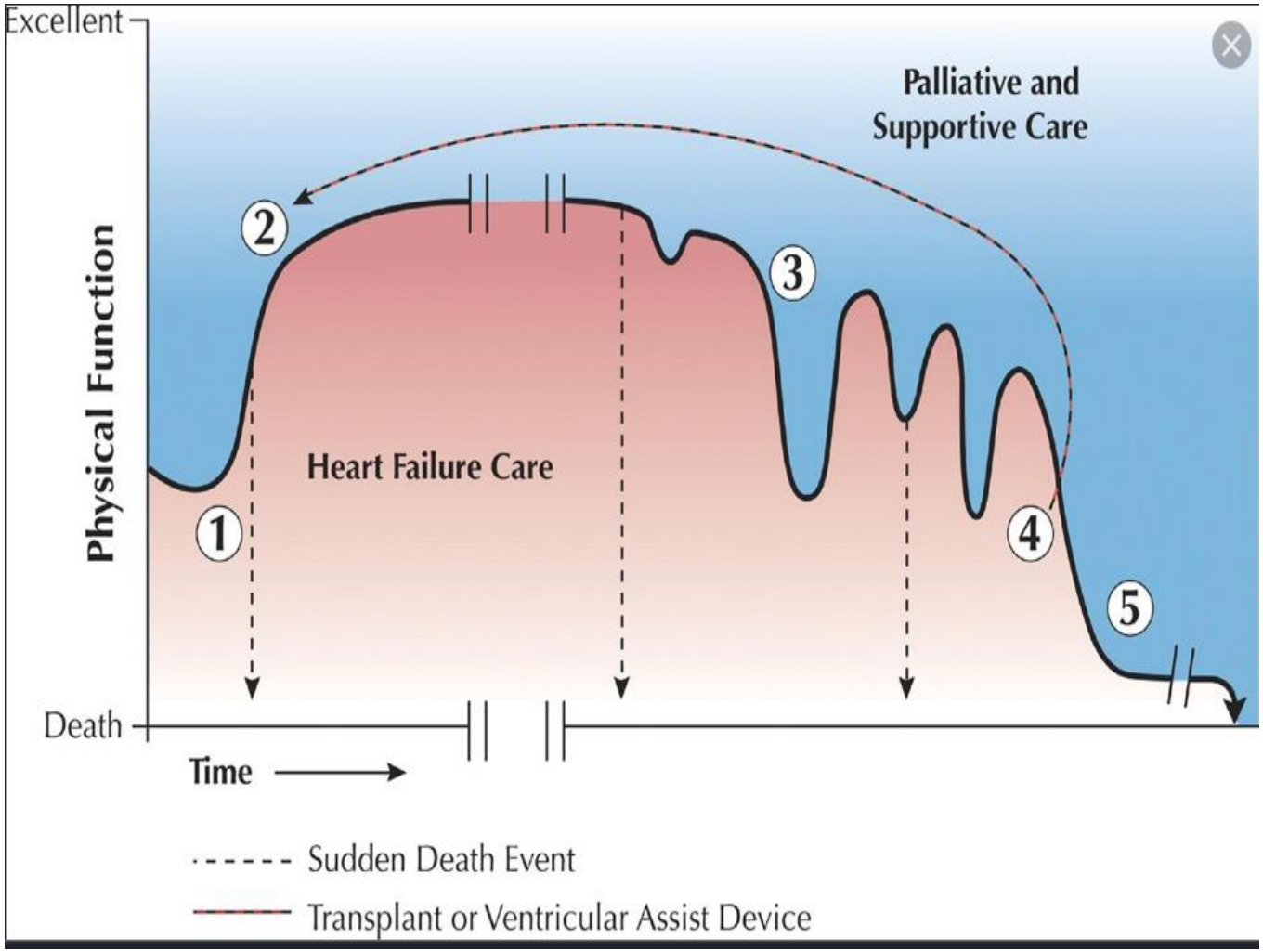
LVAD BTT och DT

Bridge To Transplant och Destination Therapy

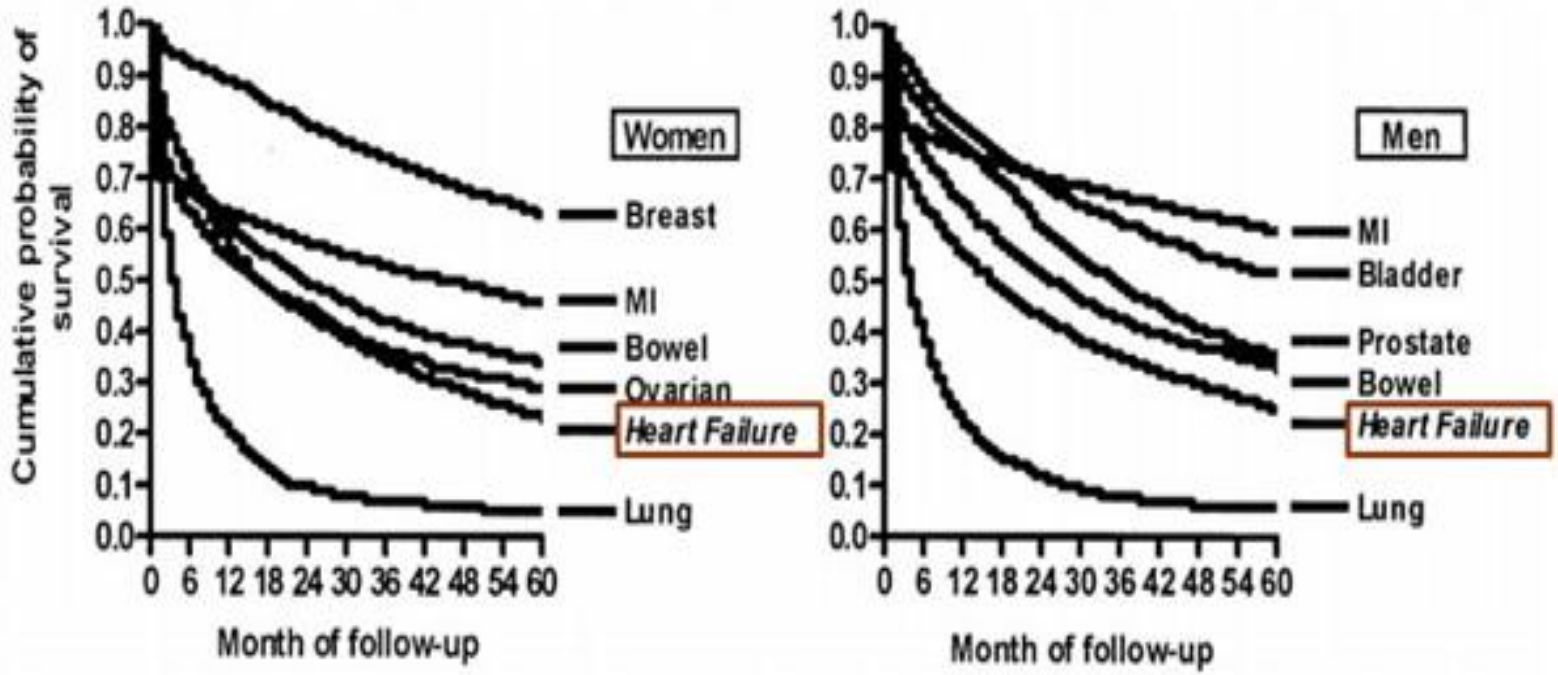
Region Östergötland

Sjukdomsförlopp hjärtsvikt



Region Östergötland

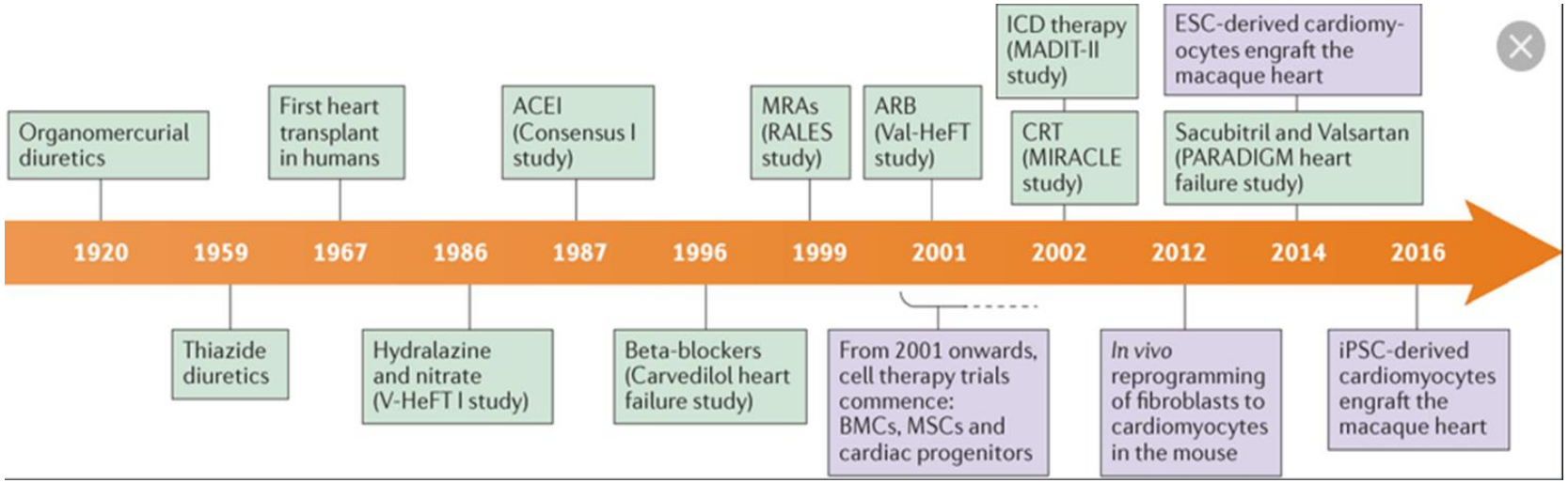
