Patient Clusters and Cost Trajectories in the Swiss Atrial Fibrillation Cohort

Authors

Aebersold, Helena[a], Serra-Burriel, Miquel[a], Foster-Witassek, Fabienne[a], Moschovitis, Giorgio[b], Aeschbacher, Stefanie[c,d], Auricchio, Angelo[e], Beer, Jürg H.[f,g], Blozik, Eva[h], Bonati, Leo H.[i,j], Conen, David[k], Felder, Stefan[l], Huber, Carola A.[m], Kühne, Michael[c,d], Müller, Andreas[n], Oberle, Jolanda[o,p], Paladini, Rebecca E.[c,d], Reichlin, Tobias[q], Rodondi, Nicolas[o,p], Springer, Anne[c,d], Stauber, Annina[n], Sticherling, Christian[c,d], Szucs, Thomas[r], Osswald, Stefan[c,d], Schwenkglenks, Matthias[a,r], on behalf of the Swiss-AF Investigators

[a] Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland

[b] Division of Cardiology, Ente Ospedaliero Cantonale (EOC), Ospedale Regionale di Lugano, Lugano, Switzerland

[c] Cardiology Division, Department of Medicine, University Hospital Basel, Switzerland

[d] Cardiovascular Research Institute Basel, University Hospital Basel, Switzerland

[e] Department of Cardiology, Instituto Cardiocentro Ticino, Ente Ospedaliero Cantonale (EOC), Lugano, Switzerland

[f] Department of Medicine, Cantonal Hospital of Baden, Switzerland

[g] Center for Molecular Cardiology, University of Zürich, Switzerland

[h] Institute of Primary Care, University of Zurich, Zurich, Switzerland

[i] Department of Neurology, University Hospital Basel, Basel Switzerland

[j] Research Department, Reha Rheinfelden, Rheinfelden, Switzerland

[k] Population Health Research Institute, McMaster University, Hamilton, Canada

[l] University of Basel, Faculty of Business and Economics, Switzerland

[m] Department of Health Sciences, Helsana Group, Zurich, Switzerland

[n] Department of Cardiology, Triemli Hospital Zurich, Switzerland

[o] Institute of Primary Health Care (BIHAM), University of Bern, Switzerland

[p] Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland

[q] Department of Cardiology, Inselspital, Bern University Hospital, University of Bern, Switzerland

[r] Institute of Pharmaceutical Medicine (ECPM), University of Basel, Basel, Switzerland

Correspondence: Helena Aebersold, University of Zurich, Epidemiology, Biostatistics & Prevention Institute (EBPI), Hirschengraben 84, 8001 Zurich, helena.aebersold@uzh.ch

Abstract

Objective

Evidence on long-term costs of atrial fibrillation (AF) and associated factors is scarce. As part of the Swiss-AF prospective cohort study we aimed to characterise AF costs and their development over time, and to assess specific patient clusters and their cost trajectories.

Methods

Swiss-AF enrolled 2,415 patients with variable duration of AF between 2014 and 2017. Patient clusters were identified using hierarchical cluster analysis of baseline characteristics. Ongoing yearly follow-ups include health insurance clinical and claims data. An algorithm was developed to adjudicate costs to AF and related complications.

Results

A subpopulation of 1,024 Swiss-AF patients with available claims data was followed up for a median [interquartile range] of 3.24 [1.09] years. Average yearly AF-adjudicated costs amounted to CHF 5,679 (EUR 5,163), remaining stable across the observation period. AF-adjudicated costs consisted mainly of in- and outpatient AF treatment costs (CHF 4,078; EUR 3,707), followed by costs of bleeding (CHF 696; EUR 633) and heart failure (CHF 494; EUR 449). Hierarchical analysis identified three patient clusters: cardiovascular (CV; N=253 with claims), isolated-symptomatic (IS; N=586), and severely morbid without cardiovascular disease (SM; N=185). The CV cluster and SM cluster depicted similarly high costs across all cost outcomes, IS patients accrued the lowest costs.

Conclusion

Our results highlight three well-defined patient clusters with specific costs that could be used for stratification in both clinical and economic studies. Patient characteristics associated with adjudicated costs as well as cost trajectories may enable an early understanding of the magnitude of upcoming AF-related healthcare costs.

Keywords

atrial fibrillation, cost of illness, cost trajectories, hierarchical clustering, patient cluster

What is already known on this topic

Atrial fibrillation (AF) is a complex disease and constitutes a major economic and societal challenge due to its high prevalence worldwide.

What this study adds

This study, based on a large prospective cohort study, provides evidence on real-world AF costs and their development over time. Data-derived patient clusters are linked to costs and their respective cost trajectories are assessed.

How this study might affect research, practice or policy

The identified patient clusters and their characteristics may help clinicians and payers to gain an early insight and understanding of the magnitude of the expected AF-related healthcare costs.

Introduction

Atrial fibrillation (AF) is the most prevalent arrhythmia worldwide,[1] and its prevalence is expected to double by 2050.[2,3] AF patients face increased risk of stroke, cognitive dysfunction, and impaired quality of life.[4,5]

AF also constitutes a major economic and societal challenge. Only a limited number of AF cost-of-illness studies[6] is available, indicating that costs are predominantly driven by AF-related hospitalisations.[7] Hospitalisation costs were reported to amount to 50-70% of total costs,[8] while medication costs were comparatively low.[9] Drivers of hospitalisations in AF patients were identified to be multifaceted and diverse.[10,11] They include age, previous history of heart failure and myocardial infarction, non-cardiovascular conditions, i.e. sleep apnoea and chronic kidney disease, as well as lifestyle factors.

Despite these insights, evidence on real-world AF-related costs and their components remains scarce. Most results stem from retrospective studies. Even less evidence is available on cost trajectories over time, especially in prevalent AF patients. Patient characterisation based on AF subtypes is known to not encompass the full spectrum of AF,[12,13] and data-driven characterisation of patients has not yet been used for costing.

The Swiss-AF Economics project, part of the prospective Swiss Atrial Fibrillation cohort study[14,15] (Swiss-AF), aims to assess AF-related economic burden. Clinical data are combined with health insurance claims to characterise the Swiss-AF study population from an economic perspective. Focusing on the direct medical cost per patient from the perspective of the Swiss statutory health insurance system, this analysis aims to describe AF costs and their trajectories, and to build data-driven patient clusters and assess their respective cost trajectories.

Methods

Study Design and Data Sources

Swiss-AF is an ongoing prospective multicentre observational cohort study across 14 clinical centres in Switzerland. The detailed study setup and methodology have been described earlier.[14] In short, 2,415 patients were enrolled between April 2014 and August 2017. Eligibility criteria for Swiss-AF were based on history of documented AF and being older than 65 years; 228 patients who were potentially part of the active workforce were enrolled at age 45-64 to enable the study of socio-economic aspects of AF.[14] This analysis used a 2014-2020 data cut; a summary of the study design and main outcomes is shown in **Figure 1**.

Health economic data include medical resource use at the enrolling centres – e.g. number of hospitalisations, interventions, medication – and health insurance claims data from four cooperating insurance companies, covering 1,024 patients (42.4% of the study population). The claims data cover all services submitted for reimbursement by the Swiss statutory health insurance, which is obligatory for all residents and has a comprehensive benefit package covering inpatient and outpatient services.

Claims relating to inpatient services were based on the Swiss flat-fee reimbursement scheme for acute care hospitalisations (SwissDRG[16]). Data related to inpatient services in rehabilitation clinics were based on tariffs per day negotiated between each service provider and insurer, and claims related to nursing home care services were based on daily contributions fixed by the Swiss Federal Council. Outpatient services were covered with detailed information for each cost component, based on national tariff codes and price lists. Relevant comorbidities not collected by the Swiss-AF study were derived from the drug utilisation information present in the claims data, using the pharmaceutical cost groups (PCGs) method.[17]

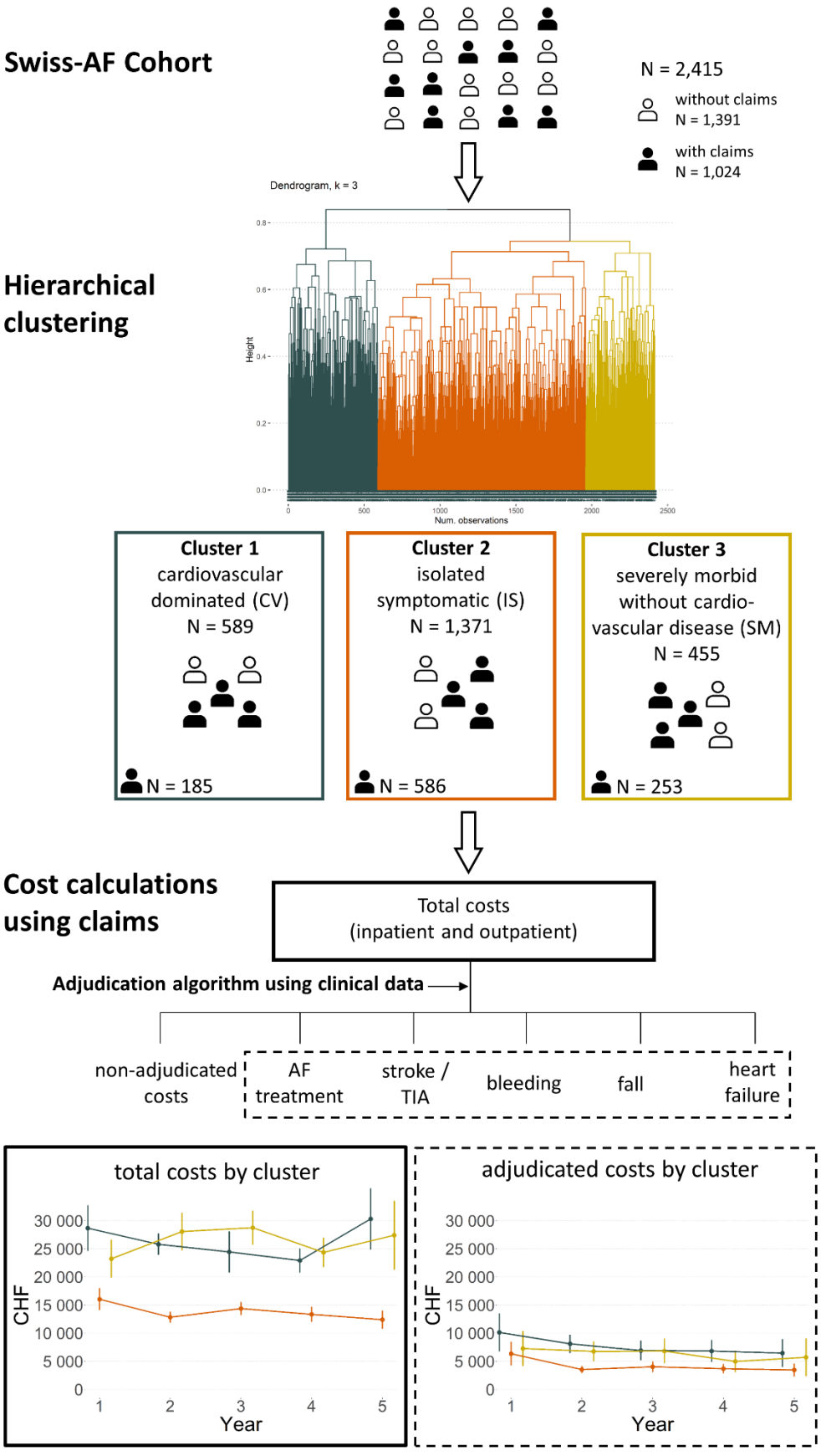


Figure 1. Summary of the study design and main outcomes.

Notes: An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries.

Abbreviations: AF: atrial fibrillation.

Outcome Measures

Our main outcome of interest was total AF-adjudicated costs from the Swiss statutory health insurance perspective. Costs in AF patients are, typically, partially related to AF and its potential complications, partially related to other comorbidities. To distinguish these components, an adjudication algorithm (**Table S10**) was developed through an iterative process, involving clinical experts, health economists, and claims data specialists. The adjudication algorithm combined clinical events, e.g. date of a bleeding event, with information from the health insurance claims, e.g. SwissDRG based. Inpatient costs were either non-related or adjudicated to one of five groups: (1) AF, (2) stroke or transient ischemic attack (TIA), (3) bleeding, (4) fall, (5) heart failure. Similarly, outpatient costs were either non-related or classified into one of six groups: (1) AF without medication, (2) AF medication, (3) stroke or TIA without medication, (4) stroke or TIA medication, (5) bleeding, (6) fall. As it was not possible to distinguish between complications (e.g. strokes) caused by AF or other reasons, complication costs were considered in full.

We thus considered the sum of all costs adjudicated to groups (1) to (6) as total AF-adjudicated costs. Secondary outcomes included the subcategories AF-adjudicated inpatient costs, AF-adjudicated outpatient costs excluding drug costs, and AF-adjudicated outpatient drug costs. We also considered total costs, equivalent sub-categories, and non-adjudicated costs, i.e. the costs not adjudicated to AF or its complications. All outcome variables and their relationship can be found in **Figure S1**. Main cost results are presented in Euros (EUR) in addition to Swiss francs (CHF), based on an exchange rate (averaged 2014-2020) of EUR 1.0 = CHF 1.1, to facilitate comparison with other countries.

Covariates

Baseline covariates, measured at enrolment, included the following types:

(1) patient characteristics: age, sex, body mass index (BMI), AF type, AF symptoms, time since AF diagnosis, risk of stroke for non-valvular atrial fibrillation (CHA_2DS_2-VASc score).

(2) medical history: previous major bleeding, stroke or TIA, systemic embolism, heart failure, myocardial infarction, diabetes, hypertension, renal insufficiency, sleep apnoea.

(3) treatments and implanted devices: percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), electro-conversion, pulmonary vein isolation (PVI), loop recorder, pacemaker (PM), cardiac resynchronisation therapy (CRT) with or without ICD, implantable cardioverter defibrillator (ICD).

(4) anticoagulation medication: vitamin K antagonist (VKA), direct-acting oral anticoagulant (DOAC).
(5) other medication: antiplatelets, aspirin, statins, diuretics, beta-blockers, digoxin.
(6) socioeconomic factors: education, greater area of residence, smoking, alcohol consumption.

Statistical analysis

First, the characteristics of the included Swiss-AF patients were described. Baseline characteristics were presented with mean and standard deviation for normally distributed variables, median and interquartile range for continuous non-normally distributed variables, and N (%) for categorical ones. Kaplan-Meier curves of overall survival were used to depict mortality and cohort attrition.

Second, costs and their trajectories since enrolment were described. Cost components are shown as bar charts and boxplot distributions of mean annual costs. Cost trajectories are depicted as line plots with mean estimates and 95% confidence intervals. All costs considered individual follow-up times and were aggregated to a yearly level. Given the relative stability of prices over the observation period, costs were taken as reported. Costs as a function of time since diagnosis were also explored graphically.

Third, to gain an understanding of different patterns in the Swiss-AF population, clusters of patients and their respective cost composition and cost trajectories were determined. A hierarchical cluster analysis was run (**Table S5**). The unsupervised learning model[18] considered the full Swiss-AF population and all baseline covariates except greater area of residence. Gower distances were used with a complete linkage method, choosing optimal clusters according to elbow and silhouette methods.[18] Differences in baseline characteristics between patient clusters were compared with standardised mean difference, t-test for continuous and roughly normally distributed variables, Mann-Whitney U test for continuous non-normally distributed variables, and fisher's exact test for categorical variables. Cluster-specific overall survival was compared using Kaplan-Meier curves and age-adjusted cox regression. A complementary multivariable regression-based cost analysis is reported in the supplement (**Figures S7-S8**, **Tables S6-S9**).

A 5% significance level was pre-specified, and no adjustments for multiple testing were performed on between-cluster comparisons of patient characteristics. Given the usage of baseline data and observed claims there were no missing data. The cost analyses conditioned on patients being alive. Data management, variable derivations and all statistical analyses were conducted using R version 3.6.3.

Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

Results

Patient population

For the 1,024 Swiss-AF patients with available claims data, included in the cost analyses, baseline characteristics are shown in **Table 1**. The mean age at baseline was 73 ± standard deviation (SD) 8 years and 28% were female. On average, patients were diagnosed with AF 6.3 years prior to enrolment, and the majority had AF symptoms (62%). Patients without available claims data, additionally used in the hierarchical cluster analysis, had comparable characteristics (**Table S1**). **Figure S2** depicts the average monthly cost evolution alongside the Kaplan-Meier curve of overall survival, across the full observation period of 2014 to 2020. For subsequent analyses, individual patient follow-up was censored at five years after enrolment (median follow-up: 3.24 years), given sparse data thereafter.

Cost structures and cost trajectories

Figure 2 shows mean annual costs and cost trajectories for different cost outcomes. More details on all cost outcomes and costs by time since AF diagnosis are provided in **Tables S2**, **Figures S3-S4**. The average total per-patient costs amounted to CHF 19,037 (EUR 17,306) yearly, of which roughly half corresponded to outpatient services. Inpatient costs appeared to be higher than outpatient costs only during the first year, remaining stable and at a similar level thereafter.

Total AF-adjudicated costs (**Figure S1**), amounted to CHF 5,679 (EUR 5,163) annually, roughly 30% of the total costs. AF-adjudicated costs consisted mainly of in- and outpatient AF treatment costs (CHF 4,078; EUR 3,707), followed by costs of bleeding (CHF 696; EUR 633) and heart failure (CHF 494; EUR 449). As the total costs, the AF-adjudicated costs remained stable across the whole analysed period of five years. AF-adjudicated inpatient costs were higher than AF-adjudicated outpatient costs in the first year.

Table 1. Baseline characteristics of all included AF patients and each cluster.

	Overall	Cardiovascular dominated (CV)	Isolated Symptomatic (IS)	Severely morbid without cardiovascular disease (SM)		
N	1 024	253	586	185	p	SMD
Characteristics						
Age *mean (SD)*	73.00 (8.17)	75.39 (6.81)	70.92 (8.30)	76.32 (7.48)	<0.001	0.467
Sex Female *N (%)*	283 (27.6)	29 (11.5)	177 (30.2)	77 (41.6)	<0.001	0.48
BMI *median [IQR]*	26.98 [24.43, 30.52]	28.65 [25.61, 31.94]	26.21 [24.06, 29.72]	27.13 [24.69, 30.81]	<0.001	0.276
Type of AF *N (%)*					<0.001	0.508
Paroxysmal	471 (46.0)	97 (38.3)	314 (53.6)	60 (32.4)		
Permanent	243 (23.7)	87 (34.4)	73 (12.5)	83 (44.9)		
Persistent	310 (30.3)	69 (27.3)	199 (34.0)	42 (22.7)		
AF symptoms *N (%)*	632 (61.8)	125 (49.4)	429 (73.2)	78 (42.2)	<0.001	0.437
Years since AF Dx *mean (SD)*	6.33 (7.91)	7.72 (9.21)	5.32 (6.99)	7.66 (8.32)	<0.001	0.202
CHA_2DS_2-VASc *mean (SD)*	3.44 (1.73)	4.90 (1.42)	2.67 (1.48)	3.92 (1.39)	<0.001	1.036
Prev. Major Bleeding *N (%)*	61 (6.0)	22 (8.7)	21 (3.6)	18 (9.7)	0.001	0.166
Prev. Stroke or TIA *N (%)*	212 (20.7)	68 (26.9)	109 (18.6)	35 (18.9)	0.02	0.132
Prev. Sys. Embolism *N (%)*	60 (5.9)	27 (10.7)	16 (2.7)	17 (9.2)	<0.001	0.216
Prev. Heart Failure *N (%)*	254 (24.8)	126 (49.8)	49 (8.4)	79 (42.7)	<0.001	0.675
Prev. Myocardial Inf. *N (%)*	161 (15.7)	140 (55.3)	17 (2.9)	4 (2.2)	<0.001	0.971
Diabetes *N (%)*	176 (17.2)	96 (37.9)	41 (7.0)	39 (21.1)	<0.001	0.53
Hypertension *N (%)*	692 (67.6)	222 (87.7)	319 (54.4)	151 (81.6)	<0.001	0.523
Renal Insufficiency *N (%)*	213 (20.8)	101 (39.9)	39 (6.7)	73 (39.5)	<0.001	0.57
Sleep Apnea *N (%)*	154 (15.0)	63 (24.9)	65 (11.1)	26 (14.1)	<0.001	0.244
Prev. PTCA or CABG *N (%)*	288 (28.1)	219 (86.6)	63 (10.8)	6 (3.2)	<0.001	1.897
Prev. Electroconversion *N (%)*	355 (34.7)	80 (31.6)	223 (38.1)	52 (28.1)	0.023	0.142
Prev. PVI *N (%)*	210 (20.5)	23 (9.1)	176 (30.0)	11 (5.9)	<0.001	0.442
Implanted Device *N (%)*					<0.001	0.42
No device or Loop recorder	841 (82.1)	183 (72.3)	529 (90.3)	129 (69.7)		
PM	121 (11.8)	37 (14.6)	44 (7.5)	40 (21.6)		
ICD	31 (3.0)	16 (6.3)	8 (1.4)	7 (3.8)		
CRT (ICD)	31 (3.0)	17 (6.7)	5 (0.9)	9 (4.9)		
Medication *N (%)*						
Antiplateletes	53 (5.2)	37 (14.6)	13 (2.2)	3 (1.6)	<0.001	0.331
Aspirin	171 (16.7)	103 (40.7)	50 (8.5)	18 (9.7)	<0.001	0.537
Statins	529 (51.7)	228 (90.1)	228 (38.9)	73 (39.5)	<0.001	0.843
Diuretics	459 (44.8)	177 (70.0)	116 (19.8)	166 (89.7)	<0.001	1.217
Beta-blockers	726 (70.9)	210 (83.0)	379 (64.7)	137 (74.1)	<0.001	0.283
Digoxin	39 (3.8)	13 (5.1)	9 (1.5)	17 (9.2)	<0.001	0.235
Anticoagulation					<0.001	0.586
None	93 (9.1)	28 (11.1)	55 (9.4)	10 (5.4)		
VKA	414 (40.4)	148 (58.5)	151 (25.8)	115 (62.2)		
DOAC	517 (50.5)	77 (30.4)	380 (64.8)	60 (32.4)		
Comorbidities (PCG; %)						

