Medium Term Survival and Functional Status in Patients with Severe Aortic Stenosis Treated by Transcatheter Aortic Valvular Implantation in the PARTNER EU Trial

Bernard De Bruyne, MD, PhD

Cardiovascular Center Aalst

OLV-Clinic Aalst, Belgium

Data Extract 7 Aug 09

Disclosure Statement

Nothing to disclose

Participating Investigators

Aalst – *OLV-Clinic*
IC: B. De Bruyne, Marc Vanderheyden
CV: I. Degrieck, F. Casselman, H. Vanermen

Essen - *University Clinics-West German Heart Center*
IC: S. Sack, R. Erbel, H. Eggebrecht, P. Kahlert
CV: M. Thielmann, D. Wendt, H. Jakob

Frankfurt a.M. - *J. W. Goethe University*
IC: V. Schächinger, S. Fichtlscherer
CV: G. Wimmer-Greinecker, M. Doss

London - *Kings College Hospital*
IC: M. Thomas, P. MacCarthy
CV: A. El-Gamel, O. Wendler

Massy - *Institut Hospitalier Jacques Cartier*
IC: T. Lefevre, M-C. Morice
CV: P. Donzeau-Gouge, A. Farge, M. Romano

Paris - *Hôpital Bichat*
IC: A. Vahanian, D. Himbert
CV: P. Nataf, N. Al-Attar

Rotterdam - *Erasmus Medical Center*
IC: P. DeJaegere
CV: A.P. Kappetein

Rouen - *Charles Nicole Hôpital*
IC: A. Cribier, H. Eltchaninoff
CV: J-P Bessou, Y-P Litzler

Vienna - *Medical University (AKH)*
IC: D. Glogar, H. Baumgartner
CV: E. Wolner, P. Simon, W. Wisser , M.T. Kasimir

Steering Committee:
Wimmer-Greinecker, Schächinger, Lefevre, De Bruyne, Nataf, DeJaegere

Data Extract 7 Aug 09

Trial Overview & Methods

Purpose

- Establish interventional cardiology/ cardiac surgery partnerships to identify, jointly screen and treat adult severe aortic stenosis patients by transfemoral or transapical TAVI

Design

- Prospective, multicenter, non- randomized, observational trial of the Edwards SAPIEN™ THV

Primary Safety Endpoint

- Freedom from death from the index procedure to 30 days and 6 months

Primary Efficacy Endpoint

- Hemodynamic, QOL and NYHA improvement at 12 months

Trial Conduct

- Enrollment period
  - April 2007 – January 2008 – initiated in pre-commercialization period
- Investigator and Site Training
  - 2 day didactic, simulator training, case observations
  - 2 proctored cases each approach (TF/TA)
- Follow-up and Monitoring
  - 30 day, 6, 12 and 18 month intervals
  - 100% monitoring in progress

Trial Oversite

- Echo Corelab – Columbia University Medical Center, NYC (Dr. L. Gillam)
- CEC and DSMB - independent committees to review safety & adjudicate events
  - Administration- European Center for Cardiovascular Research (CERC), Paris
  - 100% event adjudication in progress

Data Extract 7 Aug 09

Key Inclusion/Exclusion Criteria

- **Inclusion Criteria**
  - Logistic EuroSCORE ≥20% and/or STS score ≥10
  - Comorbidities – if EuroSCORE <20
    - Porcelain aorta, surgically unmanageable ascending aortic calcification
    - Chest deformities that preclude open chest procedures
  - Senile degenerative symptomatic aortic valve stenosis with a documented AVA < 0.8 cm^2, mean gradient > 40mmHg and/or jet velocity > 4.0 m/s
- **Exclusion Criteria**
  - Evidence of an acute myocardial infarction within 14 days of the intended treatment
  - Any therapeutic invasive cardiac procedure, other than BAV, performed within 30 days of the index procedure
  - Native aortic annulus <16 mm or >25 mm (per baseline ECHO)
  - Life expectancy <12 months due to non-cardiac co-morbid conditions
  - Unprotected left main disease (>70%)
  - Active infection or endocarditis
  - Acute coronary insufficiency