Mortalitet



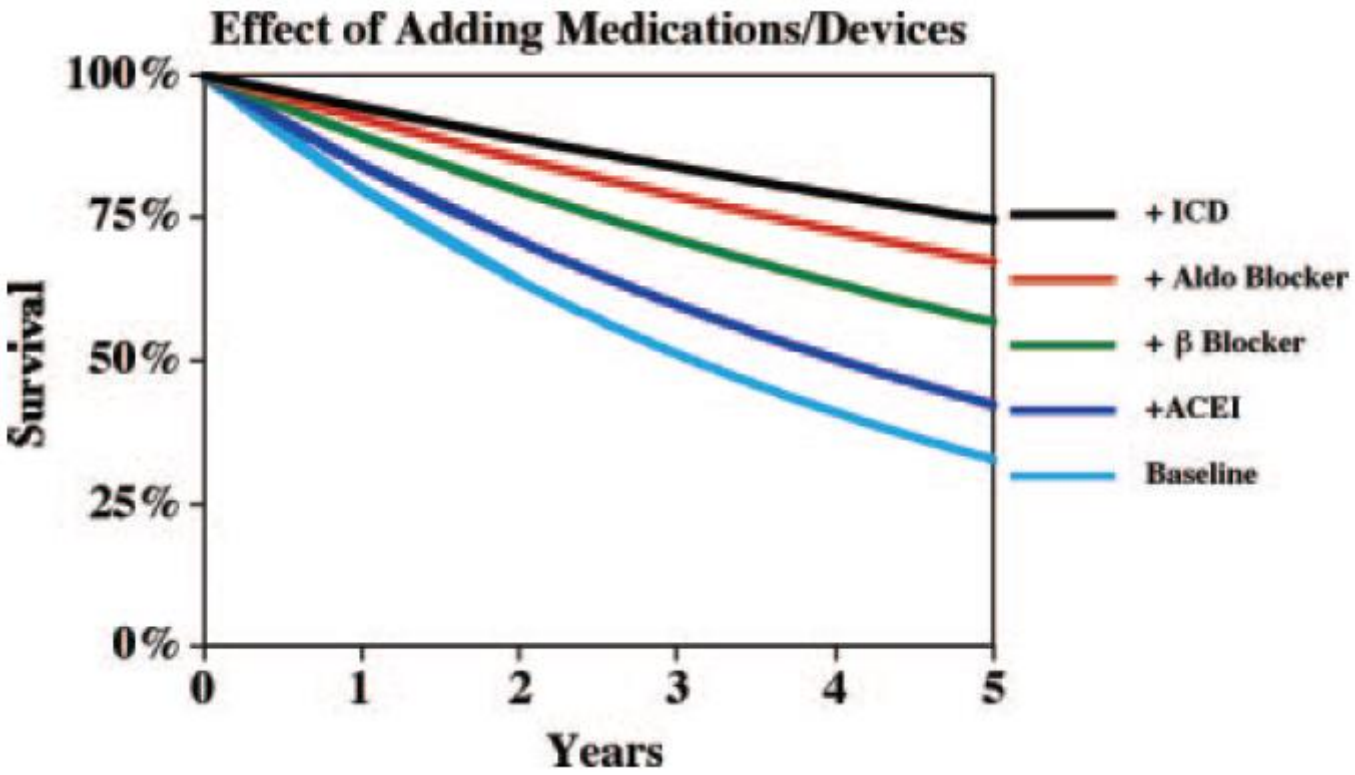
Stewart S,et al. More malignant than cancer? Five-year survival following a first admission for heart failure in Scotland. European Jouranl of Heart Failure 3 (2001) 315-322

