The UK TAVI Registry

Jan Kovac MD FACC FESC
University Hospitals of Leicester
United Kingdom

on behalf of

UK TAVI data monitoring and analysis group
UK TAVI Registry
The United Kingdom Transcatheter Aortic Valve Implantation Registry

- To guide the introduction of TAVI in the UK
- Collaborative program
  - Professional Societies (BCIS and SCTS)
  - Department of Health and Specialist Commissioners
  - Health Technology Assessment and Regulators (NICE)
- 100% of consecutive UK TAVI implants (commissioning req.)
- Data collection via Central Cardiac Audit Database
- Data entered prospectively
- Mortality tracking
  - linkage MRIS Medical Records Information Service
    (formerly NHS Central Register, ONS)
The UK TAVI Registry

100% of consecutive UK TAVI implants
(1st Jan 2007 to 31st Dec 2011)

N = 2,732

- Collaborative program
  - Professional Societies (BCIS and SCTS)
  - Department of Health and Specialist Commissioners
  - Health Technology Assessment and Regulators (NICE)

Prospective Data collection via CCAD within NICOR with mortality tracking via Office of National Statistics
## Demographics (cohort to end 2011)

<table>
<thead>
<tr>
<th></th>
<th>Edwards Femoral</th>
<th>CoreValve Femoral</th>
<th>Edwards Apical</th>
<th>CoreValve Subclavian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>49.1</td>
<td>53.3</td>
<td>56.3</td>
<td>71.4</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>81.8 (7.3)</td>
<td>80.7 (7.6)</td>
<td>81.1 (7.7)</td>
<td>80.6 (6.7)</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>21.1</td>
<td>23.5</td>
<td>21.1</td>
<td>26.3</td>
</tr>
<tr>
<td>Previous MI, %</td>
<td>20.9</td>
<td>22.6</td>
<td>19.5</td>
<td>25.0</td>
</tr>
<tr>
<td>Prior cardiac surgery, %</td>
<td>26.8</td>
<td>31.9</td>
<td>42.7</td>
<td>32.3</td>
</tr>
<tr>
<td>PVD, %</td>
<td>15.7</td>
<td>19.3</td>
<td>45.7</td>
<td>55.6</td>
</tr>
</tbody>
</table>
UK TAVI Registry Totals

Total = 2,353 as 18-11-2011
UK TAVI Registry
The United Kingdom Transcatheter Aortic Valve Implantation Registry

Data at 17-10-2012

Number of TAVI by year

- 2007: 66
- 2008: 296
- 2009: 560
- 2010: 778
- 2011: 1052
UK TAVI Registry

100% consecutive UK TAVI procedures 1st Jan 2007 – 31st Dec 2011

- Edwards (n=1,353)
- Medtronic (n=1,350)
- St Jude (n=13)

- Other
- SC
- TA
- TF

Medtronic has the majority of procedures, with Edwards and St Jude following.
UK TAVI Registry

Access route by Year

Data to end 2010 Provisional Analysis as Sept 2011
UK TAVI: Access Route by Year

Medtronic CoreValve

Edwards Sapien
UK TAVI Registry
Logistic Euroscore

Data to end 2010 Provisional Analysis as Sept 2011

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Median</th>
<th>IQR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards Femoral</td>
<td>16</td>
<td>[11-24]</td>
<td>0.42</td>
</tr>
<tr>
<td>CoreValve Femoral</td>
<td>17</td>
<td>[12-26]</td>
<td>0.09</td>
</tr>
<tr>
<td>Edwards Transapical</td>
<td>21</td>
<td>[14-31]</td>
<td>0.09</td>
</tr>
<tr>
<td>CoreValve Subclavian</td>
<td>22</td>
<td>[13-39]</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Median, %
[IQR]
UK TAVI Registry
Logistic Euroscore

Data to end 2010 Provisional Analysis as Sept 2011

P<0.001

Median, %
[IQR]

