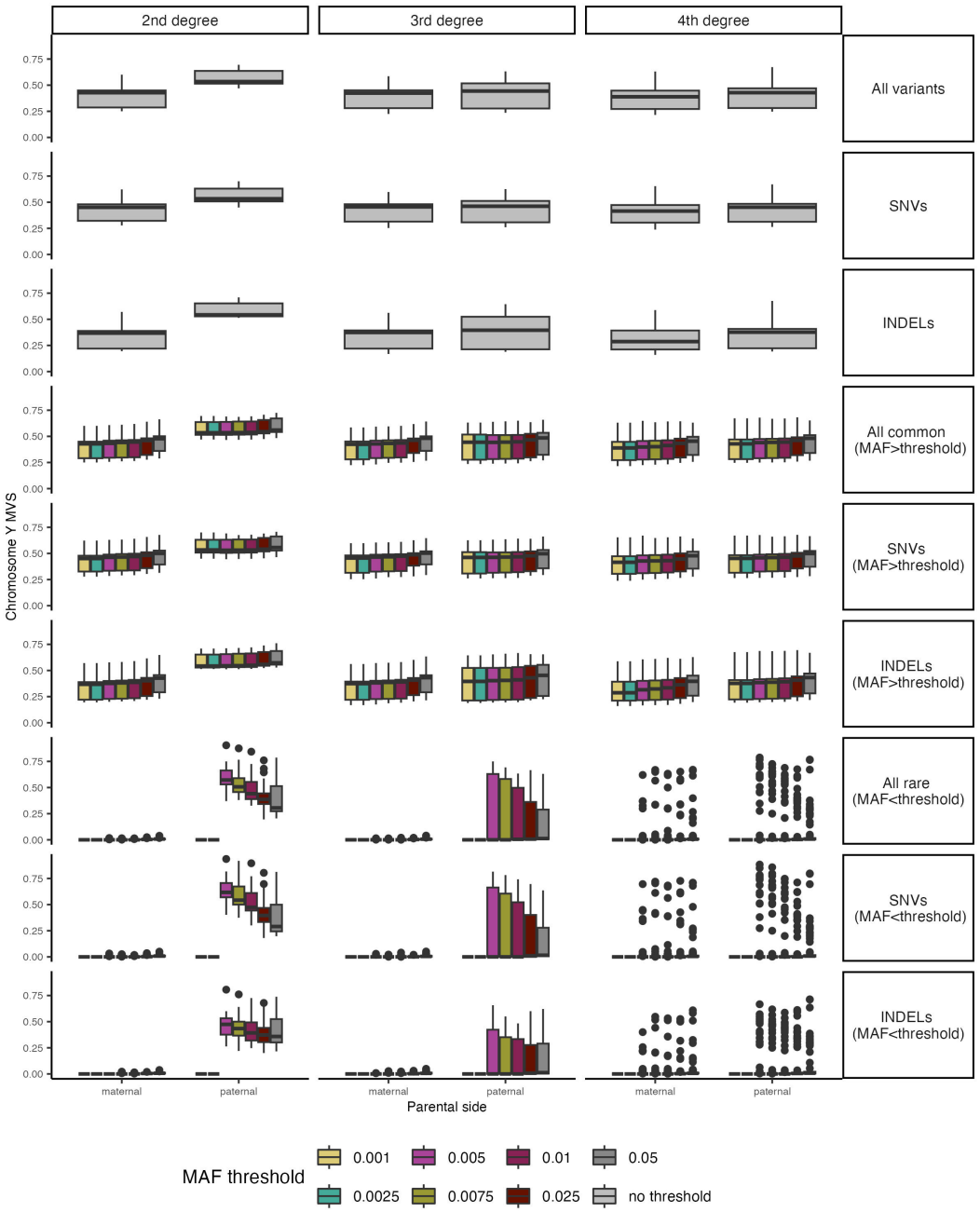
Supplementary Fig. 6 | Parental side assignment from mitochondrial DNA Minor Variant Sharing (MVS) analysis in 3^{rd} degree relative pairs. a) Density distribution of mtDNA Minor Variant Sharing (MVS) between targets and 3^{rd} degree surrogate father (blue) and targets and 3^{rd} degree surrogate mother (red) across the validation cohort's individuals. Boxes indicate the interquartile range (IQR), with the bottom and top of the box representing the 25th (Q1) and 75th (Q3) percentiles, respectively. The horizontal line within the box represents the median (50th percentile). Whiskers extend to the smallest and largest values within $Q1-1.5\times IQR$ and $Q3+1.5\times IQR$. Each point represent a target-relative pair. **b**) Parental side probabilities depending on mtDNA MVS derived from the validation cohort. Selected and unselected maternal (red) and paternal (blue) probabilities for a given x-axis value are indicated by solid and dotted lines, respectively. **c**) Accuracy of parental side predictions (y-axis) as a function of the parental side probability (x-axis). **d**) Distribution of maternal (red) and paternal (blue) side assignment probabilities derived from mtDNA MVS across 114,965 UK Biobank 3^{rd} degree relative pairs.



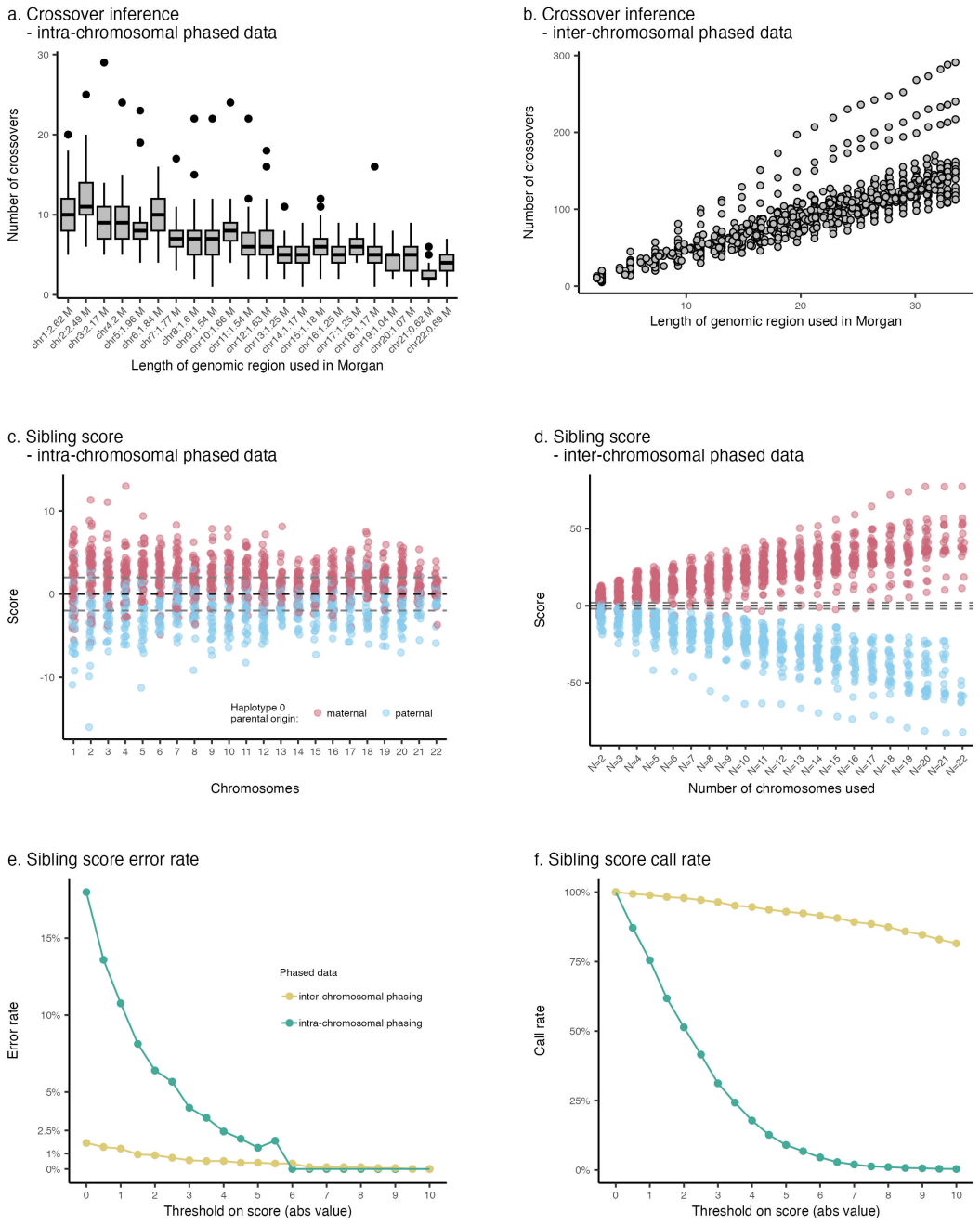
Supplementary Fig. 7 | Parental side assignment from mitochondrial DNA Minor Variant Sharing (MVS) analysis in 4^{th} degree relative pairs. a) Density distribution of mtDNA Minor Variant Sharing (MVS) between targets and 4^{th} degree surrogate father (blue) and targets and 4^{th} degree surrogate mother (red) across the validation cohort's individuals. Boxes indicate the interquartile range (IQR), with the bottom and top of the box representing the 25th (Q1) and 75th (Q3) percentiles, respectively. The horizontal line within the box represents the median (50th percentile). Whiskers extend to the smallest and largest values within $Q1-1.5\times IQR$ and $Q3+1.5\times IQR$. Each point represent a target-relative pair. **b**) Parental side probabilities depending on mtDNA MVS derived from the validation cohort. Selected and unselected maternal (red) and paternal (blue) probabilities for a given x-axis value are indicated by solid and dotted lines, respectively. **c**) Accuracy of parental side predictions (y-axis) as a function of the parental side probability (x-axis). **d**) Distribution of maternal (red) and paternal (blue) side assignment probabilities derived from mtDNA MVS across 312,447 UK Biobank 4^{th} degree relative pairs.



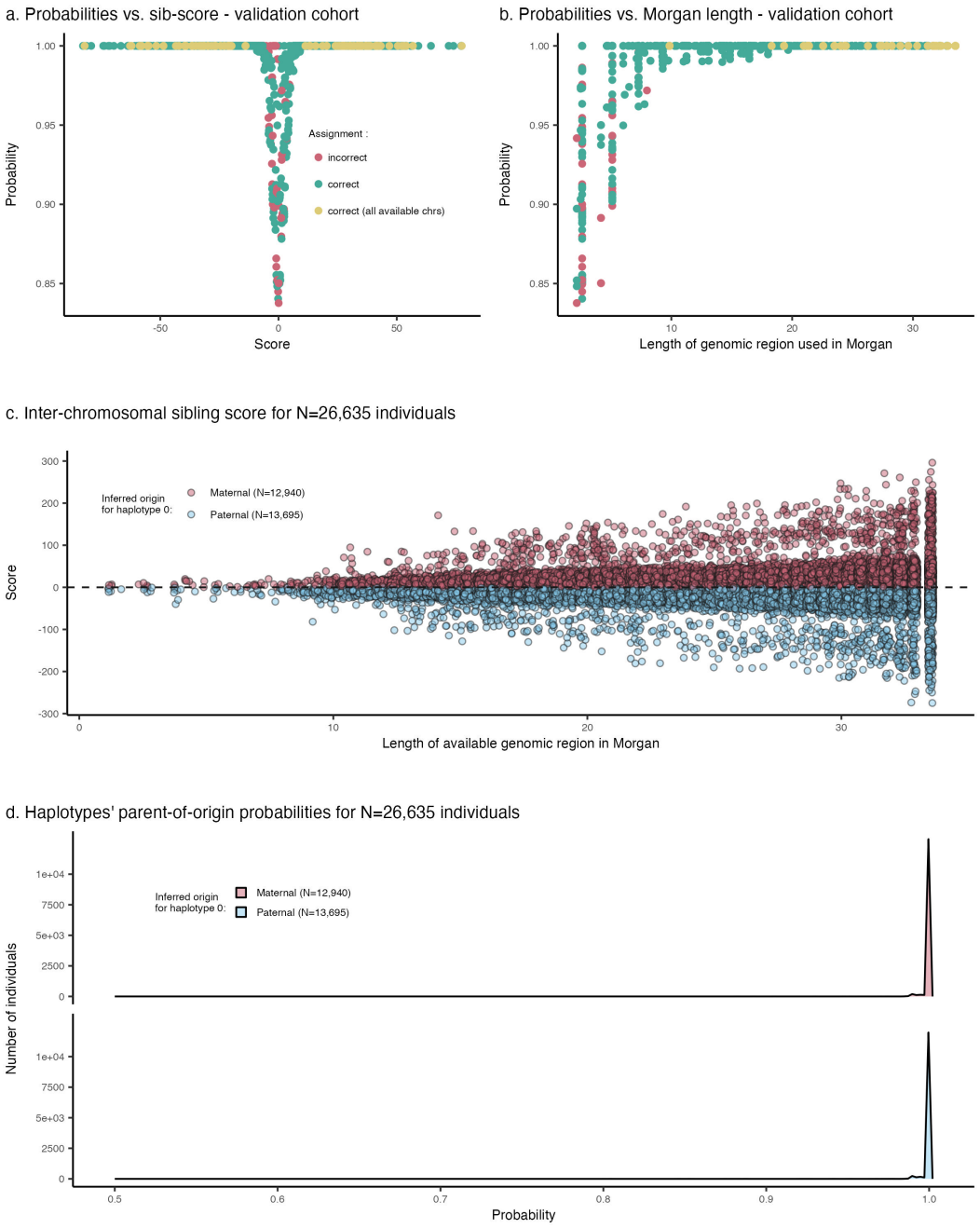
Supplementary Fig. 8 | Selection of mitochondrial DNA (mtDNA) Minor Variant Sharing (MVS) predictors for parental side assignments. a) Distribution of parental side assignment probabilities for 316,700 target-relative pairs, stratified by relatedness degree (2^{nd}, 3^{rd}, and 4^{th} degree). For individuals with multiple relatives of the same degree, only the relative with the highest predicted accuracy was retained. Probabilities are binned at intervals of 0.01 for visualization. **b**) Log-scale distribution of the number of target individuals (y-axis) based on the number of relatives (x-axis) supporting the same parental side assignment, further stratified by degree of relatedness.