Acid	397 (38.8)	115 (45.6)	207 (35.4)	75 (40.5)	0.018	0.14
Bone	44 (4.3)	7 (2.8)	22 (3.8)	15 (8.1)	0.015	0.159
Cancer	35 (3.4)	9 (3.6)	17 (2.9)	9 (4.9)	0.438	0.068
Cardiovascular	754 (73.8)	191 (75.8)	417 (71.3)	146 (78.9)	0.085	0.118
Dementia	27 (2.6)	3 (1.2)	16 (2.7)	8 (4.3)	0.127	0.13
Diabetes	122 (11.9)	63 (25.0)	27 (4.6)	32 (17.3)	<0.001	0.401
Epilepsy	66 (6.5)	22 (8.7)	35 (6.0)	9 (4.9)	0.207	0.103
Glaucoma	103 (10.1)	29 (11.5)	54 (9.2)	20 (10.8)	0.565	0.05
Gout	96 (9.4)	43 (17.1)	27 (4.6)	26 (14.1)	<0.001	0.274
Hyperlipidemia	425 (41.6)	169 (67.1)	190 (32.5)	66 (35.7)	<0.001	0.489
Iron deficiency	66 (6.5)	22 (8.7)	27 (4.6)	17 (9.2)	0.021	0.121
Pain	386 (37.8)	105 (41.7)	199 (34.0)	82 (44.3)	0.014	0.141
Psychiatric	266 (26.0)	72 (28.6)	143 (24.4)	51 (27.6)	0.399	0.062
Antipsychotic	16 (1.6)	3 (1.2)	10 (1.7)	3 (1.6)	0.855	0.029
Respiratory	144 (14.1)	44 (17.5)	69 (11.8)	31 (16.8)	0.05	0.107
Rheumatic	406 (39.7)	111 (44.0)	223 (38.1)	72 (38.9)	0.266	0.08
Thyroid	87 (8.5)	20 (7.9)	49 (8.4)	18 (9.7)	0.789	0.042
Sparse	27 (2.6)	8 (3.2)	12 (2.1)	7 (3.8)	0.366	0.069
Socioeconomic						
Education *N (%)*					<0.001	0.337
Basic	139 (13.6)	25 (9.9)	75 (12.8)	39 (21.1)		
Middle	505 (49.4)	147 (58.1)	258 (44.1)	100 (54.1)		
Advanced	379 (37.0)	81 (32.0)	252 (43.1)	46 (24.9)		
Mother tongue *N (%)*					0.005	0.213
German	755 (73.7)	203 (80.2)	415 (70.8)	137 (74.1)		
French	141 (13.8)	29 (11.5)	80 (13.7)	32 (17.3)		
Italian	128 (12.5)	21 (8.3)	91 (15.5)	16 (8.6)		
Smoking *N (%)*					<0.001	0.295
Never	453 (44.2)	73 (28.9)	290 (49.5)	90 (48.6)		
In the past	495 (48.3)	160 (63.2)	253 (43.2)	82 (44.3)		
Active	76 (7.4)	20 (7.9)	43 (7.3)	13 (7.0)		
Alcohol *mean (SD)*	1.12 (1.53)	1.08 (1.40)	1.14 (1.52)	1.14 (1.72)	0.845	0.028
Greater Region *N (%)*					<0.001	0.352
Zurich	125 (12.2)	46 (18.2)	63 (10.8)	16 (8.6)		
Lake Geneva Region	56 (5.5)	12 (4.7)	28 (4.8)	16 (8.6)		
Espace Mitelland	289 (28.2)	68 (26.9)	166 (28.3)	55 (29.7)		
Northwestern Switzerland	310 (30.3)	84 (33.2)	159 (27.1)	67 (36.2)		
Eastern Switzerland	67 (6.5)	9 (3.6)	48 (8.2)	10 (5.4)		
Southern Switzerland	125 (12.2)	21 (8.3)	89 (15.2)	15 (8.1)		
Central Switzerland	52 (5.1)	13 (5.1)	33 (5.6)	6 (3.2)		

Notes: Alcohol in drinks per day. Abbreviations: AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-valvular atrial fibrillation), CRT: Cardiac resynchronization therapy, DOAC: direct-acting oral anticoagulant, Dx: diagnosis, ICD: Implantable cardioverter defibrillator, IQR: interquartile range, PCG: pharmaceutical cost groups, PM: Pacemaker, Prev.: previous history of, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, SD: standard deviation, SMD: standardized mean difference, TIA: transient ischemic attack, VKA: vitamin K antagonist**.**

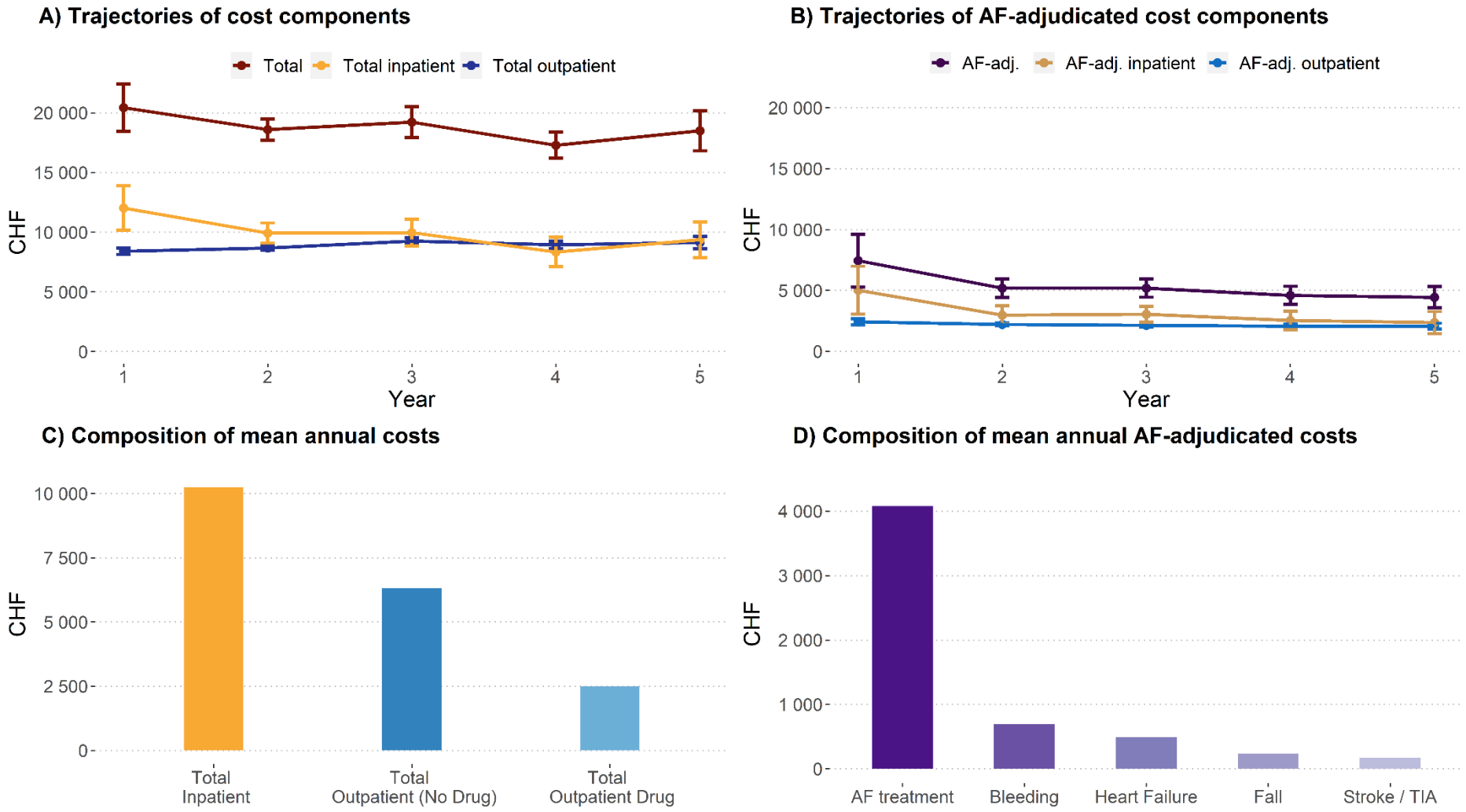


Figure 2. Cost compositions and cost trajectory of different outcome variables. A) Cost trajectory of total, total inpatient and total outpatient costs during five years of follow-up. B) Cost trajectory of AF-adjudicated total, AF-adjudicated total inpatient and AF-adjudicated total outpatient costs during five years of follow-up. C) Composition of mean annual total costs. D) Composition of mean annual total AF-adjudicated costs. AF treatment costs include AF medication, and stroke / TIA costs include stroke / TIA medication. All cost components include inpatient and outpatient services, except for heart failure. Heart failure costs were calculated only from inpatient services.
Notes: An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries.
Abbreviations: adj.: adjudicated, AF: atrial fibrillation.

Patient clusters and their cost trajectories

Three hierarchical analysis-based clusters were identified to be optimal according to the elbow and silhouette methods. **Table 1** shows baseline characteristics by cluster. Cluster-specific Kaplan-Meier curves of overall survival and results of age-adjusted cox regression are depicted in **Figure S5** and **Table S3**.

The first cluster included 253 patients and may be characterised as “cardiovascular dominated” (CV). CV patients displayed many risk factors and indicators for cardiovascular diseases – e.g., a high proportion of past smokers (63%), low proportion of never smokers (29%), high prevalence of diabetes (38%); high cardiovascular drug therapy – i.e. aspirin (41%), statins (90%), and beta-blockers (83%); the highest proportion of prior myocardial infarction (55%). Most patients in this cluster had previous PTCA or CABG (87%). Until the five-year follow-up 55 (21.7%) were deceased and 11 (4.3%) lost.

The second cluster included 586 patients we characterised as “isolated symptomatic” (IS). IS patients were the youngest among the three clusters (mean age: 71). They had the highest occurrence of paroxysmal AF (54%) and presence of AF symptoms (73%). However, they had few medical history items present, few comorbidities, low medication use, and had been diagnosed with AF more recently (mean years: 5.3). Until the 5-year follow-up 36 (6.1%) were deceased and 14 (2.4%) lost.

The third cluster included 185 “severely morbid without cardiovascular disease” (SM) patients. These patients were characterised by the highest occurrence of permanent AF (45%), the highest proportion with a pacemaker (22%), and the highest use of diuretics (90%). Moreover, they featured the lowest presence of AF symptoms (42%), had practically no previous myocardial infarctions (2.2%), and relatively low prevalence of diabetes (21%). The presence of heart failure was similar as in cluster 1 (43% vs. 50%). Until the 5-year follow-up 35 (18.9%) were deceased and 12 (6.5%) lost.

Cost trajectories per cluster are shown in **Figure 3**, and more details on the cost outcomes by cluster in **Table S4** and **Figure S6**. Throughout all cost trajectories, IS patients accrued the lowest costs. Moreover, the pattern in the IS group resembled the overall cost trajectory (**Figure 2**): after an initial high, all costs remained stable across the observation period. Compared to the SM cluster, the CV patients depicted slightly higher AF-adjudicated costs. The results are consistent with the results of the complementary multivariable regression-based cost analysis, which provided estimates of average covariate effects across all patients (**Figures S7-S8**, **Tables S5-S8**).

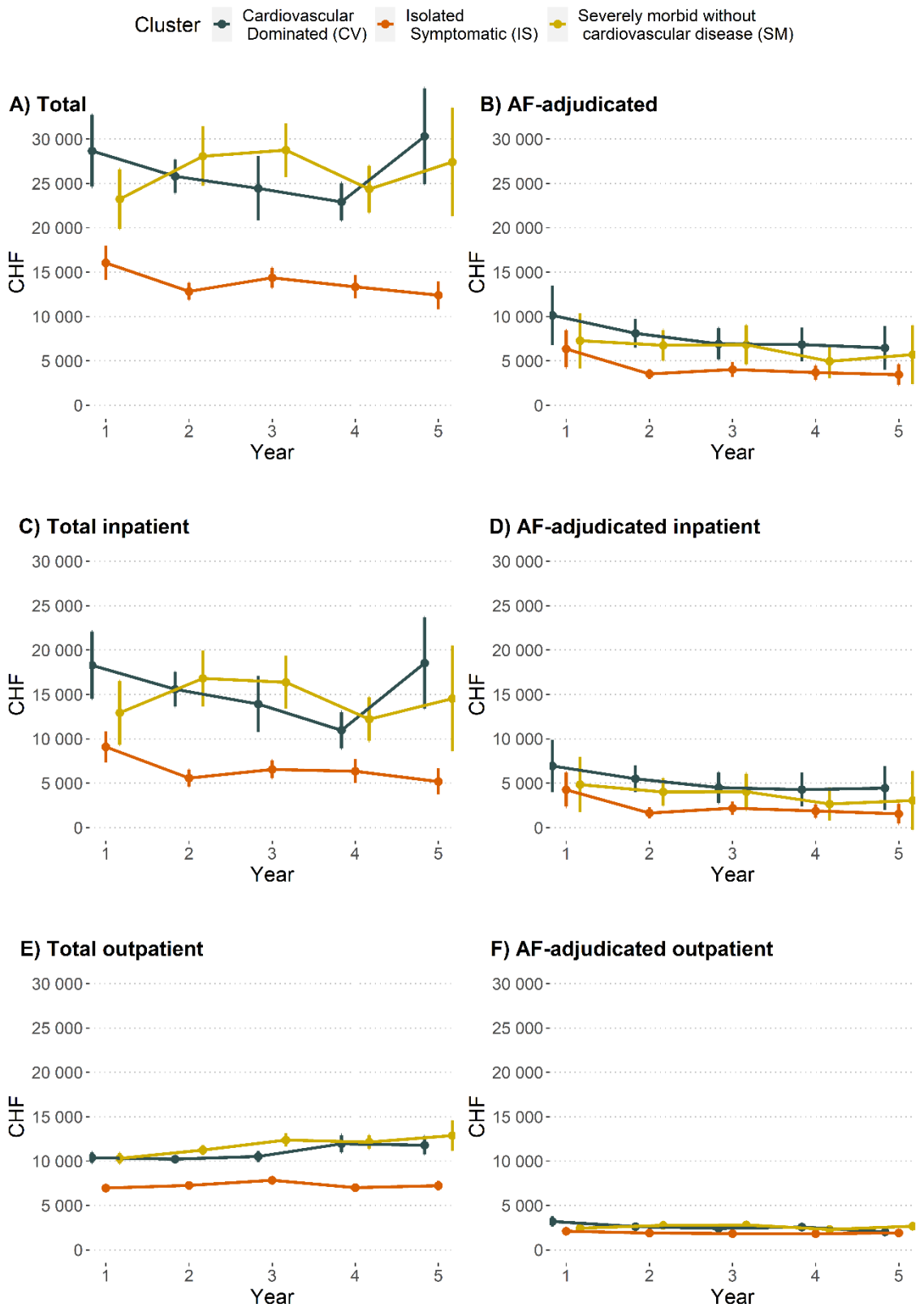


Figure 3. Cost trajectories by patient clusters. Three patient clusters were identified: cardiovascular dominated (CV), isolated symptomatic (IS), and severely morbid without cardiovascular disease (SM). The cost trajectory for different cost outcomes are shown for a follow-up period of five years: A) total costs, B) total AF-adjudicated costs, C) total inpatient costs, D) total AF-adjudicated inpatient costs, E) total outpatient costs, and F) total AF-adjudicated outpatient costs.
Notes: An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries.
Abbreviations: adj.: adjudicated, AF: atrial fibrillation.

Discussion

This study presents recent evidence on real-world AF costs. To our knowledge, it is the first to link data-derived patient clusters with cost trajectories. We observed mean annual and AF-adjudicated healthcare costs to remain stable over several years. Furthermore, among three clinically well-defined patient clusters cost levels differed but were also stable throughout the observation period.

Mean annual total costs amounted to CHF 19,037 (EUR 17,306) per AF patient (~23% of the Swiss Gross Domestic Product per capita), whereof CHF 5,679 (EUR 5,163) were attributable to AF and its complications. Across the entire observation period, these costs remained relatively stable. Inpatient and outpatient costs were of similar magnitude; this applied to both, AF-adjudicated and non-adjudicated costs. This finding is in line with existing literature, where inpatient costs incurred at least half of the total costs.[19–22] A stable proportion across five years, also apparent in AF-adjudicated costs, has not been previously reported.

Of the AF-adjudicated costs, 71.8% were directly related to AF, followed by bleeding, heart failure, fall, and stroke / TIA costs. In the literature so far, AF-related costs were mostly assessed through various excess cost calculations[23] and a clinically-based bottom-up approach was missing. Even though our adjudication algorithm was unable to distinguish between the costs of care episodes for potential AF complications triggered by AF versus by other causes, we believe that this bottom-up approach contributes to a more realistic understanding of AF and related costs. Also, in contrast to most studies,[19,21,24,25] our observed contribution of AF-adjudicated costs to overall healthcare costs was smaller. One reason may be that we analysed prevalent AF patients while the literature focussed mainly on incident patients.

Our analysis yielded three patient clusters, each with distinct characteristics and cost trajectories: CV with rather high costs, SM with similarly high costs, and IS with substantially lower costs. Some attempts to cluster the heterogeneity of AF patients were reported previously, but not linked with cost trajectories.[12,26–28] To facilitate an understanding of observed trajectories, we based our analysis on patient baseline characteristics. The characteristics of the CV patients were roughly comparable to those of the Atherosclerotic Comorbid AF cluster found in two other clusterings[12,26]; while patients in the IS cluster resemble the Younger Paroxysmal AF cluster identified in a Japanese cohort[26] and the Low Comorbidity cluster identified in a US cohort[12]. The SM cluster was not yet reported by other AF clustering studies[12,26].

Costs in the CV and SM clusters were substantial across the full observation period, indicating very high longer-term, AF-adjudicated as well as non-adjudicated costs for these patients. Non-adjudicated costs are likely to confirm additional, substantial comorbidity. In IS patients, all cost categories – including AF-adjudicated costs – were clearly lower. One plausible interpretation may be that AF treatment becomes more expensive in generally sicker

patients and should therefore be managed and contained early on. This remains to be confirmed by longer-term cost analyses of different AF treatment strategies in future research. Moreover, future work should confirm the costs of AF in comparisons with the general population.

The prospective cohort study patients we report on differ from the patient populations underlying recent AF cost studies in four ways, with implications for the interpretation of the results. Firstly, most studies to-date relied on administrative databases only[21,25,29]; secondly, they were often retrospective[19,21,25,27]; and thirdly, had short follow-up times between 0.5 to 3 years[19,24]. By combining clinical and health insurance claims data prospectively, we add information on the longer-term healthcare costs of AF patients. Fourthly, we examined prevalent patients with varying disease duration (including 13% enrolled within six months after first AF diagnosis), providing real-world insights into the longer-term cost impact of AF in a substantially wider spectrum of AF patients than previous studies. Differences in cultural settings, healthcare organisation and price structures limit the direct transferability of our Swiss cost results to other countries. However, we expect the relative role of different cost components and types of resource consumption to be comparable in socioeconomically similar countries. This should be particularly true for Europe, given the application of the European Society of Cardiology AF guideline also in Switzerland[30]. The characterisation of different patient clusters and their characteristics is also likely to be of relevance beyond Switzerland.

Several limitations inherent to our study require discussion. First, patients in Swiss-AF are heterogeneous. We tried to account for the heterogeneity with the clustering method, and covariate selection was based on the current literature as well as discussions with clinicians from the Swiss-AF study centres. Second, the study population is not fully representative of all Swiss AF patients. However, efforts were made to achieve a high degree of representativeness of diagnosed Swiss AF patients. Inclusion criteria were wide, ensuring a similar degree of diversity as found in daily clinical routine. Patients were enrolled in 14 clinical centres all over the country. Small centres and primary care physicians were invited to contribute patients. Third, given deductible levels in the Swiss statutory health insurance system, the possibility that not all claims were handed in for reimbursement exists, which may have led to an underestimation of true costs. However, as AF patients have substantial costs, it is rather unlikely that claims were not submitted. A fourth limitation lies in the adjudication algorithm, which was developed carefully and considered clinical information together with claims data. Still, it may not fully reflect the true causation of costs by AF and its complications, and could not distinguish which specific complications, e.g. strokes, were truly due to AF or not.

In conclusion, this study analysed real-world AF costs, patient clusters and their cost trajectories. We observed mean annual AF-adjudicated costs of roughly CHF 6,000 (EUR 5,500) per patient and stable relative contributions of different cost categories during five

years. Three well-defined patient clusters were identified using a hierarchical clustering method: cardiovascular, isolated-symptomatic, and severely morbid without cardiovascular disease. The cost levels for AF-adjudicated and overall healthcare costs depended on patient cluster, but interestingly also remained stable over time. Cardiovascular patients accrued the highest costs, severely morbid patients without cardiovascular disease featured similarly high costs, while isolated-symptomatic patients had substantially lower costs. This suggests that AF becomes more expensive to treat in sicker patients and should therefore be managed early on. These insights may help clinicians and payers to develop an early understanding of the magnitude of to be expected AF-related healthcare costs.

Funding

This work is supported by grants of the Swiss National Science Foundation (grant numbers 105318_189195 / 1, 33CS30_148474, 33CS30_177520, 32473B_176178, and 32003B_197524), the Swiss Heart Foundation, the Foundation for Cardiovascular Research Basel (FCVR), and the University of Basel.

Acknowledgements

We thank Lukas Kauer from the health insurance CSS, Pascal Godet from the health insurance Sanitas, Beat Brüngger and Andri Signorell from the health insurance Helsana, and the health insurance KPT for providing the claims data for this study. The full list of Swiss-AF investigators is provided in the supplementary material.

Contributors

All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

Disclosures

Dr. Auricchio is a consultant with Abbott, Boston Scientific, Backbeat, Cairdac, Corvia, EP Solutions, Medtronic, Microport CRM, Philips, XSpline; he participates in clinical trials sponsored by Boston Scientific, Medtronic, Microport CRM, Philips and XSpline; and has intellectual properties assigned to Boston Scientific, Biosense Webster, and Microport CRM. Dr. Beer reports grant support from the Swiss National Foundation of Science, The Swiss Heart Foundation and the Stiftung Kardio; grant support, speakers- and consultation fees to the institution from Bayer, Sanofi and Daichii Sankyo. Dr. Conen received consulting fees from Roche Diagnostics, and speaker fees from Servier and BMS/Pfizer, all outside of the current work. Dr. Kühne reports personal fees from Bayer, personal fees from Böhringer Ingelheim, personal fees from Pfizer BMS, personal fees from Daiichi Sankyo, personal fees from Medtronic, personal fees from Biotronik, personal fees from Boston Scientific, personal fees from Johnson&Johnson, personal fees from Roche, grants from Bayer, grants from Pfizer, grants from Boston Scientific, grants from BMS, grants from Biotronik, grants from Daiichi Sankyo. Dr. Moschovitis has received consultant fees for taking part to advisory boards from Novartis, Boehringer Ingelheim, Bayer, Astra Zeneca and Daiichi Sankyo, all outside of the presented work. Dr. Müller reports fellowship and training support from Biotronik, Boston Scientific, Medtronic, Abbott/St. Jude Medical, and Biosense Webster; speaker honoraria from Biosense Webster, Medtronic, Abbott/St. Jude Medical, AstraZeneca, Daiichi Sankyo, Biotronik, MicroPort, Novartis, and consultant honoraria for Biosense Webster, Medtronic, Abbott/St. Jude

Medcal, and Biotronik. Dr. Reichlin has received research grants from the Swiss National Science Foundation, the Swiss Heart Foundation, and the sitem insel support fund, all for work outside the submitted study. Speaker/consulting honoraria or travel support from Abbott/SJM, Astra Zeneca, Brahms, Bayer, Biosense-Webster, Biotronik, Boston-Scientific, Daiichi Sankyo, Medtronic, Pfizer-BMS and Roche, all for work outside the submitted study. Support for his institution's fellowship program from Abbott/SJM, Biosense-Webster, Biotronik, Boston-Scientific and Medtronic for work outside the submitted study. Dr. Schwenkglenks reports grants from Swiss National Science Foundation, for the conduct of the study; grants from Amgen, grants from MSD, grants from Novartis, grants from Pfizer, grants from Roche, grants and personal fees from BMS, personal fees from Sandoz, all outside the submitted work. Dr. Serra-Burriel reports grants from the European Commission outside of the present work. Dr. Sticherling has received speaker honoraria from Biosense Webster and Medtronic and research grants from Biosense Webster, Daiichi-Sankyo, and Medtronic. The remaining authors have nothing to disclose.

Ethics and Data availability statement

The Swiss-AF study protocol was approved by the local ethics committee (Ethikkommission Nordwest- und Zentralschweiz, 2014-067, PB_2016-00793), and written informed consent was obtained from each participant. The patient informed consent forms state that the data, containing personal and medical information, are exclusively available for research institutions in an anonymized form and are not allowed to be made publicly available. Researchers interested in obtaining the data for research purposes can contact the Swiss-AF scientific lead. Contact information is provided on the Swiss-AF website (http://www.swissaf.ch/contact.htm). Authorization of the responsible ethics committee is mandatory before the requested data can be transferred to external research institutions.

