

Supplementary Materials:

Table S1: ICD-10-GM Codes/ OPS diagnosis and procedure codes/ATC codes relevant for analysis.

Antiarrhythmic drugs	
Class Ia	ATC: C01BA
Class Ib	ATC: C01BB
Class Ic	ATC: C01BC
Class III excluding amiodarone	ATC: C01BCD excluding C01BD01
Amiodarone	ATC: C01BD01
Arrhythmia	
Atrial re-entrant tachycardia	ICD-10-GM: I47.1
Atrial fibrillation	ICD-10-GM: I48.0 - I48.2
Atrial flutter	ICD-10-GM: I48.3, I48.4
Ventricular re-entrant tachycardia	ICD-10-GM: I47.0
Ventricular tachycardia (other)	ICD-10-GM: I47.2
Ventricular extrasystole	ICD-10-GM: I49.3
Ventricular flutter/ fibrillation	ICD-10-GM: I49.0
Cardiac arrest (not specified further)	ICD-10-GM: I46.1, I46.1, I46.9
Baseline characteristics	
Left heart failure	ICD-10-GM: I50.1
Right heart failure	ICD-10-GM: I50.0
Implantation of a pacemaker	OPS: 5-377.0- 5-377.4
Implantation of an implantable cardioverter defibrillator	OPS: 5-377.5, 5-377.7
Obesity	ICD-10-GM: E66
Smoking	ICD-10-GM: F17
Alcohol abuse	ICD-10-GM: F10
Chronic kidney disease	ICD-10-GM: N18.4, N18.5
Liver dysfunction	ICD-10-GM: K72.1, K72.7
Heart failure drug therapy	
ACE-Inhibitors/ Angiotensin II receptor blockers	ATC: C09
Diuretics	ATC: C03
Betablockers excluding sotalol	ATC: C07A excluding C07AA07
Cardiac glycosides	ATC: C01AA
Calcium channel blockers	ATC: C08
Thyroid dysfunction	
Hyperthyroidism	ICD-10-GM: E05
Hypothyroidism	ICD-10-GM: E03
Thyroiditis	ICD-10-GM: E06
Thyroid radiotherapy	OPS: 8- 53
Thyroid surgery	OPS: 5- 06
Drug therapy/catheter ablation	
Catheter ablation	OPS: 1-26
Levothyroxine	ATC: H03AA01
Thiamazole	ATC: H03BB02
Propylthiouracil	ATC: H03BA02
Sodiumperchlorate	ATC: H03BC02

Table S2: ICD-10 GM-Codes used for identification and grouping of patients with congenital heart disease (CHD).

Simple CHD	
Isolated ventricular septal defect	Q21.0
Persistent arterial duct	Q25.0
Isolated congenital valve disease	Q23.0, Q23.1, Q22.4, Q22.8, Q22.9, Q23.2, Q23.3, Q22.1, Q22.2, Q22.3
Other congenital malformation of the great arteries	Q25.8, Q25.9
Moderate complexity CHD	
Tetralogy of Fallot	Q21.3, Q21.80, (Q22.0 and Q21.0)
Ebstein's anomaly	Q22.5
Aortic isthmus stenosis, interrupted aortic arch	Q25.1, Q25.2
Atrioventricular septal defect	Q21.2
Partial anomalous pulmonary venous connection	Q26.3, Q26.4
Severely complex CHD	
Univentricular heart	Q20.1, Q20.2, Q20.4, Q22.6, Q23.4, (Q22.0 without Q21.0) I27.8 and at least one further Q-Code with the exception of Q21.1
Eisenmenger's syndrome	or Q21.88 and at least one further Q-Code with the exception of Q21.1
Transposition of the great arteries (TGA)	Q20.3, Q20.5
Other complex heart malformation, e.g. total anomalous pulmonary venous connection, common arterial trunk	Q20.0, Q26.2

Figure S1: Study design.