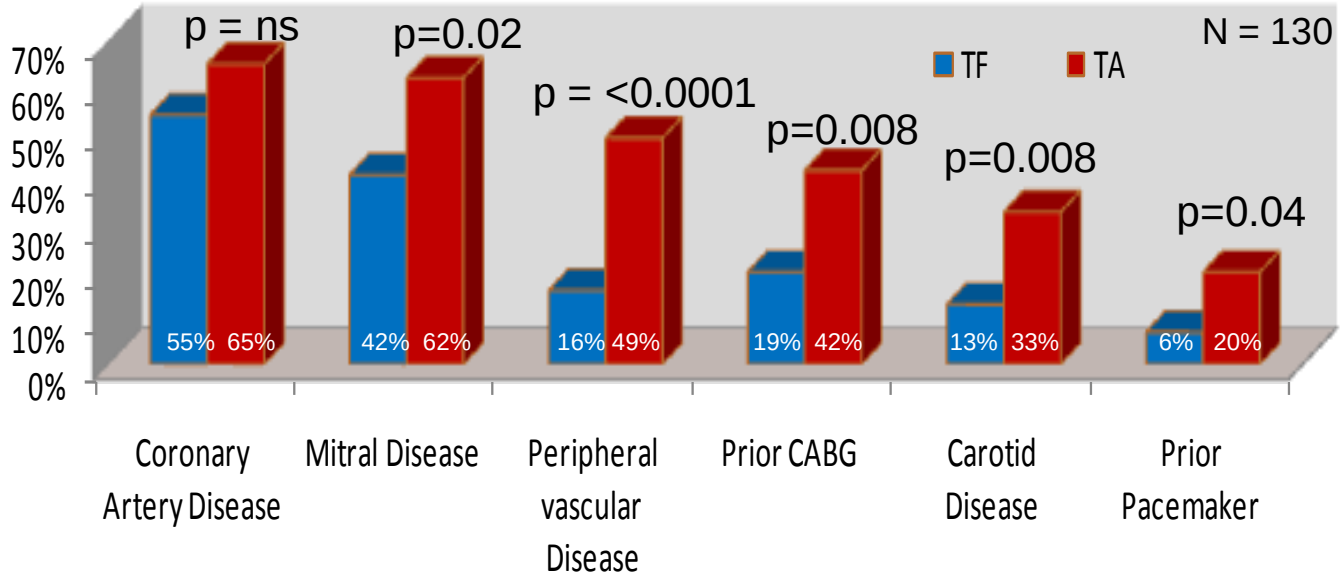
Data Extract 7 Aug 09

Baseline Demographics – ITT

	Transfemoral n = 61	Transapical n = 69
Mean Age (yrs)	82.3 ± 5.2 (Range: 69.1-92.5)	81.9 ± 5.7 (Range: 67.7-93.3)
Gender	Female: 61% Male: 39%	Female: 51% Male: 49%
NYHA	I: 2% III: 68% II: 15% IV: 16%	I: 1% III: 68% II: 13% IV: 17%
Mean Aortic Valve Area	0.7 ± 0.2 (Range: 0.3-1.2)	0.7 ± 0.4 (Range: 0.3-2.7)
Mean Gradient	47.3 ± 19.9 (Range: 10-120)	46.7 ± 18.6 (Range: 18-87)
Mean Ejection Fraction	52.7 ± 17.7 (Range: 15.0-86.1)	53.0 ± 14.6 (Range: 17.3-77.0)
Logistic EuroSCORE	25.7 ± 11.5 (Range: 6.4-65.5) Median = 24.4	33.8 ± 14.4 (Range: 5.1-72.1) Median = 29.8
STS Score	11.3 ± 6.1 (Range: 3.7-32.7)	11.8 ± 6.8 (Range: 2-41)

Data Extract 7 Aug 09

Comorbidities



- **TA Cohort had greater comorbidities with higher:**
  CAD, Mitral disease, PVD, Prior CABG, Carotid Disease, Prior Pacemaker

- **At least one-third of patients enrolled had underlying:**
  - Systemic hypertension (71% TF, 77% TA)
  - Pulmonary disease (48% TF, 35% TA)
  - Chronic kidney disease (37% TF, 46% TA)

Data Extract 7 Aug 09

Study Flow Chart

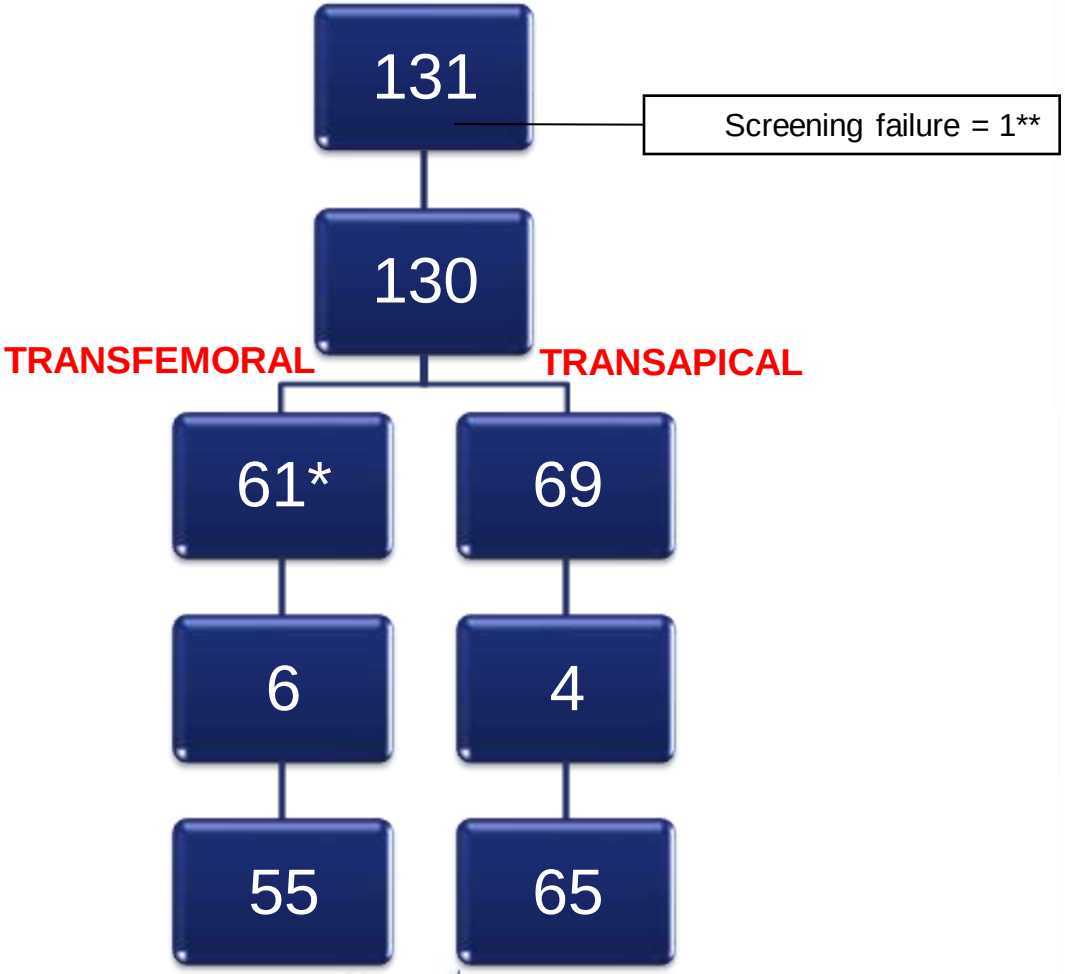
- Signed Informed Consent

INTENTION-TO-TREAT (ITT)

- Attempted Procedure
- Aborted Procedure
  (No valve implant attempted)

DEVICE IMPLANT PERFORMED

- Patient followed per protocol "as intended" (AI)