Region Östergötland

Utveckling av behandlingen

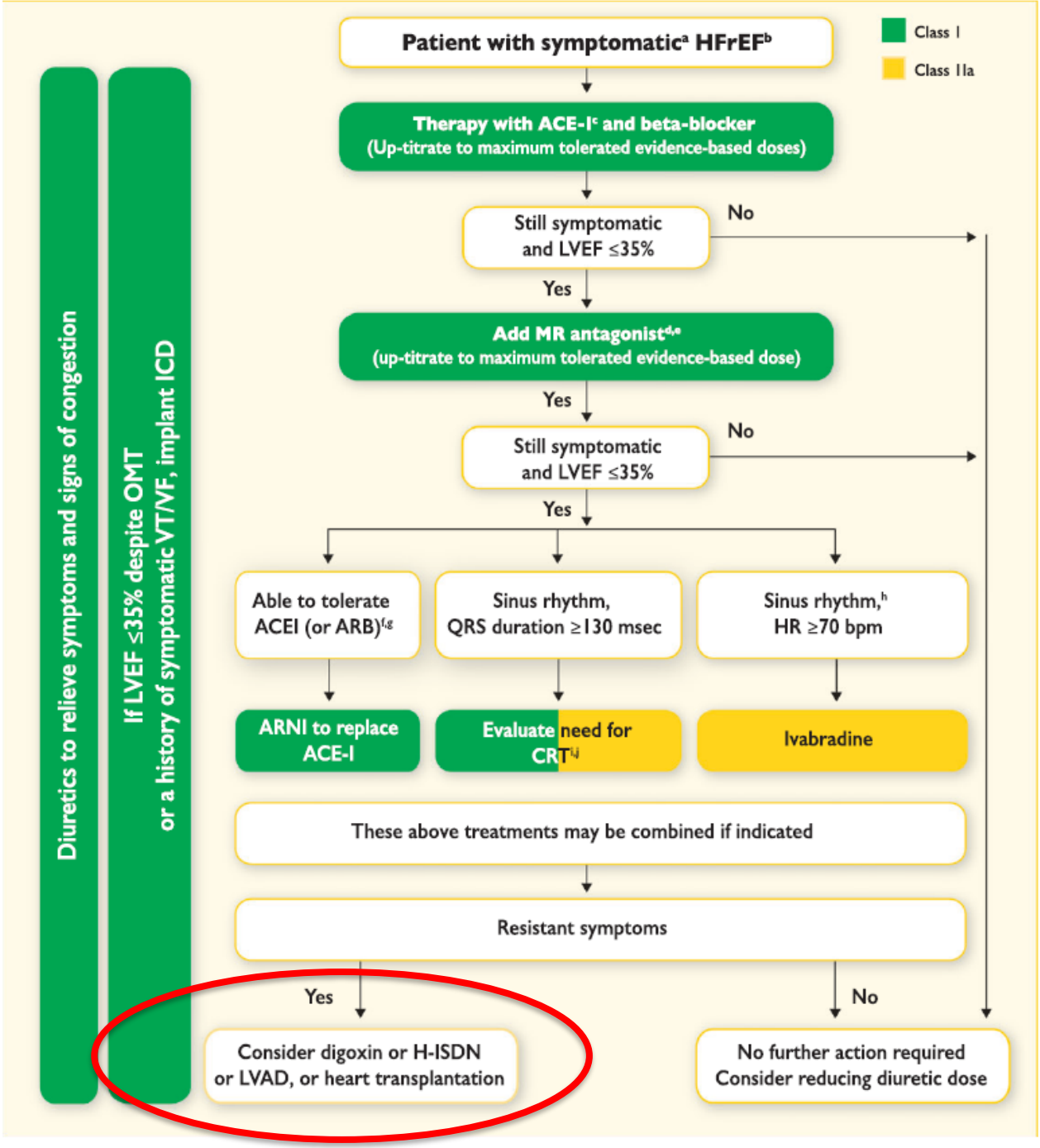


Överlevnad vid kronisk hjärtsvikt



Seattle Heart Failure Model, Circulation 2009

Region Östergötland



ESC guidelines

Region Östergötland

Patient selektion
Peak VO2 (ml/kg x min)

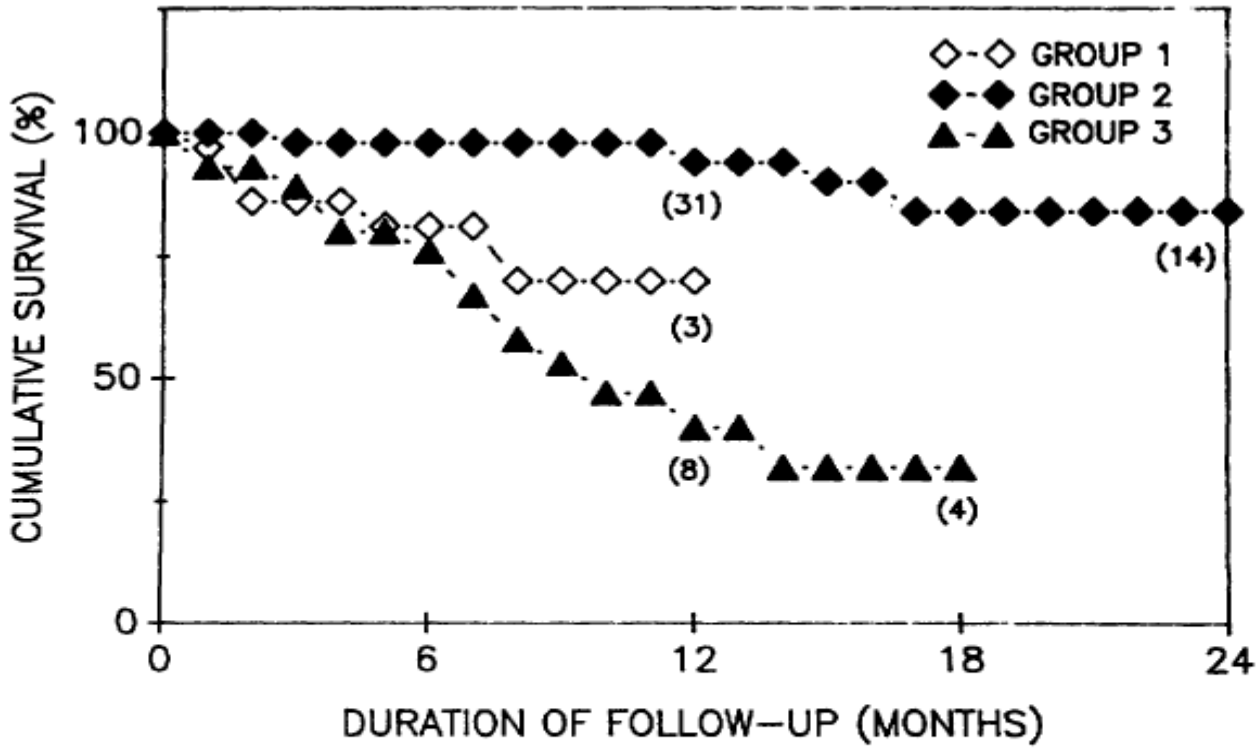
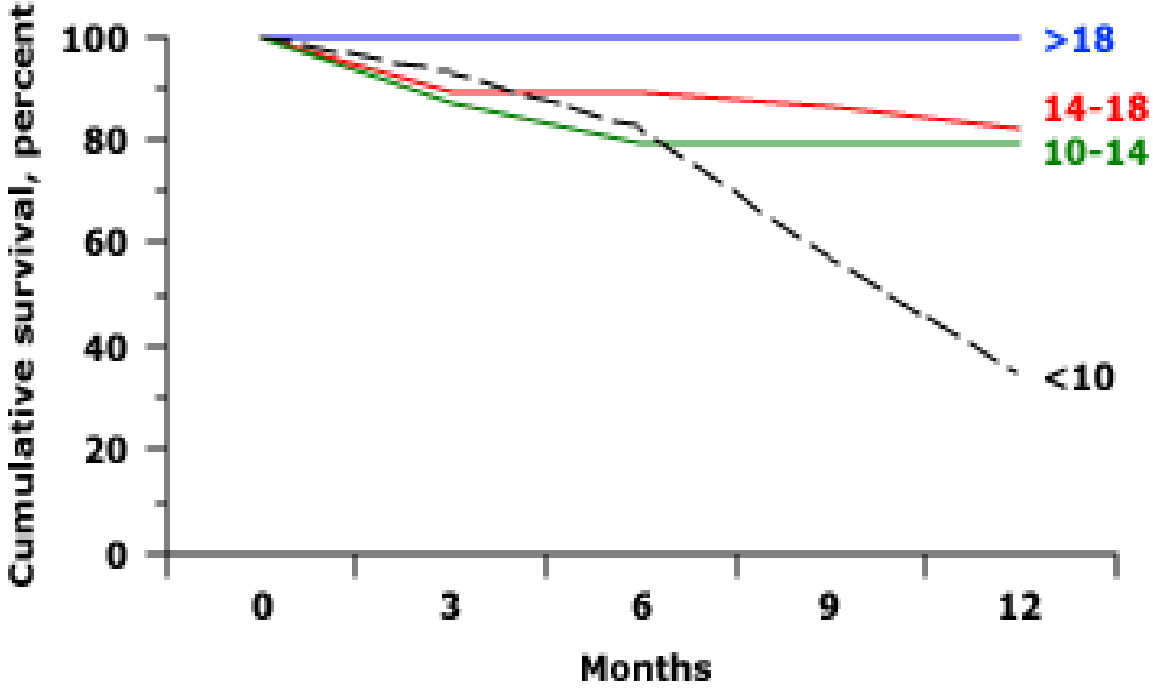


FIGURE 2. *Survival curves comparing groups 1, 2, and 3. Survival curves for groups accepted (1) and rejected for transplant (3) are similar but are significantly reduced compared with group 2* ($p<0.001$).

