**Full Title:** Initial experience of a second-generation self-expanding transcatheter aortic valve:

The UK & Ireland EvolutTM R Implanters’ Registry

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**Word Count:** 2467

**Brief Title:** The UK & Ireland EvolutTM R Implanters’ Registry

**Conflicts of Interest:**

Dr Blackman – proctor and consultant for Medtronic and Boston Scientific

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**ABSTRACT**

**Objectives**

This study presents the United Kingdom and Ireland real-world learning curve experience of the EvolutTM R (Medtronic, Minneapolis, Minnesota, USA) transcatheter heart valve.

**Background**

The EvolutTM R is a self-expanding, repositionable and fully recapturable second-generation transcatheter heart valve with several novel design features to improve outcome, and reduce complications.

**Methods**

Clinical, procedural, and 30-day outcome data were prospectively collected for the first 264 patients to receive an Evolut RTM valve in the United Kingdom and Ireland.

**Results**

264 consecutive EvolutTM R implants were performed across 9 centers. Mean age was 81.1 ± 7.8 years and mean Logistic EuroScore was 19.9 ± 13.7%. Procedural indications included aortic stenosis (72.0%), mixed aortic valve disease (17.4%) and failing aortic valve bioprostheses (10.6%).

Conscious sedation was used in 39.8% of cases and transfemoral access in 93.6%. The procedural success rate was 91.3%, and paravalvular leak immediately after implantation was mild or less in 92.3%. Major complications were rare: cardiac tamponade 0.4%; conversion to sternotomy 0.8%; annular rupture 0.0%; coronary occlusion 0.8%; major vascular 5.3%; acute kidney injury 6.1%; new permanent pacemaker implantation 14.7%; and procedural-related death 0.0%.

At 30-day follow-up survival was 97.7%, paravalvular leak was mild or less in 92.3% and stroke rate was 3.8%.

**Conclusions**

This registry represents the largest published real-world experience of the EvolutTM R valve. Procedural success rate was high and safety was excellent, comparable to previous studies of the EvolutTM R valve and other second-generation devices. The low rate of complications represents an improvement on first-generation devices.

**CONDENSED ABSTRACT**

The EvolutTM R is a self-expanding, repositionable and fully recapturable second-generation transcatheter heart valve with several improvements on first generation devices. This registry represents the largest real-world experience of the EvolutTM R valve to date.

264 consecutive EvolutTM R implants were performed across 9 centres in the United Kingdom and Ireland. The procedural success rate was 91.3%. At 30-day follow-up survival was 97.7%, paravalvular leak was mild or less in 92.3% and stroke rate was 3.8%.

Procedural success rate was high and safety was excellent, comparable to previous studies of the EvolutTM R valve and other second-generation devices.

**KEYWORDS**

Aortic Stenosis

Transcatheter Heart Valve

Transcatheter Aortic Valve Replacement

Evolut R

Outcome

Complication

**ABBREVIATIONS**

AKIN Acute Kidney Injury Network

MSCT Multislice Computed Tomography

NYHA New York Heart Association

PPM permanent pacemaker

PVL paravalvular leak

STS Society of Thoracic Surgeons

TAVR transcatheter aortic valve replacement

VARC-2 Valve Academic Research Consortium 2

**INTRODUCTION**

Transcatheter aortic valve replacement (TAVR) is an established therapy for severe aortic stenosis in patients considered high- or extreme-risk for surgical aortic valve replacement, on the basis of trials and registries of first generation devices. For self-expanding technology with the CoreValve® (Medtronic, Minneapolis, Minnesota, USA), this evidence includes the ADVANCE Registry1 and US Pivotal Trial2, 3 amongst others.

The trials and registries of first generation TAVR devices demonstrated important limitations and peri-procedural complications4. Second generation TAVR devices are designed to improve on these limitations and complications.

The EvolutTM R is a self-expanding, repositionable and fully recapturable second-generation TAVR prosthesis. It incorporates several design changes from the first-generation CoreValve® 5. Firstly, vascular access is achieved with a 14-French equivalent system (incorporating an In-LineTM sheath). The lower profile system is designed to improve deliverability and reduce vascular complications. Secondly, the EnveoTM R delivery system provides a more predictable 1:1 deployment response, and allows for repositioning and full recapture. This novel delivery system permits optimal valve deployment. Thirdly, the valve has an extended inflow skirt and the frame exhibits more consistent radial force. These adaptations aim to reduce paravalvular leak (PVL) and the need for permanent pacemakers (PPM).

