SURTAVI: Transaortic Valve Replacement Compared to Surgical Aortic Valve Replacement in Medium-Risk Patients

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On behalf of SURTAVI Investigators

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Thursday, April 30, 7:50-7:58 AM

Room 104, Level 1

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EU		USA	
CE mark access to multiple TAVR systems		**FDA approval IDE for intermediate risk**	
Boston Scientific	**Lotus**	**Edwards**	**SAPIEN-XT**
Direct Flow	**DFM**	**Medtronic**	**CoreValve Evolut**
Edwards	**SAPIEN-XT, -THV, -3**		
Jena Valve	**Jena Valve TAVI-TA/Tao**		
Medtronic	**CoreValve, Evolut, Evolut R, Engager-TA**		
ST. Jude	**Portico-TF**		
SYMETIS	**ACURATE neo+TF, TA**		
Health authority requests that the manufacturer pays for the investigated device. (e.g. Italy not included in SURTAVI)		In the context of IDE Reimbursement at the pro rata of a similar treatment. (e.g. surgical treatment)	
26 competent authorities 70 notifying Bodies (BfArM refused to follow the adjustment of the FDA)		FDA has agreed to adjust the inclusion criteria from 4-10 STS PROM to heart team judgement	

Valve specific European registry reports

Medtronic CoreValve

Authors	Published year	Patients number	EuroSCORE	STS PROM
Piazza N et al.	2008	646	23.1±13.8	-
Pertronio AS et al.	2010	514	20.1(12.8-30.5)	-
Buellesfeld L et al.	2011	126	23.43±13.80	-
Tamburino C et al.	2011	599	23.0±13.7	-
Usia GP et al.	2012	181	24.0±13.5	11.4±9.9
Linke A et al.	2014	1015	19.4±12.3	-

Edwards SAPIEN

Authors	Published year	Patients number	EuroSCORE	STS PROM
Walther T et al.	2009	168	27±12.7	-
Thomas M et al.	2010	1038	TF 25.8±14.4 TA 29.1±16.2	-
Lefevre T et al.	2011	130	TF 33.8±14.4 TA 25.7±11.5	TF 11.8±6.8 TA 11.3±6.1
Wendler O et al.	2012	2307	TF 23.9±14.2 TA 27.6±16.1	-
Wendler O et al.	2012	2706	TF 19.9±12.0 TA 21.8±13.8	TF 8.4±7.0 TA 8.7±7.2

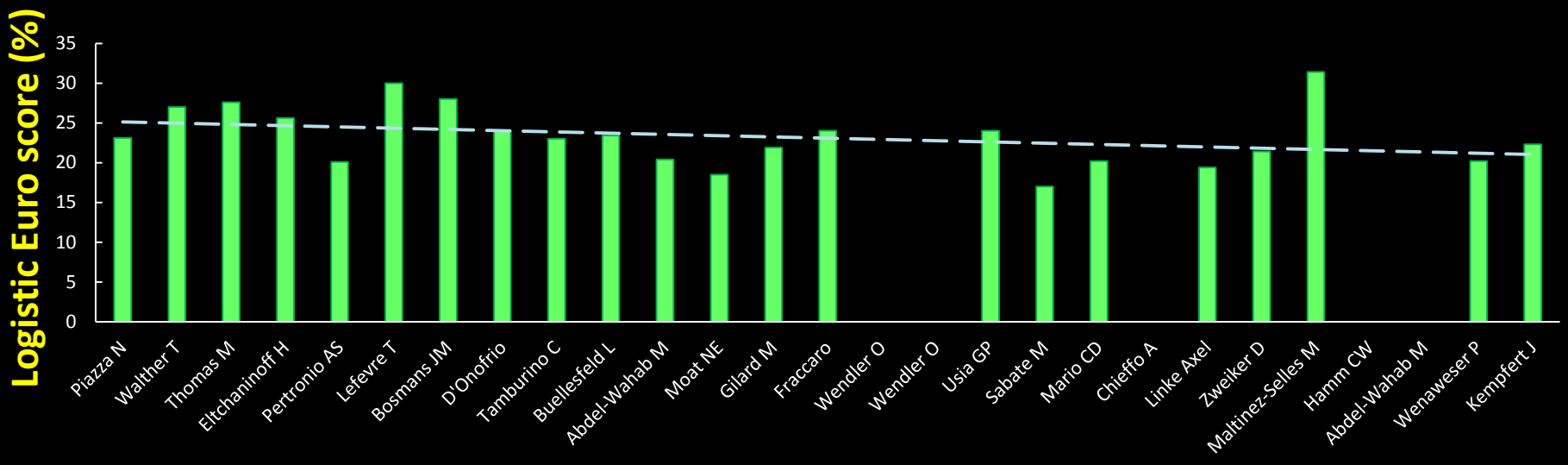
National and international registry reports

