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# Use of linked registry claims data for long term surveillance of devices after endovascular abdominal aortic aneurysm repair: observational surveillance study

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## Abstract

### OBJECTIVE

To evaluate long term outcomes (reintervention and late rupture of abdominal aortic aneurysm) of aortic endografts in real world practice using linked registry claims data.

### DESIGN

Observational surveillance study.

### SETTING

282 centers in the Vascular Quality Initiative Registry linked to United States Medicare claims (2003-18).

### PARTICIPANTS

20 489 patients treated with four device types used for endovascular abdominal aortic aneurysm repair (EVAR): 40.6% (n=8310) received the Excluder (Gore), 32.2% (n=6606) the Endurant (Medtronic), 16.0% (n=3281) the Zenith (Cook Medical), and 11.2% (n=2292) the AFX (Endologix). Given modifications to AFX in late 2014, patients who received the AFX device were categorized into two groups: the early AFX group (n=942) and late AFX group (n=1350) and compared with patients who received the other devices, using propensity matched Cox models.

### MAIN OUTCOME MEASURES

Reintervention and rupture of abdominal aortic aneurysm post-EVAR; all patients (100%) had complete follow-up via the registry or claims based outcome assessment, or both.

### RESULTS

Median age was 76 years (interquartile range (IQR) 70-82 years), 80.0% (16 386/20 489) of patients

were men, and median follow-up was 2.3 years (IQR 0.9-4.1 years). Crude five year reintervention rates were significantly higher for patients who received the early AFX device compared with the other devices: 14.9% (95% confidence interval 13.7% to 16.2%) for Excluder, 19.5% (18.1% to 21.1%) for Endurant, 16.7% (15.0% to 18.6%) for Zenith, and early 27.0% (23.7% to 30.6%) for the early AFX. The risk of reintervention for patients who received the early AFX device was higher compared with the other devices in propensity matched Cox models (hazard ratio 1.61, 95% confidence interval 1.29 to 2.02) and analyses using a surgeon level instrumental variable of >33% AFX grafts used in their practice (1.75, 1.19 to 2.59). The linked registry claims surveillance data identified the increased risk of reintervention with the early AFX device as early as mid-2013, well before the first regulatory warnings were issued in the US in 2017.

### CONCLUSIONS

The linked registry claims surveillance data identified a device specific risk in long term reintervention after EVAR of abdominal aortic aneurysm. Device manufacturers and regulators can leverage linked data sources to actively monitor long term outcomes in real world practice after cardiovascular interventions.

### Introduction

In the United States, the Food and Drug Administration studies medical devices in both pre-market and post-market approval pathways to ensure that they are effective and have minimal risk of complications.<sup>1</sup> Endovascular abdominal aortic aneurysm repair (EVAR) has become a key treatment option for patients with abdominal aortic aneurysm.<sup>2</sup> For EVAR devices, which are designed to exclude the abdominal aortic aneurysm from blood flow, the FDA has used data from industry sponsored clinical trials to examine the risks of complications, such as the need for reinterventions to keep blood from leaking into the abdominal aortic aneurysm—called an endoleak, and late rupture of the aneurysm despite repair.<sup>3-5</sup>

Between 2015 and 2022, several investigator initiated publications and reports from physicians who carry out implants emerged related to the early versions of the AFX device.<sup>6-11</sup> These reports detailed frequent reinterventions and late abdominal aortic aneurysm ruptures and varied from single center reports to a large integrated health system level summary. These endoleaks were presumed to be due to poor durability

## WHAT IS ALREADY KNOWN ON THIS TOPIC

Few large, multicenter observational analyses have examined the role of device type on long term outcomes after endovascular repair of abdominal aortic aneurysm

## WHAT THIS STUDY ADDS

This study leverages linked claims registry data sources to provide long term outcome assessment after endovascular abdominal aortic aneurysm repair (EVAR), which may be a model for future device surveillance

Differences were found in performance of the four most commonly used devices in the United States over time, suggesting that better long term active surveillance of EVAR devices is necessary in real world practice

Using linked registry claims data sources might help to identify signals of device failure before current regulatory pathways

of the expanded polytetrafluoroethylene fabric used to cover the stents in AFX.<sup>6,7</sup> Endologix changed the expanded polytetrafluoroethylene fabric in all AFX devices manufactured after 1 July 2014, and most early generation AFX devices were not used after 2015.<sup>6,7,12,13</sup>

However, it remains uncertain if AFX failed more commonly than other devices in real world practice.<sup>12</sup> At present, no systematic surveillance structure exists to evaluate long term outcomes of aortic endografts in real world practice. Therefore, we studied reintervention and rupture of abdominal aortic aneurysm after EVAR across four major endoprostheses: the Excluder (Gore), Endurant (Medtronic), Zenith (Cook Medical), and AFX (Endologix). AFX was divided into two categories (early, before the fabric change; and late, after the fabric change). We used data from the Vascular Quality Initiative (VQI) linked to Medicare claims as part of the Vascular Implant Surveillance and Interventional Outcomes Network project (VQI-VISION),<sup>14</sup> and studied the associations between device, reintervention, and rupture of abdominal aortic aneurysm.

