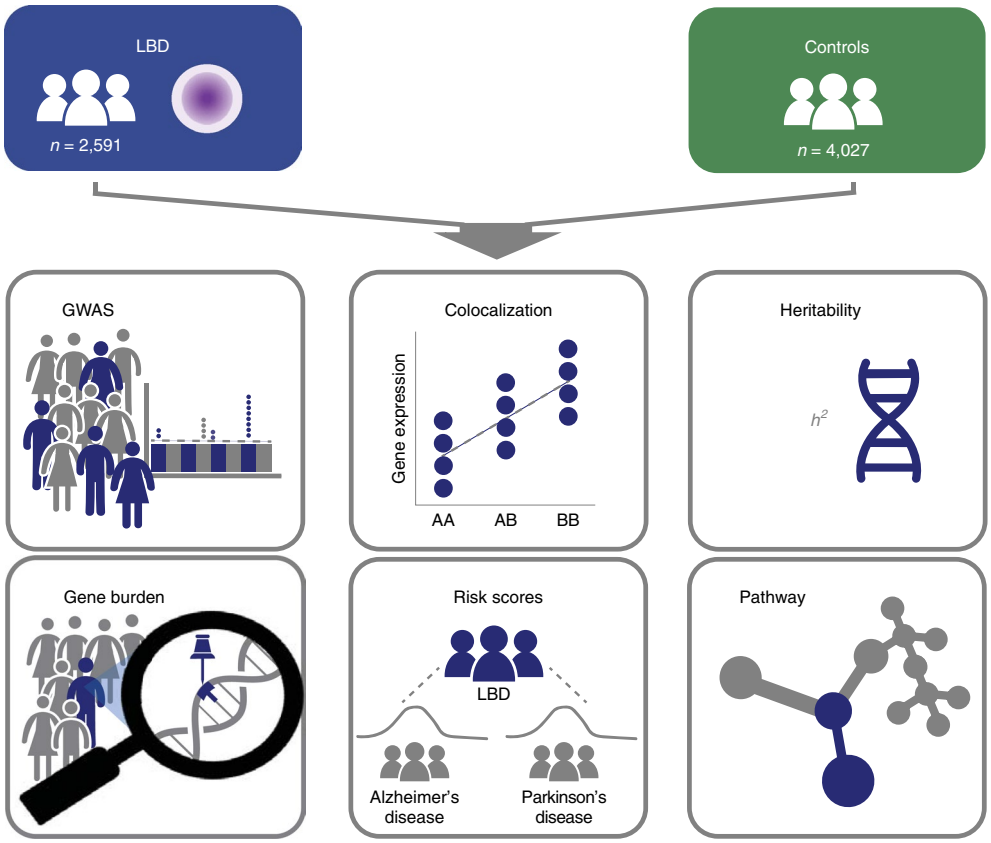

Fig. 1 | Analysis workflow. Schematic illustration of the analytical workflow.

Table 1 | Genome-wide-significant association signals in LBD GWAS

				Whole-genome discovery cohort				Replication cohort				Meta-analysis
Chr	Position (SNP ID)	Closest gene	Alleles (A1, A2)	EAF		OR (95% CI)	*P*	EAF		OR (95% CI)	*P*	*P*
				Cases	Controls			Cases	Controls			
1	155,236,376 (rs2230288)	*GBA*	C, T	0.028	0.009	2.89 (2.16–3.87)	1.28×10^{-12}	0.031	0.013	2.01 (1.46–2.78)	1.95×10^{-5}	4.63×10^{-16}
2	127,135,234 (rs6733839)	*BIN1*	C, T	0.416	0.362	1.25 (1.16–1.35)	4.16×10^{-9}	0.413	0.382	1.16 (1.05–1.28)	3.28×10^{-3}	1.04×10^{-10}
4	945,299 (rs6599388)	*TMEM175*	C, T	0.338	0.310	1.25 (1.15–1.35)	3.54×10^{-8}	0.337	0.286	1.15 (1.03–1.28)	1.03×10^{-2}	2.61×10^{-9}
4	89,842,209 (rs7680557)	*SNCA-AS1*	A, C	0.440	0.504	0.79 (0.73–0.85)	9.73×10^{-11}	0.435	0.509	0.76 (0.64–0.90)	5.27×10^{-8}	3.28×10^{-17}
19	44,906,745 (rs769449)	*APOE*	G, A	0.213	0.100	2.46 (2.22–2.74)	4.65×10^{-63}	0.222	0.110	2.32 (2.05–2.63)	3.27×10^{-40}	2.57×10^{-101}

For each of the five loci, the variant with the lowest *P* value is listed. The gene in closest proximity to the top variant at each locus is represented. The chromosomal position is shown according to hg38. Genome-wide significance was defined as $P<5\times10^{-8}$. A1, other allele; A2, effect allele; Chr, chromosome; EAF, effect allele frequency.

loci (eQTL) were obtained from eQTLGen and PsychENCODE[18,19], the largest available human blood and brain eQTL datasets. We found evidence of colocalization between the *TMEM175* locus and an eQTL regulating *TMEM175* expression in blood (posterior probability for H_4 (PPH4) = 0.99; Fig. 3a and Supplementary Table 1). There was also colocalization between the association signal at the *SNCA* locus and an eQTL regulating *SNCA-AS1* expression in the brain (PPH4 = 0.96; Fig. 3b and Supplementary Table 1). Interestingly, the index variant at the *SNCA* locus was located within the *SNCA-AS1* gene, which overlaps with the 5′ end of *SNCA* and encodes a long noncoding antisense RNA species known to regulate *SNCA* expression. Sensitivity analyses confirmed that these colocalizations were robust to changes in the previous probability of a variant associating with both traits (Extended Data Fig. 4).

We interrogated the effect of each single-nucleotide polymorphism (SNP) in the region surrounding *SNCA-AS1* on LBD risk using our GWAS data, and *SNCA-AS1* expression using the PsychENCODE data (Extended Data Fig. 5a). All genome-wide-significant-risk