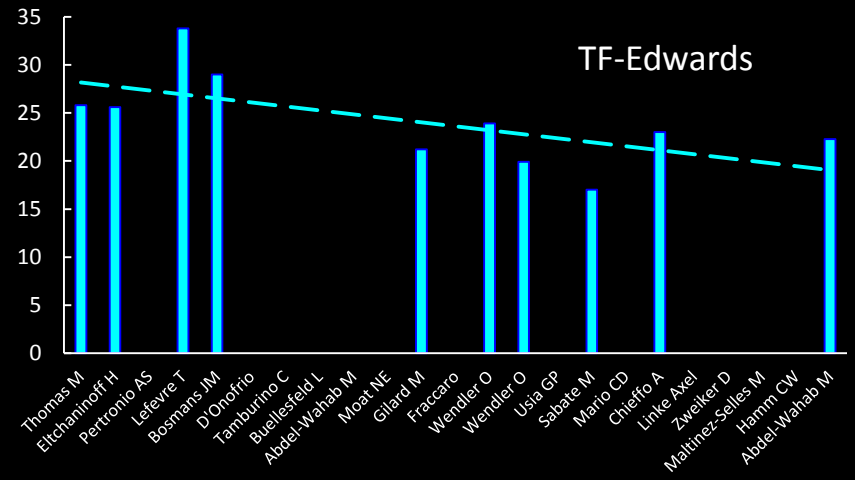
Mixed Registry

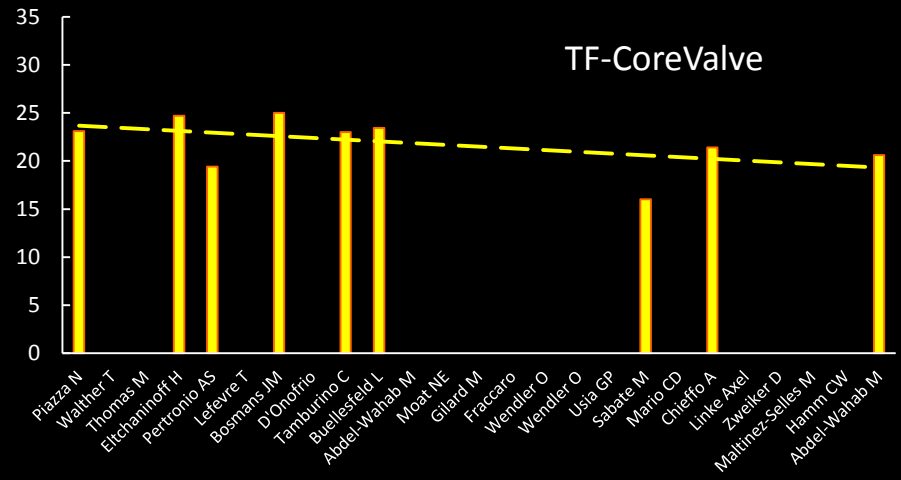
Authors	Published year	Patients number	EuroSCORE	STS PROM
Eltchaninoff H et al.	2010	244	25.6±11.4	18.9±12.8
Bosmans JM et al.	2011	328	28±16	-
D'Onofrio et al.	2011	504	24±16	11±4
Moat NE et al.	2011	870	18.5(11.7)	-
Abdel-Wahab M et al.	2011	697	20.4±13.1	-
Fraccaro et al.	2012	384	24.0±15.6	9.8±8.8
Gilard M et al.	2012	3195	21.9±14.3	14.4±11.9
Chieffo A et al.	2013		SA 23.0±13.8 21.4±12.6	SAP 8.9±6.5 Core 8.1±6.2
Mario CD et al.			.2±13	-
Sabate M et al.	2013	1416	17±11	-
Abdel-Wahab M et al.	2014	394	SAP 22.27±13.39 Core 20.61±13.93	-
Zweiker D et al.	2014	959	21.4±13.2	15.4±11.0
Maltinez-Selles M et al.	2014	261	31.4±17.9	-
Hamm CW et al.	2014	3876	TV 25.9 TA 24.5	-
Wenaweser P et al.	2014	697	20.2±12.7	8.2±7.1
D'Ascenzo F et al.	2015	674	sPAP≦40mmHg 17.2±13.1 sPAP > 40mmHg 18.5±18.9	sPAP≦40mmHg 9.4±8.4 sPAP > 40mmHg 8.7±6.7