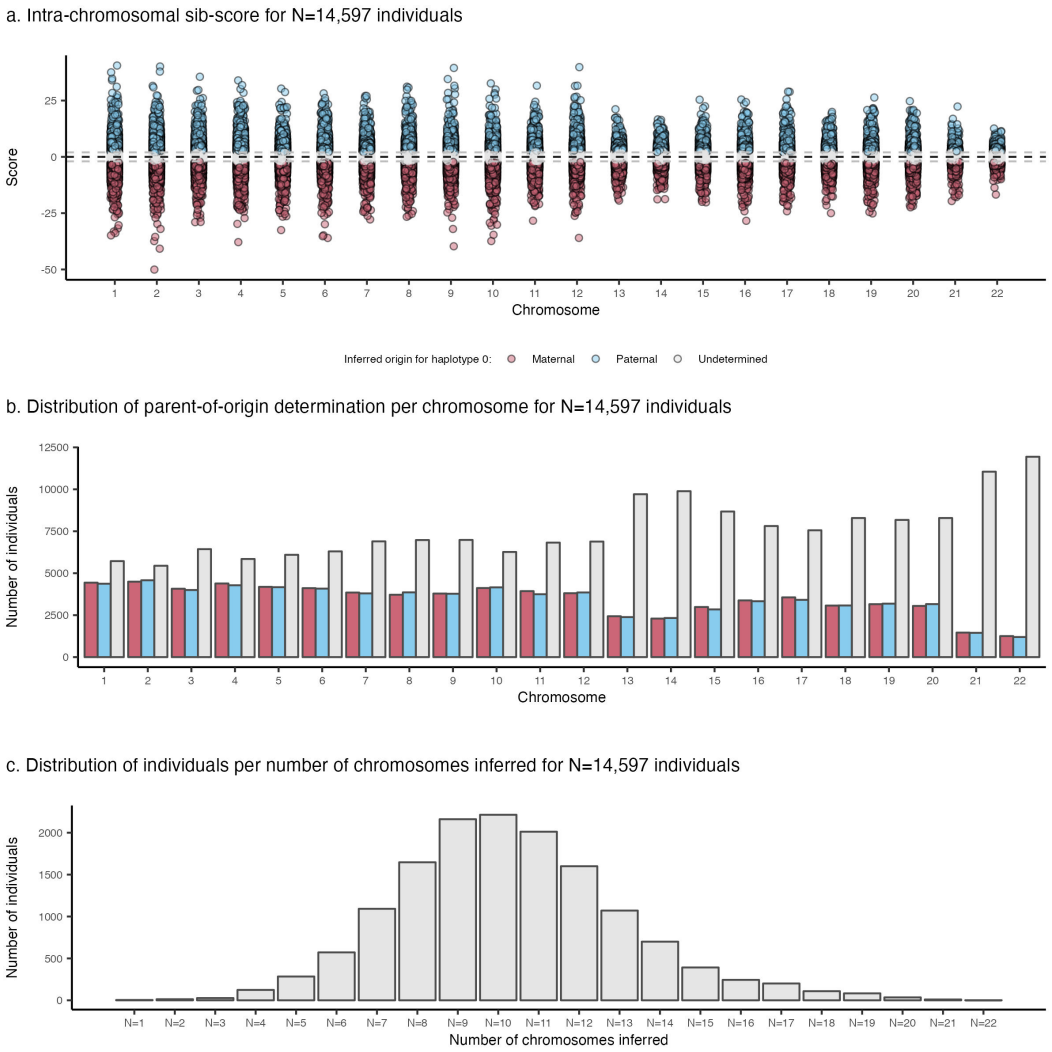
Supplementary Fig. 9 | Chromosome Y Minor Variant Sharing (MVS) analysis. The y-axis represents the proportion of chromosome Y minor variants shared (MVS), stratified by parental side assignments (maternal or paternal, x-axis), relatedness degrees (columns: 2^{nd}, 3^{rd}, and 4^{th} degree), variant categories (rows), and minor allele frequency (MAF) thresholds (color-coded). Categories include all variants, single nucleotide variants (SNVs), insertions/deletions (INDELs), common variants (MAF > threshold), and rare variants (MAF < threshold). The MAF thresholds are denoted in the legend for clearer distinction of variant frequencies.



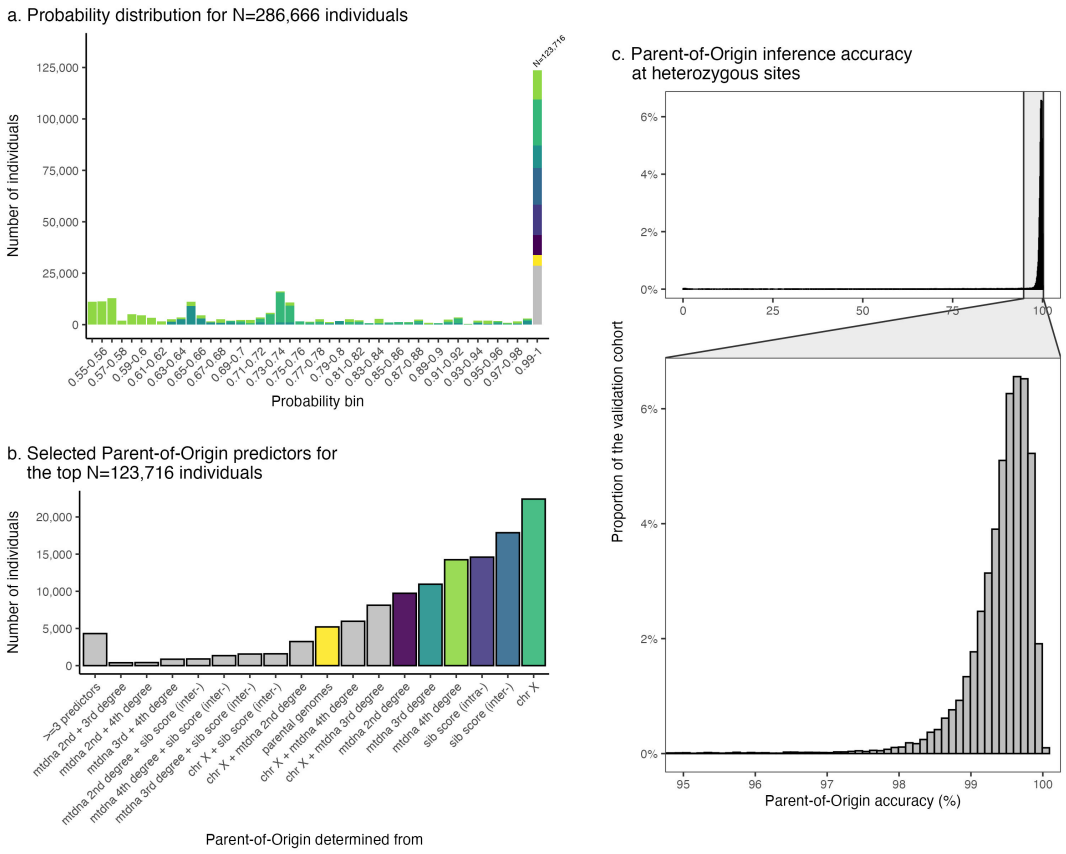
Supplementary Fig. 10 | Evaluation of sibling scores from intra- and inter-chromosomal phasing in N=88 individuals of the validation cohort. **a**) Distribution of the number of inferred crossovers (y-axis) per chromosome (x-axis) derived from intra-chromosomally phased data. **b**) Distribution of the number of inferred crossovers (y-axis) relative to the genomic length used (in Morgans, x-axis) derived from inter-chromosomally phased data. **c**) Distribution of sibling scores (y-axis) per chromosome (x-axis) using intra-chromosomally phased data. Maternal and paternal haplotypes are color-coded in red and blue, respectively. **d**) Distribution of sibling scores (y-axis) relative to the number of chromosomes included in inter-chromosomally phased data (x-axis). **e**) Error rates (y-axis) of sibling scores for varying score thresholds (absolute values, x-axis). For example, excluding ambiguous scores between -2 and 2 reduced error rates to 1.4% with inter-chromosomal phasing, compared to 6.4% with intra-chromosomal phasing. **f**) Call rates (y-axis) of sibling scores for varying score thresholds (absolute values, x-axis), showing the proportion of individuals meeting the threshold criteria.



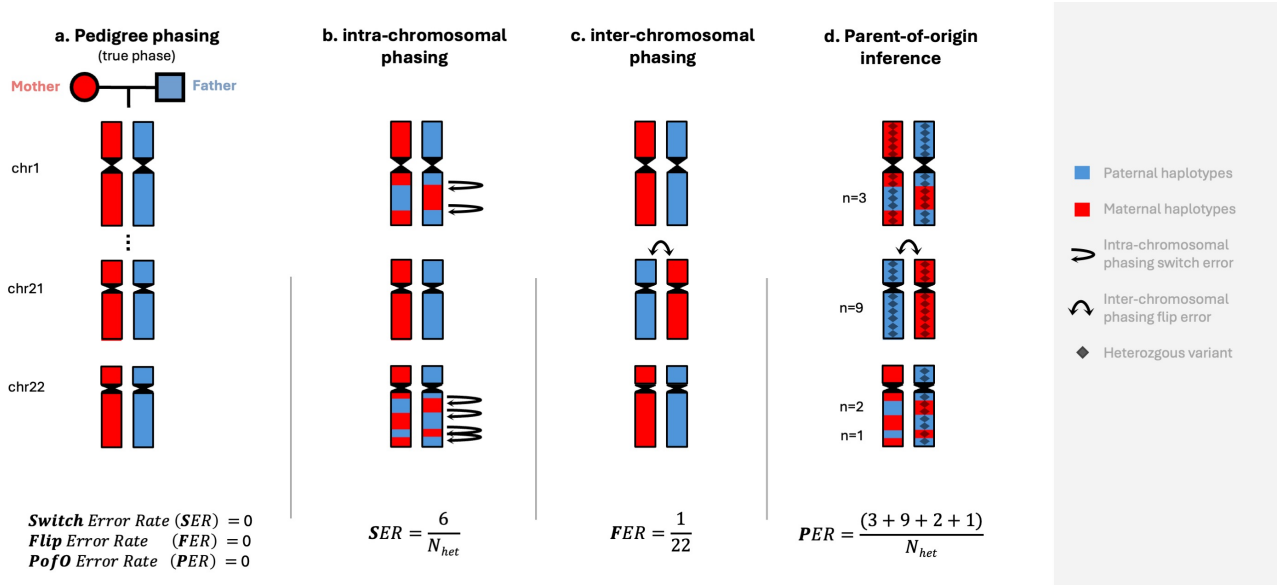
Supplementary Fig. 11 | Validation and derivation of parent-of-origin probabilities using sibling scores from inter-chromosomal phased data. **a**) PofO probabilities (y-axis) as a function of sibling scores (x-axis) in the validation cohort. Each dot represents a specific configuration (an individual with a given number of chromosomes used). We varied the number of chromosome used per individual to assess the accuracy of different configurations (see Supplementary Figure **??**D). Red dots indicate incorrect parental assignments, green dots indicate correct assignments, and yellow dots denote correct assignments using the maximum available chromosomes (N_{max}, corresponds to the full set of inter-chromosomally phased chromosome for a given individual). No errors were observed when N_{max} chromosomes were used. **b**) PofO probabilities (y-axis) plotted against the total available genomic length in Morgans (x-axis) for sibling score calculation in the validation cohort. Each configuration is represented as a dot (color-coded as in panel a). Increasing genomic length results in higher assignment accuracy, with perfect accuracy achieved at N_{max} (yellow dots). **c**) Sibling scores (y-axis) derived for N=26,635 individuals across available genomic lengths (x-axis). Most configurations (99.5%) cover more than 10 Morgans and include over 30 inferred crossover events, ensuring high assignment accuracy (as indicated in the validation panels a and b). **d**) Distribution of PofO probabilities for 26,635 individuals. A majority of individuals (>95%) exhibit probabilities of 1, resulting in perfect accuracy within the validation cohort (see yellow dots in panel a).



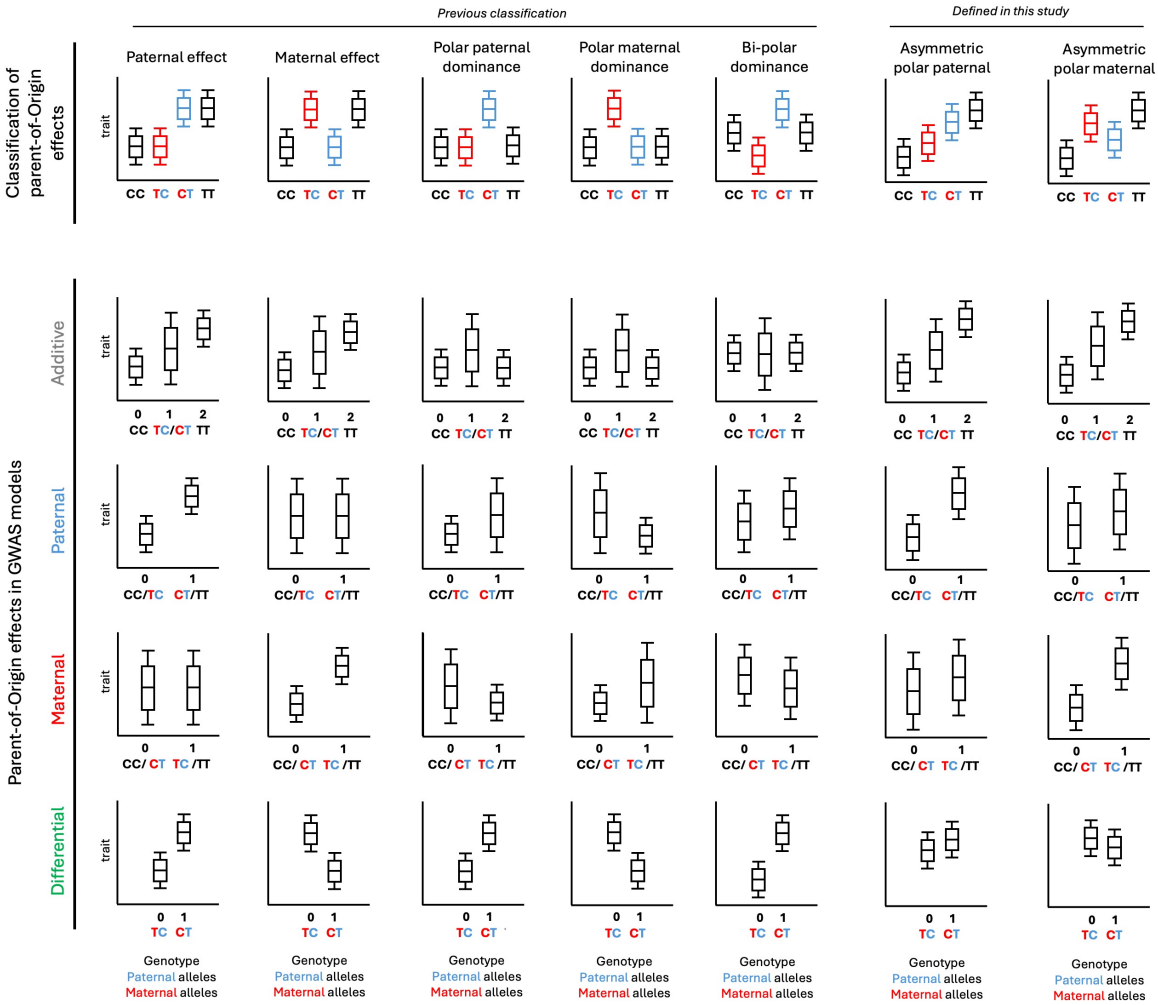
Supplementary Fig. 12 | Derivation of parent-of-origin probabilities using sibling scores from intra-chromosomal phased data. **a**) Sibling scores calculated for each chromosome independently (x-axis). Each dot corresponds to a single chromosome, with blue and red dots indicating paternal and maternal assignment, respectively, for the first haplotype. Undetermined assignments are shown in gray. **b**) Distribution of the number of individuals (y-axis) with inferred PofO for each chromosome (x-axis). Larger chromosomes exhibit higher numbers of PofO inference (e.g., 8,811 individuals for chromosome 1), while smaller chromosomes show fewer inferences (e.g., 2,450 individuals for chromosome 22), reflecting the increased likelihood of crossovers on larger chromosomes. **c**) Distribution of the number of chromosomes with inferred PofO per individual (x-axis), with counts shown on the y-axis. On average, individuals have 10.3 chromosomes with PofO inferred. This is lower compared to the average of 16 chromosomes inferred using inter-chromosomal phasing (see Supplementary Figure **??**B).