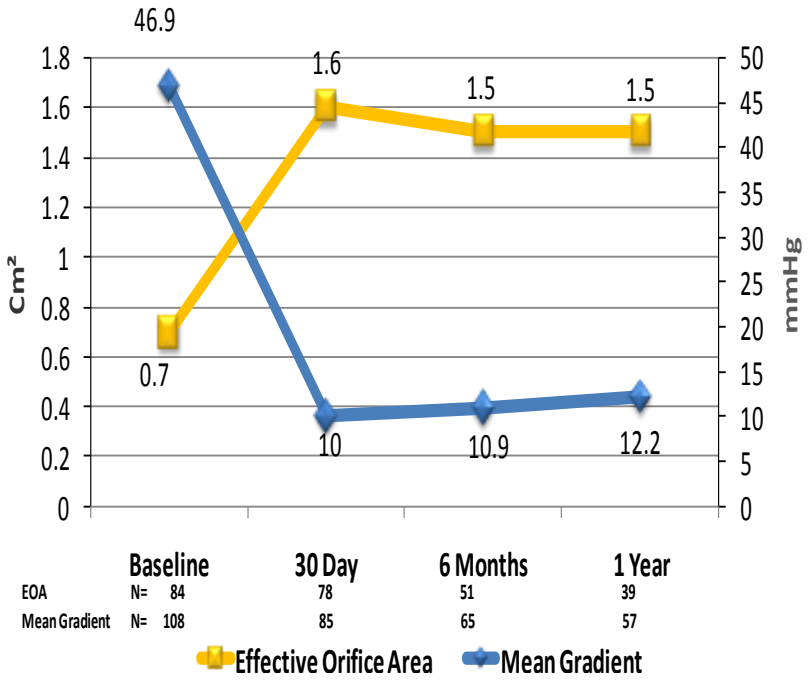


Data Extract 7 Aug 09

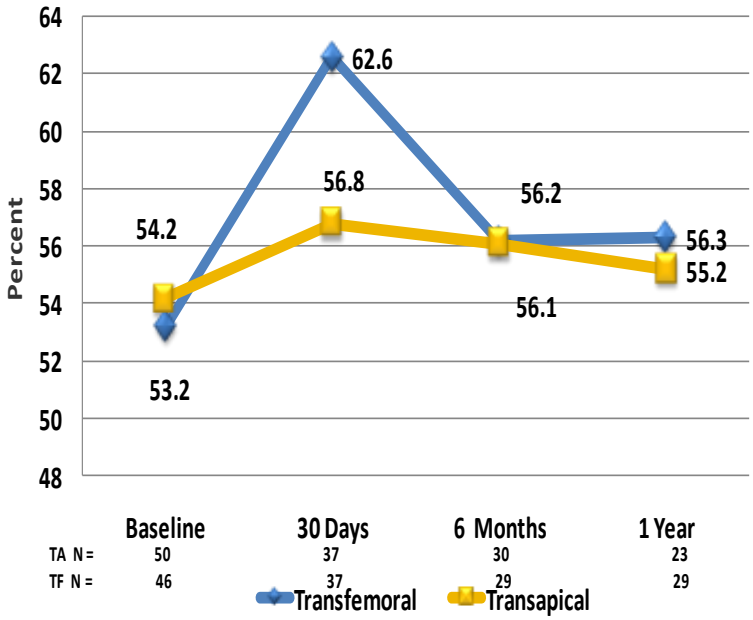
* One TF cross-over to TA analyzed is in TF cohort per PARTNER EU Trial Executive Committee ruling
** One screening failure – active endocarditis - 131 patients signed informed consents

Hemodynamics and Valve Performance

Mean Gradient and AVA



LVEF

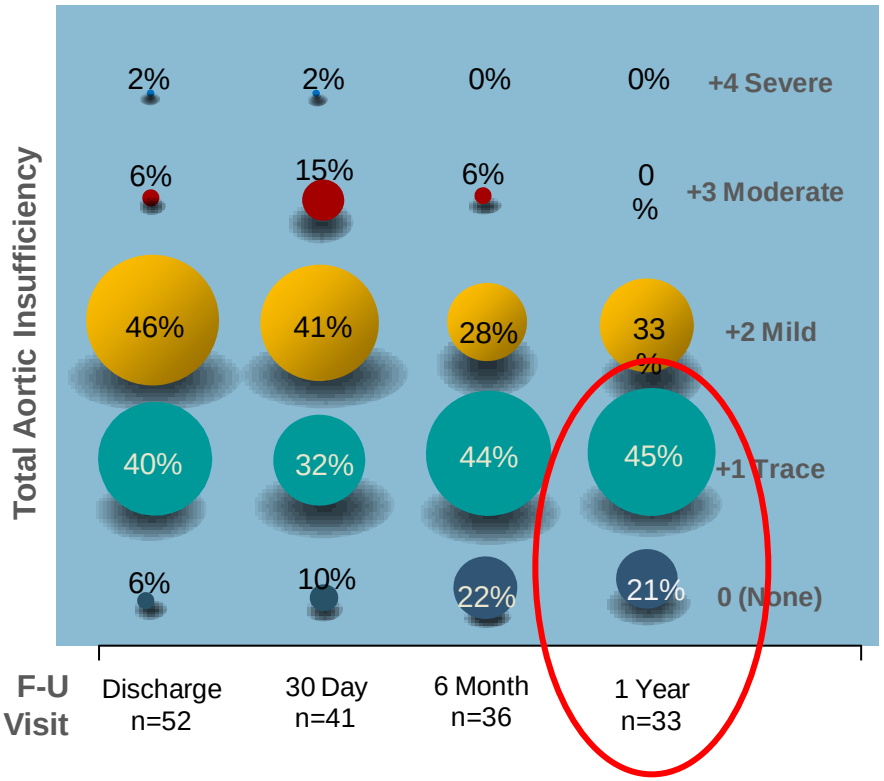


Valve performs as intended with relief of severe stenosis and return to low gradients