19863 pts

A trend in clinical European registries







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New Inclusion Criteria Following agreement with the FDA

Version 6: (first patient was enrolled with version 3 on 19th Jun 2012)

1. Subject must have an STS mortality risk score ≥4% and ≤10

Medtronic SURTAVI Trial. Version 6.0

Version 8: (*now applied in 81 centers out of 82 centers; Jan 26th 2015*)

1. Subject must have *co-morbidities such that Heart Team agrees predicted risk of operative mortality is ≥3% at 30 days*

Medtronic SURTAVI Trial. Version 8.0

Activation and Enrollment Overview

- 78 sites activated
  - US: 59
  - Europe: 14
  - Canada: 5
- 1173 subjects (included before randomization)
  - US: 957
  - Europe: 174
  - Canada: 42

Data derived from "Executive committee meeting" on 8th Apr 2015

Heart Team Review and Decision (continued)

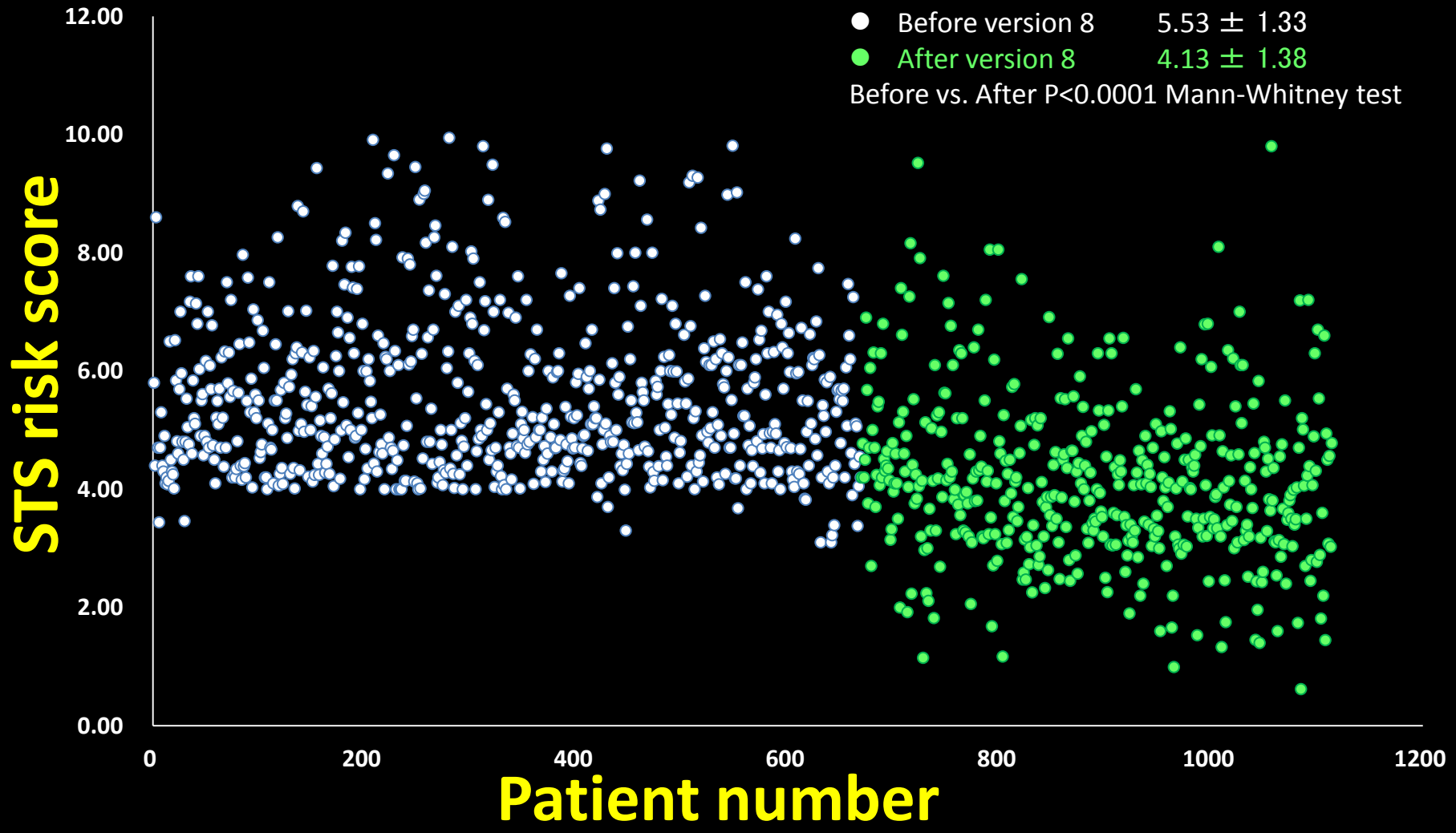
Version 8:

- **Any additional risk factors not accounted for in the STS risk calculator that may increase the level of surgical risk:**
  - **Heart Team should consider the following potential incremental risks:**
    - ***Age ≥ 75***
    - **BNP ≥ 550pg/mL or NT proBNP ≥ 3200pg/mL**
    - ***Prior Stroke/TIA***
    - **FEV1 750-1000cc**
    - **Home / Supplemental oxygen**
    - **Nocturnal Bi-level Positive Airway Pressure**
    - **5-Meter Gait Speed ≥ 6 seconds**
    - **Severe Diastolic Dysfunction (Grade III or IV)**
    - **Liver Disease (Child A or B)**
    - **Pulmonary Hypertension (systolic pressure 60-80mmHg)**
    - ***Frailty (e.g. BMI <21, Albumin <3.3, etc.)***
    - ***Other risks, as deemed applicable***
  - **Confirm the incremental risk, *as determined by the Heart Team, does not result in a risk definition higher than* intermediate risk**

Medtronic SURTAVI Trial. Version 8.0

Yellow indicates it was already in STS

SURTAVI-Baseline characteristics
STS risk score



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Data derived from "Intelemage inteleGRID" on 7th April 2015

SURTAVI-Baseline characteristics Potential incremental risks

Variable	Before version 8	After version 8
Age ≥ 75	86.4%	77.3% ↓
BNP>550 pg/ml	13.8%	13.9% →
NT proBNP ≥ 3200 pg/mL	13.8%	14.1% →
Severe diastolic dysfunction	1.6%	1.8% →
Pulmonary Hypertension (systolic pressure ≥ 60 mmHg)	3.0%	2.2% ↓
Prior Stroke/TIA	15.5%	10.8% ↓
Home/Supplemental oxygen	2.5%	2.0% ↓
Nocturnal Bi-PAP	4.5%	6.8% ↑
FEV1 750-1000 cc	2.4%	1.8% ↓
5-meter gait speed ≥ 6 seconds	26.0%	48.9% ↑
Liver disease (Child A, or B)	0.4%	0.4% →
Severe Aortic Calcification	8.1%	11.5% ↑

