Figure 1. PRISMA Flowchart

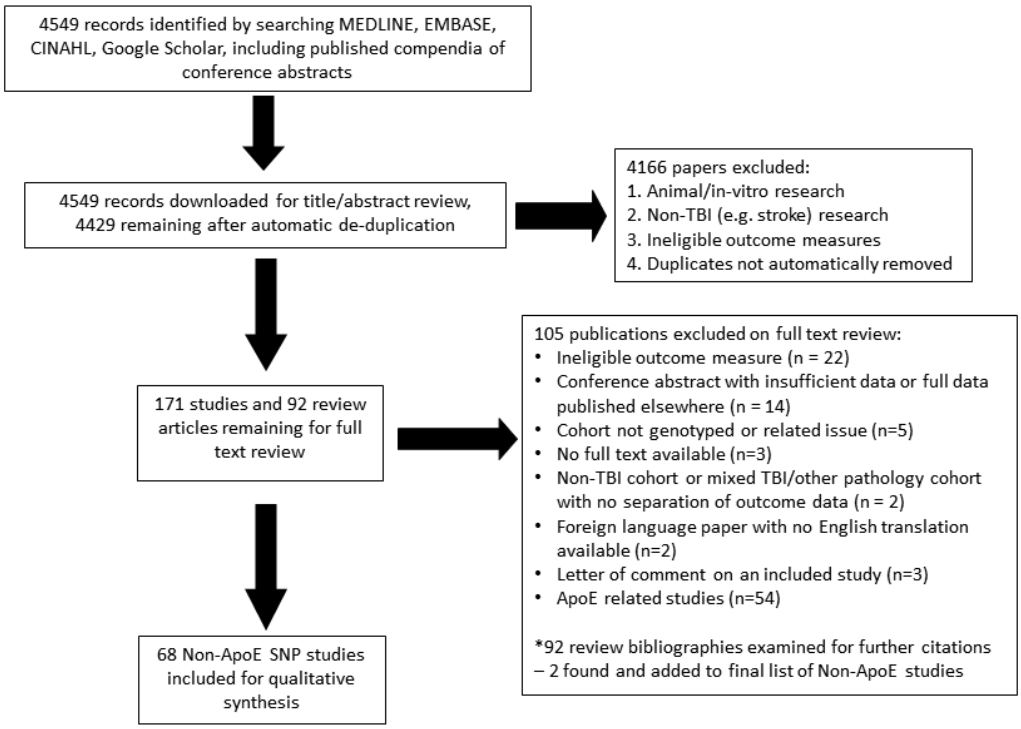
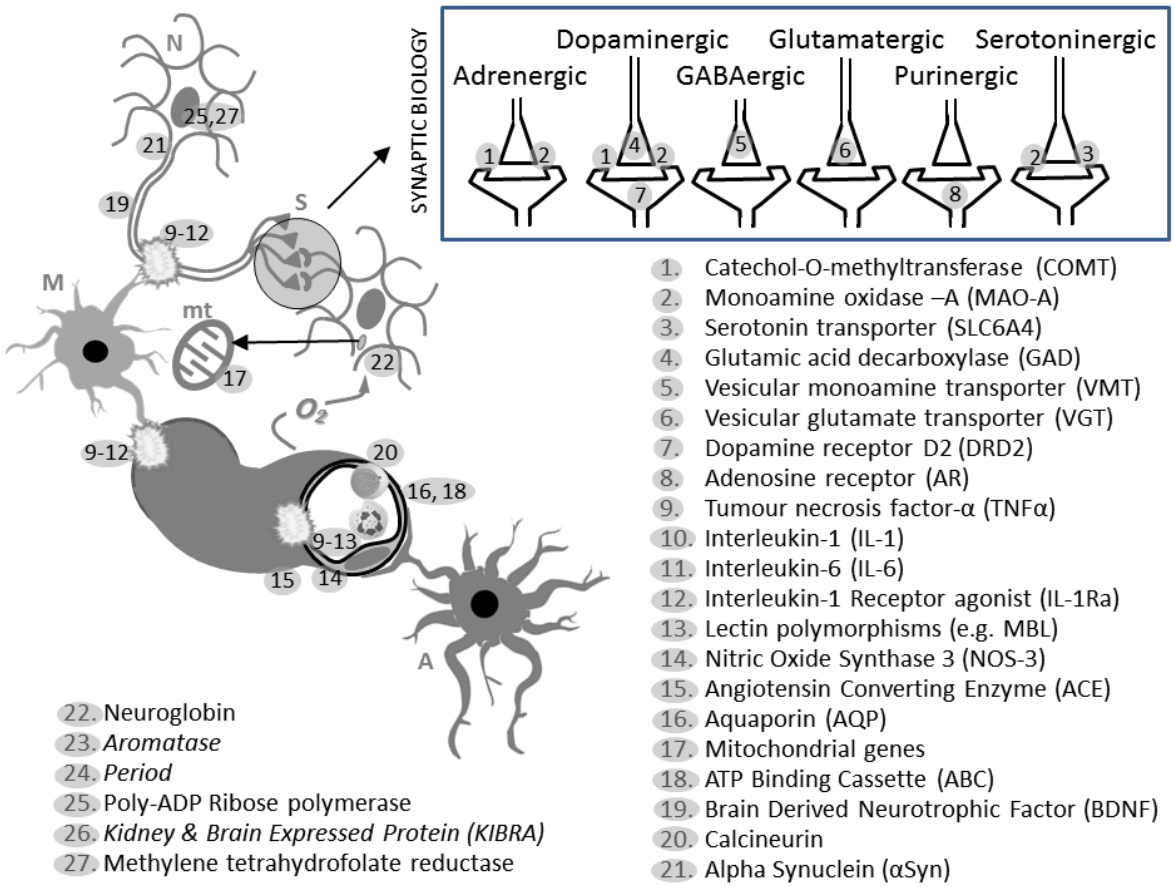
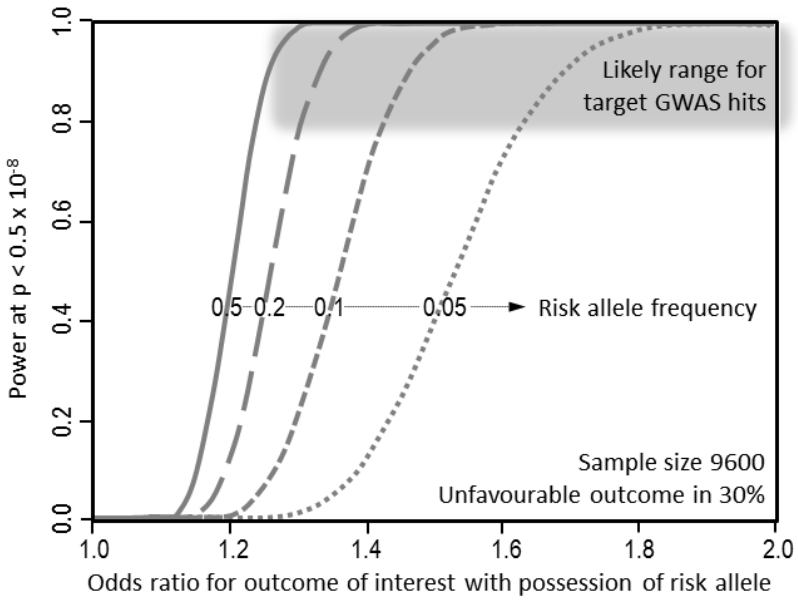


