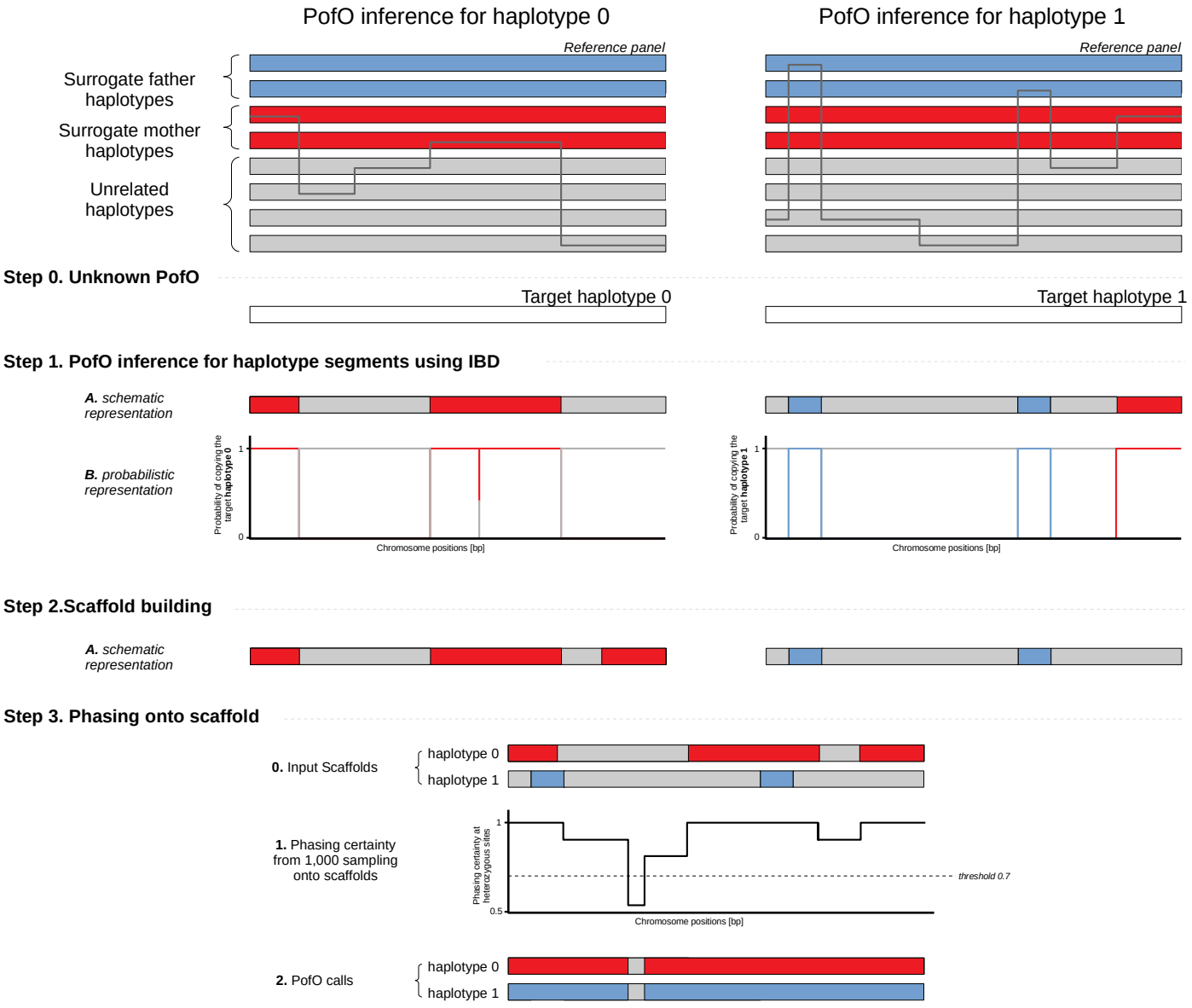
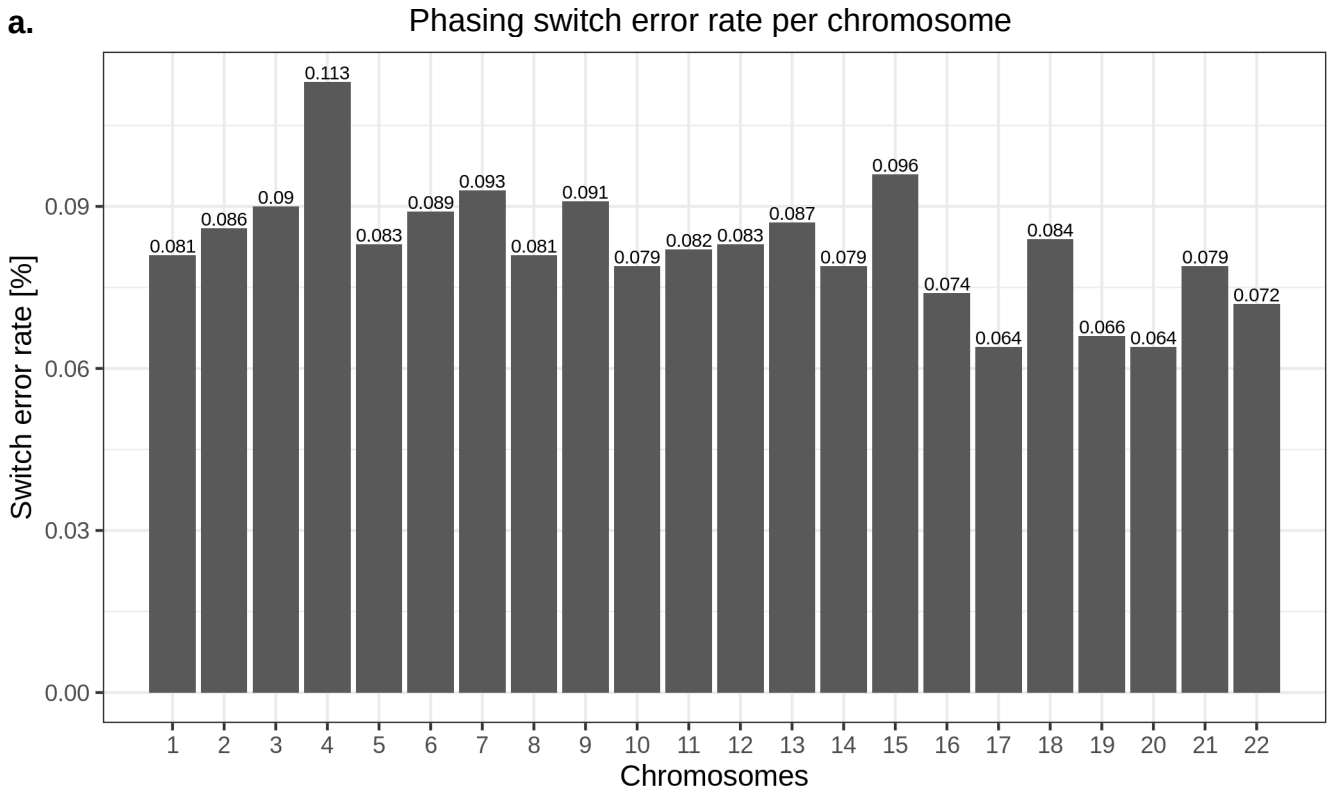
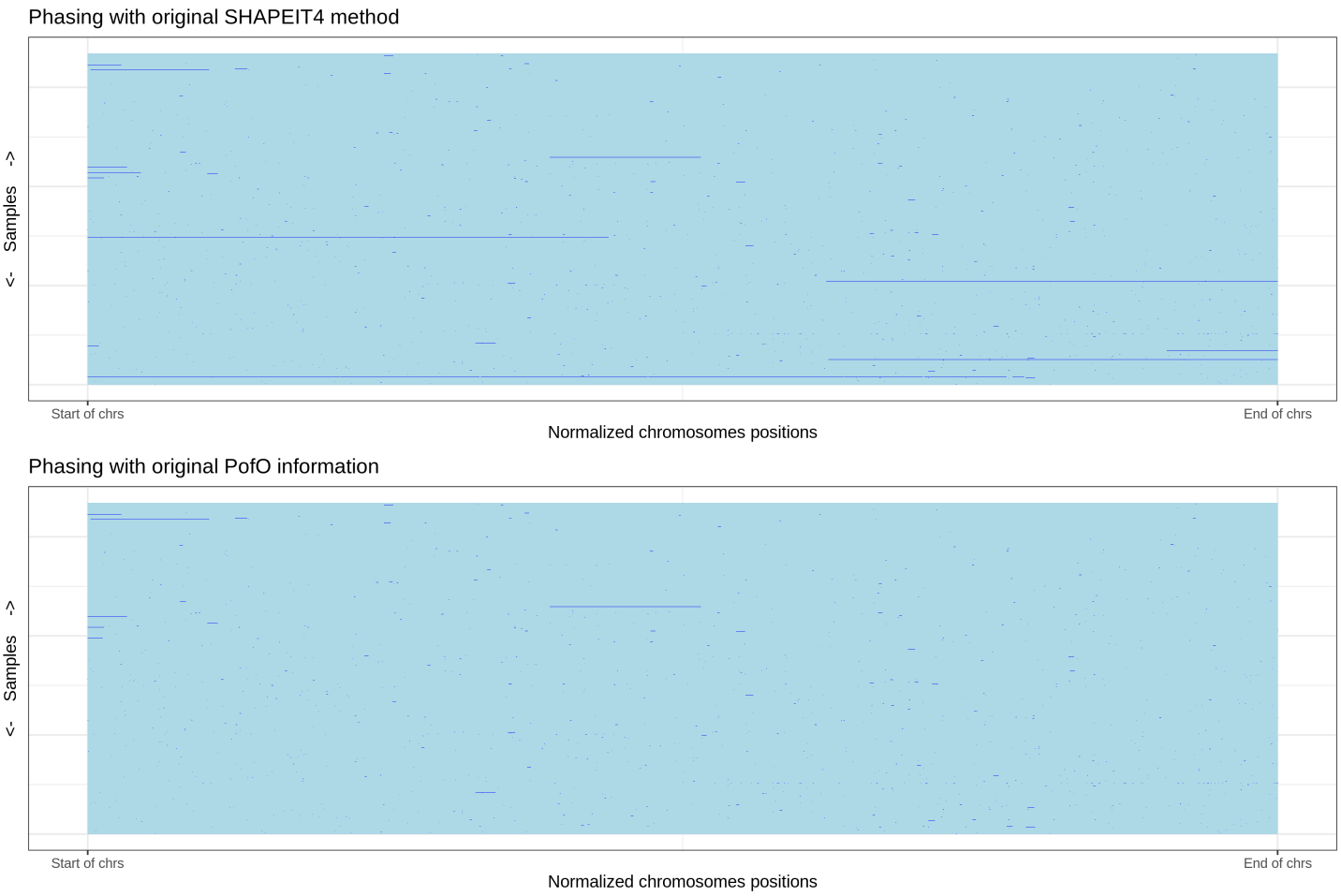
# Supplementary information