References

1. Patel, N. J., Atti, V., Mitrani, R. D., Viles-Gonzalez, J. F. & Goldberger, J. J. Global rising trends of atrial fibrillation: a major public health concern. *Heart* **104**, 1989–1990 (2018).
2. Krijthe, B. P. *et al.* Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *European Heart Journal* **34**, 2746–2751 (2013).
3. Miyasaka, Y. *et al.* Secular Trends in Incidence of Atrial Fibrillation in Olmsted County, Minnesota, 1980 to 2000, and Implications on the Projections for Future Prevalence. *Circulation* **114**, 119–125 (2006).
4. Conen, D. *et al.* Risk of Death and Cardiovascular Events in Initially Healthy Women With New-Onset Atrial Fibrillation. *JAMA* **305**, 2080–2087 (2011).

5. Stewart, S., Murphy, N. F., Walker, A., McGuire, A. & McMurray, JJ. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. *Heart* **90**, 286–292 (2004).

6. Wodchis, W. P., Bhatia, R. S., Leblanc, K., Meshkat, N. & Morra, D. A Review of the Cost of Atrial Fibrillation. *Value in Health* **15**, 240–248 (2012).

7. Ball, J., Carrington, M. J., McMurray, J. J. V. & Stewart, S. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *International Journal of Cardiology* **167**, 1807–1824 (2013).

8. Wolowacz, S. E., Samuel, M., Brennan, V. K., Jasso-Mosqueda, J. G. & van Gelder, I. C. The cost of illness of atrial fibrillation: a systematic review of the recent literature. *Europace* **13**, 1375–1385 (2011).

9. Wong, C. X., Brooks, A. G., Leong, D. P., Roberts-Thomson, K. C. & Sanders, P. The Increasing Burden of Atrial Fibrillation Compared With Heart Failure and Myocardial Infarction: A 15-Year Study of All Hospitalizations in Australia. *Arch Internal Medicine* **172**, 739–741 (2012).

10. Bhat, A. *et al.* Drivers of hospitalization in atrial fibrillation: A contemporary review. *Heart Rhythm* **17**, 1991–1999 (2020).

11. Steinberg, B. A. *et al.* Drivers of hospitalization for patients with atrial fibrillation: Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *American Heart Journal* **167**, 735-742.e2 (2014).

12. Inohara, T. *et al.* Association of of Atrial Fibrillation Clinical Phenotypes With Treatment Patterns and Outcomes: A Multicenter Registry Study. *JAMA Cardiology* **3**, 54–63 (2018).

13. Lip, G., Nieuwlaat, R., Pisters, R., Lane, D. & Crijns, H. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* **137**, 263–272 (2010).

14. Conen, D. *et al.* Design of the Swiss Atrial Fibrillation Cohort Study (Swiss-AF): structural brain damage and cognitive decline among patients with atrial fibrillation. *Swiss Medical Weekly* **147**, (2017).

15. Conen, D. *et al.* Relationships of Overt and Silent Brain Lesions With Cognitive Function in Patients With Atrial Fibrillation. *J Am Coll Cardiol* **73**, 989–999 (2019).

16. SwissDRG. https://www.swissdrg.org/de/akutsomatik/swissdrg-system-1002021 (2021).

17. Huber, C. A., Szucs, T. D., Rapold, R. & Reich, O. Identifying patients with chronic conditions using pharmacy data in Switzerland: an updated mapping approach to the classification of medications. *BMC Public Health* **13**, 1–10 (2013).

18. Hastie, T., Tibshirani, R. & Friedman, J. *Springer Series in Statistics The Elements of Statistical Learning Data Mining, Inference, and Prediction*.

19. Reinhold, T., Lindig, C., Willich, S. N. & Brüggenjürgen, B. The costs of atrial fibrillation in patients with cardiovascular comorbidities--a longitudinal analysis of German health insurance data. *Europace* **13**, 1275–1280 (2011).

20. Zoni-Berisso, M. *et al.* The cost of atrial fibrillation in Italy: a five-year analysis of healthcare expenditure in the general population. From the Italian Survey of Atrial Fibrillation Management (ISAF) study. *European Review for Medical and Pharmacological Sciences* **21**, 175–183 (2017).

21. Kim, M., Lin, J., Hussein, M., Kreilick, C. & Battleman, D. Cost of atrial fibrillation in United States managed care organizations. *Advances in Therapy* **26**, 847–857 (2009).

22. Ringborg, A. *et al.* Costs of atrial fibrillation in five European countries: Results from the Euro Heart Survey on atrial fibrillation. *Europace* **10**, 403–411 (2008).

23. Becker, C. Cost-of-illness studies of atrial fibrillation: methodological considerations. *Expert Review of Pharmacoeconomics & Outcomes Research* **14**, 661–684 (2014).

24. Johnsen, S. P., Dalby, L. W., Täckström, T., Olsen, J. & Fraschke, A. Cost of illness of atrial fibrillation: a nationwide study of societal impact. *BMC Health Services Research* **17**, 1–8 (2017).

25. Kim, M., Johnston, S., Chu, B., Dalal, M. R. & Schulman, K. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. *Circulation. Cardiovascular Quality and Outcomes* **4**, 313–320 (2011).

26. Inohara, T. *et al.* A Cluster Analysis of the Japanese Multicenter Outpatient Registry of Patients With Atrial Fibrillation. *The American Journal of Cardiology* **124**, 871–878 (2019).

27. Suzuki, S. *et al.* Identifying risk patterns in older adults with atrial fibrillation by hierarchical cluster analysis: A retrospective approach based on the risk probability for clinical events. *IJC Heart & Vasculature* **37**, 100883 (2021).

28. Karwath, A. *et al.* Redefining β-blocker response in heart failure patients with sinus rhythm and atrial fibrillation: a machine learning cluster analysis. *The Lancet* **398**, 1427–1435 (2021).

29. Bennell, M. C. *et al.* Identifying predictors of cumulative healthcare costs in incident atrial fibrillation: A population-based study. *J Am Heart Assoc* **4**, (2015).

30. Hindricks, G. *et al.* 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *European Heart Journal* **42**, 373–498 (2021)

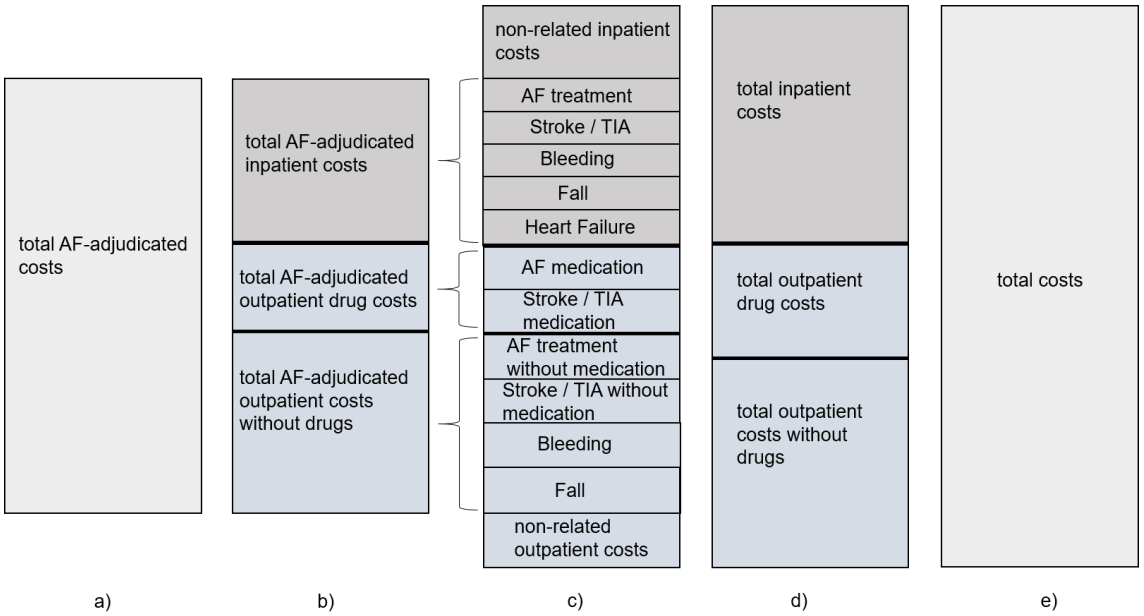


Figure S1. Outcome definition scheme. Main outcome of interest was (a) total AF-adjudicated costs, which is (b) the sum of total AF-adjudicated inpatient costs and total AF-adjudicated outpatient costs. Total inpatient costs (d) are either adjudicated into five groups or non-related (c), while total outpatient costs (d) are either adjudicated into six groups or non-related (c). The sum of all costs account for total costs (e).

Table S1. Baseline characteristics of patients with and without claims data.

		Claims	No claims		
	n	1 024	1 391	p	SMD
Characteristics					
Age *mean (SD)*		73.00 (8.17)	73.42 (8.61)	0.232	0.049
Sex Female *N (%)*		283 (27.6)	379 (27.2)	0.868	0.009
BMI *median [IQR]*		26.98 [24.43, 30.52]	26.99 [24.34, 30.25]	0.849	0.001
Type of AF *N (%)*				0.536	0.046
Paroxysmal		471 (46.0)	611 (43.9)		
Permanent		243 (23.7)	353 (25.4)		
Persistent		310 (30.3)	427 (30.7)		
AF symptoms *N(%)*		632 (61.8)	862 (62.0)	0.964	0.004
Years since AF Dx *mean (SD)*		6.33 (7.91)	6.06 (7.49)	0.399	0.035
CHA_2DS_2-VASc score *mean (SD)*		3.44 (1.73)	3.50 (1.68)	0.411	0.034
Prev. Major Bleeding *N (%)*		91 (6.5)	61 (6.0)	0.617	0.024
Previous Stroke or TIA *N (%)*		212 (20.7)	267 (19.2)	0.396	0.037
Prev. Sys. Embolism *N (%)*		67 (4.8)	60 (5.9)	0.299	0.046
Prev. Heart Failure *N (%)*		254 (24.8)	372 (26.8)	0.306	0.044
Prev. Myocardial Inf. *N (%)*		229 (16.5)	161 (15.7)	0.665	0.02
Diabetes *N (%)*		176 (17.2)	245 (17.6)	0.827	0.011
Hypertension *N (%)*		692 (67.6)	995 (71.5)	0.041	0.086
Renal Failure *N (%)*		213 (20.8)	297 (21.4)	0.784	0.013
Sleep Apnea *N (%)*		206 (14.8)	154 (15.0)	0.927	0.006
Prev. PTCA *N (%)*		335 (24.1)	235 (22.9)	0.548	0.027
Prev. CABG *N (%)*		132 (9.5)	105 (10.3)	0.579	0.026
Previous Electroconversion *N (%)*		355 (34.7)	506 (36.4)	0.410	0.036
Prev. PVI *N (%)*		279 (20.1)	210 (20.5)	0.825	0.011
Medication *N (%)*					
Antiplatelets		53 (5.2)	97 (7.0)	0.085	0.075
Aspirin		171 (16.7)	233 (16.8)	1.000	0.001
Statins		529 (51.7)	665 (47.8)	0.067	0.077
Diuretics		459 (44.8)	671 (48.2)	0.105	0.068
Betablockers		726 (70.9)	972 (69.9)	0.619	0.022
Digoxin		39 (3.8)	70 (5.0)	0.183	0.060
VKA		414 (40.4)	537 (38.6)	0.387	0.037
DOAC		517 (50.5)	713 (51.3)	0.739	0.015
Implanted Device *N (%)*				0.909	0.051
No device		831 (81.2)	1103 (79.3)		
Loop recorder		10 (1.0)	14 (1.0)		
PM		121 (11.8)	187 (13.4)		
CRT		12 (1.2)	17 (1.2)		
ICD		31 (3.0)	44 (3.2)		
CRT-ICD		19 (1.9)	26 (1.9)		
Socioeconomic					
Mother tongue *N (%)*				0.075	0.094
German		755 (73.7)	1 075 (77.7)		
French		141 (13.8)	163 (11.8)		
Italian		128 (12.5)	145 (10.5)		
Education *N (%)*				0.086	0.091
Basic		139 (13.6)	149 (10.7)		
Middle		505 (49.4)	692 (49.9)		
Advanced		379 (37.0)	547 (39.4)		
Smoking *N (%)*				0.882	0.021

Never	453 (44.2)	606 (43.6)		
In the past	495 (48.3)	686 (49.3)		
Active	76 (7.4)	99 (7.1)		
Alcohol *mean (SD)*	1.12 (1.53)	1.04 (1.48)	0.15	0.059
Greater Region			<0.001	0.293
Zurich	56 (5.5)	103 (7.4)		
Lake Geneva Region	289 (28.2)	275 (19.9)		
Espace Mittelland	310 (30.3)	568 (41.1)		
Northwestern Switzerland	67 (6.5)	85 (6.1)		
Eastern Switzerland	125 (12.2)	141 (10.2)		
Southern Switzerland	125 (12.2)	124 (9.0)		
Central Switzerland	52 (5.1)	87 (6.3)		

Notes: Alcohol in drinks per day. Abbreviations: AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-valvular atrial fibrillation), CRT: Cardiac resynchronization therapy, DOAC: direct-acting oral anticoagulant, Dx: diagnosis, ICD: Implantable cardioverter defibrillator, IQR: interquartile range, PCG: pharmaceutical cost groups, PM: Pacemaker, Prev.: previous history of, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, SD: standard deviation, SMD: standardized mean difference, TIA: transient ischemic attack, VKA: vitamin K antagonist.

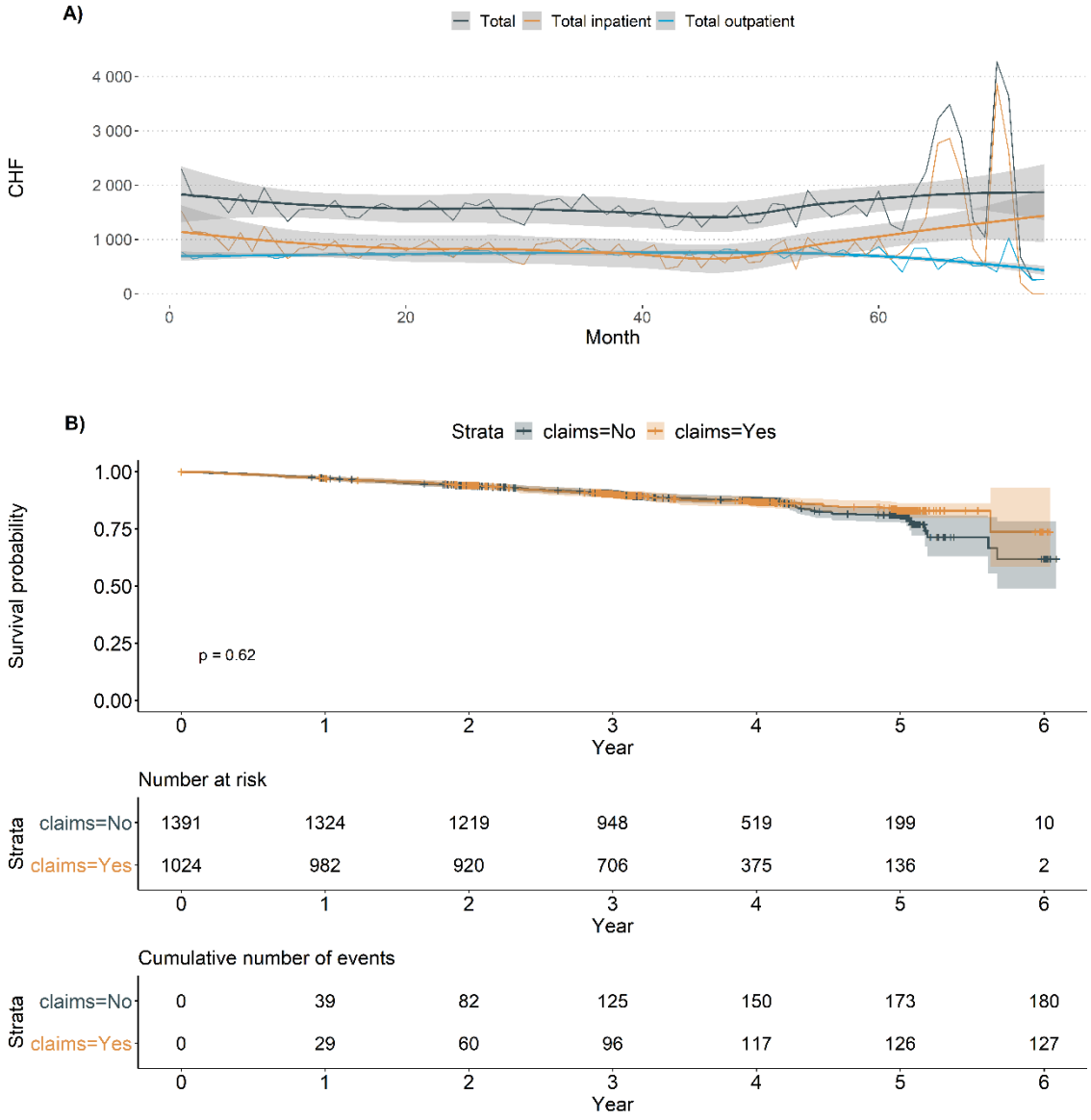


Figure S2. Trajectory of monthly costs and Kaplan-Meier curve. A) Temporal evolution of monthly costs for patients with claims data across all follow-ups. B) Overall survival and follow-up for all Swiss-AF patients: Kaplan-Meier curve, risk table, and cumulative number of events. *Notes:* median follow-up: 3.24 years; total patient-years of follow-up: 8 343.10. An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries.

Table S2. Annual costs in Swiss Francs (CHF) by cost component.

Cost component	*Median [IQR]*	*Mean (SD)*
Total	4 518 [825, 11 771]	19 037 (59 998)
Total inpatient	0 [0, 0]	10 235 (56 327)
Total outpatient drugs	508 [0, 2 956]	2 495 (7 382)
Total outpatient without drugs	2 282 [59, 7 225]	6 307 (13 154)
Total AF-adj.	400 [0, 3 213]	5 679 (36 135)
Total AF-adj. inpatient	0 [0, 0]	3 458 (35 188)
Total AF-adj. outpatient drugs	0 [0, 250]	591 (1 392)
Total AF-adj. outpatient without drugs	0 [0, 1 251]	1 630 (6 899)
Total AF treatment	226 [0, 2 773]	4 078 (28 640)
Total stroke or TIA	0 [0, 0]	174 (9 124)
Total bleeding	0 [0, 0]	696 (17 462)
Total fall	0 [0, 0]	237 (4 434)
Total heart failure	0 [0, 0]	494 (8 469)

Notes: Heart failure costs include inpatient services only. An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries. Abbreviations: adj.: adjudicated, AF: atrial fibrillation, IQR: interquartile range, SD: standard deviation, TIA: transient ischemic attack.

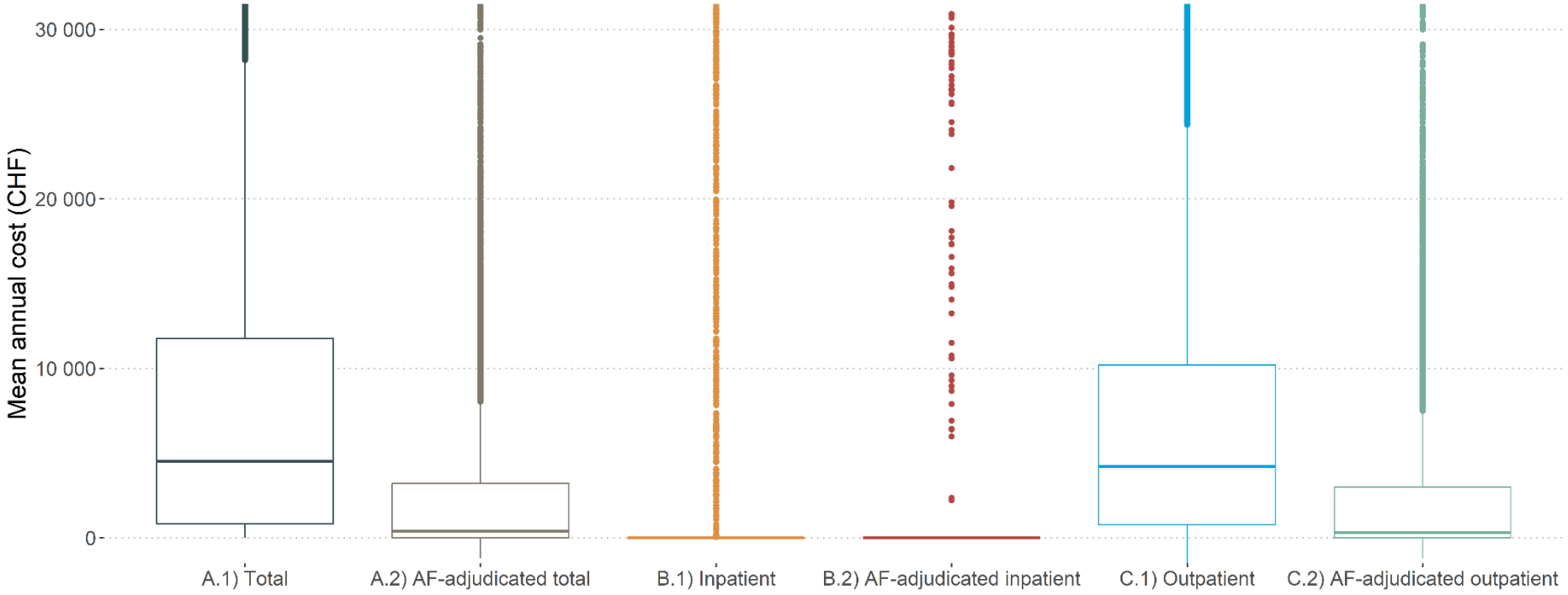


Figure S3. Boxplot distribution of mean annual costs by cost outcome.
Notes: An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries.

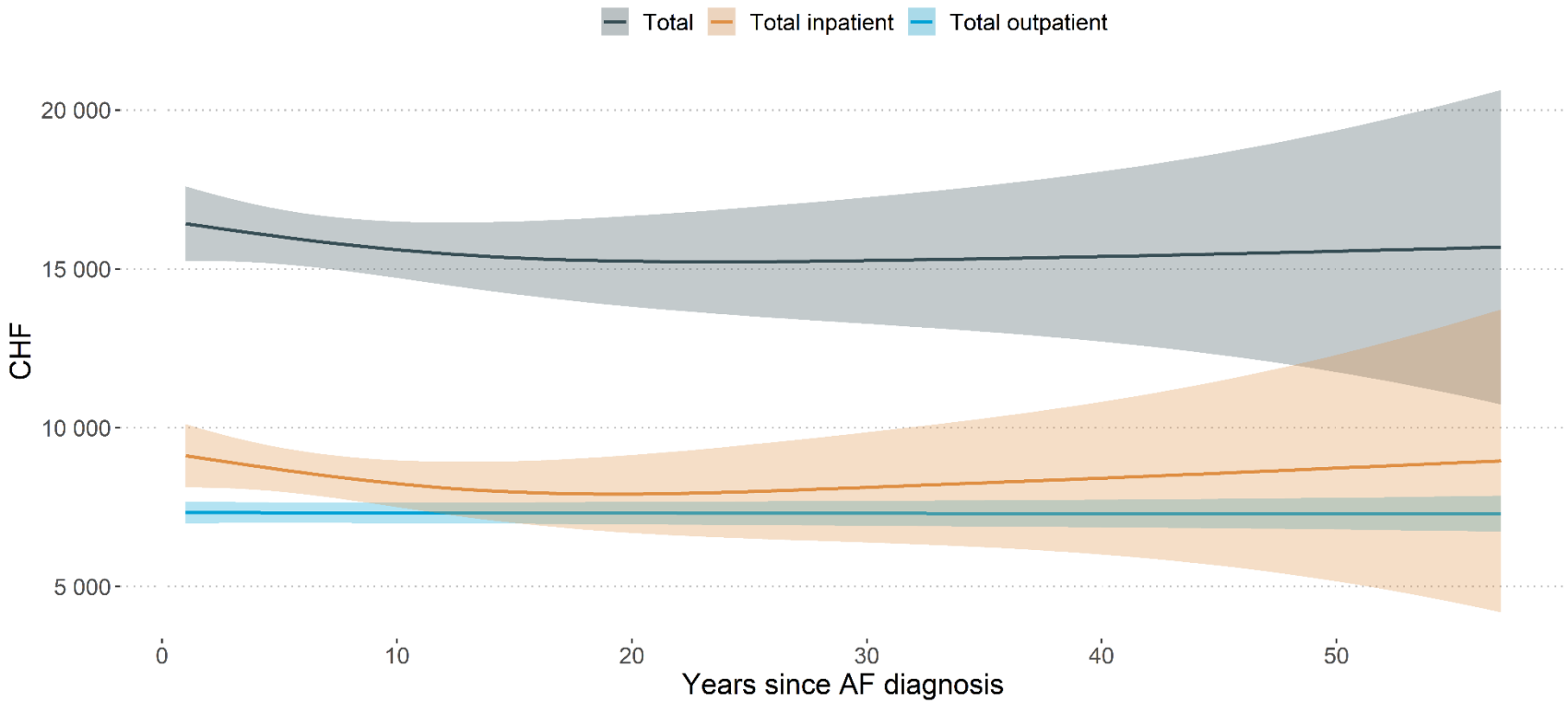


Figure S4. Trajectory of mean annual costs since AF diagnosis.
Notes: An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries.

