SUPPLEMENTARY DATA

TriNetX database

The TriNetX data are collected from member health care organizations (HCOs) and originate from their primary electronic health records system. A typical HCO is a large academic health center, with data coming from the majority of its affiliates. A single HCO frequently has more than one facility, including main and satellite hospitals. The data are stored on the TriNetX database via a physical server at the institution's data center or a virtual hosted appliance. The TriNetX platform comprises a series of these appliances connected into a federated network. This network can broadcast queries to each appliance. Results are subsequently collected and aggregated. Once the data are sent to the network, they are mapped to a standard and controlled set of clinical terminologies and undergo a data quality assessment, including 'data cleaning' that rejects records that do not meet the TriNetX quality standards. The TriNetX database performs an internal and extensive data quality assessment with every refresh based on conformance, completeness, and plausibility (http://doi.org/10.13063/2327-9214.1244). HIPAA (Health Insurance Portability and Accountability Act) compliance of the clinical patient data is achieved using deidentification. Available data types within the network include demographics, diagnoses (represented by ICD-10-CM codes), procedures (coded in ICD-10-PCS or Current Procedural Terminology (CPT)), and measurements (coded to LOINC). While extensive information is provided about patients' diagnoses and procedures, other variables (such as socioeconomic and lifetime factors) are not comprehensively represented. The advantage of electronic health record data over insurance claim data is that both insured and uninsured patients are included. An advantage of electronic health record data over survey data is that the former represents the diagnostic rates in the population presenting to health care facilities. This provides an accurate account of the burden of specific diagnoses on health care systems. One primary limitation of relying on diagnoses is that they do not account for undiagnosed patients who might have a condition but have not yet received medical support. Another general limitation of electronic health record data is that a

patient may be seen in different HCOs for different components of their care. If one health care organization is not part of the federated network, then part of their medical records may not be available. Using a network of HCOs, rather than a single site, limits this possibility but does not fully remove it.

Propensity Score Matched Analyses Using logistic regression [Logistic Regression of the scikit-learn package in Python (version 3.7)], TriNetX performs a 1:1 greedy nearest neighbor matching model, with a caliper of 0.1 pooled standard deviations. To eliminate bias resulting from nearest neighbor algorithms, the orders of rows are randomized. Any baseline characteristic with a standardized mean difference between cohorts lower than 0.1 is deemed well matched (https://www.tandfonline.com/doi/full/10.1080/00273171.2011.568786).

Schoenfeld residuals test

This test evaluates whether the relationship between the predictor variables and the hazard function remains constant over time. The null hypothesis was that the effect of amyloidosis on the hazard was constant over time. The chi-square statistic quantifies the difference between the observed and expected Schoenfeld residuals. A larger chi-square value suggests a greater deviation from the expected values, indicating a potential violation of the proportional hazards assumption. Conversely, a smaller chi-square value indicates that the observed residuals closely match the expected values, supporting the proportional hazard assumption. The *P*-value, derived from the chi-square statistic, reflects the probability of observing such deviations under the null hypothesis. A *P* value for proportionality (*P* prop.)> .05 suggests that the observed deviations are likely due to random variation, and thus, the proportional hazards assumption holds. In contrast, a *P* prop. < .05 indicates that the observed deviations are unlikely to be due to random variation, implying that the proportional hazards assumption has been violated.

Table 1 of the supplementary data. ICD-10-CM and CPT codes for inclusion and exclusion criteria in patients with amyloidosis who had transcatheter aortic valve replacement

	ICD-10-CM and CPT codes
Patients with amyloidosis	
Inclusion criteria	1. Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve (CPT code 1021150) and 2. Amyloidosis (ICD-10-CM code E85.0)
Exclusion criteria	None
Patients without amyloidosis	
Inclusion criteria	1. Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve (CPT code 1021150)
Exclusion criteria	2. Amyloidosis (ICD-10-CM code E85.0)