Mancini et al
Circulation 1991

Region Östergötland

Patient selektion
peak VO2 (ml/kg x min)

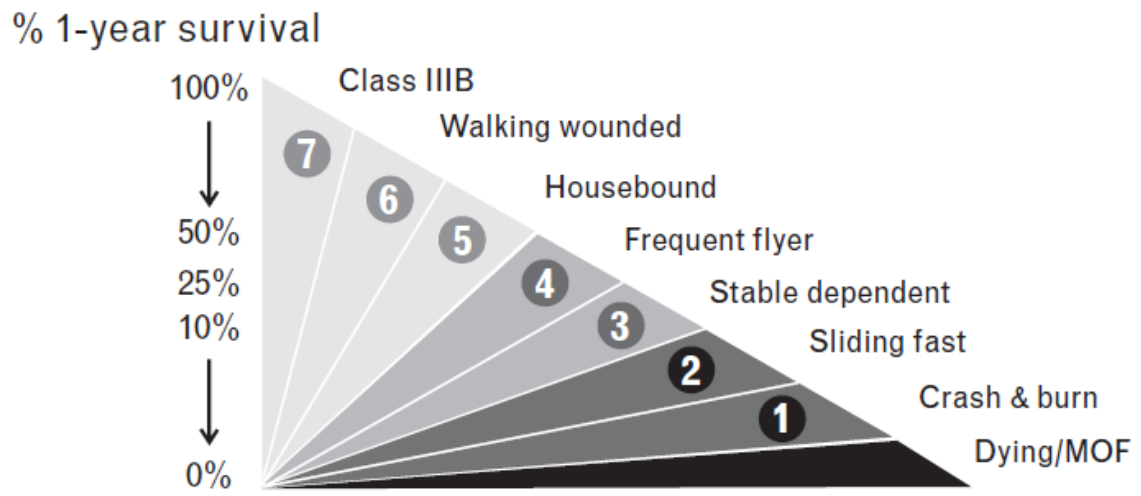


Mancini et al Circulation 1991

Region Östergötland

INTERMACS profil

Interagency Registry for Mechanically Assisted Circulatory Support



Intermacs level	Survival	VAD benefit
5–7	Months to years	Not established
3–4	Weeks to months	Yes
1–2	Hours to weeks	Yes
MOF	Hours to days	Bridge to decision in selected cases

Leitz, Miller. Curr opin cardiol 2009

Region Östergötland

Bridge To Transplantation

Table 3 One-Year Outcomes of the Waiting List in UNOS Status 1 and Status 2 Candidates for Heart Transplantation Across Eras: I = 1990 to 1994, II = 1995 to 1999, and III = 2000 to 2005: U.S. Scientific Registry for Transplant Recipients (n = 48,982)

	UNOS Status 1			UNOS Status 2		
	Era I (n = 4,541) (%)	Era II (n = 6,087) (%)	Era III (n = 7,376) (%)	Era I (n = 11,904) (%)	Era II (n = 10,843) (%)	Era III (n = 8,231) (%)
Transplant	60	64.9	67.6	45.8	39.9	45.0
Death	25.6	20.4	15.4	12.5	11.2	7.5
Removed: improvement	<0.1	2.0	1.7	2.0	1.1	1.3
Removed: worsening	3.2	2.0	3.3	0.1	1.8	1.7
Ongoing >1 yr	4.5	7.7	7.8	33.1	43.0	38.7
Ongoing <1 yr	6.6	2.8	4.1	6.4	3.0	5.7

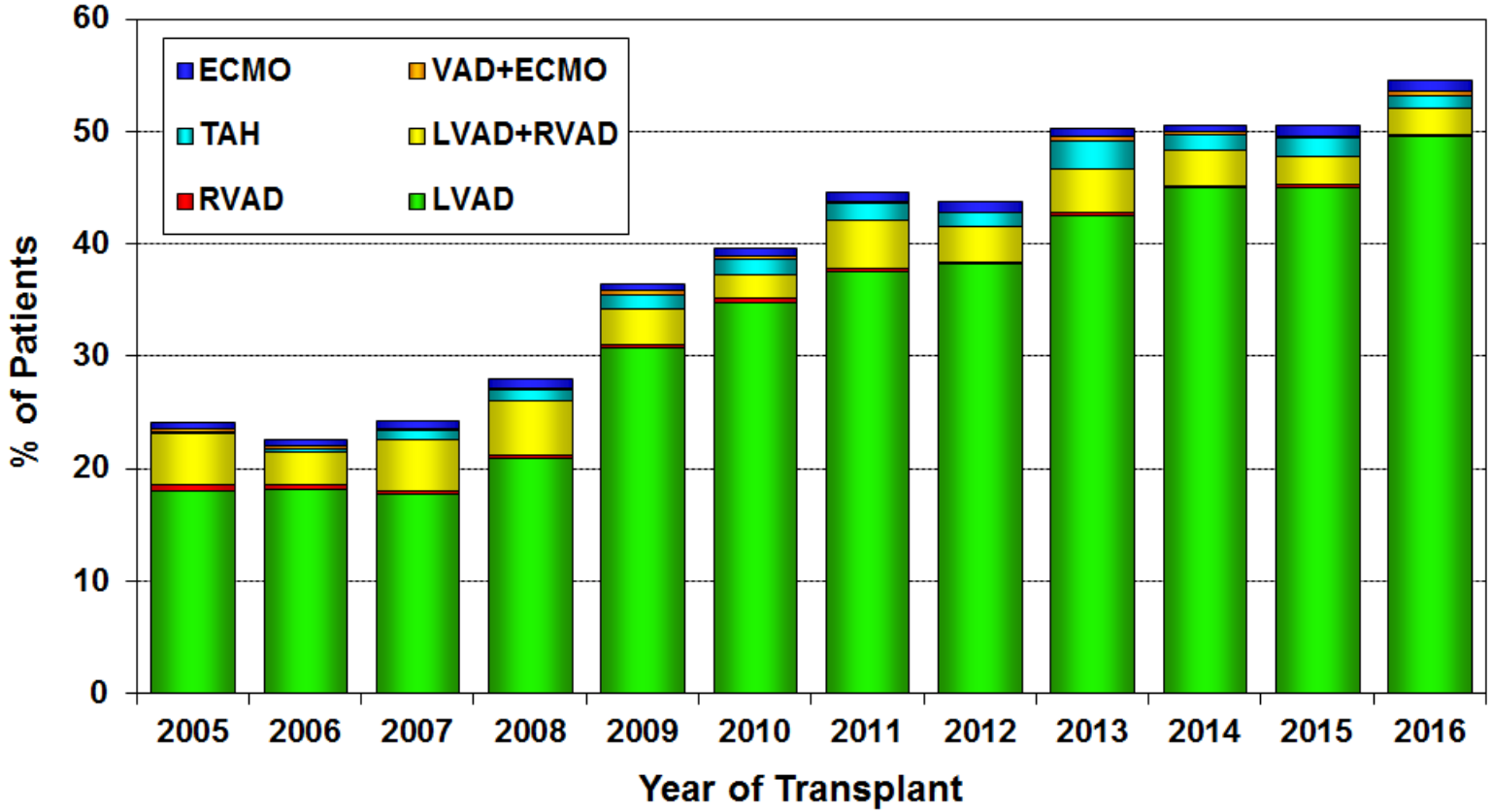
UNOS = United Network of Organ Sharing.