## Methods

### Data sources

We used the most recent 2018 VQI-VISION Medicare claims linkage data for this study. The VQI registry collects individual level personal and clinical details for patients receiving common vascular procedures at more than 600 centers in the US and Canada.<sup>15</sup> The EVAR module began recording device identifiers in 2003, with linkage to the Global Universal Device Identifier. Medicare claims data include all inpatient, outpatient, and provider billing data for the care that Medicare beneficiaries receive.<sup>16</sup> Patients in the VQI were linked to their respective Medicare claims file at patient level.<sup>17</sup> The linkage between these two databases combines the clinical information from the registry with long term follow-up from Medicare claims. Detailed linkage methods and peer reviewed publications using the linkage data have been reported elsewhere.<sup>5,18-21</sup>

### Study population

From the linked data we identified patients who underwent EVAR as their first abdominal aortic aneurysm repair from 1 January 2003 to 31 December 2018. Patients whose index EVAR procedure was converted to an open repair were included. Patients who were not enrolled in fee-for-service Medicare at the time of the EVAR procedure were excluded. We restricted the cohort to patients undergoing EVAR using grafts from four major manufacturers, including AFX. Patients who received grafts from manufacturers that were less commonly used (<100 devices collected in VQI) were excluded; these patients represented less than 1% of all individuals entered in the VQI's EVAR registry module.

### Main exposure variable

The main exposure variable was the device type manufactured by four companies: the Excluder (Gore),

Endurant (Medtronic), Zenith (Cook Medical), and AFX (Endologix). AFX was modified in July 2014, after reports of poor durability of the expanded polytetrafluoroethylene fabric used in the endograft. To improve durability, Endologix changed how the fabric was manufactured after mid-2014.<sup>13</sup> An FDA class 2 recall was issued on 19 January 2017 related to the fabric.<sup>22</sup> Given the modifications to this graft, we examined patients who received AFX devices before and after 1 January 2015, defined as early AFX and late AFX, respectively.

The comparator devices, Excluder, Endurant, and Zenith, underwent only minor modifications during the period studied, such as changes to the limbs in Zenith. Because outcomes did not differ over time in adjusted analyses between the Excluder, Endurant, and Zenith, we pooled these devices in comparisons with the early and late AFX devices, in accordance with the VQI approved protocol for identification of devices used in research studies.<sup>15</sup>

### Main outcome measures

Our primary outcomes were reintervention and late rupture of abdominal aortic aneurysm after EVAR occurring after hospital discharge from the initial repair. Our secondary outcomes were conversion to open repair and overall patient survival. We also assessed post-procedure surveillance of EVAR as a covariate to ensure all devices were monitored similarly after implantation.

Measurement of each of these outcomes has been validated in previous work using a combination of data from the VQI dataset and Medicare claims.<sup>5,23-25</sup> Specifically, reintervention was defined as any procedure related to either the aneurysm or the index aneurysm repair, and this definition has been validated using a clinical chart review as published in our previous work, with greater than 92% specificity and 96% sensitivity.<sup>23,26</sup> Rupture of an abdominal aortic aneurysm after EVAR was defined as having a diagnosis of ruptured abdominal aortic aneurysm after discharge, in conjunction with a reintervention or death that occurred 14 days before or after the procedure.<sup>5</sup> Mortality was identified from the Medicare Master Beneficiary Summary File.<sup>16</sup> Conversion to open repair was defined as an open aneurysm repair after the index EVAR, including open repairs performed during the hospital admission of the index procedure.<sup>25</sup>

Finally, to ensure all patients who received EVAR devices were monitored similarly after implantation, we examined the occurrence of failures in surveillance, defined as the end of a 15 month period after EVAR during which no abdominal computed tomography, magnetic resonance imaging, or ultrasonography was performed.<sup>24</sup> For each outcome, we censored patients at the time of death, the end of Medicare fee-for-service entitlement, or the end of the study (31 December 2018), whichever came first.

### Clinical covariates for risk adjustment

Baseline characteristics were identified from the VQI as well as Medicare claims. These included personal

information (age, sex, race), procedure year, urgency of presentation (elective, urgent, or rupture), body mass index (BMI), smoking status (none, former, current), comorbidities (hypertension, congestive heart failure, diabetes, coronary artery disease, chronic obstructive pulmonary disease, dialysis), previous aneurysm repair, preoperative drug use (statin, antiplatelet, anticoagulation,  $\beta$  blocker), aneurysm morphology, ability to undergo open repair, and maximum aneurysm diameter.

### Statistical analysis

Patient baseline characteristics by device type were reported using counts and percentages for categorical variables and medians and interquartile ranges for continuous variables. We used  $\chi^2$  tests and Wilcoxon rank-sum tests to compare categorical and continuous variables across groups, respectively. Kaplan-Meier analyses assessed cumulative risks of death, reintervention, imaging surveillance failure, conversion to open repair, and late aneurysm rupture. Estimated event rates over time were compared across groups with log-rank tests.

We adjusted for differences in baseline patient characteristics across device types and accounted for differences in patients in different time periods. This was done using propensity score matching in combination with a time dependent approach, wherein we performed survival analyses on patient outcomes before and after 2015, in AFX and other time matched comparator devices.

A standard difference-in-difference approach was not feasible as the outcome was measured using survival analysis. The difference in the hazard ratios obtained from these two comparisons would indicate the impact of the change in AFX. We matched and compared the early AFX group with patients receiving grafts from the other three manufacturers to the end of 2014 and the late AFX group with patients receiving grafts from the other manufacturers in and after 2015. For each comparison we created a logistic regression model to obtain the propensity of receiving an AFX graft based on patient characteristics. We then performed a 1:1 nearest neighbor matching between patients treated with an AFX graft and those treated with grafts from the other manufacturers, using a caliper width of 0.2 of the standard deviation of the logit of the propensity score.

To examine cohort balance after each match, we calculated standardized mean differences and further adjusted for unbalanced covariates if present. When analyzing matched data with Cox regression models, we used robust sandwich estimators to account for the matching. We performed a sensitivity analysis using a multivariable Cox regression model to compare patients treated with early AFX grafts, late AFX grafts, and grafts from other manufacturers, adjusting for the time effect. Although comparisons were performed across all device types, for clarity we grouped together the Excluder, Endurant, and Zenith devices and compared them with early and late AFX devices, adjusting for multiple comparisons.

