Table S1: Diagnosis and procedure codes used for this analysis

OPS codes	
5-351.0*	Surgical aortic valve replacement
5-35a.0*	Transcatheter aortic valve replacement
5-361.*, 5-362.*, 5-363.*,	Coronary artery bypass graft
5-351.1*, 5-351.2*, 5-353.1, 5-353.2	Surgical mitral valve replacement/reconstruction
5-351.4*	Surgical tricuspid valve replacement
5-377.0 et seqq.	Permanent pacemaker implantation
8-800.7* since 2010: 8-800.c*	Transfusion of RBC

Diagnosis	
I35.0, I06.0	Aortic valve stenosis (degenerative/rheumatic)
I35.2, I06.2	Combined aortic valve diseases (degenerative/rheumatic)
I50.1*	Left ventricular congestive heart failure *(according to NYHA classes)*
I10*	Arterial Hypertension
I25.11, I25.12, I25.13	Coronary artery disease
I25.20, I25.21, I25.22	Previous myocardial infarction *(within 4 months/1 year/after 1 year)*
Z95.1	Previous coronary artery bypass graft
Z95.1 – Z95.4	Previous cardiac surgery
I70.20-I70.25, I70.8, I70.9, I73.9	Peripheral vascular disease
I65.2	Carotid disease
I21*	Acute myocardial infarction *(within the last 28 days)*
J44*	Chronic obstructive pulmonary disease
I27*	Pulmonary hypertension
N18*	Renal disease
N17*	Acute kidney injury
I48.1*	Atrial fibrillation
E10* - E14*	Diabetes
I63*, I64	Stroke or cerebral infarction incl. occlusion and stenosis of cerebral and precerebral arteries, resulting in cerebral infarction

Table S2: Results of the logistic regression model, transformation into discrete event probabilities and subsequent meta regressions

First step: Logistic regression model on 43,996 TAVI cases with in-hospital mortality as dependent variable, an interaction term (n_ik_year_50_100#year) between categorical time (in years) and volume categories and 22 predefined patient and procedural characteristics as potential confounder.

n_ik_year_50_100	OR	p-value	95% CI
procedure volume <50	1		
procedure volume 50-99	0.989	0.98	0.437 - 2.241
procedure volume >=100	0.668	0.004	0.506 - 0.882
year			
2008	1		
2009	0.929	0.671	0.661 - 1.305
2010	0.844	0.376	0.579 - 1.229
2011	0.686	0.032	0.486 - 0.968
2012	0.525	0.004	0.340 - 0.812
2013	0.465	0.001	0.302 - 0.718
2014	0.453	0.001	0.288 - 0.712
n_ik_year_50_100#year			
procedure volume 50-99 # 2009	0.929	0.874	0.376 - 2.298
procedure volume 50-99 # 2010	0.909	0.828	0.384 - 2.151
procedure volume 50-99 # 2011	1.105	0.822	0.464 - 2.631
procedure volume 50-99 # 2012	1.280	0.597	0.512 - 3.202
procedure volume 50-99 # 2013	1.141	0.781	0.452 - 2.877
procedure volume 50-99 # 2014	0.908	0.845	0.346 - 2.385
procedure volume >=100 # 2009	1.007	0.981	0.583 - 1.740
procedure volume >=100 # 2010	1.120	0.598	0.735 - 1.705
procedure volume >=100 # 2011	1.260	0.223	0.869 - 1.827
procedure volume >=100 # 2012	1.399	0.164	0.872 - 2.244
procedure volume >=100 # 2013	1.606	0.046	1.009 - 2.558
procedure volume >=100 # 2014	1.100	0.687	0.692 - 1.749
Female	0.902	0.045	0.815 - 0.998
Age in years	1.009	0.155	0.997 - 1.022
Estimated logistic EuroSCORE	1.022	0.000	1.015 - 1.029
Aortic valve stenosis	0.636	0.000	0.504 - 0.802
Combined aortic valve diseases	0.553	0.000	0.447 - 0.685
NYHA II	0.551	0.000	0.423 - 0.717
NYHA III or IV	1.550	0.000	1.264 - 1.900
CAD	1.034	0.517	0.934 - 1.144
Hypertension	0.698	0.000	0.612 - 0.797
Previous MI (within 4 months)	0.683	0.048	0.467 - 0.997
Previous MI (within 1 year)	1.042	0.881	0.608 - 1.785
Previous MI (after 1 year)	0.979	0.816	0.821 - 1.169
Previous CABG	1.017	0.884	0.809 - 1.278
Previous cardiac surgery	0.808	0.117	0.619 - 1.055
Peripheral vascular disease	1.118	0.140	0.964 - 1.295
Carotid disease	0.896	0.165	0.768 - 1.046
COPD	0.979	0.744	0.863 - 1.111
Pulmonary hypertension	0.852	0.021	0.744 - 0.976
GFR <15%	1.770	0.000	1.443 - 2.170
GFR <30%	1.414	0.000	1.167 - 1.714
Atrial fibrillation	1.211	0.000	1.115 - 1.315
Diabetes	1.024	0.640	0.926 - 1.133