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Median</th>
<th>IQR</th>
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<tbody>
<tr>
<td>Edwards Femoral</td>
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</tr>
<tr>
<td>CoreValve Subclavian</td>
<td>22</td>
<td>13-39</td>
</tr>
</tbody>
</table>
Change in logEUROSCORE with time in UK

Trendline suggests 0.6% reduction in LES
Per year
TAVI – trend in 30-day mortality over time

- 2007: 13.9%
- 2008: 8.5%
- 2009: 5.4%
- 2010: 6.2%
- 2011: 5.8%
UK TAVI Registry to end 2009
Moat N E, Ludman PF, DeBelder MA et al JACC 2011:58;2130

EXPEDITED PUBLICATIONS

Long-Term Outcomes After Transcatheter Aortic Valve Implantation in High-Risk Patients With Severe Aortic Stenosis

The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry

Neil E. Moat, MBBS, MS,* Peter Ludman, MA, MD,† Mark A. de Beelder, MA, MD;‡ Ben Bridgewater, PhD,§ Andrew D. Cunningham, PhD,¶¶ Christopher P. Young, MD,¶ Martyn Thomas, MD,¶¶ Jan Kovac, MD,# Tom Spyts, MD,# Philip A. MacCarthy, BS, PhD,**, Olaf Wendler, MD, PhD,** David Hildick-Smith, MD,†† Simon W. Davies, MBBS, MD,* Uday Trivedi, MBBS,†† Daniel J. Blackman, MD,‡‡ Richard D. Levy, MD,§ Stephen J. D. Brecker, MD, §§ Andreas Baumbach, MD,¶ Tim Daniel, MB, ChB,¶¶ Huon Gray, MD,¶¶ Michael J. Mullen, MBBS, MD***

London, Birmingham, Bristol, Middlesbrough, Manchester, Leicester, Brighton, Leeds, and Southampton, United Kingdom

870 Patients having 877 TAVI procedures 100% mortality tracking
Thirty-day mortality (cohort to end 2011)

- Edwards Femoral
- CoreValve Femoral: p = ns
- Edwards Transapical: p 0.04
- CoreValve Subclavian
UK TAVI Registry

Log Euroscore 0-20%

Log Euroscore 20-40%

Log Euroscore >40%

p<0.00001
One-year Survival – Alternative Access

### Non-Transfemoral TAVI Cases

<table>
<thead>
<tr>
<th>Survival</th>
<th>0 Days</th>
<th>30 Days</th>
<th>6 Months</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transapical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number at Risk</td>
<td>410</td>
<td>355</td>
<td>313</td>
<td>235</td>
</tr>
<tr>
<td>Survival Subclavian</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number at Risk</td>
<td>91</td>
<td>87</td>
<td>74</td>
<td>48</td>
</tr>
</tbody>
</table>

*TF vs non-TF

p<0.001*
Two-year Survival – Alternative Access

Transfemoral
Subclavian
Transapical

$p < 0.00001$
UK TAVI Registry
New Permanent Pacemaker

Data to end 2010 Provisional Analysis as Sept 2011

- Edwards Femoral: 6.2%
- CoreValve Femoral: 21.6%
- Edwards Transapical: 5.6%
- CoreValve Subclavian: 22.1%

P<0.001
UK TAVI Registry
Aortic Regurgitation Grade ≥2+

Data to end 2010 Provisional Analysis as Sept 2011
UK TAVI Registry

Planned Research

• Applications to use dataset for research
  – Data Sharing agreement
  – www.bcis.org.uk

• 3 projects approved:
  – Cost effectiveness analysis based on UK TAVI Registry
  – Gender and Outcomes
  – Previous open heart surgery and outcomes from TAVI
Males – more:
- Ex smokers
- Previous MI
- Previous Revasc
- Concomitant CAD
- Poorer LV
- Moderate AR
Conclusions

- Successful collaborative implementation of a National Registry
- All Valve types represented with complete coverage of TAVI in GB
- Both valve types implanted via FA have similar medium term mortality
- Interesting initial analysis of outcome following alternative access routes
UK SATIRE

The combined UK cardiac Surgical And TavI REgistries.