Lietz, Miller. JACC 2007

Region Östergötland

Adult Heart Transplants

% of Patients Bridged with Mechanical Circulatory Support* by Year and Device Type

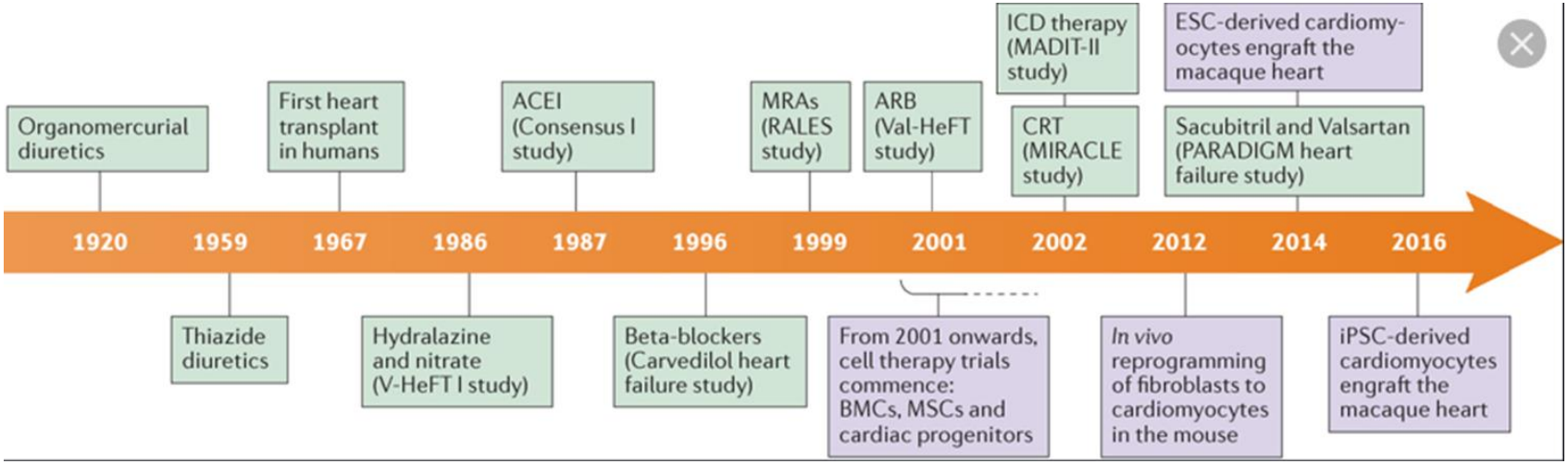


Region Östergötland

Bridge to transplant

- Kortvarigt, i väntan på hjärttransplantation
- Normalisering av hemodynamik
- Förbättrar end-organ dysfunktion
- Förbättrar ansträngningstolerans
- Poliklinisk vård
- Acceptabel livskvalité
- Relativ få ’major adverse events’

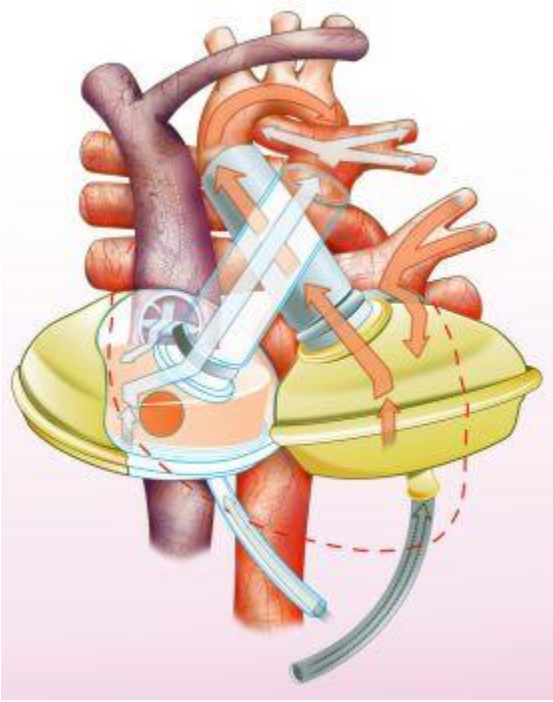
Utveckling MCS



Första lyckad MCS implantation i 1966

Region Östergötland

Historia



- 1984 Total artificial heart (Jarvik 7-100)
- Pneumatisk
- 1991 moratorium

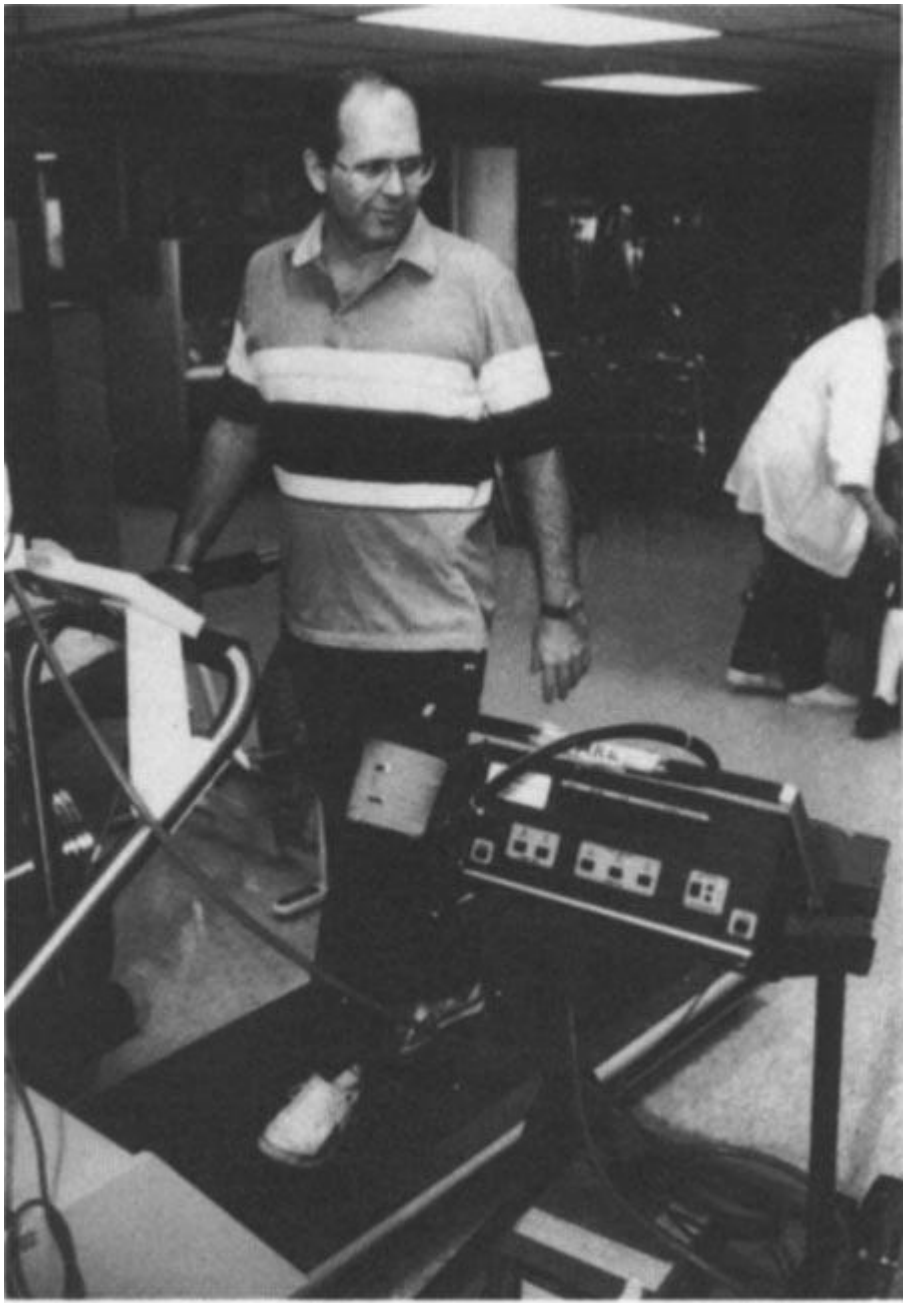
- 1994 pneumatisk LVAD
- Elektrisk
- Möjligheten att utveckla bärbar
- Patient selektion