Data derived from "Intelemage inteleGRID" on 7th April 2015

SURTAVI Heart-Team

Initial screening: 1616 patients approached

1492 Patients in review process

Patients in screening process 124

Further assessment and additional tests

1236 Patients suitable

Unsuitable or unwilling 256

Local Heart-Team review

1151 Eligible for enrolment

Ineligible for enrolment 85

Central (Virtual) Heart- Team review

1124 APPROVED

DENIED - Not enrolled 27

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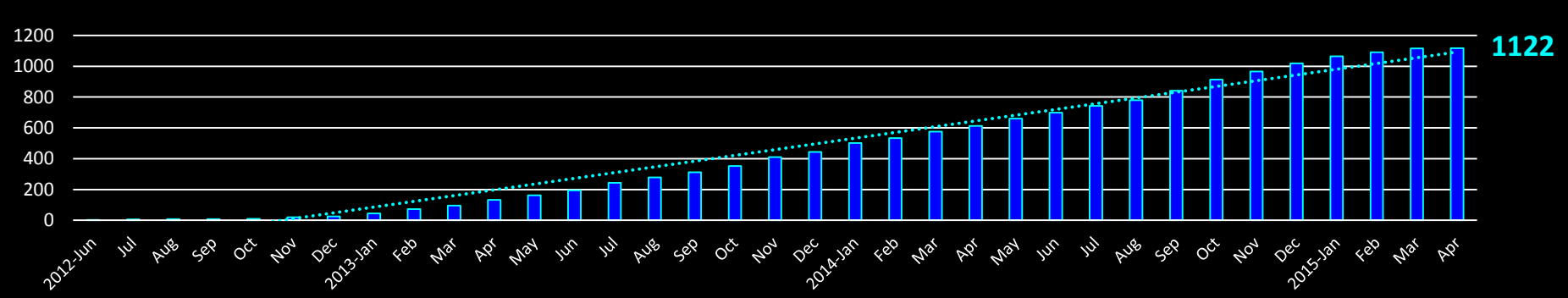
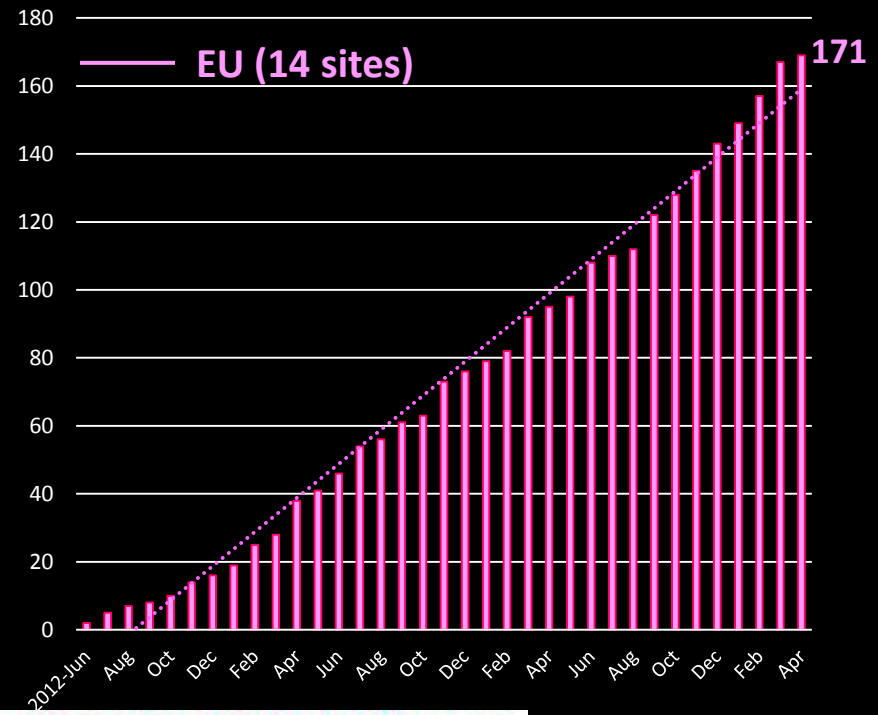
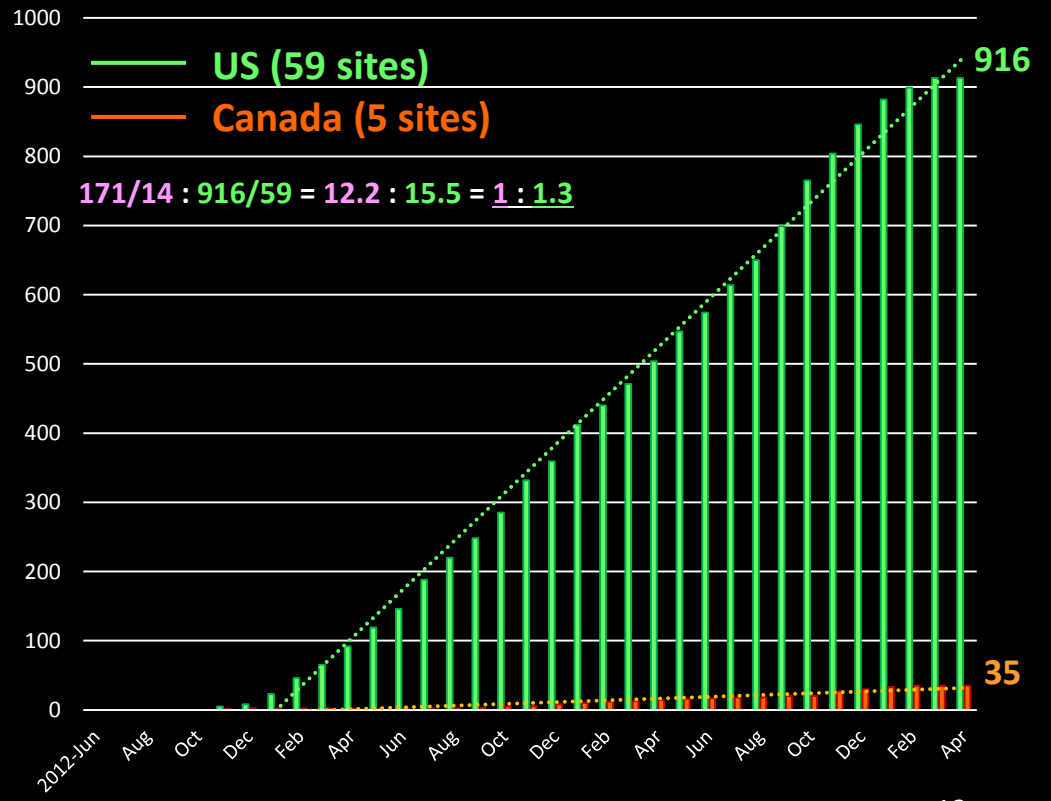
Enrollment overview