Second step: Predicted probabilities are calculated by setting each confounder to its mean value (prediction at the means) using Stata's margins command with application of the atmeans option.

n_ik_year_50_100#year	Prob.	p-value	95% CI
procedure volume <50 # 2008	0.090	0.000	0.068 - 0.113
procedure volume <50 # 2009	0.085	0.000	0.071 - 0.098
procedure volume <50 # 2010	0.077	0.000	0.059 - 0.095
procedure volume <50 # 2011	0.064	0.000	0.048 - 0.08
procedure volume <50 # 2012	0.050	0.000	0.033 - 0.066
procedure volume <50 # 2013	0.044	0.000	0.029 - 0.059
procedure volume <50 # 2014	0.043	0.000	0.027 - 0.059
procedure volume 50-99 # 2008	0.090	0.006	0.026 - 0.153
procedure volume 50-99 # 2009	0.078	0.000	0.058 - 0.098
procedure volume 50-99 # 2010	0.070	0.000	0.059 - 0.082
procedure volume 50-99 # 2011	0.069	0.000	0.057 - 0.082
procedure volume 50-99 # 2012	0.062	0.000	0.049 - 0.076
procedure volume 50-99 # 2013	0.050	0.000	0.038 - 0.061
procedure volume 50-99 # 2014	0.039	0.000	0.026 - 0.052
procedure volume >=100 # 2008	0.062	0.000	0.060 - 0.064
procedure volume >=100 # 2009	0.058	0.000	0.034 - 0.083
procedure volume >=100 # 2010	0.059	0.000	0.044 - 0.074
procedure volume >=100 # 2011	0.054	0.000	0.047 - 0.061
procedure volume >=100 # 2012	0.047	0.000	0.039 - 0.054
procedure volume >=100 # 2013	0.047	0.000	0.040 - 0.055
procedure volume >=100 # 2014	0.032	0.000	0.028 - 0.036

Third step: A random effects meta regression (using Stata's command metareg) with time and volume as continuous covariates was applied to the estimated rates.

	Coeff	p-value	95% CI
Volume effect	-0.007	0.002	-0.012 - -0.003
Annual change	-0.006	0.000	-0.008 - -0.004

Fourth step: A second random effects meta regression model was applied including also an interaction term.

	Coeff	p-value	95% CI
Volume effect	-4.536	0.026	-8.473 - -0.600
Annual change	-0.011	0.000	-0.016 - -0.006
Annual change of volume effect	0.002	0.027	0.000 - 0.004

Table S3: Results of the logistic regression model, transformation into discrete event probabilities and subsequent meta regressions

First step: Logistic regression model on 43,996 TAVI cases with stroke as dependent variable, an interaction term (n_ik_year_50_100#year) between categorical time (in years) and volume categories and 22 predefined patient and procedural characteristics as potential confounder.