Table 2 of the supplementary data. Codes for the 1-year risk of adverse events

	ICD-10-CM, ICD-10-PCS, CPT, HCPCS, and SNOMED codes
All-cause death	• Deceased (TriNetX variable)
Acute heart failure	• ICD-10-CM code: I50.21 (Acute systolic (congestive) heart failure) • ICD-10-CM code: I50.23 (Acute on chronic systolic (congestive) heart failure) • ICD-10-CM code: I50.31 (Acute diastolic (congestive) heart failure) • ICD-10-CM code: I50.33 (Acute on chronic diastolic (congestive) heart failure) • ICD-10-CM code: I50.41 (Acute combined systolic (congestive) and diastolic (congestive) heart failure) • ICD-10-CM code: I50.43 (Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure)
Ischemic stroke	• ICD-10-CM code I63: (Ischemic stroke) • ICD-10-CM code: G45 (Transient cerebral ischemic attacks and related syndromes)
Pacemaker implantation	• CPT code:1006075 (Pacemaker or Implantable Defibrillator Procedures) • HCPCS code: C1785 (Pacemaker, dual chamber, rate-responsive) • HCPCS code: C1786 (Pacemaker, single chamber, rate-responsive) • HCPCS code: C2621 (Pacemaker, other than single or dual chamber) • CPT code: 1027823 (Pacemaker-Leadless and Pocketless System) • HCPCS code: C2620 (Pacemaker, single chamber, nonrate-responsive) • HCPCS code: C2619 (Pacemaker, dual chamber, nonrate-responsive)

	• ICD-10-PCS code: 02HL3JZ (Insertion of Pacemaker Lead into Left Ventricle, Percutaneous Approach) • ICD-10-PCS code: 02H73JZ (Insertion of Pacemaker Lead into Left Atrium, Percutaneous Approach) • CPT code: 33207 (Insertion of new or replacement of permanent pacemaker with transvenous electrode(s); ventricular) • SNOMED code: 233174007 (Cardiac pacemaker procedure) • CPT code: 33216 (Insertion of a single transvenous electrode, permanent pacemaker, or implantable defibrillator) • ICD-10-PCS code: 0JH604Z (Insertion of Pacemaker, Single Chamber into Chest Subcutaneous Tissue and Fascia, Open Approach) • SNOMED code: 307280005 (Implantation of cardiac pacemaker)
Aute kidney injury	• ICD10CM code: N17 (Acute kidney failure)

Table 3 of the supplementary data. Risk of primary and secondary outcomes in TAVR patients with and without amyloidosis after propensity score matching from 2005 to 2019

	With amyloidosis events	Without amyloidosis - events	HR (95%CI)	Chi-square	*P*
Composite	116 (19.7)	90 (15.3)	1.35 (1.03-1.78)	0.863	.353
Acute HF	64 (10.8)	47 (7.2)	1.37 (0.94-1.99)	0.466	.495
Stroke	31 (5.2)	17 (2.8)	1.84 (1.02-3.32)	3.521	.061
Acute kidney injury	35 (5.8)	28 (4.7)	1.19 (0.73-1.96)	2.347	.126
PM implantation	27 (4.5)	23 (3.9)	1.18 (0.67-2.06)	0.230	.632
All-cause death	15 (2.5)	13 (2.2)	1.09 (0.52-2.28)	2.088	.148

HF, heart failure; HR, hazard ratio; PM, pacemaker.

Unless otherwise indicated, the data are expressed as No. (%).

Table 4 of the supplementary data. Risk of primary and secondary outcomes in TAVR patients with and without amyloidosis after propensity score matching from 2020 to 2023.

	With amyloidosis events	Without amyloidosis - events	HR (95%CI)	Chi-square	*P*
Composite	228 (38.7)	205 (34.8)	1.17 (1.00-1.42)	0.308	.579
Acute HF	126 (21.4)	102 (17.3)	1.26 (0.97-1.64)	2.886	.089
Stroke	64 (10.8)	54 (9.1)	1.13 (0.79-1.63)	0.463	.496
Acute kidney injury	90 (15.3)	74 (12.5)	1.19 (0.88-1.62)	0.889	.346
PM implantation	60 (10.2)	48 (8)	1.22 (0.84-1.78)	1.165	.281
All-cause death	40 (6.8)	48 (8)	0.77 (0.51-1.18)	2.542	.111

HF, heart failure; HR, hazard ratio; PM, pacemaker.

Unless otherwise indicated, the data are expressed as No. (%).