Ferric carboxymaltose for the treatment of iron deficiency in heart failure: a multinational cost-effectiveness analysis utilising AFFIRM-AHF

Authors: Phil McEwan, Jason A. Davis, Piotr Ponikowski, Giuseppe Rosano, Andrew J. Stewart Coats, Fabio Dorigotti, Donal O'Sullivan, Antonio Ramirez de Arellano, Ewa A. Jankowska

Supplementary Material

Deterministic sensitivity analysis

Results of the deterministic sensitivity analysis (DSA) are presented in Table S1. In this analysis, individual parameters are varied to assess the effect on model outcomes imposed by base case assumptions. Parameters assessed for impact included the time horizon of the model, discounting rates, variations in costs and utilities, adverse events, and different implementations of mortality. Most analyses resulted in dominant incremental cost-effectiveness ratios (ICERs) indicating that the scenario resulted in reduced costs and increases in quality-adjusted life years (QALYs) gained.

Table S1. Deterministic sensitivity results

Country	UK	USA	Switzerland	Italy
Time horizon				
Lifetime (base case)	Dominant	Dominant	Dominant	EUR 1,269
1 year	Dominant	Dominant	Dominant	Dominant
10 years	Dominant	Dominant	Dominant	EUR 111
Discounting				
Costs (0.00%)	GBP 14	Dominant	Dominant	EUR 2,199
Costs (6.00%)	Dominant	Dominant	Dominant	EUR 612
Benefits (0.00%)	Dominant	Dominant	Dominant	EUR 1,064
Benefits (6.00%)	Dominant	Dominant	Dominant	EUR 1,484
Costs				
Health state (50% of mean)	Dominant	Dominant	Dominant	Dominant
Health state (150% of mean)	GBP 174	Dominant	Dominant	EUR 3,175
Adverse event (50% of mean)	Dominant	Dominant	Dominant	EUR 1,121
Adverse event (150% of mean)	Dominant	Dominant	Dominant	EUR 1,416
Intervention (50% of mean)	Dominant	Dominant	Dominant	EUR 1,038
Intervention (150% of mean)	Dominant	Dominant	Dominant	EUR 1,499
Adverse events and utilities				
Health state utility (50% of mean)	Dominant	Dominant	Dominant	EUR 2,457
Health state utility (150% of mean)	Dominant	Dominant	Dominant	EUR 855
Event disutility (50% of mean)	Dominant	Dominant	Dominant	EUR 1,289
Event disutility (150% of mean)	Dominant	Dominant	Dominant	EUR 1,249
Adverse event disutility (50% of mean)	Dominant	Dominant	Dominant	EUR 1,269
Adverse event disutility (150% of mean)	Dominant	Dominant	Dominant	EUR 1,268
Adverse events (excluded)	Dominant	Dominant	Dominant	EUR 973
Adverse events (included)	Dominant	Dominant	Dominant	EUR 1,269
Distribution and mortality				
Weibull (base case)	Dominant	Dominant	Dominant	EUR 1,269
Gompertz	Dominant	Dominant	Dominant	Dominant
Log-logistic	Dominant	Dominant	Dominant	Dominant
Lognormal	Dominant	Dominant	Dominant	Dominant
Exclude life tables from analysis	Dominant	Dominant	Dominant	EUR 1,395

Deterministic sensitivity analysis results. Shown are the resulting incremental cost effectiveness ratios (ICERs) for each country according to the scenario indicated. Those that are dominant indicate a decrease in incremental costs accompanied by an increase in incremental quality adjusted life years (QALYs). EUR, Euros; GBP, Great Britain Pounds Sterling.

Modelling mortality

To estimate events beyond the trial follow-up period of 52 weeks, parametric survival equations using different distributions were fitted to patient data from the AFFIRM-AHF trial. All-cause and cardiovascular- (CV-) specific mortality were modelled as time to event. Covariables for adjustment in the survival modelling were chosen based on clinical specification of patient characteristics that were expected to affect outcomes, and the same set of parameters were used in modelling of repeat events (see section “Modelling repeat events”).

