

SUPPLEMENTARY RESULTS

Results for the New Oral Coagulants (NOACs)

Apixaban

With routine use of apixaban the average QALYs over 5 years were 2.23 per patient treated compared with 2.19 QALYs under current practice, resulting in a QALY gain of 0.04 per AF patient.

At the population level, the total QALYs across the 32 European countries were 15.6 million with routine use of apixaban and 15 million with current practice, an increase of around 0.3 million QALYs (**Table S1**). For all countries, routine use of apixaban generated additional QALYs, compared to current practice.

Table S1. QALYs gained at the population level

	Routine use of apixaban	Current practice	Difference
Austria	325,014	317,547	7,468
Belgium	307,069	299,159	7,910
Bulgaria	200,264	195,557	4,707
Croatia	100,544	98,250	2,293
Cyprus	23,264	22,726	538
Czech Republic	317,893	311,210	6,683
Denmark	170,331	166,375	3,956
Estonia	37,643	36,733	909
Finland	199,345	194,715	4,629
France	1,833,743	1,787,222	46,521
Germany	2,660,951	2,591,201	69,750
Greece	304,496	296,145	8,350
Hungary	281,900	274,937	6,963
Ireland	98,251	96,106	2,145
Italy	1,872,808	1,823,832	48,975
Latvia	59,742	58,335	1,407
Lithuania	82,826	80,761	2,065
Luxembourg	17,278	16,867	411
Malta	12,744	12,453	291
Netherlands	452,570	442,127	10,443
Poland	1,145,395	1,119,657	25,738
Portugal	227,401	221,484	5,917
Romania	443,190	432,131	11,059
Slovakia	144,124	141,157	2,967
Slovenia	72,787	71,241	1,546
Spain	1,306,107	1,271,932	34,175
Sweden	396,282	387,020	9,263
Total EU-27	13,025,092	12,762,893	262,199
United Kingdom	2,124,231	2,073,206	51,025
Total EU-28	15,136,770	14,835,975	300,795
Iceland	7,873	7,698	175
Israel	142,068	138,784	3,284
Norway	152,832	148,869	3,963
Switzerland	184,185	179,852	4,332
Total 32 countries	15,613,474	15,311,120	302,354

The average therapy cost per AF patient for apixaban was €1,426 compared with €64.90 for current practice (€10 billion as opposed to €453 million at the population level). However,

subsequent health and social care costs were lower under routine use of apixaban than current practice (€8 billion vs. €14 billion, respectively).

So, over a 5-year period, the incremental health and social care costs would be €3.1 billion across Europe. However, in six of the 32 countries under study, the intervention would generate health and social care cost savings: Germany €499 million, Switzerland €65 million, Norway €61 million, Finland €10 million, Luxembourg at €3 million and Iceland at €1 million (**Table S2**).

Table S2. Population-level health and social care costs for patients routinely receiving apixaban and current practice, € thousands

	Routine use of apixaban							Current practice						
	Therapy	Bleeding	Subsequent costs			TOTAL costs	Therapy	Bleeding	Subsequent costs			TOTAL costs		
			Inpatient	Outpatient	A&E				Social care	Inpatient	Outpatient		A&E	Social care
Austria	205,955	9,304	135,922	2,218	845	716	354,960	9,424	9,396	247,703	4,025	1,539	1,306	273,394
Belgium	196,090	10,567	161,814	980	208	52,686	422,345	8,839	10,650	295,782	1,791	382	97,780	415,224
Bulgaria	122,621	223	7,965	158	25	663	131,654	5,670	225	14,484	286	46	1,220	21,930
Croatia	61,148	311	5,374	93	134	897	67,956	2,841	314	9,775	169	243	1,653	14,995
Cyprus	14,175	75	824	134	55	987	16,252	656	76	1,498	244	101	1,820	4,393
Czech Republic	191,693	3,825	54,043	1,024	59	3,912	254,557	8,984	3,866	97,984	1,851	107	7,183	119,975
Denmark	107,461	3,628	73,704	477	181	37,669	223,120	4,902	3,663	134,174	866	330	69,486	213,422
Estonia	23,187	356	4,973	192	39	1,242	29,988	1,072	359	9,050	348	72	2,293	13,193
Finland	126,849	7,519	109,109	3,400	691	45,358	292,926	5,762	7,592	198,864	6,185	1,261	83,861	303,525
France	1,206,272	33,388	588,328	12,085	2,751	175,437	2,018,262	53,766	33,674	1,077,758	22,128	5,038	326,167	1,518,530
Germany	1,713,263	98,786	2,130,913	33,964	739	408,619	4,386,283	76,800	99,565	3,889,376	61,962	1,350	756,746	4,885,798
Greece	200,152	3,630	89,095	292	465	9,702	303,336	8,857	3,657	163,073	534	851	18,012	194,984
Hungary	171,299	1,473	28,049	357	92	9,712	210,982	7,924	1,484	50,895	645	166	17,865	78,980
Ireland	60,280	2,499	29,023	532	502	10,153	102,988	2,789	2,525	52,841	966	914	18,758	78,793
Italy	1,237,352	47,641	686,458	12,201	8,105	173,970	2,165,726	54,902	48,036	1,253,872	22,268	14,819	322,726	1,716,623
Latvia	36,542	141	2,439	97	14	546	39,779	1,700	142	4,436	176	26	1,006	7,487
Lithuania	50,785	269	5,793	166	14	1,993	59,020	2,348	272	10,553	301	26	3,681	17,181
Luxembourg	10,950	777	11,698	154	14	4,673	28,267	499	784	21,375	282	26	8,664	31,629
Malta	8,096	272	3,568	24	14	958	12,932	368	275	6,499	43	25	1,769	8,979
Netherlands	283,437	13,579	192,360	5,366	345	93,255	588,341	12,958	13,711	350,443	9,758	629	172,369	559,869
Poland	693,200	5,175	85,220	4,549	185	33,282	821,611	32,322	5,224	155,180	8,257	338	61,460	262,780
Portugal	147,903	2,298	30,257	961	875	2,651	184,944	6,607	2,316	55,285	1,756	1,599	4,920	72,484
Romania	274,700	951	21,102	656	49	8,026	305,484	12,587	959	38,419	1,192	89	14,814	68,060
Slovakia	85,081	621	10,925	864	52	3,510	101,053	4,041	628	19,835	1,560	95	6,453	32,611
Slovenia	45,242	829	12,142	163	52	4,696	63,124	2,092	838	22,126	296	95	8,674	34,122
Spain	855,846	22,812	362,478	11,495	7,568	71,924	1,332,122	38,155	22,992	663,896	21,058	13,871	133,787	893,759
Sweden	254,006	8,844	137,586	7,692	1,964	95,392	505,482	11,487	8,932	250,613	13,967	3,577	176,202	464,778
Total EU-27	8,325,665	275,585	4,731,587	125,786	23,943	1,360,973	14,843,539	378,195	279,120	8,671,383	230,051	43,890	2,528,095	12,130,736
United Kingdom	1,344,698	60,629	766,446	13,929	4,824	262,717	2,453,243	61,111	61,184	1,397,868	25,373	8,819	486,455	2,040,810
Total EU-28	9,659,919	323,950	5,491,078	150,586	28,692	1,628,382	17,282,607	439,302	328,168	10,063,412	275,392	52,600	3,024,743	14,183,617
Iceland	4,883	374	4,471	118	27	1,917	11,791	225	378	8,160	214	49	3,553	12,579
Israel	88,720	1,866	16,506	361	664	5,171	113,287	4,062	1,884	30,098	652	1,209	9,581	47,486
Norway	100,303	6,227	115,504	995	259	71,096	294,383	4,458	6,278	210,836	1,812	473	131,701	355,558
Switzerland	117,417	8,589	147,603	303	198	64,503	338,613	5,322	8,672	269,598	553	363	119,509	404,017
Total 32 countries	9,962,606	341,836	5,670,952	146,923	29,884	1,762,664	17,914,867	453,367	346,438	10,396,422	268,728	54,796	3,274,972	14,794,723

When we include health, social and informal care costs and productivity losses, the overall societal costs were estimated to be €20 billion with routine use of apixaban compared with €18 billion for current practice (**Table S3**).