## Supplementary figures

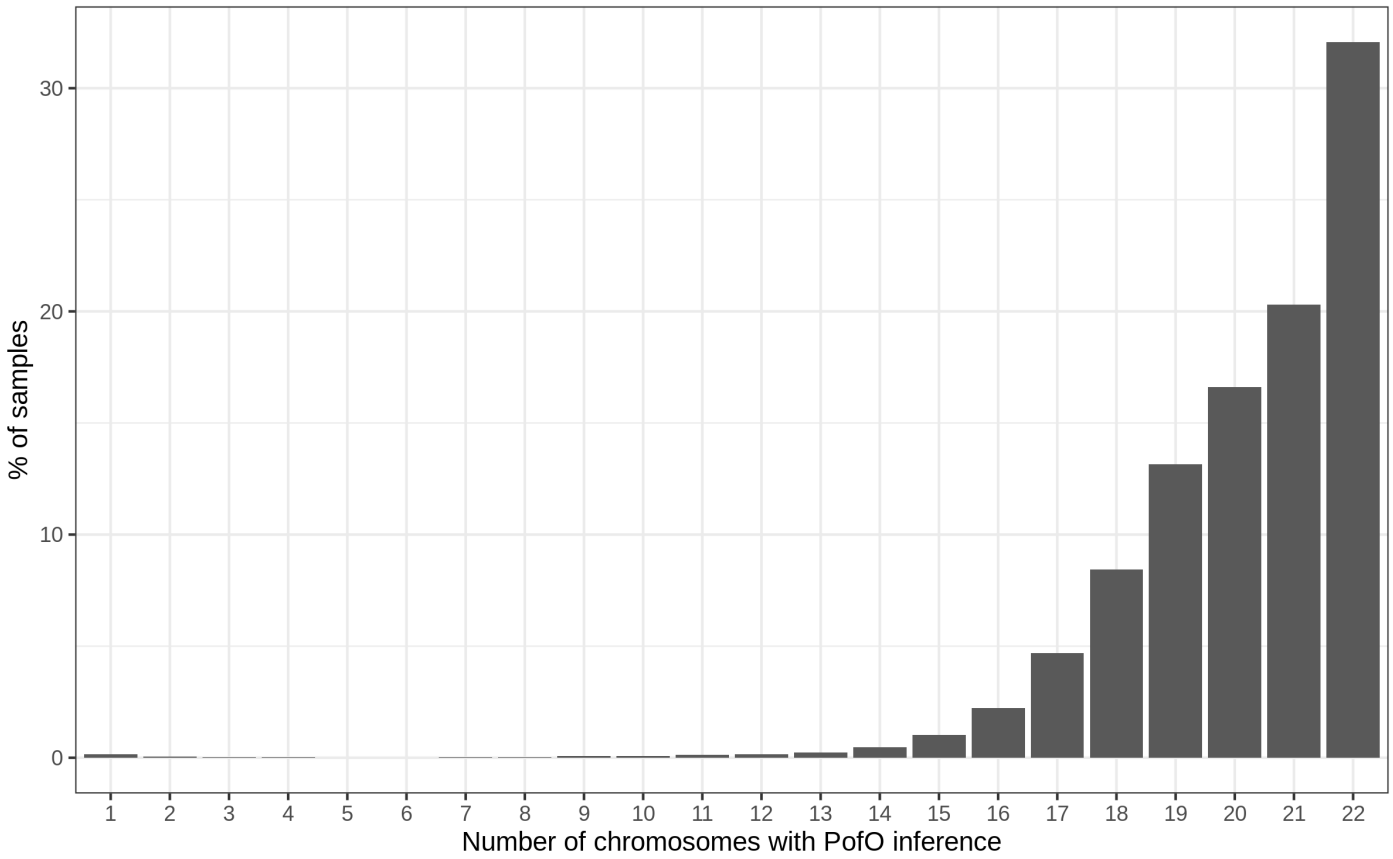



**<u>Supplementary Figure 1:</u> PofO inference from surrogate parents.**
Schematic representation of the PofO inference performed for each of the two haplotypes of a target sample. In **step 1**, the PofO of haplotype segments is inferred from the surrogate parents using a HMM that computes IBD sharing between the target haplotype and a reference panel comprising haplotypes from the surrogate parents and 100 unrelated haplotypes. In **step 2**, the resulting IBD segments are used to assemble a haplotype scaffold to inform another round of phasing. In **step 3**, we sampled 1,000 haplotype pairs per target as part of the last phasing round in order to compute the frequency at which unassigned alleles co-localize onto the maternal/paternal scaffold, thereby deriving confidence scores for their PofO extrapolation.