Lastly, to adjust for surgeon level effects in the choice of device used, we created a surgeon level instrumental variable defined as surgeons who used more than 33% AFX grafts in their practice, in both the pre-2015 period and the post-2015 period. The  $\kappa$  statistics from these models indicated reasonable agreement between the instrumental variables and the treatment variables for both the pre-2015 period ( $\kappa=0.55$ ) and the post-2015 period ( $\kappa=0.59$ ). We then included this instrumental variable in our main effects analysis, using a two stage residual inclusion estimation within a parametric Weibull model.

### Signal surveillance sensitivity analysis

We performed a signal surveillance analysis to assess the ability to detect the increased rate of reintervention. For each year between 2010 and 2018, we compared reinterventions after EVAR using early AFX devices manufactured before 2015 with devices from the other manufacturers during the same period, using follow-up events identified up to then. The surveillance comparisons were made at intervals of six months from the beginning of 2010. For the comparison at each time point, we performed a propensity score matched analysis using data available up to that time point. A Cox regression model was then used to compare reinterventions after the use of AFX devices with devices from the other manufacturers. To show when significant differences in reintervention rates would be detectable, we sequentially plotted the hazard ratios and 95% confidence intervals obtained from these Cox regression models. All analyses were carried out using SAS version 9.4 (SAS Institute, Cary, NC).

### Patient and public involvement

Two patient advisors, one of whom received an early generation AFX device and experienced complications, were involved in the development of this research question. They reviewed study protocols, outcome measures, and the value of these outcomes, especially reintervention, risk of abdominal aortic aneurysm rupture, information sources about rupture and repair, and surveillance burden after EVAR. Patients were given study materials and examples of the outcome measures that are collected by the registry and asked if these were the appropriate outcomes and best represented the outcomes that mattered most to patients. The patients were appraised of the need for the study, as well as the outcome of the study. A family member of one of the patient advisors also reviewed study protocols, outcomes, and results.

## Results

### Personal characteristics, by device type

We identified 20 489 patients in the VQI-VISION dataset who underwent EVAR and had linkages to Medicare claims (table 1). Overall, 40.6% (n=8310) of patients received the Excluder, 32.2% (n=6606) the Endurant, 16.0% (n=3281) the Zenith, and 11.2% (n=2292) the AFX (4.6% (n=942) received the early AFX and 6.6% (n=1350) the late AFX).

Table 1 | Personal and clinical characteristics of patients by type of device to repair abdominal aortic aneurysm

Characteristics	Overall (n=20 489)	Excluder (Gore) (n=8310)	Endurant (Medtronic) (n=6606)	Zenith (Cook Medical) (n=3281)	AFX (Endologix)*		P value
					Early device (n=942)	Late device (n=1350)	
Median (IQR) age (years)	76 (70-82)	76 (70-81)	76 (71-82)	76 (71-82)	76 (70-82)	76 (70-81)	0.15
Men	16 386 (80.0)	6703 (80.7)	5243 (79.4)	2718 (82.8)	703 (74.6)	1019 (75.5)	<0.001
Whitet†	19 029 (92.9)	7687 (92.5)	6141 (93.0)	3061 (93.3)	887 (94.2)	1253 (92.8)	0.29
Procedure year:							
2003-09	946 (4.6)	394 (4.7)	291 (4.4)	227 (6.9)	34 (3.6)	0 (0.0)	
2010-14	7702 (37.6)	2552 (30.7)	2545 (38.5)	1697 (51.7)	908 (96.4)	0 (0.0)	<0.001
2015-18	11 841 (57.8)	5364 (64.5)	3770 (57.1)	1357 (41.4)	0 (0.0)	1350 (100.0)	
Urgency of presentation:							
Elective	17 759 (86.8)	7199 (86.8)	5600 (84.9)	2858 (87.1)	868 (92.1)	1234 (91.5)	
Symptomatic	1620 (7.9)	661 (8.0)	571 (8.7)	251 (7.7)	53 (5.6)	84 (6.2)	<0.001
Ruptured AAA	1088 (5.3)	438 (5.3)	426 (6.5)	172 (5.2)	21 (2.2)	31 (2.3)	
Median (IQR) BMI	27.2 (24.2-30.8)	27.3 (24.2-30.9)	27.1 (24.0-30.7)	27.3 (24.2-30.7)	26.8 (24.0-30.6)	27.1 (24.2-30.7)	0.02
Preoperative smoking status:							0.19
Never	3151 (15.4)	1295 (15.6)	967 (14.7)	541 (16.5)	138 (14.6)	210 (15.6)	
Former	11 685 (57.1)	4712 (56.8)	3780 (57.3)	1891 (57.8)	542 (57.5)	760 (56.3)	
Current	5625 (27.5)	2291 (27.6)	1851 (28.1)	841 (25.7)	262 (27.8)	380 (28.1)	
Comorbidities:							
Hypertension	16 987 (83.4)	6846 (82.9)	5503 (83.8)	2715 (83.1)	802 (85.7)	1121 (83.4)	0.18
Congestive heart failure	2748 (13.4)	1065 (12.8)	875 (13.3)	474 (14.5)	142 (15.1)	192 (14.2)	0.07
Diabetes mellitus	4166 (20.3)	1715 (20.6)	1331 (20.2)	641 (19.6)	197 (20.9)	282 (20.9)	0.69
Coronary artery disease	6115 (29.9)	2411 (29.0)	2047 (31.0)	973 (29.7)	310 (32.9)	374 (27.7)	0.007
COPD	6890 (33.7)	2726 (32.9)	2283 (34.6)	1065 (32.5)	321 (34.1)	495 (36.7)	0.01
Dialysis	290 (1.4)	111 (1.3)	91 (1.4)	59 (1.8)	17 (1.8)	12 (0.9)	0.11
Preoperative aneurysm repair‡	≥11	189 (2.3)	132 (2.0)	44 (1.4)	<11	53 (3.9)	<0.001
Preoperative statin†	14 125 (69.1)	5713 (68.8)	4511 (68.5)	2273 (69.4)	686 (72.8)	942 (69.8)	0.09
Preoperative antiplatelet†:							<0.001
No	6633 (32.4)	2728 (32.9)	2232 (33.9)	984 (30.1)	263 (27.9)	426 (31.6)	
Aspirin only	11 316 (55.3)	4542 (54.8)	3550 (53.9)	1905 (58.2)	576 (61.1)	743 (55.1)	
P2Y only	609 (3)	259 (3.1)	198 (3.0)	87 (2.7)	26 (2.8)	39 (2.9)	
Aspirin and P2Y	1891 (9.2)	766 (9.2)	609 (9.2)	298 (9.1)	77 (8.2)	141 (10.5)	
Preoperative anticoagulation:							<0.001
No	≥11	6258 (75.3)	4932 (74.7)	2216 (67.5)	620 (65.8)	≥11	
Yes	2336 (11.4)	974 (11.7)	742 (11.2)	337 (10.3)	78 (8.3)	205 (15.2)	
Missing	≥11	1078 (13.0)	932 (14.1)	728 (22.2)	244 (25.9)	<11	
Preoperative β blockert	11 877 (58.1)	4751 (57.2)	3842 (58.3)	1968 (60.1)	586 (62.3)	730 (54.1)	<0.001
Median (IQR) maximum AAA diameter†	55 (51-61)	55 (51-60)	55 (51-62)	55 (52-61)	55 (50-60)	54 (50-58)	<0.001

