Table 1. Probabilities

Parameter	Base case	Range	Distribution	Source
Genotype				
Wild-type	0.28	0.23 to 0.33	Dirichlet	a
1 variant allele	0.36	0.31 to 0.41	Dirichlet	a
≥2 variant alleles	0.36	0.31 to 0.42	Dirichlet	a
Risk of bleeding (yearly)				
INR < 2	0.015	0.007 to 0.030	Beta	[21]
INR within range	0.014	0.009 to 0.023	Beta	[21]
INR 3.0-5.0	0.037	0.022 to 0.063	Beta	[21]
INR > 5	0.301	0.149 to 0.609	Beta	[21]
Aspirin	0.012	0.008 to 0.019	Beta	[19]
Risk of TE (yearly)				
INR < 2	0.081	0.043 to 0.151	Beta	[21]
INR within range	0.024	0.012 to 0.049	Beta	[21]
INR 3.0-5.0	0.027	0.012 to 0.062	Beta	[21]
INR > 5	0.073	0.039 to 0.136	Beta	[21]
Aspirin	0.030	0.020 to 0.044	Beta	[19]
Bleeding outcomes (if bleeding occurs)				
ICH	0.20	0.19 to 0.21	Beta	[16]
Fatal	0.45	0.42 to 0.49	Dirichlet	[16]
Sequelae	0.50	0.46 to 0.54	Dirichlet	[17]
Death/month	0.056	0.04 to 0.07	Beta	[11]
ECH	0.80	0.79 to 0.81	Beta	[17]
TE outcomes (if TE occurs)				
Stroke	0.72	0.69 to 0.75	Beta	[14,15]
Fatal	0.10	0.08 to 0.13	Dirichlet	[16]
Sequelae	0.47	0.44 to 0.51	Dirichlet	[11]
Death/month	0.056	0.04 to 0.07	Beta	[11]
TIA	0.28	0.25 to 0.31	Beta	[14,15]
INR measurements				
First month	6	4.27 to 7.73	Normal	a
Months 2 and 3, per month	3	1.15 to 4.85	Normal	a
Consecutive months, per month	1.75	1.23 to 2.14	Normal	[16]
Extra measurement after event	1	0 to 2	Uniform	Assumption
Age at start of treatment, years	70	50 to 90	Normal	[8,13]

a: authors' own analysis of data from the EU-PACT trial [8]

INR= International Normalized Ratio, ICH=intracranial haemorrhage, ECH=extra cranial haemorrhage, TE=thromboembolic event, TIA=transient ischaemic attack.

Table 2. Utilities and costs

Parameter	Base case	Range	Distribution	Source
Utilities				
Atrial fibrillation	0.81	0.7784 to 0.8430	Beta	[22]
Coumarin use	-0.013	-0.005 to -0.021	Beta	[24]
Aspirin use	-0.002	0.000 to -0.006	Beta	[24]
ECH	-0.06	-0.02 to -0.10	Beta	[11]
ICH	-0.1814	-0.1550 to -0.2089	Beta	[22]
TIA	-0.1032	-0.0881 to -0.1189	Beta	[22]
Stroke	-0.1385	-0.1182 to -0.1600	Beta	[22]
Sequelae after ICH or stroke	-0.374	-0.160 to -0.588	Beta	[22]
Costs (euro)				
Genotyping	40	20 to 60	Gamma	[26]
Phenprocoumon tablets per month	1.78	1.53 to 2.03	Gamma	[26]
Acenocoumarol tablets per month	1.49	1.24 to 1.74	Gamma	[26]
Aspirin tablets per month	0.90	0.79 to 1.01	Gamma	[26]
INR measurement + visit to anticoagulant clinic	12.07	10 to 14	Gamma	[12,25,27]
ECH	13,690	10,952 to 16,428	Gamma	[12,25,27]
ICH	19,672	15,737 to 23,606	Gamma	[12,25,29]
TIA	949	759 to 1139	Gamma	a
Stroke	10,282	8226 to 12,338	Gamma	[12,25,28]
Sequelae - first month	9254	7403 to 11,105	Gamma	[12,25]
Sequalae - subsequent months	463	370 to 555	Gamma	[12,25]

a: Buisman *et al.* , forthcoming

ECH=extra cranial haemorrhage, ICH=intracranial haemorrhage, TIA=transient ischaemic attack, INR= International Normalized Ratio.

Table 3. Results of the cost-effectiveness analysis – base case

Population		First year incidence of adverse events per 100 patients		Lifelong outcomes		
Phenprocoumon	Strategy	Haemorrhagic	Thromboembolic	Costs (€)	QALYs	ICER (€/QALY gained)
Overall	Clinical	2	3.03	9644	9.5198	
	PGx	1.97	3.01	9677	9.5210	
	Δ	-0.03	-0.02	33	0.0012	28,349
Wild-type	Clinical	1.92	3.18	9647	9.5160	
	PGx	1.94	3.08	9679	9.5192	
	Δ	0.02	-0.10	32	0.0033	9788
1 variant	Clinical	1.90	3.06	9633	9.5205	
	PGx	1.93	3.01	9671	9.5219	
	Δ	0.03	-0.05	38	0.0014	27,820
2 variants	Clinical	2.17	2.9	9652	9.5221	
	PGx	2.06	2.97	9682	9.5215	
	Δ	-0.11	0.07	29	-0.0007	Clinical dosing dominates
Acenocoumarol	Strategy	Haemorrhagic	Thromboembolic	Costs (€)	QALYs	ICER (€/QALY gained)
Overall	Standard	2.05	3.05	9616	9.5187	
	PGx	2.02	3.03	9649	9.5201	
	Δ	-0.03	-0.02	33	0.0014	24,427
Wild-type	Standard	1.86	3.2	9605	9.5164	
	PGx	1.91	3.08	9638	9.5201	
	Δ	0.05	-0.12	34	0.0037	9,069
1 variant	Standard	1.97	3.02	9604	9.5211	
	PGx	2.01	3.03	9652	9.5197	
	Δ	0.04	0.01	48	-0.0014	Clinical dosing dominates
2 variants	Standard	2.26	2.96	9637	9.5182	
	PGx	2.10	2.98	9656	9.5204	
	Δ	-0.16	0.02	18	0.0022	8,101

Table 4. Threshold values for age and costs of genotyping at which the ICER would be below €20,000 per QALY gained

	ICER≤€20,000	ICER>20,000
Phenprocoumon		
Age	≤58 years	>58 years
Cost of the test	≤€30	>€30
Acenocoumarol		
Age	≤64 years	>64 years
Cost of the test	≤€33	>€33