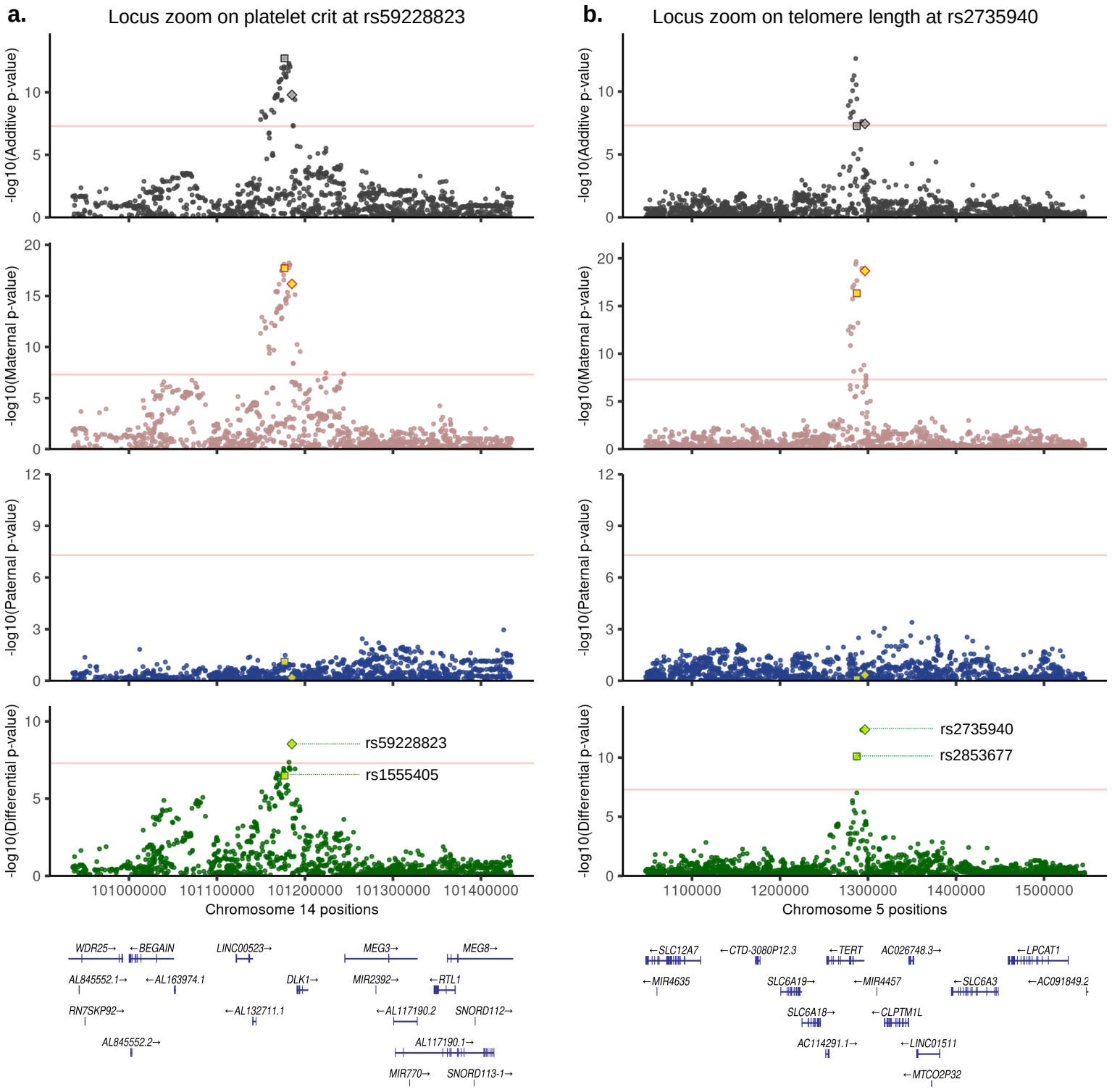



**<u>Supplementary Figure 2:</u> Phasing accuracy with known PofO information.**
**a.** Phasing switch error rates per chromosome. **b.** Genomic location of switch errors along the chromosomes for 308 samples with both surrogate parents and genotyped parents (y-axis). Positions are normalized between 0 and 1 (x-axis). Continuous segments with the same color represent segments correctly phased. Switches between two colors represent switch errors.




**<u>Supplementary Figure 3:</u> Coverage of PofO inference across samples.**
Proportion of samples (y-axis) having PofO inference across N chromosomes (x-axis).

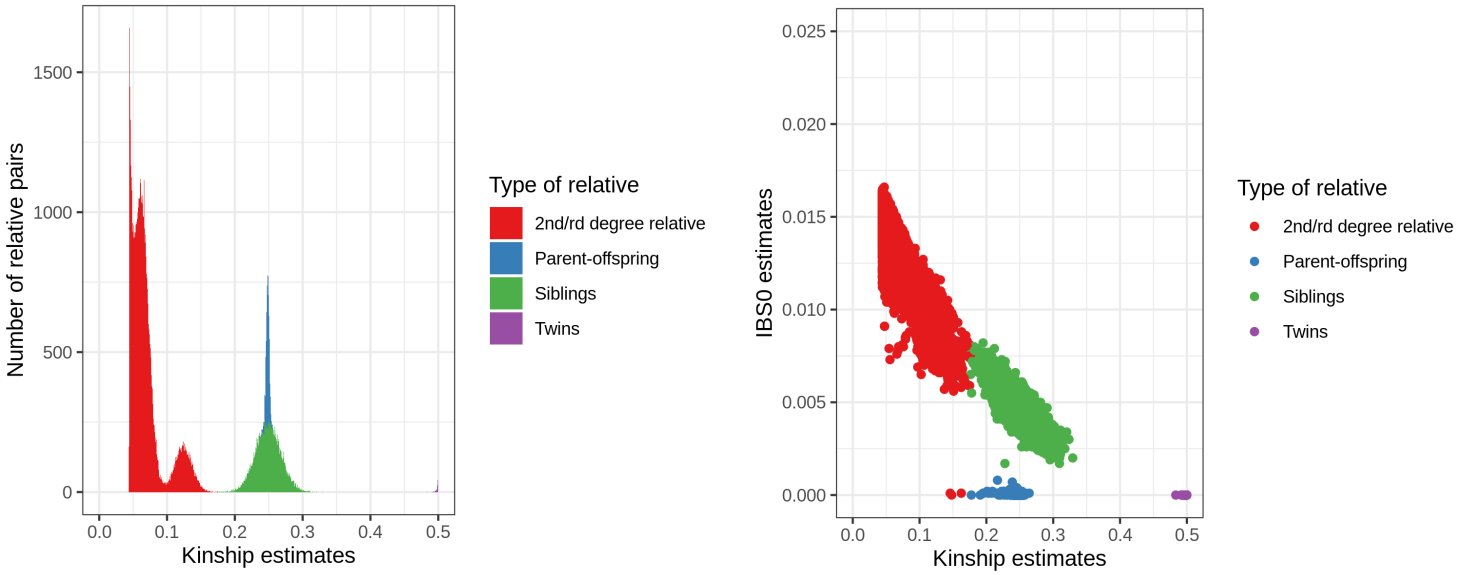



**<u>Supplementary Figure 4:</u> Locus zoom**

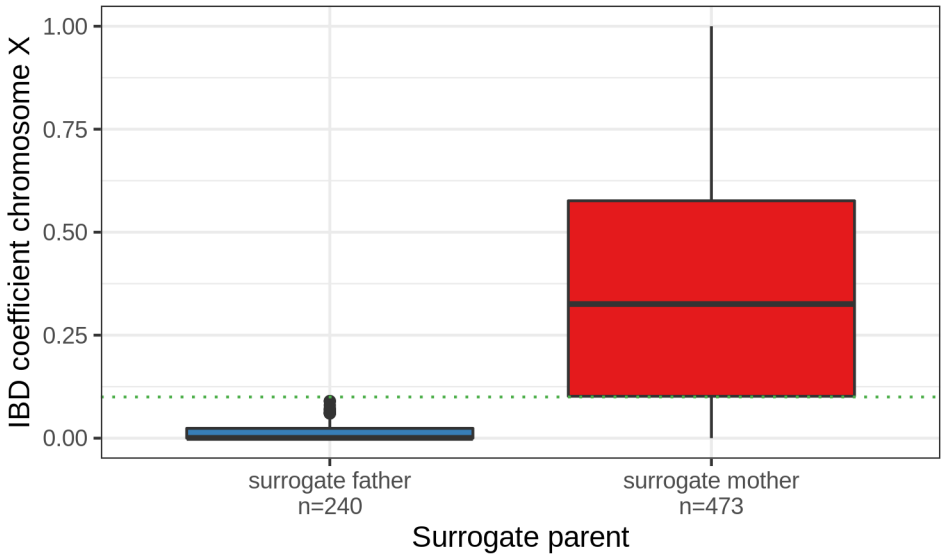
Locus zoom on (**a.**) platelet crit at rs59228823 and (**b.**) telomere length at rs2735940 along a 500kb window centered on the variant (diamond) across the additive (black), maternal (red), paternal (blue) and differential (green) scans. Alternative causal variants previously reported and assessed in this study are shown with a square.