An analysis of activity, trend and outcomes in 37,020 patients who underwent aortic valve intervention in the 5 years from 2006 -2010.

Neil E Moat, D Cunningham, M de Belder, P Ludman, B Bridgewater, G Hickey.
The UK Registries

• All cardiac surgical procedures and all TAVI’s in the UK are entered into National Registries hosted by NICOR (National Institute for Cardiovascular Outcomes Research)

• The datasets and databases were designed to be compatible and comparable

• The dataset definitions can be found at http://www.ucl.ac.uk/nicor/audits
All Surgical Aortic valve Interventions (AVR + AVR&CABG)

- 2006: 6217
- 2007: 7548
- 2008: 7252
- 2009: 7252
- 2010: 7252
All Aortic valve Interventions (AVR + AVR&CABG + TAVI)

2006: 6217
2007: 8000
2008: 8201
2009: 9000
2010: 8201
All Aortic valve Interventions (AVR + AVR&CABG + TAVI)
in patients aged 80 or over

2006 2007 2008 2009 2010

2035

1055
In 2010 9% of all aortic valve interventions (AVR + AVR&CABG + TAVI) were by TAVI.
## Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>AVR</th>
<th>AVR&amp;CABG</th>
<th>TAVI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67.8</td>
<td>73.1</td>
<td>81.4</td>
</tr>
<tr>
<td>Female</td>
<td>28.2</td>
<td>41.2</td>
<td>46.7</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>8.3</td>
<td>23.9</td>
<td>81.2</td>
</tr>
<tr>
<td>LVEF &lt;30%</td>
<td>5.1</td>
<td>7.2</td>
<td>8.7</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>14.2</td>
<td>15.1</td>
<td>27.6</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>6.3</td>
<td>14.6</td>
<td>27.2</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>0.7</td>
<td>0.6</td>
<td>7.4</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>4.8</td>
<td>10.2</td>
<td>32.8</td>
</tr>
<tr>
<td>Non-elective procedure</td>
<td>20.5</td>
<td>27.1</td>
<td>9.2</td>
</tr>
</tbody>
</table>
## Demographics in patients aged 80 or over

<table>
<thead>
<tr>
<th></th>
<th>AVR</th>
<th>AVR&amp;CABG</th>
<th>TAVI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>83.0</td>
<td>83</td>
<td>85.5</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>56</td>
<td>37</td>
<td>51</td>
</tr>
<tr>
<td><strong>NYHA III/IV</strong></td>
<td>9.3</td>
<td>23.4</td>
<td>83.2</td>
</tr>
<tr>
<td><strong>LVEF &lt;30%</strong></td>
<td>4.1</td>
<td>6.6</td>
<td>6.7</td>
</tr>
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<td>8.8</td>
<td>14.5</td>
<td>25.8</td>
</tr>
<tr>
<td><strong>Renal dysfunction</strong></td>
<td>0.4</td>
<td>0.3</td>
<td>6.5</td>
</tr>
<tr>
<td><strong>Previous cardiac surgery</strong></td>
<td>8.0</td>
<td>3.2</td>
<td>24.0</td>
</tr>
<tr>
<td><strong>Non-elective procedure</strong></td>
<td>23.0</td>
<td>32.7</td>
<td>11.0</td>
</tr>
</tbody>
</table>
30-day mortality for all patients and for those over 80 years undergoing AVR or AVR&CABG

AVR: 2.2% (all), 4.1% (over 80)
AVR&CABG: 4.5% (all), 6.4% (over 80)
TAVI: 6.7% (all)
Kaplan-Meier survival distributions for TAVI, isolated AVR and AVR&CABG
Survival over the first year for AVR, AVR&CABG and for TAVI
Survival over the first year for AVR, AVR&CABG in patients over 80 and for all TAVI
Risk model performance was assessed by evaluating model calibration and discrimination

• For each of the 10 deciles of data the mean observed and predicted mortality was plotted and a non-parametric smoothing curve overlaid to show general trend.

• The overall observed-to-expected (O:E) ratio was also calculated; departures from unity indicate a lack of overall calibration.