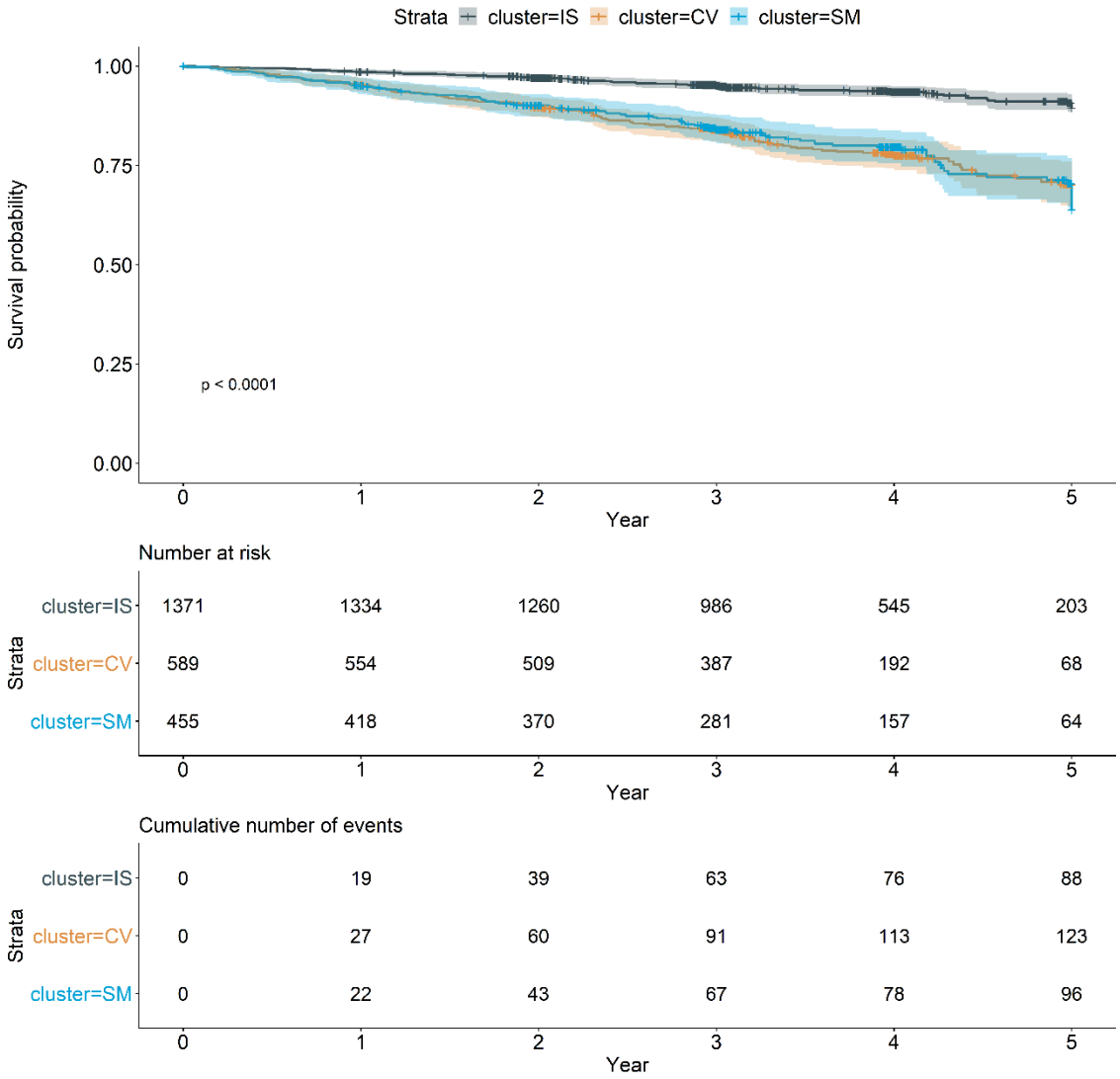


Figure S5. Kaplan-Meier curve, risk table and cumulative number of events by patient cluster. Cluster: CV = Cardiovascular Dominated, IS = Isolated Symptomatic, SM = severely morbid without cardiovascular disease.

Table S3. Hazard Ratio of the Cox Regression. Reference cluster = Isolated Symptomatic (IS).

	HR
Age	1.09 [1.06, 1.11]
Time since Diagnosis	1.01 [0.99, 1.03]
Cluster: Cardiovascular Dominated (CV)	2.75 [1.79, 4.23]
Cluster: Severely morbid without cardiovascular disease (SM)	2.10 [1.30, 3.39]
Observations	1 016
R^2	0.081

Table S4. Annual costs (CHF) of AF-adjudicated cost groups by patient cluster.

	Cardiovascular Dominated (CV)		Isolated Symptomatic (IS)		Severely morbid without cardiovascular disease (SM)	
Cost group	*Median [IQR]*	*Mean (SD)*	*Median [IQR]*	*Mean (SD)*	*Median [IQR]*	*Mean (SD)*
Total AF treatment	702 [0, 3 218]	5 146 (36 440)	0 [0, 2 423]	3 637 (25 289)	791 [0, 3 078]	4 153 (27 545)
Total stroke / TIA	0 [0, 0]	170 (5 379)	0 [0, 0]	94 (7 010)	0 [0, 0]	447 (16 378)
Total bleeding	0 [0, 0]	1 512 (28 820)	0 [0, 0]	371 (10 593)	0 [0, 0]	713 (16 142)
Total fall	0 [0, 0]	252 (3 699)	0 [0, 0]	229 (4 911)	0 [0, 0]	247 (3 547)
Total heart failure	0 [0, 0]	1 104 (12 308)	0 [0, 0]	102 (3 513)	0 [0, 0]	1 005 (12 834)

Notes: Heart failure costs include inpatient services only. An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries. Abbreviations: AF: atrial fibrillation, IQR: interquartile range, SD: standard deviation, TIA: transient ischemic attack.

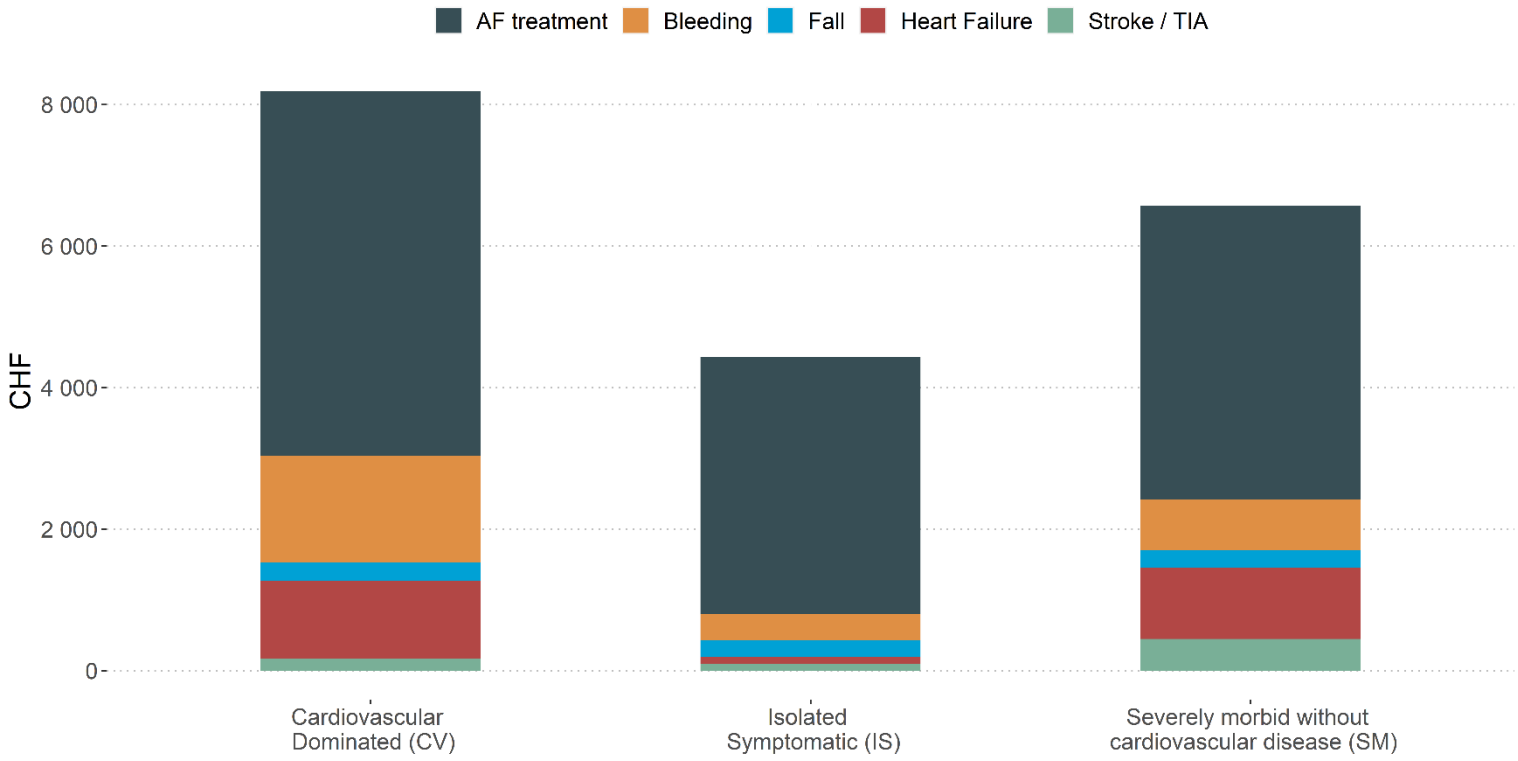


Figure S6. Mean annual costs of adjudicated cost group by patient cluster. Heart failure costs include inpatient services only. *Notes:* An exchange rate of EUR 1.0 = CHF 1.1 can be used to convert the costs into Euros to facilitate comparison with other countries. Abbreviations: AF: atrial fibrillation, TIA: transient ischemic attack.

Table S5: Hierarchical Clustering method.

Hierarchical Clustering

The underlying logic of hierarchical clustering is to create a hierarchy of clusters with the highest possible degree of similarity within the clusters and the highest possible degree of dissimilarity between the clusters.[1,2] In our case, the purpose was to classify AF patients into different types. The clusters were created following a divisive, top-down, approach. This implies that all observations were first classified into one cluster and then recursively split into binary subgroups. As the measure of similarity we employed the Gower's distance, and the optimal number of clusters was simultaneously decided with the elbow and silhouette methods.[1,2]

Gower's distance

The Gower's distance is a comprehensive similarity measure in which for each feature $k = 1, \dots, p$ we create a score that ranges between 0 and 1, $s_{ijk} \in [0,1]$. If two observations (x_i, x_j) have a similar feature, k, then the score for that feature will be approaching 1, while 0 if the contrary occurs. Gower's distance allows for variables with different measurement levels, k. For numeric variables the score is $s_{ijk} = 1 - |x_{i,k} - x_{j,k}|/R_k$, where R_k is the difference between the sample's maximum and minimum value for variable k. For factor variables, the score takes value 1 if the features match and 0 otherwise, $s_{ijk} = 1\{x_{i,k} = x_{j,k}\}$. The Gower's distance between two observations (x_i, x_j) is then the average of the scores.

$$S_{i,j} = \frac{\sum_{k=1}^{p} s_j(x_1, x_2)}{p}$$

Our choice of Gower's distance was motivated by the nature of our dataset, where both quantitative and qualitative features of patients are present, allowing us to combine them into a simple numeric distance metric.

Elbow method

The elbow method is a heuristic that computes the intra-cluster variation (also known as within-cluster sum of squares, WSS) for each of the potential cluster groupings. The location of the bend or "knee", meaning the inflexion point, is usually chosen as the indicator of the appropriate number of clusters (see Figure panel A below).

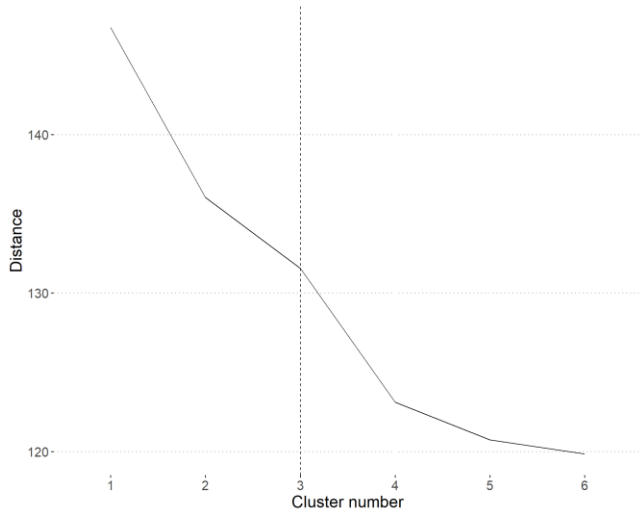
Silhouette method

The silhouette method computes a silhouette value that considers how close each observation is to its own cluster compared to the others and the value ranges from -1 to 1,

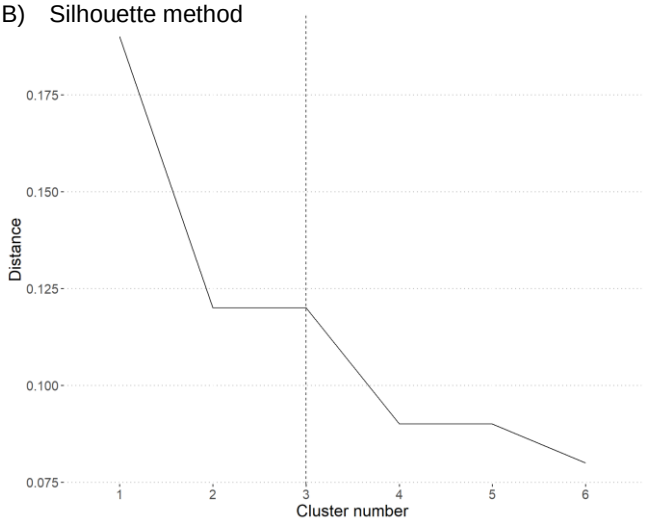
with higher values indicating better clustering for each iteration on the number of clusters (see Figure panel B below).

In case of contradiction of these methods, the clinically more plausible solution would have been selected.

A) Elbow method



B) Silhouette method



References:

[1] Hastie, T., Tibshirani, R. & Friedman, J. Springer Series in Statistics The Elements of Statistical Learning Data Mining, Inference, and Prediction.

[2] James, G., Witten, D., Hastie, T., & Tibshirani, R. (2013). An introduction to statistical learning (Vol. 112, p. 18). New York: springer.

Table S6: Covariates associated with AF costs.

Introduction

Complementary to the analysis in the main manuscript we aimed to evaluate the covariates associated with costs. For this, a multivariable regression-based analysis was run.

Methods

The covariates associated with costs were assessed using multivariable generalised linear models with quasi-poisson link distribution. Our model choice was motivated by the expected skewness of the outcome distributions[1,2] and by the straightforward interpretation of the exponentiated coefficients as rate ratios (RR), i.e. relative increases in cost.[3-6] Additional to the covariates listed in the manuscript we also considered further relevant comorbidities not collected by the Swiss-AF study. These were derived from the drug utilisation present in the claims data, using the pharmaceutical cost groups (PCGs) method[7]: acid related disorders, bone diseases, cancer, dementia, epilepsy, respiratory illness, rheumatic conditions, glaucoma, gout, iron deficiency, chronic pain, psychiatric diseases, use of antipsychotic drugs, thyroid disease, other rare diseases.

Several sensitivity analyses were carried out to assess the robustness of the results. As they are direct correlates of costs, covariates representing anticoagulation, other medication, treatment and implanted devices were left out to assess the isolated impact of medical history. In another sensitivity analysis, all but medical history predictors were included to assess treatment factors. Moreover, a gamma distribution was assumed instead of the quasi-poisson link to confirm appropriateness of the model choice. And last, the influence of the study centres as well as insurance characteristics on regression results were checked.

Results

Multivariable regression-based associations between covariates and AF-adjudicated costs are shown in **Figure S7**, while all numerical estimates are depicted in **Table S6**. The covariate patterns for AF-adjudicated total and AF-adjudicated inpatient costs were similar; however, associations with AF-adjudicated outpatient costs differed at some points. The significant effects for all three AF-adjudicated cost types include active smoking (RR 1.67; RR 1.77; RR 1.3), and AF symptoms (RR 1.43; RR 1.66; RR 1.08). An increase in AF-adjudicated total and AF-adjudicated inpatient costs arose also from permanent AF (RR 1.36; RR 1.61), previous myocardial infarction (RR 1.37; RR 1.66), and previous heart failure (RR 1.2; RR 1.43). In contrast, AF-adjudicated outpatient costs were significantly driven by the presence of any cardiac device (PM RR 1.22; ICD RR

1.76; CRT/CRT-ICD RR 1.62), and anticoagulation (VKA RR 1.45; DOAC RR 1.36). Two covariates were significantly associated with lower AF-adjudicated outpatient costs: history of stroke or TIA (RR 0.67), and being female (RR 0.77). The results of the sensitivity analyses can be found in **Figure S8**, and **Table S6-S8**. All results remained stable when insurance characteristics were additionally included.

Discussion

In our patient population, the factors most strongly associated with higher AF-adjudicated costs were active smoking and AF symptoms. Further associations were found to differ between AF-adjudicated inpatient versus outpatient costs. Estimates in the literature so far focussed on drivers of hospitalisation and total costs only.[8–11] Our estimates of a positive RR for permanent AF, BMI, and myocardial infarction are in line with the literature for AF-adjudicated inpatient and AF-adjudicated total costs. Unsurprisingly, medication like VKA or DOAC increased AF-adjudicated outpatient costs but had a small effect on AF-adjudicated inpatient costs. The association between presence of cardiac devices (pacemaker, ICD, and CRT) and AF-adjudicated outpatient costs was presumably due to routine controls and maintenance. Our estimates of sex-specific AF costs were inconclusive, in line with previous studies.[8,12]

Limitations for this analysis include the unfortunate case that we could not acquire insurance characteristics from one insurer and decided to only consider these in a sensitivity analysis. However, there was no indication of a distortion of our results. Another limitation lies therein, that some covariates were correlated and not all conceivable covariates were measured. This limited our ability to identify isolated effects. Even though different sensitivity analyses were run to check the robustness of the results, the observed associations should be interpreted cautiously.

References

1. Venables, W. N. & Ripley, B. D. *Modern Applied Statistics with S* . (Springer, 2002). doi:https://doi.org/10.1007/978-0-387-21706-2.
2. Miquel, L. *et al.* Alcohol, tobacco and health care costs: a population-wide cohort study (n = 606 947 patients) of current drinkers based on medical and administrative health records from Catalonia. *European Journal of Public Health* **28**, 674–680 (2018).
3. Mihaylova, B., Briggs, A., O'Hagan, A. & Thompson, S. G. Review of Statistical Methods for Analysing Healthcare Resources and Costs. *Health Economics* **20**, 897 (2011).
4. Austin, P., Ghali, W. A. & Tu, J. v. A comparison of several regression models for analysing cost of CABG surgery. *Statistics in Medicine* **22**, 2799–2815 (2003).
5. Bennell, M. C. *et al.* Identifying predictors of cumulative healthcare costs in incident atrial fibrillation: A population-based study. *J Am Heart Assoc* **4**, (2015).

6. Blough, D. K. & Ramsey, S. D. Using generalized linear models to assess medical care costs. *Health Services and Outcomes Research Methodology* **1**, 185–202 (2000).

7. Huber, C. A., Szucs, T. D., Rapold, R. & Reich, O. Identifying patients with chronic conditions using pharmacy data in Switzerland: an updated mapping approach to the classification of medications. *BMC Public Health* **13**, 1–10 (2013).

8. Bhat, A. *et al.* Drivers of hospitalization in atrial fibrillation: A contemporary review. *Heart Rhythm* **17**, 1991–1999 (2020).

9. Steinberg, B. A. *et al.* Drivers of hospitalization for patients with atrial fibrillation: Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *American Heart Journal* **167**, 735-742.e2 (2014).

10. DeVore, A. D. *et al.* Hospitalizations in patients with atrial fibrillation: an analysis from ROCKET AF. *Europace* **18**, 1135–1142 (2016).

11. le Heuzey, J.-Y. *et al.* Cost of care distribution in atrial fibrillation patients: the COCAF study. *American Heart journal* **147**, 121–126 (2004).

12. Schnabel, R. B. *et al.* Gender differences in clinical presentation and 1-year outcomes in atrial fibrillation. *Heart* **103**, 1024–1030 (2017).