**a.** Distribution of the kinship estimate for UK Biobank relatives pairs

**b.** Kinship estimate ~ IBS0 for UK Biobank relatives pairs



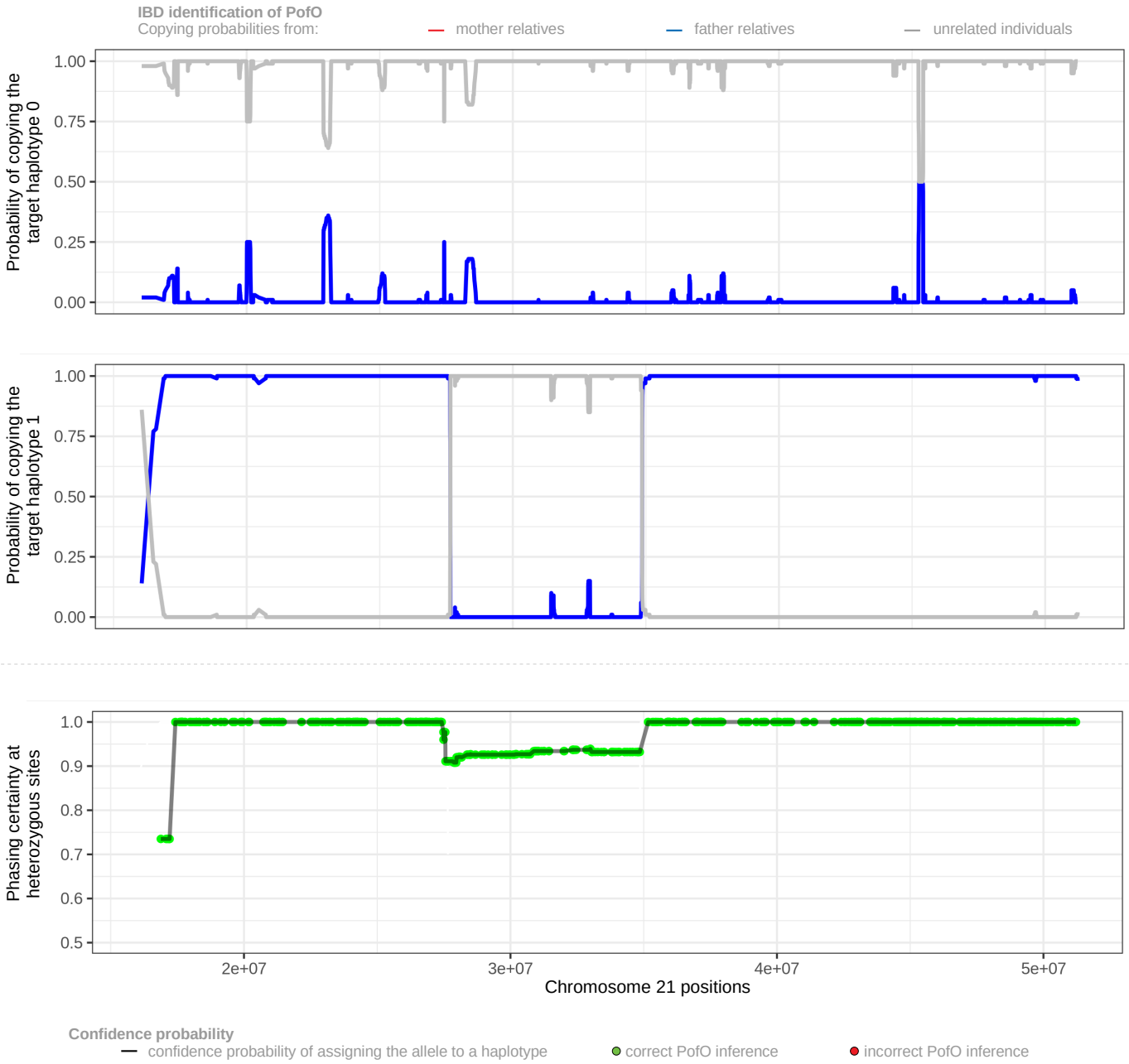

**<u>Supplementary Figure 5:</u> Relatedness in UK biobank.**
**a.** Distribution of the kinship estimate across all UK Biobank relative pairs up to the third degree.
**b.** Kinship estimates in function of the IBS0 estimates in all UK biobank relative pairs up to the third degree. Colors indicate the classification used in our analysis.




**<u>Supplementary Figure 6:</u> Validation of chromosome X IBD.**
IBD coefficient on chromosome X (y-axis) for targets with genotyped parents and surrogate parents (i.e. validation cohort). The IBD is estimated between these targets and their surrogate mother or surrogate father (x-axis). Dotted green line indicates the cut-off used in our analysis (=0.1). Boxes bound the 25$^{th}$, 50$^{th}$ (median) and 75$^{th}$ quantile. Whiskers range from minima (lower) and maxima (upper).