n_ik_year_50_100	OR	p-value	95% CI
procedure volume <50	1		
procedure volume 50-99	0.929	0.886	0.339 - 2.5473
procedure volume >=100	0.969	0.945	0.398 - 2.3631
year			
2008	1		
2009	1.140	0.643	0.654 - 1.989
2010	0.732	0.308	0.401 - 1.335
2011	0.678	0.211	0.369 - 1.246
2012	0.659	0.197	0.350 - 1.241
2013	0.574	0.114	0.289 - 1.142
2014	0.759	0.426	0.385 - 1.496
n_ik_year_50_100#year			
procedure volume 50-99 # 2009	1.079	0.896	0.344 - 3.384
procedure volume 50-99 # 2010	1.310	0.637	0.428 - 4.009
procedure volume 50-99 # 2011	1.233	0.715	0.400 - 3.796
procedure volume 50-99 # 2012	1.247	0.706	0.396 - 3.921
procedure volume 50-99 # 2013	1.332	0.631	0.414 - 4.288
procedure volume 50-99 # 2014	0.957	0.942	0.290 - 3.162
procedure volume >=100 # 2009	0.779	0.649	0.265 - 2.287
procedure volume >=100 # 2010	1.134	0.810	0.407 - 3.159
procedure volume >=100 # 2011	1.640	0.331	0.606 - 4.440
procedure volume >=100 # 2012	1.209	0.712	0.441 - 3.312
procedure volume >=100 # 2013	1.769	0.282	0.626 - 4.995
procedure volume >=100 # 2014	1.099	0.857	0.393 - 3.076
Female	0.648	0.000	0.565 - 0.744
Age in years	0.900	0.000	0.890 - 0.910
Estimated logistic EuroSCORE	68461	0.000	33804 - 138650
Aortic valve stenosis	1.278	0.067	0.983 - 1.663
Combined aortic valve diseases	1.329	0.045	1.006 - 1.755
NYHA II	0.949	0.675	0.744 - 1.211
NYHA III or IV	1.096	0.166	0.962 - 1.249
CAD	1.011	0.875	0.885 - 1.154
Hypertension	0.910	0.148	0.802 - 1.034
Previous MI (within 4 months)	0.278	0.000	0.167 - 0.464
Previous MI (within 1 year)	1.246	0.491	0.667 - 2.328
Previous MI (after 1 year)	1.005	0.975	0.742 - 1.360
Previous CABG	0.857	0.350	0.620 - 1.184
Previous cardiac surgery	0.120	0.000	0.089 - 0.161
Peripheral vascular disease	0.395	0.000	0.325 - 0.480
Carotid disease	0.461	0.000	0.362 - 0.587
COPD	0.355	0.000	0.295 - 0.429
Pulmonary hypertension	0.198	0.000	0.164 - 0.239
GFR <15%	0.266	0.000	0.183 - 0.387
GFR <30%	0.297	0.000	0.226 - 0.391
Atrial fibrillation	1.093	0.165	0.964 - 1.239
Diabetes	1.079	0.260	0.945 - 1.231

Second step: Predicted probabilities are calculated by setting each confounder to its mean value (prediction at the means) using Stata's margins command with application of the atmeans option.

n_ik_year_50_100#year	Prob.	p-value	95% CI
procedure volume <50 # 2008	0.022	0.000	0.012 - 0.031
procedure volume <50 # 2009	0.025	0.000	0.017 - 0.032
procedure volume <50 # 2010	0.016	0.000	0.010 - 0.022
procedure volume <50 # 2011	0.015	0.000	0.009 - 0.021
procedure volume <50 # 2012	0.014	0.000	0.008 - 0.021
procedure volume <50 # 2013	0.013	0.000	0.006 - 0.019
procedure volume <50 # 2014	0.016	0.000	0.008 - 0.025
procedure volume 50-99 # 2008	0.020	0.026	0.002 - 0.038
procedure volume 50-99 # 2009	0.025	0.000	0.014 - 0.035
procedure volume 50-99 # 2010	0.019	0.000	0.014 - 0.025
procedure volume 50-99 # 2011	0.017	0.000	0.012 - 0.022
procedure volume 50-99 # 2012	0.017	0.000	0.011 - 0.022
procedure volume 50-99 # 2013	0.015	0.000	0.011 - 0.020
procedure volume 50-99 # 2014	0.015	0.000	0.009 - 0.021
procedure volume >=100 # 2008	0.021	0.009	0.005 - 0.037
procedure volume >=100 # 2009	0.019	0.000	0.009 - 0.028
procedure volume >=100 # 2010	0.017	0.000	0.012 - 0.023
procedure volume >=100 # 2011	0.023	0.000	0.019 - 0.028
procedure volume >=100 # 2012	0.017	0.000	0.014 - 0.020
procedure volume >=100 # 2013	0.021	0.000	0.018 - 0.025
procedure volume >=100 # 2014	0.018	0.000	0.015 - 0.020

Third step: A random effects meta regression (using Stata's command metareg) with time and volume as continuous covariates was applied to the estimated rates.

	Coeff	p-value	95% CI
Volume effect	0.001	0.196	-0.001 - 0.003
Annual change	-0.001	0.029	-0.002 - 0.000

Fourth step: A second random effects meta regression model was applied including also an interaction term.