AAA=abdominal aortic aneurysm; BMI=body mass index; COPD=chronic obstructive pulmonary disease; IQR=interquartile range.

Median (IQR) follow-up for entire cohort was 838(348 1508) days.

\*Because of poor durability, the expanded polytetrafluoroethylene fabric used in AFX devices was changed after 1 July 2014: early devices and late devices relate to before and after this change, respectively.

†<1.5% missing.

The median age of patients was 76 years (interquartile range (IQR) 70-82 years); 80.0% (n=16 386) were men. Most patients were former or current smokers (84.5%; n=17 310). The median diameter of treated aneurysms was 55 (IQR 51-61) mm. The reasons for repair varied: 86.8% (n=17 759/20 489) for elective repair, 7.9% (n=1620) owing to symptoms, and 5.3% (n=1088) for ruptured abdominal aortic aneurysm. The median follow-up was 2.3 (IQR 0.95-4.13) years; no patients were lost to follow-up. The rates of imaging surveillance failures did not differ between devices (see supplementary appendix 1).

### Crude reintervention

*Early and late AFX versus each comparator device*—Crude five year reintervention rate for patients who received the early AFX was significantly higher than for patients who received the comparator devices (Excluder 14.9% (95% confidence interval 13.7% to

16.2%), Endurant 19.5% (18.1% to 21.1%), Zenith 16.7% (15.0% to 18.6%), and late AFX 27.0% (23.7% to 30.6%) (P<0.001) (fig 1). In crude comparisons, the hazard ratio for reintervention with the early AFX was higher than with the other devices (Excluder 1.85 (95% confidence interval 1.57 to 2.19), Endurant 1.33 (1.13 to 1.57), and Zenith 1.56 (1.30 to 1.86); P<0.001 for all). No differences were observed between patients who received the late AFX and those who received comparator devices, although these results were limited to follow-up for three years.

*Early and late AFX versus comparator devices collectively*—When we grouped patients who received the Excluder, Endurant, and Zenith devices collectively, the rate of reintervention within three years after implantation was significantly higher among patients who received the early AFX (17.4%, 95% confidence interval 14.9% to 20.2%) versus other devices (11.4%, 10.8% to 12.0%) or the late AFX (11.5%, 9.3% to