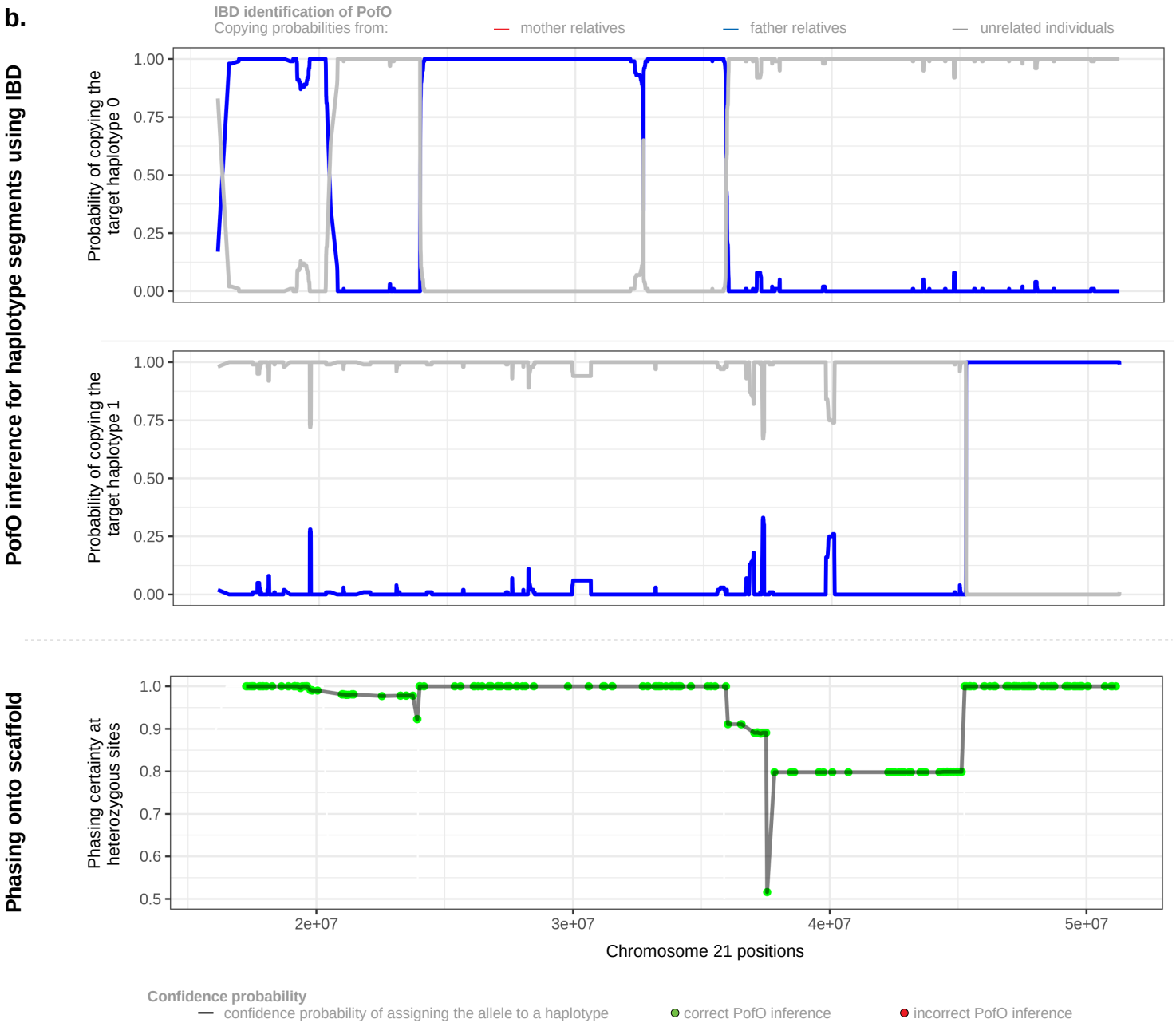
**a.**

**PofO inference for haplotype segments using IBD**

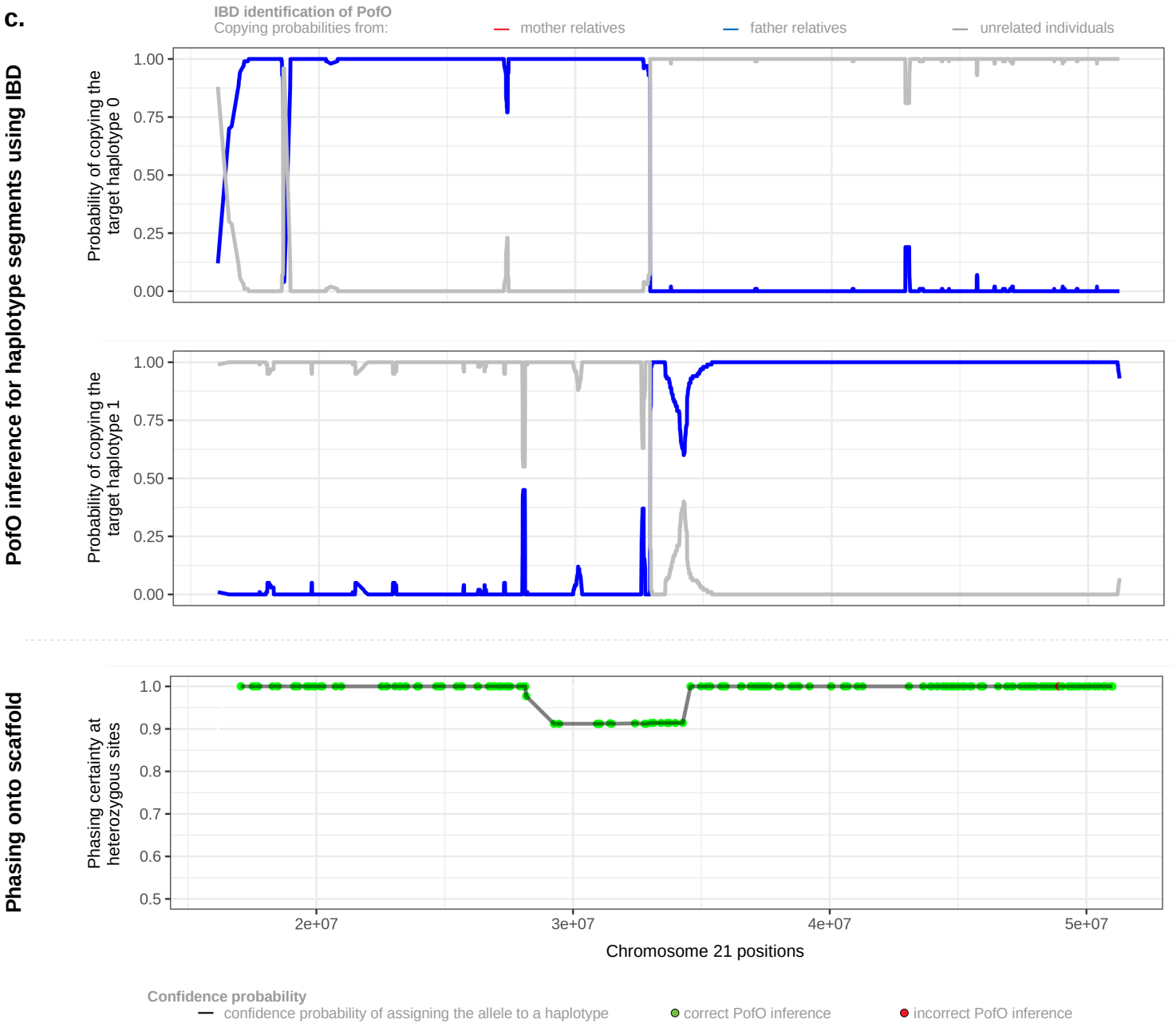



**Phasing onto scaffold**

**b.**


PofO inference for haplotype segments using IBD
IBD identification of PofO
Copying probabilities from:
mother relatives
father relatives
unrelated individuals
Probability of copying the target haplotype 0
1.00
0.75
0.50
0.25
0.00
Probability of copying the target haplotype 1
1.00
0.75
0.50
0.25
0.00
Phasing onto scaffold
Phasing certainty at heterozygous sites
1.0
0.9
0.8
0.7
0.6
0.5
2e+07
3e+07
4e+07
5e+07
Chromosome 21 positions
Confidence probability
confidence probability of assigning the allele to a haplotype
correct PofO inference
incorrect PofO inference

c.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0.75
0.50
0.25
0.00
Phasing onto scaffold
Phasing certainty at heterozygous sites
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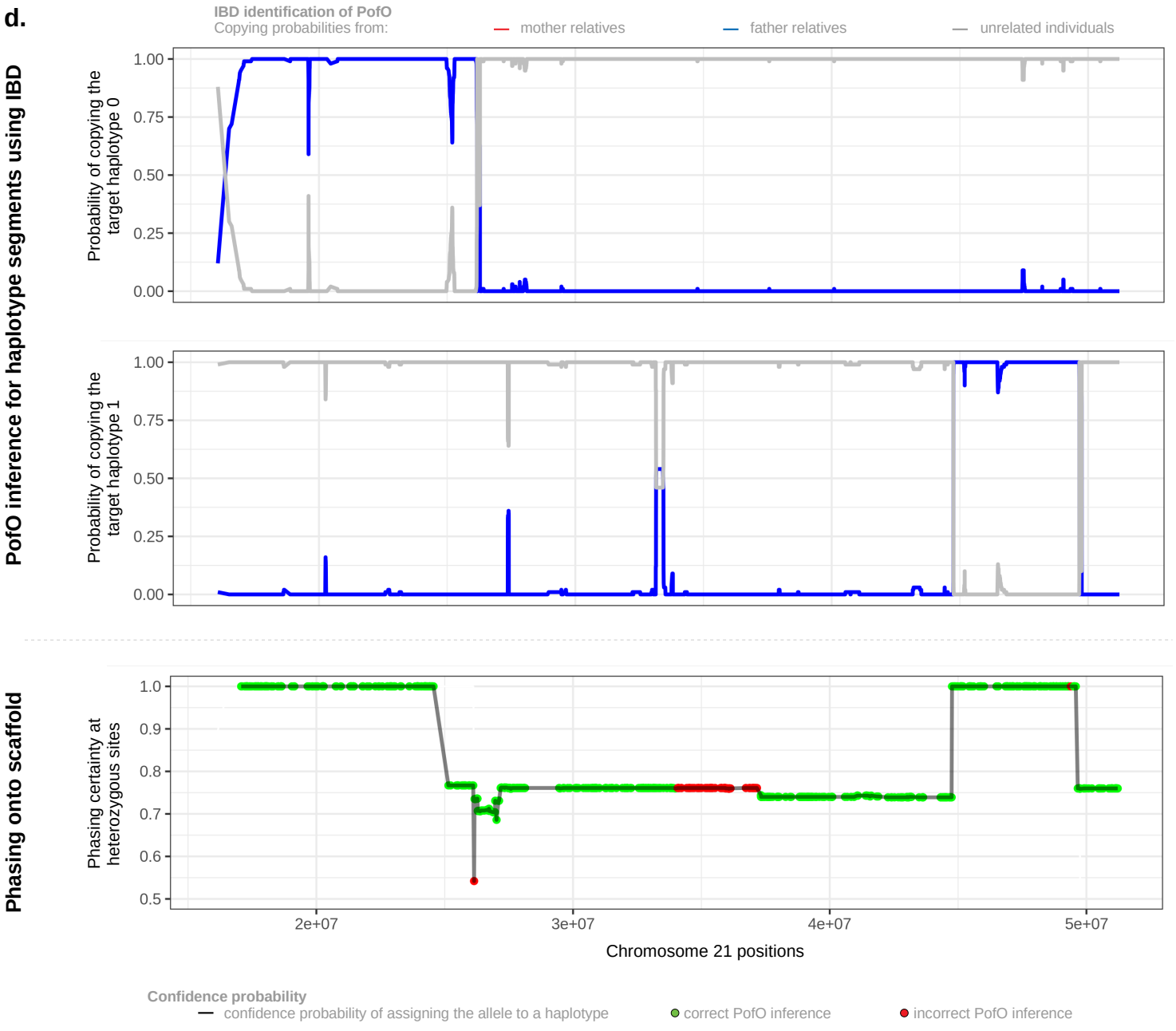
0.8
0.7
0.6
0.5
2e+07
3e+07
4e+07
5e+07
Chromosome 21 positions
Confidence probability
confidence probability of assigning the allele to a haplotype
correct PofO inference
incorrect PofO inference