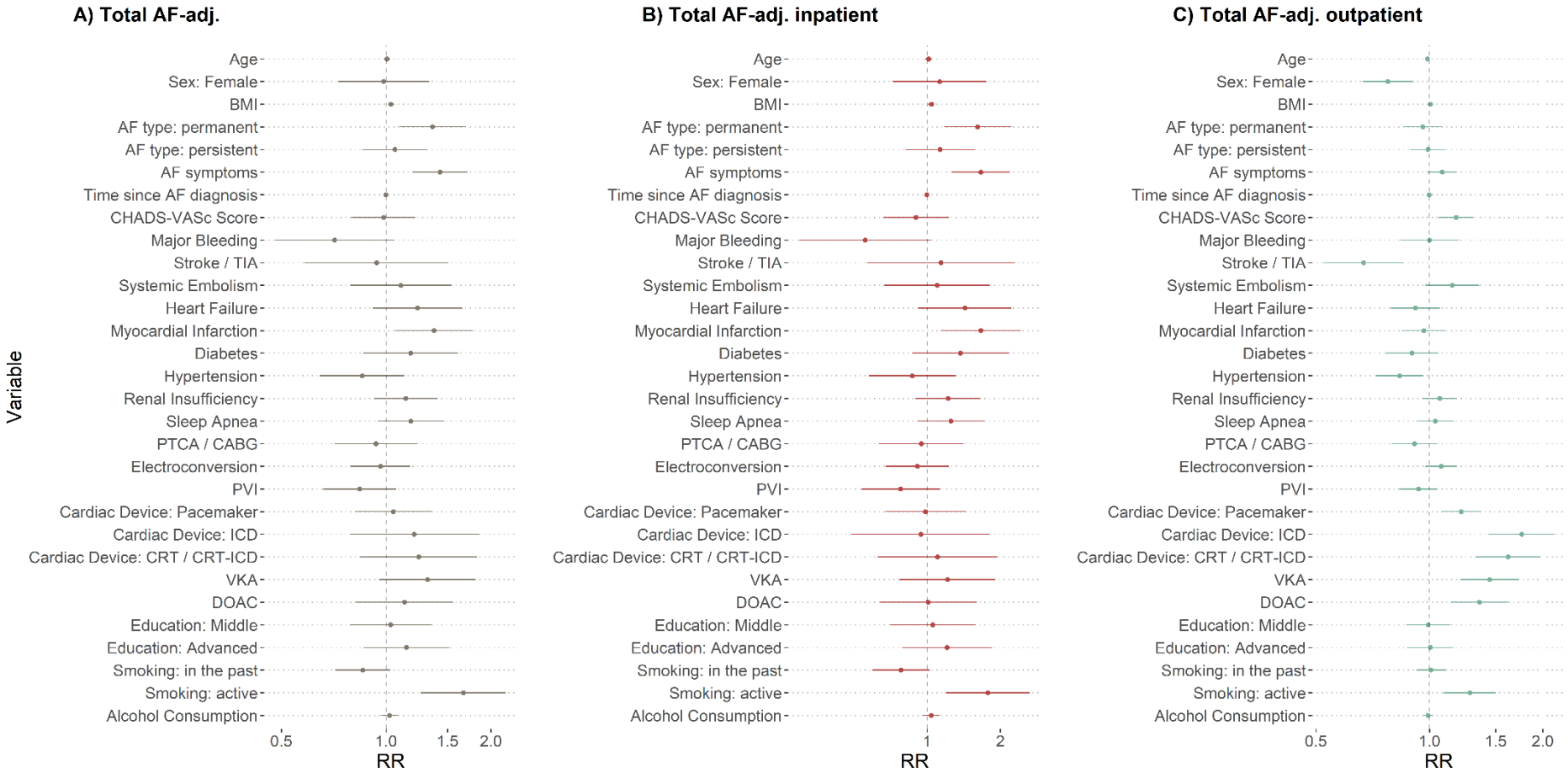


Figure S7. Rate ratios (RR) and corresponding confidence intervals (CI) for the multivariable cost models. A) RR and CI for factors associated with total AF-adjudicated costs. B) RR and CI for factors associated with total AF-adjudicated inpatient costs. C) RR and CI for factors associated with total AF-adjudicated outpatient costs.
Notes: Abbreviations: adj.: adjudicated, AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-valvular atrial fibrillation), CRT: Cardiac resynchronization therapy, DOAC: direct-acting oral anticoagulant, ICD: Implantable cardioverter defibrillator, PCG: pharmaceutical cost groups, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, TIA: transient ischemic attack, VKA: vitamin K antagonist.

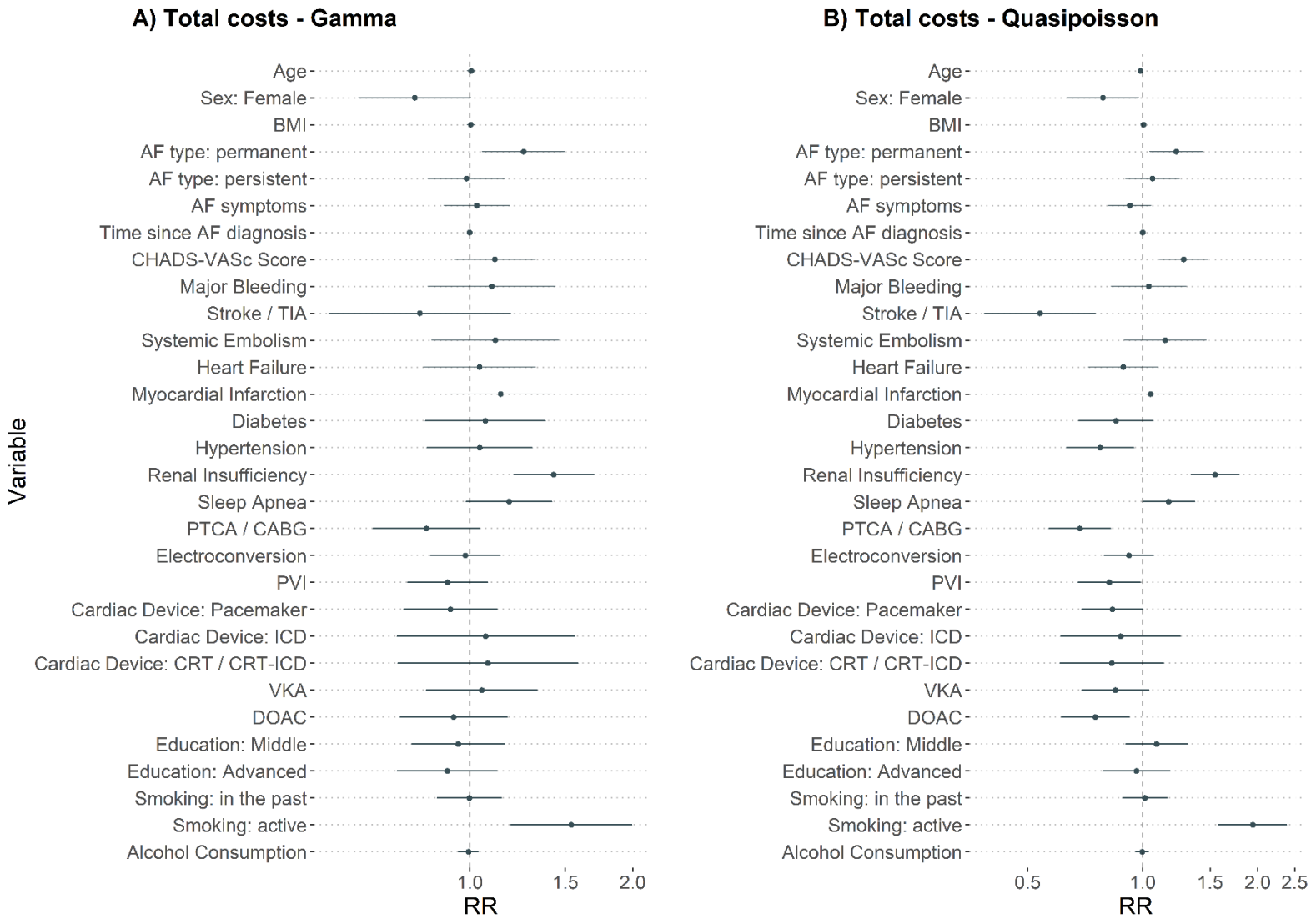


Figure S8. Regression estimates for total costs using GLM Gamma (link = log) and Quasipoisson (link = log).
Notes: Abbreviations: adj.: adjudicated, AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-valvular atrial fibrillation), CRT: Cardiac resynchronization therapy, DOAC: direct-acting oral anticoagulant, ICD: Implantable cardioverter defibrillator, PCG: pharmaceutical cost groups, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, TIA: transient ischemic attack, VKA: vitamin K antagonist.

Table S7. Estimates (RR) and confidence interval (95%) of multivariable cost models for different cost outcomes.

	Dependent variable:					
	Total costs	**Total AF-adj. costs**	**Total inpatient costs**	**Total AF-adj. inpatient costs**	**Total outpatient costs**	**Total AF-adj. outpatient costs**
Age	0.99 [0.97, 1.00]	1.01 [0.99, 1.03]	0.99 [0.97, 1.01]	1.01 [0.98, 1.04]	0.99 [0.97, 1.00]	0.99 [0.98, 1.00]
Sex: Female	0.79 [0.64, 0.97]	0.98 [0.73, 1.33]	0.84 [0.63, 1.12]	1.13 [0.72, 1.76]	0.69 [0.57, 0.83]	0.78 [0.67, 0.90]
BMI	1.01 [0.99, 1.02]	[1.01, 1.05]	1.00 [0.98, 1.02]	1.04 [1.01, 1.07]	1.01 [1.00, 1.02]	1.01 [1.00, 1.02]
AF type: permanent	1.22 [1.05, 1.43]	[1.09, 1.68]	1.36 [1.10, 1.68]	1.61 [1.18, 2.21]	1.09 [0.95, 1.26]	0.96 [0.86, 1.08]
Af type: persistent	1.06 [0.90, 1.25]	1.06 [0.85, 1.31]	1.13 [0.90, 1.41]	1.13 [0.82, 1.57]	1.01 [0.88, 1.17]	0.99 [0.89, 1.10]
AF symptoms	0.92 [0.81, 1.05]	1.43 [1.19, 1.71]	0.93 [0.78, 1.11]	1.66 [1.27, 2.18]	0.99 [0.88, 1.11]	1.08 [0.99, 1.18]
Years since AF diagnosis	1.00 [0.99, 1.01]	1.00 [0.99, 1.01]	1.00 [0.99, 1.01]	1.00 [0.98, 1.01]	1.00 [0.99, 1.01]	1.00 [0.99, 1.00]
CHA_2DS_2-VASc	1.28 [1.10, 1.48]	0.98 [0.80, 1.21]	1.26 [1.03, 1.53]	0.90 [0.66, 1.23]	1.26 [1.11, 1.44]	1.18 [1.06, 1.31]
Major Bleeding	1.04 [0.83, 1.30]	0.71 [0.48, 1.05]	0.98 [0.72, 1.32]	0.56 [0.30, 1.04]	1.16 [0.95, 1.43]	1.00 [0.84, 1.19]
Stroke / TIA	0.54 [0.38, 0.75]	0.94 [0.58, 1.51]	0.54 [0.35, 0.85]	1.14 [0.57, 2.29]	0.59 [0.44, 0.80]	0.67 [0.52, 0.85]
Systemic Embolism	1.15 [0.89, 1.47]	1.10 [0.79, 1.54]	1.22 [0.88, 1.69]	1.10 [0.67, 1.81]	1.09 [0.87, 1.36]	1.15 [0.98, 1.36]
Heart Failure	0.89 [0.72, 1.10]	1.23 [0.92, 1.66]	1.01 [0.76, 1.34]	1.43 [0.92, 2.22]	0.70 [0.58, 0.85]	0.92 [0.79, 1.06]
Myocardial Infarction	1.05 [0.87, 1.27]	1.37 [1.06, 1.77]	1.11 [0.86, 1.43]	1.66 [1.14, 2.42]	1.02 [0.87, 1.21]	0.97 [0.85, 1.10]
Diabetes	0.85 [0.68, 1.07]	1.18 [0.86, 1.61]	0.86 [0.64, 1.16]	1.37 [0.87, 2.16]	0.92 [0.75, 1.13]	0.90 [0.77, 1.06]

Hypertension	0.77 [0.63, 0.95]	0.85 [0.65, 1.13]	0.79 [0.60, 1.03]	0.87 [0.58, 1.31]	0.80 [0.67, 0.95]	0.83 [0.72, 0.96]
Renal Insufficiency	1.55 [1.34, 1.79]	1.14 [0.92, 1.40]	1.66 [1.36, 2.02]	1.22 [0.89, 1.66]	1.35 [1.19, 1.54]	1.07 [0.96, 1.19]
Sleep Apnea	1.17 [1.00, 1.37]	1.18 [0.95, 1.46]	1.24 [1.01, 1.53]	1.25 [0.91, 1.72]	1.12 [0.97, 1.29]	1.04 [0.93, 1.16]
PTCA / CABG	0.69 [0.57, 0.83]	0.94 [0.71, 1.23]	0.67 [0.52, 0.85]	0.95 [0.64, 1.41]	0.72 [0.60, 0.85]	0.91 [0.79, 1.05]
Electroconversion	0.92 [0.79, 1.07]	0.96 [0.79, 1.17]	0.93 [0.76, 1.14]	0.91 [0.68, 1.23]	0.92 [0.81, 1.05]	1.07 [0.97, 1.19]
PVI	0.82 [0.68, 0.99]	0.84 [0.66, 1.07]	0.71 [0.54, 0.93]	0.78 [0.54, 1.13]	0.98 [0.84, 1.14]	0.94 [0.83, 1.05]
Cardiac Device: PM	0.83 [0.69, 1.00]	1.05 [0.82, 1.35]	0.70 [0.54, 0.91]	0.98 [0.67, 1.44]	1.09 [0.93, 1.27]	1.22 [1.07, 1.38]
Cardiac Device: ICD	0.88 [0.61, 1.26]	1.20 [0.79, 1.84]	0.74 [0.45, 1.20]	0.94 [0.49, 1.81]	1.21 [0.88, 1.65]	1.76 [1.44, 2.14]
Cardiac Device: CRT / CRT-ICD	0.83 [0.61, 1.13]	1.24 [0.84, 1.83]	0.68 [0.44, 1.04]	1.10 [0.63, 1.95]	1.14 [0.87, 1.49]	1.62 [1.33, 1.97]
VKA	0.85 [0.69, 1.04]	1.31 [0.95, 1.81]	0.76 [0.58, 0.99]	1.21 [0.77, 1.91]	1.15 [0.94, 1.42]	1.45 [1.21, 1.73]
DOAC	0.75 [0.61, 0.92]	1.13 [0.82, 1.56]	0.64 [0.49, 0.84]	1.01 [0.64, 1.60]	1.08 [0.88, 1.33]	1.36 [1.14, 1.62]
PCG acid related disorders	1.15 [1.00, 1.33]	1.24 [1.02, 1.50]	1.11 [0.91, 1.35]	1.20 [0.90, 1.61]	1.23 [1.09, 1.40]	1.32 [1.20, 1.45]
PCG bone diseases	1.46 [1.16, 1.84]	0.77 [0.50, 1.17]	1.30 [0.93, 1.81]	0.59 [0.30, 1.17]	1.75 [1.45, 2.12]	1.15 [0.96, 1.39]
PCG cancer	1.62 [1.26, 2.09]	1.87 [1.30, 2.69]	1.62 [1.14, 2.30]	2.16 [1.28, 3.66]	1.80 [1.46, 2.22]	1.51 [1.25, 1.83]
PCG dementia	0.99 [0.68, 1.42]	1.14 [0.69, 1.88]	0.86 [0.50, 1.47]	0.99 [0.45, 2.20]	1.19 [0.89, 1.58]	1.32 [1.05, 1.65]

PCG epilepsy	1.64 [1.35, 2.00]	1.88 [1.44, 2.47]	1.83 [1.41, 2.38]	2.16 [1.47, 3.16]	1.35 [1.13, 1.62]	1.18 [1.01, 1.38]
PCG glaucoma	0.99 [0.82, 1.21]	0.88 [0.66, 1.16]	0.86 [0.65, 1.14]	0.79 [0.52, 1.22]	1.19 [1.01, 1.39]	1.01 [0.88, 1.16]
PCG gout	0.92 [0.76, 1.11]	0.89 [0.67, 1.17]	0.89 [0.69, 1.15]	0.85 [0.57, 1.28]	1.01 [0.85, 1.19]	0.97 [0.84, 1.11]
PCG iron deficiency	1.39 [1.14, 1.70]	1.08 [0.80, 1.46]	1.32 [1.00, 1.74]	1.07 [0.69, 1.67]	1.56 [1.32, 1.84]	1.15 [0.99, 1.33]
PCG pain	1.04 [0.90, 1.20]	1.01 [0.83, 1.23]	0.97 [0.80, 1.18]	0.97 [0.73, 1.30]	1.17 [1.03, 1.32]	1.07 [0.97, 1.18]
PCG psychiatric	1.11 [0.96, 1.27]	1.12 [0.92, 1.36]	1.05 [0.86, 1.28]	1.13 [0.84, 1.50]	1.16 [1.03, 1.30]	1.12 [1.02, 1.23]
PCG antipsychotic	0.81 [0.52, 1.26]	0.65 [0.34, 1.26]	0.90 [0.50, 1.63]	0.54 [0.20, 1.49]	0.76 [0.52, 1.11]	0.85 [0.62, 1.18]
PCG respiratory	1.00 [0.85, 1.18]	0.88 [0.70, 1.12]	0.91 [0.73, 1.14]	0.85 [0.60, 1.21]	1.19 [1.04, 1.36]	0.99 [0.88, 1.11]
PCG rheumatic conditions	1.05 [0.91, 1.21]	0.94 [0.77, 1.14]	1.07 [0.88, 1.30]	0.89 [0.67, 1.19]	1.04 [0.92, 1.17]	1.02 [0.93, 1.13]
PCG thyroid disorders	1.22 [1.00, 1.50]	1.41 [1.08, 1.84]	1.27 [0.96, 1.68]	1.64 [1.11, 2.40]	1.21 [1.01, 1.44]	1.12 [0.97, 1.28]
PCG sparse	1.08 [0.80, 1.47]	0.56 [0.32, 0.96]	0.89 [0.56, 1.40]	0.49 [0.21, 1.15]	1.29 [1.01, 1.65]	0.75 [0.58, 0.97]
Education: Middle	1.09 [0.90, 1.31]	1.03 [0.79, 1.34]	1.09 [0.85, 1.40]	1.06 [0.71, 1.57]	1.07 [0.91, 1.27]	0.99 [0.87, 1.13]
Education: Advanced	0.96 [0.79, 1.18]	1.14 [0.86, 1.52]	0.88 [0.67, 1.16]	1.21 [0.79, 1.84]	1.08 [0.90, 1.29]	1.01 [0.87, 1.16]
Smoking: In the past	1.01 [0.88, 1.16]	0.86 [0.71, 1.03]	1.06 [0.88, 1.27]	0.78 [0.59, 1.03]	0.92 [0.82, 1.04]	1.01 [0.92, 1.11]

Smoking: Active	1.94 [1.58, 2.39]	1.67 [1.26, 2.20]	2.44 [1.87, 3.18]	1.78 [1.19, 2.64]	1.15 [0.94, 1.42]	1.28 [1.09, 1.50]
Alcohol	1.00 [0.96, 1.04]	1.02 [0.97, 1.08]	1.00 [0.95, 1.06]	1.04 [0.96, 1.12]	1.00 [0.96, 1.03]	0.99 [0.96, 1.02]
Greater Region: Lake Geneva	1.17 [0.83, 1.64]	0.85 [0.54, 1.32]	1.14 [0.70, 1.88]	0.82 [0.41, 1.65]	1.16 [0.88, 1.53]	0.98 [0.80, 1.19]
Greater Region: Espace Mittelland	1.32 [1.05, 1.65]	1.16 [0.88, 1.54]	1.50 [1.09, 2.07]	1.35 [0.88, 2.08]	1.09 [0.91, 1.31]	0.92 [0.80, 1.05]
Greater Region: Northwestern Switzerland	1.67 [1.34, 2.07]	1.14 [0.86, 1.51]	2.13 [1.56, 2.91]	1.40 [0.91, 2.15]	1.13 [0.95, 1.35]	0.86 [0.75, 0.98]
Greater Region: Eastern Switzerland	1.12 [0.80, 1.57]	0.84 [0.54, 1.31]	1.27 [0.79, 2.03]	0.90 [0.46, 1.78]	0.98 [0.74, 1.29]	0.80 [0.65, 0.98]
Greater Region: Southern Switzerland	1.12 [0.86, 1.47]	0.70 [0.49, 1.01]	1.11 [0.75, 1.64]	0.68 [0.39, 1.20]	1.15 [0.93, 1.44]	0.78 [0.66, 0.93]
Greater Region: Central Switzerland	0.98 [0.65, 1.48]	0.97 [0.60, 1.56]	1.26 [0.71, 2.23]	1.11 [0.53, 2.31]	0.73 [0.51, 1.02]	0.79 [0.63, 0.99]
Observations	1013	1013	1013	1013	1013	1013

Notes: Alcohol in drinks per day. Abbreviations: AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-vavluar atrial fibrillation), CRT: Cardiac resynchronization therapy, DOAC: direct-acting oral anticoagulant, Dx: diagnosis, ICD: Implantable cardioverter defibrillator, PCG: pharmaceutical cost groups, PM: Pacemaker, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, TIA: transient ischemic attack, VKA: vitamin K antagonist.

Table S8. Regression estimates for total costs using GLM Gamma (link = log) and Quasipoisson (link = log).

	Total costs	
	Gamma	*Quasipoisson*
Age	1.01 [0.99, 1.02]	0.99 [0.97, 1.00]
Sex: Female	0.79 [0.62, 1.00]	0.79 [0.64, 0.97]
BMI	1.00 [0.99, 1.02]	1.01 [0.99, 1.02]
AF type: permanent	1.26 [1.06, 1.50]	1.22 [1.05, 1.43]
AF type: persistent	0.99 [0.84, 1.16]	1.06 [0.90, 1.25]
AF symptoms	1.03 [0.90, 1.18]	0.92 [0.81, 1.05]
Years since AF diagnosis	1.00 [0.99, 1.01]	1.00 [0.99, 1.01]
CHA_2DS_2-VASc	1.11 [0.94, 1.32]	1.28 [1.10, 1.48]
Major Bleeding	1.10 [0.84, 1.43]	1.04 [0.83, 1.30]
Stroke / TIA	0.81 [0.55, 1.19]	0.54 [0.38, 0.75]
Systemic Embolism	1.11 [0.85, 1.46]	1.15 [0.89, 1.47]
Heart Failure	1.04 [0.82, 1.32]	0.89 [0.72, 1.10]
Myocardial Infarction	1.14 [0.92, 1.41]	1.05 [0.87, 1.27]
Diabetes	1.07 [0.83, 1.38]	0.85 [0.68, 1.07]
Hypertension	1.04 [0.83, 1.31]	0.77 [0.63, 0.95]
Renal Insufficiency	1.43 [1.20, 1.69]	1.55 [1.34, 1.79]
Sleep Apnea	1.18 [0.98, 1.42]	1.17 [1.00, 1.37]
PTCA / CABG	0.83 [0.66, 1.04]	0.69 [0.57, 0.83]
Electroconversion	0.98 [0.84, 1.14]	0.92 [0.79, 1.07]
PVI	0.91 [0.77, 1.08]	0.82 [0.68, 0.99]
Cardiac Device: PM	0.92 [0.75, 1.12]	0.83 [0.69, 1.00]
Cardiac Device: ICD	1.07 [0.73, 1.56]	0.88 [0.61, 1.26]
Cardiac Device: CRT / CRT-ICD	1.08 [0.73, 1.58]	0.83 [0.61, 1.13]
VKA	1.05 [0.83, 1.33]	0.85 [0.69, 1.04]
DOAC	0.93 [0.74, 1.17]	0.75 [0.61, 0.92]
Education: Middle	0.95 [0.78, 1.16]	1.09 [0.90, 1.31]
Education: Advanced	0.91 [0.73, 1.12]	0.96 [0.79, 1.18]
Smoking: In the past	1.00 [0.87, 1.14]	1.01 [0.88, 1.16]
Smoking: Active	1.54 [1.19, 1.99]	1.94 [1.58, 2.39]
Alcohol Consumption	0.99 [0.95, 1.04]	1.00 [0.96, 1.04]

Notes: Alcohol in drinks per day. Abbreviations: AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-valvular atrial fibrillation), CRT: Cardiac resynchronization therapy, Dx: diagnosis, ICD: Implantable cardioverter defibrillator, DOAC: direct-acting oral anticoagulant, PCG: pharmaceutical cost groups, PM: Pacemaker, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, TIA: transient ischemic attack, VKA: vitamin K antagonist.

Table S9. Comparison of three multivariable cost models for total AF-adjudicated costs.

