

Gene	Study	Total n	Outcome assessed	SNPs explored	Findings
DRD2/ANKK1	Fallia et al. 2015 <sup>24</sup>	160	GOSE at 6-12 months	ANKK1:rs1800497 DRD2: rs6279; rs2734838; rs17529477; rs4245147; rs7131056; rs4630328	ANKK1 rs1800497 Taq1A polymorphism modifies outcome (better 6 month GOSE for heterozygotes, but no impact for either homozygotes. Did not survive FDR correction).  No impact from DRD2 SNPs on global outcome.
	Neilson et al. 2017 <sup>75</sup>		GOSE 3/6 months	ANKK1:rs1800497; rs4938016; rs11604671 DRD2: rs6277	Complex topological analysis. Different outcomes depending on CT findings: In CT negative patients – better outcomes with ANKK1 TAQ1ars11604671 A/A genotype and ANKK1 Taq1A C/G genotype and DRD2 rs6277 T/T genotype. In CT positive patients - better outcomes with ANKK1 TAQ1ars11604671 A/G genotype and ANKK1 Taq1A C/C genotype and DRD2 rs6277 C/C genotype associated with better outcome in CT positive patients.
COMT	Wilmott et al. 2014 <sup>18</sup>	211	GOSE at 1-2 years	COMT Val158Met: rs4680	No impact of polymorphisms on global outcome.
	Winkler et al. 2016 <sup>19</sup>	93	GOSE at 6 months	COMT Val158Met: rs4680	Met allele carriers have better outcomes at 6 months.
	Neilson et al. 2017 <sup>75</sup>	586	GOSE 3/6 months	COMT Val158Met: rs4680	Complex topological analysis with multiple genes. COMT rs4680 M/V genotype associated with better GOSE in CT negative patients; M/M genotype associated with better outcomes in CT positive patients.
5HT2AR	Neilson et al. 2017 <sup>75</sup>	586	GOSE 3/6 months	rs6311	Complex topological analysis with multiple genes. No impact of rs6311 polymorphism on outcome.
μ opioid receptor	Neilson et al. 2017 <sup>75</sup>	586	GOSE 3/6 months	OPRM1: rs1799971	Complex topological analysis with multiple genes. No impact of rs1799971 polymorphism on outcome.
IL1A	Tanriverdi et al. 2006 <sup>36</sup>	71	GOS at 6 months	IL-1A -889: rs1800587	No significant effect of polymorphism on outcome.
	Dardoitis et al. 2006 <sup>38</sup>	215	GOS at 6 months	IL-1A -889: rs1800587	No significant effect of polymorphism on outcome.
	Waters et al. 2013 <sup>45</sup>	937	GOS at 6 months	IL-1A -889: rs1800587	No significant effect of polymorphism on outcome.
IL1B	Uzan et al. 2005 <sup>40</sup>	69	GOS at 6 months	IL1B +3953: rs1143634 IL1B -511: rs16944	IL1B +3953 Allele 2 showed worse outcomes. No statistically significant impact of rs16944 on outcome.
	Waters et al. 2013 <sup>45</sup>	937	GOS at 6 months	IL1B -31: rs1143627 IL1B -511: rs16944 IL1B +3953: rs1143634	No statistically significant impact of any of these polymorphisms on global outcome.
IL1RN	Hadigeorgiou et al. 2005 <sup>41</sup>	151	GOS at 6 months	VNTR in IL1RN gene	IL-1RN VNTR Allele 2 has no impact on global outcome at predefined significance level (p < 0.01), but associated with more haemorrhage.
IL-6	Minambres et al. 2003 <sup>43</sup>	40	Mortality	IL-6 174: rs1800795	No association between IL-6 174 GG/CC polymorphism.
	Dallia Libera et al. 2011 <sup>42</sup>	77	GOS at ICU discharge	IL-6 174: rs1800795	GG homozygotes at IL-6 174 locus show reduced mortality in ICU survivors.
	Waters et al. 2013 <sup>45</sup>	937	GOS at 6 months	IL6 -174:rs1800795 IL6 -572: rs1800796 IL6 -597: rs1800797	No impact of any polymorphism on global outcome.
	Sinha et al. 2015 <sup>44</sup>	456	GOS & FIM	IL-6 174: rs1800795	C allele possession at IL-1 74 locus associated with improved survival at 6 months.
TNFA	Waters 2013 <sup>45</sup>	937	GOS at 6 months	TNFA – 238: rs361525 TNFA – 308: rs1800629	TNFA – 308: rs1800629 Allele 2 carriers showed worse outcome. No effect of rs1800629 polymorphism .
TGFB	Waters 2013 <sup>45</sup>	937	GOS at 6 months	TGFB -509: rs1800469 TGFB -800: rs1800468	No impact of either polymorphism on global outcome.
Mitochondrial Haplotype	Conley 2014 <sup>55</sup>	255	GOS, NRS and DRS at 6/12 months	mtDNA -10398	mtDNA -10398 G Haplotype carriers less disabled on DRS than mtDNA -10398 A Haplotype at 6 and 12 months.