Frazier, Rose et al 1992

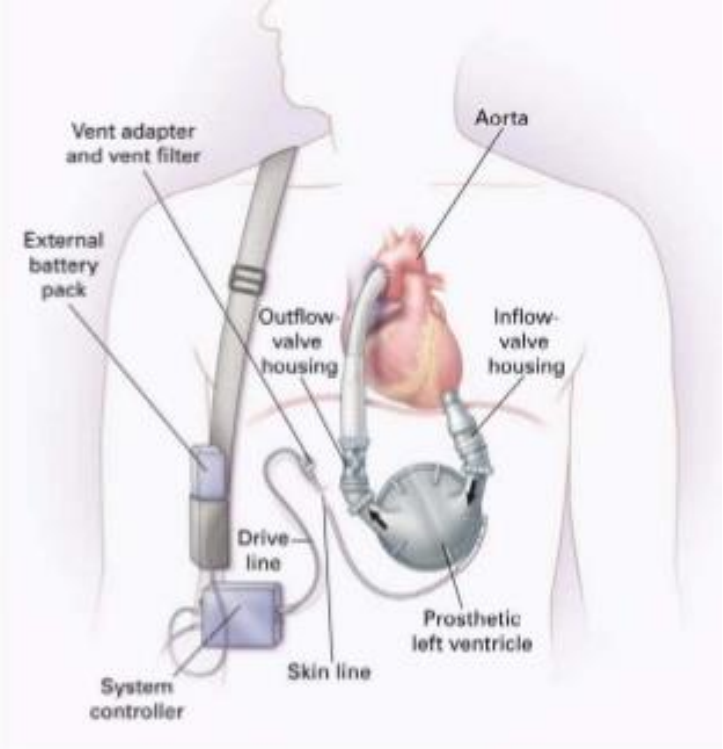
	LVAD (26)	BTT LVAD (8)	Kontroll (6)
Tid med LVAD	1-233	1-84	
Dör innan HTx	6	5	3
Dör <60d efter HTx	2	2	2
Överlever > 60 d efter HTx	15	1	1 (77d)

Utveckling LVAD

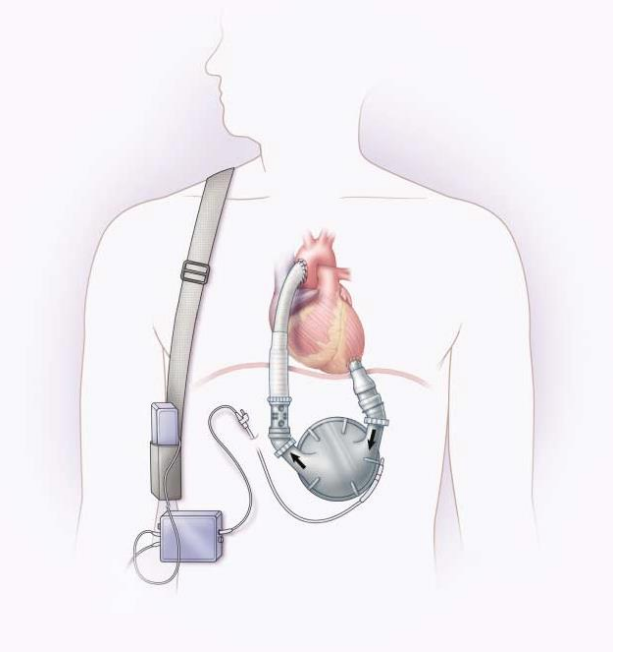
1992



1998



REMATCH



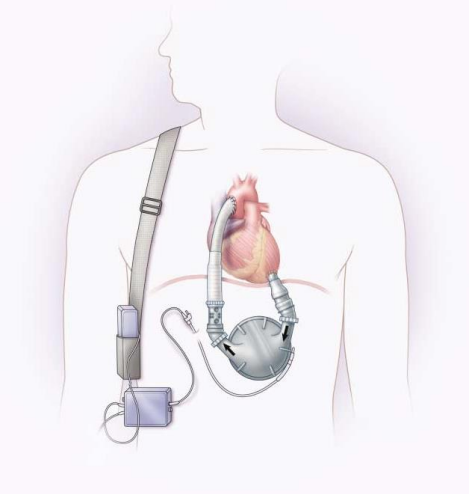
- 129 pat NYHA IV
- LVEF < 25%
- VO2 < 12-14 ml/min x kg
- 68 pat LVAD, 61 pat OMT
- HM I pulsativ LVAD

	OMT	LVAD
Concomitant medications (%)		
Digoxin	85	87
Loop diuretics	97	96
Spironolactone	39	34
ACE inhibitors	51	62
A-II antagonists	18	10
Amiodarone	46	45
Beta-blockers	20	24
Intravenous inotropic agents	72	65

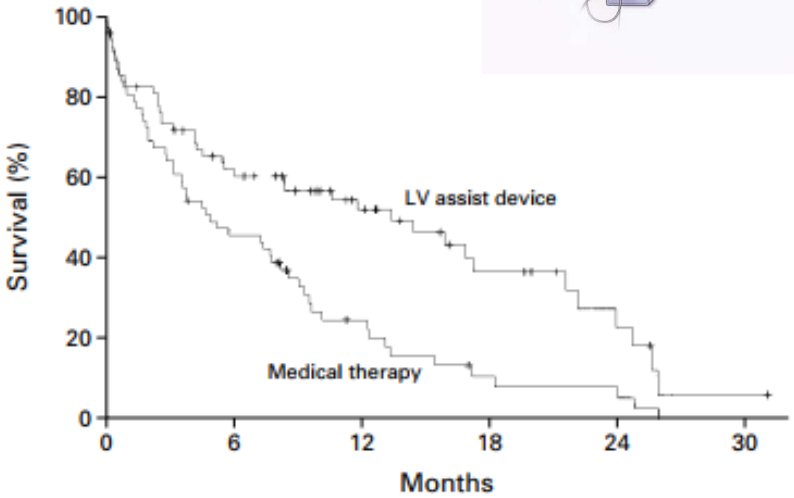
NEJM 2001

Region Östergötland

REMATCH
HM1 vs OMT



Cause of Death	Medical-Therapy Group	LVAD Group	Total
	no. of patients		
Left ventricular dysfunction	50	1	51
Sepsis	1	17	18
Failure of LVAD	0	7	7
Miscellaneous noncardiovascular causes	0	5	5
Cerebrovascular disease	0	4	4
Miscellaneous cardiovascular causes	1	2	3
Pulmonary embolism	0	2	2
Acute myocardial infarction	1	0	1
Cardiac procedure	1	0	1
Perioperative bleeding	0	1	1
Unknown	0	2	2
Total	54	41	95



No. at Risk						
LV assist device	68	38	22	11	5	1
Medical therapy	61	27	11	4	3	0

Figure 2. Kaplan–Meier Analysis of Survival in the Group That Received Left Ventricular (LV) Assist Devices and the Group That Received Optimal Medical Therapy.

Crosses depict censored patients. Enrollment in the trial was terminated after 92 patients had died; 95 deaths had occurred by the time of the final analysis.