	Coeff	p-value	95% CI
Volume effect	-1.103	0.307	-3.311 - 1.106
Annual change	-0.002	0.086	-0.005 - 0.000
Annual change of volume effect	0.001	0.306	-0.001 - 0.002

Table S4: Results of the logistic regression model, transformation into discrete event probabilities and subsequent meta regressions

First step: Logistic regression model on 43,996 TAVI cases with bleeding as dependent variable, an interaction term (n_ik_year_50_100#year) between categorical time (in years) and volume categories and 22 predefined patient and procedural characteristics as potential confounder.

n_ik_year_50_100	OR	p-value	95% CI
procedure volume <50	1		
procedure volume 50-99	0.806	0.366	0.506 - 1.286
procedure volume >=100	0.485	0.006	0.291 - 0.811
year			
2008	1		
2009	0.942	0.677	0.711 - 1.248
2010	0.775	0.086	0.579 - 1.037
2011	0.574	0.000	0.422 - 0.781
2012	0.502	0.000	0.363 - 0.696
2013	0.559	0.001	0.399 - 0.785
2014	0.340	0.000	0.226 - 0.511
n_ik_year_50_100#year			
procedure volume 50-99 # 2009	0.992	0.978	0.571 - 1.724
procedure volume 50-99 # 2010	1.176	0.541	0.699 - 1.980
procedure volume 50-99 # 2011	1.224	0.458	0.718 - 2.087
procedure volume 50-99 # 2012	1.321	0.321	0.762 - 2.293
procedure volume 50-99 # 2013	0.894	0.693	0.511 - 1.563
procedure volume 50-99 # 2014	1.265	0.463	0.675 - 2.374
procedure volume >=100 # 2009	1.070	0.828	0.581 - 1.970
procedure volume >=100 # 2010	1.078	0.799	0.605 - 1.920
procedure volume >=100 # 2011	2.198	0.006	1.249 - 3.866
procedure volume >=100 # 2012	1.669	0.080	0.941 - 2.960
procedure volume >=100 # 2013	1.371	0.286	0.768 - 2.447
procedure volume >=100 # 2014	1.540	0.174	0.827 - 2.868
Female	1.096	0.032	1.008 - 1.193
Age in years	0.982	0.000	0.974 - 0.990
Estimated logistic EuroSCORE	5.813	0.000	3.386 - 9.979
Aortic valve stenosis	0.738	0.000	0.639 - 0.852
Combined aortic valve diseases	0.677	0.000	0.580 - 0.790
NYHA II	0.665	0.000	0.562 - 0.786
NYHA III or IV	1.313	0.000	1.216 - 1.418
CAD	1.062	0.137	0.981 - 1.149
Hypertension	0.798	0.000	0.741 - 0.861
Previous MI (within 4 months)	0.866	0.324	0.650 - 1.153
Previous MI (within 1 year)	1.071	0.742	0.711 - 1.614
Previous MI (after 1 year)	0.869	0.137	0.721 - 1.046
Previous CABG	0.530	0.000	0.447 - 0.629
Previous cardiac surgery	1.275	0.005	1.077 - 1.509
Peripheral vascular disease	1.255	0.000	1.118 - 1.409
Carotid disease	1.182	0.022	1.024 - 1.364
COPD	0.998	0.969	0.896 - 1.111
Pulmonary hypertension	0.833	0.002	0.741 - 0.935
GFR <15%	2.045	0.000	1.725 - 2.423
GFR <30%	1.446	0.000	1.240 - 1.685
Atrial fibrillation	1.418	0.000	1.316 - 1.528
Diabetes	0.968	0.418	0.894 - 1.048

Second step: Predicted probabilities are calculated by setting each confounder to its mean value (prediction at the means) using Stata's margins command with application of the atmeans option.

n_ik_year_50_100#year	Prob.	p-value	95% CI
procedure volume <50 # 2008	0.134	0.000	0.108 - 0.161
procedure volume <50 # 2009	0.128	0.000	0.109 - 0.146
procedure volume <50 # 2010	0.107	0.000	0.090 - 0.125
procedure volume <50 # 2011	0.082	0.000	0.066 - 0.097
procedure volume <50 # 2012	0.072	0.000	0.057 - 0.088
procedure volume <50 # 2013	0.080	0.000	0.062 - 0.098
procedure volume <50 # 2014	0.050	0.000	0.034 - 0.066
procedure volume 50-99 # 2008	0.111	0.000	0.071 - 0.151
procedure volume 50-99 # 2009	0.105	0.000	0.082 - 0.128
procedure volume 50-99 # 2010	0.102	0.000	0.089 - 0.116
procedure volume 50-99 # 2011	0.081	0.000	0.069 - 0.093
procedure volume 50-99 # 2012	0.077	0.000	0.064 - 0.090
procedure volume 50-99 # 2013	0.059	0.000	0.049 - 0.069
procedure volume 50-99 # 2014	0.051	0.000	0.039 - 0.063
procedure volume >=100 # 2008	0.070	0.000	0.040 - 0.100
procedure volume >=100 # 2009	0.071	0.000	0.052 - 0.090
procedure volume >=100 # 2010	0.059	0.000	0.048 - 0.070
procedure volume >=100 # 2011	0.087	0.000	0.078 - 0.096
procedure volume >=100 # 2012	0.059	0.000	0.053 - 0.066
procedure volume >=100 # 2013	0.055	0.000	0.049 - 0.060
procedure volume >=100 # 2014	0.038	0.000	0.034 - 0.042

Third step: A random effects meta regression (using Stata's command metareg) with time and volume as continuous covariates was applied to the estimated rates.