• Model discrimination was evaluated by deriving the receiver operating characteristic (ROC) curve and calculating the area under the curve (AUC) summary statistics.
<table>
<thead>
<tr>
<th>Group</th>
<th>Model</th>
<th>Predicted mortality (%)</th>
<th>O:E</th>
<th>Discrimination AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI</td>
<td>EuroSCORE</td>
<td>21</td>
<td>0.34</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>EuroSCORE II</td>
<td>4.1</td>
<td>1.68</td>
<td>0.59</td>
</tr>
<tr>
<td>Isolated sAVR</td>
<td>EuroSCORE</td>
<td>7.9</td>
<td>0.29</td>
<td>0.783</td>
</tr>
<tr>
<td></td>
<td>EuroSCORE II</td>
<td>2.6</td>
<td>0.87</td>
<td>0.78</td>
</tr>
<tr>
<td>sAVR + CABG</td>
<td>EuroSCORE</td>
<td>9.8</td>
<td>0.48</td>
<td>0.717</td>
</tr>
<tr>
<td></td>
<td>EuroSCORE II</td>
<td>4.7</td>
<td>1</td>
<td>0.732</td>
</tr>
</tbody>
</table>
Summary

• Significant growth in all aortic valve interventions (~30%)
• Half of this increase occurred in patients 80+ years old
• Predictably large differences in demographics
• As expected patients coming to TAVI are older and higher risk than those for conventional surgery, but there is significant overlap between the groups
• Median PLOS was similar in both cohorts
• Survival is worse following TAVI, as would be expected by the elderly and high risk nature of these patients.
Summary

- The logistic EuroSCORE does not predict operative outcomes for surgery or TAVI and should not be used.
- The EuroSCORE 2 gives good prediction for conventional surgery but does not have satisfactory discriminatory ability for predicting mortality outcomes for TAVI.
- Early and late survival were worse in the AVR&CABG cohort than in those having an isolated AVR.
- The presence of concomitant CAD did not affect early or late survival following TAVI.
The UK TAVI Trial
UK TAVI - Aim

To assess the clinical effectiveness and cost-utility of TAVI as an alternative to conventional surgical AVR in patients with severe symptomatic aortic stenosis who are at intermediate or high operative risk.
UK TAVI - Key Questions

- Is TAVI superior with respect to early QoL, post-procedure recovery, hospital stay and cost?
- Does TAVI have comparable long-term benefit and morbidity and mortality at least as good as surgery?
UK TAVI - Design

- Prospective
- Multi-centre UK
- Open-label
- Parallel group
- Pragmatic trial of TAVI strategy vs surgical AVR
- Non-inferiority
Inclusion Criteria

• Severe symptomatic aortic stenosis
• Age ≥80 years  or  Age ≥70 years + intermediate or high operative risk  
  (guideline STS score 4% - 12% but MDT has discretion)
• Both AVR and TAVI deemed to be acceptable options
• Concurrent coronary disease amenable to PCI or CABG
• Fully informed written consent

Eligibility will be determined by the MDT
Exclusion Criteria

- Intervention inappropriate due to comorbidity or frailty
- Life expectancy less than one year
- Technically unsuitable for either AVR or TAVI
- Dementia or cognitive impairment (consent/ compliance)
- Previous AVR or TAVI
- Non-availability of suitable TAVI option (may refer on)
- Participation in conflicting study
MDT - typical composition

• ≥ 2 cardiac surgeons
• One or more interventional cardiologists skilled in TAVI
• One or more experts in cardiac imaging
• Cardiac anaesthetist
• Geriatrician
• Specialist nurse
MDT process

Risk factors to consider include but not limited to:

- Frailty or general debility
- Chronic pulmonary disease
- Previous cardiac surgery or hostile mediastinum
- Extra-cardiac arteriopathy
- Neurological dysfunction
- Impaired renal function
- Impaired left ventricular function
- Diabetes mellitus
- Pulmonary hypertension
- Low BMI
UK TAVI – trial design