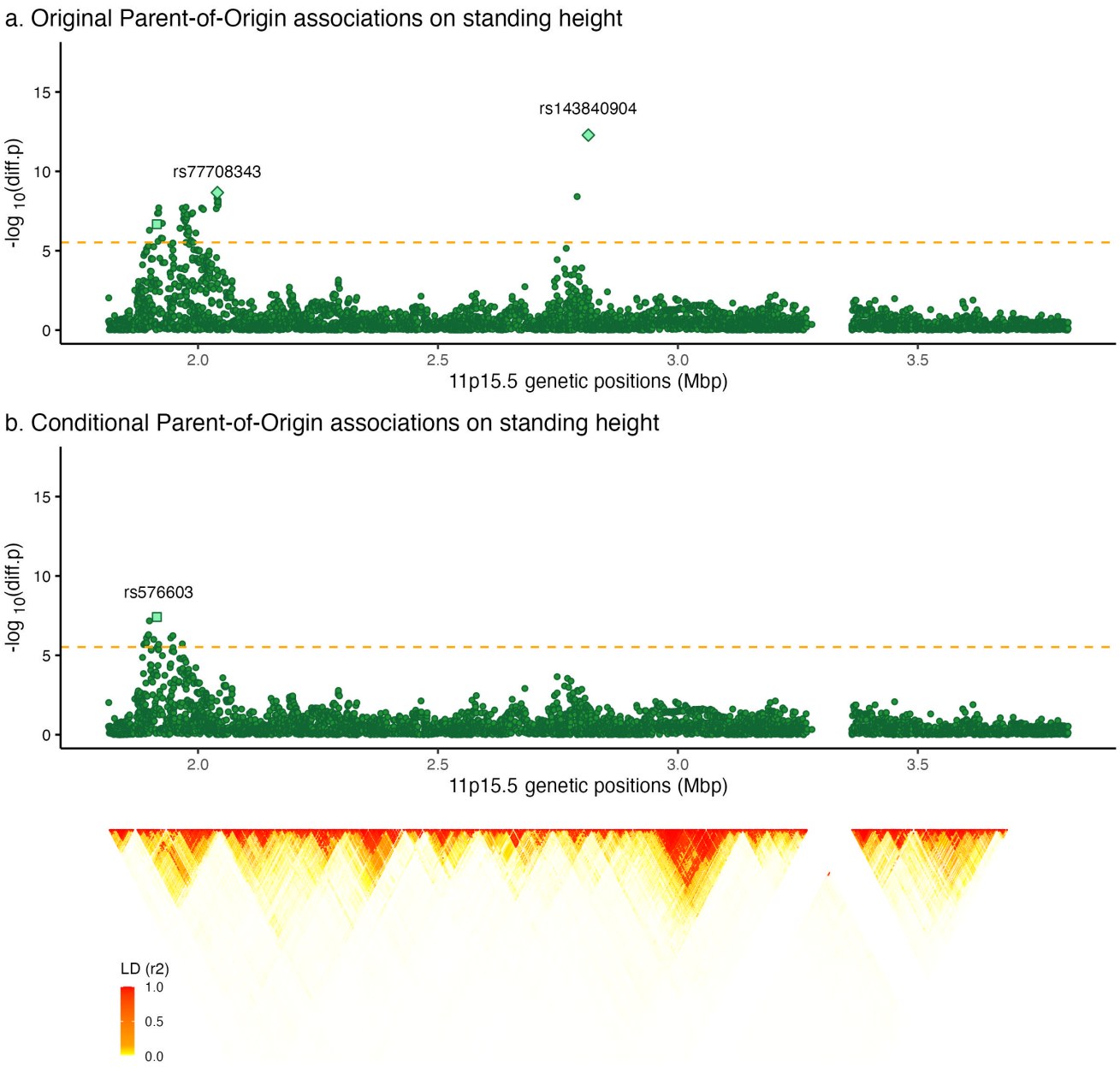
Supplementary Fig. 13 | Selected parent-of-origin predictors and error rate. **a**) Distribution of PofO probabilities for N=286,666 individuals. The x-axis represents probability bins, and the y-axis shows the number of individuals. Colors correspond to the predictors used for PofO determination, as indicated in panel (b). **b**) Distribution of selected PofO predictors for individuals having a PofO probability greater than 0.99. **c**) Distribution of the PofO inference accuracy. Errors were computed at heterozygous site only by comparing the PofO determined using our approach to the one obtained from parental genomes. We found an average accuracy of 97.94%. This rate is impacted by individuals for which entire haplotypes are incorrect, resulting from inter-chromosomal phasing errors, totaling 64 haplotypes (in the validation cohort). These are likely due to the presence of relatives sharing both paternal and maternal IBD segments, which may be due to consanguinity, and were not filtered out during the construction of the validation cohort. As a result, only a few individuals' haplotypes decrease the global accuracy, and most individuals have a PofO correctly assigned. Indeed, the majority of haplotypes (83.9%) exhibit accuracy above 99%, and half of the haplotypes have more than 0.52% accuracy.



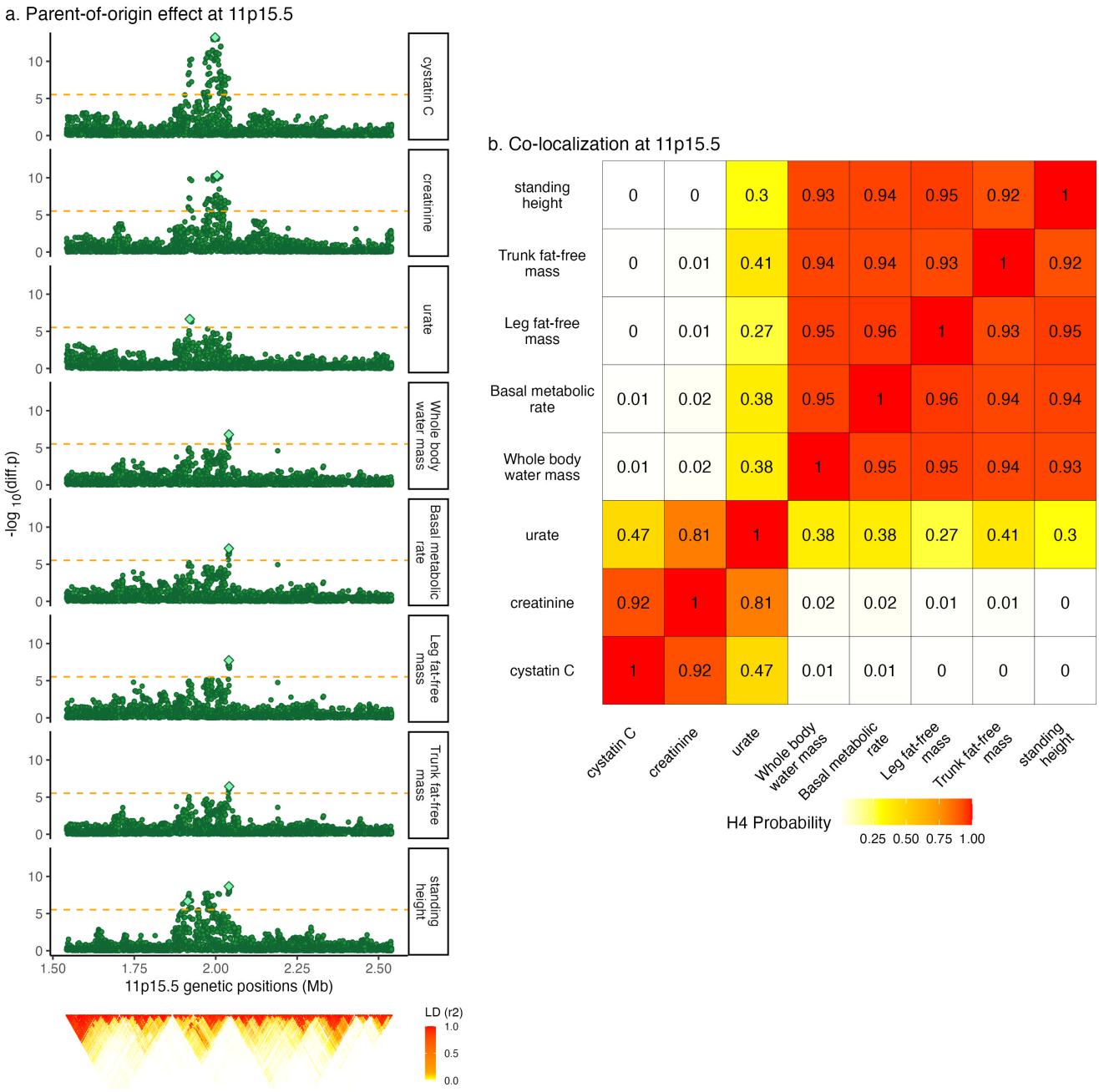
Supplementary Fig. 14 | Illustration of errors in statistical methods. **a**) A perfectly phased individual (both intra- and inter-chromosomally). Phasing is performed using the parental genomes: maternal (red) and paternal (blue). In this scenario, the PofO is directly inferred alongside the phasing process without errors. **b**) An individual with intra-chromosomal phasing errors introduced by traditional phasing software (e.g., SHAPEIT5[1]). These errors are represented as switches between parental haplotypes within the same chromosome (horizontal arrows), with 6 switches shown here. Since switches occur only at heterozygous sites, the switch error rate (SER) is calculated as $SER = 6/N_{het}$, where N_{het} is the total number of heterozygous sites. **c**) An individual with inter-chromosomal phasing errors but assumed perfect intra-chromosomal phasing (no switches within the same chromosome). Errors in this case are represented as flips of entire parental haplotypes across chromosomes (vertical arrow), with one flip shown here. The flip error rate (FER) is calculated as the proportion of chromosomes flipped relative to the majority, ranging from 0% to 50%. **d**) An individual with combined intra- and inter-chromosomal phasing errors. PofO inference errors aggregate contributions from both switch and flip errors. The PofO error rate (PER) is computed as the proportion of heterozygous sites (grey diamonds) incorrectly assigned. For example, in this scenario, assigning the first haplotype as maternal and the second as paternal results in a total of 15 errors.



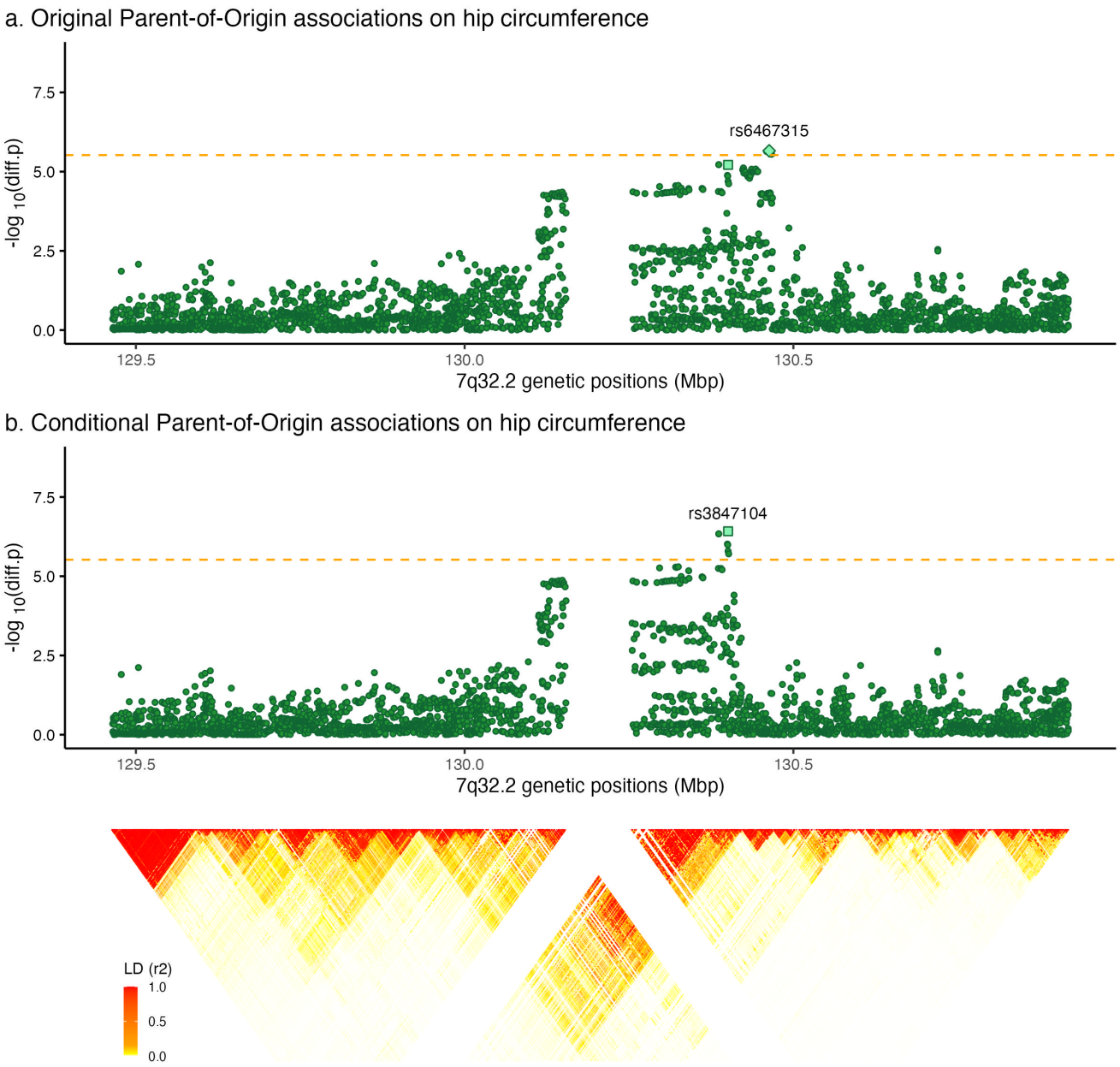
Supplementary Fig. 15 | Classification and detection of parent-of-origin effects in GWAS. Top panel illustrates the classification of POEs[2] and shows the variation in trait values (y-axis) across genotypes and parental origin of alleles (x-axis). Maternal alleles are shown in red, and paternal alleles are shown in blue. Boxplots represent the distribution of trait values for different genotypes: black boxes for homozygotes, red boxes for maternal heterozygotes, and blue boxes for paternal heterozygotes. Each boxplot includes the 25th, 50th (median), and 75th percentiles, with whiskers extending to the minimum and maximum values. **Bottom panels** show the interpretation of the different POEs (x-axis) using various GWAS models (y-axis), including additive, paternal, maternal, and differential models. In this study, we identified POEs using the differential GWAS model.



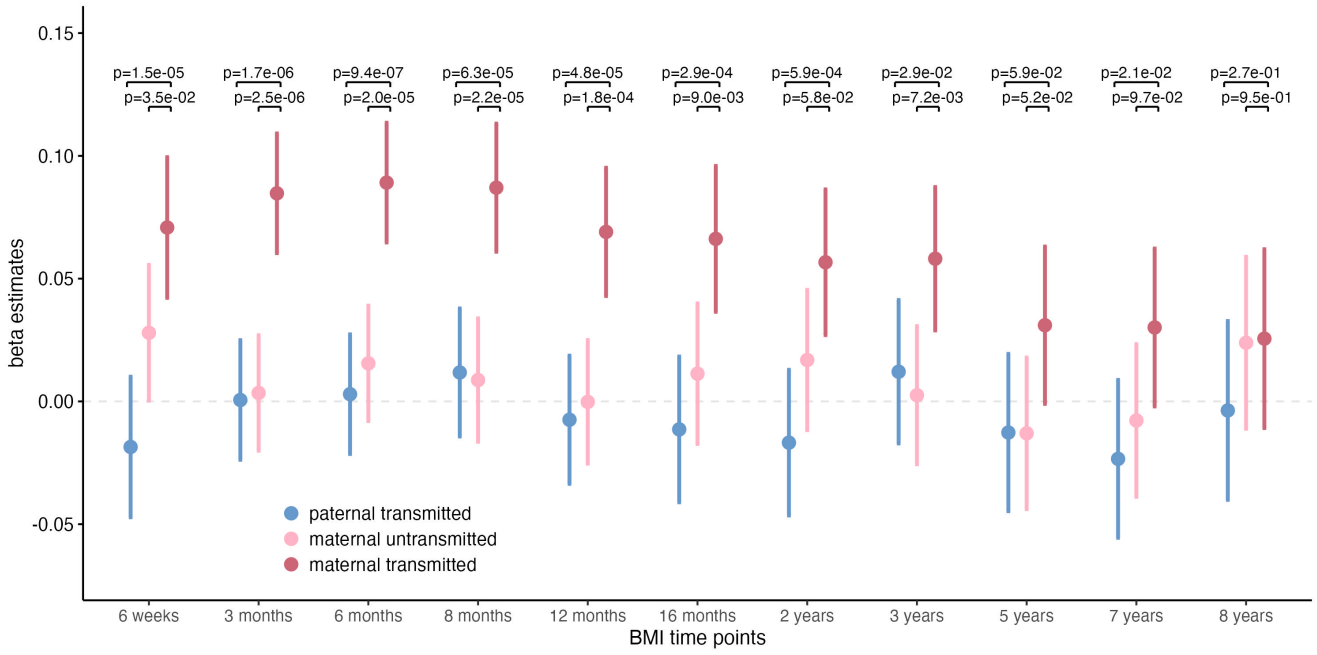
Supplementary Fig. 16 | Conditional analysis on standing height at 11p15.5. a) Original, and **b**) Conditional differential GWAS show the association strength ($-log_{10}(p - value)$, y-axis) against the genomic position (x-axis) at the 11p15.5 region. Each point represents a genetic variant. Diamonds indicate the variants with independent, significant POE on standing height found in this study in the primary GWAS scan. The square represents the variant with significant and independent POE identified in the conditional analysis. Orange dashed lines represent the significance threshold used in this study when focusing on imprinted regions (3.1×10^{-06}). Bottom panel shows the Linkage Disequilibrium (LD) pattern, ranging from LD=0 (white) to LD=1 (red).