	Coeff	p-value	95% CI
Volume effect	-0.011	0.001	-0.016 - -0.0049
Annual change	-0.011	0.000	-0.013 - -0.0083

Fourth step: A second random effects meta regression model was applied including also an interaction term.

	Coeff	p-value	95% CI
Volume effect	-4.84852	0.169	-11.97 - 2.27482
Annual change	-0.01589	0.001	-0.024 - -0.0076
Annual change of volume effect	0.0024	0.170	-0.001 - 0.00595

Table S5: Results of the logistic regression model, transformation into discrete event probabilities and subsequent meta regressions

First step: Linear regression model on 43,996 TAVI cases with Length of hospital stay as dependent variable, an interaction term (n_ik_year_50_100#year) between categorical time (in years) and volume categories and 22 predefined patient and procedural characteristics as potential confounder.

n_ik_year_50_100	Coeff	p-value	95% CI
procedure volume <50	0		
procedure volume 50-99	2.959	0.001	1.133 - 4.786
procedure volume >=100	-4.148	0.000	-5.574 - -2.721
year			
2008	0		
2009	2.179	0.001	0.950 - 3.409
2010	1.472	0.019	0.247 - 2.697
2011	0.507	0.422	-0.731 - 1.745
2012	-1.002	0.100	-2.197 - 0.193
2013	0.382	0.580	-0.970 - 1.734
2014	-0.060	0.931	-1.433 - 1.312
n_ik_year_50_100#year			
procedure volume 50-99 # 2009	-5.745	0.000	-7.942 - -3.547
procedure volume 50-99 # 2010	-4.872	0.000	-6.926 - -2.819
procedure volume 50-99 # 2011	-3.555	0.001	-5.622 - -1.488
procedure volume 50-99 # 2012	-2.174	0.037	-4.219 - -0.130
procedure volume 50-99 # 2013	-4.452	0.000	-6.576 - -2.327
procedure volume 50-99 # 2014	-3.947	0.000	-6.110 - -1.783
procedure volume >=100 # 2009	1.066	0.242	-0.721 - 2.853
procedure volume >=100 # 2010	0.788	0.365	-0.915 - 2.490
procedure volume >=100 # 2011	1.972	0.021	0.292 - 3.652
procedure volume >=100 # 2012	2.929	0.000	1.302 - 4.557
procedure volume >=100 # 2013	0.970	0.275	-0.773 - 2.713
procedure volume >=100 # 2014	0.390	0.662	-1.358 - 2.139
Female	-0.483	0.000	-0.725 - -0.241
Age in years	-0.247	0.000	-0.276 - -0.218
Estimated logistic EuroSCORE	25.503	0.000	23.345 - 27.661
Aortic valve stenosis	-6.255	0.000	-6.912 - -5.598
Combined aortic valve diseases	-6.592	0.000	-7.263 - -5.921
NYHA II	0.154	0.365	-0.179 - 0.487
NYHA III or IV	2.597	0.000	2.374 - 2.821
CAD	-0.037	0.740	-0.259 - 0.184
Hypertension	-0.888	0.000	-1.111 - -0.666
Previous MI (within 4 months)	-3.355	0.000	-4.175 - -2.534
Previous MI (within 1 year)	0.015	0.980	-1.172 - 1.203
Previous MI (after 1 year)	-0.303	0.250	-0.819 - 0.213
Previous CABG	-2.938	0.000	-3.596 - -2.280
Previous cardiac surgery	-1.710	0.000	-2.405 - -1.015
Peripheral vascular disease	-0.917	0.000	-1.345 - -0.489
Carotid disease	-1.110	0.000	-1.614 - -0.606
COPD	-0.618	0.001	-0.973 - -0.263
Pulmonary hypertension	-2.226	0.000	-2.624 - -1.827
GFR <15%	1.941	0.000	0.958 - 2.923
GFR <30%	0.725	0.034	0.054 - 1.396
Atrial fibrillation	2.575	0.000	2.365 - 2.785
Diabetes	0.932	0.000	0.702 - 1.161