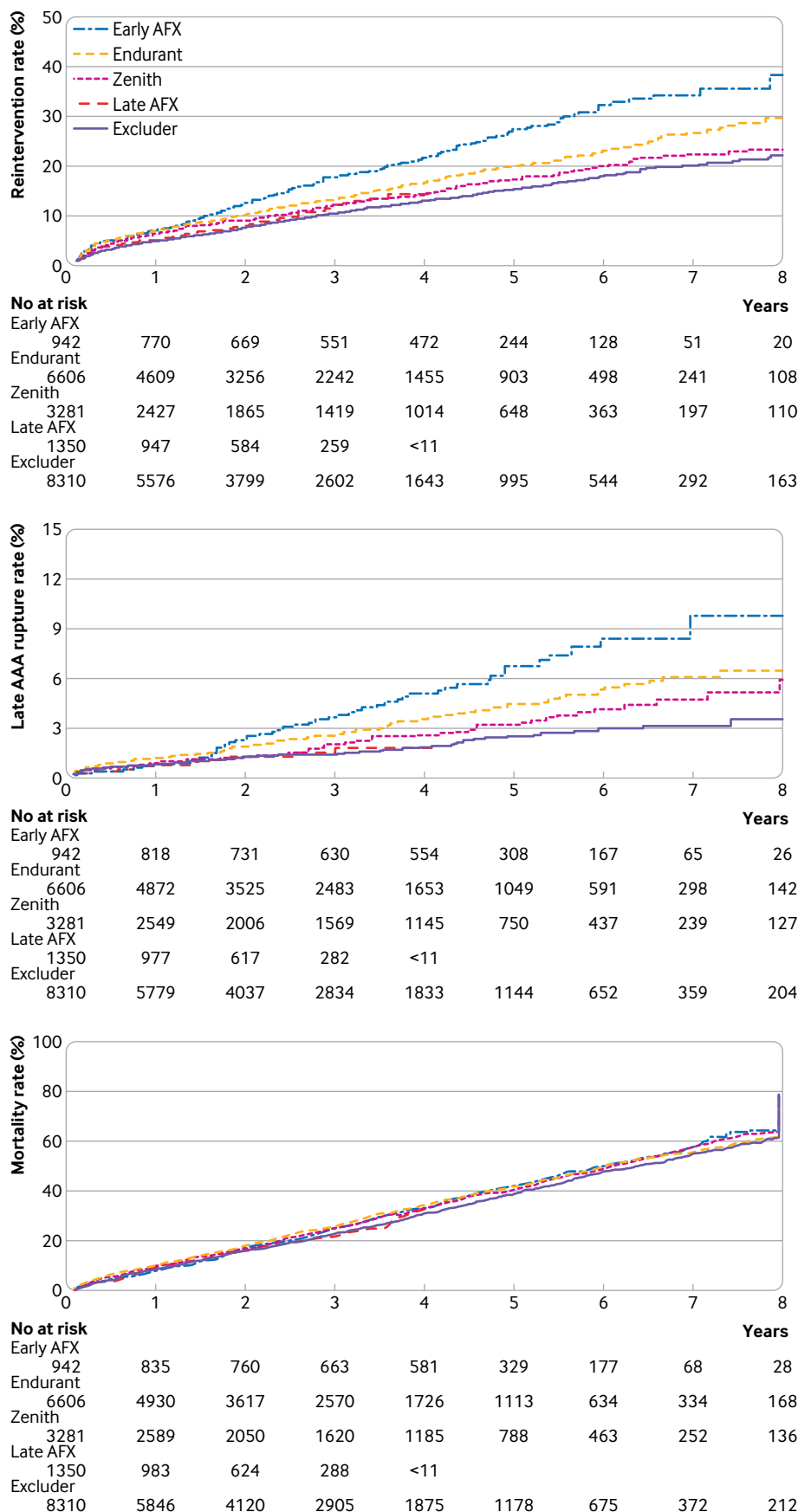


Fig 1 | Kaplan-Meier survival curves for reintervention, late rupture, and overall survival after endovascular repair of abdominal aortic aneurysm, by device type: Excluder (Gore), Endurant (Medtronic), Zenith (Cook Medical), and AFX (Endologix)

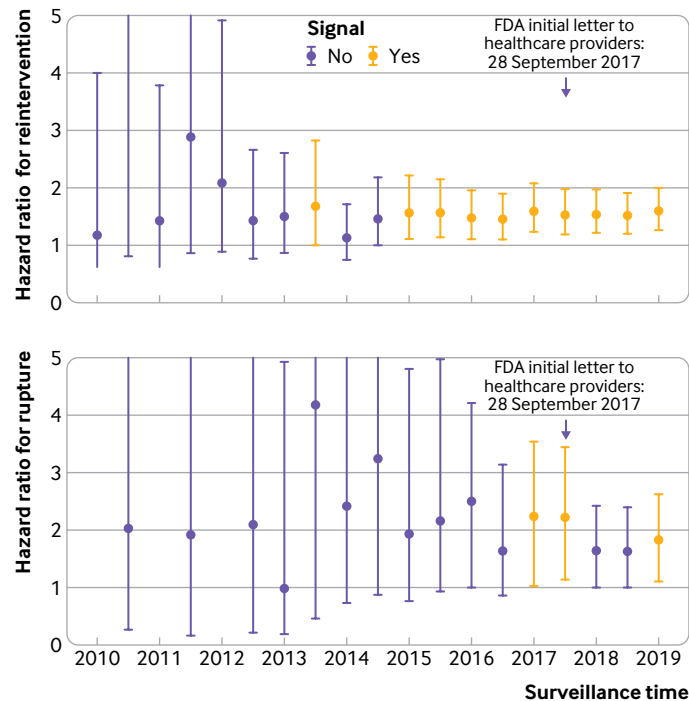


Fig 2 | Number of years to detect complications signal for the early AFX (Endologix) device for endovascular repair. Whiskers represent 95% confidence intervals. FDA=Food and Drug Administration

14.1%) (log rank  $P < 0.001$ ). The reintervention rate for patients who received the late AFX at three years after implantation was 11.5% ( $P < 0.001$ ). No significant difference was observed for reintervention rate between the late AFX and the pooled devices, either individually or collectively. No clinically relevant differences persisted in risk adjusted analyses (see supplementary appendix 3).

#### Crude late abdominal aortic aneurysm rupture

*Early and late AFX versus each comparator device*—Crude five year rupture rates were higher for patients who received the early AFX (6.6%, 95% confidence interval 4.9% to 8.9%) versus other devices (Excluder 2.4% (95% confidence interval 1.8% to 3.0%), Endurant 4.3% (3.6% to 5.2%), Zenith 3.0% (2.3% to 4.0%) ( $P < 0.001$  for all) (fig 1). The rate of rupture was lowest in patients who received the Excluder (3.0%, 2.3% to 3.9%;  $P < 0.0001$ ). In crude comparisons, the hazard ratio for late rupture with the early AFX device was significantly higher than for each of the other devices (Excluder 3.08, 95% confidence interval 2.08 to 4.57,  $P < 0.001$ ; Endurant 1.43, 1.01 to 2.01,  $P = 0.042$ ; Zenith 1.92, 1.30 to 2.83,  $P = 0.001$ ).