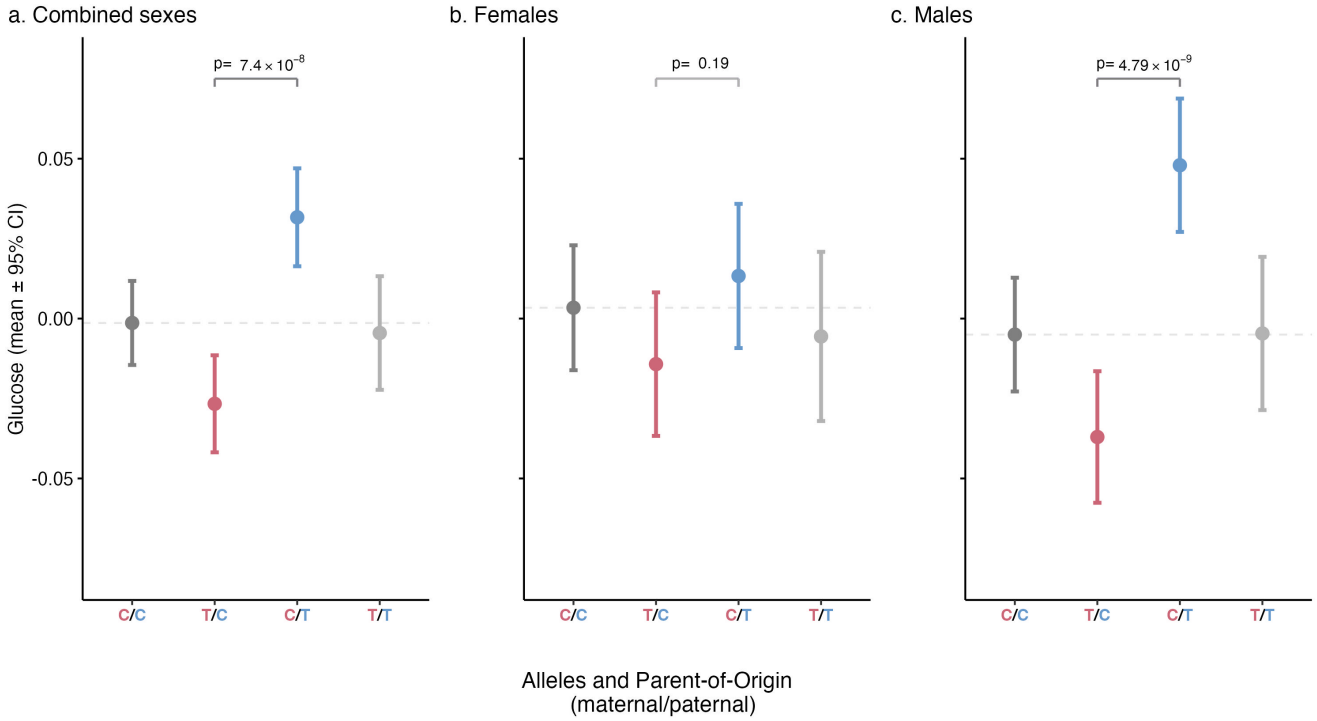
Supplementary Fig. 17 | Co-localization analyses at 11p15.5. **a**) Parent-of-origin associations across traits at 11p15.5 show the differential GWAS association strength ($-log_{10}(p-value)$, y-axis) against the genomic position (x-axis). Orange dashed lines represent the significance threshold used in this study when focusing on imprinted regions (3.1×10^{-6}). Each point represents a genetic variant. Light green diamonds shows lead POE reported in Table **??**. **b**) Co-localization probability heatmap (i.e, shared causal variant probability H_4).



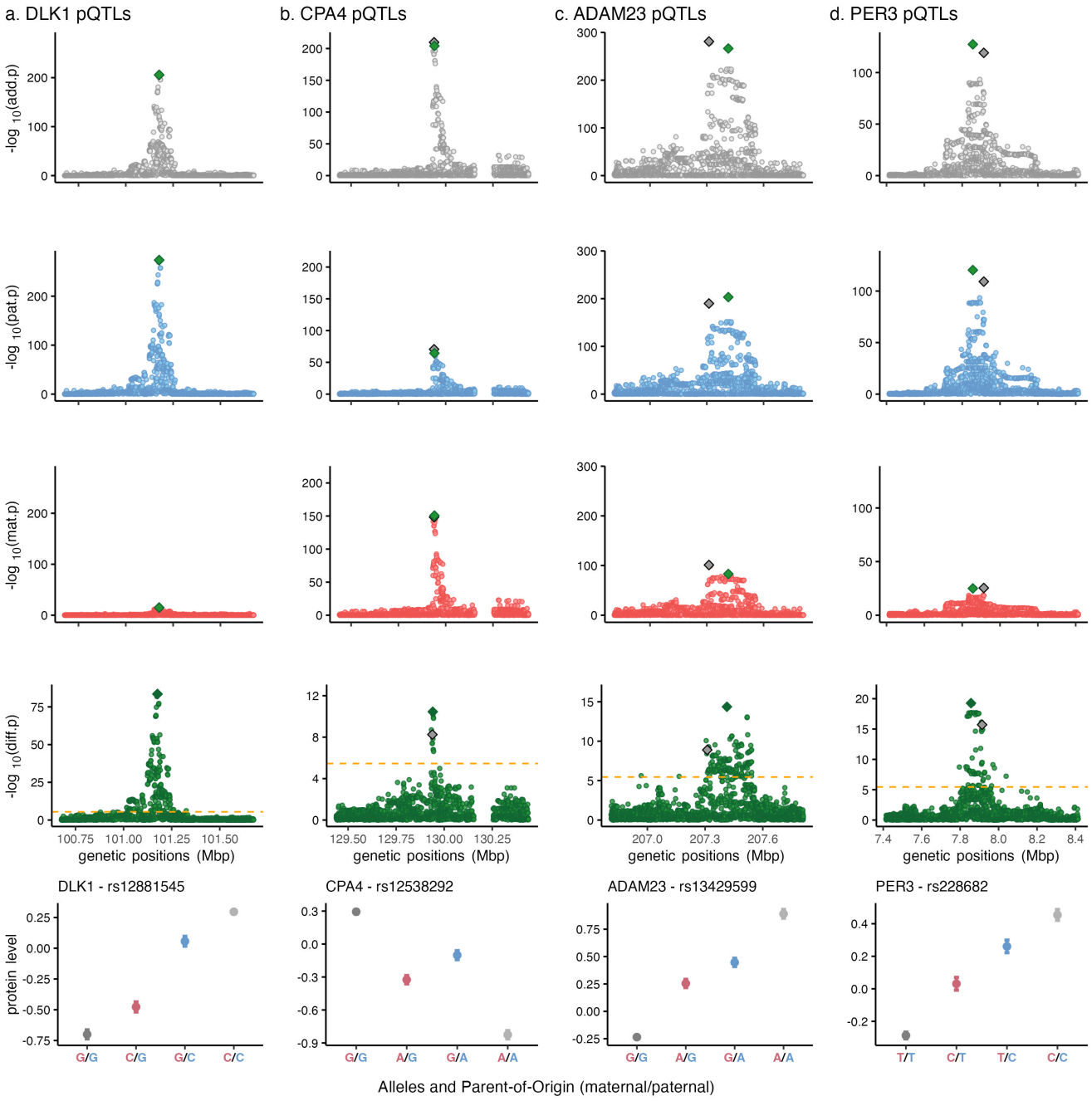
Supplementary Fig. 18 | Conditional analysis on hip circumference at 7q32.2. **a**) Original, and **b**) Conditional differential GWAS show the association strength ($-log_{10}(p-value)$, y-axis) against the genomic position (x-axis) at the 7q32.2 region. Each point represents a genetic variant. The diamond indicates the variant with significant POE on hip circumference found in this study in the primary GWAS scan. The square indicates the variant with significant and independent POE identified in the conditional analysis. Orange dashed lines represent the significance threshold used in this study when focusing on imprinted regions (3.1×10^{-6}). Bottom panel shows the Linkage Disequilibrium (LD) pattern, ranging from LD=0 (white) to LD=1 (red).



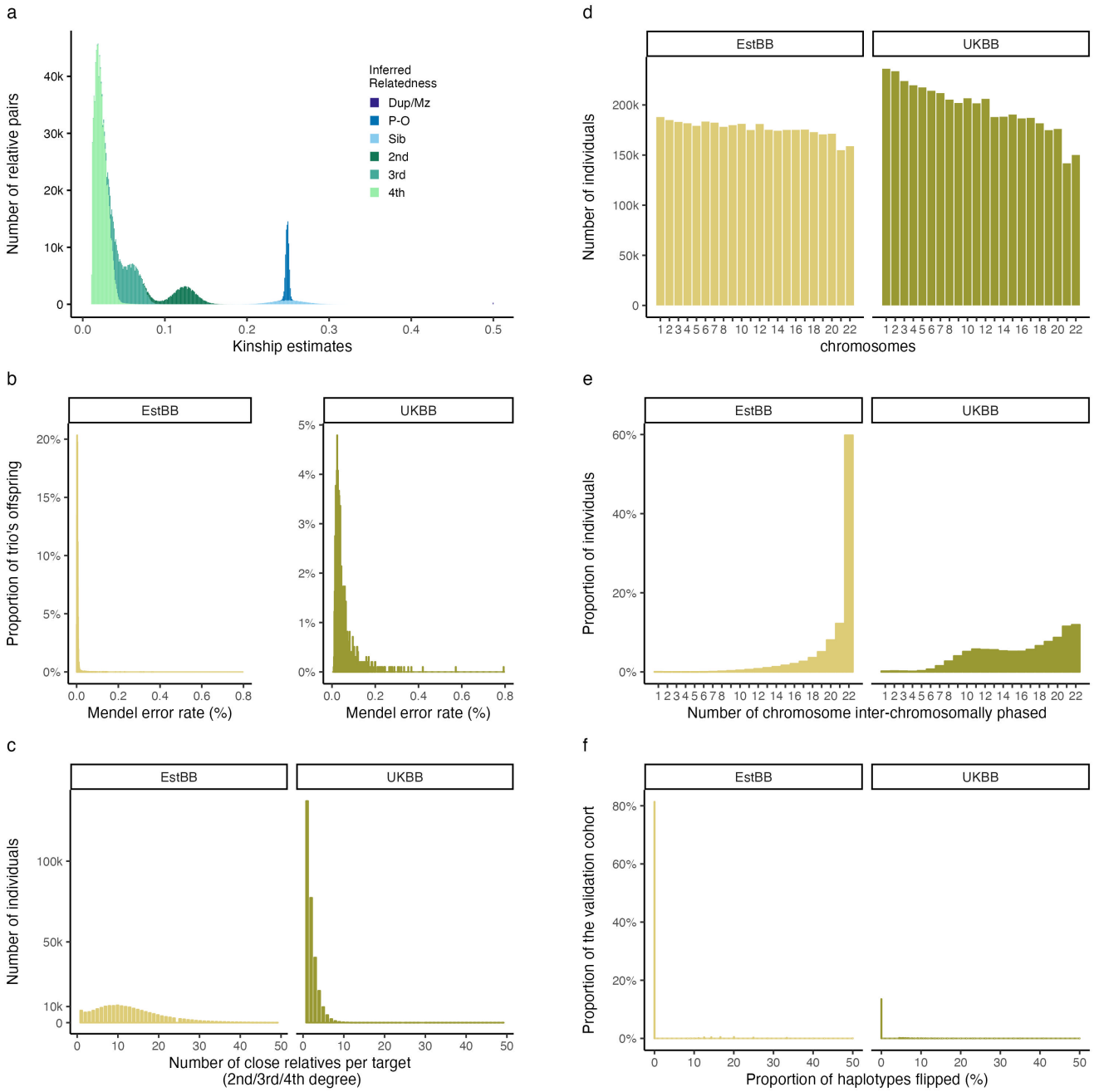
Supplementary Fig. 19 | Parent-of-origin effects of rs6467315 on different BMI time points. Beta estimates and 95% confidence intervals (y-axis) of paternal transmitted (blue), maternal transmitted (red) and maternal untransmitted (pink) alleles effects on different BMI time points (x-axis). We assessed the differences in effects between (i) maternal and paternal transmitted alleles and (ii) maternal transmitted and untransmitted alleles using a Z-score approach, analogous to a differential GWAS test.



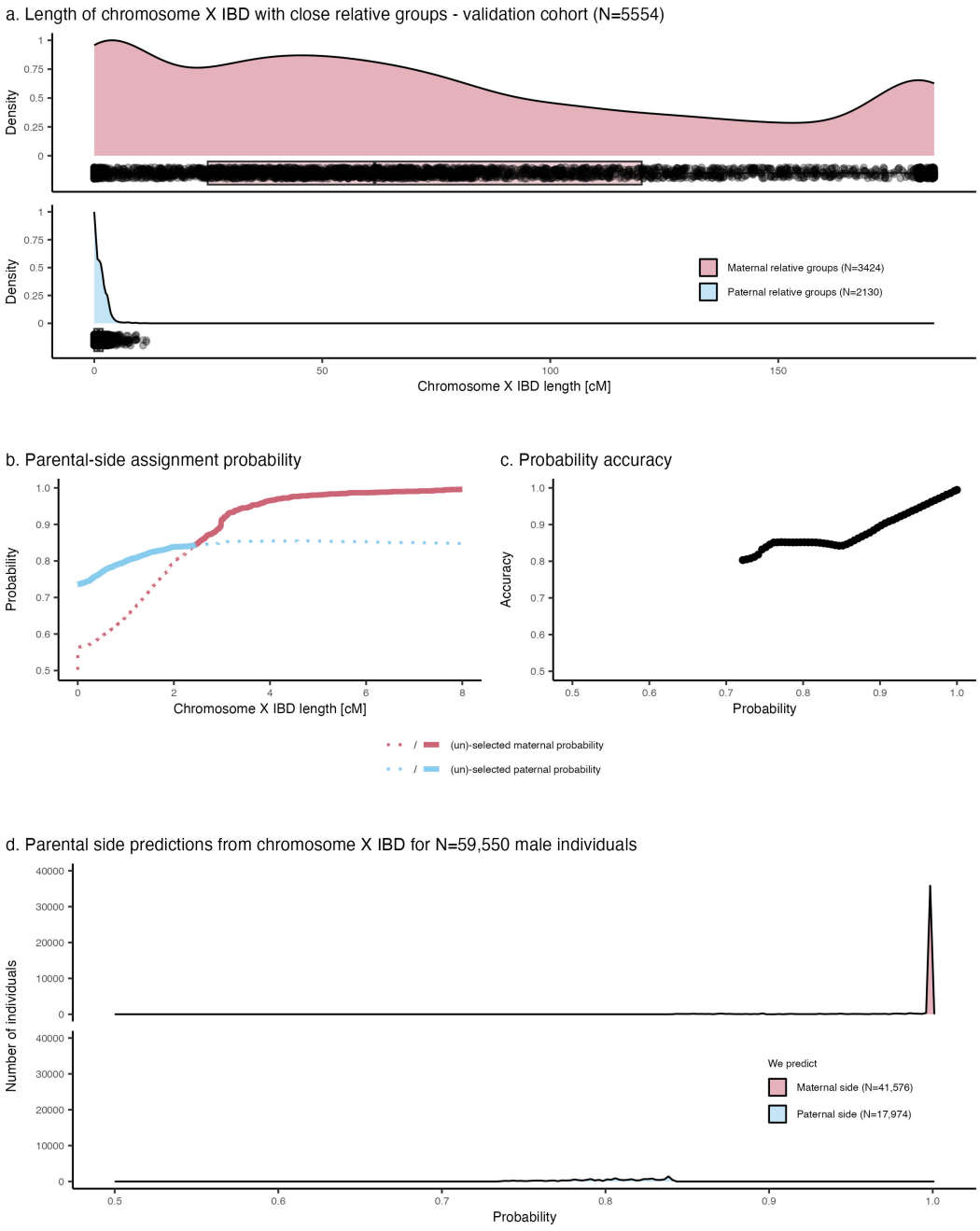
Supplementary Fig. 20 | Sex-specific POE of rs4417225 on glucose levels. Effects of genotypes and PofO of alleles (x-axis) on glucose level (y-axis) for (**a**) both sexes combined, (**b**) females only, and (**c**) males only. Red markers represent maternal heterozygotes, blue markers represent paternal heterozygotes, and dark and light grey represent homozygotes. The data points show the mean glucose levels, with error bars indicating the 95% confidence intervals. A grey dashed line represents the mean glucose level for individuals with the reference genotype (C/C). Significance values from the differential GWAS tests are annotated within each panel.