Early studies of the EvolutTM R suggest reduced complication rates compared to the first generation device6, 7. In this study we report the real-world learning curve experience of implanting the EvolutTM R in consecutive unselected patients in the United Kingdom and Ireland.

**METHODS**

Prospective clinical, procedural, and outcome data were collected for the first 264 consecutive patients receiving an EvolutRTM valve across 9 centers in the United Kingdom and Ireland, between December 2013 and May 2016.

Choice of TAVR as treatment and pre-procedural assessment for TAVR was undertaken by the Heart Team at each implantation centre. Implantation was carried out as previously described8, 9. Procedural success was defined according to the Valve Academic Research Consortium 2 (VARC-2) criteria4 – (1) absence of procedural mortality, and (2) correct positioning of a single prosthetic heart valve, and (3) intended performance of the prosthetic heart valve (no prosthesis-patient mismatch and mean aortic valve gradient <20mmHg), and (4) no moderate or severe PVL. Peri-procedural complications were also classified according to the VARC-2 criteria4. Mortality, cerebrovascular accident and PVL rates were collected at post-discharge 30-day follow up.

**Statistical Analysis**

Statistical analysis was performed using SPSS software (IBM, USA). Continuous variables were reported as mean ± SD and categorical variables as percentages. Continuous variables were compared using a two-tailed Student t test with a 95% confidence interval.

**RESULTS**

**Baseline Characteristics**

The baseline pre-procedural patient characteristics are summarized in Table 1. The mean age was 81.1 ± 7.8 years and 58.3% of patients were female. Important co-morbidities included diabetes mellitus (25.0%), coronary artery disease > 1 vessel (19.3%), previous cardiac surgery (31.1%), chronic pulmonary disease (26.9%), previous cerebrovascular disease (11.7%), extracardiac arteriopathy (23.9%), and poor left ventricular systolic function (9.1%). Pre-operative cardiac rhythm disturbances included atrial fibrillation (22.0%), other conduction disease (23.7% - conduction disturbances including atrioventricular node disease, bundle branch disease or fascicle hemiblock), and prior permanent pacemaker (7.2%). The mean Logistic EuroScore was 19.9 ± 13.7% and the mean Society of Thoracic Surgery (STS) predicted risk of mortality score was 6.0 ± 5.6%.

New York Heart Association (NYHA) functional class III or IV was evident in 86.7%, and 16.2% of cases were performed urgently (during an acute hospital admission for decompensated heart failure).

Isolated aortic stenosis was the most common indication (72.0%), though mixed aortic valve disease (17.4%), and failing aortic valve bioprostheses (10.6%) were also treated. The mean aortic valve gradient was 47.0 ± 16.2 mmHg and the mean aortic valve area was 0.68 ± 0.23 cm2 (see Figure 1). Screening multislice computed tomography (MSCT) was performed in 90.9% of cases.

**Procedural Characteristics**

The procedural characteristics are summarized in Table 2. Conscious sedation was used in 39.8% of cases. Vascular access was predominantly via the transfemoral route (93.6%), with subclavian (5.3%) and direct aortic (1.1%) access also used. Most transfemoral cases used percutaneous access (96.8%), and 69.5% of these cases were completed using the 14F In-LineTM sheath only. Dedicated closure devices (Prostar [Abbott Vascular, USA] or ProGlide [Abbott Vascular, USA]) were used in 95.8% of the percutaneous transfemoral procedures, and in the remaining 4.2% planned/unplanned surgical repair was undertaken.

More than half (58.7%) of the cases were guided by intra-procedural transoesophageal echocardiography. Pre-implantation balloon aortic valvuloplasty was performed in 27.7% of the procedures. All three EvolutTM R valve sizes were used in this cohort: 23mm (18.2%), 26mm (28.8%) and 29mm (53.0%). Valve deployment was successful in 91.3% of the cases, as defined by VARC-2 criteria4. In the 3 unsuccessful cases there was 1 case of a detached nose cone, 1 case of an end-cap separation, and 1 case of clinical instability necessitating the procedure to be abandoned. Valve repositioning was required in 20.5% of cases, as defined by partial recapture of the valve after initial deployment. Full valve recapture (valve retrieval) was necessary in 17.2% and post implantation balloon dilatation was performed in 23.0%. Post-procedural PVL was mild or less 92.3% of patients (see Figure 2). At the end of the procedure the mean aortic valve gradient was 8.3 ± 6.0 mmHg (47.0 ± 16.1 mmHg pre-procedurally) and mean valve area was 1.7 ± 0.45 cm2 (0.68 ± 0.23 cm2 pre-procedurally) – see Figure 1.