	Total AF-adjudicated costs		
	Main	*Medical History*	*Treatment*
Observation time	0.98 [0.98, 0.99]	0.98 [0.98, 0.99]	0.98 [0.98, 0.99]
Age	1.01 [0.99, 1.03]	1.01 [0.99, 1.03]	1.00 [0.99, 1.01]
Sex: Female	0.98 [0.73, 1.33]	1.00 [0.76, 1.30]	0.90 [0.72, 1.12]
BMI	1.03 [1.01, 1.05]	1.03 [1.01, 1.05]	1.03 [1.01, 1.04]
AF type: permanent	1.36 [1.09, 1.68]	1.45 [1.18, 1.79]	1.29 [1.04, 1.61]
Af type: persistent	1.06 [0.85, 1.31]	1.07 [0.88, 1.30]	1.06 [0.85, 1.31]
AF symptoms	1.43 [1.19, 1.71]	1.42 [1.18, 1.70]	1.52 [1.27, 1.82]
Years since AF diagnosis	1.00 [0.99, 1.01]	1.00 [0.99, 1.01]	1.00 [0.99, 1.01]
CHA_2DS_2-VASc	0.98 [0.80, 1.21]	0.96 [0.81, 1.14]	-
Major Bleeding	0.71 [0.48, 1.05]	0.70 [0.47, 1.03]	-
Stroke / TIA	0.94 [0.58, 1.51]	0.97 [0.65, 1.45]	-
Systemic Embolism	1.10 [0.79, 1.54]	1.11 [0.80, 1.55]	-
Heart Failure	1.23 [0.92, 1.66]	1.32 [1.02, 1.72]	-
Myocardial Infarction	1.37 [1.06, 1.77]	1.40 [1.10, 1.79]	-
Diabetes	1.18 [0.86, 1.61]	1.23 [0.93, 1.63]	-
Hypertension	0.85 [0.65, 1.13]	0.85 [0.66, 1.10]	-
Renal Insufficiency	1.14 [0.92, 1.40]	1.17 [0.95, 1.44]	-
Sleep Apnea	1.18 [0.95, 1.46]	1.17 [0.94, 1.45]	-
PTCA / CABG	0.94 [0.71, 1.23]	-	0.99 [0.80, 1.23]
Electroconversion	0.96 [0.79, 1.17]	-	0.98 [0.80, 1.19]
PVI	0.84 [0.66, 1.07]	-	0.85 [0.67, 1.08]
Cardiac Device: PM	1.05 [0.82, 1.35]	-	1.03 [0.80, 1.33]
Cardiac Device: ICD	1.20 [0.79, 1.84]	-	1.28 [0.84, 1.95]
Cardiac Device: CRT / CRT-ICD	1.24 [0.84, 1.83]	-	1.46 [1.00, 2.11]
Antiplatelet	-	-	1.54 [1.08, 2.19]
Aspirin	-	-	0.96 [0.74, 1.24]
Statin	-	-	1.11 [0.92, 1.33]
Diuretics	-	-	1.52 [1.27, 1.83]
Betablocker	-	-	0.96 [0.79, 1.16]
Digoxin	-	-	0.69 [0.43, 1.09]
VKA	1.31 [0.95, 1.81]	-	1.30 [0.91, 1.84]
DOAC	1.13 [0.82, 1.56]	-	1.12 [0.79, 1.59]
PCG acid related disorders	1.24 [1.02, 1.50]	1.23 [1.01, 1.49]	1.22 [1.00, 1.49]
PCG bone diseases	0.77 [0.50, 1.17]	0.79 [0.52, 1.20]	0.71 [0.47, 1.09]
PCG cancer	1.87 [1.30, 2.69]	1.89 [1.32, 2.72]	1.80 [1.25, 2.59]
PCG dementia	1.14 [0.69, 1.88]	1.14 [0.69, 1.87]	1.06 [0.64, 1.75]
PCG epilepsy	1.88 [1.44, 2.47]	1.89 [1.44, 2.47]	1.84 [1.41, 2.41]
PCG glaucoma	0.88 [0.66, 1.16]	0.89 [0.67, 1.18]	0.89 [0.67, 1.17]

PCG gout	0.89 [0.67, 1.17]	0.90 [0.68, 1.17]	0.90 [0.68, 1.17]
PCG iron deficiency	1.08 [0.80, 1.46]	1.12 [0.84, 1.51]	1.10 [0.81, 1.48]
PCG pain	1.01 [0.83, 1.23]	1.00 [0.83, 1.22]	1.07 [0.88, 1.29]
PCG psychiatric	1.12 [0.92, 1.36]	1.12 [0.92, 1.36]	1.09 [0.90, 1.32]
PCG antipsychotic	0.65 [0.34, 1.26]	0.71 [0.37, 1.34]	0.62 [0.32, 1.20]
PCG respiratory	0.88 [0.70, 1.12]	0.88 [0.70, 1.10]	0.88 [0.70, 1.12]
PCG rheumatic conditions	0.94 [0.77, 1.14]	0.92 [0.76, 1.11]	0.96 [0.79, 1.16]
PCG thyroid disorders	1.41 [1.08, 1.84]	1.43 [1.10, 1.87]	1.39 [1.07, 1.81]
PCG sparse	0.56 [0.32, 0.96]	0.54 [0.31, 0.94]	0.59 [0.34, 1.03]
Education: Middle	1.03 [0.79, 1.34]	1.02 [0.78, 1.32]	1.04 [0.80, 1.36]
Education: Advanced	1.14 [0.86, 1.52]	1.09 [0.82, 1.44]	1.18 [0.89, 1.57]
Smoking: In the past	0.86 [0.71, 1.03]	0.85 [0.71, 1.02]	0.82 [0.69, 0.99]
Smoking: Active	1.67 [1.26, 2.20]	1.65 [1.25, 2.18]	1.58 [1.19, 2.10]
Alcohol	1.02 [0.97, 1.08]	1.03 [0.97, 1.08]	1.01 [0.96, 1.07]
Greater Region: Lake Geneva	0.85 [0.54, 1.32]	0.90 [0.58, 1.40]	0.92 [0.59, 1.43]
Greater Region: Espace Mittelland	1.16 [0.88, 1.54]	1.22 [0.92, 1.61]	1.19 [0.90, 1.58]
Greater Region: Northwestern Switzerland	1.14 [0.86, 1.51]	1.21 [0.92, 1.60]	1.16 [0.88, 1.54]
Greater Region: Eastern Switzerland	0.84 [0.54, 1.31]	0.87 [0.56, 1.35]	0.89 [0.57, 1.38]
Greater Region: Southern Switzerland	0.70 [0.49, 1.01]	0.73 [0.51, 1.06]	0.68 [0.48, 0.98]
Greater Region: Central Switzerland	0.97 [0.60, 1.56]	0.96 [0.60, 1.55]	0.86 [0.53, 1.39]
Observations	1013	1013	1013

Notes: Alcohol in drinks per day. Abbreviations: AF: atrial fibrillation, CABG: coronary artery bypass grafting, CHA_2DS_2-VASc: risk of stroke (for non-valvular atrial fibrillation), CRT: Cardiac resynchronization therapy, DOAC: direct-acting oral anticoagulant, Dx: diagnosis, ICD: Implantable cardioverter defibrillator, PCG: pharmaceutical cost groups, PM: Pacemaker, PTCA: Percutaneous transluminal coronary angioplasty, PVI: Pulmonary vein isolation, TIA: transient ischemic attack, VKA: vitamin K antagonist.

Table S10: Adjudication algorithm.

The aim of the adjudication algorithm was to distinguish in- and outpatient care episodes and medical resource use related to AF and its potential complications, from episodes related to other morbidities. Mainly clinical understanding of disease specifics and procedures, and understanding of technical terms were necessary to develop the algorithm. As such, clinical experts, i.e. cardiologists, from the Swiss-AF study centres were involved by the health economics team. The adjudication process development included the following steps:

- In a first meeting, possible cost categories (e.g. directly AF-related, fall-related, Stroke/TIA-related) were established together with the Swiss-AF study coordinator and a MD-PhD student. The prerequisites for a meaningful cost category were the connection with AF and a sufficient possibility to identify corresponding care episodes and resource use items.
- Two members of the health economics team separated and listed relevant and not relevant tariff codes and diagnosis-related group codes, the relevant ones serving to assign care episodes and resource use items to cost categories. This process was supported by iterative plausibility checks and done in regular exchange with a cardiologist from the Swiss-AF study team, to address cases of uncertainty and arising questions. For questions regarding the interpretation of insurance data, our health insurance contact persons were involved.
- The adjudication of AF-related and stroke-related medication was done by the MD-PhD student using ATC codes.
- After finishing a first draft of the adjudication algorithm, it was sent to five clinicians and the Swiss-AF study coordinator for review. Open questions and possibilities for improvement were discussed in a meeting until a consensus was found.
- The technical implementation of the adjudication algorithm was done by members of the health economics team, merging clinical and claims data.

At the time of development of the algorithm, cost results were not available; the only interest was in the classification of clinical episodes and claims as related to AF and its potential complications, or not. I.e., the development of the algorithm was not influenced by any knowledge of actual cost results.

A) Adjudication of inpatient costs. *Allocation of inpatient costs related to AF and AF complications.*

Costs were determined in 4 separate blocks:

AF-related costs exclusive of Stroke/TIA, Bleeding, falls	**Stroke/TIA-related costs**	**Bleeding-related costs**	**Fall-related costs**
Included DRG* codes listed below that suggested an AF-related treatment.	DRG* codes listed below were defined as stroke/TIA-related if they occurred within two weeks of the stroke/TIA.	DRG* codes listed below were defined as bleeding-related if they occurred within two weeks of the bleeding.	DRG* codes listed below were defined as fall-related if the patient had at least one fall in the same follow-up year as the inpatient episode (information from FU visit).

Abbreviations (also used on the next pages): AF: atrial fibrillation, CC: complications or comorbidities, DRG: diagnosis related group, FU: follow-up, IMC: intermediate care, OR: operating room, TIA: transient ischemic attack

* SwissDRG. https://www.swissdrg.org/de/akutsomatik/swissdrg-system-1002021 (2021).

AF-related costs (excluding costs for Stroke/TIA, bleeding, falls)

In principle, inpatient episodes were classified as AF-related if the following episodes occurred. Specific details are reported in the table as applicable.

Inpatient episodes considered as related to AF	SwissDRG
AF ablation	
Ablative Massnahmen bei Tachyarrhythmie mit bestimmter Ablation und komplexem Eingriff, Alter < 16 Jahre	F50A
Ablative Massnahmen bei Tachyarrhythmie mit bestimmter Ablation, Alter > 15 Jahre	F50B
Ablative Massnahmen bei Tachyarrhythmie mit komplexem Eingriff, Alter > 15 Jahre	F50C
Ablative Massnahmen bei Tachyarrhythmie, Alter > 15 Jahre	F50D, F50E
Implantation, revision or change of pace maker	
Implantation eines Herzschrittmachers mit einer Drei- oder Zwei-Kammer-Stimulation mit komplexem Eingriff oder Alter < 16 Jahre oder bestimmter Prozedur	F12A
Implantation eines Herzschrittmachers mit äusserst schweren CC	F12B
Implantation eines Herzschrittmachers mit einer Drei-Kammer-Stimulation	F12C
Implantation eines Herzschrittmachers mit einer Zwei-Kammer-Stimulation oder einem sondenlosen System	F12D
Implantation eines Herzschrittmachers mit einer Ein-Kammer-Stimulation	F12E
Implantation eines Herzschrittmachers, Ein-Kammersystem	F12F
Wechsel eines Herzschrittmachers, Mehrkammersystem	F17A
Wechsel eines Herzschrittmachers, Einkammersystem	F17B
Revision eines Herzschrittmachers oder Kardioverters / Defibrillators (AICD) ohne Aggregatwechsel, mit äusserst schweren CC oder bestimmtem Eingriff oder Alter < 16 Jahre	F18A
Revision eines Herzschrittmachers oder Kardioverters / Defibrillators (AICD) ohne Aggregatwechsel, Alter > 15 Jahre	F18B
Implantation of a cardioverter	
Neuimplantation Kardioverter / Defibrillator (AICD), Zwei- oder Drei-Kammer-Stimulation, mit zusätzlichem Herz- oder Gefässeingriff	F01A
Neuimplantation Kardioverter / Defibrillator (AICD), Drei-Kammer-Stimulation	F01B
Neuimplantation Kardioverter / Defibrillator (AICD), Ein-Kammer-Stimulation, mit zusätzlichem Herz- oder Gefässeingriff	F01C
Neuimplantation Kardioverter / Defibrillator (AICD), Zwei-Kammer-Stimulation	F01D
Neuimplantation Kardioverter / Defibrillator (AICD), Ein-Kammer-Stimulation mit äusserst schweren CC	F01E
Neuimplantation Kardioverter / Defibrillator (AICD), Ein-Kammer-Stimulation	F01F
Aggregatwechsel eines Kardioverters / Defibrillators (AICD), Zwei- oder Drei-Kammer-Stimulation	F02A
Aggregatwechsel Kardioverters / Defibrillators (AICD), Ein-Kammer-Stimulation	F02B
Aggregatwechsel eines Kardioverters / Defibrillators (AICD), Zwei- oder Drei-Kammer-Stimulation	F02Z
Aggregatwechsel eines Kardioverters / Defibrillators (AICD), Ein-Kammer-Stimulation	F10Z
Not severe / severe arrhytmia	
Schwere Arrhythmie und Herzstillstand, mit äusserst schweren CC	F70A
Schwere Arrhythmie und Herzstillstand	F70B
Nicht schwere kardiale Arrhythmie und Erregungsleitungsstörungen, Koronararteriosklerose und instabile Angina pectoris, mit äusserst schweren CC	F71A

Nicht schwere kardiale Arrhythmie und Erregungsleitungsstörungen mit schweren CC	F71B
Koronararteriosklerose, kardiale Arrhythmien, Angina Pectoris mit äusserst schweren CC oder komplexer Diagnose oder Alter < 16 Jahre, mehr als ein Belegungstag	F66A
Koronararteriosklerose, kardiale Arrhythmien, Angina Pectoris, Alter > 15 Jahre, mehr als ein Belegungstag	F66B
Mitral valve operation	
Herzklappeneingriff mit Herz-Lungen-Maschine, mit komplizierender Prozedur oder Herzschrittmacher mit bestimmtem Herzklappenersatz	F03A
Herzklappeneingriff mit Herz-Lungen-Maschine, mit Dreifacheingriff oder Alter < 1 J. od. mit tiefer Hypothermie od. Bioprothese, od. Zweifacheingriff mit angeb. Herzfehler od. best. Eingriff od. Alter < 16 J. mit äuss. schw. CC	F03C
Herzklappeneingriff mit Herz-Lungen-Maschine und Zweifacheingriff mit angeb. Herzfehler oder bestimmtem Eingriff oder Alter < 16 J.	F03D
Herzklappeneingriff mit Herz-Lungen-Maschine	F03E
Endovaskuläre Implantation eines Herzklappenersatzes mit Impl. eines Herzschrittmachers / Graft oder Alter < 16 Jahre	F98B
Endovaskuläre Implantation eines Herzklappenersatzes, Alter > 15 Jahre	F98C
Invasive diagnostics	
Invasive kardiologische Diagnostik ausser bei akutem Myokardinfarkt mit komplexem Eingriff oder mit komplizierender Diagnose und äusserst schwere CC, oder komplizierender Prozedur	F49A
Invasive kardiologische Diagnostik ausser bei akutem Myokardinfarkt mit äusserst schweren CC oder Alter < 14 Jahre	F49B
Invasive kardiologische Diagnostik ausser bei akutem Myokardinfarkt mit komplexem Eingriff oder mit komplizierender Diagnose	F49C
Invasive kardiologische Diagnostik ausser bei akutem Myokardinfarkt, Alter > 13 Jahre	F49D
Invasive kardiologische Diagnostik ausser bei akutem Myokardinfarkt, 2 Belegungstage oder bestimmte Verfahren	F49E
Invasive kardiologische Diagnostik ausser bei akutem Myokardinfarkt, ein Belegungstag ohne bestimmten Verfahren	F49F
Hypertension	
Hypertonie mit äusserst schweren CC und mehr als ein Belegungstag	F67A
Hypertonie	F67B, F67C
Heart failure and shock (only if the study centre indicated AF as reason)	
Herzinsuffizienz und Schock mit äusserst schweren CC, mit Dialyse oder Reanimation oder komplizierender Diagnose	F62A
Herzinsuffizienz und Schock mit äusserst schweren CC	F62B
Herzinsuffizienz und Schock	F62C
Syncope	
Synkope und Kollaps, mit äusserst schweren CC	F73A
Synkope und Kollaps	F73B
Synkope und Kollaps oder Herzklappenerkrankungen ohne äusserst schwere oder schwere CC	F73Z
Other episodes	
Koronare Bypass-Operation mit invasiver kardiologischer Diagnostik oder intraoperativer Ablation, mit komplizierenden Prozeduren oder Karotiseingriff oder bestimmte Eingriffe mit Herz-Lungen-Maschine in tiefer Hypothermie	F05Z

Andere Krankheiten des Kreislaufsystems mit Intensivmedizinischer Komplexbehandlung oder IMC Komplexbehandlung > 196/184 Aufwandspunkte	F75A
Andere Krankheiten des Kreislaufsystems mit äusserst schweren CC, Alter > 17 Jahre, mehr als ein Belegungstag	F75B
Andere Krankheiten des Kreislaufsystems oder Gefässeingriff, Alter < 18 Jahre, mehr als ein Belegungstag	F75C
Andere Krankheiten des Kreislaufsystems oder Gefässeingriff, Alter > 17 Jahre	F75D
Rehabilitation (if directly following a hospitalisation with one of the above codes)	-

Stroke/TIA-related cost

The following SwissDRG codes were classified as Stroke/TIA-related if …

- … the patient had a stroke/TIA within two weeks (14 days) before the start date of inpatient episode.
- … the patient had a stroke/TIA during the inpatient episode.

Inpatient episodes considered as related to stroke/TIA	**SwissDRG**
Intensive care	
Beatmung > 499 Stunden mit komplexer OR-Prozedur oder Polytrauma oder komplexer Vakuumbehandlung, oder Alter < 16 Jahre oder Intensivmedizinische Komplexbehandlung > 1764/2484 Aufwandspunkte	A07B
Beatmung > 249 Std. mit aufwendigen Prozeduren, oder Beatmung < 95 Std. mit bestimmten Konstellationen od. kompliz. Prozeduren, od. Alter < 6 Jahre, od. IntK > 1470/1656 Aufwandspunkte mit erschw. Diagnose	A11C
Beatmung > 249 Stunden od. Beatmung > 95 Std. mit bestimmten Konstellationen, Alter > 5 Jahre	A11D
Beatmung > 95 und < 250 Stunden mit hochkomplexen Konstellationen mit IntK > 980/1104 Aufwandspunkte oder mehrzeitige Eingriffe oder Alter < 16 Jahre oder IntK > 1470/1656 Aufwandspunkte	A13A
Beatmung > 95 und < 250 Stunden mit bestimmten komplizierenden Konstellationen, Alter > 15 Jahre oder IntK > 392/552 Aufwandspunkte oder Alter < 16 Jahre, oder nicht verstorben oder verlegt oder Verweildauer > 8 Tage	A13C
Intensivmedizinische Komplexbehandlung > 392/552 und < 981/1105 Aufwandspunkte bei bestimmten Krankheiten und Störungen	A36B
Geriatric and palliative care	
Geriatrische Akutrehabilitation ab 14 Behandlungstagen od. neurologische Komplexbehandlung des akuten Schlaganfalls, mit bestimmter OR Prozedur od. Intensivmedizinische Komplexbehandlung > 184 Aufwandspunkte	A95B
Geriatrische Akutrehabilitation ab 14 Behandlungstagen oder neurologische Komplexbehandlung des akuten Schlaganfalls, mit schwerer motorischer Funktionseinschränkung oder bestimmtem Eingriff	A95C
Geriatrische Akutrehabilitation ab 14 Behandlungstagen oder neurologische Komplexbehandlung des akuten Schlaganfalls	A95D
Palliativmedizinische Komplexbehandlung ab 7 Behandlungstage mit komplizierender Prozedur, oder palliativmed. KBH ab 14 Behandlungstage mit bestimmter OR Prozedur od. bestimmtem Eingriff	A97C
Palliativmedizinische Komplexbehandlung ab 21 Behandlungstage	A97D
Palliativmedizinische Komplexbehandlung ab 7 Behandlungstage mit bestimmter Prozedur oder schwere motorische Funktionseinschränkung oder bestimmtem EingrifF	A97F
Palliativmedizinische Komplexbehandlung ab 7 Behandlungstage	A97G
Complex craniotomy	

Komplexe Kraniotomie oder Wirbelsäulen-Operation, Alter < 6 Jahre oder < 18 Jahre mit grossem intrakraniellen Eingriff, mit äusserst schweren CC, oder Intensivmedizinische Komplexbehandlung > 196/184 Aufwandspunkte	B02A
Komplexe Kraniotomie oder Wirbelsäulen-Operation mit intraop. Monitoring oder kompliz. Prozedur oder grossem intrakraniellen Eingriff	B02B
Komplexe Kraniotomie oder Wirbelsäulen-Operation	B02C, B02D
Acute stroke	
Neurologische Komplexbehandlung des akuten Schlaganfalls mit bestimmter Prozedur od. Apoplex /TIA mit Herzschrittmacher, mehr als 72 Stunden mit komplexem Eingriff oder mit komplizierender Prozedur	B39A
Neurologische Komplexbehandlung des akuten Schlaganfalls mit bestimmter Prozedur, bis 72 Stunden mit komplexem Eingriff, oder mehr als 72 Stunden	B39B
Neurologische Komplexbehandlung des akuten Schlaganfalls mit bestimmter Prozedur od. Apoplex/TIA mit ASD Verschluss	B39C
Transient ischemic attack	
Transitorische ischämische Attacke (TIA) und extrakranielle Gefässverschlüsse mit neurologischer Komplexbehandlung des akuten Schlaganfalls > 72 Stunden	B69A
Transitorische ischämische Attacke (TIA) und extrakranielle Gefässverschlüsse mit neurologischer Komplexbehandlung des akuten Schlaganfalls < 73 Stunden	B69B
Transitorische ischämische Attacke (TIA) und extrakranielle Gefässverschlüsse mit anderer neurologischer Komplexbehandlung des akuten Schlaganfalls od. neurolog. Komplexdiagnostik	B69C
Transitorische ischämische Attacke (TIA) und extrakranielle Gefässverschlüsse	B69D
Apoplexy	
Apoplexie mit neurologischer Komplexbehandlung des akuten Schlaganfalls > 72 Std. oder Intensivmedizinische Komplexbehandlung >184 Aufwandspunkte, mit komplizierender Diagnose od. schw. motor. Funktionsstörung	B70A
Apoplexie mit neurologischer Komplexbehandlung des akuten Schlaganfalls > 72 Std. od. Intensivmedizinische Komplexbehandlung > 184 Aufwandspunkte od. neurolog. Komplexdiagn.	B70B
Apoplexie mit neurologischer Komplexbehandlung des akuten Schlaganfalls < 73 Std., mit komplizierender Diagnose oder Thrombolyse oder schw. motor. Funktionsstörung	B70C
Apoplexie mit neurologischer Komplexbehandlung des akuten Schlaganfalls < 73 Std., oder mit anderer neurolog. Komplexbehandlung > 72 Std.	B70D
Apoplexie mit anderer neurologischer Komplexbehandlung des akuten Schlaganfalls < 73 Std. od. neurolog. Komplexdiagnostik	B70E
Apoplexie, mehr als ein Belegungstag oder Thrombolyse mit komplizierender Diagnose oder schw. motor. Funktionsstörung	B70F
Apoplexie, mehr als ein Belegungstag	B70G
Apoplexie, mehr als ein Belegungstag oder Thrombolyse, verstorben < 5 Tage nach Aufnahme, mit neurologischer Komplexbehandlung des akuten Schlaganfalls oder anderer neurologischer Komplexbehandlung	B70H
Apoplexie, mehr als ein Belegungstag oder Thrombolyse, verstorben < 5 Tage nach Aufnahme	B70I
Apoplexie, ein Belegungstag	B70J
Apoplexie mit neurologischer Komplexbehandlung des akuten Schlaganfalls < 24 Std., ein Belegungstag	B70K
Other	

Eingriffe an den extrakraniellen Gefässen mit äusserst schweren CC oder mit beidseitigem Eingriff an den extrakraniellen Gefässen oder bei Hirninfarkt	B04B
Operative Eingriffe bei Para- / Tetraplegie, zerebrale Erkrankung u. Eingriffe b. zerebraler Lähmung, Muskeldystrophie, Neuropathie od. Eingriffe an WS u. RM, u. IntK > 196/119 Pkt. od. IMCK > 196/184 Pkt., od. Alter < 16 Jahre	B03A
Operative Eingriffe bei Para- / Tetraplegie, zerebrale Erkrankung und Eingriffe b. zerebraler Lähmung, Muskeldystrophie, Neuropathie od. Eingriffe an WS u. RM, und kompliz. Proz.	B03B
Operative Eingriffe bei Para- / Tetraplegie, zerebrale Erkrankung und Eingriffe b. zerebraler Lähmung, Muskeldystrophie, Neuropathie od. Eingriffe an Wirbelsäule u. Rückenmark	B03C
Rehabilitation (if directly following a hospitalisation for any reason above)	-

Bleeding-related costs

Bleeding-related costs were assumed if a patient took anticoagulants ...