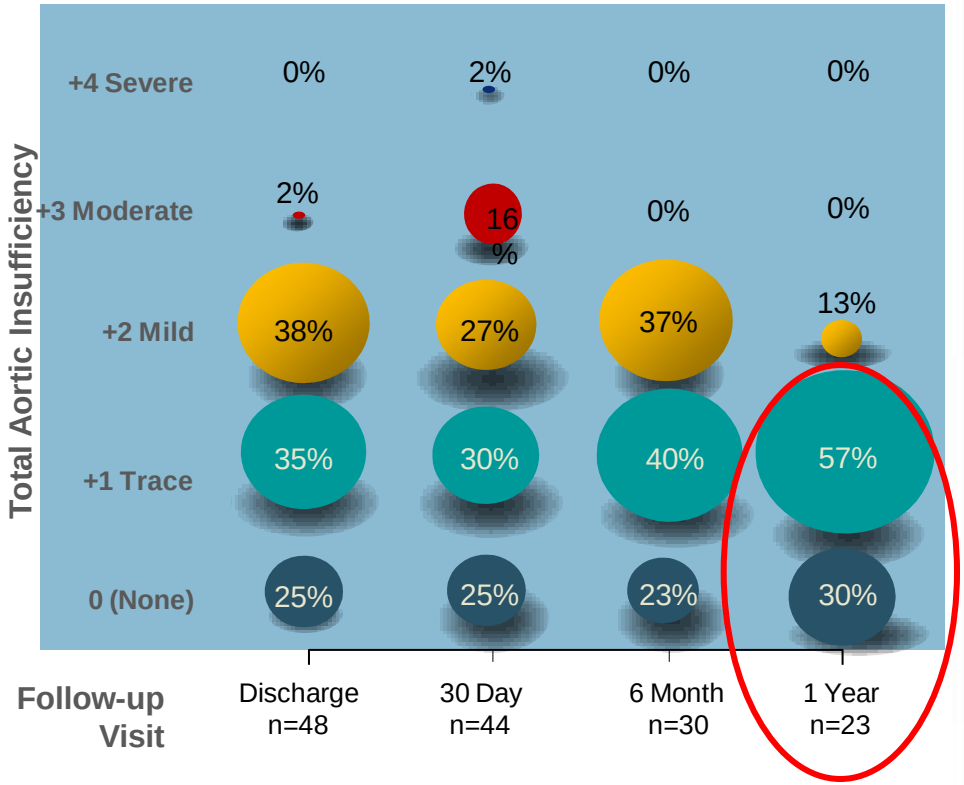
Data Extract 7 Aug 09

Aortic Insufficiency

Transfemoral



Transapical



At one year post implant: 66%: 0 or 1+

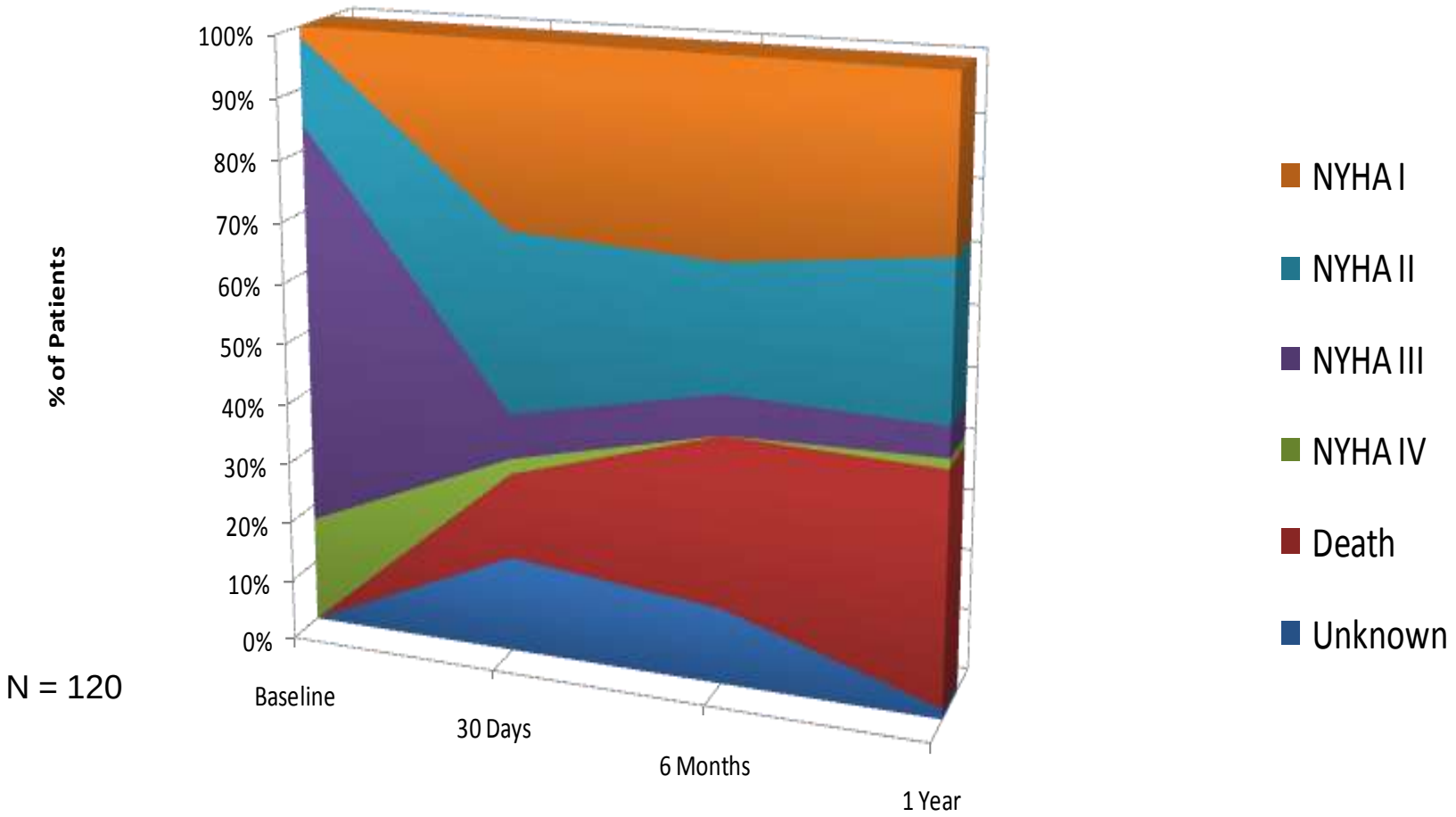
At one year post implant: 87%: 0 or 1+

Data Extract 7 Aug 09

Functional Status

Data Extract 7 Aug 09

1-Year NYHA Classification