Mitochondrial Haplogroup	Bulstrode 2014 <sup>54</sup>	805	GOS at 6 months	Haplogroups: H,J,T,U,K,other	Haplogroup K associated with better GOS at 6 months. Complex interactions of other Haplogroups with age and APOE genotype on outcome.
BCL2	Hoh 2010 <sup>56</sup>	205	GOS, NRS and DRS at 3/6/12 months	BCL2: rs1026825, rs12454712, rs12968517, rs1381548, rs1481031, rs17756073, rs17759659, rs1801018, rs1944419, rs3810027, rs4456611, rs4941185, rs7230970, rs7236090, rs8083946, rs899968, rs949037	Multivariate analysis demonstrates that there were four SNPs of significant interest which had impact on outcome: rs17759659, rs1801018, rs7236090, and rs949037.
	Neilson et al. 2017 <sup>75</sup>	586	GOSE 3/6 months	rs17759659	No outcome impact reported for polymorphism at rs1775659.
BDNF	Fallia 2015 <sup>48</sup>	568	Mortality at 7 days & 1 year	rs6265; rs7124442	No impact of individual polymorphisms on mortality. However, Gene Risk Score (GRS) developed from multivariate Cox regression shows association of combined possession of rs7124442 C allele and rs6265 M allele significantly associated with acute mortality, regardless of age. Post-acutely, BDNF-GRS interacted with age: in the no-risk group younger participants had highest survival probability, while older participants had lowest survival probability.
	Fallia 2016 <sup>79</sup>	295	GOS at 6/12 months; Time to death	rs6265; rs7124442	GRS score from Fallia et al 2015 shown to interact with age and serum BDNF to predict mortality.
	Munoz 2017 <sup>77</sup>	234	GOS at 6 months; Time to death	rs6265; rs7124442	GRS score from Fallia et al 2015 used with CSF BDNF levels and cortisol trajectories to create a mediation model. GRS mediates outcome through BDNF differently in low and high cortisol trajectory groups.
ATP Binding Cassette	Cousar 2013 <sup>59</sup>	556	GOS at 6 months	ABCB1: rs1045642, rs1128503; ABCC1: rs212093, rs35621, rs4148382; ABCC2: rs2273697	When controlled for GCS, age, sex, and ISS; the ABCC1 G/G and the ABCB1 T/T genotype were associated with better outcome.
	Wang 2015 <sup>61</sup>	182	GOS at 6 months	ABCB1: rs1045642; ABCB1: rs2032582	Patients carrying C/T or C/C genotype of ABCB1 C3435T were more likely to have a better neurological outcome when compared with the T/T genotype
Neuroglobin	Chuang 2010 <sup>63</sup>	196	GOS, DRS, NRS at 6/12 months	rs3783988, rs10133981	Haplotype block represented by rs3783988 in NGB (which codes for oxygen binding region of neuroglobin) have better DRS and GOS at 3,6,12, 24 months. rs10133981 not significantly related to functional outcome.
ACE	Dardoitis 2015 <sup>58</sup>	363	GOS at 6 months	rs4343, rs4461142, rs7221780, rs8066276, rs8066114	rs4461142, rs7221780 and rs8066276 showed significantly worse outcomes for heterozygous variants carrying the risk allele compared with the common alleles; outcomes were also significantly worse for rs7221780 C/C homozygotes and rs8066276 T/T homozygotes.
AQP4	Dardoitis 2014 <sup>64</sup>	363	GOS at 6 months	rs335929, rs3763043, rs11661256, rs335931, rs3763040, rs4800773, rs3875089	rs3763043 T/T genotype carriers showed worse outcomes; and rs3875089 C allele carriers showed better outcomes.
Aromatase	Garringer 2013 <sup>65</sup>	110	GOS at 6 months	rs700519, rs28757184, rs2236722, rs56658716, rs2470144, rs2470152, rs4646, rs6493496, rs7168331, rs8041933, rs2470151, rs3751592, rs12901187, rs1062033,	rs2470152 T/T and T/C genotype, rs4646 C/C genotype, and rs2470144 A/A genotype were associated with worse outcomes, and those with > 1 risk SNP variant had a higher risk for poor outcome, compared with those with one risk variant.

				rs7172156, rs11632036, rs12591359, rs10459592, rs12592697, rs2899472, rs6493487, rs2899470.	
p53	Martinez-Lucas 2005 <sup>68</sup>	90	GOS at ICU discharge	rs1042522	Arg/Arg genotype of the Arg72Pro polymorphism at rs1042522 was associated with increased likelihood of a bad outcome at ICU discharge.
Calcineurin	Osier 2017 <sup>81</sup>	380	GOS at 3/6/12 months	PPP3CC: rs2443504, rs2461491, rs2469749, rs10108011	Calcineurin A-gamma gene (PPP3CC) rs2443504 AA genotype univariately associated with GCS ( p = 0.022), GOS at 3, 6, and 12 months, and mortality; significance for GOS retained in multivariate analysis (including age and sex) at 3 and 6 months.
Lectin system	Osthoff 2017 <sup>80</sup>	44	GOSE at 3 months	MBL2: rs1800451, rs1800450, rs5030737, rs7096206 FCN-2: rs3124953, rs17514136, rs17549193, rs7851696	No impact of any polymorphism on outcome.
PARP-1	Sarnaik 2010 <sup>70</sup>	191	GOS at 6 months	rs1109032, rs3219090, rs3219119, rs2271347	rs3219119 A/A genotype independently predicted favourable outcome. rs2271347 A allele carriage resulted in higher CSF PAR-modified protein level, but did not affect outcome.
	Neilson et al. 2017 <sup>75</sup>	586	GOSE 3/6 months	rs3219119	Complex topological analysis. Rs3219119 T/T and A/T genotypes had worse outcomes at 3-6 months

**Table1.** Non-APOE candidate gene studies which used global outcome as phenotype of interest. GOS: Glasgow Outcome Score; GOSE: Glasgow Outcome Score- Extended; FIM: Functional Independence Measure; DRS: Disability Rating Scale; NRS: Numerical Rating Scale; ICU: intensive Care Unit; FDR: False Discovery Rate. Other abbreviations as in text.