

# Dissecting COPD subtypes using multi-trait genetics

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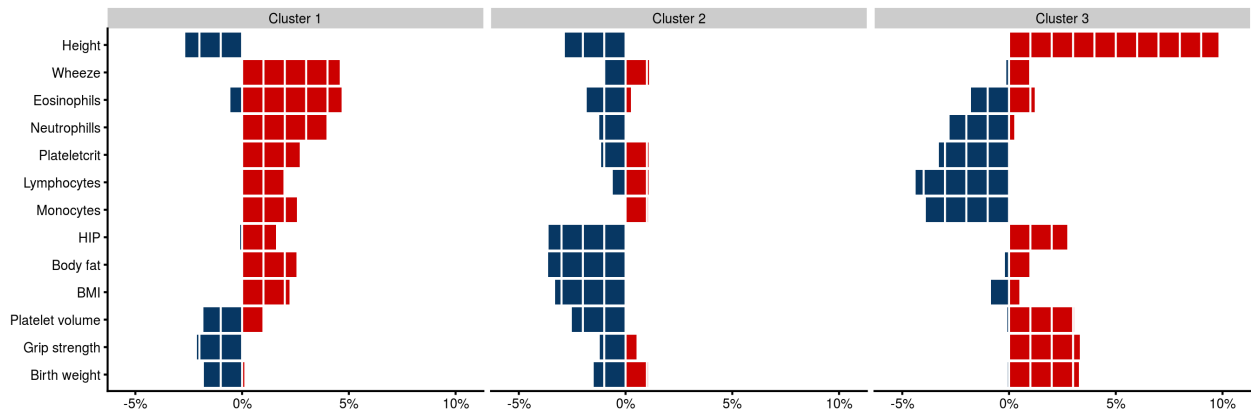
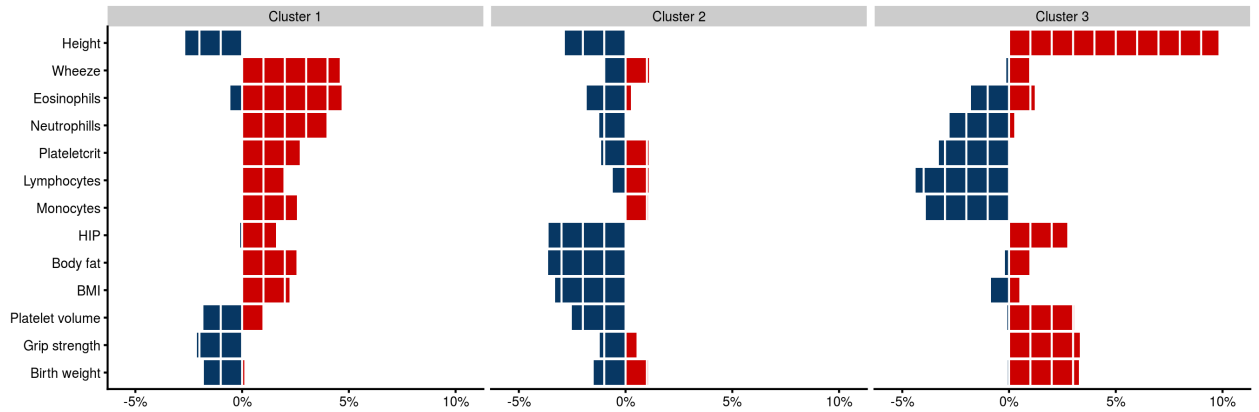