Model coefficients are listed in Table S2. Weibull distributions were used in base case analysis as they result in the most plausible estimates of long-term survival when compared with previously published estimates. Deterministic sensitivity analysis results (see main text) showed the base case results were robust to the choice of model, resulting in demonstration of dominance or cost-effectiveness across all model choices investigate. In addition to the Weibull distribution in the base case, parameterisations were also performed for Gompertz, Lognormal and Log-logistic distributions.

Table S2. Parameterisations for the adjusted mortality equations

Distribution	All-cause mortality				Cardiovascular mortality		
	Parameter	Coefficient	SE	p-value	Coefficient	SE	p-value
Weibull	shape	1.098	0.092	--	1.136	0.084	--
	scale	1293.758	398.825	--	907.779	229.220	--
	FCM	0.1271	0.1702	0.2276	0.0669	0.1447	0.3219
	Female	0.1532	0.1915	0.2119	0.2282	0.1645	0.0827
	anaemic	-0.0762	0.1844	0.3396	0.0946	0.1539	0.2694
	De novo HF	0.1414	0.2401	0.2780	-0.0442	0.1918	0.4088
	Ischaemic HF	-0.4127	0.1868	0.0136	-0.3430	0.1576	0.0148
	LVEF (centred)	0.0204	0.0094	0.0150	0.0182	0.0081	0.0119
	Quartile2	0.2867	0.2524	0.1280	0.2442	0.2180	0.1314
	Quartile3	0.6766	0.2451	0.0029	0.6173	0.2121	0.0018
	Quartile4	1.4138	0.2487	< 0.0000	1.3537	0.2142	< 0.0000
	eGFR (centred)	0.0095	0.0047	0.0223	0.0092	0.0040	0.0110
	Age (centred)	-0.0128	0.0100	0.1001	-0.0135	0.0085	0.0565

Distribution	All-cause mortality				Cardiovascular mortality		
Gompertz	shape	-3.89E-05	8.48E-04	--	4.88E-04	6.43E-04	--
	rate	6.76E-04	2.27E-04	--	8.61E-04	2.55E-04	--
	FCM	-0.1447	0.1867	0.2192	-0.0769	0.1643	0.3198
	Female	-0.1702	0.2098	0.2086	-0.2583	0.1860	0.0824
	anaemic	0.0812	0.2021	0.3440	-0.1023	0.1748	0.2793
	De novo HF	-0.1660	0.2630	0.2639	0.0419	0.2179	0.4238
	Ischaemic HF	0.4457	0.2015	0.0135	0.3908	0.1767	0.0135
	LVEF (centred)	-0.0224	0.0101	0.0135	-0.0208	0.0090	0.0106
	Quartile2	-0.3166	0.2759	0.1255	-0.2747	0.2469	0.1329
	Quartile3	-0.7234	0.2657	0.0032	-0.6811	0.2382	0.0021
	Quartile4	-1.5136	0.2563	< 0.0000	-1.4967	0.2289	< 0.0000
	eGFR (centred)	-0.0106	0.0051	0.0188	-0.0105	0.0045	0.0091
	Age (centred)	0.0143	0.0109	0.0941	0.0156	0.0096	0.0517
Log-logistic	shape	1.167	0.095	--	1.221	0.087	--
	scale	1022.786	324.980	--	686.144	181.999	--
	FCM	0.1377	0.1767	0.2179	0.0840	0.1514	0.2896
	Female	0.1599	0.1985	0.2101	0.2473	0.1714	0.0745
	Anaemic	-0.0850	0.1886	0.3261	0.0991	0.1598	0.2676
	De novo HF	0.1359	0.2399	0.2856	-0.0405	0.1940	0.4172
	Ischaemic HF	-0.4126	0.1914	0.0155	-0.3359	0.1624	0.0193
	LVEF (centred)	0.0218	0.0098	0.0135	0.0199	0.0085	0.0092
	Quartile2	0.3423	0.2742	0.1059	0.2943	0.2411	0.1111
	Quartile3	0.7278	0.2619	0.0027	0.6791	0.2298	0.0016
	Quartile4	1.4808	0.2559	< 0.0000	1.4329	0.2228	< 0.0000
	eGFR (centred)	0.0105	0.0048	0.0139	0.0101	0.0041	0.0065
	Age (centred)	-0.0126	0.0102	0.1090	-0.0140	0.0088	0.0555
Lognormal	Mean (log)	7.104	0.350	--	6.632	0.291	--
	sd (log)	1.749	0.129	--	1.630	0.105	--
	FCM	0.1904	0.1841	0.1505	0.1342	0.1580	0.1977
	Female	0.2349	0.2042	0.1250	0.2962	0.1764	0.0466
	Anaemic	-0.0889	0.1940	0.3234	0.1093	0.1663	0.2556
	De novo HF	0.1637	0.2364	0.2444	-0.0010	0.1957	0.4980
	Ischaemic HF	-0.3553	0.1948	0.0341	-0.2688	0.1667	0.0534
	LVEF (centred)	0.0192	0.0103	0.0303	0.0187	0.0088	0.0168
	Quartile2	0.3549	0.3048	0.1221	0.2977	0.2659	0.1314
	Quartile3	0.7113	0.2858	0.0064	0.6695	0.2497	0.0037
	Quartile4	1.5496	0.2668	< 0.0000	1.5032	0.2321	< 0.0000
	eGFR (centred)	0.0117	0.0048	0.0074	0.0109	0.0041	0.0040
	Age (centred)	-0.0104	0.0104	0.1596	-0.0127	0.0090	0.0793