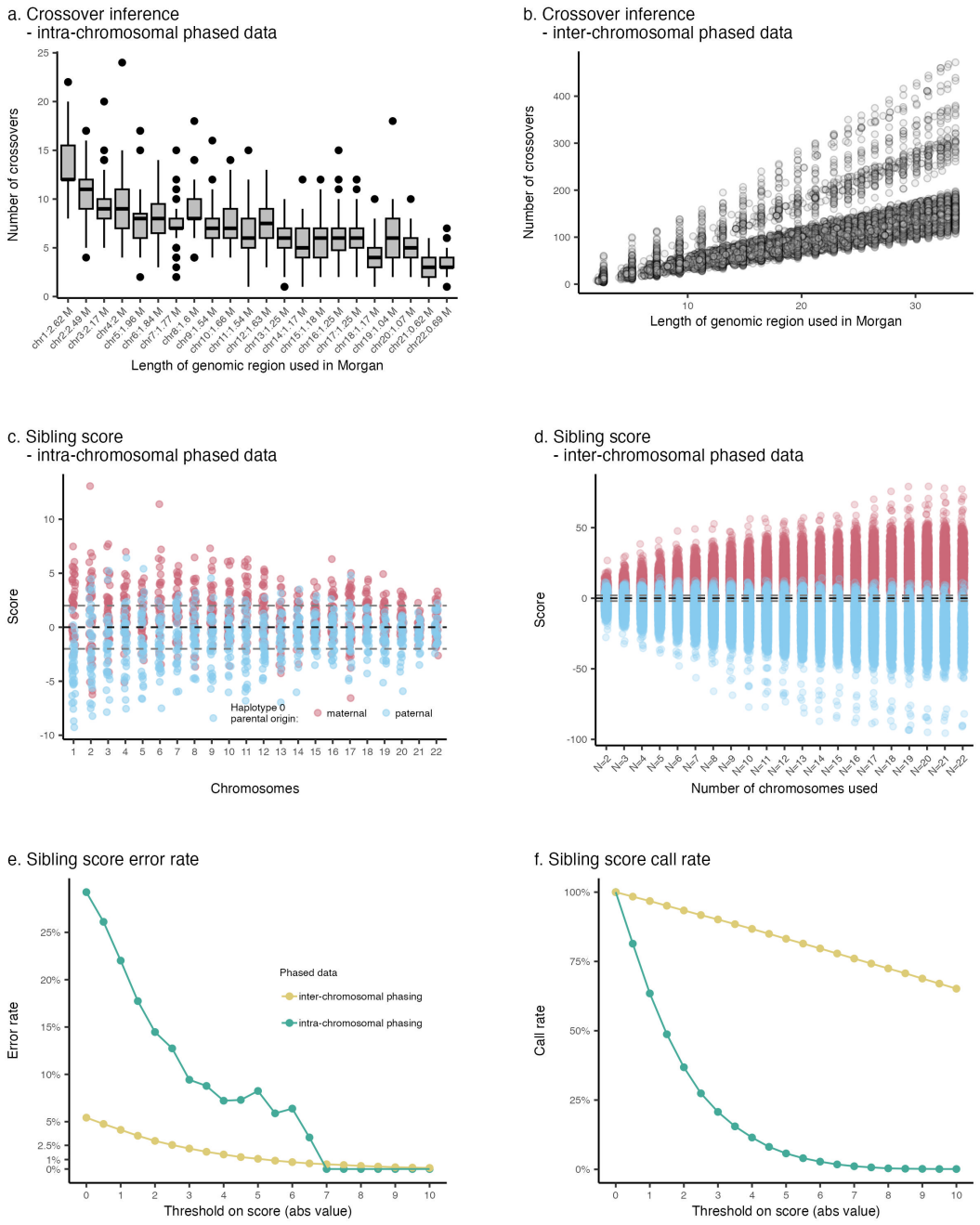
Supplementary Fig. 21 | Significant Parent-of-Origin pQTLs. Association strength ($-log_{10}(p-value)$, y-axis) against the genomic position (x-axis) for additive (grey), paternal (blue), maternal (red) and differential (green) GWAS on (**a**) DLK1, (**b**) CPA4, (**c**) ADAM23 and (**d**) PER3. Diamonds show the primary additive association previously reported[3] (grey) and the primary POE-pQTL detected in this study (green). Orange dashed line indicate the significance threshold ($P_D < 0.05/14285 = 3.5 \times 10^{-6}$). **Bottom panel** show the effects of alleles and PofO on normalized protein levels.



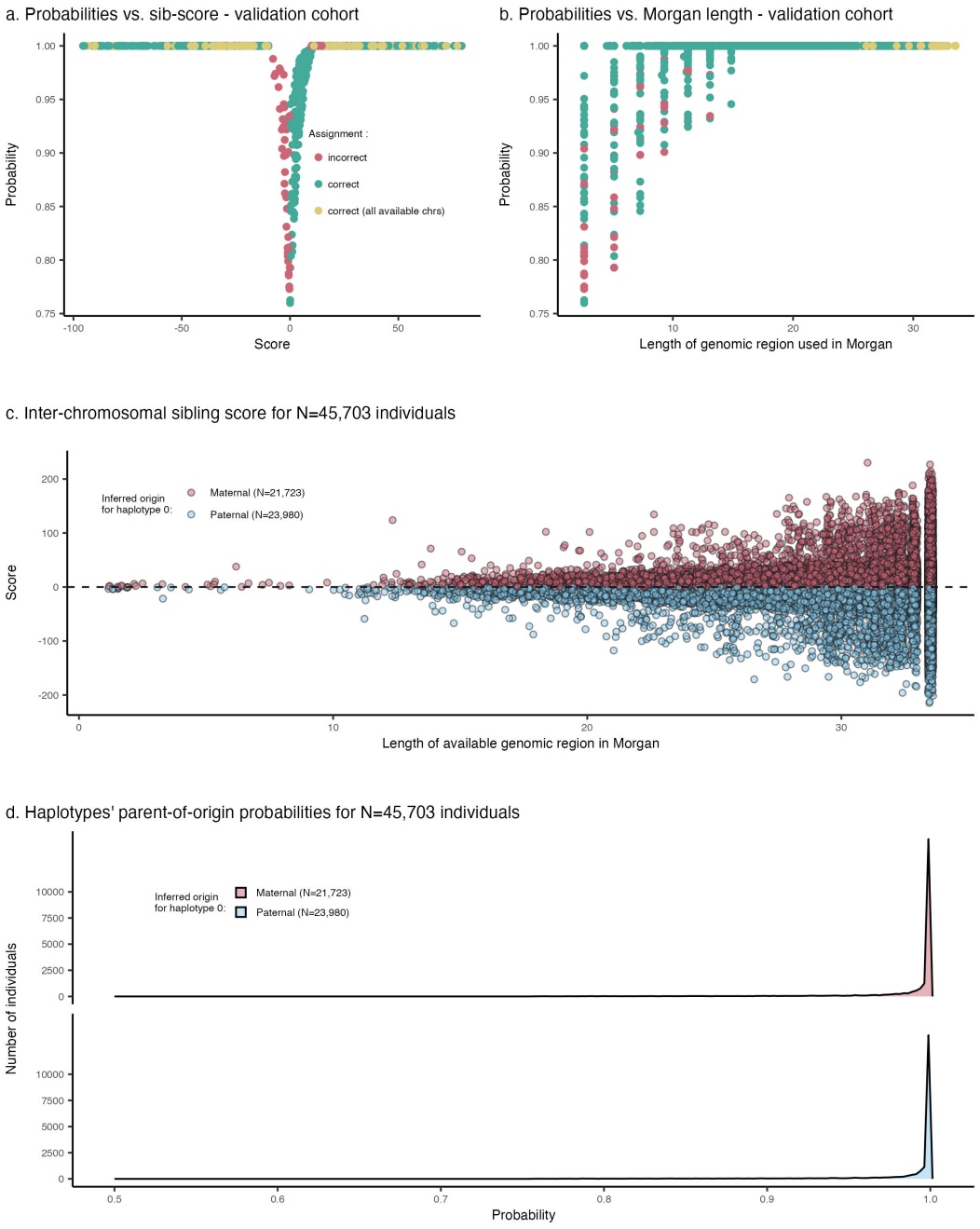
Supplementary Fig. 22 | Overview of relatedness metrics and inter-chromosomal phasing in the Estonian Biobank (EstBB), with comparisons to the UK Biobank (UKBB). a) Distribution of inferred relatedness across the EstBB cohort. Dup/MZ=monozygotic twins; P-O=parent-offspring; Sib=sibling; 2nd=2nd degree relative pairs; 3rd=3rd degree relative pairs; 4th=4th degree relative pairs. Relatedness was inferred using the KING software v2.2.7[4]. **b**) Distribution of Mendel error in trio's offspring for both the EstBB and UKBB cohorts. **c**) Distribution of the number of close relative per individual. **d**) Distribution of the number of individuals (y-axis) with a given chromosome (x-axis) successfully included in the inter-chromosomal phasing. **e**) Distribution of the number of individuals with N chromosomes (x-axis) successfully included in the inter-chromosomal phasing. **f**) Distribution of inter-chromosomal phasing error rate in the validation cohorts, calculated by comparing phasing results from surrogate parents to those obtained using parental genomes as the ground truth.



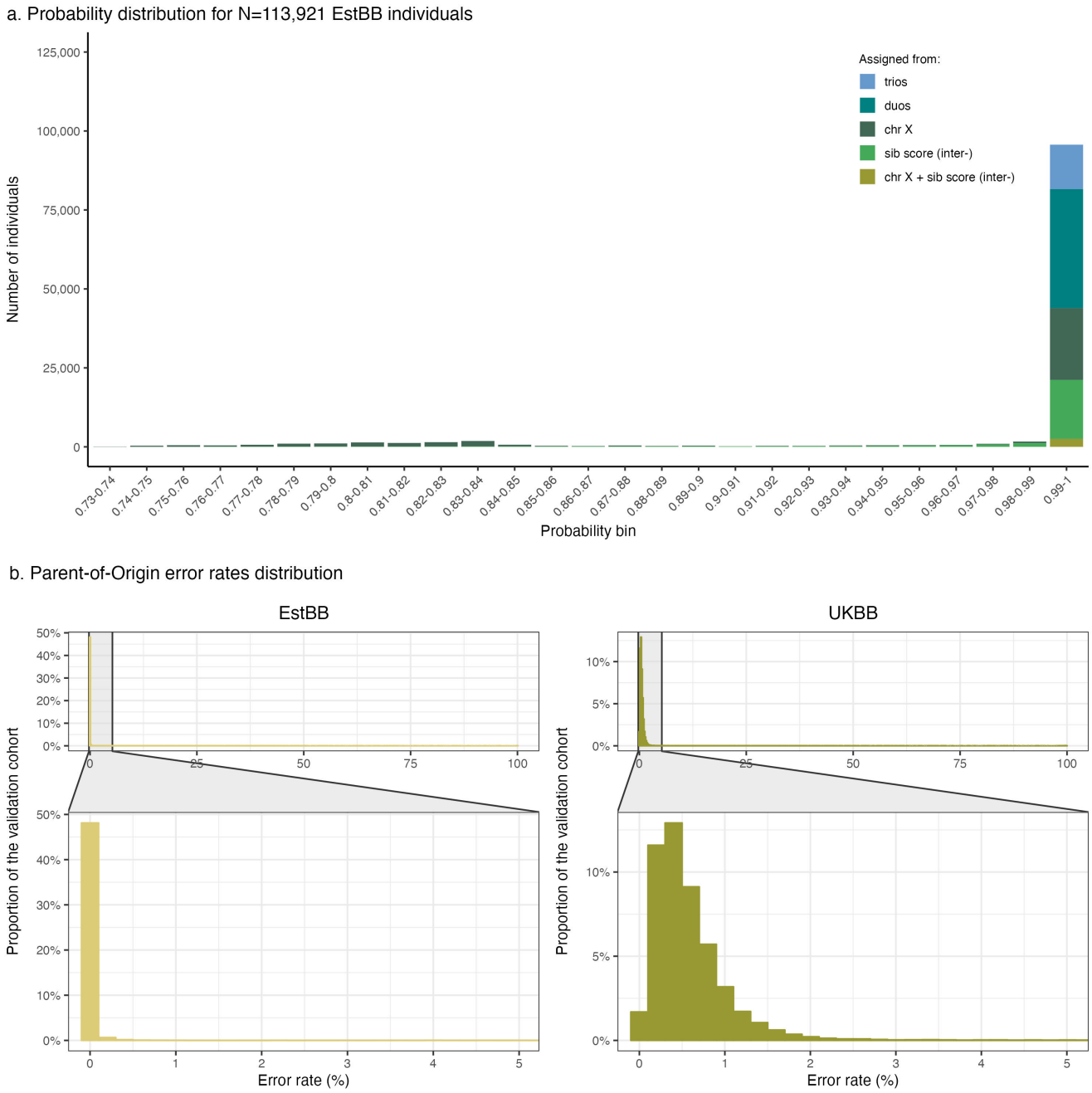
Supplementary Fig. 23 | Parental side assignment from chromosome X IBD analysis in male individuals in the Estonian Biobank. **a**) Density distribution of chromosome X IBD segment length in centimorgan (cM) between targets and surrogate father (blue) and targets and surrogate mother (red) across the validation cohort's male individuals. Boxes indicate the interquartile range (IQR), with the bottom and top of the box representing the 25th (Q1) and 75th (Q3) percentiles, respectively. The horizontal line within the box represents the median (50th percentile). Whiskers extend to the smallest and largest values within $Q1-1.5 \times IQR$ and $Q3 + 1.5 \times IQR$. Each point represent a target-relative pair. **b**) Parental side probabilities depending on chromosome X IBD segment length derived from the validation cohort. Selected and unselected maternal (red) and paternal (blue) probabilities for a given x-axis value are indicated by solid and dotted lines, respectively. **c**) Accuracy of parental side predictions (y-axis) as a function of the parental side probability (x-axis). **d**) Distribution of maternal (red) and paternal (blue) side assignment probabilities derived chromosome X IBD across 59,550 Estonian Biobank male individuals.