- … and the bleeding date fell into an inpatient episode (from start until end). In this case, any Swiss DRG code for this inpatient episode was counted as bleeding-related.
- … and had a bleeding within two weeks before the start date of an inpatient episode. In this case, the following SwissDRG codes were classified as bleeding-related.

Inpatient episodes considered as bleeding-related	**SwissDRG**
Intensive care	
Beatmung > 499 Stunden mit komplexer OR-Prozedur oder Polytrauma oder komplexer Vakuumbehandlung, oder Alter < 16 Jahre oder Intensivmedizinische Komplexbehandlung > 1764/2484 Aufwandspunkte	A07B
Beatmung > 249 Std. mit aufwendigen Prozeduren, oder Beatmung < 95 Std. mit bestimmten Konstellationen od. kompliz. Prozeduren, od. Alter < 6 Jahre, od. IntK > 1470/1656 Aufwandspunkte mit erschw. Diagnose	A11C
Beatmung > 249 Stunden od. Beatmung > 95 Std. mit bestimmten Konstellationen, Alter > 5 Jahre	A11D
Beatmung > 95 und < 250 Stunden mit hochkomplexen Konstellationen mit IntK > 980/1104 Aufwandspunkte oder mehrzeitige Eingriffe oder Alter < 16 Jahre oder IntK > 1470/1656 Aufwandspunkte	A13A
Beatmung > 95 und < 250 Stunden mit bestimmten komplizierenden Konstellationen, Alter > 15 Jahre oder IntK > 392/552 Aufwandspunkte oder Alter < 16 Jahre, oder nicht verstorben oder verlegt oder Verweildauer > 8 Tage	A13C
Intensivmedizinische Komplexbehandlung > 392/552 und < 981/1105 Aufwandspunkte bei bestimmten Krankheiten und Störungen	A36B
Gastroscopy	
Kompl. Gastroskopie mit äusserst schw. CC oder kompliz. Proz. bei schw. Erkrankung, oder äusserst schw. CC oder kompl. Gastroskopie verbunden mit kompliz. Eingriff, Alter < 15 Jahre	G46A
Kompl. Gastroskopie verbunden mit kompliz. Eingriff oder äusserst schw. CC, Alter > 14 Jahre, oder schw. Erkrankung der Verdauungsorgane und Alter < 15 Jahre	G46B
Gastroskopie oder endoskopisches Antirefluxverfahren	G46C
Andere Gastroskopie bei schweren Krankheiten der Verdauungsorgane ohne äusserst schwere oder schwere CC oder Gastroskopie, Alter < 15 Jahre	G47Z
Koloskopie mit schweren CC oder komplizierendem Eingriff oder Alter < 15 Jahre mit bestimmter Diagnose oder komplizierender Prozedur, mehr als ein Belegungstag	G48A

Koloskopie mit schweren CC oder komplizierendem Eingriff oder Alter < 15 Jahre, mehr als ein Belegungstag	G48B
Gastrointestinal bleeding	
Ulkuserkrankung mit gastrointest. Blutung mehr als ein BT und äusserst schw. CC, oder best. Diagnose mit Dialyse od. Alter < 3 J. od. Para-/Tetrapl., od. IntK > 196/119 Pkt. od. IMCK > 196/184 Pkt.	G67A
Verschiedene Erkrankungen der Verdauungsorgane oder gastrointestinale Blutung oder Ulkuserkrankung, mit Dialyse oder Alter < 3 Jahre oder Para-/Tetraplegie	G67B
Verschiedene Erkrankungen der Verdauungsorgane oder gastrointestinale Blutung oder Ulkuserkrankung	G67C
Verschiedene Erkrankungen der Verdauungsorgane oder gastrointestinale Blutung, ein Belegungstag oder Ulkuserkrankung, ohne äusserst schweren CC	G67D
Gastrointestinale Blutung oder Ulkuserkrankung mit äusserst schweren CC, mehr als ein Belegungstag	G73Z
Epistaxis	
Epistaxis oder Otitis media/Infektionen der oberen Atemwege und Alter > 2 Jahre mit äusserst schweren CC, mehr als ein Belegungstag	D62A
Epistaxis oder Otitis media/Infektionen der oberen Atemwege, Alter > 2 Jahre und Alter < 12 Jahre oder komplizierender Prozedur oder bestimmter Diagnose, mehr als ein Belegungstag	D62B
Epistaxis oder Otitis media/Infektionen der oberen Atemwege und Alter >11 Jahre, mehr als ein Belegungstag	D62C
Other	
Erkrankungen des retikuloendothelialen Systems, des Immunsystems und Gerinnungsstörungen mit bestimmter komplexer Diagnose oder komplizierender Prozedur und mehr als ein Belegungstag	Q60A
Erkrankungen des retikuloendothelialen Systems, des Immunsystems und Gerinnungsstörungen mit komplexer Diagnose oder äusserst schweren CC, und mehr als ein Belegungstag	Q60B
Erkrankungen des retikuloendothelialen Systems, des Immunsystems und Gerinnungsstörungen, mehr als ein Belegungstag	Q60C
Rehabilitation (if directly following a hospitalisation for any reason above)	-

Fall related costs

The following SwissDRG codes were classified as fall-related if …

- … the patient had at least one fall in the same follow-up year

Inpatient episodes considered as fall-related	**SwissDRG**
Head / intracranial injury	
Intrakranielle Verletzung, mehr als ein Belegungstag, Intensivmedizinische Komplexbehandlung > 196/119 Aufwandspunkte oder IMCK > 196/184 Aufwandspunkte	B78A
Intrakranielle Verletzung, mehr als ein Belegungstag, Alter < 12 Jahre	B78B
Intrakranielle Verletzung, mehr als ein Belegungstag, Alter > 11 Jahre	B78C
Schädelfrakturen	B79Z
Andere Kopfverletzungen, mehr als ein Belegungstag	B80A, B80Z
Andere Kopfverletzungen, ein Belegungstag	B80B
Syncope	

Synkope und Kollaps, mit äusserst schweren CC	F73A
Synkope und Kollaps	F73B
Synkope und Kollaps oder Herzklappenerkrankungen ohne äusserst schwere oder schwere CC	F73Z
Musculoskeletal system	
Andere Eingriffe an Hüftgelenk und Femur mit Mehrfacheingriff, komplexer Prozedur, komplexer Diagnose oder bestimmtem Eingriff oder äusserst schwere CC	I08C
Andere Eingriffe an Hüftgelenk und Femur	I08D
Eingriffe an Humerus, Tibia, Fibula und Sprunggelenk, mit Mehrfacheingriff, bestimmtem beidseitigen Eingriff oder komplexer Prozedur/Diagnose	I13B
Eingriffe an Humerus, Tibia, Fibula und Sprunggelenk mit komplizierendem Eingriff, Alter > 15 Jahre	I13D
Eingriffe an Humerus, Tibia, Fibula und Sprunggelenk	I13E
Eingriffe am Fuss mit komplexem Eingriff mit kompl. Diagnose, od. Osteomyelitis / Arthritis, Alter < 16 Jahre, mehr als ein BT	I20C
Eingriffe am Fuss mit mehreren komplexen Eingriffen od. mit hochkomplexem Eingriff mit komplexer Diagnose, Alter > 15 Jahre, mehr als ein BT	I20D
Eingriffe am Fuss, mit komplexem Eingriff od. Weichteilschaden mehr als ein Belegungstag, Alter > 15 Jahre, oder bestimmter Eingriff od. kompliz. Diagnose	I20E
Eingriffe am Fuss, mehr als ein Belegungstag, Alter < 16 Jahre	I20F
Eingriffe am Fuss, mehr als ein Belegungstag, Alter > 15 Jahre	I20G
Bestimmte Eingriffe an Hüftgelenk und Femur oder komplexe Eingriffe an Ellenbogengelenk und Unterarm	I21C
Komplexe Eingriffe am Schultergelenk	I29Z
Eingriffe an Handgelenk und Hand mit komplexem Eingriff od. kompliz. Diagnose, Alter < 6 Jahre und mehr als ein Belegungstag	I32B
Eingriffe an Handgelenk und Hand, Alter > 5 Jahre und mehr als ein Belegungstag	I32C
Eingriffe an Handgelenk und Hand, ein Belegungstag	I32D
Eingriffe an Handgelenk und Hand	I32E
Muskel- und Sehnenerkrankungen oder Verstauchung, Zerrung und Luxation an Hüftgelenk, Becken und Oberschenkel, mehr als ein Belegungstag	I71Z
Verletzungen an Unterarm, Handgelenk, Hand oder Fuss mit schweren CC, mehr als ein Belegungstag	I74A
Verletzungen an Unterarm, Handgelenk, Hand oder Fuss, mehr als ein Belegungstag	I74B
Verletzungen an Unterarm, Handgelenk, Hand oder Fuss, Alter > 9 Jahre	I74C
Schwere Verletzungen an oberen oder unteren Extremitäten oder Entzündungen von Sehnen, Muskeln und Schleimbeuteln, Alter > 15 Jahre und mehr als ein Belegungstag	I75C
Mässig schwere Verletzungen an oberen oder unteren Extremitäten, mehr als ein Belegungstag	I77Z
Leichte bis moderate Verletzungen an oberen oder unteren Extremitäten, mehr als ein Belegungstag	I78Z
Rehabilitation (if directly following a hospitalisation for any reason above)	-

B) Adjudication of outpatient costs. *Allocation of outpatient costs related to AF and AF-related complications*

Costs were determined in 6 separate blocks:

AF-related costs exclusive of costs for medication and complications (Stroke/TIA, bleeding, falls)

Included all outpatient visits with tariff codes* that suggested an AF related treatment/control at the general practitioner or in hospital outpatient clinic.

Stroke/TIA-related costs without medication

Listed tariff codes* identified a Stroke/TIA-relevant visit or were in general classified as Stroke/TIA-related if the start of treatment (not the service date!) occurred within 3 months after the event (event date available from clinical data).

Bleeding-related costs

Listed tariff codes* identified a bleeding-related visit if they occurred within the first month after a bleeding event.
Additionally, certain laboratory tests were included in the costs if performed within 3 months after bleeding.

AF-related medication costs

Using ATC codes, the costs of all medications listed were considered as AF-related.

Stroke/TIA-related medication costs

Using ATC codes, the costs of all medications listed were considered as stroke/TIA-related if the medication was purchased within 6 months after the event.
Oral anticoagulation & beta blockers were not considered here due to overlap with AF-related medication costs.

Fall-related costs

Defined service providers and tarif codes* were classified as fall-related if the patient had at least one fall in the same follow-up year.

Abbreviations: AF: atrial fibrillation, ATC: Anatomical Therapeutic Chemical Classification, CC: complications or comorbidities, FU: follow-up, OR: operating room, TIA: transient ischemic attack

* Tarif codes (TARMED). https://www.bag.admin.ch/bag/de/home/versicherungen/krankenversicherung/krankenversicherung-leistungen-tarife/Aerztliche-Leistungen-in-der-Krankenversicherung/Tarifsystem-Tarmed.html (2021).

Hypothetical examples of how outpatient visits were represented in the health insurance data:

Example 1

Pat-ID	*Leistungsdatum*	*Leistungserbringer Obergruppe*	*Leistungserbringer Untergruppe*	*Tarifziffer*	*Text*
1	24.04.2014	Ärzte	Allg. Innere Med.	00.0010	Konsultation, erste 5 Min. (Grundkonsultation)
1	24.04.2014	Ärzte	Allg. Innere Med.	00.0030	+ Konsultation, letzte 5 Min. (Konsultationszuschlag)
1	24.04.2014	Ärzte	Allg. Innere Med.	00.2285	Nicht formalisierter Bericht, 11 bis 35 Zeilen Text
1	24.04.2014	Ärzte	Allg. Innere Med.	4707.00	Präsenztaxe für das ärztliche Praxislaboratorium, pro Patient mit Konsultation inkl. Laboranalysen und pro Tag; nur anwendbar bei Durchführung der Laboruntersuchungen im eigenen Praxislaboratorium nach Artikel 54 Absatz 1 Buchstabe a Ziffer 3 KVV
1	24.04.2014	Ärzte	Allg. Innere Med.	1700.00	Thromboplastinzeit nach Quick/INR
1	24.04.2014	Ärzte	Allg. Innere Med.	4707.10	Zuschlag für jede Analyse, die das Suffix C aufweist; nur anwendbar in Verbindung mit der Präsenztaxe nach 4707.00 bei Durchführung der Laboruntersuchungen im eigenen Praxislaboratorium nach Artikel 54 Absatz 1 Buchstabe a Ziffer 3 KVV und in Form der
1	24.04.2014	Ärzte	Allg. Innere Med.	4707.20	Zuschlag für jede Analyse, die das Suffix C aufweist; nur anwendbar in Verbindung mit der Präsenztaxe nach 4707.00 bei Durchführung der Laboruntersuchungen im eigenen Praxislaboratorium nach Artikel 54 Absatz 1 Buchstabe a Ziffer 3 KVV und in Form der

Identified this visit as AF-related visit. The total costs of this visit will be considered.

Example 2

Pat-ID	*Leistungsdatum*	*Leistungserbringer*	*Leistungserbringer*	*Tarifziffer*	*Text*
2	24.04.2014			00.0025	+ Konsultation bei Kindern unter 6 Jahren und Personen über 75 Jahren, jede weiteren 5 Min.
2	24.04.2014			00.0015	+ Zuschlag für hausärztliche Leistungen in der Arztpraxis
2	24.04.2014	Ärzte	Allg. Innere Med.	17.0010	Elektrokardiogramm ({EKG})
2	24.04.2014			00.0416	Kleine Untersuchung durch den Facharzt für Grundversorgung bei Kindern unter 6 Jahren und Personen über 75 Jahren, pro 5 Min.
2	24.04.2014			00.0010	Konsultation, erste 5 Min. (Grundkonsultation)
2	24.04.2014			00.0715	Punktion, venös, zwecks Blutentnahme, jede Lokalisation durch nichtärztliches Personal
2	24.04.2014			00.0135	Überweisungen an Konsiliarärzte in Abwesenheit des Patienten bei Kindern unter 6 Jahren und Personen über 75 Jahren, pro 1 Min.
2	24.04.2014	Ärzte	Allg. Innere Med.	6847571	NITROGLYC Streuli Kaukaps 0.8 mg Blist 30 Stk

Identifies this visit as AF-related visit. The total costs of this visit will be considered.

Costs of medication are not considered within the visits. Costs of AF relevant medications are calculated separately.

AF-related costs (excluding costs for Stroke/TIA, bleeding, falls)

Outpatient services at specialists outside the hospital
In principle, all services outside the hospital were classified as AF related if the following applied:

- *Leistungserbringer Kardiologie* (Leistungserbringer Obergruppe „Ärzte“ + Leistungserbringer Untergruppe „Kardiologie“)

Outpatient services in hospitals & at general practitioners/specialists not in hospital
In addition, the following rules applied to all outpatient services:
The services (tariff codes) in the table below were used to identify outpatient treatment episodes as AF-relevant treatment episodes. This means that as soon as one of these services occurred, all services of a treatment episode were classified as AF relevant.
However, if these services occurred in connection with a non-AF-specific X-ray (e.g. lower/upper extremities) or within an oncological examination, the treatment episode was considered non-AF-related (see list Contra-AF).

Outpatient services indicating an AF-related visit	Tarif code
Thromboplastinzeit nach Quick/INR	1700
EKG	17.0010
+ Zuschlag für physikalische Provokations-Tests bei Elektrokardiogramm ({EKG})	17.0020
+ Zuschlag für medikamentöse Provokations-Tests bei Elektrokardiogramm ({EKG})	17.0030
Kardiale medikamentöse Intervention unter kontinuierlicher Registrierung mittels 12-Ableitungs-EKG, als alleinige Leistung	17.0050
ELEKTROKARDIOGRAMM (EKG) DURCH FACHARZT AUSSERHALB PRAXIS/SPITAL	17.0060
Belastungs-{EKG}, Ergometrie	17.0090
EKG-Rhythmusstreifen, pro 5 Min.	17.0120
Holter-{EKG}, Anlegen inkl. Entfernen	17.0130
Holter-{EKG}, 8 bis 16 Std., Auswertung	17.0140
Holter-{EKG}, 16 bis 24 Std., Auswertung	17.0150
Patientenaktiviertes Langzeit-{EKG}, Anlegen inkl. Entfernen, Instruktion	17.0160
+ Zuschlag für Programmierung bei patientenaktiviertem Langzeit-{EKG}	17.0170
Patientenaktiviertes Langzeit-{EKG}, Auswertung	17.0180
Elettrocardiogramma ({ECG}) con elettrodo esofageo, incl. inserimento sonde	17.0200
Echokardiografie, transthorakal, qualitative und quantitative Untersuchung beim Erwachsenen älter als 16 Jahre	17.0210
+ Zuschlag für venöse echokardiografische Kontrastdarstellung	17.0220
Echokardiografie, transthorakal, Kontrolluntersuchung	17.0230
Echokardiografie, transoesophageal	17.0260
Stressechokardiografie, physische Belastung	17.0280
Stressechokardiografie, medikamentöse Belastung	17.0290
Echokardiografie mit advanced techniques	17.0300
Arterieller Gefässstatus mittels CW-Doppler, obere und untere Extremitäten	17.0410
Blutdruckmessung, 24 Std	17.0510
Auswertung einer nuklearkardiologischen Untersuchung des Herzens durch den Facharzt Kardiologie	17.0670
Auswertung einer {MRI}-Untersuchung des Herzens durch den Facharzt Kardiologie	17.0680
Kardangiografie, Grundleistung I	17.0710
Kardangiografie, arterieller Zugang, Grundleistung II	17.0740
+ Zuschlag zur Grundleistung II für anderen arteriellen Zugang als femoral (z.B. brachial usw.)	17.0750
+ Zuschlag zur Grundleistung II für zusätzlich venösen Zugang	17.0760
+ Zuschlag zur Grundleistung II für endovaskuläre Intervention	17.0778
+ Zuschlag zur Grundleistung II für endovaskuläre Intervention	17.0780
Kardangiografie, venöser Zugang, Grundleistung IV	17.0830

+ Zuschlag zur Grundleistung IV für transseptale Punktion	17.0840
+ Zuschlag zur Grundleistung IV für endovaskuläre Intervention	17.0850
Rechtsherzkatheter in Ruhe, Grundelement	17.0910
+ Zuschlag für Shunt-Bestimmung, Links-Rechts-Shunt und Rechts-Links-Shunt, jede Methode	17.0940
Linksherzkatheter, Grundelement	17.1010
+ Zuschlag für die supravalvuläre Aortografie zur Darstellung von Aortenwurzel u/o Aorteninsuffizienz	17.1080
Selektive Koronarografie, Grundelement	17.1090
+ Supplément pour la mise en place d'un cathéter de perfusion lors de {PTCA}	17.1150
Elektrophysiologische kardiale Diagnostik u/o Therapie	17.1310
+ Zuschlag für Vorhofstimulation	17.1320
+ Zuschlag für Kammerstimulation	17.1340
+ Zuschlag für Kontrollstimulation	17.1360
+ Zuschlag für pharmakologische Interventionen bei elektrophysiologischen Untersuchungen	17.1370
+ Zuschlag für Kontrolluntersuchung nach Ablatio	17.1400
Kardioversion bei Vorhofflimmern/Vorhofflattern, als alleinige Leistung	17.1510
Einlage eines provisorischen Schrittmachers, als alleinige Leistung	17.1530
Einlage eines definitiven Schrittmachers, eine Elektrode, als alleinige Leistung	17.1540
+ Zuschlag für zweite Elektrode bei definitivem Schrittmacher	17.1550
Batteriewechsel bei definitivem Schrittmacher	17.1560
Schrittmacherkontrolle, Einkammersystem, mit Parameterprogrammierung	17.1590
Schrittmacherkontrolle, Zweikammersystem, mit Parameterprogrammierung	17.1600
Schrittmacherkontrolle, Einkammersystem, ohne Parameterprogrammierung	17.1610
Schrittmacherkontrolle, Zweikammersystem, ohne Parameterprogrammierung	17.1620
Mise en place d'un défibrillateur cardioverteur implantable ({DCI})	17.1630
{ICD}-Kontrolle, Einkammersystem, ohne Schockauslösung	17.1640
{ICD}-Kontrolle, Zweikammersystem, ohne Schockauslösung	17.1650
{ICD}-Kontrolle, mit Schockauslösung	17.1660
Implantation eines Ereignisrekorders	17.1670
Datenübertragung und Auswertung bei implantiertem Ereignisrekorder, pro Abgriff	17.1680
Explantation eines Ereignisrekorders	17.1690
Technische Grundleistung 0, Kardangiografie/kardiologisch-interventionelle Radiologie, ambulanter Patient	17.1810
MRI Herz (Auswertung unter 17.0680)	39.5100

If one of the following drugs was dispensed during a treatment episode, the treatment episode was classified as AF-relevant. Purchases from the pharmacy were not considered here as they did not identify relevant visits and the cost of medication was calculated separately! The costs of medication were not included in the costs of the visit, as the costs of the medication were determined separately → only serveed as identification of an AF-relevant visit:

	ATC code				
Medication	Level 1	Level 2	Level 3	Level 4	Level 5
Oral anticoagulats					
Marcoumar (Phenprocoumon)	B	01	A	A	04
Sintrom (Acenocoumarol)	B	01	A	A	04
Pradaxa (Dabigatran)	B	01	A	E	07
Xarelto (Rivaroxaban)	B	01	A	F	01

Lixiana (Edoxaban)	B	01	A	F	03
Eliquis (Apixaban)	B	01	A	F	02
Beta-blockers					
Bilol (Bisoprolol)	C	07	A	B	07
Concor (Bisoprolol)	C	07	B	B	07
Carvedilol	C	07	A	G	02
Dilatrend (Carvedilol)	C	07	A	G	02
Beloc Zok (Metoprolol)	C	07	A	B	02
Lopresor (Metoprolol)	C	07	A	B	02
Meto Zerok (Metoprolol)	C	07	A	B	02
Nebilet (Nebivolol)	C	07	A	B	12
Brevibloc (Esmolol)	C	07	A	B	09
Inderal (Propanolol)	C	07	A	A	05
Atenil (Atenolol)	C	07	A	B	03
Tenormin (Atenolol)	C	07	A	B	03
Calcium-channel blockers					
Dilzem (Diltiazem)	C	08	D	B	01
Flamon (Verapamil)	C	08	D	A	01
Isoptin (Verapamil)	C	08	D	A	01
Antiarrythmics					
Tambocor (Flecainid)	C	01	B	C	04
Rhytmonorm (Propafenon)	C	01	B	C	03
Corvert (Ibutilid)	C	01	B	D	05
Brinavess (Vernakalant)	C	01	B	G	11
Sotalol	C	07	A	A	07
Multaq (Dronedaron)	C	01	B	D	07
Digoxin (Digoxin)	C	01	A	A	05
Amiodaron	C	01	B	D	01
Cordarone (Amiodaron)	C	01	B	D	01
Escodaron (Amiodaron)	C	01	B	D	01

Contra-AF related
If the following services were included in a visit, the entire visit was classified as non-AF-relevant, even if the visit included an AF-relevant service:

Outpatient services indicating a non-AF-related visit	**Tarif code**
Behandlung durch den Facharzt für Onkologie, pro 5 Min.	00.1530
Röntgen: Obere Extremität	39.02.01.04
Röntgen: Untere Extremität	39.02.01.05
Röntgen: Becken/Sakrum, erste Aufnahme	39.0210
Röntgen: Schultergelenk/Scapula/AC-Gelenk, erste Aufnahme	39.0220
Röntgen: Ellbogengelenk, erste Aufnahme	39.0240
Röntgen: Handgelenk, erste Aufnahme	39.0260
Röntgen: Hand, erste Aufnahme	39.0270
Röntgen: Finger, erste Aufnahme	39.0280
Röntgen: Hüfte, erste Aufnahme	39.0290
Röntgen: Knie, erste Aufnahme	39.0310
Röntgen: oberes Sprunggelenk (OSG), erste Aufnahme	39.0330
Röntgen: Fuss inkl. Calcaneus, erste Aufnahme	39.0340
Röntgen: Mammografie	39.02.04
MRI Mamma(e)	39.5130
MRI Schultergelenk und/oder Oberarme	39.5140
MRI Ellbogengelenke und/oder Vorderarme	39.5150
MRI Handgelenke und/oder Hand/Hände	39.5160

MRI Hüfte und/oder Oberschenkel	39.5170
MRI Kniegelenk und/oder Unterschenkel	39.5180
MRI Fuss und/oder Sprunggelenke, Fussgelenke inkl. Achillessehne	39.5190
Ultraschallgelenkuntersuchung Schultergelenk, pro Seite	39.3400
Ultraschallgelenkuntersuchung Kniegelenk, pro Seite	39.3402
Hémodialyse full care	33.0010
Blutstillung bei Epistaxis am Locus Kiesselbachi, jede Methode	10.0670
Blutstillung bei Epistaxis an anderer Lokalisation als Locus Kiesselbachi, jede Methode	10.0680
Wundversorgung ohne Einbezug komplexer Strukturen, Gesicht, Hals, Hand (ohne Nacken, Kopfhaut), erste 3 cm	04.1010
Obere gastrointestinale Endoskopie ({GI}-Endoskopie)	19.0410
Koloskopie, vollständig	19.1010

- ➔ Remark: some of these services were relevant for fall-related and bleeding-related costs, which were determined separately.