Second step: Marginal means are calculated by setting each confounder to its mean value (prediction at the means) using Stata's margins command with application of the atmeans option.

n_ik_year_50_100#year	Coeff	p-value	95% CI
procedure volume <50 # 2008	19.184	0.000	18.241 - 20.13
procedure volume <50 # 2009	21.364	0.000	20.577 - 22.15
procedure volume <50 # 2010	20.656	0.000	19.874 - 21.44
procedure volume <50 # 2011	19.691	0.000	18.890 - 20.49
procedure volume <50 # 2012	18.182	0.000	17.448 - 18.92
procedure volume <50 # 2013	19.566	0.000	18.599 - 20.53
procedure volume <50 # 2014	19.124	0.000	18.128 - 20.12
procedure volume 50-99 # 2008	22.144	0.000	20.579 - 23.71
procedure volume 50-99 # 2009	18.578	0.000	17.650 - 19.51
procedure volume 50-99 # 2010	18.743	0.000	18.221 - 19.27
procedure volume 50-99 # 2011	19.095	0.000	18.554 - 19.64
procedure volume 50-99 # 2012	18.967	0.000	18.413 - 19.52
procedure volume 50-99 # 2013	18.074	0.000	17.576 - 18.57
procedure volume 50-99 # 2014	18.137	0.000	17.545 - 18.73
procedure volume >=100 # 2008	15.036	0.000	13.964 - 16.11
procedure volume >=100 # 2009	18.281	0.000	17.543 - 19.02
procedure volume >=100 # 2010	17.296	0.000	16.791 - 17.8
procedure volume >=100 # 2011	17.515	0.000	17.137 - 17.89
procedure volume >=100 # 2012	16.964	0.000	16.696 - 17.23
procedure volume >=100 # 2013	16.389	0.000	16.136 - 16.64
procedure volume >=100 # 2014	15.366	0.000	15.179 - 15.55

Third step: A random effects meta regression (using Stata's command metareg) with time and volume as continuous covariates was applied to the estimated means.

	Coeff	p-value	95% CI
Volume effect	-1.488	0.000	-2.021 - -0.9555
Annual change	-0.269	0.029	-0.507 - -0.0307

Fourth step: A second random effects meta regression model was applied including also an interaction term.

	Coeff	p-value	95% CI
Volume effect	22.5075	0.935	-554.1 - 599.146
Annual change	-0.23991	0.452	-0.898 - 0.41837
Annual change of volume effect	-0.01193	0.931	-0.299 - 0.2748

Table S6: Results of the logistic regression model, transformation into discrete event probabilities and subsequent meta regressions

First step: Linear regression model on 43,996 TAVI cases with reimbursement as dependent variable, an interaction term (n_ik_year_50_100#year) between categorical time (in years) and volume categories and 22 predefined patient and procedural characteristics as potential confounder.

n_ik_year_50_100	Coeff	p-value	95% CI
procedure volume <50	0		
procedure volume 50-99	-905.1	0.024	-1689.5 - -120.7
procedure volume >=100	-1792.9	0.000	-2614.4 - -971.4
year			
2010	0		
2011	-1104.3	0.026	-2078.5 - -130.1
2012	-1872.9	0.000	-2810.5 - -935.4
2013	-1339.7	0.007	-2316.5 - -362.9
2014	-1240.5	0.015	-2235.4 - -245.5
n_ik_year_50_100#year			
procedure volume 50-99 # 2011	349.5	0.545	-783.6 - 1482.5
procedure volume 50-99 # 2012	598.9	0.269	-464.0 - 1661.8
procedure volume 50-99 # 2013	-162.6	0.775	-1276.2 - 950.9
procedure volume 50-99 # 2014	-51.3	0.928	-1159.3 - 1056.7
procedure volume >=100 # 2011	994.4	0.082	-127.8 - 2116.7
procedure volume >=100 # 2012	994.3	0.063	-55.5 - 2044.2
procedure volume >=100 # 2013	614.5	0.267	-471.3 - 1700.4
procedure volume >=100 # 2014	803.0	0.150	-289.3 - 1895.4
Female	-816.4	0.000	-1022.5 - -610.4
Age in years	-134.0	0.000	-159.5 - -108.6
Estimated logistic EuroSCORE	9498.4	0.000	7514.7 - 11482.1
Aortic valve stenosis	-1480.8	0.000	-2097.4 - -864.3
Combined aortic valve diseases	-1671.1	0.000	-2296.6 - -1045.6
NYHA II	-420.2	0.001	-665.2 - -175.3
NYHA III or IV	686.8	0.000	501.3 - 872.2
CAD	133.6	0.153	-49.7 - 316.8
Hypertension	-427.8	0.000	-614.4 - -241.3
Previous MI (within 4 months)	-1677.0	0.000	-2134.6 - -1219.4
Previous MI (within 1 year)	295.6	0.574	-733.9 - 1325.2
Previous MI (after 1 year)	-483.1	0.009	-843.2 - -123.0
Previous CABG	-1118.8	0.000	-1687.9 - -549.8
Previous cardiac surgery	-574.4	0.061	-1174.8 - 25.9
Peripheral vascular disease	86.9	0.649	-287.8 - 461.7
Carotid disease	-365.0	0.106	-807.3 - 77.3
COPD	-0.6	0.997	-318.6 - 317.4
Pulmonary hypertension	-951.6	0.000	-1302.7 - -600.4
GFR <15%	1849.2	0.000	921.0 - 2777.4
GFR <30%	322.0	0.258	-235.7 - 879.6
Atrial fibrillation	913.0	0.000	741.8 - 1084.1
Diabetes	223.8	0.020	34.7 - 412.9