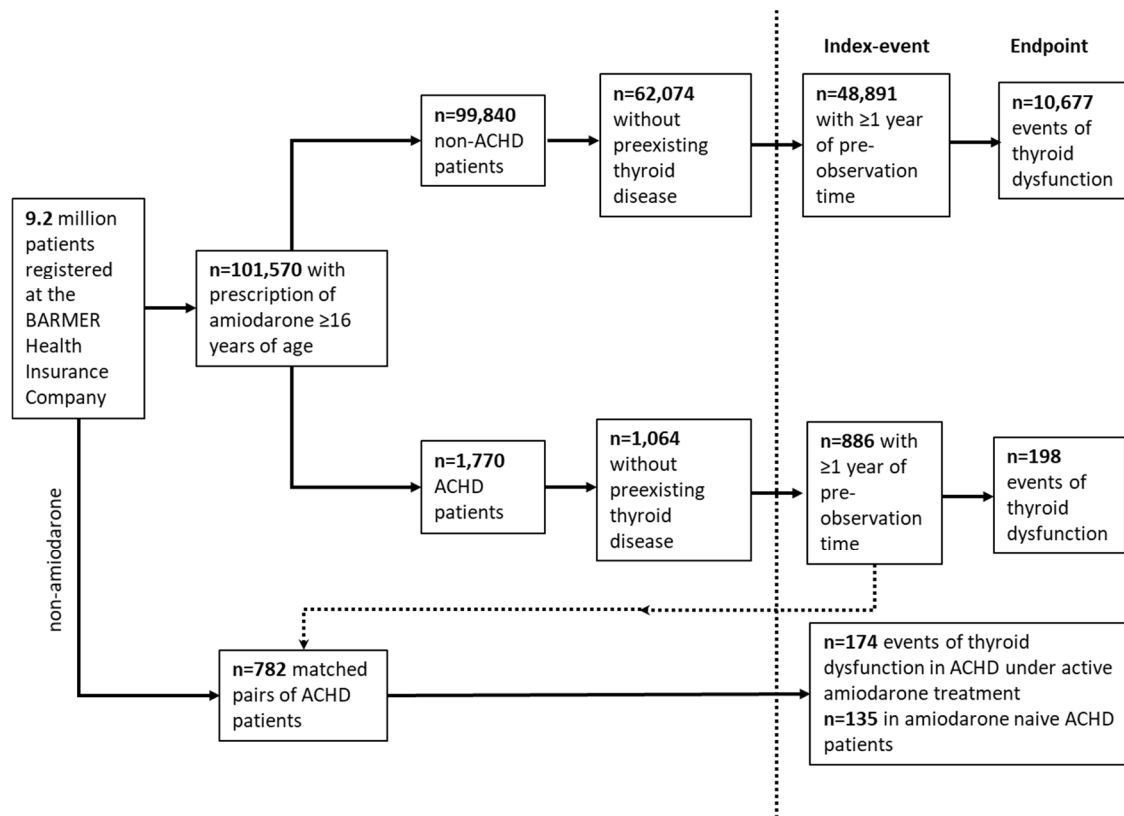


Table S3: Risk factors for occurrence of **hyperthyroidism** after amiodarone intake in **all patients**; results of the multivariable Cox regression analysis.

*active amiodarone intake defined as prescription of amiodarone within 90 days before and after analyzation time. To avoid the problem of non-proportional hazards, a stepwise analysis showing yearly intervals was used, thus allowing the corresponding coefficient to be time-varying.