Region Östergötland

Heartmate II

- HM I vs HM II
  (pulsativ vs kontinuerlig)
- LVEF < 25%
- VO2 < 12 ml/min x kg
- 200 pat (66 vs 134)

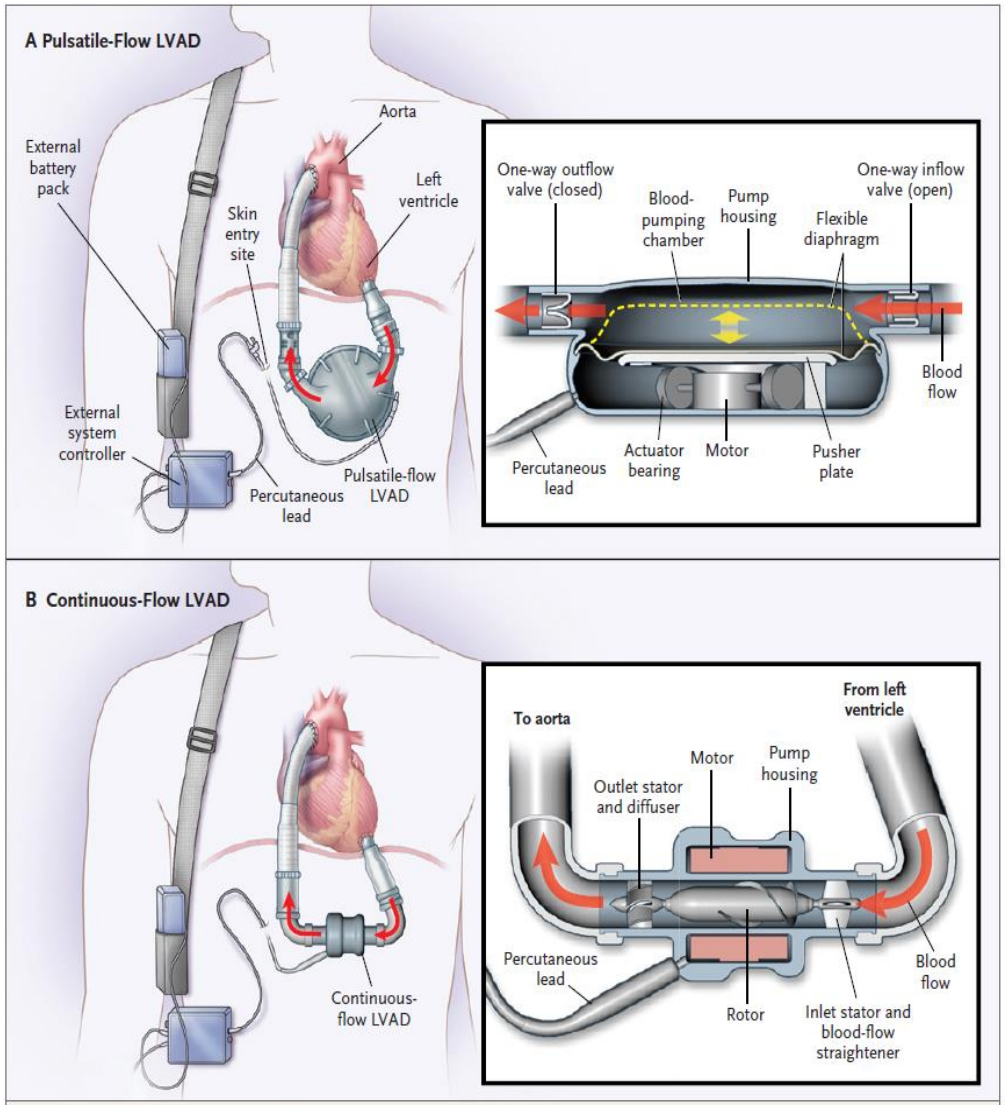


Figure 1. Pulsatile-Flow (Panel A) and Continuous-Flow (Panel B) Left Ventricular Assist Devices (LVADs).

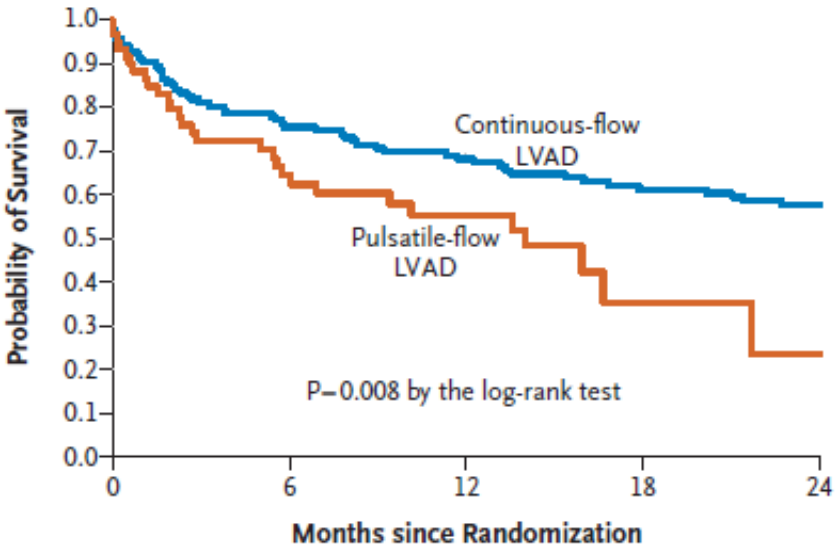
NEJM 2009

Region Östergötland

HM II vs HM I

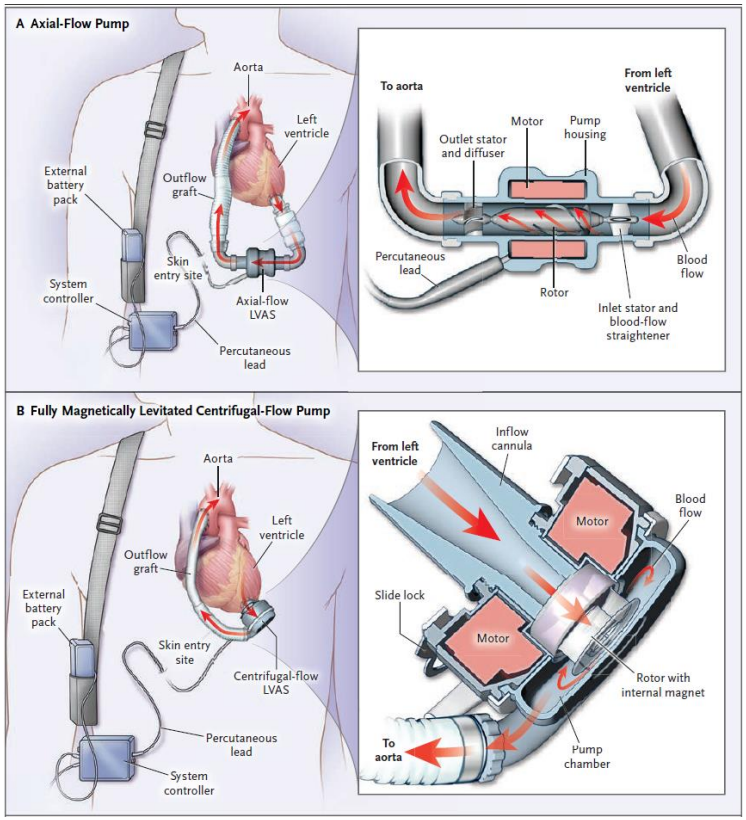
Concomitant medication or intervention — no. (%)			
Intravenous inotropic agent	103 (77)	55 (83)	0.36
Diuretic	123 (92)	57 (86)	0.32
ACE inhibitor	43 (32)	22 (33)	0.87
Angiotensin II–receptor antagonist	12 (9)	3 (5)	0.39
Beta-blocker	71 (53)	38 (58)	0.55
Biventricular pacemaker	85 (63)	39 (59)	0.64
ICD	111 (83)	52 (79)	0.56
IABP	30 (22)	15 (23)	1.00
Mechanical ventilation	9 (7)	6 (9)	0.57

End point	HM II (n=134)	HM I (n=66)
Överlevnad utan stroke och reoperation	62 (46%)	7 (11%)
Stroke	15 (11)	8 (12)
Reoperation	13 (10)	24 (36)
Avliden < 2 år	44 (33)	27 (41)
Total	72 (54)	59 (89)



No. at Risk					
Continuous-flow LVAD	133	95	82	69	62
Pulsatile-flow LVAD	59	32	19	5	2