**d.**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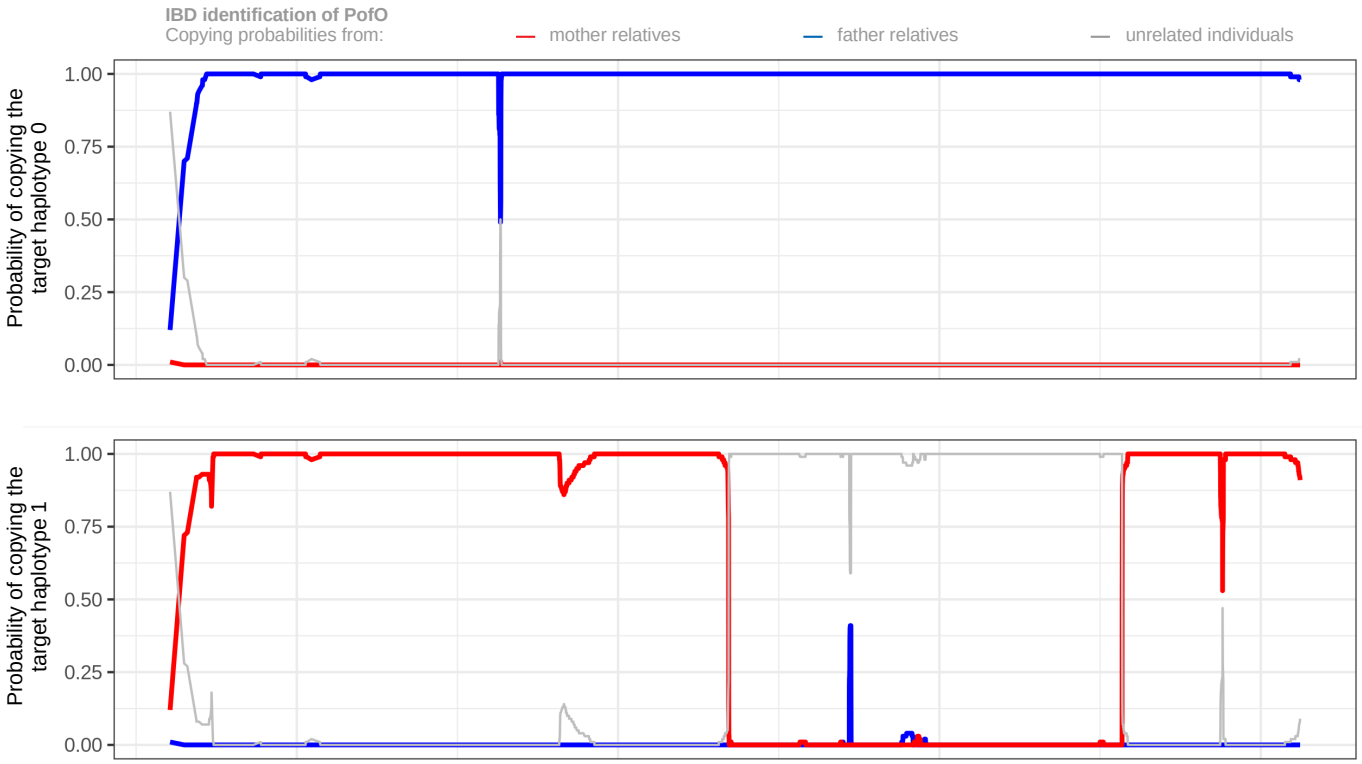
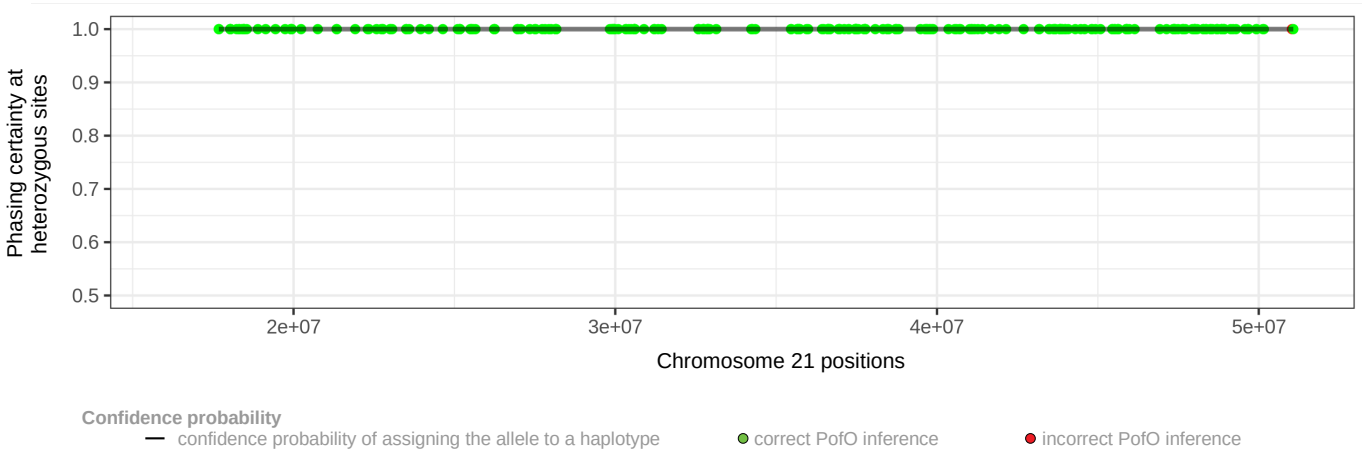
0.8
0.7
0.6
0.5
2e+07
3e+07
4e+07
5e+07
Chromosome 21 positions
Confidence probability
confidence probability of assigning the allele to a haplotype
correct PofO inference
incorrect PofO inference

e.