Variable	Hazard ratio (95% CI)	p-value
Active amiodarone intake (year 1)*	1.45 (1.23-1.71)	<0.001
Active amiodarone intake (year 2)*	1.40 (1.23-1.59)	<0.001
Active amiodarone intake (year 3)*	2.70 (2.37-3.07)	<0.001
Active amiodarone intake (year ≥ 4)*	3.33 (2.99-3.70)	<0.001
Age /10 years	0.89 (0.86-0.91)	<0.001
Female gender	1.13 (1.06-1.19)	<0.001
Congenital heart disease	0.95 (0.78-1.15)	0.60
Pacemaker therapy	1.06 (0.96-1.17)	0.27
Implantable cardioverter defibrillator	1.15 (1.05-1.26)	0.003
Chronic kidney disease	0.90 (0.75-1.09)	0.28
Liver dysfunction	0.83 (0.26-2.61)	0.75
Alcohol abuse	0.96 (0.84-1.08)	0.48
Smoking	1.13 (1.04-1.22)	0.004
Obesity	0.88 (0.83-0.93)	<0.001

Table S4: Risk factors for occurrence of **hyperthyroidism** after amiodarone intake in adults with **congenital heart disease only** (CHD); results of the multivariable Cox regression analysis.
*active amiodarone intake defined as prescription of amiodarone within 90 days before and after analyzation time. To avoid the problem of non-proportional hazards, a stepwise analysis showing yearly intervals was used, thus allowing the corresponding coefficient to be time-varying.

Variable	Hazard ratio (95% CI)	<i>p</i> -value
Active amiodarone intake (year 1)*	1.01 (0.33-3.10)	0.98
Active amiodarone intake (year 2)*	2.09 (1.00-4.40)	0.05
Active amiodarone intake (year 3)*	4.21 (1.61-10.99)	0.003
Active amiodarone intake (year ≥4)*	4.12 (2.02-8.40)	<0.001
Age /10 years	0.93 (0.82-1.07)	0.32
Female gender	1.36 (0.90-2.05)	0.15
Medium complexity CHD vs. simple	1.06 (0.67-1.68)	0.81
High complexity CHD vs. simple	1.33 (0.74-2.39)	0.33
Pacemaker therapy	1.39 (0.77-2.49)	0.27
Implantable cardioverter defibrillator	1.32 (0.72-2.41)	0.37
Alcohol abuse	0.28 (0.04-2.16)	0.22
Smoking	0.93 (0.48-1.79)	0.82
Obesity	0.79 (0.49-1.27)	0.33

Table S5: Risk factors for occurrence of hypothyroidism after amiodarone intake in all patients; results of the multivariable Cox regression analysis.

*active amiodarone intake defined as prescription of amiodarone within 90 days before and after analyzation time. To avoid the problem of non-proportional hazards, a stepwise analysis showing yearly intervals was used, thus allowing the corresponding coefficient to be time-varying.

Variable	Hazard ratio (95% CI)	p-value
Active amiodarone intake (year 1)*	2.44 (2.05-2.90)	<0.001
Active amiodarone intake (year 2)*	2.31 (2.02-2.64)	<0.001
Active amiodarone intake (year 3)*	2.09 (1.82-2.40)	<0.001
Active amiodarone intake (year ≥ 4)*	2.87 (2.66-3.10)	<0.001
Age /10 years	1.04 (1.01-1.07)	0.005
Female gender	1.63 (1.56-1.72)	<0.001
Congenital heart disease	1.08 (0.91-1.28)	0.36
Pacemaker therapy	1.12 (1.03-1.22)	0.005
Implantable cardioverter defibrillator	1.38 (1.27-1.49)	<0.001
Chronic kidney disease	1.89 (1.68-2.12)	<0.001
Liver dysfunction	0.57 (0.19-1.75)	0.33
Alcohol abuse	1.45 (1.31-1.60)	<0.001
Smoking	1.11 (1.03-1.20)	0.005
Obesity	1.11 (1.06-1.16)	<0.001

Table S6: Risk factors for occurrence of **hypothyroidism** after amiodarone intake in **adults with congenital heart disease only** (CHD); results of the multivariable Cox regression analysis.

*active amiodarone intake defined as prescription of amiodarone within 90 days before and after analyzation time. To avoid the problem of non-proportional hazards, a stepwise analysis showing yearly intervals was used, thus allowing the corresponding coefficient to be time-varying.