Therefore, routinely prescribing AF-patients with apixaban would result in incremental costs of €2.2 billion to European societies. However, for nine countries, the intervention would generate societal cost savings: Germany (€739 million), Switzerland (€85 million), Norway (€73 million), Finland (€22 million), Belgium (€17 million), Denmark (€7 million), Luxembourg (€5 million), The Netherlands (€2 million), and Iceland (€1 million).

Table S3. Societal costs under routine use of apixaban vs current practice, € thousands

	Routine use of apixaban				Current practice			
	Health & social care	Informal care	Productivity losses	TOTAL costs	Health & social care	Informal care	Productivity losses	TOTAL costs
Austria	354,960	10,838	39,448	405,246	273,394	19,898	55,442	348,734
Belgium	422,345	8,017	39,856	470,218	415,224	14,779	57,222	487,225
Bulgaria	131,654	1,058	7,182	139,894	21,930	1,935	8,996	32,861
Croatia	67,956	1,154	5,076	74,186	14,995	2,113	6,830	23,939
Cyprus	16,252	428	1,734	18,414	4,393	784	2,386	7,564
Czech Republic	254,557	4,637	19,501	278,695	119,975	8,461	25,118	153,554
Denmark	223,120	6,203	33,510	262,833	213,422	11,368	45,163	269,953
Estonia	29,988	418	3,141	33,546	13,193	766	3,997	17,955
Finland	292,926	2,226	25,747	320,898	303,525	4,084	35,672	343,282
France	2,018,262	42,297	173,548	2,234,107	1,518,530	78,111	250,350	1,846,992
Germany	4,386,283	87,082	453,941	4,927,306	4,885,798	160,187	620,448	5,666,433
Greece	303,336	6,680	15,237	325,253	194,984	12,325	22,151	229,461
Hungary	210,982	2,064	18,722	231,769	78,980	3,770	23,268	106,019
Ireland	102,988	3,323	14,225	120,536	78,793	6,099	19,793	104,685
Italy	2,165,726	59,155	128,922	2,353,803	1,716,623	109,013	188,753	2,014,390
Latvia	39,779	553	4,322	44,655	7,487	1,013	5,378	13,879
Lithuania	59,020	693	5,658	65,371	17,181	1,272	7,040	25,493
Luxembourg	28,267	527	2,215	31,009	31,629	970	3,297	35,896
Malta	12,932	233	669	13,834	8,979	428	957	10,364
Netherlands	588,341	6,796	67,704	662,841	559,869	12,477	92,360	664,706
Poland	821,611	6,931	73,029	901,571	262,780	12,708	93,061	368,550
Portugal	184,944	3,063	11,725	199,732	72,484	5,648	16,326	94,458
Romania	305,484	3,613	18,262	327,359	68,060	6,624	23,292	97,976
Slovakia	101,053	1,184	9,170	111,407	32,611	2,162	11,764	46,537
Slovenia	63,124	1,122	4,808	69,054	34,122	2,059	6,723	42,904
Spain	1,332,122	44,701	91,206	1,468,029	893,759	82,596	132,832	1,109,188
Sweden	505,482	5,156	46,632	557,270	464,778	9,459	65,177	539,414
Total EU-27	14,843,539	301,076	1,466,709	16,611,323	12,130,736	555,769	1,964,786	14,651,292
United Kingdom	2,453,243	47,355	264,305	2,764,903	2,040,810	87,105	362,068	2,489,983
Total EU-28	17,282,607	348,235	1,745,585	19,376,427	14,183,617	642,818	2,336,102	17,162,537
Iceland	11,791	110	1,247	13,148	12,579	202	1,740	14,521
Israel	113,287	4,092	13,491	130,870	47,486	7,533	18,555	73,574
Norway	294,383	2,939	21,280	318,603	355,558	5,405	30,829	391,792
Switzerland	338,613	6,802	36,485	381,900	404,017	12,519	51,103	467,639
Total 32 countries	17,914,867	362,062	1,829,563	20,106,491	14,794,723	668,535	2,445,367	17,908,625

Overall, routine use of apixaban was cost-effective in the majority of the remaining countries and in Europe as a whole, compared to current practice (**Table S4**). For Croatia, the Czech Republic, Hungary, Latvia, Lithuania, Poland, Romania and Slovakia the decision on whether the intervention is good value for money was dependent on which cost-effectiveness threshold was applied. Only for Bulgaria, the incremental cost-effectiveness ratio (ICER) was estimated to be higher than the NICE cost-effectiveness threshold.

Table S4. Incremental cost per QALY gained from a health & social care and societal perspectives

Country	Health and social care	Cost-effective at € €22,727 per additional QALY?	Society	Cost-effective at € €22,727 per additional QALY?	Cost-effective compared to GDP per capita?
Austria	€ 10,935	yes	€ 8	yes	yes
Belgium	€ 911	yes	Apixaban dominates	yes	yes
Bulgaria	€ 23,312	no	€ 22,740	no	no
Croatia	€ 23,096	no	€ 21,911	yes	no
Cyprus	€ 22,054	yes	€ 20,178	yes	yes
Czech Republic	€ 20,143	yes	€ 18,725	yes	no
Denmark	€ 2,460	yes	Apixaban dominates	yes	yes
Estonia	€ 18,473	yes	€ 17,145	yes	yes
Finland	Apixaban dominates	yes	Apixaban dominates	yes	yes
France	€ 10,748	yes	€ 8,321	yes	yes
Germany	Apixaban dominates	yes	Apixaban dominates	yes	yes
Greece	€ 12,979	yes	€ 11,472	yes	yes
Hungary	€ 18,959	yes	€ 18,059	yes	no
Ireland	€ 11,292	yes	€ 7,390	yes	yes
Italy	€ 9,178	yes	€ 6,930	yes	yes
Latvia	€ 22,953	no	€ 21,874	yes	no
Lithuania	€ 20,262	yes	€ 19,311	yes	no
Luxembourg	Apixaban dominates	yes	Apixaban dominates	yes	yes
Malta	€ 13,570	yes	€ 11,906	yes	yes
The Netherlands	€ 2,739	yes	Apixaban dominates	yes	yes
Poland	€ 21,715	yes	€ 20,710	yes	no
Portugal	€ 19,010	yes	€ 17,792	yes	yes
Romania	€ 21,470	yes	€ 20,743	yes	no
Slovakia	€ 23,068	no	€ 21,862	yes	no
Slovenia	€ 18,768	yes	€ 16,918	yes	yes
Spain	€ 12,832	yes	€ 10,500	yes	yes
Sweden	€ 4,404	yes	€ 1,928	yes	yes
Total EU-27	€ 10,360	yes	€ 7,475	yes	yes
United Kingdom	€ 8,094	yes	€ 5,388	yes	yes
Total EU-28	€ 10,317	yes	€ 7,360	yes	yes
Iceland	Apixaban dominates	yes	Apixaban dominates	yes	yes
Israel	€ 20,041	yes	€ 17,446	yes	yes
Norway	Apixaban dominates	yes	Apixaban dominates	yes	yes
Switzerland	Apixaban dominates	yes	Apixaban dominates	yes	yes
Total 32 countries	€ 10,335	yes	€ 7,269	yes	yes

Dabigatran

With routine use of dabigatran the average QALYs over 5 years were 2.24 per patient treated compared with 2.19 QALYs under current practice, resulting in a QALY gain of 0.05 per AF patient.