*Early and late AFX versus comparator devices collectively*—When the Excluder, Endurant, and Zenith were pooled the rate of abdominal aortic aneurysm rupture was observed to be significantly higher among patients with the early AFX (3.7%, 95% confidence interval 2.5% to 5.3%) compared with the other devices (1.8%, 1.6% to 2.1%) by three years after implantation as well as with the late AFX (1.7%, 0.9% to 3.1%) (log rank  $P = 0.004$ ). In patients who received the late AFX,

the rate of rupture at three years after implantation was 1.7% (fig 1). The rate of late rupture did not differ between the late AFX and Excluder, Endurant, and Zenith, either individually or collectively.

#### Surveillance sensitivity analysis

In the surveillance sensitivity analysis, an increased risk of reintervention associated with the early AFX is detectable as early as 2013 (fig 2), and the signal of increased reintervention becomes consistent from 2015 onwards. Similar findings were evident for late rupture. These findings indicate that between three and five years had elapsed before the risk of reintervention became evident using linked registry claims data. Based on conventional reporting mechanisms, the FDA issued its first written communication warnings based on reports from the manufacturer in 2017, more than two years after the signal was evident in our surveillance analyses based on linked registry claims data.<sup>27</sup> Supplementary appendix 5 outlines the regulatory summary documents related to the device. Reintervention events clustered early (less than two years after initiation of surveillance) or late (after two years of surveillance) did not influence our findings (see supplementary appendix 6).

#### Propensity matched and instrumental variable adjusted comparisons

We used propensity score matching to create two cohorts, each with 895 patients: one cohort comprised those who received the early AFX and the other cohort those who received one of the other devices implanted before 2015. Matched cohorts were also created, each with 1311 patients: one cohort comprised those who

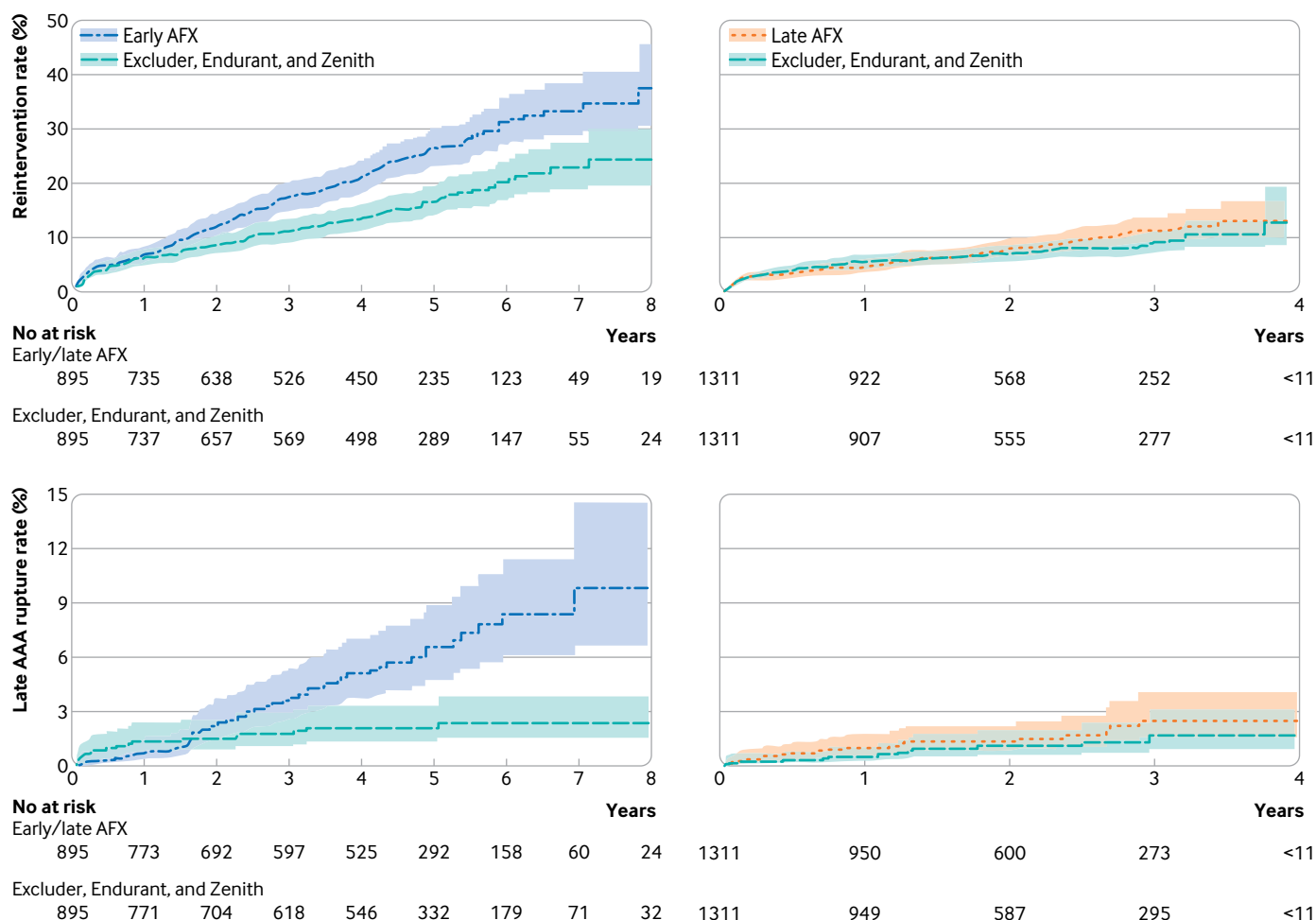


Fig 3 | Propensity matched comparisons of reintervention and late rupture after endovascular repair of abdominal aortic aneurysm, by device type: Excluder (Gore), Endurant (Medtronic), Zenith (Cook Medical), and AFX (Endologix)