**Complications and Outcomes**

Two patients required emergency sternotomy – one case for left ventricular wire perforation with cardiac tamponade and the other case for acute occlusion of the right coronary artery which could not be treated with bailout angioplasty. There were no annular ruptures. There was one further case of acute coronary artery occlusion, which was treated with bailout angioplasty. VARC-2 defined major vascular complications occurred in 5.3%. Acute kidney injury (stages 1-3 as defined by the Acute Kidney Injury Network - AKIN10) occurred in 6.1% of the cases and two (0.8%) required renal replacement therapy. New PPM implantation was required in 14.7% of patients, at a median time of 3-days post procedure. The indications for new PPM implantation included 3rd degree heart block (38.9%), 2nd degree heart block (22.2%) and new left bundle branch block (38.9%). There were no procedural-related deaths.

At 30-days the survival rate was 97.7% (4/6 deaths occurred during the hospital admission but were unrelated to the procedure), the stroke rate was 3.8% (all non-disabling, as per VARC-2 definition4) and PVL was mild or less in 92.3% (see Figure 2).

**DISCUSSION**

This study describes the cohort of consecutive real-world patients treated with the Medtronic EvolutTM R transcatheter heart valve in 9 experienced TAVR centres in the UK and Ireland. The major findings of this study were a high procedural success rate (successful valve deployment 91.3%), low procedural related complications (major vascular 5.3%, new PPM implantation 14.7% and no procedural-related deaths) and excellent 30-day outcome (mild or less PVL 92.3%, mortality 2.3% and stroke 3.8%)

Although the baseline patient characteristics are broadly similar to previous TAVR registries, there were some important differences in this cohort. Firstly, there was a high proportion of patients treated for mixed aortic valve disease (17.4%) or failing surgical aortic valve bioprostheses (10.6%). Secondly, a large proportion of cases (16.2%) were undertaken in urgently, in patients who presented acutely with decompensated cardiac function. Thirdly, despite a high incidence of cardiac conduction disease at baseline (23.7%), the pre-existing PPM prevalence was low (7.2%) and there was no routine practice of prophylactic implantation of PPMs in this at-risk subgroup. Fourthly, there was high, but importantly not universal, use of pre-procedural MSCT (90.9%) to assess aortic annulus geometry to guide valve size selection.

A large proportion of cases (39.8%) were undertaken using conscious sedation only, a trend which is becoming increasingly common in contemporary TAVR practice6, 7, 11-15. This represents an increase in the use of sedation in UK practice16. The rate of transfemoral vascular access was unusually high (93.6%) compared to previous TAVR registries, and the majority of cases were completed percutaneously using the lower profile 14-French equivalent InLineTM sheath. Successful haemostasis was achieved in 95.8% of the percutaneous transfemoral access cases using closure devices, again mirroring the paradigm shift in seen in current TAVR practice. Historically transfemoral access has been associated with high rates of major vascular complications (6.2% – 16.4%)1-3, 17-19 and associated morbidity/mortality. The low rate of major vascular complications (5.3%), compared to other second-generation devices11, 13-15, may reflect the lower profile 14-French equivalent sheath and the routine practice of percutaneous closure (95.8%). The low rate of alternative access suggests that many of the patients in this cohort treated transfemorally may have a burden of vascular disease which in the past would have dictated alternative access - the 14-French equivalent sheath makes it possible to perform transfemoral TAVR in arteries as small as 5mm. Despite this, vascular complications were gratifyingly low.

In this intermediate risk population (STS Score 6.0 + 5.6%), mortality at 30-days was low in this cohort (2.3%) compared to studies of the first generation device (8.0%)1-3 and similar to recent other studies of the EvolutTM R (2.5% - 3.1%)6, 7. None of the deaths were directly related to the procedure. This must reflect generic experience with TAVR, improved patient selection, improved pre-procedural analysis with CT, effective complication management and improved devices.