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Data derived from "Intelemage inteleGRID" on 7th April 2015

STS PROM estimate
CoreValve US Pivotal Trial

	As – Treated Population	
STS PROM estimate	TAVR Group (N = 390)	Surgical Group (N = 357)
Mean estimate - %	7.3 ± 3.0	7.5 ± 3.4
< 4% - no. (%)	33 (8.5)	40 (11.2)
4 ~ 10% - no. (%)	304 (77.9)	251 (70.3)
> 10% - no. (%)	53 (13.6)	66 (18.5)

Adams DH et al. N Engl J Med 2014;370:1790-1798

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Based on STS: > 80% of patients would have been SURTAVI Eligible!

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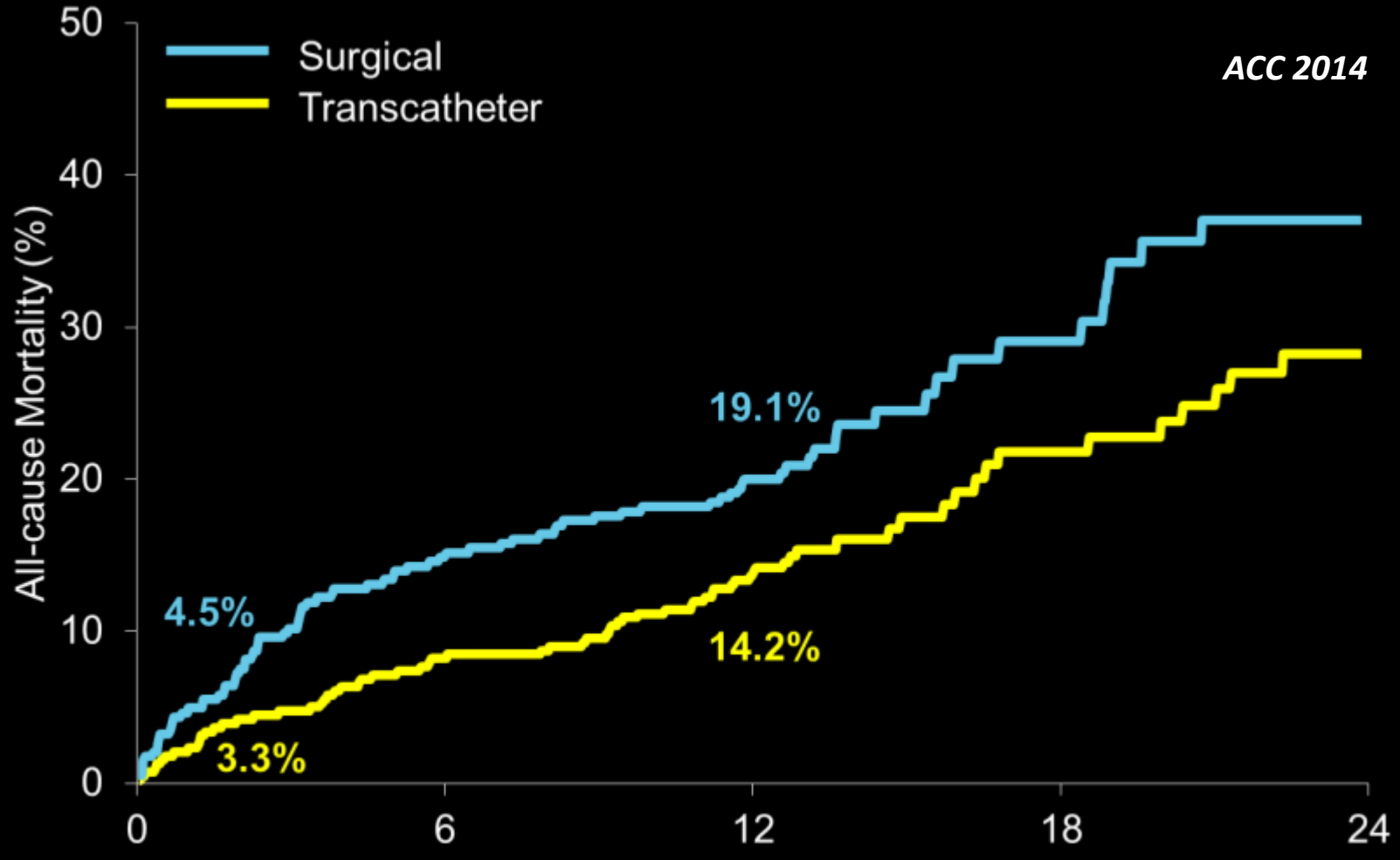
2-Year All-cause Mortality: CoreValve US Pivotal Trial



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Summary

- After introduction of version-8, lower objective scores (STS etc.)
- Quantification of the "incremental risk" may minimise subjectivity
- Increases of incremental risks were expected after introduction of version-8, however cardiovascular-related incremental risks (BNP, pulmonary hypertension, or prior Stroke/TIA) did decrease concertedly with STS score.
- Considering the overlap in STS and the outcome at 1year of the patients, recruited in the CoreValve US Pivotal Trial (n = 795 pts) with the patients recruited in the SURTAVI (n = 1122 pts: 650 pts for before version 8; 472 pts for after version 8, 7th Apr 2015), an interim analysis would be advisable.