Supplementary Fig. 24 | Evaluation of sibling scores from intra- and inter-chromosomal phasing in the Estonian Biobank validation cohort. **a**) Distribution of the number of inferred crossovers (y-axis) per chromosome (x-axis) derived from intra-chromosomally phased data. **b**) Distribution of the number of inferred crossovers (y-axis) relative to the genomic length used (in Morgans, x-axis) derived from inter-chromosomally phased data. **c**) Distribution of sibling scores (y-axis) per chromosome (x-axis) using intra-chromosomally phased data. Maternal and paternal haplotypes are color-coded in red and blue, respectively. **d**) Distribution of sibling scores (y-axis) relative to the number of chromosomes included in inter-chromosomally phased data (x-axis). **e**) Error rates (y-axis) of sibling scores for varying score thresholds (absolute values, x-axis). **f**) Call rates (y-axis) of sibling scores for varying score thresholds (absolute values, x-axis), showing the proportion of individuals meeting the threshold criteria.



Supplementary Fig. 25 | Validation and derivation of parent-of-origin probabilities using sibling scores from inter-chromosomal phased data in the Estonian Biobank. a) PofO probabilities (y-axis) as a function of sibling scores (x-axis) in the validation cohort. Each dot represents a specific configuration (an individual with a given number of chromosomes used). We varied the number of chromosome used per individual to assess the accuracy of different configurations. Red dots indicate incorrect parental assignments, green dots indicate correct assignments, and yellow dots denote correct assignments using the maximum available chromosomes (N_{max}, corresponds to the full set of inter-chromosomally phased chromosome for a given individual). No errors were observed when N_{max} chromosomes were used. **b**) PofO probabilities (y-axis) plotted against the total available genomic length in Morgans (x-axis) for sibling score calculation in the validation cohort. Each configuration is represented as a dot (color-coded as in panel a). Increasing genomic length results in higher assignment accuracy, with perfect accuracy achieved at N_{max} (yellow dots). **c**) Sibling scores (y-axis) derived for N=45,703 individuals across available genomic lengths (x-axis). **d**) Distribution of PofO probabilities for 45,703 Estonian Biobank individuals.



Supplementary Fig. 26 | Parent-of-origin probability distribution and error rates in the Estonian Biobank. a) Distribution of PofO probabilities for N=113,921 individuals in the Estonian Biobank, color-coded by the source of inference (e.g., chromosome X data, sibling score from inter-chromosomal phased data, duos, and trios). Most individuals exhibit high PofO probabilities, reflecting the accuracy of the approach. **b**) Comparison of PofO error rate distributions between the Estonian Biobank (EstBB) and UK Biobank (UKBB) validation cohorts. The EstBB shows consistently lower error rates, likely attributed to the higher number of close relatives per individual, which enhances IBD detection and improves inter-chromosomal phasing accuracy. Zoomed panels show the error rates below 5%, highlighting the robustness of PofO inference in both biobanks.

Supplementary Tables

TRAIT	N	N males	N females
Telomere length	109355	58552	50803
Sodium in urine	109372	58565	50807
Creatinine	109379	58568	50811
Microalbumin in urine	109379	58568	50811
Vitamin D	109385	58572	50813
Urate	109385	58572	50813
Triglycerides	109385	58572	50813
Total protein	109385	58572	50813
Testosterone	109385	58572	50813
Total bilirubin	109385	58572	50813
SHBG	109385	58572	50813
Rheumatoid factor	109385	58572	50813
Phosphate	109385	58572	50813
Oestradiol	109385	58572	50813
Lipoprotein A	109385	58572	50813
LDL direct	109385	58572	50813
IGF-1	109385	58572	50813
HDL cholesterol	109385	58572	50813
Glycated haemoglobin	109385	58572	50813
Glucose	109385	58572	50813
Gamma glutamyltransferase	109385	58572	50813
Cystatin C	109385	58572	50813
C-reactive protein	109385	58572	50813
Creatinine	109385	58572	50813
Cholesterol	109385	58572	50813
Calcium	109385	58572	50813
Urea	109385	58572	50813
Direct bilirubin	109385	58572	50813
Aspartate aminotransferase	109385	58572	50813
Apoliprotein B	109385	58572	50813
Apoliprotein A	109385	58572	50813
Alanine aminotransferase	109385	58572	50813
Alkaline phosphatase	109385	58572	50813
Albumin	109385	58572	50813
Reticulocyte count	109385	58572	50813
Nucleated red blood cell count	109385	58572	50813
Basophill count	109385	58572	50813
Eosinophill count	109385	58572	50813
Neutrophill count	109385	58572	50813
Monocyte count	109385	58572	50813
Lymphocyte count	109385	58572	50813
Platelet count	109385	58572	50813
Red blood cell	109385	58572	50813
White blood cell	109385	58572	50813
Standing height	109385	58572	50813
Hip circumference	109385	58572	50813
Waist circumference	109385	58572	50813
Trunk fat-free mass	109385	58572	50813
Trunk fat percentage	109385	58572	50813
Arm fat-free mass	109385	58572	50813
Arm fat percentage	109385	58572	50813
Leg fat-free mass	109385	58572	50813
Leg fat percentage	109385	58572	50813
Basal metabolic rate	109385	58572	50813
Whole body water mass	109385	58572	50813
Body fat percentage	109385	58572	50813
Body mass index	109385	58572	50813
Birth weight	109385	58572	50813
Type 2 diabetes	9189 (99007)	6265 (51513)	2925 (47495)

Supplementary Table 1 | UK Biobank traits selected for this study.
TRAIT: phenotype name; N: number of individuals (selected as (i) self-reported as white British, confirmed by PCA, according to UK Biobank field 22006; (ii) having a PofO probability > 0.99, as defined for the differential GWAS[5]). For type 2 diabetes, we indicated cases and controls. TS ratio: Relative leucocyte telomere length; SHBG: Sex Hormone-Binding Globulin.

				Published studies					Current study				
	TRAIT	RSID	ID	BETA PAT	P PAT	BETA MAT	P MAT	P DIFF	BETA PAT	P PAT	BETA MAT	P MAT	P DIFF
Kim et al., HGG Adv 2021	HDL-C	rs12154627*	7_130422934_T_C	0.0300	6.40E-02	0.1300	2.10E-16	3.10E-06	0.0139	2.76E-02	0.0463	1.93E-13	6.20E-04
	triglyceride	rs12154627*	7_130422934_T_C	-0.0100	5.60E-01	-0.1000	1.40E-09	1.30E-04	-0.0151	2.69E-02	-0.0465	8.94E-12	1.00E-03
	platelets	rs10146962*	14_101170540_T_C	0.0400	6.30E-02	-0.1000	2.30E-11	7.80E-10	-0.0180	9.17E-03	-0.0964	3.73E-44	9.22E-16
Zoledziewska et al., Nat Genet 2015	Height	rs143840904*	11_2813322_C_T	0.0021	9.65E-01	-0.2740	3.98E-08	7.55E-05	-0.0226	1.37E-01	-0.1831	9.13E-32	5.21E-13
	Height	rs2075870*	11_2790019_G_A	-0.0172	7.93E-01	-0.2730	6.97E-08	2.00E-04	-0.0246	8.31E-02	-0.1439	3.00E-23	3.89E-09
	Height	rs149658560*	11_2767262_G_A	-0.0121	8.18E-01	-0.2970	2.93E-07	3.00E-04	-0.0066	6.13E-01	-0.0917	6.47E-12	7.09E-06
Granot-Hershkovitz et al., EJHG 2020	Height	rs1042136	6_33048628_A_C	-0.0230	1.55E-08	0.0050	4.21E-01	1.39E-04	-0.0160	3.54E-03	-0.0062	2.57E-01	1.90E-01
Benonisdottir et al., Nat Comm 2016	Height	rs147239461*	11_1986402_G_T	-0.1200	5.90E-13	0.0560	9.40E-04	1.20E-13	-0.0484	2.80E-05	0.0395	4.92E-04	4.89E-08
	Height	rs7482510	11_2190591_C_G	-0.0650	5.10E-11	0.0180	7.60E-02	4.70E-09	-0.0189	2.71E-04	0.0002	9.71E-01	4.15E-03
	Height	rs143840904*	11_2813322_C_T	0.0570	4.20E-02	-0.2600	2.00E-17	1.60E-14	-0.0226	1.37E-01	-0.1831	9.13E-32	5.21E-13
	Height	rs41286560*	14_101349454_G_T	-0.1200	2.20E-08	0.0670	1.70E-03	7.40E-10	-0.0519	5.03E-05	0.0168	1.87E-01	1.46E-04
Kong et al., Nature 2009	T2D	rs2334499*	11_1696849_C_T	1.35 (OR)	4.70E-10	0.86 (OR)	2.00E-03	4.10E-11	0.1391	2.19E-07	-0.0737	6.05E-03	2.16E-08
Hofmeister et al., Nat Comm 2022	telomere length	rs2735940*	5_1296486_A_G	0.0088	4.60E-01	-0.1215	2.10E-19	4.30E-13	0.014	4.59E-02	-0.100	3.12E-49	2.84E-32
	platelets	rs59228823*	14_101185187_G_C	-0.0110	5.80E-01	-0.1230	6.80E-16	2.30E-08	-0.015	4.68E-02	-0.104	2.14E-42	2.42E-16
Juliusdottir et al., Nat Genet 2021	birth weight	rs9855896	3_14287150_A_G	0.039	4.90E-05	-0.017	1.30E-01	1.65E-04	-0.009	4.29E-01	0.019	8.74E-02	7.59E-02
	birth weight	rs6575803	14_101257755_C_T	0.094	8.30E-17	0.009	5.20E-01	6.00E-07	-0.049	2.03E-03	-0.014	3.75E-01	1.48E-01
	birth weight	rs2296528	20_57274151_G_C	0.037	3.80E-06	-0.012	2.10E-01	4.72E-05	0.032	1.64E-03	0.022	3.45E-02	4.68E-01
	birth weight	rs76094073	6_109288036_C_G	-0.007	5.20E-01	0.06	1.60E-05	2.80E-04	0.042	2.89E-03	0.039	5.84E-03	8.63E-01
	birth weight	rs2529415	7_50736662_C_T	-0.004	6.70E-01	0.039	1.50E-04	7.86E-04	-0.001	9.25E-01	-0.017	8.40E-02	2.39E-01
	birth weight	rs2901307	10_124128443_C_T	0.001	8.50E-01	0.044	2.20E-06	7.03E-05	0.026	5.52E-03	0.031	7.07E-04	6.63E-01
	birth weight	rs231848	11_2735557_A_G	-0.003	7.00E-01	0.051	8.10E-08	9.70E-06	0.005	6.19E-01	-0.019	4.41E-02	7.32E-02
	birth weight	rs2928148	15_41401550_G_A	0.002	8.00E-01	0.045	1.30E-06	1.62E-04	0.016	8.77E-02	0.026	7.09E-03	4.88E-01

Supplementary Table 2 | Replication of previously published Parent-of-origin effects.

TRAIT: phenotype name; RSID: variant rs id; ID: chromosome_position(hg19)_reference allele_alternative allele; BETA and P denote effect sizes and P-values; PAT, MAT, and DIFF denote paternal, maternal and differential tests; *: associations replicated in our study.

Chromosome	Region start	Region end	Genes overlapping region
chr1	68011644	69016459	ARHI
chr2	80015483	81031487	LRRTM1
chr4	89117065	90118980	NAPIL5
chr6	56682421	57691161	PRIM2
chr6	143761436	144885734	PLAGL1,HYMAI
chr6	159890130	161376014	IGF2R,SLC22A2,SLC22A3
chr7	50154712	51361157	GRB10
chr7	93714535	95425726	SGCE,PEG10,PPP1R9A
chr7	96149701	97154142	DLX5
chr7	129432993	130918860	CPA4,MEST,KLF14
chr8	949568	2156642	DLGAP2
chr8	140113081	141215299	KCNK9
chr11	1516405	3686539	H19,IGF2,IGF2AS,INS,KCNQ1,KCNQ1DN,CDKN1C,SLC22A1LS,SLC22A1L,PHLDA2,OSBPL5
chr11	5911654	7479277	SMPD1,ZNF215
chr11	31909324	32957086	WT1
chr14	100693252	101827367	DLK1,MEG3
chr15	23310105	24432449	MKRN3,MAGEL2,NDN
chr15	24700069	26608348	SNURF,IPW,UBE3A,ATP10A
chr16	2986109	3993490	ZNF597
chr18	44054572	45056448	TCEB3C
chr19	56785919	57852075	ZIM2,PEG3
chr20	35649606	36652091	NNAT
chr20	41643052	42670534	L3MBTL
chr20	56914783	57986249	NESP55,GNAS1

Supplementary Table 3 | Imprinted regions.

Imprinted regions extracted from Kong *et al.*[6] and lifted over to hg19.

CHR	POS	SNP ID	A0	A1	A1FREQ	BETA PAT	SE PAT	P PAT	BETA MAT	SE MAT	P MAT	BETA DIFF	SE DIFF	P DIFF	BETA ADD	SE ADD	P ADD	TRAIT
11	1918083	rs7105710	T	C	0.546	0.001	0.005	8.18E-01	-0.013	0.005	8.00E-03	0.014	0.007	4.10E-02	-0.006	0.003	8.70E-02	Sitting height
11	2040272	rs77708343	A	G	0.039	-0.055	0.012	8.51E-06	0.046	0.012	1.21E-04	-0.101	0.017	4.17E-09	-0.003	0.009	6.95E-01	Sitting height
11	2813322	rs143840904	C	T	0.019	-0.044	0.018	1.30E-02	-0.131	0.018	6.61E-13	0.087	0.025	3.80E-04	-0.086	0.013	1.06E-11	Sitting height

Supplementary Table 4 | Replication of standing height association with sitting height.

CHR: chromosome; POS: genetic position (hg19); SNP ID: variant rs id; A0: reference allele; A1: assessed allele; A1FREQ: A1 allele frequency. BETA, SE and P denote effect sizes, standard errors and P-values; PAT, MAT, DIFF and ADD denote paternal, maternal, differential and additive tests. TRAIT: phenotype name.

CHR	POS	SNP ID	A0	A1	A1FREQ	BETA PAT	SE PAT	P PAT	BETA MAT	SE MAT	P MAT	BETA DIFF	SE DIFF	P DIFF	BETA ADD	SE ADD	P ADD	TRAIT	Status	Locus
2	54422548	rs7562908	A	G	0.026	0.148	0.021	1.06E-12	0.043	0.021	3.86E-02	-0.104	0.029	4.17E-04	-0.099	0.015	2.80E-11	TS ratio	novel	ACYP2
3	46058335	rs6809223	T	C	0.734	-0.049	0.007	1.62E-11	-0.015	0.007	4.20E-02	-0.034	0.010	8.80E-04	-0.032	0.005	5.24E-10	Basophill count	novel	CCR1, CCR3, XCR1
3	156795468	rs13322435	A	G	0.403	-0.072	0.009	1.05E-14	-0.038	0.009	3.15E-05	-0.033	0.013	1.12E-02	-0.055	0.007	4.24E-17	Birth weight	novel	TIPARP
5	72399063	rs10223082	T	C	0.667	-0.052	0.008	9.54E-12	-0.014	0.008	6.50E-02	-0.037	0.011	5.12E-04	-0.033	0.005	9.51E-10	Calcium	novel	FCHO2
7	73026378	rs17145750	C	T	0.162	0.015	0.009	9.68E-02	0.063	0.009	9.07E-13	-0.048	0.013	1.18E-04	0.039	0.006	4.60E-10	IGF-1	novel	MLXIPL
11	2157793	rs3213217	A	T	0.236	0.096	0.008	1.44E-34	0.058	0.008	2.01E-13	0.038	0.011	5.72E-04	0.077	0.006	7.74E-44	IGF-1	novel	IGF2

Supplementary Table 5 | Parent-of-origin effect within additively associated regions, per phenotype.
CHR: chromosome; POS: genetic position (hg19); SNP ID: variant rs id; A0: reference allele; A1: assessed allele; A1FREQ: A1 allele frequency. BETA, SE and P denote effect sizes, standard errors and P-values; PAT, MAT, DIFF and ADD denote paternal, maternal, differential and additive tests. TRAIT: phenotype name.