At the population level, the total QALYs across the 32 European countries were 16 million with routine use of dabigatran and 15 million with current practice, an increase of around 0.3 million QALYs (**Table S5**). For all countries, routine use of dabigatran generated additional QALYs, compared to current practice.

Table S5. QALYs gained at the population level

	Routine use of dabigatran	Current practice	Difference
Austria	325,231	317,547	7,684
Belgium	307,294	299,159	8,135
Bulgaria	200,376	195,557	4,819
Croatia	100,597	98,250	2,347
Cyprus	23,276	22,726	550
Czech Republic	318,052	311,210	6,842
Denmark	170,437	166,375	4,062
Estonia	37,666	36,733	933
Finland	199,476	194,715	4,760
France	1,835,240	1,787,222	48,018
Germany	2,662,785	2,591,201	71,585
Greece	304,733	296,145	8,587
Hungary	282,054	274,937	7,117
Ireland	98,306	96,106	2,199
Italy	1,874,265	1,823,832	50,432
Latvia	59,778	58,335	1,443
Lithuania	82,878	80,761	2,117
Luxembourg	17,290	16,867	423
Malta	12,752	12,453	300
Netherlands	452,844	442,127	10,717
Poland	1,146,024	1,119,657	26,367
Portugal	227,573	221,484	6,089
Romania	443,458	432,131	11,326
Slovakia	144,194	141,157	3,037
Slovenia	72,831	71,241	1,589
Spain	1,307,195	1,271,932	35,263
Sweden	396,542	387,020	9,522
Total EU-27	13,034,130	12,762,893	271,237
United Kingdom	2,125,643	2,073,206	52,437
Total EU-28	15,147,194	14,835,975	311,219
Iceland	7,878	7,698	180
Israel	142,159	138,784	3,375
Norway	152,946	148,869	4,077
Switzerland	184,309	179,852	4,457
Total 32 countries	15,624,209	15,311,120	313,089

On average the average therapy cost per patient treated with dabigatran was €1,279 compared with €64.90 for current practice. At the population level, this translated to costs of €9 billion as opposed to €453 million with current practice.

Over a 5-year period, treating with dabigatran would result in additional health and social care costs of €1.4 billion across Europe (**Table S6**). In ten of the 32 countries under study, the intervention was estimated to generate health and social care cost savings: Germany €908 million, Switzerland €97 million, Norway €88 million, Finland €38 million, Belgium €37 million, the Netherlands €27 million, Denmark €11 million, Sweden €7 million, Luxembourg €6 million and Iceland €2 million.

Table S6. Population-level health and social care costs for patients routinely receiving dabigatran and current practice, € thousands

	Routine use of dabigatran							Current practice						
	Drug	Bleeding	Subsequent costs			TOTAL costs	Drug	Bleeding	Subsequent costs			TOTAL costs		
			Inpatient	Outpatient	A&E				Social care	Inpatient	Outpatient		A&E	Social care
Austria	184,724	10,994	123,778	2,024	770	652	322,941	9,424	9,396	247,703	4,025	1,539	1,306	273,394
Belgium	175,881	12,529	147,157	892	190	47,821	384,470	8,839	10,650	295,782	1,791	382	97,780	415,224
Bulgaria	109,971	262	7,259	144	23	603	118,262	5,670	225	14,484	286	46	1,220	21,930
Croatia	54,840	366	4,897	85	122	816	61,125	2,841	314	9,775	169	243	1,653	14,995
Cyprus	12,713	88	751	123	50	898	14,623	656	76	1,498	244	101	1,820	4,393
Czech Republic	171,920	4,497	49,296	936	54	3,563	230,266	8,984	3,866	97,984	1,851	107	7,183	119,975
Denmark	96,378	4,289	67,141	435	165	34,257	202,665	4,902	3,663	134,174	866	330	69,486	213,422
Estonia	20,797	419	4,529	175	36	1,129	27,084	1,072	359	9,050	348	72	2,293	13,193
Finland	113,769	8,899	99,347	3,101	630	41,225	266,971	5,762	7,592	198,864	6,185	1,261	83,861	303,525
France	1,082,005	39,693	534,843	11,002	2,502	159,187	1,829,232	53,766	33,674	1,077,758	22,128	5,038	326,167	1,518,530
Germany	1,536,562	117,080	1,938,745	30,942	672	371,091	3,995,092	76,800	99,565	3,889,376	61,962	1,350	756,746	4,885,798
Greece	179,517	4,316	80,990	266	423	8,804	274,316	8,857	3,657	163,073	534	851	18,012	194,984
Hungary	153,627	1,734	25,566	326	83	8,837	190,174	7,924	1,484	50,895	645	166	17,865	78,980
Ireland	54,063	2,947	26,437	485	457	9,231	93,620	2,789	2,525	52,841	966	914	18,758	78,793
Italy	1,109,791	56,605	624,354	11,113	7,372	157,931	1,967,167	54,902	48,036	1,253,872	22,268	14,819	322,726	1,716,623
Latvia	32,775	166	2,222	89	13	496	35,762	1,700	142	4,436	176	26	1,006	7,487
Lithuania	45,550	318	5,274	151	13	1,812	53,117	2,348	272	10,553	301	26	3,681	17,181
Luxembourg	9,822	920	10,643	141	13	4,244	25,783	499	784	21,375	282	26	8,664	31,629
Malta	7,261	322	3,250	22	12	871	11,738	368	275	6,499	43	25	1,769	8,979
Netherlands	254,205	16,049	175,169	4,894	314	84,763	535,395	12,958	13,711	350,443	9,758	629	172,369	559,869
Poland	621,721	6,094	77,627	4,151	169	30,260	740,023	32,322	5,224	155,180	8,257	338	61,460	262,780
Portugal	132,658	2,728	27,516	875	795	2,406	166,979	6,607	2,316	55,285	1,756	1,599	4,920	72,484
Romania	246,366	1,123	19,217	598	45	7,296	274,645	12,587	959	38,419	1,192	89	14,814	68,060
Slovakia	76,309	729	9,963	789	48	3,196	91,034	4,041	628	19,835	1,560	95	6,453	32,611
Slovenia	40,577	979	11,060	149	47	4,270	57,082	2,092	838	22,126	296	95	8,674	34,122
Spain	767,691	27,117	329,475	10,462	6,880	65,249	1,206,873	38,155	22,992	663,896	21,058	13,871	133,787	893,759
Sweden	227,809	10,472	125,297	7,018	1,789	86,719	459,103	11,487	8,932	250,613	13,967	3,577	176,202	464,778
Total EU-27	7,467,251	326,542	4,305,053	114,624	21,788	1,235,987	13,471,246	378,195	279,120	8,671,383	230,051	43,890	2,528,095	12,130,736
United Kingdom	1,206,074	71,767	697,576	12,698	4,391	238,659	2,231,166	61,111	61,184	1,397,868	25,373	8,819	486,455	2,040,810
Total EU-28	8,663,943	383,799	4,996,265	137,230	26,111	1,478,893	15,686,241	439,302	328,168	10,063,412	275,392	52,600	3,024,743	14,183,617
Iceland	4,380	442	4,070	107	25	1,742	10,766	225	378	8,160	214	49	3,553	12,579
Israel	79,575	2,207	15,022	330	605	4,697	102,435	4,062	1,884	30,098	652	1,209	9,581	47,486
Norway	89,960	7,396	105,090	907	236	64,565	268,154	4,458	6,278	210,836	1,812	473	131,701	355,558
Switzerland	105,312	10,172	134,322	276	180	58,590	308,853	5,322	8,672	269,598	553	363	119,509	404,017
Total 32 countries	8,935,411	404,991	5,159,961	133,895	27,197	1,600,852	16,262,307	453,367	346,438	10,396,422	268,728	54,796	3,274,972	14,794,723