Indicated patient parameters (eGFR, age, LVEF, etc) correspond to patient characteristics at baseline in the study. Quartiles refer to Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score (CSS) scores divided into quartiles according to baseline reading and are presented with the lowest quartile (Quartile1) as reference. eGFR, estimated glomerular filtration rate in mL/min/1.73m^2; FCM, ferric carboxymaltose; HF, heart failure; LVEF, left ventricular ejection fraction.

KCCQ-CSS transition probabilities

Health states in the model were determined according to quartiles of Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score (CSS) values. At baseline, data from all patients, independently of treatment arm, were used to determine quartile cut-offs for the four model states. Examination of the mean KCCQ-CSS values revealed an inflection point at approximately 3 months, indicating a steep initial increase in scores (improving health state) and later a more level score distribution over time.

Probabilities for transition were determined using trial data and patient counts to characterise movement among the states (increasing or decreasing KCCQ-CSS). To reflect the different phases of KCCQ-CSS value change, one set of transitions was determined for patients on average from cycle 0 to 3 (12 weeks), and a second set for cycles 4 onwards.

Resulting transition probabilities for ferric carboxymaltose and placebo are shown in Table S3.

Table S3. KCCQ-CSS transition probabilities

State transitions [From, To]	Ferric carboxymaltose				Placebo			
	Cycle 0 - 3		Cycle 4+		Cycle 0 - 3		Cycle 4+	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
KCCQ[1,1]	0.24610	0.00017	0.26570	0.00028	0.26050	0.00015	0.44600	0.00027
KCCQ[1,2]	0.22480	0.00015	0.34340	0.00028	0.19060	0.00013	0.22920	0.00022
KCCQ[1,3]	0.17640	0.00013	0.18760	0.00024	0.22340	0.00014	0.16840	0.00020
KCCQ[1,4]	0.35270	0.00019	0.20330	0.00026	0.32550	0.00016	0.15640	0.00018
KCCQ[2,1]	0.13430	0.00012	0.19130	0.00020	0.13920	0.00012	0.24670	0.00022
KCCQ[2,2]	0.18520	0.00013	0.24500	0.00022	0.19270	0.00014	0.29390	0.00025
KCCQ[2,3]	0.17590	0.00013	0.34070	0.00024	0.20630	0.00014	0.23540	0.00023
KCCQ[2,4]	0.50460	0.00017	0.22300	0.00022	0.46170	0.00017	0.22400	0.00023
KCCQ[3,1]	0.06472	0.00007	0.10990	0.00011	0.07392	0.00008	0.12120	0.00011
KCCQ[3,2]	0.10330	0.00009	0.20230	0.00016	0.09007	0.00008	0.21960	0.00014
KCCQ[3,3]	0.31070	0.00013	0.33520	0.00018	0.32790	0.00013	0.39030	0.00017
KCCQ[3,4]	0.52120	0.00014	0.35270	0.00018	0.50810	0.00013	0.26890	0.00015