Second step: Marginal means are calculated by setting each confounder to its mean value (prediction at the means) using Stata's `margins` command with application of the `atmeans` option.

n_ik_year_50_100#year	Coeff	p-value	95% CI
procedure volume <50 # 2010	36999.8	0.000	36302.5 - 37697.1
procedure volume <50 # 2011	35895.5	0.000	35214.3 - 36576.7
procedure volume <50 # 2012	35126.9	0.000	34499.5 - 35754.2
procedure volume <50 # 2013	35660.1	0.000	34979.4 - 36340.7
procedure volume <50 # 2014	35759.3	0.000	35049.7 - 36469.0
procedure volume 50-99 # 2010	36094.7	0.000	35738.1 - 36451.3
procedure volume 50-99 # 2011	35339.9	0.000	34882.3 - 35797.5
procedure volume 50-99 # 2012	34820.7	0.000	34470.7 - 35170.6
procedure volume 50-99 # 2013	34592.3	0.000	34198.2 - 34986.4
procedure volume 50-99 # 2014	34803.0	0.000	34459.0 - 35147.0
procedure volume >=100 # 2010	35206.9	0.000	34775.2 - 35638.7
procedure volume >=100 # 2011	35097.1	0.000	34744.3 - 35449.8
procedure volume >=100 # 2012	34328.3	0.000	34128.7 - 34527.9
procedure volume >=100 # 2013	34481.7	0.000	34285.1 - 34678.4
procedure volume >=100 # 2014	34769.5	0.000	34623.4 - 34915.6

Third step: A random effects meta regression (using Stata's command metareg) with time and volume as continuous covariates was applied to the estimated means.

	Coeff	p-value	95% CI
Volume effect	-503.8	0.005	-826.4 - -181.2
Annual change	-257.6	0.011	-444.3 - -70.9

Fourth step: A second random effects meta regression model was applied including also an interaction term.

	Coeff	p-value	95% CI
Volume effect	-245427.3	0.262	-702076.0 - 211221.4
Annual change	-518.0	0.050	-1036.3 - 0.2
Annual change of volume effect	121.7	0.263	-105.2 - 348.7

Table S7: Results of the logistic regression model, transformation into discrete event probabilities and subsequent meta regressions

First step: Logistic regression model on 43,996 TAVI cases with ventilation as dependent variable, an interaction term (n_ik_year_50_100#year) between categorical time (in years) and volume categories and 22 predefined patient and procedural characteristics as potential confounder.