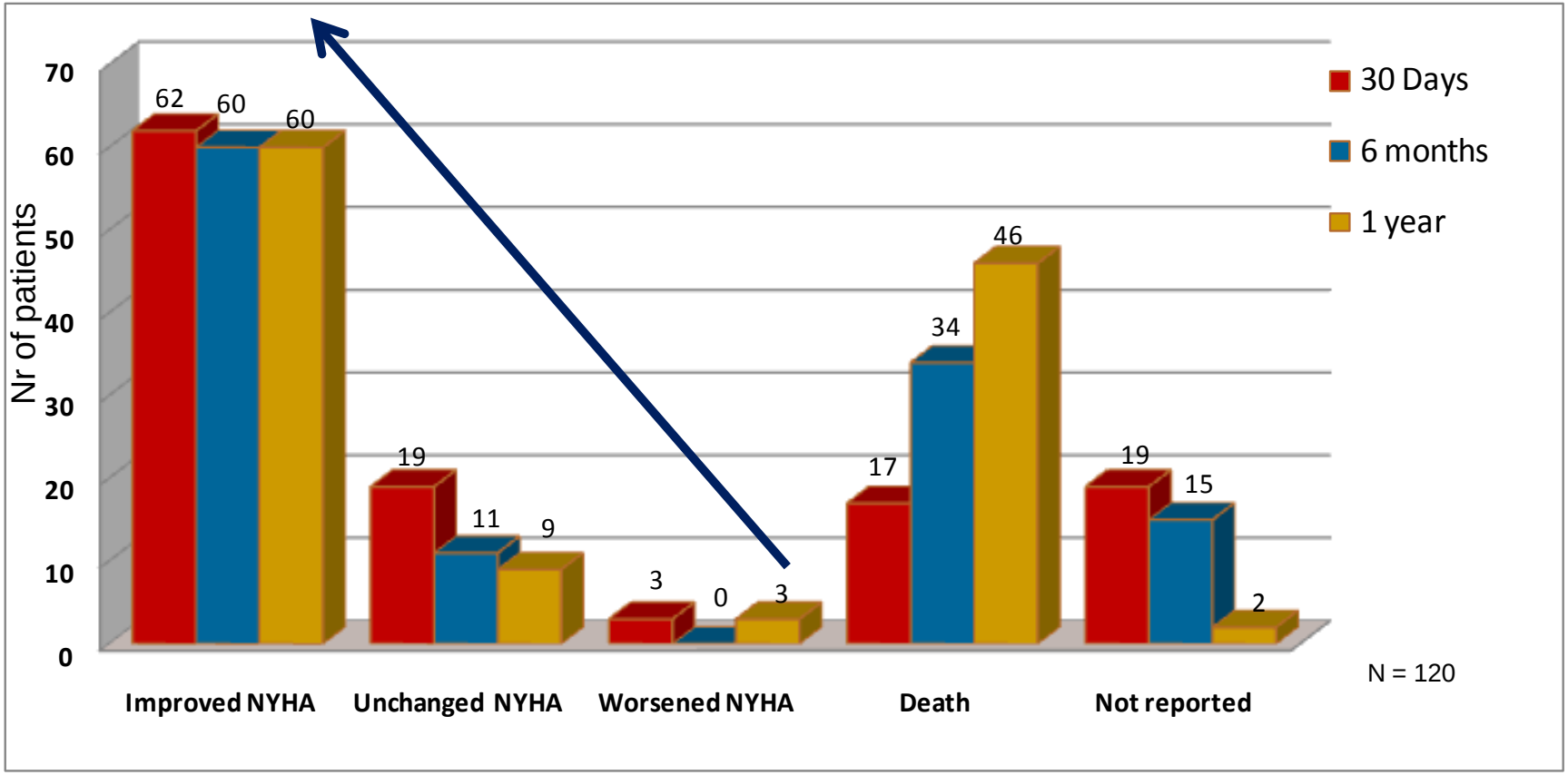


N = 120

89% of surviving patients in NYHA Class 1 or 2

Data Extract 7 Aug 09

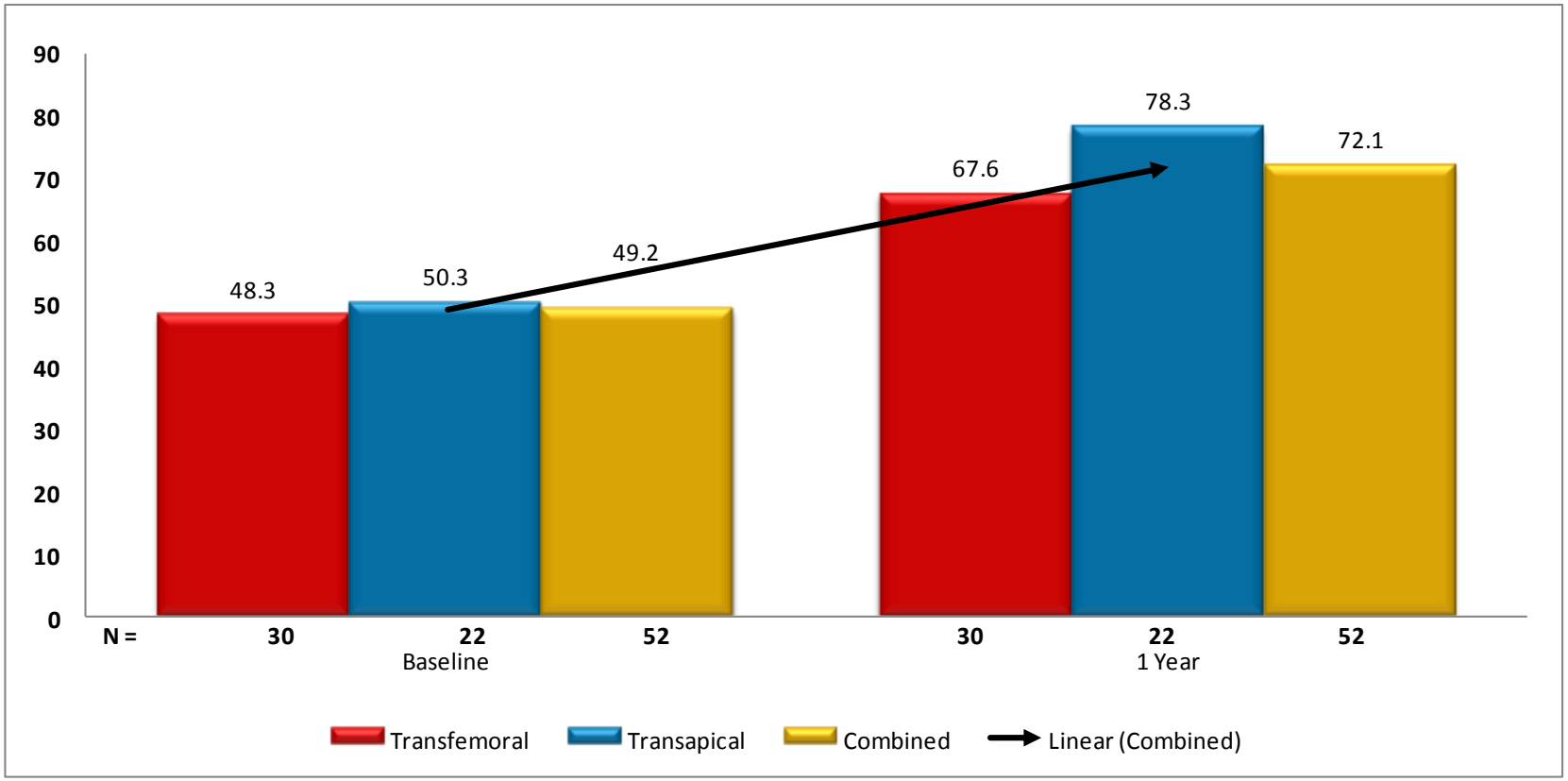
1-Year NYHA Classification



81% had improved NYHA class at 12 months

Data Extract 7 Aug 09

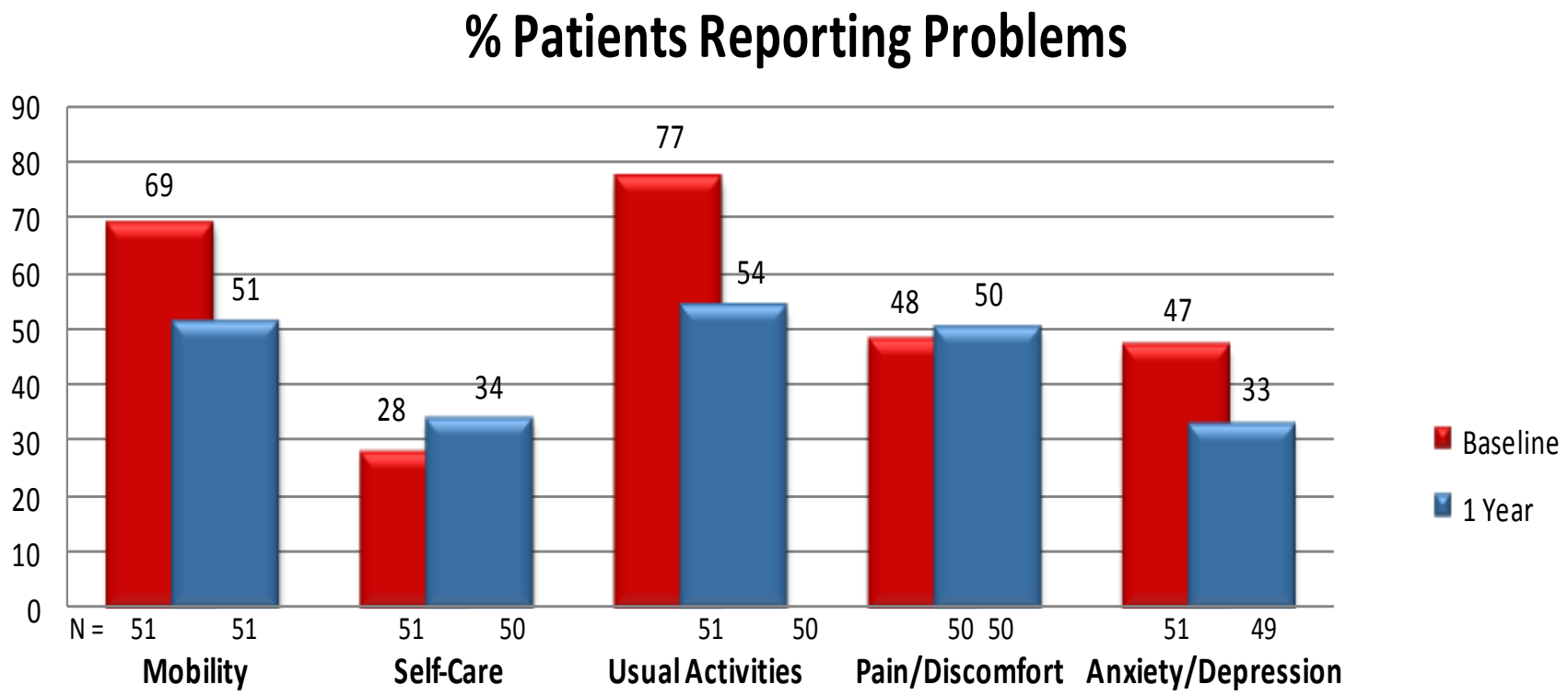