KCCQ[4,1]	0.01868	0.00002	0.09879	0.00005	0.02451	0.00003	0.09761	0.00005
KCCQ[4,2]	0.03989	0.00003	0.09207	0.00005	0.02711	0.00003	0.09878	0.00005
KCCQ[4,3]	0.09583	0.00005	0.14970	0.00006	0.11100	0.00006	0.15000	0.00006
KCCQ[4,4]	0.84560	0.00006	0.65940	0.00008	0.83740	0.00007	0.65360	0.00007

Cycles defined in the model as KCCQ CSS: Kansas City Cardiomyopathy Questionnaire clinical summary score; SE, standard error.

Modelling repeat hospitalisation events

To account for repeat events, generalised estimating equations with a negative binomial distribution were fit to the AFFIRM-AHF full analysis set patient data to estimate hospitalisation for heart failure (HHF) and hospitalisation for non-heart failure (HnHF) events. Covariables for adjustment were selected based on clinical specification; that is, those primary patient parameters expected to impact hospitalisation events, as mentioned above in modelling for mortality. The AFFIRM-AHF data included labelling of HHF events and hospitalisation for any other reason. The hospitalisation for HnHF events were thus determined as the set of hospitalisations that were not labelled HHF. Model coefficients are presented in Table S4.

Table S4. Regression models developed for HHF and HnHF

	Hospitalisation for heart failure			Hospitalisation for non-heart failure		
Parameter	**Coefficient**	**SE**	**p-value**	**Coefficient**	**SE**	**p-value**
Intercept	-2.3827	0.2035	<0.0000	-2.8267	0.2772	<0.0000
Time	-0.0011	0.0005	0.0307	-0.0032	0.0006	0.0000
FCM	-0.2220	0.1242	0.0739	-0.0621	0.1512	0.6814
Female	-0.1766	0.1376	0.1993	-0.7550	0.1661	<0.0000
Anaemic	0.0579	0.1288	0.6529	-0.1008	0.1578	0.5229
De novo HF	-0.8082	0.1876	<0.0000	0.0377	0.1895	0.8423
Ischaemic HF	0.1360	0.1332	0.3071	0.2863	0.1822	0.1162
LVEF (centred)	-0.0229	0.0068	0.0007	-0.0114	0.0091	0.2097
Quartile2	-0.1796	0.1825	0.3248	-0.0960	0.2582	0.7101
Quartile3	-0.4488	0.1670	0.0072	-0.3191	0.2372	0.1785
Quartile4	-1.0908	0.1793	<0.0000	-0.4805	0.2089	0.0214
eGFR (centred)	-0.0082	0.0032	0.0112	-0.0109	0.0036	0.0026
Age (centred)	-0.0041	0.0070	0.5608	-0.0014	0.0085	0.8734

Quartiles refer to Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score (CSS) scores divided into quartiles according to baseline reading and are presented with the lowest quartile (Quartile1) as reference. eGFR, estimated glomerular filtration rate in mL/min/1.73m²; FCM, ferric carboxymaltose; HF, heart failure; LVEF, left ventricular ejection fraction; SE, standard error.