Figure 1: workflow



## **Supplementary Figures**

## Supplementary Tables

**Table S1:** COPDGene traits with evidence of cluster-specific GRS effect at FDR < 0.1

Trait	Group	Type	N	P(GRS0)	P(GRS1-3)	Q(GRS1-3)	Cluster
Height_CM	Basic	num	6,725	0.0029	8.7e-17	2.1e-14	3
PEF_utah	Basic	num	6,703	6.9e-39	4.1e-07	5e-05	3
pre_FEF2575	Basic	num	6,658	1.9e-78	1.2e-06	8.7e-05	3
FEF2575_utah	Basic	num	6,703	4.4e-71	1.4e-06	8.7e-05	3
Emph_Extent_P1	Basic	num	5,241	4e-14	1.6e-05	7e-04	3
eosinphl_calc	Counts	num	3,889	0.81	1.7e-05	7e-04	1
FEV1_FVC_utah	Basic	num	6,703	2.9e-75	2.1e-05	0.00073	3
pre_FEV1_FVC	Basic	num	6,658	3.9e-80	7.6e-05	0.0023	3
Severe.Centrilobular_P1	Basic	num	6,553	1.9e-24	0.00014	0.0038	3
pctEmph_UpperThird_Slicer	Basic	num	6,240	8.4e-24	0.00048	0.012	3
TreatSteroids	Basic	bin01	6,721	3.5e-12	0.00059	0.013	1
UpperThird_LowerThird_Slicer	Basic	num	6,240	0.0015	0.00063	0.013	3
Weight_KG	Basic	num	6,725	0.88	0.00084	0.016	2
DLCOpp_P2	Basic	num	3,578	1.4e-05	0.00096	0.017	3
wbc_calc	Counts	num	3,889	0.17	0.0015	0.022	1
Moderate.Centrilobular_P1	Basic	num	6,553	2.4e-21	0.0015	0.022	3
Panlobular_P1	Basic	num	6,553	2.6e-27	0.002	0.028	3
CRP	Biomarker_RBM	num	601	0.53	0.0021	0.028	1
BronchTimes	Basic	num	3,181	0.12	0.0029	0.038	2
Slicer_15pctIn_Total	Basic	num	6,348	2.2e-24	0.0036	0.043	3
Normal_P1	Basic	num	6,552	2.1e-17	0.0038	0.043	3
CoronaryArtery	Basic	bin01	6,722	0.8	0.0044	0.048	2
pctEmph_Slicer	Basic	num	6,348	4e-25	0.0045	0.048	3
Insp_Below950_Slicer	Basic	num	6,348	8.6e-24	0.0049	0.049	3
eosinphl_pct_calc	Counts	num	3,889	0.36	0.005	0.049	1
SGRQ_scoreImpact	Basic	num	6,721	2.9e-13	0.0067	0.062	3
Slicer_15pctEx_Total	Basic	num	5,842	2e-31	0.0075	0.066	3
SGRQ_scoreTotal	Basic	num	6,721	2.1e-13	0.0076	0.066	3
prm_emphysema	Basic	num	5,598	8.5e-26	0.0089	0.075	3
FumesJobEver	Basic	bin013	6,356	0.21	0.0097	0.077	1
distwalked	Basic	num	6,617	3.7e-05	0.01	0.077	1
SleepApnea	Basic	bin013	5,909	0.95	0.01	0.077	2
SELE	Biomarker_RBM	num	601	0.73	0.013	0.094	1

Out of 311 tested COPDGene traits, 33 traits show a significant effect of three cluster-specific GRSs (GRS1-3) in addition to unweighted GRS (GRS0) cluster-specific GRS effects after multiple-testing correction.

Four types of nested models are compared by the Likelihood Ratio Test (LRT): (model 1) trait-specific covariates; (model 2) trait-specific covariates and unweighted GRS (GRS0); (model 3) trait-specific covariates, unweighted GRS (GRS0) and three cluster-specific GRS (GRS1-3); and (models 4) trait-specific covariates, unweighted GRS (GRS0) and a single cluster-specific GRS (either GRS1, GRS2 or GRS3).

Columns:  $P(\text{GRS0})$ , p-value of comparison between models 1 and 2;  $P(\text{GRS1-3})$ , (heterogeneity) p-value of comparison between models 2 and 3; and  $Q(\text{GRS1-3})$  (q-value) adjusted  $P(\text{GRS1-3})$  using the Benjamini-Hochberg (FDR) method with the number of comparisons equal to 311; *Cluster*, the cluster with the strongest marginal cluster-specific GRS assessed by p-value from comparison between model 2 and each model 4.