received the late AFX and the other cohort those who received one of the three devices implanted after 2015 (see supplementary appendix 2). The rates of reintervention and late rupture were higher among patients who received the early AFX than among those who received the other devices during the same period (hazard ratio 1.61, 95% confidence interval 1.29 to 2.02;  $P<0.001$ , and 2.79, 1.56 to 4.89;  $P<0.001$ , respectively) (fig 3). The rates of reintervention and late rupture did not, however, differ when we compared the late AFX with the three other devices during the same period (1.11, 0.83 to 1.49;  $P=0.47$ ).

Similar findings were found for both reinterventions and late rupture when individual devices were compared (see supplementary appendix 3). The propensity matched models for reinterventions adjusted for aneurysm size, urgency of presentation, and patients' personal characteristics were similar to those of the collective analysis (hazard ratios: Excluder 1.91, 95% confidence interval 1.49 to 2.45,  $P<0.001$ ; Endurant 1.45, 1.16 to 1.81,  $P=0.001$ ; Zenith 1.63, 1.30 to 2.06,  $P<0.001$ ). Propensity matched models for late rupture showed similar findings (Excluder 2.36, 1.40 to 3.99,  $P=0.001$ ; Endurant 1.69, 1.05 to 2.73,  $P=0.031$ ; Zenith 2.33, 1.36 to 3.98,  $P=0.002$ ).

Finally, results from our multivariable Cox regressions were consistent with the propensity score matched analysis (table 2). When compared with patients receiving all other grafts, those receiving the early AFX were 58% more likely to require reintervention (hazard ratio 1.58, 95% confidence interval 1.35 to 1.85,  $P<0.001$ ) and more than twice as likely to experience a late ruptured abdominal aortic aneurysm (2.47, 1.78 to 3.44,  $P<0.001$ ). However, when patients who received the late AFX were compared with those who received all the other devices, we found no significant difference in reintervention (1.07, 0.86 to 1.32,  $P=0.56$ ), or late ruptured abdominal aortic aneurysm (1.01, 0.88 to 1.16,  $P=0.98$ ). Even when including our instrumental variable to adjust for clustering of device choice within surgeons, the reintervention risk associated with the early AFX was still significantly higher than the comparator devices (hazard ratio 1.75, 1.19 to 2.59,  $P=0.005$ ), whereas for the late AFX this difference was not present (1.28, 0.75 to 2.17,  $P=0.36$ ).

#### Overall survival and conversion to open repair

Mortality was similar within the first decade after EVAR, at about 75% in patients treated with all devices

**Table 2 | Hazard ratio estimates from adjusted Cox model\* or adjusted hazard ratios for reintervention, late rupture of abdominal aortic aneurysm, mortality, and conversion to open repair, for early and late AFX device (Endologix) versus three other devices for endovascular repair†**

	Point estimate (95% CI)‡	P value
Propensity score matched analysis		
Reintervention:		
Early AFX v early other devices	1.61 (1.29 to 2.02)	<0.001
Late AFX v late other devices	1.11 (0.83 to 1.49)	0.47
Late rupture:		
Early AFX v early other devices	2.79 (1.60 to 4.88)	<0.001
Late AFX v late other devices	0.64 (0.31 to 1.32)	0.23
Death:		
Early AFX v early other devices	1.08 (0.95 to 1.24)	0.25
Late AFX v late other devices	1.02 (0.85 to 1.22)	0.83
Multivariable regression		
Reintervention:		
Early AFX v all other devices	1.58 (1.35 to 1.85)	<0.001
Late AFX v all other devices	1.07 (0.86 to 1.32)	0.56
Late rupture:		
Early AFX v all other devices	2.47 (1.78 to 3.44)	<0.001
Late AFX v all other devices	1.01 (0.55 to 1.83)	0.98
Death:		
Early AFX v all other devices	1.04 (0.94 to 1.15)	0.45
Late AFX v all other devices	1.01 (0.88 to 1.16)	0.92

\*Adjusted for age, sex, race, urgency of presentation, procedure year, comorbidities, statin treatment, antiplatelet agents, anticoagulation,  $\beta$  blockade, and anatomical characteristics of aneurysm, such as size, extent, and neck angle, when available in the Vascular Quality Initiative dataset.

†Excluder (Gore), Endurant (Medtronic), and Zenith (Cook Medical).

‡Wald confidence limits.

(fig 1). The rates of conversion to open repair after EVAR also did not differ in patients treated with AFX devices and those treated with the other devices. Each had a rate of conversion of about 3% during the study period (see supplementary appendix 4).

## Discussion

We used real world evidence from a linked registry claims dataset to examine associations between device type used for EVAR and long term reintervention and late abdominal aortic aneurysm rupture. In crude, propensity matched, and instrumental variable adjusted analyses we found that the need for reintervention in patients receiving an early AFX manufactured before 2015 was 61% higher (hazard ratio 1.61, 95% confidence interval 1.29 to 2.02) than for the other devices within five years after implantation. This translates into nearly 10% higher risk of reintervention in absolute terms. Furthermore, the risk of late rupture in the same period was more than twice as high as patients receiving any other device. Finally, the ability to detect this signal of adverse events among multiple EVAR devices was made possible by linking VQI registry data to Medicare claims. These data revealed the first signal was detectable as early as 2013, and consistently began in 2015, two years before the FDA issued its initial warnings related to the device in 2017.