Adverse event rates

No adverse events of special clinical interest were indicated a priori in the study. Selection of adverse events for consideration was therefore determined by rate of occurrence overall in the entire study population, independently of study arm. A criterion of 1% was selected as the threshold for inclusion and 10 events met this threshold (Table S5) using the safety analysis set.

Table S5. Adverse event rates

Adverse event	Overall	FCM	Placebo
Cardiac failure	33.7%	29.0%	38.5%
Cardiac failure congestive	5.9%	5.5%	6.4%
Cardiac failure acute	4.2%	4.5%	4.0%
Pneumonia	2.4%	2.0%	2.9%
Death	1.9%	1.4%	2.4%
Cardiac arrest	1.7%	1.3%	2.2%
Sepsis	1.4%	1.3%	1.6%
Atrial fibrillation	1.4%	2.0%	0.7%
Acute kidney injury	1.2%	1.4%	0.9%
Sudden death	1.1%	0.9%	1.3%

FCM, ferric carboxymaltose.

Adverse event data included intervention and outcome of each AE; most of these were associated with hospitalisation. Those events classified as cardiac in origin (cardiac failure congestive or acute, cardiac arrest) and those indicated as death (death, sudden death) were excluded from the AE analysis as these events were expected to be captured elsewhere (HHF events and mortality). AEs considered in the model were thus atrial fibrillation, pneumonia, sepsis, and acute kidney injury. Due to the comparatively low incidence of these AEs, adjusted equations were not used. The events were instead characterised by constant rates estimated separately for each treatment arm and determined from the rate of occurrence within the 52-week trial period divided by number of patients on an intention-to-treat basis.

Derivation of patient health state and event utility

As described (see main text) four health states were defined for the model according to quartiles of KCCQ-CSS recorded at baseline. Data available from the AFFIRM-AHF trial included EQ-5D-5L date to which UK tariffs had already been applied to generate utility indices. This utility weighting permits the accumulation of quality adjusted life years (QALYs) according to the proportion of patients spending time (cycles) in each state as they progress through the model according to the transition probabilities described above (Table S3). Baseline utilities were estimated as the mean utility index for patients who had been assigned to each KCCQ-CSS-defined health state.

To determine the event-related impact on utility, a mixed effect regression modelling approach was used, adjusting for covariates expected to have an impact on utility prediction (age, follow-up time, sex, geographical region, health state). Note that the value determined for sepsis (0.212) suggested an increase in utility, which was not considered plausible. The result is likely due to the low frequency of events, combined with the requirement that an EQ-5D-5L measurement had to occur within 1 cycle (4 weeks) of the event. A value for this utility decrement was sourced from the literature.[1] Utility values used in the model are listed in Table S6.

Table S6. Estimation of utility values

Parameter	Coefficient	SE	p-value
Intercept	0.6608	0.0325	< 0.0000
Time (study day)	4.902E-06	1.858E-05	0.7919
Age	-0.0014	0.0004	0.0012
Female	-0.0264	0.0098	0.0068
Eastern Europe	-0.0369	0.0117	0.0017
Latin America	0.0376	0.0191	0.0499
Rest of World	-0.0456	0.0143	0.0014
Quartile2	0.1009	0.0108	< 0.0000
Quartile3	0.1402	0.0101	< 0.0000
Quartile4	0.2490	0.0096	< 0.0000
Events			
Hospitalisation for heart failure	-0.0708	0.0162	< 0.0000
Hospitalisation for non-heart failure	-0.0152	0.0186	0.4148
Atrial fibrillation	-0.0175	0.1143	0.8783
Acute kidney injury	-0.0365	0.0929	0.6945
Pneumonia	-0.0976	0.0793	0.2186
Sepsis	0.2120	0.1754	0.2268

Region coefficients are relative to Western Europe as reference. Quartiles refer to Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score (CSS) scores divided into quartiles according to baseline reading and are presented with the lowest quartile (Quartile1) as reference. SE, standard error. Note that the positive value for sepsis (0.212) indicating an increase in utility was not used in the model. See text for details.