When productivity losses were included, overall societal costs were €18.4 billion with routine use of dabigatran compared with €17.9 billion for current practice (**Table S7**) - an additional cost of €0.5 billion to the European society. In ten countries, routine use of dabigatran would generate cost savings relative to current practice: Germany €1 billion, Switzerland €117 million, Norway €100 million, Finland €49 million, Belgium €57 million, the Netherlands €57 million, Sweden at €30 million, Denmark €29 million, Luxembourg at €7 million and Iceland at €2 million, relative to current practice.

Table S7. Societal costs under routine use of dabigatran vs current practice, € thousands

	Routine use of dabigatran				Current practice			
	Health & social care	Informal care	Productivity losses	TOTAL costs	Health & social care	Informal care	Productivity losses	TOTAL costs
Austria	322,941	9,864	38,288	371,093	273,394	19,898	55,442	348,734
Belgium	384,470	7,285	38,514	430,269	415,224	14,779	57,222	487,225
Bulgaria	118,262	963	7,079	126,305	21,930	1,935	8,996	32,861
Croatia	61,125	1,051	4,953	67,129	14,995	2,113	6,830	23,939
Cyprus	14,623	390	1,691	16,704	4,393	784	2,386	7,564
Czech Republic	230,266	4,227	19,181	253,674	119,975	8,461	25,118	153,554
Denmark	202,665	5,648	32,757	241,069	213,422	11,368	45,163	269,953
Estonia	27,084	380	3,089	30,554	13,193	766	3,997	17,955
Finland	266,971	2,026	25,039	294,036	303,525	4,084	35,672	343,282
France	1,829,232	38,424	167,503	2,035,159	1,518,530	78,111	250,350	1,846,992
Germany	3,995,092	79,170	442,377	4,516,639	4,885,798	160,187	620,448	5,666,433
Greece	274,316	6,068	14,695	295,079	194,984	12,325	22,151	229,461
Hungary	190,174	1,880	18,472	210,526	78,980	3,770	23,268	106,019
Ireland	93,620	3,025	13,851	110,496	78,793	6,099	19,793	104,685
Italy	1,967,167	53,759	124,418	2,145,343	1,716,623	109,013	188,753	2,014,390
Latvia	35,762	504	4,263	40,528	7,487	1,013	5,378	13,879
Lithuania	53,117	631	5,579	59,327	17,181	1,272	7,040	25,493
Luxembourg	25,783	479	2,129	28,391	31,629	970	3,297	35,896
Malta	11,738	212	649	12,598	8,979	428	957	10,364
Netherlands	535,395	6,185	66,109	607,688	559,869	12,477	92,360	664,706
Poland	740,023	6,310	71,832	818,166	262,780	12,708	93,061	368,550
Portugal	166,979	2,783	11,394	181,156	72,484	5,648	16,326	94,458
Romania	274,645	3,288	17,952	295,885	68,060	6,624	23,292	97,976
Slovakia	91,034	1,079	9,014	101,127	32,611	2,162	11,764	46,537
Slovenia	57,082	1,021	4,666	62,770	34,122	2,059	6,723	42,904
Spain	1,206,873	40,597	88,009	1,335,479	893,759	82,596	132,832	1,109,188
Sweden	459,103	4,693	45,402	509,197	464,778	9,459	65,177	539,414
Total EU-27	13,471,246	273,737	1,430,287	15,175,269	12,130,736	555,769	1,964,786	14,651,292
United Kingdom	2,231,166	43,068	257,806	2,532,040	2,040,810	87,105	362,068	2,489,983
Total EU-28	15,686,241	316,626	1,702,686	17,705,553	14,183,617	642,818	2,336,102	17,162,537
Iceland	10,766	100	1,216	12,083	12,579	202	1,740	14,521
Israel	102,435	3,721	13,163	119,319	47,486	7,533	18,555	73,574
Norway	268,154	2,673	20,561	291,388	355,558	5,405	30,829	391,792
Switzerland	308,853	6,186	35,492	350,530	404,017	12,519	51,103	467,639
Total 32 countries	16,262,307	329,199	1,784,659	18,376,165	14,794,723	668,535	2,445,367	17,908,625

Overall, routine use of dabigatran was cost-effective in all the 32 European countries under studies when using a €22,727 per QALY gained threshold (**Table S8**), but for Bulgaria, Croatia, Hungary, Latvia, Lithuania, Poland, Romania and Slovakia, the incremental cost-effectiveness ratio (ICER) was estimated to be higher than the country-specific GDP per capita.

Table S8. Incremental cost per QALY gained from a health & social care and societal perspectives

Country	Health and social care	Cost-effective at € €22,727 per additional QALY?	Society	Cost-effective at € €22,727 per additional QALY?	Cost-effective compared to GDP per capita?
Austria	€ 6,240	yes	€ 3	yes	yes

Belgium	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Bulgaria	€ 19,984	yes	€ 19,392	yes	no
Croatia	€ 19,635	yes	€ 18,405	yes	no
Cyprus	€ 18,575	yes	€ 16,617	yes	yes
Czech Republic	€ 16,027	yes	€ 14,633	yes	yes
Denmark	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Estonia	€ 14,829	yes	€ 13,508	yes	yes
Finland	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
France	€ 6,345	yes	€ 3,919	yes	yes
Germany	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Greece	€ 9,161	yes	€ 7,641	yes	yes
Hungary	€ 15,589	yes	€ 14,684	yes	no
Ireland	€ 6,550	yes	€ 2,642	yes	yes
Italy	€ 4,798	yes	€ 2,597	yes	yes
Latvia	€ 19,573	yes	€ 18,464	yes	no
Lithuania	€ 16,955	yes	€ 15,984	yes	no
Luxembourg	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Malta	€ 9,048	yes	€ 7,457	yes	yes
The Netherlands	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Poland	€ 18,067	yes	€ 17,052	yes	no
Portugal	€ 15,450	yes	€ 14,237	yes	yes
Romania	€ 18,225	yes	€ 17,473	yes	no
Slovakia	€ 19,201	yes	€ 17,973	yes	no
Slovenia	€ 14,358	yes	€ 12,499	yes	yes
Spain	€ 8,762	yes	€ 6,417	yes	yes
Sweden	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Total EU-27	€ 4,767	yes	€ 1,932	yes	yes
United Kingdom	€ 3,428	yes	€ 802	yes	yes
Total EU-28	€ 4,649	yes	€ 1,745	yes	yes
Iceland	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Israel	€ 16,186	yes	€ 13,555	yes	yes
Norway	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Switzerland	Dabigatran dominates	yes	Dabigatran dominates	yes	yes
Total 32 countries	€ 4,500	yes	€ 1,493	yes	yes

Edoxaban

Routinely treating AF patients with edoxaban would generate average QALYs over 5 years of 2.23 per patient treated compared with 2.19 QALYs under current practice, resulting in a QALY gain of 0.04 per AF patient. At the population level, the total QALYs across the 32 European countries were 16 million and 15 million with current practice, an increase of 0.3 million QALYs (**Table S9**). For all countries, routine use of edoxaban generated additional QALYs relative to current practice.