Quality of Life – Overall Summary Score



At 1 year post implantation, a large treatment effect is noted by a 22.9 point improvement

Data Extract 7 Aug 09

Quality of Life – EQ-5D

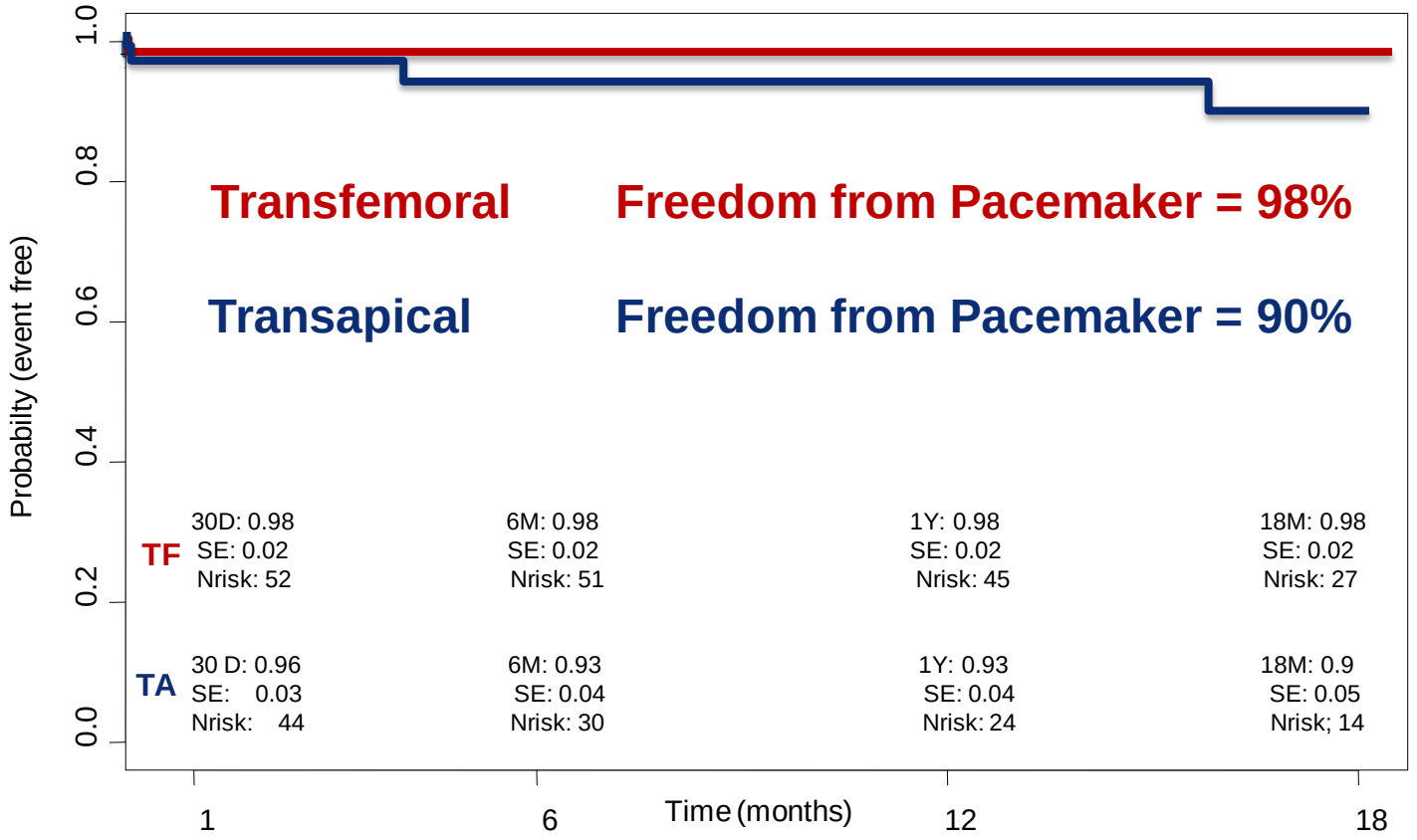


At 1 year post implantation, a meaningful improvement in most activities of daily living is noted