Cost inputs for the model

Searches were conducted to identify relevant sources for model cost inputs (Table S7). . Costs as shown were adjusted to 2020 currency units of the respective countries (UK, USA, Switzerland, Italy) using the Campbell and Cochrane Economics Methods Group cost converter.[2] Costs were as reported in the referenced sources, or if derivative calculations were performed, these are described in the table or caption. The cost for background resource use associated with heart failure is applied uniformly across all KCCQ-CSS-defined states. Although it is expected that costs may be higher for patients in worse states (for example quartile 1 versus the best health in quartile 4), the indicated value is taken as an average for any patient diagnosed with heart failure. Additional costs as a function of health state are captured in the model, since risk of heart failure hospitalisation and non-heart failure hospitalisation (see section on modelling of repeat hospitalisation events) is modelled on health state as a covariate. Rates of these events are thus expected to be higher as patients experience poorer health states, thereby capturing additional costs associated with each state.

Treatment costs for ferric carboxymaltose were applied for 1,000 mg of ferric carboxymaltose in cycle 1 (spanning weeks 1 to 4) as the most frequently administered dosage among patients. Dosage was converted to costs using country-specific data provided by Vifor Pharma. For cycle 2, as described in the main text, the remainder of the average total dose per patient (354 mg) was applied, scaled according the unit cost per mg of the drug.

Adverse event costs in the model (Table S7) were for the event only, intended to be exclusive of hospitalisation. The events modelled were classified as serious and according to records, most resulted in hospitalisation. The hospitalisation component of cost is therefore expected to be captured in the hospitalisation for non-heart failure event cost, with an additional cost attributable to the specific AE. In cases where such a hospitalisation-independent cost could not be identified, surrogates were used as described in the table.

Table S7. Cost inputs for the model

Cost item	Mean (SE)	Source
UK		
FCM – treatment costs (first cycle)	GBP 178.58 (4.45)	Vifor Pharma data on file
FCM – treatment costs (second cycle)	GBP 64.41 (10.21)	Vifor Pharma data on file
Placebo – treatment costs	GBP 0	Vifor Pharma data on file
Background HF management	GBP 877.56 (87.76)#	McMurray et al.[3], NHS Reference Costs[4] per McEwan et al.[5]
Hospitalisation for heart failure	GBP 2,832 (283.20)#	NHS Reference Costs[4] per McEwan et al.[5]
Hospitalisation for non-heart failure	GBP 1,327.07 (132.71)#	NHS Reference Costs[4] per McEwan et al.[5]
Cardiovascular disease death	GBP 3,126 (312.60)	Alva et al.[6] per McEwan et al.[5]
Atrial fibrillation	GBP 674.71 (67.47)	Stewart et al.[7]
Pneumonia	GBP 6,810.06 (681.01)	Luckraz et al.[8]
Acute kidney injury	GBP 3,161.37 (316.14)	NHS reference costs[4], Kerr et al.[9]
Sepsis	GBP 4,423.56 (442.36)	NHS Reference Costs[4]
USA		
FCM – treatment costs (first cycle)	USD 1, 563.74 (39.01)	Vifor Pharma data on file
FCM – treatment costs (second cycle)	USD 555.23 (89.44)	Vifor Pharma data on file
Placebo – treatment costs	USD 0	Vifor Pharma data on file
Background HF management	USD 1916.12 (191.61)	Liu et al.[10]
Hospitalisation for heart failure	USD 27,374.07 (2,737.407)	Kansal et al.[11]
Hospitalisation for non-heart failure	USD 16,640.04 (1,664.004)	Kansal et al.[11]
Cardiovascular disease death	USD 25,210 (2,521)	Naccareli Clinical Cardiology 2010
Atrial fibrillation	USD 405.98 (40.60)	Kansal et al.[11]
Pneumonia	USD 3,178.12 (317.81)	Tong et al.[12]
Acute kidney injury	USD 9,098.44 (909.84)	Silver et al.[13]
Sepsis	USD 4,851.9 (485.19)	Paoli et al.[14]