In addition, some service providers were classified as non-AF-relevant. This means that even if an AF-relevant service occurred during a visit of the service providers marked with "x", the visit was still classified as non-AF-relevant.

- ➔ Remark: some of the excluded service providers were considered for stroke/TIA costs (e.g. physiotherapists, ergo therapists), for bleeding costs (e.g. gastroenterologists), or for fall costs (e.g. orthopaedics).

Subgroups service providers, Data 2019	**Frequency of services in the data**	**Not AF-relevant (x)**
Anästhesiologie	1556	
Chirurgie	2820	
Dermatologie und Venerologie	9470	x
Gynäkologie	2650	x
Endokrinologie	4659	
Pneumologie	4339	
Neurochirurgie	476	
Neurologie	1159	
Psychatrie und Psychotherapie	1211	
Kinder- und Jugendpsychiatrie und -psychotherapie	45	x
Ophthalmologie	30988	x
Orthopädische Chirurgie und Traumatologie des Bewegungsapparates	4725	x
Oto-Rhino-Laryngologie	3526	x
Kinder- und Jugendmedizin	868	x
Radiologie	3161	
Tropen- und Reisemedizin	239	x
Urologie	6184	
Rheumatologie	5139	x
Allgemeine Innere Medizin	204096	
Angiologie	1084	
Kardiologie	15723	
Haematologie	1366	

Gastroenterologie	3576	x
Radio-Onkologie und Strahlentherapie	412	x
Nuklearmedizin	118	
Physikalische Medizin und Rehabilitation	130	
praktischer Arzt / Aerztin	21694	
Allergologie und klinische Immunologie	139	x
Arbeitsmedizin	65	
Herz- und thorakale Gefaesschirurgie	31	
Infektiologie	543	x
Kiefer- und Gesichtschirurgie	55	x
Medizinische Onkologie	2207	x
Nephrologie	1735	
Pathologie	3685	
Plastische, Rekonstruktive und Aesthetische Chirurgie	1084	x
Prävention und Gesundheitswesen	7	
Handchirurgie	188	x
Gruppenpraxen	27198	
Ärzte, Spezialfälle	103	
Zahnaerzte	218	x
ZAHNAERZTE-INSTITUTIONEN	12	x
Chiropraktoren	1495	x
Zentrumsversorgung, Niveau 1 (Universitaetsspitaeler)	61980	
Zentrumsversorgung, Niveau 2	115666	
Grundversorgung, Niveau 3	7286	
Grundversorgung, Niveau 4	7662	
Grundversorgung, Niveau 5	8781	
Spezialkliniken Chirurgie	4159	
Spezialkliniken Pädiatrie	13	x
Rehabilitationskliniken	1701	
Diverse Spezialkliniken	3926	
Spezialkliniken Geriatrie	460	
Psychiatrische Kliniken, Niveau 1	274	
Psychiatrische Kliniken, Niveau 2	98	
Spezialfaelle	255	
Pflegeheime	212	
Alters- und Pflegeheime	52	
AKUT- UND UEBERGANGSPFLEGE AUEP	9	
Apotheken	135845	
Spezialfaelle, Apotheken	608	
Privatlaboratorien	14948	
Blutspendezentren	219	
Mikrobiologie-Laboratorien	5862	
Genetik-Laboratorien	113	
Mikrobiologie/Genetik-Laboratorien	11688	

PhysiotherapeutInnen	13328	x
Organisationen der Physiotherapie	4436	x
Pflegefachpersonen	2510	
HEBAMMEN	22	x
Organisationen der Ergotherapie	772	x
ErgotherapeutInnen	455	x
LogopädInnen	66	x
Haus- und Krankenpflegevereine Spitex	42173	
Tages- oder Nachtstruktur	62	
Akut- und Uebergangspflege AUeP	55	
Ernaehrungsberatung	33	x
Diabetesgesellschaften	38	x
Organisationen der Ernaehrungsberatung	15	x
Abgabestellen Mittel und Gegenstaende	3397	
Spezialfaelle	310	
Transport- und Rettungsunternehmen	203	
Spezialfaelle	33	
Heilbaeder	18	
Uebrige Rechnungssteller	143	
Ausland	63	
Gemeinsame Einrichtung KVG	52	
SVK	426	
Optiker	443	x
Spezialfaelle	3	
ASCA	22	

Not used as marker (either too unspecific or not relevant for AF):

Outpatient services not relevant for allocation	**Tarif code**
Tilt-Test	17.0100
Echokardiografie foetal, qualitative und quantitative Untersuchung	17.0310
+ Zuschlag für einfache Belastung bei arteriellem Gefässstatus	17.0420
+ Zuschlag für Laufbandbelastung bei arteriellem Gefässstatus	17.0430
+ Zuschlag für Messung an einem zusätzlichen Segment bei arteriellem Gefässstatus, pro Segment	17.0440
Registrazione comparativa delle curve dei flussi arteriosi di segmenti vascolari simmetrici, mediante doppler CW/doppler PW bidirezionale, per singolo segmento	17.0460
Bidirektionale Doppleruntersuchung der oberflächlichen u/o tiefen Venen einer oberen/unteren Extremität, pro Seite	17.0490
Oszillometrische, automatische simultane Blutdruckmessung, vier Extremitäten	17.0500
Gefässplethysmografie, pro Extremität	17.0520
Gefässoszillografie, pro Extremitätenpaar	17.0530
+ Zuschlag für Provokations-Test bei Gefässoszillografie	17.0540
Statische Kapillarmikroskopie am Nagelfalz	17.0560
Transkutane Messung des Sauerstoffpartialdruckes	17.0590
+ Provokations-Test bei transkutaner Messung des Sauerstoffpartialdruckes	17.0600

Angiologische Volumetrie, pro Extremitätenabschnittspaar	17.0640
Hydrostatische Druckmessung mit Doppler-Ultraschall (Pole Pressure) oder Pulsabnehmer	17.0660
+ Zuschlag für Pulmonalisangiografie, selektive Darstellung	17.0950
+ Supplément pour la visualisation non sélective de l'artère mammaire interne, par côté	17.1020
+ Supplément pour visualisation de l'artère mammaire interne, injection sélective, par côté	17.1030
+ Zuschlag für die angiografische Darstellung der abdominellen Aorta, bzw. A. subclavia, Übersicht	17.1040
+ Zuschlag für Darstellung der Beckenarterien, Übersicht	17.1050
+ Supplément pour la visualisation de greffons de by-pass, injection sélective, par greffon	17.1070
+ Zuschlag für selektive Darstellung Arteria renalis, erster Abgang	17.1085
+ Zuschlag für selektive Darstellung Arteria renalis, jeder weitere Abgang	17.1086
{PTCA} bei Koronarstenosen oder Koronarverschlüssen, erstes dilatiertes Gefässsegment	17.1110
+ Zuschlag {PTCA} bei Koronarstenosen oder Koronarverschlüssen, jedes weitere dilatierte Gefässsegment	17.1130
+ Zuschlag für Stenteinlage bei {PTCA}, pro Stent	17.1140
+ Zuschlag für intrakoronare medikamentöse Therapie bei {PTCA}, pro Gefässsegment	17.1160
+ Supplément pour examen échographique intracoronarien lors de {PTCA}, par segment vasculaire	17.1180
Atriale Septostomie, jede Methode	17.1270
Myokardbiopsie	17.1280
+ Zuschlag für Abklärung von supraventrikulären Reentrytachykardien	17.1330
+ Ablatio einer akzessorischen Verbindung, erste Verbindung	17.1380
+ Ablatio einer akzessorischen Verbindung, jede weitere Verbindung	17.1390

AF related medication costs

The costs of all medications included in this list were considered as AF related medication costs. The medications were identified with the ATC code.

	ATC code				
AF related medication	Level 1	Level 2	Level 3	Level 4	Level 5
Oral anticoagulations					
Marcoumar (Phenprocoumon)	B	01	A	A	04
Sintrom (Acenocoumarol)	B	01	A	A	04
Pradaxa (Dabigatran)	B	01	A	E	07
Xarelto (Rivaroxaban)	B	01	A	F	01
Lixiana (Edoxaban)	B	01	A	F	03
Eliquis (Apixaban)	B	01	A	F	02
Beta-blockers					
Bilol (Bisoprolol)	C	07	A	B	07
Concor (Bisoprolol)	C	07	B	B	07
Carvedilol	C	07	A	G	02
Dilatrend (Carvedilol)	C	07	A	G	02
Beloc Zok (Metoprolol)	C	07	A	B	02
Lopresor (Metoprolol)	C	07	A	B	02
Meto Zerok (Metoprolol)	C	07	A	B	02
Nebilet (Nebivolol)	C	07	A	B	12
Brevibloc (Esmolol)	C	07	A	B	09

Inderal (Propanolol)	C	07	A	A	05
Atenil (Atenolol)	C	07	A	B	03
Tenormin (Atenolol)	C	07	A	B	03
Calcium-channel blockers					
Dilzem (Diltiazem)	C	08	D	B	01
Flamon (Verapamil)	C	08	D	A	01
Isoptin (Verapamil)	C	08	D	A	01
Antiarrythmics					
Tambocor (Flecainid)	C	01	B	C	04
Rhytmonorm (Propafenon)	C	01	B	C	03
Corvert (Ibutilid)	C	01	B	D	05
Brinavess (Vernakalant)	C	01	B	G	11
Sotalol	C	07	A	A	07
Multaq (Dronedaron)	C	01	B	D	07
Digoxin (Digoxin)	C	01	A	A	05
Amiodaron	C	01	B	D	01
Cordarone (Amiodaron)	C	01	B	D	01
Escodaron (Amiodaron)	C	01	B	D	01

The costs for the services “Bezugs-Check”, “Medikamenten-Check” and “Effizienzbeitrag” will not be considered in the cost calculation.

Stroke/TIA related cost excluding medication

The following services were classified as Stroke/TIA relevant if the start of treatment (not the service date!) occurred within 3 months after the event (date from clinical data).

1. Tarifs that identified a stroke/TIA-relevant visit:

Tarifs that identify a stroke/TIA-relevant visit	Tarif code
{CT} Neurokranium	39.4020
{MRI} Neurokranium Übersicht	39.5050
Duplex-Sonografie der intracraniellen Arterien, beidseits	39.3540
PW-Sonografie der intracraniellen Arterien beidseits	39.3550
Eintrittspauschale in die anerkannte Notfallaufnahme	35.0610
Notfall-Inkonvenienzpauschale C, Mo-So 22-7	00.2540
Lumbalpunktion	05.0100
Langzeit-EEG, ambulant (Kassetten-EEG-Recording), mehr als 20 Std.	05.0450
Neuromonotoring EEG	05.0500
Intrakraniales-EEG, pro 60 Min.	05.0530

2. Drugs that identified a stroke/TIA-relevant visit (the costs of stroke/TIA-relevant drugs were calculated separately). Statins and aspirin were not considered for identification because they are too unspecific for stroke/TIA:

Drugs that identify a stroke/TIA-relevant visit	Tarif code
Clopidogrel	B01AC04

3. Services of the following service providers were generally classified as stroke/TIA-relevant treatment started within 3 months of the event):
   Remark: If a service provider was not marked here, it does not mean that the services were not considered at all. For service providers without marking, the relevant visits were identified via the single tariff numbers and were not generally classified as stroke/TIA (e.g. radiology is taken

into account via the tariff number "CT Neurocranium" etc. so that not too many non-relevant X-ray examinations were classified as stroke/TIA-relevant).

Leistungserbringer Untergruppe, Daten 2019	Häufigkeit in Daten 2019	Stroke/TIA relevant (✓)
Anästhesiologie	1556	
Chirurgie	2820	
Dermatologie und Venerologie	9470	
Gynäkologie	2650	
Endokrinologie	4659	
Pneumologie	4339	
Neurochirurgie	476	✓
Neurologie	1159	✓
Psychatrie und Psychotherapie	1211	
Kinder- und Jugendpsychiatrie und -psychotherapie	45	
Ophthalmologie	30988	
Orthopädische Chirurgie und Traumatologie des Bewegungsapparates	4725	
Oto-Rhino-Laryngologie	3526	
Kinder- und Jugendmedizin	868	
Radiologie	3161	
Tropen- und Reisemedizin	239	
Urologie	6184	
Rheumatologie	5139	
Allgemeine Innere Medizin	204096	
Angiologie	1084	
Kardiologie	15723	
Haematologie	1366	
Gastroenterologie	3576	
Radio-Onkologie und Strahlentherapie	412	
Nuklearmedizin	118	
Physikalische Medizin und Rehabilitation	130	
praktischer Arzt / Aerztin	21694	
Allergologie und klinische Immunologie	139	
Arbeitsmedizin	65	
Herz- und thorakale Gefaesschirurgie	31	
Infektiologie	543	
Kiefer- und Gesichtschirurgie	55	
Medizinische Onkologie	2207	
Nephrologie	1735	
Pathologie	3685	
Plastische, Rekonstruktive und Aesthetische Chirurgie	1084	
Prävention und Gesundheitswesen	7	
Handchirurgie	188	

Gruppenpraxen	27198	
Ärzte, Spezialfälle	103	
Zahnaerzte	218	
ZAHNAERZTE-INSTITUTIONEN	12	
Chiropraktoren	1495	
Zentrumsversorgung, Niveau 1 (Universitaetsspitaeler)	61980	
Zentrumsversorgung, Niveau 2	115666	
Grundversorgung, Niveau 3	7286	
Grundversorgung, Niveau 4	7662	
Grundversorgung, Niveau 5	8781	
Spezialkliniken Chirurgie	4159	
Spezialkliniken Pädiatrie	13	
Rehabilitationskliniken	1701	✓
Diverse Spezialkliniken	3926	
Spezialkliniken Geriatrie	460	✓
Psychiatrische Kliniken, Niveau 1	274	
Psychiatrische Kliniken, Niveau 2	98	
Spezialfaelle	255	
Pflegeheime	212	✓
Alters- und Pflegeheime	52	✓
AKUT- UND UEBERGANG-SPFLEGE AUEP	9	✓
Apotheken	135845	
Spezialfaelle, Apotheken	608	
Privatlaboratorien	14948	
Blutspendezentren	219	
Mikrobiologie-Laboratorien	5862	
Genetik-Laboratorien	113	
Mikrobiologie/Genetik-Laboratorien	11688	
PhysiotherapeutInnen	13328	✓
Organisationen der Physiotherapie	4436	✓
Pflegefachpersonen	2510	✓
HEBAMMEN	22	
Organisationen der Ergotherapie	772	✓
ErgotherapeutInnen	455	✓
LogopädInnen	66	✓
Haus- und Krankenpflegevereine Spitex	42173	✓
Tages- oder Nachtstruktur	62	
Akut- und Uebergangspflege AUeP	55	✓
Ernaehrungsberatung	33	
Diabetesgesellschaften	38	
Organisationen der Ernaehrungsberatung	15	
Abgabestellen Mittel und Gegenstaende	3397	✓
Spezialfaelle	310	

Transport- und Rettungsunternehmen	203	✓
Spezialfaelle	33	
Heilbaeder	18	
Uebrige Rechnungssteller	143	
Ausland	63	
Gemeinsame Einrichtung KVG	52	
SVK	426	
Optiker	443	
Spezialfaelle	3	
ASCA	22	
Gesamt	821074	

Stroke/TIA related medication costs

The costs of the following medications were considered as stroke/TIA relevant if they were purchased within 6 months after a stroke/TIA. Oral anticoagulation and beta-blockers were not considered here, as these medications were included in the AF medication costs.

The costs for the services “Bezugs-Check”, “Medikamenten-Check” and “Effizienzbeitrag” were not considered in the cost calculation.

	ATC code				
Medication Stroke/TIA	Level 1	Level 2	Level 3	Level 4	Level 5
Thrombozytenaggregationshemmer					
Aspirin cardio (Acetylsalicylsäure)	B	01	A	C	06
Plavix (Clopidogrel)	B	01	A	C	04
Lipidlowering drugs					
Atorvastatin	C	10	A	A	05
Fluvastatin	C	10	A	A	04
Rosuvastatin	C	10	A	A	07
Simvastatin	C	10	A	A	01
Pravastatin	C	10	A	A	03
Pitavastatin	C	10	A	A	08
Rosuvastatin + Ezetimibe	C	10	B	A	06
Atorvastatin + Ezetimibe	C	10	B	A	05
Ezetimibe	C	10	A	X	09
Alirocumab	C	10	A	X	14
Evolocumab	C	10	A	X	13

Swiss-AF investigators

University Hospital Basel and Basel University: Stefanie Aeschbacher, Katalin Bhend, Steffen Blum, Leo Bonati, David Conen, Ceylan Eken, Urs Fischer, Corinne Girroy, Elisa Hennings, Elena Herber, Vasco Iten, Philipp Krisai, Michael Kühne, Maurin Lampart, Mirko Lischer, Nina Mäder, Christine Meyer-Zürn, Pascal Meyre, Andreas U. Monsch, Luke Mosher, Christian Müller, Stefan Osswald, Rebecca E. Paladini, Anne Springer, Christian Sticherling, Thomas Szucs, Gian Völlmin.
Principal Investigator: Stefan Osswald; Local Principal Investigator: Michael Kühne

University Hospital Bern: Faculty: Drahomir Aujesky, Juerg Fuhrer, Laurent Roten, Simon Jung, Heinrich Mattle; Research fellows: Seraina Netzer, Luise Adam, Carole Elodie Aubert, Martin Feller, Axel Loewe, Elisavet Moutzouri, Claudio Schneider;
Study nurses: Tanja Flückiger, Cindy Groen, Lukas Ehrsam, Sven Hellrigl, Alexandra Nuoffer, Damiana Rakovic, Nathalie Schwab, Rylana Wenger, Tu Hanh Zarrabi Saffari.
Local Principal Investigator: Nicolas Rodondi, Tobias Reichlin

Stadtspital Triemli Zurich: Christopher Beynon, Roger Dillier, Michèle Deubelbeiss,
Franz Eberli, Christine Franzini, Isabel Juchli, Claudia Liedtke, Samira Murugiah, Jacqueline Nadler, Thayze Obst, Jasmin Roth, Fiona Schlomowitsch, Xiaoye Schneider, Katrin Studerus, Noreen Tynan, Dominik Weishaupt.
Local Principal Investigator: Andreas Müller

Kantonspital Baden: Simone Fontana, Corinne Friedli, Silke Kuest, Karin Scheuch, Denise Hischier, Nicole Bonetti, Alexandra Grau, Jonas Villinger, Eva Laube, Philipp Baumgartner, Mark Filipovic, Marcel Frick, Giulia Montrasio, Stefanie Leuenberger, Franziska Rutz.
Local Principal Investigator: Jürg-Hans Beer

Cardiocentro Lugano: Angelo Auricchio, Adriana Anesini, Cristina Camporini, Giulio Conte, Maria Luce Caputo, Francois Regoli.
Local Principal Investigator: Tiziano Moccetti

Kantonsspital St. Gallen: Roman Brenner, David Altmann, Michaela Gemperle.
Local Principal Investigator: Peter Ammann

Hôpital Cantonal Fribourg: Mathieu Firmann, Sandrine Foucras, Martine Rime.
Local Principal Investigator: Daniel Hayoz

Luzerner Kantonsspital: Benjamin Berte, Kathrin Bühler, Virgina Justi, Frauke Kellner-Weldon, Brigitta Mehmann, Sonja Meier, Myriam Roth, Andrea Ruckli-Kaeppeli, Ian Russi, Kai Schmidt, Mabelle Young, Melanie Zbinden.
Local Principal Investigator: Richard Kobza

Ente Ospedaliero Cantonale Lugano: Elia Rigamonti, Carlo Cereda, Alessandro Cianfoni, Maria Luisa De Perna, Jane Frangi-Kultalahti, Patrizia Assunta Mayer Melchiorre, Anica Pin,Tatiana Terrot, Luisa Vicari.
Local Principal Investigator: Giorgio Moschovitis.

University Hospital Geneva: Georg Ehret, Hervé Gallet, Elise Guillermet, Francois Lazeyras, Karl-Olof Lovblad, Patrick Perret, Philippe Tavel, Cheryl Teres.
Local Principal Investigator: Dipen Shah

University Hospital Lausanne: Nathalie Lauriers, Marie Méan, Sandrine Salzmann, Jürg Schläpfer.

Local Principal Investigator: Alessandra Pia Porretta

Bürgerspital Solothurn: Andrea Grêt, Jan Novak, Sandra Vitelli.
Local Principal Investigator: Frank-Peter Stephan

Ente Ospedaliero Cantonale Bellinzona: Jane Frangi-Kultalahti, Augusto Gallino, Luisa Vicari.
Local Principal Investigator: Marcello Di Valentino

University of Zurich/University Hospital Zurich: Helena Aebersold, Fabienne Foster, Matthias Schwenkglenks.

Medical Image Analysis Center AG Basel: Jens Würfel (Head), Anna Altermatt, Michael Amann, Marco Düring, Petra Huber, Esther Ruberte, Tim Sinnecker, Vanessa Zuber.

Clinical Trial Unit Basel: Michael Coslovsky (Head), Pascal Benkert, Gilles Dutilh, Milica Markovic, Pia Neuschwander, Patrick Simon

Schiller AG Baar: Ramun Schmid