**PofO inference for haplotype segments using IBD**

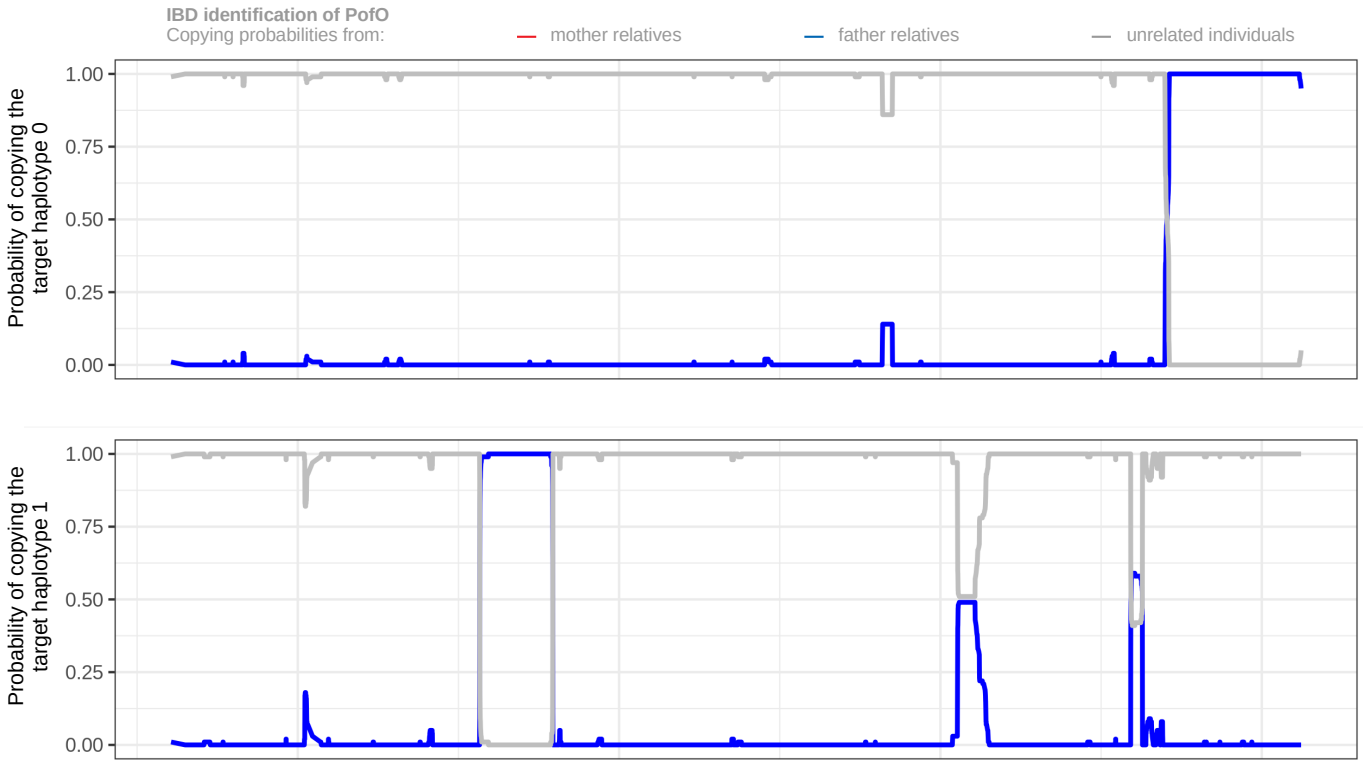



**Phasing onto scaffold**

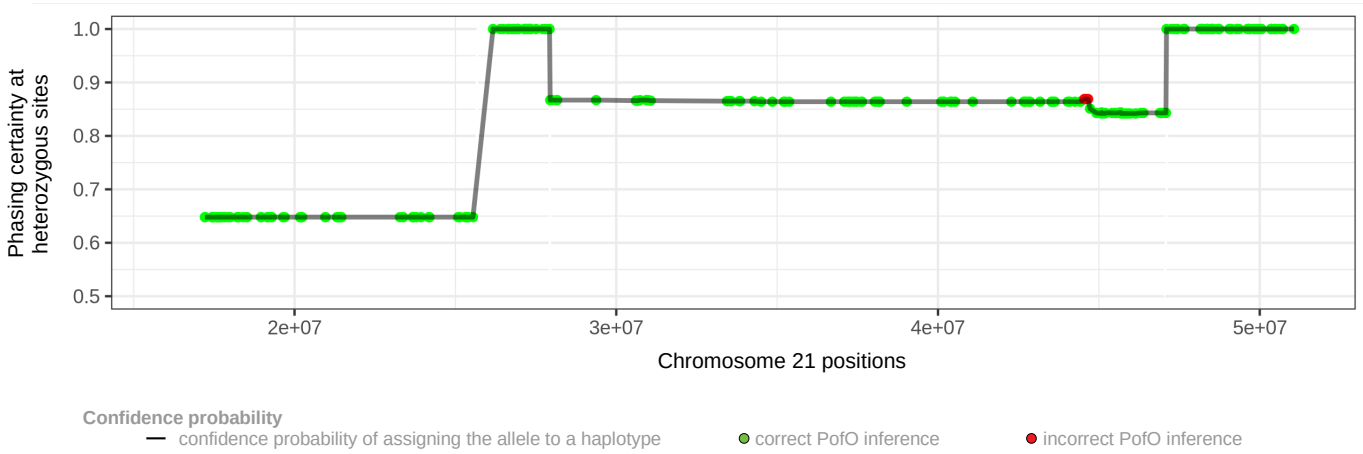


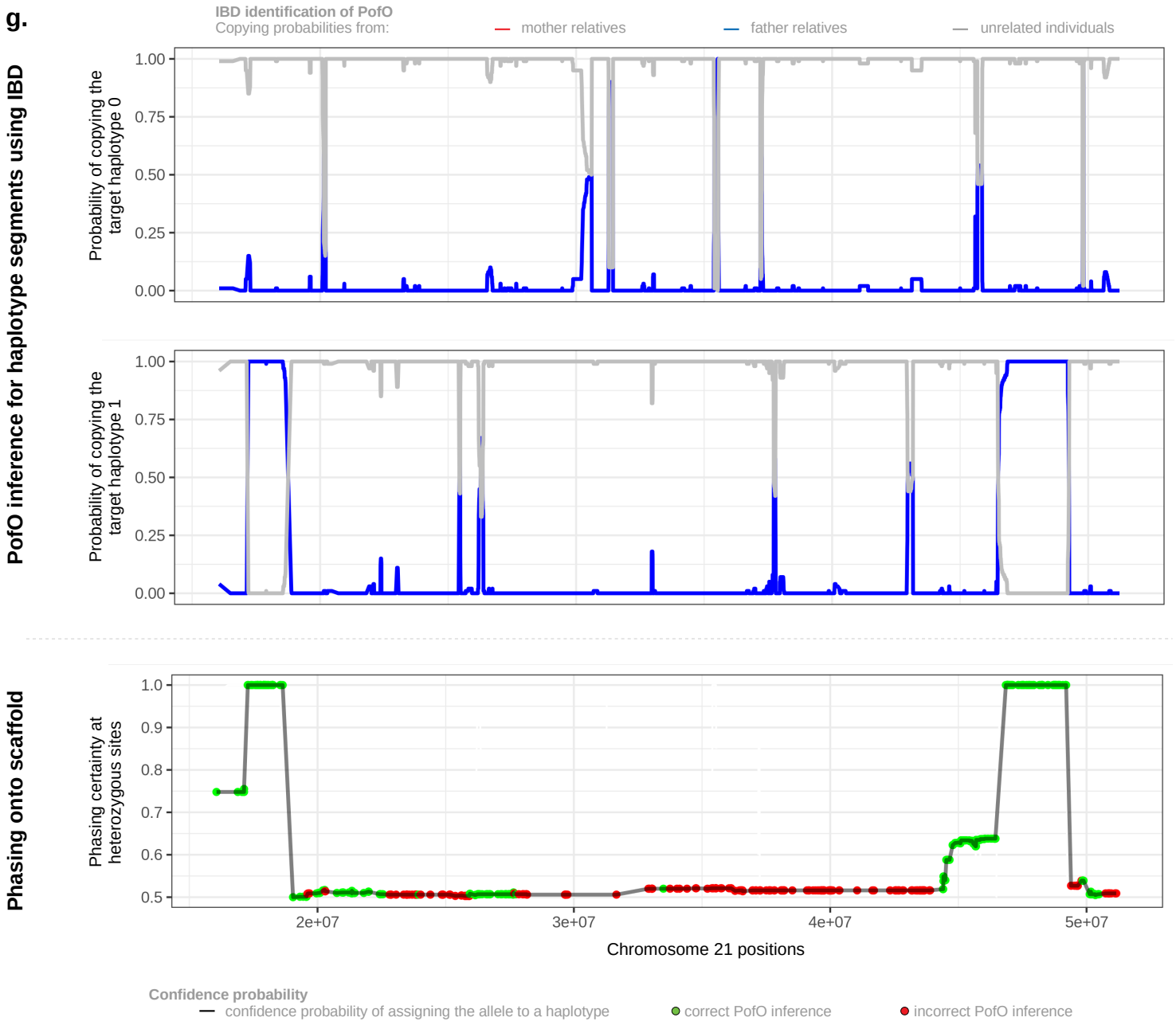
**f.**

**PofO inference for haplotype segments using IBD**




**Phasing onto scaffold**






**<u>Supplementary Figure 7a-g.</u> PofO inference from the surrogate parents for chromosome 21 across 8 validation individuals.** Panels 1-2 show the probability given by our HMM (y-axis) that each target haplotype copies from the surrogate father(s) in blue, the surrogate mother(s) in red or unrelated individuals in grey as we move along chromosome 21. Panel 3 shows the phasing certainty resulting from 1,000 sampling onto scaffold. Red dots show errors in the PofO inference while green dots show correct PofO inference