Severe Symptomatic Aortic Stenosis

- Intervention appropriate? [Y/N]
  - Surgery feasible? [Y/N]
    - High operative risk? [Y/N]
      - TAVI feasible? [Y/N]
        - Consent [Y/N]
          - RCT
            - Surgery
            - TAVI
      - TAVI feasible? [Y/N]
    - TAVI feasible? [Y/N]
  - TAVI feasible? [Y/N]

MDT

- TAVI feasible? [Y/N]
Randomisation

- Web-based
- Stratified by:
  - Age
  - Centre
  - Presence/absence of CAD requiring revascularisation
Interventions

• Control group:
  Surgical AVR (any valve except sutureless)
  Concomitant revascularisation, if appropriate

• Intervention group:
  TAVI  - any CE-marked valve deemed appropriate by MDT
  - any access route deemed appropriate by MDT
  - PCI pre-TAVI (or post) at investigator’s discretion

*UK TAVI is a pragmatic trial of a TAVI strategy*
Primary end-point

- All-cause mortality at one year

  Peri-procedural = TAVI advantage?

  Post-discharge = Equivalence?

  Long-term = AVR proven; TAVI uncertain
Secondary outcomes (VARC 2 definitions)

- All-cause mortality (30 d & annually to 5 years)
- Cardiovascular mortality (30 d & annually to 5 years)
- Quality adjusted survival (3/12 & annually to 5 years)
- Stroke (30 d & annually to 5 years)
- Re-intervention (30 d & annually to 5 years)
- Death from any cause or disabling stroke (30 d & annually to 5 years)
- Death from any cause, stroke or re-intervention (30 d & annually to 5 years)
- Quality of life (MLWHF, EQ-5D, SF-12)
- Symptoms/ functional capacity (CCS, NYHA, Nottingham EADL, 6-min walk)
- Cognitive function (MMS Index)
- Procedural success and in-hospital complications
- Conduction disturbance requiring permanent pacemaker
- Echo measures (LV EF, mass, dimensions, volumes, AR, AV grad & area)
- Costs, cost-utility, incremental C/E ratio (1 yr, 5yrs, estimated lifetime)
Assessments

- Baseline (include frailty - Fried criteria)
- Follow-up: - 6 weeks, one-year (as per clinical practice)

  Clinical
  QoL/ functional
  Echocardiographic
  Resource use/ cost-utility

  - Interim telephone QoL 7d, 3m, 6m
  - Annual telephone QoL & CV events for 5y
Fried Frailty Criteria (phenotype)

- Weight loss >5kg in past year
- Grip strength using dynamometer
- Exhaustion
- Walk time (2.4m)
- Low activity level

Frail: ≥ 3 criteria
Pre-frail: 1 or 2 criteria
Non-frail: 0 criteria
Sample size calculation

- Assumed one-year mortality after AVR 15%
- Non-inferiority margin 7.5%
- 90% power
- Alpha 0.05
- Sample size 808 patients
- Interim review of sample size by DMC
Timeline

Sep 2012: Funding approval
Mar 2013: Final protocol
May 2013: Ethics and regulatory approvals
Aug 2013: First patient enrolled
Aug 2016: 808 patients recruited
Dec 2017: Completion of one-year follow-up
Summary

• The registries are national and publically funded, and as such they are free from any commercial bias.
• The Registries are not voluntary and thus are free of any selection bias.
• The two registries combined give a large sample for analysis and benefit from robust independent long-term mortality tracking.
• The datasets have been specifically configured to have identical definitions for the appropriate fields and have good data on pre-operative patient characteristics, procedural data and mortality, hospital length of stay and long term survival.
### Peak Gradient (mmHg) vs Mean gradient (mmHg)

<table>
<thead>
<tr>
<th>Year</th>
<th>Peak Gradient</th>
<th>Mean Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-TAVI</td>
<td>96</td>
<td>54</td>
</tr>
<tr>
<td>01/2007</td>
<td>11</td>
<td>5.5</td>
</tr>
<tr>
<td>2009</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>2011</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>2012</td>
<td>19</td>
<td>9</td>
</tr>
</tbody>
</table>

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**Thank You**
The End