Data Extract 7 Aug 09

18 Months - Arrhythmias Requiring Pacemaker

N = 130



30 day pacemaker in conventional AVR = 3.2% – 8.5% [1]

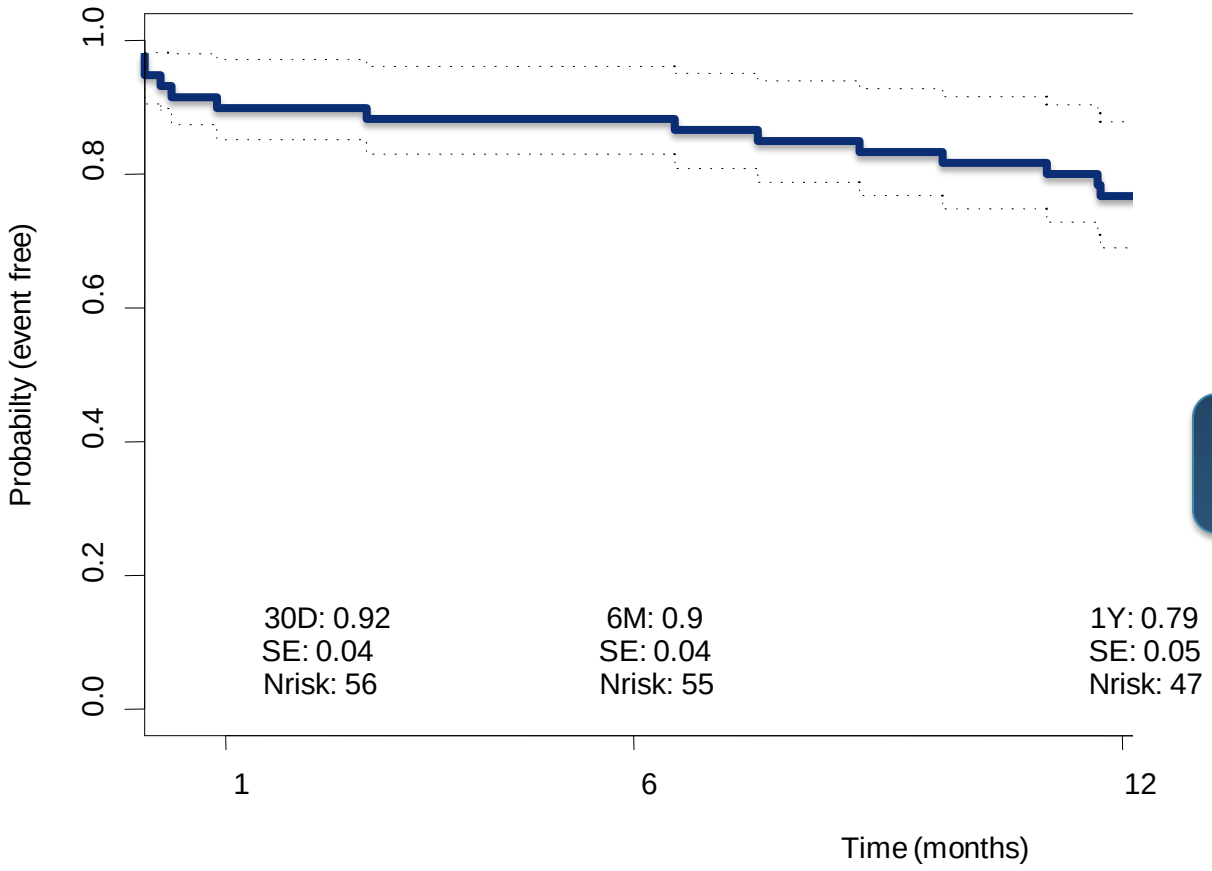
Data Extract 7 Aug 09

1. Dawkins et al. Permanent Pacemaker Implantation After Isolated AVR, Ann Thorac Surg, 2008, 85:108-12

Survival at 18 months

Data Extract 7 Aug 09

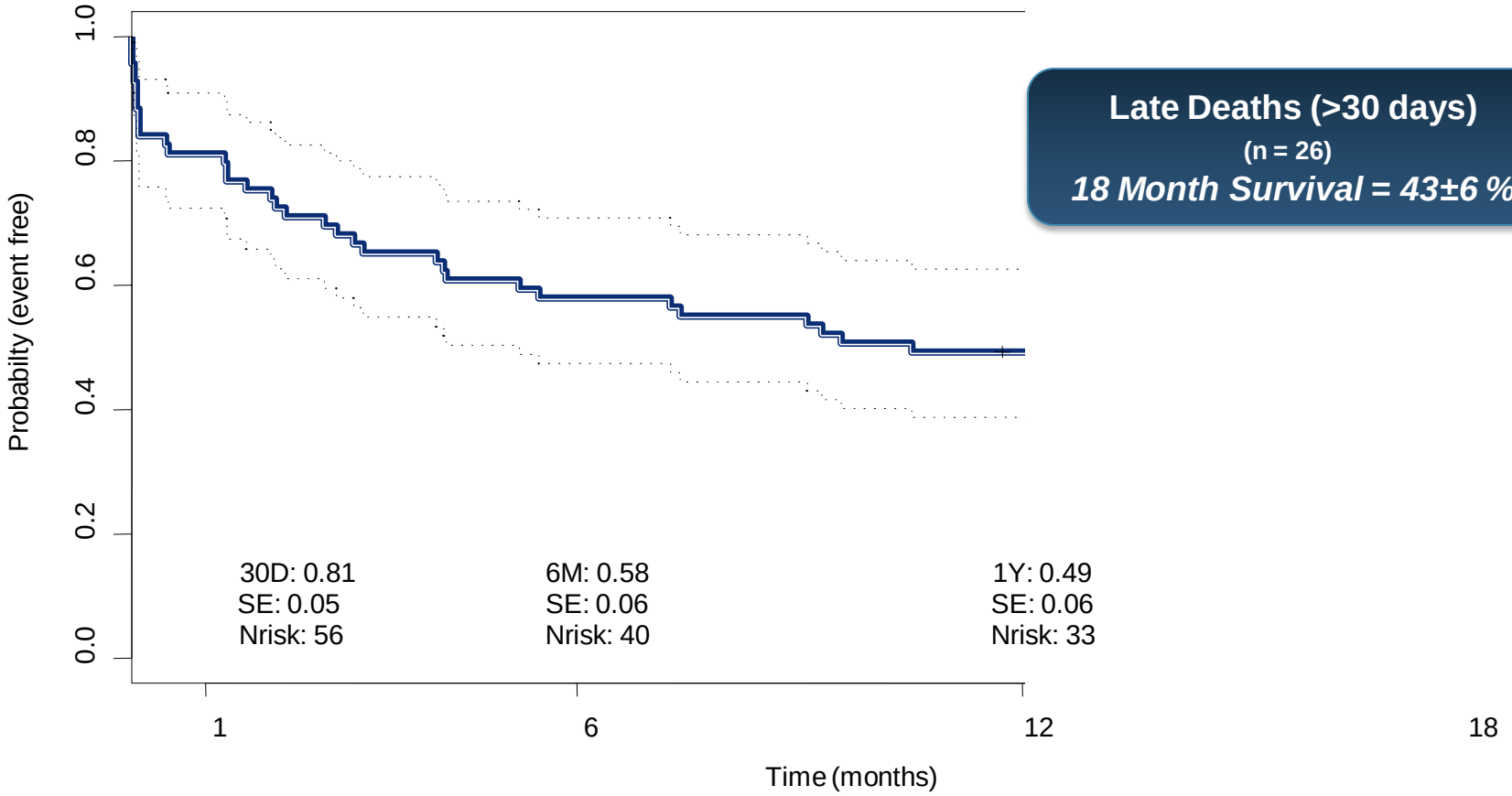
Transfemoral Survival to 18 Months



Late Deaths (>30 days)
(n = 12)
18 Month Survival = 71 ± 6%

Data Extract 7 Aug 09

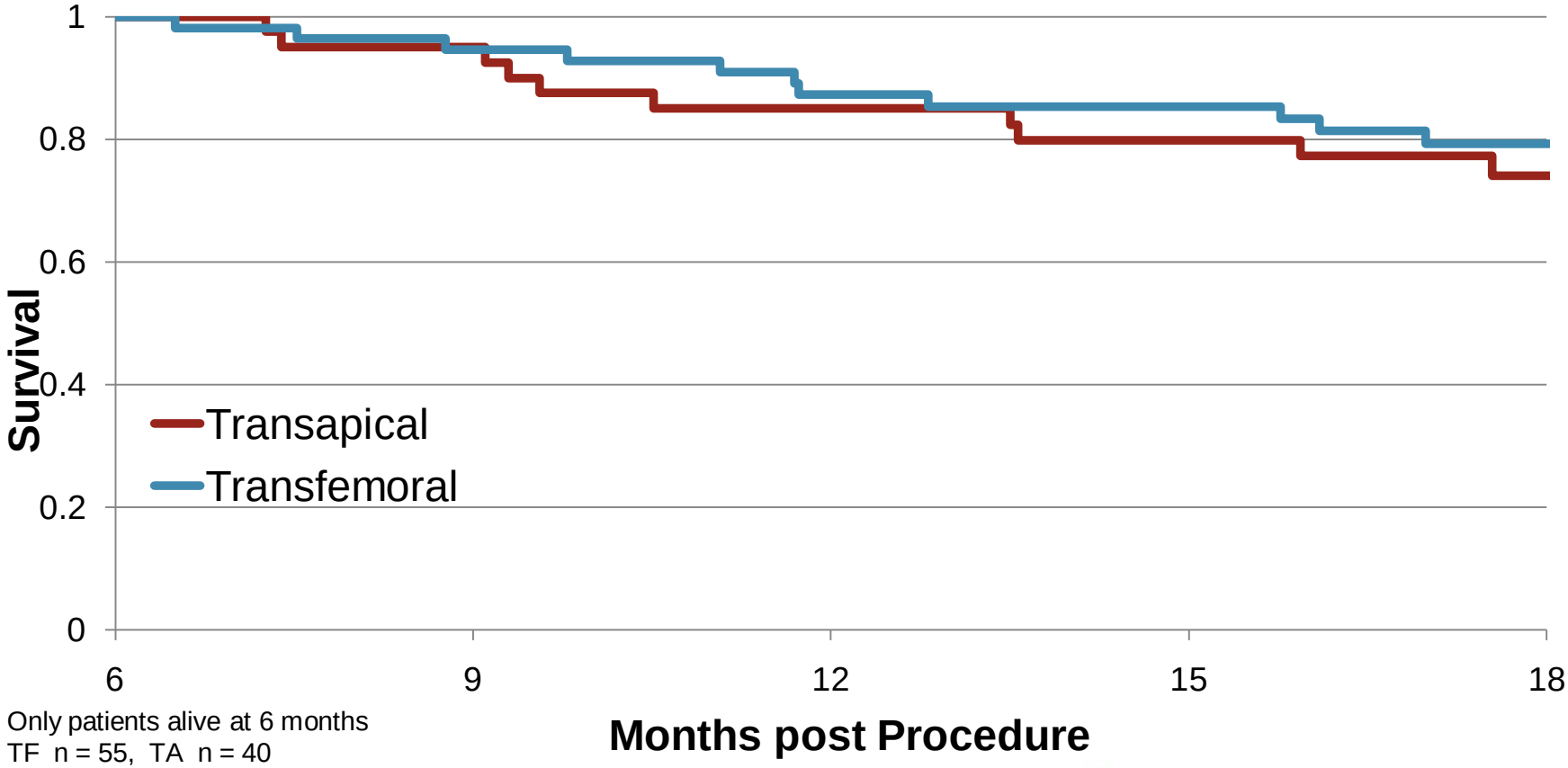
Transapical Survival to 18 Months



Late Deaths (>30 days)
(n = 26)
18 Month Survival = 43±6 %

Data Extract 7 Aug 09

KM Survival Estimate Between 6 and 18 months



Only patients alive at 6 months
TF n = 55, TA n = 40

Data Extract 7 Aug 09

Conclusions

- The PARTNER EU Trial is the first TAVI trial where implant approach (TF or TA) was determined jointly by interventional cardiologists and cardiac surgeons.
- Comparison of survival between TF and TA is problematic due to variability in baseline co morbidity.
- The Edwards SAPIEN™ THV valve shows excellent hemodynamic performance (AR 0 or 1 in the majority of patients), which translates into a marked improvement in functional status and physical and mental wellbeing.
- The Kaplan-Meier survival estimates between 6 to 18 months after implantation are very favorable with no signs of valve deterioration.

Data Extract 7 Aug 09