### Advantages of hybrid data sources in detecting failures and measuring improvement

Obtaining long term follow-up data after clinical trials is expensive and challenging. However, coordinated

registry networks, such as VQI-VISION, may offer an alternative for long term surveillance at lower cost compared with clinical trials. Several trials on abdominal aortic aneurysms, such as the EVAR-1 and EVAR-2 randomized trials, have leveraged claims based data sources to measure long term outcomes.<sup>4 28</sup>

These approaches offer the ability to monitor the long term results of interventions using real world data sources—a strategy that has been used after several other types of interventional treatments, such as transcatheter aortic valve repair.<sup>5 20 21 29</sup> Cost modeling exercises suggest registry based follow-up leveraging claims based resources would yield cost savings of up to 70% compared with typical mechanisms for collection of clinical trial data.<sup>30</sup>

### Considerations for longitudinal assessment of device performance after EVAR

Our data and other recent meta-analyses suggest that the risks of endoleak and late rupture do not plateau after EVAR, but rather they are linear and additive over time.<sup>5 31 32</sup> Whereas variables such as aneurysm anatomy and concordance with device specific instructions for use are of primary importance,<sup>33</sup> post-EVAR surveillance must consider a continual risk for reintervention over the patient and the device's life cycle, as well as patient preferences about surveillance and reintervention, particularly at the end of life. Finally, the timing of device failures, censoring, and attrition during a surveillance programme must be considered as well, based on experience from data safety monitoring during clinical trials. As outlined by several authors, multiple events may cluster in the initial period of surveillance, whereas rates could be lower later during surveillance, and attrition can influence these effects as well.<sup>34-36</sup> Consideration of a non-linear nature of these estimates during a surveillance programme would be necessary to best inform decisions about stopping use of a device or continuing surveillance.

### Limitations of this study

Our study has several limitations. First, Medicare claims datasets are not available to researchers for a year or more after billing events occur, making immediate signal detection difficult. However, more rapid processing of Medicare claims datasets may help to improve this interval to less than a year, and previous studies have illustrated the value in vascular care of early signal detection in real world practice.<sup>37 38</sup> Second, although our algorithms provide a strong assessment of mortality, reintervention, and late rupture,<sup>5 23</sup> future work will be necessary to best understand other outcomes such as aneurysm related mortality or overall cause of death for patients deaths after EVAR. Third, although we are certain of the date of implantation, our study design cannot ensure that devices manufactured before 2015 were not analyzed within the late AFX group, although device replacement in the field by the manufacturer may have minimized this occurrence.<sup>13 22</sup> Finally, certain



descriptive variables, such as aortic neck angle could not be included in all models as these data were not collected in all registry sites and in all years of the study.<sup>15</sup> However, our effect size remained constant in crude, propensity adjusted, and instrumental variable adjusted approaches, suggesting that our findings were similar even when accounting for measurable or unmeasurable confounders.

## Conclusion

Long term reintervention and rupture after EVAR varies by device manufacturer, and failures are common, especially for early generation devices. More broadly, for patients facing invasive cardiovascular procedures, distributed research networks incorporating hybrid claims based registry data sources offer an efficient pathway for systematic surveillance of long term outcomes in real world practice. Using similar methodology to provide efficient long term surveillance after other invasive procedures may help provide better data for regulatory agencies and providers, and for patients treated with medical devices.

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**Contributors:** PG is senior author and guarantor. PG, JM, BS, MS, MM, BB, SS, SA, ES, OA, AB, BG, KM, XZ, JE-J, and AS conceived and designed the study. JM, XZ, and BG did the statistical analysis. PG, JM, BS, MS, MM, BB, SS, SA, ES, OA, AB, BG, KM, XZ, JE-J, AS, KG, JB, WDC, DS, RD, NM, GW, KW, LM, MD, JM, CC, YD, DB, CM, KS, SB, NO, PH, and JC critically revised the manuscript and approved the final version. PG, JE-J, and AS acquired funding. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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**Competing interests:** All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: support from the Food and Drug Administration, National Heart, Lung and Blood Institute, and Society for Vascular Surgery; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

**Ethical approval:** This study was approved by the institutional review board at Weill Cornell Medical Center for this proposal with waiver of informed consent to analyze secondary data sources (protocol # IRB: 20-12023018). A STROBE cohort study checklist was completed. The

data use agreement at the Vascular Quality Initiative was developed to allow receipt of patient level data from the endograf manufacturer. This contained fields necessary for matching to Medicare claims, which uniquely identify the patient in both the industry dataset and the Medicare claims files.<sup>17</sup>

**Data sharing:** This study is based on data sources obtained with specific data use agreements from the Society for Vascular Surgery's Patient Safety Organization (SVS-PSO) and the Centers for Medicare and Medicaid Services (CMS) (CMS DUA# 57451). Although the data use agreements prohibit sharing of individual level data, aggregate files, methods, coding algorithms, and analytic code used to generate the tables, figures, and results in this manuscript will be made available upon requests to the corresponding author. Individual patient level data files may be requested directly from the SVS-PSO and CMS. According to CMS requirements, reuse of the Vascular Quality Initiative-Medicare linked dataset is possible only through collaboration with the original requestor at Weill Cornell Medicine. Further details are publicly available at <https://www.vqi.org/data-analysis/vision/>.

The manuscript's guarantor (PG) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained.

**Dissemination to participants and related patient and public communities:** The results of our study will be disseminated in the public forum through research reports describing device specific outcomes. These will be made available at the registry website <https://www.vqi.org/data-analysis/vision/>, where the registry already disseminates summary findings directly to patients who have been entered on the system.

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**Supplementary information:** Appendices 1-6  
**Supplementary information:** List of collaborators