Variable	Hazard ratio (95% CI)	<i>p</i> -value
Active amiodarone intake (year 1)*	3.37 (0.97-11.74)	0.06
Active amiodarone intake (year 2)*	2.36 (1.12-5.00)	0.02
Active amiodarone intake (year 3)*	2.47 (0.85-7.21)	0.10
Active amiodarone intake (year ≥4)*	2.39 (1.40-4.11)	0.002
Age/10 years	0.87 (0.77-0.99)	0.03
Female gender	1.79 (1.27-2.52)	0.001
Medium complexity CHD vs. simple	1.27 (0.86-1.89)	0.23
High complexity CHD vs. simple	1.73 (1.11-2.70)	0.02
Pacemaker therapy	1.27 (0.74-2.18)	0.39
Implantable cardioverter defibrillator	1.29 (0.71-2.33)	0.41
Chronic kidney disease	2.97 (1.16-7.59)	0.02
Alcohol abuse	1.31 (0.54-3.18)	0.55
Smoking	1.41 (0.87-2.31)	0.17
Obesity	1.06 (0.73-1.54)	0.77

Table S7: Use of catheter ablation and antiarrhythmic drug treatment around the time of diagnosis of thyroid dysfunction in adults with congenital heart disease (ACHD) versus non-ACHD.

	Non-ACHD, n=48,891		ACHD, n=886	
	6 months before endpoint	6 months after endpoint	6 months before endpoint	6 months after endpoint
Combined endpoint thyroid dysfunction, n (%)	10,677 (21.8)		198 (22.3)	
Catheter ablation, n (%)	858 (8.0)	1,352 (12.7)	23 (11.6)	31 (15.7)
Intake of antiarrhythmic drugs				
Class Ia, n (%)	5 (0.0)	4 (0.0)	0 (0.0)	0 (0.0)
Class Ib, n (%)	9 (0.1)	6 (0.1)	0 (0.0)	0 (0.0)
Class Ic, n (%)	199 (1.9)	221 (2.1)	7 (3.5)	8 (4.0)
Class III, n (%)	7,904 (74.0)	5,171 (48.4)	129 (65.2)	80 (40.4)
Amiodarone only, n (%)	7,842 (73.4)	5,022 (47.0)	128 (64.6)	75 (37.9)
Hyperthyroidism, n (%)	5,094 (10.4)		103 (11.6)	
Catheter ablation, n (%)	425 (8.3)	714 (14.0)	13 (12.6)	17 (16.5)
Intake of antiarrhythmic drugs				
Class Ia, n (%)	3 (0.1)	3 (0.1)	0 (0.0)	0 (0.0)
Class Ib, n (%)	5 (0.1)	5 (0.1)	0 (0.0)	0 (0.0)
Class Ic, n (%)	118 (2.3)	149 (2.9)	3 (2.9)	6 (5.8)
Class III, n (%)	3,613 (70.9)	1,990 (39.1)	64 (62.1)	32 (31.1)
Amiodarone only, n (%)	3,574 (70.2)	1,882 (36.9)	64 (62.1)	29 (28.2)
Hypothyroidism, n (%)	7,079 (14.5)		138 (15.6)	
Catheter ablation, n (%)	587 (8.3)	863 (12.2)	16 (11.6)	22 (15.9)
Intake of antiarrhythmic drugs				
Class Ia, n (%)	2 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)
Class Ib, n (%)	7 (0.1)	4 (0.1)	0 (0.0)	0 (0.0)
Class Ic, n (%)	117 (1.7)	109 (1.5)	3 (2.2)	1 (0.7)
Class III, n (%)	4,978 (70.3)	3,628 (51.3)	82 (59.4)	61 (44.2)
Amiodarone only, n (%)	4,925 (69.6)	3,554 (50.2)	81 (58.7)	59 (42.8)