The rate of >mild PVL at 30-days (7.7%) was lower than seen with the first generation device (11.4% - 14.2%)1-3 and similar to other studies of the EvolutTM R (3.9% - 5.4%)6, 7. The EvolutTM R has important design changes compared to the first generation device. The novel Nitinol cell design means the frame exerts a more consistent radial force across the operating range of annulus size for a given implant size. The inflow skirt is extended downwards, and the frame design is straighter at the inflow. All of these factors contribute to the reduced PVL rate compared to the first generation CoreValve®. However the >mild PVL rate in this cohort (7.7% - see Figure 2) is higher than that reported for the LotusTM valve (0.6% - 1.0% [Boston Scientific, Natick, Massachusetts, USA])11, 13, 20-22, and the SAPIENTM 3 (1.0% – 3.4% [Edwards Lifesciences, Irivine, California, USA])14, 15. Unlike the Evolut R, the LotusTM and SAPIENTM 3 valves have sealing skirts outside to reduce PVL. Future iterations of the EvolutTM R will have to consider this feature, however this may increase the profile of the delivery catheter and could be associated with higher pacing rates14, 15, 20, 22. There are some other considerations as well. Firstly this study reflected real-world practice and a number of patients were implanted urgently rather than electively, and secondly more than 10% of patients did not have pre-procedure CT scans. Both of these may have impacted on a slightly higher PVL rate than the CE Mark6 and US7 Studies.

The rate of new PPM implantation in this study at 30-days was 13.6% which is considerably lower than seen with the first generation device (26.4%)1 and comparable to other studies of the Evolut R (11.7% - 16.4%)6, 7. This pacemaker rate is similar to that of the SAPIENTM 3 valve and is greatly lower than the LotusTM valve11, 13-15, 20-22. The novel design features of the Evolut R, including repositionability and cell design enabling a more consistent radial force appears to translate to lower rates of pacing overall.

Cerebrovascular accidents remain an important concern post-TAVR and principally occurs during balloon dilatation and valve implantation. In this study, the stroke rate was low (3.8%) and comparable to other TAVR series of second generation devices6, 7, 11, 13-15. Importantly, the requirement to recapture and reposition the device did not appear to increase the risk of stroke.

In this study, pre-implantation balloon valvuloplasty was carried out in only 27.7% reflecting that in the vast majority of cases this valve can be deployed without pre-implantation valvuloplasty. Post-deployment valvuloplasty was required in 23.0%.

**Study Limitations**

The study findings should be interpreted in light of the study design. Participation in this registry was voluntary and all data was self-reported by each center without core-lab validation. This study has however considerable strengths, including prospective granular data collection and the enrolment of real-world unselected participants that reflect day-to-day clinical practice. Further study is required to demonstrate the longer-term durability of this prosthesis.

**CONCLUSIONS**

This study presents the largest experience of unselected real-world patients treated with the Medtronic EvolutTM R valve. Our data demonstrate high procedural success and excellent safety with low rates of complications.

**CLINCAL PERSPECTIVES**

**What’s Known?** Early studies of the EvolutTM R TAVR prosthesis suggested a higher procedural success rates and reduced complication rates compared to first generation devices.

**What’s New?** This registry represents the largest real-world world experience of the EvolutTM R valve to date. The procedural success rate was high (91.3%) and the safety profile was excellent (30-day survival 97.7%, paravalvular leak mild or less in 92.3% and stroke rate 3.8%).

**What’s Next?** Future studies of the EvolutTM R valve are needed to evaluate the longer-term durability of this prosthesis beyond 30 days. Additionally, formal clinical trials of this device in low- and intermediate-risk groups of patients would corroborate its procedural success rate and safety for wider use.

**TABLES**

|  |  |
| --- | --- |
| **Table 1 – Baseline Patient Characteristics** | **N = 264** |
|  |  |
| **A. DEMOGRAPHICS** |  |
| Age (years) | 81.1 ± 7.8 |
| Female Gender | 154 (58.3) |
| Body Mass Index (kg/m2) | 26.9 ± 5.5 |
|  |  |
| **B. CO-MORBIDITY** |  |
| Diabetes Mellitus | 66 (25.0) |
| Creatinine (mmol/L) | 99.6 ± 53.8 |
| Coronary Artery Disease >1 Vessel ^ | 51 (19.3) |
| Previous Cardiac Surgery | 82 (31.1) |
| Chronic Pulmonary Disease | 71 (26.9) |
| Previous Cerebrovascular Disease | 31 (11.7) |
| Extracardiac Arteriopathy | 63 (23.9) |
| Pre-Operative Cardiac Rhythm Disturbances |  |
| *Atrial Fibrillation* | 58 (22.0) |
| *Conduction Disease §* | 58 (23.7) |
| *Pre-existing Permanent Pacemaker* | 19 (7.2) |
| Left Ventricular Function |  |
| *≥ 50%* | 177 (67.0) |
| *30% - 50%* | 63 (23.9) |
| *< 30%* | 24 (9.1) |
| Logistic EuroScore (%) | 19.9 ± 13.7 |
| STS Score (%) | 6.0 ± 5.6 |
|  |  |
| **C. AORTIC VALVE** |  |
| Aortic Valve Pathology |  |
| *Aortic Stenosis* | 190 (72.0) |
| *Mixed Aortic Valve Disease* | 46 (17.4) |
| *Failing Aortic Valve Bioprosthesis* | 28 (10.6) |
| Mean Aortic Valve Gradient (mmHg) | 47.0 ± 16.2 |
| Aortic Valve Area (cm2) | 0.68 ± 0.23 |
| Aortic Annulus Mean Diameter (mm) | 23.3 ± 1.82 |
| MSCT assessment of Aortic Annulus Diameter | 240 (90.9) |
|  |  |
| **D. OTHER** |  |
| Elective Cases | 218 (83.8) |
| NYHA Class III or IV | 229 (86.7) |
| Values are mean ±SD or n (%)  *^ coronary artery disease defined by a stenosis >50%*  *§ conduction disturbances including atrioventricular node disease, bundle branch disease or fascicle hemiblock* | |