n_ik_year_50_100	OR	p-value	95% CI
procedure volume <50	1		
procedure volume 50-99	0.716	0.262	0.400 - 1.283
procedure volume >=100	0.492	0.026	0.263 - 0.918
year			
2008	1		
2009	0.946	0.745	0.677 - 1.322
2010	0.853	0.362	0.605 - 1.201
2011	0.765	0.135	0.539 - 1.086
2012	0.664	0.029	0.459 - 0.959
2013	0.623	0.018	0.420 - 0.923
2014	0.532	0.004	0.345 - 0.819
n_ik_year_50_100#year			
procedure volume 50-99 # 2009	1.079	0.827	0.544 - 2.141
procedure volume 50-99 # 2010	1.382	0.322	0.729 - 2.622
procedure volume 50-99 # 2011	1.43	0.277	0.751 - 2.723
procedure volume 50-99 # 2012	1.096	0.789	0.561 - 2.142
procedure volume 50-99 # 2013	0.929	0.833	0.469 - 1.841
procedure volume 50-99 # 2014	1.016	0.967	0.489 - 2.111
procedure volume >=100 # 2009	1.732	0.131	0.848 - 3.537
procedure volume >=100 # 2010	1.232	0.555	0.616 - 2.462
procedure volume >=100 # 2011	1.914	0.059	0.975 - 3.758
procedure volume >=100 # 2012	1.624	0.163	0.822 - 3.210
procedure volume >=100 # 2013	1.636	0.165	0.817 - 3.277
procedure volume >=100 # 2014	1.358	0.402	0.664 - 2.776
Female	0.713	0.000	0.651 - 0.781
Age in years	0.959	0.000	0.951 - 0.968
Estimated logistic EuroSCORE	13.81	0.000	7.797 - 24.464
Aortic valve stenosis	0.722	0.000	0.618 - 0.843
Combined aortic valve diseases	0.663	0.000	0.561 - 0.783
NYHA II	0.498	0.000	0.404 - 0.614
NYHA III or IV	1.485	0.000	1.364 - 1.617
CAD	1.094	0.044	1.002 - 1.193
Hypertension	0.697	0.000	0.642 - 0.757
Previous MI (within 4 months)	0.804	0.163	0.591 - 1.093
Previous MI (within 1 year)	0.796	0.358	0.490 - 1.294
Previous MI (after 1 year)	0.897	0.268	0.740 - 1.087
Previous CABG	0.675	0.000	0.557 - 0.816
Previous cardiac surgery	0.848	0.091	0.701 - 1.026
Peripheral vascular disease	1.198	0.004	1.060 - 1.353
Carotid disease	0.855	0.061	0.725 - 1.007
COPD	1.211	0.001	1.085 - 1.351
Pulmonary hypertension	0.758	0.000	0.669 - 0.858
GFR <15%	1.364	0.001	1.129 - 1.647
GFR <30%	1.252	0.008	1.059 - 1.479
Atrial fibrillation	1.553	0.000	1.430 - 1.687
Diabetes	1.138	0.003	1.045 - 1.239

Second step: Predicted probabilities are calculated by setting each confounder to its mean value (prediction at the means) using Stata's `margins` command with application of the `atmeans` option.

n_ik_year_50_100#year	Prob.	p-value	95% CI
procedure volume <50 # 2008	0.086	0.000	0.065 - 0.107
procedure volume <50 # 2009	0.082	0.000	0.067 - 0.096
procedure volume <50 # 2010	0.074	0.000	0.060 - 0.089
procedure volume <50 # 2011	0.067	0.000	0.053 - 0.081
procedure volume <50 # 2012	0.059	0.000	0.045 - 0.073
procedure volume <50 # 2013	0.055	0.000	0.040 - 0.070
procedure volume <50 # 2014	0.048	0.000	0.032 - 0.063
procedure volume 50-99 # 2008	0.063	0.000	0.033 - 0.094
procedure volume 50-99 # 2009	0.064	0.000	0.046 - 0.083
procedure volume 50-99 # 2010	0.074	0.000	0.062 - 0.085
procedure volume 50-99 # 2011	0.069	0.000	0.058 - 0.079
procedure volume 50-99 # 2012	0.047	0.000	0.037 - 0.057
procedure volume 50-99 # 2013	0.038	0.000	0.030 - 0.045
procedure volume 50-99 # 2014	0.035	0.000	0.025 - 0.045
procedure volume >=100 # 2008	0.044	0.000	0.020 - 0.068
procedure volume >=100 # 2009	0.070	0.000	0.052 0.089
procedure volume >=100 # 2010	0.046	0.000	0.037 0.056
procedure volume >=100 # 2011	0.063	0.000	0.056 0.071
procedure volume >=100 # 2012	0.047	0.000	0.042 0.053
procedure volume >=100 # 2013	0.045	0.000	0.040 0.050
procedure volume >=100 # 2014	0.032	0.000	0.029 0.036

Third step: A random effects meta regression (using Stata's command `metareg`) with time and volume as continuous covariates was applied to the estimated rates.

	Coeff	p-value	95% CI
Volume effect	-0.010	0.004	-0.016 - -0.004
Annual change	-0.004	0.002	-0.007 - -0.002

Fourth step: A second random effects meta regression model was applied including also an interaction term.

	Coeff	p-value	95% CI
Volume effect	-6.084	0.040	-11.870 - -0.299
Annual change	-0.011	0.004	-0.018 - -0.004
Annual change of volume effect	0.003	0.041	0.000 - 0.006