	CHR	POS	SNP ID	A0	A1	A1FREQ	BETA PAT	SE PAT	P PAT	BETA MAT	SE MAT	P MAT	BETA DIFF	SE DIFF	P DIFF	BETA ADD	SE ADD	P ADD	PHECODE	TRAIT
a	5	1296486	rs2735940	A	G	0.493	0.014	0.007	4.59E-02	-0.100	0.007	3.12E-49	0.113	0.010	2.84E-32	-0.043	0.005	1.71E-19	22191	TS ratio
	11	1702929	**rs10838787**	G	A	0.425	0.050	0.007	2.34E-14	-0.028	0.007	1.80E-05	0.078	0.009	2.77E-17	0.011	0.005	1.76E-02	30750	Glycated haemoglobin
	11	1998031	**rs170102**	G	A	0.346	-0.041	0.006	5.96E-11	0.026	0.006	3.19E-05	-0.067	0.009	5.98E-14	-0.007	0.004	9.47E-02	30720	Cystatin C
	11	2003944	2003944	T	G	0.656	0.030	0.006	2.53E-07	-0.024	0.006	2.68E-05	0.054	0.008	4.94E-11	0.003	0.004	5.04E-01	30700	Creatinine
	11	2813322	rs143840904	C	T	0.019	-0.023	0.015	1.37E-01	-0.183	0.016	9.13E-32	0.152	0.021	5.21E-13	-0.100	0.011	2.56E-20	50	Standing height
	14	101185187	rs59228823	G	C	0.245	-0.010	0.008	2.04E-01	-0.092	0.008	3.87E-34	0.082	0.011	1.92E-14	-0.051	0.005	2.36E-21	30080	Platelet count
b	7	130016470	**rs62471721**	G	A	0.351	-0.023	0.007	9.70E-04	0.033	0.007	1.57E-06	-0.057	0.010	6.51E-09	0.005	0.005	2.85E-01	30870	Triglycerides
	11	1702929	**rs10838787**	G	A	0.425	0.136	0.027	3.88E-07	-0.091	0.027	7.55E-04	0.228	0.038	1.87E-09	0.023	0.019	2.26E-01	130708	Type 2 diabetes
	11	2040272	**rs77708343**	A	G	0.040	-0.052	0.011	1.28E-06	0.033	0.011	2.06E-03	-0.085	0.015	1.80E-08	-0.009	0.008	2.29E-01	23113	Leg fat-free mass
	20	57216538	**rs80116540**	A	G	0.075	0.035	0.010	4.38E-04	-0.043	0.010	2.04E-05	0.078	0.014	3.39E-08	-0.004	0.007	6.09E-01	23119	Arm fat percentage
	1	40593883	rs145976519	A	C	0.022	0.096	0.031	2.00E-03	-0.155	0.031	5.96E-07	0.251	0.043	3.96E-09	-0.030	0.022	1.78E-01	20022	Birth weight
	1	81185936	rs2152857	A	G	0.024	-0.074	0.018	3.08E-05	0.066	0.018	1.96E-04	0.143	0.025	1.58E-08	0.007	0.014	6.03E-01	30840	Total bilirubin
	2	863453	rs73161490	T	G	0.162	-0.035	0.009	4.70E-05	0.031	0.009	2.40E-04	-0.066	0.012	4.89E-08	-0.002	0.006	7.99E-01	30770	IGF-1
	3	108030034	rs17241163	A	G	0.091	0.087	0.026	6.55E-04	-0.116	0.026	7.34E-06	0.202	0.036	2.08E-08	-0.014	0.018	4.58E-01	30800	Oestradiol
	5	127663392	5 127663392 G A	G	A	0.139	0.024	0.010	1.28E-02	-0.052	0.010	1.33E-07	0.076	0.014	4.65E-08	-0.014	0.007	4.82E-02	30140	Neutrophill count
	11	114407458	rs138298109	A	C	0.024	-0.082	0.023	3.87E-04	0.091	0.023	7.28E-05	-0.169	0.031	4.03E-08	0.005	0.016	7.52E-01	30510	Creatinine
	14	83180060	14 83180060 A C	A	C	0.120	0.059	0.020	3.43E-03	-0.099	0.020	7.11E-07	0.156	0.028	3.58E-08	-0.021	0.014	1.40E-01	30500	Microalbumin in urine

Supplementary Table 6 | Parent-of-origin effect genome-wide.

CHR: chromosome; POS: genetic position (hg19); SNP ID: variant rs id; A0: reference allele; A1: assessed allele; A1FREQ: A1 allele frequency. BETA, SE and P denote effect sizes, standard errors and P-values; PAT, MAT, DIFF and ADD denote paternal, maternal, differential and additive tests. TRAIT: phenotype name. **a**) POEs robust when correcting for the number of traits tested ($P_D < 1 \times 10^{-9}$). **b**) POEs genome-wide significant at the single trait level ($1 \times 10^{-9} < P_D < 5 \times 10^{-8}$).

CHR	POS	SNP ID	A0	A1	BETA_PAT	SE_PAT	P_PAT	BETA_MAT	SE_MAT	P_MAT	P_DIFF	TRAIT	INITIAL TRAITS WITH POE AT THIS LOCUS
11	**1914139**	**rs576603**	**C**	**T**	**-0.048**	**0.015**	**1.70E-03**	**0.041**	**0.015**	**7.26E-03**	**3.29E-05**	**CBHA10**	**Standing height**
11	**2040272**	**rs77708343**	**A**	**G**	**-0.118**	**0.039**	**2.29E-03**	**0.071**	**0.038**	**6.32E-02**	**4.40E-04**	**CBHA10**	**Standing height, Basal metabolic rate, Leg fat-free mass, Whole body water mass**
11	**2813322**	**rs143840904**	**C**	**T**	**-0.070**	**0.056**	**2.10E-01**	**-0.321**	**0.057**	**2.07E-08**	**2.70E-03**	**CBHA10**	**Standing height**
7	130017940	rs4731690	A	G	-0.014	0.009	1.23E-01	-0.010	0.009	2.57E-01	8.13E-01	birth weight	HDL cholesterol
7	130400698	rs3847104	G	A	0.005	0.014	7.47E-01	0.017	0.014	2.15E-01	5.24E-01	birth weight	Hip circumference
7	130463192	rs6467315	C	G	0.002	0.009	8.61E-01	0.004	0.009	6.25E-01	8.24E-01	birth weight	Hip circumference
11	1702929	rs10838787	G	A	-0.029	0.009	2.31E-03	0.007	0.009	4.72E-01	8.04E-03	birth weight	Type 2 diabetes, Glycated haemoglobin
11	2040272	rs77708343	A	G	-0.057	0.024	1.88E-02	0.030	0.024	1.98E-01	9.35E-03	birth weight	Standing height, Basal metabolic rate, Leg fat-free mass, Whole body water mass
11	2858295	rs2299620	C	T	0.040	0.026	1.19E-01	0.036	0.025	1.47E-01	9.03E-01	birth weight	Glycated haemoglobin
20	57226079	rs6026426	C	G	-0.020	0.019	3.02E-01	0.030	0.019	1.16E-01	6.16E-02	birth weight	Trunk fat percentage
7	130017940	rs4731690	A	G	0.032	0.013	1.34E-02	0.001	0.013	9.16E-01	1.01E-01	CBSA10	HDL cholesterol
7	130400698	rs3847104	G	A	-0.021	0.020	2.91E-01	0.033	0.019	9.26E-02	5.07E-02	CBSA10	Hip circumference
7	130463192	rs6467315	C	G	0.013	0.013	3.16E-01	0.008	0.013	5.41E-01	7.73E-01	CBSA10	Hip circumference
11	1702929	rs10838787	G	A	-0.002	0.013	8.82E-01	-0.013	0.013	3.40E-01	6.03E-01	CBSA10	Type 2 diabetes, Glycated haemoglobin
11	2040272	rs77708343	A	G	-0.026	0.034	4.42E-01	0.026	0.033	4.42E-01	2.90E-01	CBSA10	Standing height, Basal metabolic rate, Leg fat-free mass, Whole body water mass
11	2858295	rs2299620	C	T	0.049	0.035	1.62E-01	0.071	0.035	4.32E-02	7.05E-01	CBSA10	Glycated haemoglobin
20	57226079	rs6026426	C	G	0.032	0.027	2.36E-01	-0.043	0.027	1.10E-01	5.15E-02	CBSA10	Trunk fat percentage

Supplementary Table 7 | Replication of associations with early childhood traits in the UK Biobank cohort.

CHR: chromosome; POS: genetic position (hg19); SNP ID: variant rs id; A0: reference allele; A1: assessed allele; A1FREQ: A1 allele frequency. BETA, SE and P denote effect sizes, standard errors and P-values; PAT, MAT, DIFF and ADD denote paternal, maternal, differential and additive tests. TRAIT: phenotype name. Bold indicate significant POEs; CBHA10: comparative body height at age 10; CBSA10: comparative body size at age 10.

BMI time point	N
BMI at 6 Weeks	29791
BMI at 3 Months	41865
BMI at 6 Months	42346
BMI at 8 Months	36790
BMI at 1 Year	36721
BMI at 16 Months	27595
BMI at 2 Years	27435
BMI at 3 Years	27985
BMI at 5 Years	22667
BMI at 7 Years	23280
BMI at 8 Years	17888

Supplementary Table 8 | Number of individuals per BMI time points in the MoBa cohort.

ID	BMI timepoints	BETA PAT	SE PAT	P PAT	BETA MAT	SE MAT	P MAT	BETA MAT NT	SE MAT NT	P MAT NT	P DIFF	P DIFF MAT	INITIAL TRAITS WITH POE AT THIS LOCUS
rs6467315	6 weeks	-0.019	0.015	2.04E-01	0.071	0.015	1.26E-06	0.028	0.014	4.74E-02	**1.51E-05**	3.47E-02	Hip circumference
	3 months	0.001	0.012	9.62E-01	0.085	0.012	9.46E-12	0.003	0.012	7.74E-01	**1.68E-06**	2.50E-06	
	6 months	0.003	0.012	8.12E-01	0.089	0.012	7.72E-13	0.016	0.012	1.96E-01	**9.43E-07**	2.02E-05	
	8 months	0.012	0.013	3.75E-01	0.087	0.013	6.15E-11	0.009	0.013	4.97E-01	**6.30E-05**	2.23E-05	
	12 months	-0.007	0.013	5.75E-01	0.069	0.013	2.20E-07	0.000	0.013	9.88E-01	**4.85E-05**	1.82E-04	
	16 months	-0.011	0.015	4.51E-01	0.066	0.015	1.24E-05	0.011	0.015	4.39E-01	**2.90E-04**	9.05E-03	
	2 years	-0.017	0.015	2.67E-01	0.057	0.015	1.81E-04	0.017	0.015	2.47E-01	**5.95E-04**	5.81E-02	
	3 years	0.012	0.015	4.17E-01	0.058	0.015	9.60E-05	0.003	0.014	8.61E-01	2.89E-02	7.20E-03	
	5 years	-0.013	0.016	4.38E-01	0.031	0.016	5.77E-02	-0.013	0.016	4.09E-01	5.86E-02	5.24E-02	
	7 years	-0.023	0.016	1.54E-01	0.030	0.016	6.63E-02	-0.008	0.016	6.24E-01	2.10E-02	9.68E-02	
	8 years	-0.004	0.019	8.43E-01	0.026	0.019	1.69E-01	0.024	0.018	1.81E-01	2.66E-01	9.48E-01	
rs10838787	6 weeks	-0.006	0.015	6.76E-01	0.028	0.015	5.61E-02	0.016	0.014	2.57E-01	9.96E-02	5.51E-01	Type 2 diabetes, Glycated haemoglobin, Glucose
	3 months	-0.020	0.013	1.16E-01	0.019	0.013	1.28E-01	0.025	0.012	3.68E-02	2.88E-02	7.28E-01	
	6 months	-0.028	0.013	2.75E-02	0.017	0.013	1.82E-01	0.024	0.012	4.81E-02	1.23E-02	6.86E-01	
	8 months	-0.046	0.013	6.09E-04	0.011	0.013	4.20E-01	0.030	0.013	2.12E-02	2.74E-03	3.12E-01	
	12 months	-0.042	0.013	1.96E-03	0.009	0.013	5.22E-01	0.030	0.013	1.83E-02	8.24E-03	2.42E-01	
	16 months	-0.044	0.015	3.58E-03	0.008	0.015	5.91E-01	0.007	0.015	6.52E-01	1.47E-02	9.40E-01	
	2 years	-0.029	0.015	5.51E-02	0.003	0.015	8.63E-01	-0.001	0.015	9.56E-01	1.39E-01	8.70E-01	
	3 years	-0.038	0.015	1.15E-02	-0.002	0.015	8.84E-01	0.015	0.014	2.92E-01	9.21E-02	4.04E-01	
	5 years	-0.021	0.016	2.11E-01	-0.010	0.016	5.37E-01	0.013	0.016	4.12E-01	6.54E-01	3.11E-01	
	7 years	-0.018	0.017	2.71E-01	-0.004	0.017	8.24E-01	0.024	0.016	1.32E-01	5.35E-01	2.29E-01	
	8 years	-0.001	0.019	9.76E-01	-0.007	0.019	6.91E-01	0.036	0.018	4.67E-02	7.95E-01	9.61E-02	
rs2299620	6 weeks	-0.040	0.040	3.17E-01	-0.025	-0.040	5.36E-01	0.013	0.037	7.30E-01	2.53E-01	4.91E-01	Glycated haemoglobin
	3 months	0.017	0.034	6.17E-01	-0.045	-0.034	1.79E-01	0.034	0.032	2.92E-01	5.60E-01	8.92E-02	
	6 months	0.043	0.034	2.13E-01	-0.015	-0.034	6.67E-01	-0.013	0.032	6.96E-01	5.59E-01	9.65E-01	
	8 months	0.044	0.037	2.35E-01	0.016	-0.036	6.62E-01	0.007	0.034	8.36E-01	2.47E-01	8.62E-01	
	12 months	0.021	0.037	5.71E-01	0.034	-0.036	3.41E-01	0.010	0.034	7.81E-01	2.85E-01	6.20E-01	
	16 months	0.030	0.042	4.71E-01	0.050	-0.041	2.22E-01	-0.015	0.039	7.05E-01	1.71E-01	2.51E-01	
	2 years	0.036	0.042	3.83E-01	0.035	-0.041	3.92E-01	0.046	0.039	2.35E-01	2.21E-01	8.55E-01	
	3 years	0.008	0.041	8.49E-01	0.055	-0.041	1.78E-01	0.019	0.038	6.22E-01	2.80E-01	5.18E-01	
	5 years	-0.004	0.045	9.32E-01	0.020	-0.044	6.47E-01	0.012	0.041	7.79E-01	7.94E-01	8.87E-01	
	7 years	0.066	0.045	1.45E-01	0.082	-0.045	6.65E-02	0.005	0.042	8.96E-01	1.99E-02	2.10E-01	
	8 years	-0.007	0.051	8.88E-01	0.074	-0.050	1.40E-01	0.011	0.047	8.13E-01	3.53E-01	3.61E-01	
rs4731690	6 weeks	0.008	0.015	5.82E-01	0.025	0.015	8.35E-02	0.016	0.014	2.52E-01	4.04E-01	6.49E-01	HDL cholesterol, Triglycerides, SHBG
	3 months	-0.001	0.012	9.14E-01	0.034	0.012	6.90E-03	0.019	0.012	1.19E-01	4.70E-02	3.88E-01	
	6 months	0.006	0.012	6.12E-01	0.039	0.012	1.72E-03	0.007	0.012	5.86E-01	6.33E-02	6.04E-02	
	8 months	0.008	0.013	5.41E-01	0.031	0.013	2.10E-02	0.004	0.013	7.39E-01	2.30E-01	1.53E-01	
	12 months	0.004	0.013	7.40E-01	0.037	0.013	6.00E-03	-0.002	0.013	8.59E-01	8.76E-02	3.56E-02	
	16 months	0.017	0.015	2.58E-01	0.010	0.015	4.99E-01	-0.002	0.015	9.18E-01	7.48E-01	5.76E-01	
	2 years	0.036	0.015	1.87E-02	0.005	0.015	7.39E-01	-0.007	0.015	6.41E-01	1.53E-01	5.73E-01	
	3 years	0.021	0.015	1.57E-01	-0.007	0.015	6.18E-01	-0.019	0.014	1.85E-01	1.76E-01	5.75E-01	
	5 years	0.041	0.016	1.23E-02	-0.012	0.016	4.69E-01	-0.002	0.016	8.89E-01	2.25E-02	6.71E-01	
	7 years	-0.003	0.016	8.60E-01	0.015	0.016	3.54E-01	-0.020	0.016	2.07E-01	4.35E-01	1.23E-01	
	8 years	0.019	0.019	3.17E-01	0.007	0.019	7.13E-01	-0.042	0.018	1.86E-02	6.55E-01	5.77E-02	
rs6026426	6 weeks	-0.069	-0.028	1.20E-02	0.021	0.027	4.39E-01	0.006	0.026	8.33E-01	2.06E-01	4.84E-01	Trunk fat percentage, Arm, Leg and Body fat percentages
	3 months	-0.059	-0.023	1.06E-02	-0.006	0.023	7.95E-01	-0.012	0.022	5.90E-01	4.49E-02	5.74E-01	
	6 months	-0.063	-0.023	6.68E-03	-0.005	0.023	8.37E-01	-0.026	0.022	2.40E-01	3.76E-02	3.33E-01	
	8 months	-0.055	-0.025	2.57E-02	-0.008	0.024	7.39E-01	-0.034	0.024	1.54E-01	6.79E-02	2.18E-01	
	12 months	-0.058	-0.025	1.90E-02	-0.024	0.024	3.32E-01	-0.026	0.023	2.76E-01	1.85E-02	1.46E-01	
	16 months	-0.035	-0.028	2.21E-01	-0.034	0.027	2.08E-01	-0.028	0.027	3.03E-01	7.92E-02	1.05E-01	
	2 years	-0.043	-0.028	1.29E-01	-0.020	0.027	4.73E-01	-0.002	0.027	9.50E-01	1.12E-01	5.77E-01	
	3 years	-0.005	-0.028	8.60E-01	-0.036	0.027	1.76E-01	-0.002	0.026	9.37E-01	2.86E-01	3.05E-01	
	5 years	-0.065	-0.031	3.29E-02	-0.030	0.029	3.05E-01	-0.041	0.029	1.57E-01	2.44E-02	8.46E-02	
	7 years	-0.063	-0.031	3.87E-02	-0.013	0.030	6.61E-01	-0.013	0.029	6.47E-01	7.40E-02	5.26E-01	
	8 years	-0.033	-0.035	3.39E-01	-0.006	0.033	8.50E-01	-0.038	0.033	2.43E-01	4.11E-01	3.42E-01	
rs77708343	6 weeks	-0.004	0.031	8.97E-01	0.057	0.031	6.87E-02	0.017	0.030	5.61E-01	1.68E-01	3.62E-01	Standing height, Basal metabolic rate, Leg fat-free mass
	3 months	-0.055	0.027	3.88E-02	0.021	0.027	4.24E-01	0.023	0.026	3.58E-01	4.29E-02	9.54E-01	
	6 months	-0.057	0.027	3.18E-02	0.033	0.027	2.13E-01	0.025	0.026	3.21E-01	1.66E-02	8.29E-01	
	8 months	-0.077	0.029	7.56E-03	0.040	0.029	1.62E-01	0.043	0.027	1.11E-01	4.03E-03	9.40E-01	
	12 months	-0.039	0.029	1.70E-01	0.050	0.029	8.59E-02	0.043	0.027	1.13E-01	2.88E-02	8.71E-01	
	16 months	-0.043	0.032	1.88E-01	0.015	0.033	6.52E-01	0.037	0.031	2.24E-01	2.14E-01	6.23E-01	
	2 years	-0.028	0.033	3.88E-01	0.044	0.033	1.82E-01	0.003	0.030	9.18E-01	1.20E-01	3.62E-01	
	3 years	-0.014	0.032	6.67E-01	0.044	0.033	1.82E-01	0.011	0.030	7.04E-01	2.09E-01	4.65E-01	
	5 years	-0.049	0.035	1.57E-01	0.061	0.036	8.70E-02	0.038	0.033	2.48E-01	2.69E-02	6.41E-01	
	7 years	-0.038	0.035	2.82E-01	0.080	0.036	2.50E-02	0.089	0.034	8.60E-03	1.87E-02	8.63E-01	
	8 years	-0.023	0.041	5.68E-01	0.047	0.040	2.45E-01	0.060	0.038	1.11E-01	2.22E-01	8.06E-01	
rs3847104	6 weeks	0.012	0.023	5.94E-01	-0.031	0.023	1.78E-01	0.009	0.022	6.97E-01	1.85E-01	2.16E-01	Hip circumference
	3 months	-0.013	0.019	4.88E-01	-0.036	0.019	6.25E-02	-0.017	0.019	3.70E-01	4.06E-01	4.74E-01	
	6 months	0.003	0.019	8.71E-01	-0.031	0.019	1.09E-01	-0.005	0.019	7.74E-01	2.10E-01	3.40E-01	
	8 months	-0.018	0.021	3.75E-01	-0.020	0.020	3.34E-01	0.015	0.020	4.43E-01	9.57E-01	2.20E-01	
	12 months	0.004	0.021	8.42E-01	-0.010	0.021	6.33E-01	0.004	0.020	8.34E-01	6.32E-01	6.25E-01	
	16 months	0.004	0.023	8.78E-01	0.006	0.023	8.09E-01	0.024	0.023	2.93E-01	9.50E-01	5.76E-01	
	2 years	-0.001	0.023	9.63E-01	-0.037	0.023	1.16E-01	0.024	0.023	2.89E-01	2.81E-01	6.21E-02	
	3 years	0.016	0.023	4.91E-01	-0.016	0.023	4.92E-01	0.017	0.022	4.58E-01	3.31E-01	3.12E-01	
	5 years	0.016	0.025	5.32E-01	0.005	0.025	8.49E-01	0.032	0.025	1.88E-01	7.57E-01	4.33E-01	
	7 years	-0.024	0.025	3.34E-01	-0.018	0.025	4.70E-01	0.034	0.025	1.68E-01	8.61E-01	1.39E-01	
	8 years	0.029	0.029	3.03E-01	-0.025	0.028	3.89E-01	0.008	0.028	7.69E-01	1.81E-01	4.10E-01	