Cost item	Mean (SE)	Source
Italy		
FCM – treatment costs (first cycle)	EUR 199.82 (4.98)	Vifor Pharma data on file
FCM – treatment costs (second cycle)	EUR 70.95 (11.43)	Vifor Pharma data on file
Placebo – treatment costs	EUR 0	Vifor Pharma data on file
Background HF management	EUR 3,344.52 (334.45)	Rognoni et al.[15]
Hospitalisation for heart failure	EUR 6,983.91 (698.39)	Maggioni et al.[16]†
Hospitalisation for non-heart failure	EUR 2,964.87 (296.49)	Maggioni et al.[16]†
Cardiovascular disease death	EUR 2,568.63 (256.86)	Barrios et al.[17]‡
Atrial fibrillation	EUR 2,424.69 (242.47)	Rognoni et al.[15]
Pneumonia	EUR 2,964.87 (296.49)	non-HF hospitalisation cost used as surrogate
Acute kidney injury	EUR 3,812.13 (381.21)	Rognoni et al.[15]
Sepsis	EUR 2,964.87 (296.49)	non-HF hospitalisation cost used as surrogate
Switzerland		
FCM – treatment costs (first cycle)	CHF 280.25 (6.99)	Vifor Pharma data on file
FCM – treatment costs (second cycle)	CHF 99.51 (16.03)	Vifor Pharma data on file
Placebo – treatment costs	CHF 0	Vifor Pharma data on file
Background HF management	CHF 1,328.17 (132.82)	Ademi et al.[18]
Hospitalisation for heart failure	CHF 13,645 (1364.50)	Ademi et al.[18]
Hospitalisation for non-heart failure	CHF 9,705.13 (970.51)	Brunner et al.[19]
Cardiovascular disease death	CHF 25,500 (2,550)	Panczak et al.[20]*
Atrial fibrillation	CHF 1,941.24 (194.12)	Mean across other countries^
Pneumonia	CHF 6,123.94 (612.39)	Brunner et al.[19]
Acute kidney injury	CHF 16,733.64 (1673.36)	Ademi et al.[18]
Sepsis	CHF 15,054.06 (1505.41)	Schmid et al.[21]

CHF, Swiss Francs; EUR, Euros; HF, heart failure; FCM, ferric carboxymaltose; GBP, Great Britain Pounds Sterling; USD, United States Dollars.

UK costs were applied as reported by McEwan et al.[5] with original sources indicated for traceability. Please see original publication for derivation details.
† calculated from total expenditure during follow-up period (1 year) divided into patients hospitalised for HF and those for non-HF reasons. These totals were divided by the

split in number of patients experiencing each type of hospitalisation to determine mean cost per event.
‡From source, EUR 4.4 billion for 1 712 977 deaths in 2020, divided to determine cost per death.
* The cited reference is a link to the publication; the CV death specific cost was determined from a supplementary presentation of the data in a thesis of an article co-author (C. Berlin), found in Table 5, page 120, PhD thesis, “Cardiovascular disease in Switzerland – health care, mortality and geographical pattern,” Claudia Berlin, Graduate School for Health Sciences, University of Bern
^ A cost attributable to atrial fibrillation alone for Switzerland was not identified. As a surrogate, the costs across the other countries were converted to CHF and averaged. The result (1,941 CHF) is comparable to a reported value of 1,148 CHF (inflated to 2020) from Nilsson et al.[22]. The Nilsson et al. value was not used, however, as it was described in the health economic model as attributable to a health state, rather than an event as required for the present model.

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