Figure 2: Diagrammatic representation of tissue, cellular, and subcellular location of non APOE- target in candidate gene studies.



The box at top right depicts a variety of neurochemical synapses and locates the target gene products in pre-synaptic sites, post-synaptic sites, or synaptic cleft. The vessel at bottom left shows interactions with astrocytes, microglia, and egressing neutrophils and lymphocytes. The star-bursts represent sites of inflammatory injury. A = astrocyte, ADP = adenosine diphosphate, ATP = adenosine triphosphate, GABA = gamma aminobutyric acid, M = microglia, MBL = mannose binding lectin, mt = mitochondria, N = neuron, O2 = oxygen, S = synapse, SNP = single nucleotide polymorphism. Diagram depicts a theoretical framework for the interaction of various SNPs identified within the review. Diagram depicts neuronal, microglial, astrocytic, synaptic, endothelial, leukocyte, mitochondrial, nuclear and cytosolic areas impacted by various SNPs. *NOTE: SNPs that are italicized could not be slotted into the diagram but are listed secondary to their identification within the systematic review.

Figure 3: Analysis of sample size vs. power in GWAS studies for different rates of risk allele frequency.



These analyses have been conducted for a 9600 sample with a 30% unfavourable outcome. The shaded area shows the likely range of target genes in GWAS studies. Simulations were done using simple logistic regression under additive genetic association assumption. The range of effect sizes reflect typical odds ratios seen in first rounds of genetic association studies for complex diseases, such as in the original Wellcome Trust Case-Control Consortium study (WTCCC).113 With ~50% more cases (unfavorable outcome) and ~100% more controls (favorable outcome) than in the original WTCCC study, the figure illustrates that studies of this size should be well powered in this target OR range.