Supplementary Table 9 | Replication of associations with infancy and childhood BMI in the MoBa cohort.

SNP ID: variant rs id; BETA, SE and P denote effect sizes, standard errors and P-values; PAT, MAT and MAT NT denote paternal transmitted, maternal transmitted, and maternal untransmitted alleles association coefficients; P DIFF: Z-score P-value for the differential effect between paternal and maternal transmitted alleles; P DIFF MAT: Z-score P-value for the differential effect between maternal transmitted and maternal untransmitted alleles. Bold P DIFF denote significant POEs.

CHR	POS	SNP ID	A0	A1	P DIFF COMB	P DIFF MALES	P DIFF FEMALES	Pz	TRAIT
11	1914139	rs576603	C	T	3.86E-08	3.53E-04	1.77E-04	7.34E-01	Standing height
11	2040272	rs77708343	A	G	2.18E-09	2.61E-03	2.88E-08	4.51E-02	Standing height
11	2813322	rs143840904	C	T	5.21E-13	4.48E-06	1.15E-08	2.53E-01	Standing height
11	2040272	rs77708343	A	G	7.53E-08	1.43E-05	1.24E-03	6.68E-01	Basal metabolic rate
11	2040272	rs77708343	A	G	1.80E-08	1.05E-05	4.44E-04	8.22E-01	Leg fat-free mass
11	2040272	rs77708343	A	G	1.63E-07	1.11E-05	2.99E-03	4.94E-01	Whole body water mass
11	2041348	rs78507815	G	T	3.61E-07	4.57E-06	9.55E-03	2.71E-01	Trunk fat-free mass
11	**1703564**	**rs4417225**	**C**	**T**	**7.40E-08**	**4.79E-09**	**1.93E-01**	**1.38E-03**	**Glucose**
11	1702929	rs10838787	G	A	1.87E-09	7.56E-06	4.47E-05	4.49E-01	Type 2 diabetes
11	1702929	rs10838787	G	A	2.77E-17	2.29E-10	8.53E-08	4.03E-01	Glycated haemoglobin
11	2858295	rs2299620	C	T	2.23E-06	1.52E-04	4.23E-03	4.48E-01	Glycated haemoglobin
11	1920285	rs4264135	A	G	2.22E-07	1.42E-04	1.72E-04	8.67E-01	Urate
11	1998031	rs170102	G	A	5.98E-14	2.98E-09	1.69E-06	8.34E-01	Cystatin C
11	2003944	rs217215	T	G	4.94E-11	4.15E-07	2.00E-05	9.43E-01	Creatinine
7	130009312	rs10239342	T	G	1.87E-06	2.42E-06	9.73E-03	5.34E-01	SHBG
7	130016470	rs62471721	G	A	6.51E-09	2.03E-07	1.52E-03	1.54E-01	Triglycerides
7	130017940	rs4731690	A	G	1.92E-06	2.62E-04	1.89E-03	8.51E-01	HDL cholesterol
7	130400698	rs3847104	G	A	3.81E-07	3.56E-03	4.89E-04	2.55E-01	Hip circumference
7	130463192	rs6467315	C	G	2.20E-06	5.05E-02	5.03E-06	9.52E-03	Hip circumference
20	57216538	rs80116540	A	G	3.39E-08	4.70E-03	1.36E-06	3.42E-02	Arm fat percentage
20	57216538	rs80116540	A	G	2.06E-07	5.35E-03	7.47E-06	9.69E-02	Body fat percentage
20	57226079	rs6026426	C	G	1.29E-06	5.63E-03	6.97E-05	1.51E-01	Trunk fat percentage
20	57484934	rs3730173	C	T	5.32E-07	9.03E-04	1.59E-04	5.21E-01	Leg fat percentage
6	144274210	rs12528876	T	C	2.96E-06	2.68E-04	2.62E-03	8.62E-01	IGF-1
16	3412861	rs7188903	A	G	6.14E-07	6.83E-05	2.00E-03	7.25E-01	IGF-1
15	25983333	rs146982369	C	G	2.59E-06	1.12E-03	6.15E-04	7.00E-01	Total protein
14	101185187	rs59228823	G	C	1.92E-14	5.83E-08	5.43E-08	7.05E-01	Platelet count
3	169482335	rs2293607	T	C	5.70E-07	3.50E-04	4.22E-04	8.44E-01	TS ratio
4	164012901	rs11100479	C	T	6.25E-07	3.00E-04	5.41E-04	9.20E-01	TS ratio
5	1285974	rs7705526	C	A	5.82E-11	5.87E-05	1.33E-07	2.48E-01	TS ratio

Supplementary Table 10 | Sex-specificity of Parent-of-Origin effects.

CHR: chromosome; POS: genetic position (hg19); SNP ID: variant rs id; A0: reference allele; A1: assessed allele; P DIFF denote P-values for the differential test; COMB, MALES, and FEMALES denote combined sex, males only and females only. P_Z: denotes the P-values for the comparison tests between males-specific and females-specific coefficients using a Z-score approach; TRAIT: phenotype name. Bold indicates the significant sex-specific POE.

CHR	POS (hg38)	UKB SNP	ASSESSED SNP	LD	A0	A1	N	BETA PAT	SE PAT	P PAT	BETA MAT	SE MAT	P MAT	BETA DIFF	SE DIFF	P DIFF	TRAIT
14	**100718850**	**rs59228823**	**rs59228823**		**G**	**C**	**67266**	**-0.007**	**0.008**	**3.55E-01**	**-0.087**	**0.008**	**4.49E-30**	**0.078**	**0.011**	**2.97E-13**	**Platelet count**
11	**1899055**	**rs217215**	**rs4264135**	**0.613**	**A**	**G**	**77270**	**-0.028**	**0.006**	**2.21E-06**	**0.030**	**0.006**	**4.27E-07**	**-0.058**	**0.008**	**4.40E-12**	**Creatinine**
11	**2792092**	**rs143840904**	**rs143840904**		**C**	**T**	**61630**	**-0.005**	**0.020**	**7.98E-01**	**-0.175**	**0.021**	**1.70E-17**	**0.162**	**0.028**	**7.94E-09**	**Standing height**
7	**130378099**	**rs4731690**	**rs4731690**		**A**	**G**	**81884**	**0.009**	**0.002**	**1.18E-05**	**-0.007**	**0.002**	**1.01E-03**	**0.016**	**0.003**	**6.86E-08**	**HDL cholesterol**
11	**1921890**	**rs576603**	**rs735955**	**0.881**	**G**	**A**	**61630**	**-0.027**	**0.005**	**1.39E-07**	**0.005**	**0.005**	**3.11E-01**	**-0.033**	**0.007**	**6.40E-06**	**Standing height**
11	**1694102**	**rs10838787**	**rs7130416**	**0.921**	**T**	**C**	**20203**	**0.054**	**0.013**	**2.17E-05**	**-0.027**	**0.013**	**3.46E-02**	**0.079**	**0.018**	**9.51E-06**	**Glycated haemoglobin**
7	**130376629**	**rs62471721**	**rs62471721**		**G**	**A**	**81884**	**-0.012**	**0.006**	**5.21E-02**	**0.024**	**0.006**	**4.74E-05**	**-0.036**	**0.008**	**1.91E-05**	**Triglycerides**
11	**1682334**	**rs10838787**	**rs4417225**	**0.998**	**C**	**T**	**85050**	**0.092**	**0.035**	**9.60E-03**	**-0.101**	**0.035**	**4.17E-03**	**0.189**	**0.050**	**1.47E-04**	**Type 2 diabetes**
11	**1682334**	**rs4417225**	**rs4417225**		**C**	**T**	**80403**	**0.030**	**0.009**	**5.87E-04**	**-0.017**	**0.009**	**5.81E-02**	**0.046**	**0.012**	**1.92E-04**	**Glucose**
11	**1904723**	**rs170102**	**rs61868802**	**0.608**	**A**	**G**	**21851**	**0.029**	**0.011**	**6.33E-03**	**-0.015**	**0.011**	**1.66E-01**	**0.045**	**0.015**	**3.15E-03**	**Cystatin C**
11	2837065	rs2299620	rs2299620		C	T	20203	0.060	0.034	8.07E-02	-0.070	0.034	3.83E-02	0.130	0.048	6.79E-03	Glycated haemoglobin
11	1902116	rs77708343	rs145861779	0.479	C	T	61630	-0.044	0.012	2.12E-04	-0.006	0.012	6.36E-01	-0.040	0.016	1.56E-02	Standing height
7	130715870	rs3847104	rs3847104		G	A	55874	-0.010	0.010	3.29E-01	0.010	0.010	3.55E-01	-0.020	0.015	1.70E-01	Hip circumference
7	130778999	rs6467315	rs10954284	0.999	T	A	55874	0.001	0.007	8.78E-01	0.009	0.007	1.81E-01	-0.008	0.010	4.07E-01	Hip circumference

Supplementary Table 11 | Replication of parent-of-origin effects in the Estonian Biobank cohort.
CHR: chromosome; POS: genetic position (hg38); UKBB SNP: variant exhibiting POE on the trait in the UK Biobank (UKBB); ASSESSED SNP: variant tested for POE in the Estonian Biobank (EstBB); LD: Linkage Disequilibrium (LD) between the UKBB variant and the assessed variant, if not the same variant. LD was computed in the UK Biobank cohort; A0: reference allele of the assessed variant in the EstBB; A1: assessed allele of the assessed variant in the EstBB; N: number of individuals with available trait levels (includes individuals both homozygous and heterozygous for the assessed variant); BETA, SE and P denote effect sizes, standard errors and P-values; PAT, MAT and DIFF denote paternal, maternal and differential tests. TRAIT: phenotype name. Bold indicate replicated associations.