Table S9. QALYs gained at the population level

	Routine use of edoxaban	Current practice	Difference
Austria	324,147	317,547	6,600
Belgium	306,134	299,159	6,975
Bulgaria	199,698	195,557	4,141
Croatia	100,269	98,250	2,019
Cyprus	23,198	22,726	472
Czech Republic	317,103	311,210	5,893
Denmark	169,866	166,375	3,491
Estonia	37,536	36,733	802
Finland	198,802	194,715	4,087
France	1,828,385	1,787,222	41,162
Germany	2,652,640	2,591,201	61,439
Greece	303,501	296,145	7,356
Hungary	281,061	274,937	6,123
Ireland	97,996	96,106	1,889
Italy	1,867,060	1,823,832	43,227
Latvia	59,576	58,335	1,242
Lithuania	82,580	80,761	1,819
Luxembourg	17,230	16,867	363
Malta	12,710	12,453	257
Netherlands	451,332	442,127	9,204
Poland	1,142,343	1,119,657	22,685
Portugal	226,701	221,484	5,217
Romania	441,867	432,131	9,736
Slovakia	143,772	141,157	2,616
Slovenia	72,608	71,241	1,366
Spain	1,302,133	1,271,932	30,201
Sweden	395,195	387,020	8,176
Total EU-27	12,985,483	12,762,893	222,590
United Kingdom	2,118,225	2,073,206	45,019
Total EU-28	15,090,966	14,835,975	254,991
Iceland	7,852	7,698	154
Israel	141,681	138,784	2,897
Norway	152,364	148,869	3,495
Switzerland	183,676	179,852	3,824
Total 32 countries	15,566,134	15,311,120	255,015

On average, across the 32 countries under study, the average therapy cost, per patient treated with edoxaban was €1,310 compared with €64.90 for current practice. At the

population level, this translated to costs of €9 billion as opposed to €453 million with current practice (**Table S10**). Over a 5-year period, routinely treating eligible AF-patients with edoxaban would generate additional costs of €2 billion. In six countries, routine treatment with edoxaban would generate health and social care cost savings: Germany €514 million, Switzerland €64 million, Norway €60 million, Finland €13 million Luxembourg €3 million and Iceland €1 million.

When productivity losses were included (**Table S11**), overall societal costs were €20 billion compared with €18 billion for current practice, generating additional societal costs of €2 billion across Europe. In six of the 32 countries under study, edoxaban generated societal cost savings relative to current practice: Germany (€732 million), Switzerland (€83 million), Norway (€71 million), Finland (€24 million), Belgium (€20 million), Denmark (€9 million), the Netherlands (€8 million), Luxembourg (€5 million) and Iceland (€1 million).

Overall, routine use of edoxaban showed to be cost-effective in the majority of the countries and in Europe as a whole, compared to current practice (**Table S12**). For Croatia, Cyprus, Czech Republic, Hungary, Latvia, Lithuania, Poland, Romania and Slovakia the decision on whether the intervention is good value for money was dependent on which cost-effectiveness threshold was applied. Only for Bulgaria was the ICER higher than any of the cost-effectiveness thresholds.

Table S10. Population-level health and social care costs for patients routinely receiving edoxaban and current practice, € thousands

	Routine use of edoxaban							Current practice						
	Drug	Bleeding	Subsequent costs				TOTAL costs	Drug	Bleeding	Subsequent costs				TOTAL costs
			Inpatient	Outpatient	A&E	Social care				Inpatient	Outpatient	A&E	Social care	
Austria	189,262	9,792	142,444	2,323	886	751	345,457	9,424	9,396	247,703	4,025	1,539	1,306	273,394
Belgium	180,093	11,131	169,643	1,027	218	55,306	417,418	8,839	10,650	295,782	1,791	382	97,780	415,224
Bulgaria	112,664	234	8,344	165	26	695	122,128	5,670	225	14,484	286	46	1,220	21,930
Croatia	56,191	327	5,630	97	140	941	63,326	2,841	314	9,775	169	243	1,653	14,995
Cyprus	13,024	79	864	141	58	1,036	15,201	656	76	1,498	244	101	1,820	4,393
Czech Republic	176,219	4,020	56,599	1,072	62	4,101	242,073	8,984	3,866	97,984	1,851	107	7,183	119,975
Denmark	98,742	3,819	77,226	500	190	39,514	219,990	4,902	3,663	134,174	866	330	69,486	213,422
Estonia	21,303	374	5,210	201	41	1,303	28,432	1,072	359	9,050	348	72	2,293	13,193
Finland	116,557	7,918	114,348	3,561	725	47,592	290,699	5,762	7,592	198,864	6,185	1,261	83,861	303,525
France	1,108,000	35,204	616,970	12,667	2,885	184,205	1,959,931	53,766	33,674	1,077,758	22,128	5,038	326,167	1,518,530
Germany	1,573,301	104,041	2,233,414	35,583	774	428,818	4,375,932	76,800	99,565	3,889,376	61,962	1,350	756,746	4,885,798
Greece	183,755	3,827	93,411	306	488	10,185	291,972	8,857	3,657	163,073	534	851	18,012	194,984
Hungary	157,356	1,548	29,376	374	96	10,184	198,934	7,924	1,484	50,895	645	166	17,865	78,980
Ireland	55,402	2,629	30,413	557	526	10,652	100,178	2,789	2,525	52,841	966	914	18,758	78,793
Italy	1,136,304	50,219	719,617	12,784	8,497	182,609	2,110,030	54,902	48,036	1,253,872	22,268	14,819	322,726	1,716,623
Latvia	33,578	148	2,555	102	15	572	36,971	1,700	142	4,436	176	26	1,006	7,487
Lithuania	46,651	283	6,070	174	15	2,091	55,283	2,348	272	10,553	301	26	3,681	17,181
Luxembourg	10,061	818	12,263	162	15	4,905	28,225	499	784	21,375	282	26	8,664	31,629
Malta	7,440	286	3,739	25	14	1,005	12,509	368	275	6,499	43	25	1,769	8,979
Netherlands	260,441	14,292	201,581	5,619	361	97,844	580,139	12,958	13,711	350,443	9,758	629	172,369	559,869
Poland	637,071	5,441	89,296	4,763	194	34,916	771,682	32,322	5,224	155,180	8,257	338	61,460	262,780
Portugal	135,827	2,422	31,720	1,007	917	2,782	174,675	6,607	2,316	55,285	1,756	1,599	4,920	72,484
Romania	252,329	1,001	22,110	687	51	8,419	284,596	12,587	959	38,419	1,192	89	14,814	68,060
Slovakia	78,222	652	11,443	904	55	3,680	94,956	4,041	628	19,835	1,560	95	6,453	32,611
Slovenia	41,589	873	12,725	171	55	4,926	60,338	2,092	838	22,126	296	95	8,674	34,122
Spain	785,995	24,049	380,116	12,050	7,936	75,521	1,285,667	38,155	22,992	663,896	21,058	13,871	133,787	893,759
Sweden	233,385	9,314	144,178	8,055	2,058	100,079	497,069	11,487	8,932	250,613	13,967	3,577	176,202	464,778
Total EU-27	7,646,538	290,233	4,959,374	131,774	25,096	1,428,306	14,481,321	378,195	279,120	8,671,383	230,051	43,890	2,528,095	12,130,736
United Kingdom	1,235,414	63,842	803,341	14,592	5,057	275,708	2,397,953	61,111	61,184	1,397,868	25,373	8,819	486,455	2,040,810
Total EU-28	8,872,176	341,158	5,755,383	157,752	30,074	1,708,928	16,865,471	439,302	328,168	10,063,412	275,392	52,600	3,024,743	14,183,617
Iceland	4,488	394	4,687	123	28	2,012	11,733	225	378	8,160	214	49	3,553	12,579
Israel	81,524	1,964	17,301	378	696	5,427	107,290	4,062	1,884	30,098	652	1,209	9,581	47,486
Norway	92,113	6,563	121,065	1,043	271	74,613	295,668	4,458	6,278	210,836	1,812	473	131,701	355,558
Switzerland	107,883	9,046	154,727	317	208	67,698	339,878	5,322	8,672	269,598	553	363	119,509	404,017
Total 32 countries	9,150,104	359,993	5,943,866	153,911	31,324	1,849,844	17,489,041	453,367	346,438	10,396,422	268,728	54,796	3,274,972	14,794,723