# Supplementary tables

| | Number of individuals | Number of individuals with PofO inferred from both parental genome (i.e trios) | Number of individuals with PofO inferred from one parental genome (i.e duos) | Number of individuals with PofO inferred from surrogate parents and chromosome X mapping | Number of individuals with PofO deduced from siblings | mean age | sd age | median age | min age | max age |
|---|---|---|---|---|---|---|---|---|---|---|
| Both sex | 26393 | 1037 | 3872 | 20620 | 864 | 54.7 | 9.13 | 56 | 39 | 73 |
| Males | 22652 | 427 | 1516 | 20620 | 89 | 56.25 | 8.62 | 58 | 39 | 73 |
| Females | 3741 | 610 | 2356 | 0 | 775 | 46.05 | 6.81 | 44 | 39 | 70 |

**Supplementary Table 1. Study samples**

| Phenotype | SNP | Chr | Position (hg19) | Risk allele | MAF | Add.P | Add.B | Pat.P | Pat.B | Mat.P | Mat.B | Diff.P | Mapped gene | UKB phenotype code | Hoggart *et al.*, p-values | PofO effect |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mean platelet volume | rs17388591 | 2 | 7611948 | A | 0.1511 | 0.11 | 0.0151 | 2.8e-06 | 0.0755 | 0.0034 | -0.0486 | 3.3e-08 | intergenic | 30100 | 0.0020062 | paternal |
| Platelet crit | rs116403284 | 2 | 21812980 | T | 0.0325 | 0.05 | -0.0445 | 1.3e-05 | -0.158 | 0.23 | 0.0456 | 3.4e-08 | intergenic | 30090 | 0.00365278 | paternal |
| Sitting height | rs934235 | 2 | 105661013 | G | 0.4639 | 0.31 | 0.0063 | 1.5e-06 | 0.046 | 0.001 | -0.0320 | 2.9e-09 | MRPS9 | 20015 | 0.00172474 | paternal |
| Eosinophil percentage | rs77403171 | 2 | 143984854 | G | 0.0102 | 0.64 | 0.0218 | 0.00085 | 0.229 | 0.0002 | -0.256 | 1.6e-08 | ARHGAP15 | 30210 | 0.00634692 | opposite |
| Leg fat-free mass (left) | rs117968021 | 8 | 79223827 | T | 0.0117 | 0.85 | 0.0062 | 8.6e-05 | 0.151 | 0.00061 | -0.128 | 4.5e-08 | PKIA-AS1 | 23117 | 0.00585272 | opposite |
| Mean corpuscular volume | rs10763958 | 10 | 34170183 | C | 0.4968 | 0.51 | 0.0091 | 1.0e-05 | 0.0608 | 0.0005 | -0.0418 | 8.8e-09 | intergenic | 30040 | 0.00174499 | opposite |
| Sitting height | rs143543103 | 10 | 70040971 | T | 0.0432 | 0.24 | 0.0233 | 0.0029 | -0.0680 | 8.7e-06 | 0.116 | 5.5e-09 | PBLD, MYPN | 20015 | 0.00321167 | maternal |
| Platelet crit | rs1790192 | 11 | 118757191 | G | 0.3933 | 0.56 | -0.0065 | 0.0098 | 0.0312 | 0.00063 | -0.0452 | 3.9e-08 | CXCR5 | 30090 | 0.00175238 | opposite |
| Total bilirubin | rs62032857 | 16 | 20338450 | A | 0.0247 | 0.52 | 0.0317 | 0.0022 | -0.095 | 2.2e-06 | 0.193 | 3.7e-08 | GP2 | 30840 | 0.00405805 | maternal |
| Direct bilirubin | rs62032857 | 16 | 20338450 | A | 0.0247 | 0.83 | 0.0071 | 8.3e-05 | -0.147 | 8.2e-05 | 0.175 | 2.6e-08 | GP2 | 30660 | 0.00437831 | opposite |
| Impedance of arm (left) | rs432573 | 19 | 16304742 | T | 0.1527 | 0.56 | -0.0051 | 1.1e-05 | -0.058 | 0.00096 | 0.0447 | 4.2e-08 | FAM32A, AP1M1, enhancer | 23110 | 0.00207257 | opposite |
| Impedance of arm (right) | rs432573 | 19 | 16304742 | T | 0.1527 | 0.71 | -0.0029 | 1.7e-05 | -0.056 | 0.00067 | 0.0458 | 4,00E-08 | FAM32A, AP1M1, enhancer | 23109 | 0.00207230 | opposite |
| Nucleated red blood cell percentage | rs12983350 | 19 | 31383551 | A | 0.0272 | 0.00043 | 0.0284 | 5.7e-10 | 0.0754 | 0.66 | -0.0052 | 4.4e-09 | intergenic | 30230 | 0.00658008 | paternal |
| Nucleated red blood cell count | rs12985289 | 19 | 31383552 | A | 0.0272 | 0.001 | 0.0265 | 7.6e-10 | 0.0750 | 0.45 | -0.0091 | 6.5e-09 | intergenic | 30170 | 0.00658255 | paternal |

**Supplementary Table 2. Putative PofO associations not supported by additive associations.** P-values are computed using BOLT-MM[1]. Add=Additive ; Pat.=Paternal ; Mat.=Maternal ; Diff.=Differential ; P=p-values; B=betas ; Chr=Chromosome ; MAF=minor allele frequency.

| SNP | Chr | Position (hg19) | Risk allele | MAF | Add.P | Add.B | Pat.P | Pat.B | Mat.P | Mat.B | Diff.P | Phenotype | UKB phenotype code | Pofo effect |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| rs527065 | 1 | 177868882 | T | 0.3286 | 1.3e-07 | 0.0409 | 1.8e-09 | 0.067 | 0.11 | 0.018 | 0.0015 | Weight | 23098 | paternal |
| rs539515 | 1 | 177889025 | C | 0.208 | 5.3e-08 | 0.0539 | 2.6e-09 | 0.086 | 0.057 | 0.027 | 0.0043 | Arm fat mass (right) | 23120 | paternal |
| rs539515 | 1 | 177889025 | C | 0.208 | 1.3e-06 | 0.036 | 4.6e-08 | 0.060 | 0.16 | 0.016 | 0.0044 | Arm fat percentage (right) | 23119 | paternal |
| rs8030 | 1 | 177897975 | T | 0.3035 | 2.2e-07 | 0.0401 | 7e-09 | 0.065 | 0.091 | 0.018 | 0.0032 | Waist circumference | 48 | paternal |
| rs8030 | 1 | 177897975 | T | 0.3035 | 7.5e-07 | 0.0392 | 1.8e-08 | 0.06 | 0.12 | 0.018 | 0.0035 | Leg fat mass (left) | 23116 | paternal |
| rs8030 | 1 | 177897975 | T | 0.3035 | 2.7e-07 | 0.041 | 1.2e-08 | 0.066 | 0.077 | 0.021 | 0.0047 | Leg fat mass (right) | 23112 | paternal |
| rs531385 | 1 | 177904428 | C | 0.3502 | 1e-06 | 0.0404 | 4.8e-09 | 0.071 | 0.2 | 0.014 | 0.00078 | Hip circumference | 49 | paternal |
| rs531385 | 1 | 177904428 | C | 0.3502 | 5.8e-08 | 0.0411 | 8.2e-10 | 0.067 | 0.083 | 0.019 | 0.0011 | Weight | 21002 | paternal |
| rs531385 | 1 | 177904428 | C | 0.3502 | 5e-07 | 0.0280 | 1.2e-08 | 0.046 | 0.09 | 0.014 | 0.0029 | Arm fat-free mass (left) | 23125 | paternal |
| rs531385 | 1 | 177904428 | C | 0.3502 | 6.8e-07 | 0.028 | 1.8e-08 | 0.046 | 0.086 | 0.0141 | 0.0039 | Arm predicted mass (left) | 23126 | paternal |
| rs531385 | 1 | 177904428 | C | 0.3502 | 6.7e-07 | 0.0283 | 3.7e-08 | 0.045 | 0.088 | 0.0146 | 0.0049 | Basal metabolic rate | 23105 | paternal |

**Supplementary Table 3. PheWAS at 1q25.2.** P-values are computed using BOLT-MM[1]. Add=Additive ; Pat.=Paternal ; Mat.=Maternal ; Diff.=Differential ; P=p-values; B=betas; Chr=Chromosome ; MAF=minor allele frequency.

## Supplementary References

1. Loh, P.R. *et al.* Efficient Bayesian mixed-model analysis increases association power in large cohorts. *Nat Genet* **47**, 284-90 (2015).