|  |  |
| --- | --- |
| **Table 2 - Procedural Characteristics** | **N = 264** |
|  |  |
| Conscious Sedation | 105 (39.8) |
| Vascular Access Route |  |
| *Transfemoral ^* | 247 (93.6) |
| *Subclavian* | 14 (5.3) |
| *Direct Aortic* | 3 (1.1) |
| Percutaneous Transfemoral Sheath |  |
| *14F InLineTM only* | 166 (69.5) |
| *14F InLineTM and 18F Sheath* | 73 (30.5) |
| Transfemoral Percutaneous Closure Device | 229 (95.8) |
| Transoesophageal Echo Guidance | 155 (58.7) |
| Pre-Implantation Balloon Aortic Valvuloplasty | 73 (27.7) |
| Valve Size Implanted |  |
| *23mm* | 48 (18.2) |
| *26mm* | 76 (28.8) |
| *29mm* | 140 (53.0) |
| Successful Valve Deployment § | 241 (91.3) |
| Valve Repositioning \* | 46 (20.5) |
| Valve Retrieval (full recapture) | 37 (17.2) |
| Post-Implantation Balloon Dilatation | 60 (23.0) |
| End Procedure Mean Aortic Valve Gradient (mmHg) | 8.3 ± 6.0 |
| End Procedure Aortic Valve Area (cm2) | 1.7 ± 0.45 |
| End Procedure Paravalvular Leak ≤ Mild | 241 (92.3) |
| Values are n (%)  *^ 239 percutaneous transfemoral cases and 8 surgical access transfemoral cases*  *§ successful valve deployment defined as per the VARC-2 recommendations*  *\* valve repositioning defined as any counter-clockwise rotation of the Enveo RTM delivery system after initial deployment commenced* | |

|  |  |
| --- | --- |
| **Table 3 – Complications and Outcomes** | **N = 264** |
|  |  |
| Cardiac Tamponade | 1 (0.4) |
| Conversion to Sternotomy | 2 (0.8) |
| Annular Rupture | 0 (0) |
| Coronary Occlusion | 2 (0.8) |
| Major Vascular Complications ^ | 14 (5.3) |
| Acute Kidney Injury (stages 1-3) § | 16 (6.1) |
| *Requiring renal replacement therapy* | 2 (0.8) |
| New Permanent Pacemaker Implantation | 36 (14.7) |
| *New 3rd Degree Heart Block* | 14 (38.9) |
| *New 2nd Degree Heart Block* | 8 (22.2) |
| *New Left Bundle Branch Block* | 14 (38.9) |
| 30-day Cerebrovascular Accident | 10 (3.8) |
| Procedural Related Deaths | 0 (0) |
| 30-day Survival | 258 (97.7) |
| 30-day Paravalvular Leak ≤ Mild^ | 217 (92.3) |
| Values are n (%)  *^ Major vascular complications as defined by the VARC-2 criteria*  *§ Acute kidney injury as defined by the AKIN criteria*  *^ Data only available for 235/258 surviving patients* | |

**FIGURE TITLES & LEGENDS**

Figure 1: **Changes in Aortic Valve Area and Mean Aortic Valve Gradient**.  Changes in (A) Aortic Valve Area and (B) Mean Aortic Valve Gradient, pre- and post-EvolutTM R implantation

Figure 2: **Changes in Paravalvular Leak**.  Paravalvular leak post-procedurally and at 30-day follow up

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