Table S11. Societal costs under routine use of edoxaban vs current practice, € thousands

	Routine use of edoxaban				Current practice			
	Health & social care	Informal care	Productivity losses	TOTAL costs	Health & social care	Informal care	Productivity losses	TOTAL costs
Austria	345,457	11,364	40,637	397,458	273,394	19,898	55,442	348,734
Belgium	417,418	8,410	41,109	466,937	415,224	14,779	57,222	487,225
Bulgaria	122,128	1,109	7,341	130,577	21,930	1,935	8,996	32,861
Croatia	63,326	1,209	5,212	69,747	14,995	2,113	6,830	23,939
Cyprus	15,201	449	1,784	17,434	4,393	784	2,386	7,564
Czech Republic	242,073	4,858	19,975	266,905	119,975	8,461	25,118	153,554
Denmark	219,990	6,503	34,430	260,923	213,422	11,368	45,163	269,953
Estonia	28,432	438	3,213	32,083	13,193	766	3,997	17,955
Finland	290,699	2,333	26,496	319,529	303,525	4,084	35,672	343,282
France	1,959,931	44,382	179,050	2,183,364	1,518,530	78,111	250,350	1,846,992
Germany	4,375,932	91,327	466,701	4,933,961	4,885,798	160,187	620,448	5,666,433
Greece	291,972	7,008	15,730	314,710	194,984	12,325	22,151	229,461
Hungary	198,934	2,162	19,124	220,220	78,980	3,770	23,268	106,019
Ireland	100,178	3,484	14,651	118,313	78,793	6,099	19,793	104,685
Italy	2,110,030	62,053	133,220	2,305,303	1,716,623	109,013	188,753	2,014,390
Latvia	36,971	580	4,415	41,966	7,487	1,013	5,378	13,879
Lithuania	55,283	727	5,779	61,789	17,181	1,272	7,040	25,493
Luxembourg	28,225	553	2,291	31,068	31,629	970	3,297	35,896
Malta	12,509	245	691	13,444	8,979	428	957	10,364
Netherlands	580,139	7,126	69,633	656,899	559,869	12,477	92,360	664,706
Poland	771,682	7,266	74,728	853,676	262,780	12,708	93,061	368,550
Portugal	174,675	3,213	12,071	189,959	72,484	5,648	16,326	94,458
Romania	284,596	3,787	18,686	307,070	68,060	6,624	23,292	97,976
Slovakia	94,956	1,240	9,388	105,584	32,611	2,162	11,764	46,537
Slovenia	60,338	1,176	4,950	66,464	34,122	2,059	6,723	42,904
Spain	1,285,667	46,907	94,194	1,426,768	893,759	82,596	132,832	1,109,188
Sweden	497,069	5,405	48,048	550,522	464,778	9,459	65,177	539,414
Total EU-27	14,481,321	315,761	1,507,342	16,304,424	12,130,736	555,769	1,964,786	14,651,292
United Kingdom	2,397,953	49,664	271,898	2,719,516	2,040,810	87,105	362,068	2,489,983
Total EU-28	16,865,471	365,218	1,793,987	19,024,675	14,183,617	642,818	2,336,102	17,162,537
Iceland	11,733	115	1,286	13,134	12,579	202	1,740	14,521
Israel	107,290	4,292	13,886	125,468	47,486	7,533	18,555	73,574
Norway	295,668	3,083	21,968	320,719	355,558	5,405	30,829	391,792
Switzerland	339,878	7,134	37,595	384,607	404,017	12,519	51,103	467,639
Total 32 countries	17,489,041	379,717	1,880,322	19,749,081	14,794,723	668,535	2,445,367	17,908,625

Table S12. Incremental cost per QALY gained from a health & social care and societal perspectives

Country	Health and social care	Cost-effective at € €22,727 per additional QALY?	Society	Cost-effective at € €22,727 per additional QALY?	Cost-effective compared to GDP per capita?
Austria	€ 10,858	yes	€ 7	yes	yes
Belgium	€ 246	yes	Edoxaban dominates	yes	yes
Bulgaria	€ 24,195	no	€ 23,598	no	no
Croatia	€ 23,937	no	€ 22,694	yes	no
Cyprus	€ 22,885	no	€ 20,906	yes	yes
Czech Republic	€ 20,693	yes	€ 19,235	yes	no
Denmark	€ 1,837	yes	Edoxaban dominates	yes	yes
Estonia	€ 18,979	yes	€ 17,612	yes	yes
Finland	Edoxaban dominates	yes	Edoxaban dominates	yes	yes
France	€ 10,686	yes	€ 8,172	yes	yes
Germany	Edoxaban dominates	yes	Edoxaban dominates	yes	yes
Greece	€ 13,162	yes	€ 11,590	yes	yes
Hungary	€ 19,579	yes	€ 18,650	yes	no
Ireland	€ 11,265	yes	€ 7,213	yes	yes
Italy	€ 9,050	yes	€ 6,730	yes	yes
Latvia	€ 23,742	no	€ 22,622	yes	no
Lithuania	€ 20,945	yes	€ 19,958	yes	no
Luxembourg	Edoxaban dominates	yes	Edoxaban dominates	yes	yes
Malta	€ 13,692	yes	€ 11,987	yes	yes
The Netherlands	€ 2,139	yes	Edoxaban dominates	yes	yes

Poland	€ 22,423	yes	€ 21,385	yes	no
Portugal	€ 19,569	yes	€ 18,306	yes	yes
Romania	€ 22,237	yes	€ 21,476	yes	no
Slovakia	€ 23,825	no	€ 22,574	yes	no
Slovenia	€ 19,164	yes	€ 17,245	yes	yes
Spain	€ 12,942	yes	€ 10,516	yes	yes
Sweden	€ 3,903	yes	€ 1,359	yes	yes
Total EU-27	€ 10,510	yes	€ 7,427	yes	yes
United Kingdom	€ 7,874	yes	€ 5,099	yes	yes
Total EU-28	€ 10,467	yes	€ 7,303	yes	yes
Iceland	Edoxaban dominates	yes	Edoxaban dominates	yes	yes
Israel	€ 20,614	yes	€ 17,911	yes	yes
Norway	Edoxaban dominates	yes	Edoxaban dominates	yes	yes
Switzerland	Edoxaban dominates	yes	Edoxaban dominates	yes	yes
Total 32 countries	€ 10,512	yes	€ 7,217	yes	yes

Rivaroxaban

Routinely treating AF patients with rivaroxaban would generate average QALYs over 5 years of 2.4 per patient treated compared with 2.19 QALYs under current practice, resulting in a QALY gain of 0.05 per AF patient. The total QALYs gained across the 32 European countries were 16 million with routine use of rivaroxaban and 15 million with current practice, an increase of 0.4 million QALYs (**Table S13**). For all countries, routine use of rivaroxaban generated additional QALYs relative to current practice.

Table S13. QALYs gained at the population level

	Routine use of rivaroxaban	Current practice	Difference
Austria	326,217	317,547	8,670
Belgium	308,384	299,159	9,224
Bulgaria	201,097	195,557	5,540
Croatia	100,943	98,250	2,693
Cyprus	23,360	22,726	634
Czech Republic	319,048	311,210	7,838
Denmark	170,987	166,375	4,612
Estonia	37,798	36,733	1,065
Finland	200,103	194,715	5,388
France	1,840,992	1,787,222	53,770
Germany	2,672,628	2,591,201	81,427
Greece	305,882	296,145	9,737
Hungary	283,160	274,937	8,223
Ireland	98,614	96,106	2,508
Italy	1,880,686	1,823,832	56,854
Latvia	59,980	58,335	1,645
Lithuania	83,186	80,761	2,425
Luxembourg	17,343	16,867	476
Malta	12,793	12,453	340
Netherlands	454,320	442,127	12,193
Poland	1,149,858	1,119,657	30,201
Portugal	228,374	221,484	6,890
Romania	445,120	432,131	12,988
Slovakia	144,642	141,157	3,486
Slovenia	73,038	71,241	1,797
Spain	1,311,544	1,271,932	39,612
Sweden	397,789	387,020	10,769

Total EU-27	13,081,128	12,762,893	318,235
United Kingdom	2,132,627	2,073,206	59,421
Total EU-28	15,201,574	14,835,975	365,599
Iceland	7,902	7,698	204
Israel	142,612	138,784	3,828
Norway	153,484	148,869	4,616
Switzerland	184,885	179,852	5,033
Total 32 countries	15,680,499	15,311,120	369,379

Across the 32 countries under study, the average cost of therapy per patient treated with rivaroxaban was €1,359, compared with €64.90 for current practice. At the population level, this translated to costs of €10 billion as opposed to €453 million with current practice (**Table S14**). Over a 5-year period, routinely treating with rivaroxaban would generate additional health and social care costs of €3 billion across Europe. In seven of the 32 countries under study, the intervention would generate health and social care cost savings: Germany €558 million, Switzerland €69 million, Norway €64 million, Finland €15 million, Luxembourg €4 million, Iceland €1 million and Belgium at €0.2 million.

When productivity losses were included, overall societal costs were €20 billion with routine use of rivaroxaban compared with €18 billion for current practice (**Table S15**). In nine countries under study, the intervention would generate cost savings relative to current practice: Germany (€775 million), Switzerland (€88 million), Norway (€75 million), Finland (€25 million), Belgium (€22 million), Denmark (€11 million), the Netherlands (€10 million), Luxembourg (€5 million) and Iceland (€2 million).

Routine use of rivaroxaban was shown to be cost-effective in all the 32 countries under study, both under a health and social care and a societal perspective (**Table S16**). For eight countries (Bulgaria, Croatia, Hungary, Latvia, Lithuania, Poland, Romania and Slovakia), the ICER was estimated to be higher than the country-specific GDP per capita, but consistently below the €22,727 willingness-to-pay threshold.

Table S14. Population-level health and social care costs for patients routinely receiving rivaroxaban and current practice, € thousands

	Routine use of rivaroxaban							Current practice						
	Drug	Bleeding	Subsequent costs				TOTAL costs	Drug	Bleeding	Subsequent costs				TOTAL costs
			Inpatient	Outpatient	A&E	Social care				Inpatient	Outpatient	A&E	Social care	
Austria	196,115	11,679	137,030	2,235	852	722	348,633	9,424	9,396	247,703	4,025	1,539	1,306	273,394
Belgium	186,859	13,329	163,221	987	210	53,064	417,670	8,839	10,650	295,782	1,791	382	97,780	415,224
Bulgaria	116,844	279	8,029	159	25	667	126,003	5,670	225	14,484	286	46	1,220	21,930
Croatia	58,254	389	5,418	93	135	903	65,191	2,841	314	9,775	169	243	1,653	14,995
Cyprus	13,507	94	831	135	56	994	15,617	656	76	1,498	244	101	1,820	4,393
Czech Republic	182,542	4,770	54,475	1,032	59	3,938	246,817	8,984	3,866	97,984	1,851	107	7,183	119,975
Denmark	102,350	4,557	74,300	481	183	37,929	219,799	4,902	3,663	134,174	866	330	69,486	213,422
Estonia	22,093	445	5,015	193	40	1,251	29,036	1,072	359	9,050	348	72	2,293	13,193
Finland	120,806	9,459	110,014	3,424	697	45,670	290,070	5,762	7,592	198,864	6,185	1,261	83,861	303,525
France	1,148,923	42,246	593,285	12,175	2,775	176,669	1,976,073	53,766	33,674	1,077,758	22,128	5,038	326,167	1,518,530
Germany	1,632,853	124,569	2,149,131	34,224	745	411,544	4,353,065	76,800	99,565	3,889,376	61,962	1,350	756,746	4,885,798
Greece	190,790	4,597	89,867	294	469	9,773	295,790	8,857	3,657	163,073	534	851	18,012	194,984
Hungary	163,297	1,842	28,286	360	92	9,782	203,659	7,924	1,484	50,895	645	166	17,865	78,980
Ireland	57,404	3,130	29,263	535	506	10,222	101,060	2,789	2,525	52,841	966	914	18,758	78,793
Italy	1,178,924	60,256	692,431	12,296	8,175	175,206	2,127,288	54,902	48,036	1,253,872	22,268	14,819	322,726	1,716,623
Latvia	34,812	176	2,459	98	15	550	38,109	1,700	142	4,436	176	26	1,006	7,487
Lithuania	48,403	337	5,841	167	14	2,007	56,770	2,348	272	10,553	301	26	3,681	17,181
Luxembourg	10,428	978	11,795	155	14	4,706	28,077	499	784	21,375	282	26	8,664	31,629
Malta	7,711	342	3,598	24	14	964	12,653	368	275	6,499	43	25	1,769	8,979
Netherlands	269,966	17,053	193,959	5,405	348	93,897	580,628	12,958	13,711	350,443	9,758	629	172,369	559,869
Poland	660,320	6,469	85,916	4,582	187	33,511	790,984	32,322	5,224	155,180	8,257	338	61,460	262,780
Portugal	140,936	2,903	30,523	968	882	2,670	178,883	6,607	2,316	55,285	1,756	1,599	4,920	72,484
Romania	261,816	1,194	21,278	661	49	8,083	293,081	12,587	959	38,419	1,192	89	14,814	68,060
Slovakia	81,018	772	11,010	870	53	3,533	97,257	4,041	628	19,835	1,560	95	6,453	32,611
Slovenia	43,069	1,039	12,238	164	52	4,727	61,290	2,092	838	22,126	296	95	8,674	34,122
Spain	815,378	28,865	365,614	11,582	7,633	72,435	1,301,507	38,155	22,992	663,896	21,058	13,871	133,787	893,759
Sweden	241,903	11,133	138,720	7,749	1,980	96,047	497,533	11,487	8,932	250,613	13,967	3,577	176,202	464,778
Total EU-27	7,934,073	347,352	4,772,268	126,750	24,151	1,370,678	14,575,273	378,195	279,120	8,671,383	230,051	43,890	2,528,095	12,130,736
United Kingdom	1,280,893	76,295	772,975	14,033	4,864	264,547	2,413,606	61,111	61,184	1,397,868	25,373	8,819	486,455	2,040,810
Total EU-28	9,205,356	408,233	5,538,232	151,739	28,941	1,639,977	16,972,478	439,302	328,168	10,063,412	275,392	52,600	3,024,743	14,183,617
Iceland	4,651	470	4,509	119	27	1,930	11,706	225	378	8,160	214	49	3,553	12,579
Israel	84,498	2,345	16,649	364	670	5,206	109,732	4,062	1,884	30,098	652	1,209	9,581	47,486
Norway	95,576	7,873	116,492	1,003	261	71,603	292,809	4,458	6,278	210,836	1,812	473	131,701	355,558
Switzerland	111,822	10,814	148,820	305	200	64,949	336,910	5,322	8,672	269,598	553	363	119,509	404,017
Total 32 countries	9,493,952	430,780	5,719,772	148,051	30,145	1,775,228	17,597,929	453,367	346,438	10,396,422	268,728	54,796	3,274,972	14,794,723

Table S15. Societal costs under routine use of rivaroxaban vs current practice, € thousands

	Routine use of rivaroxaban				Current practice			
	Health & social care	Informal care	Productivity losses	TOTAL costs	Health & social care	Informal care	Productivity losses	TOTAL costs
Austria	348,633	10,917	39,233	398,784	273,388	19,883	55,428	348,699
Belgium	417,670	8,079	39,693	465,442	415,224	14,779	57,222	487,225
Bulgaria	126,003	1,066	7,078	134,147	21,930	1,935	8,996	32,861
Croatia	65,191	1,162	5,026	71,380	14,995	2,113	6,830	23,939
Cyprus	15,617	431	1,726	17,775	4,393	784	2,386	7,564
Czech Republic	246,817	4,670	19,270	270,757	119,975	8,461	25,118	153,554
Denmark	219,799	6,249	33,235	259,283	213,422	11,368	45,163	269,953
Estonia	29,036	421	3,098	32,554	13,193	766	3,997	17,955
Finland	290,070	2,242	25,566	317,877	303,525	4,084	35,672	343,282
France	1,976,073	42,617	172,682	2,191,372	1,518,530	78,111	250,350	1,846,992
Germany	4,353,065	87,759	450,651	4,891,475	4,885,798	160,187	620,448	5,666,433
Greece	295,790	6,733	15,189	317,712	194,984	12,325	22,151	229,461
Hungary	203,659	2,080	18,445	224,184	78,980	3,770	23,268	106,019
Ireland	101,060	3,347	14,158	118,565	78,793	6,099	19,793	104,685
Italy	2,127,288	59,609	128,757	2,315,653	1,716,623	109,013	188,753	2,014,390
Latvia	38,109	557	4,254	42,920	7,487	1,013	5,378	13,879
Lithuania	56,770	699	5,571	63,039	17,181	1,272	7,040	25,493
Luxembourg	28,077	531	2,213	30,820	31,629	970	3,297	35,896
Malta	12,653	235	667	13,555	8,979	428	957	10,364
Netherlands	580,628	6,847	67,269	654,744	559,869	12,477	92,360	664,706
Poland	790,984	6,982	72,018	869,985	262,780	12,708	93,061	368,550
Portugal	178,883	3,086	11,654	193,624	72,484	5,648	16,326	94,458
Romania	293,081	3,640	18,013	314,734	68,060	6,624	23,292	97,976
Slovakia	97,257	1,192	9,051	107,500	32,611	2,162	11,764	46,537
Slovenia	61,290	1,130	4,774	67,194	34,122	2,059	6,723	42,904
Spain	1,301,507	45,044	90,958	1,437,509	893,759	82,596	132,832	1,109,188
Sweden	497,533	5,194	46,447	549,174	464,778	9,459	65,177	539,414
Total EU-27	14,575,273	303,397	1,454,664	16,333,335	12,130,736	555,769	1,964,786	14,651,292
United Kingdom	2,413,606	47,710	262,595	2,723,912	2,040,810	87,105	362,068	2,489,983
Total EU-28	16,972,478	350,917	1,731,470	19,054,865	14,183,617	642,818	2,336,102	17,162,537
Iceland	11,706	111	1,244	13,060	12,579	202	1,740	14,521
Israel	109,732	4,123	13,413	127,268	47,486	7,533	18,555	73,574
Norway	292,809	2,962	21,221	316,991	355,558	5,405	30,829	391,792
Switzerland	336,910	6,853	36,333	380,096	404,017	12,519	51,103	467,639
Total 32 countries	17,597,929	364,852	1,814,876	19,777,658	14,794,723	668,535	2,445,367	17,908,625

Table S16. Incremental cost per QALY gained from a health & social care and societal perspectives

Country	Health and social care	Cost-effective at € €22,727 per additional QALY?	Society	Cost-effective at € €22,727 per additional QALY?	Cost-effective compared to GDP per capita?
Austria	€ 8,415	yes	€ 6	yes	yes
Belgium	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
Bulgaria	€ 18,776	yes	€ 18,282	yes	no
Croatia	€ 18,613	yes	€ 17,617	yes	no
Cyprus	€ 17,676	yes	€ 16,107	yes	yes
Czech Republic	€ 16,068	yes	€ 14,954	yes	yes
Denmark	€ 1,189	yes	Rivaroxaban dominates	yes	yes
Estonia	€ 14,801	yes	€ 13,713	yes	yes
Finland	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
France	€ 8,350	yes	€ 6,405	yes	yes
Germany	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
Greece	€ 10,257	yes	€ 9,064	yes	yes
Hungary	€ 15,119	yes	€ 14,370	yes	no
Ireland	€ 8,638	yes	€ 5,535	yes	yes
Italy	€ 7,008	yes	€ 5,299	yes	yes
Latvia	€ 18,591	yes	€ 17,651	yes	no
Lithuania	€ 16,298	yes	€ 15,483	yes	no
Luxembourg	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
Malta	€ 10,597	yes	€ 9,377	yes	yes
the Netherlands	€ 1,428	yes	Rivaroxaban dominates	yes	yes
Poland	€ 17,448	yes	€ 16,603	yes	no
Portugal	€ 15,358	yes	€ 14,393	yes	yes
Romania	€ 17,307	yes	€ 16,689	yes	no

Slovakia	€ 18,504	yes	€ 17,489	yes	no
Slovenia	€ 15,010	yes	€ 13,520	yes	yes
Spain	€ 10,145	yes	€ 8,288	yes	yes
Sweden	€ 2,837	yes	€ 906	yes	yes
Total EU-27	€ 7,467	yes	€ 5,286	yes	yes
United Kingdom	€ 6,019	yes	€ 3,937	yes	yes
Total EU-28	€ 7,409	yes	€ 5,176	yes	yes
Iceland	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
Israel	€ 16,141	yes	€ 14,027	yes	yes
Norway	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
Switzerland	Rivaroxaban dominates	yes	Rivaroxaban dominates	yes	yes
Total 32 countries	€ 7,361	yes	€ 5,060	yes	yes