Momentum 3
HM II vs HM 3



- 1:1 randomisering
- BTT eller DT

- Primära endpoint:
- Stroke frihet
- Ingen reoperation

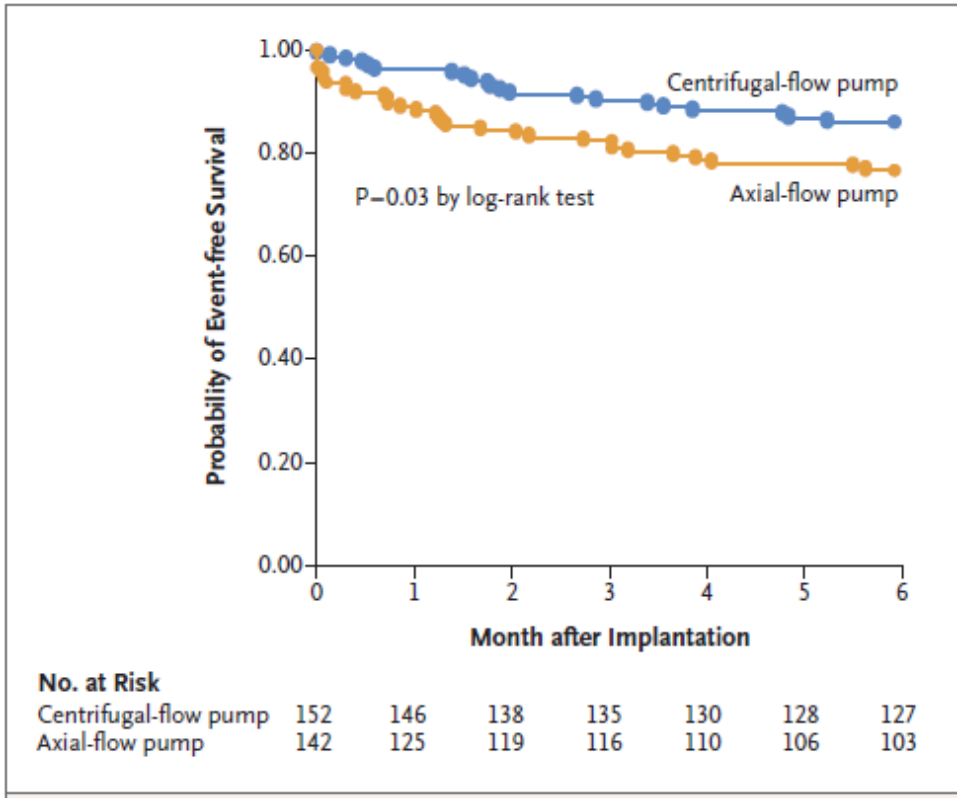
NEJM 2017

Region Östergötland

Momentum3

	HM3	vs	HMII
Concomitant medication or intervention — no. (%)			
Intravenous inotropic agents	132 (86.8)		121 (85.2)
Diuretic	134 (88.2)		136 (95.8)
Angiotensin-converting–enzyme inhibitor	37 (24.3)		38 (26.8)
Angiotensin II–receptor antagonist	10 (6.6)		18 (12.7)
Beta-blocker	91 (59.9)		79 (55.6)
Cardiac resynchronization therapy with or without defibrillator	59 (38.8)		51 (35.9)
Implantable cardioverter–defibrillator with or without cardiac resynchronization therapy	101 (66.4)		100 (70.4)
Intraaortic balloon pump	18 (11.8)		21 (14.8)
Intended goal of pump support — no. (%)			
Bridge to transplantation	41 (27.0)		37 (26.1)
Bridge to candidacy for transplantation	27 (17.8)		27 (19.0)
Destination therapy	84 (55.3)		78 (54.9)

Momentum3: 6 månader



- Ingen skillnad i blödning, stroke, sepsis, infektion, RV svikt, SVT och VT.
- Pumptrombos:

  HM II 14 pat (10%) vs

  HM 3 0 pat (0%)

Region Östergötland

Momentum3: 2 års data

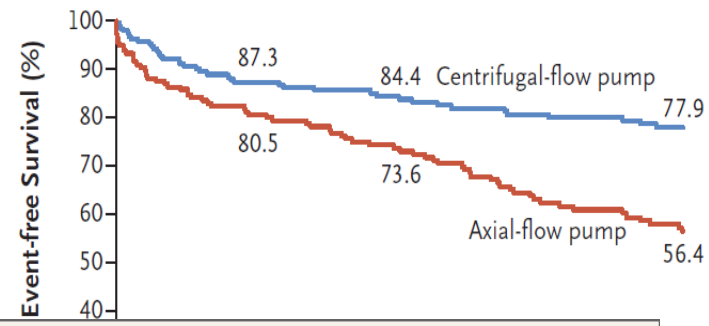


Table 3. Major Adverse Events in the Per-Protocol Population.*

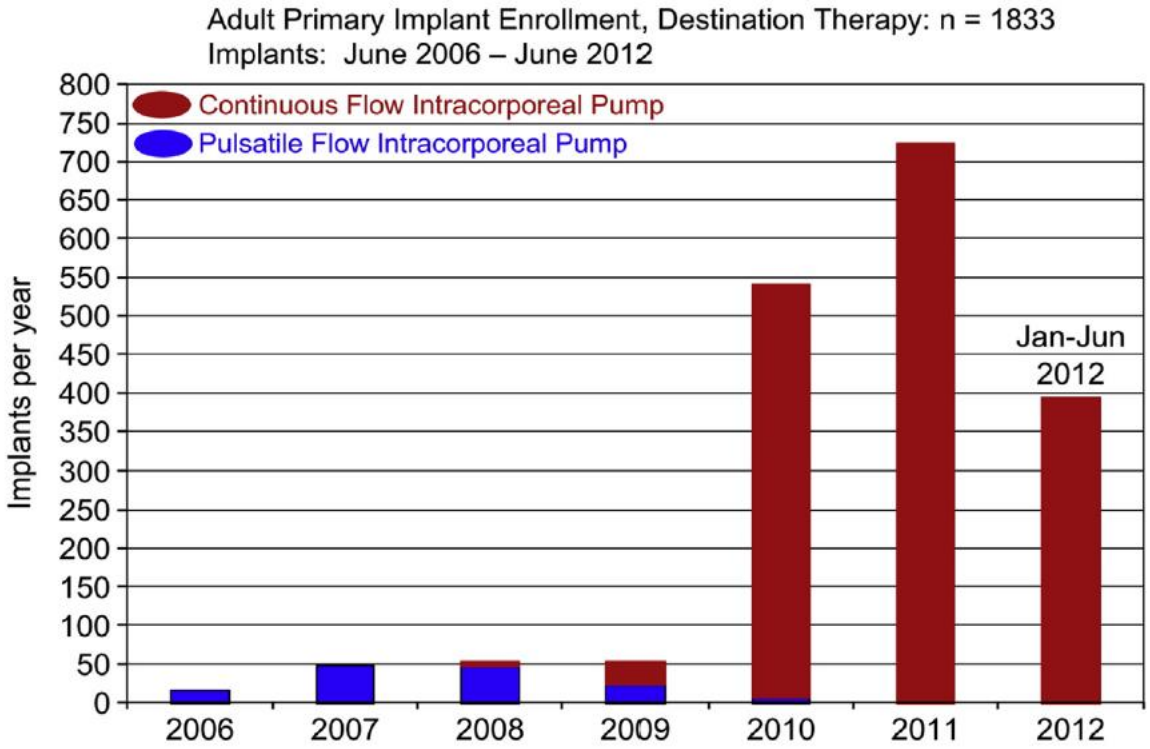
Event	Centrifugal-Flow Pump Group (N=189)		Axial-Flow Pump Group (N=172)		Hazard Ratio (95% CI)	P Value†
	no. of patients with event (%)	*no. of events*	*no. of patients with event (%)*	*no. of events*		
Suspected or confirmed pump thrombosis	2 (1.1)	2	27 (15.7)	33	0.06 (0.01–0.26)	<0.001
Pump thrombosis resulting in reoperation or removal of device	0	0	21 (12.2)	25	NA	<0.001
Stroke						
Any stroke	19 (10.1)	22	33 (19.2)	43	0.47 (0.27–0.84)	0.02
Hemorrhagic stroke	8 (4.2)	8	16 (9.3)	17	0.42 (0.18–0.98)	0.06
Ischemic stroke	12 (6.3)	14	23 (13.4)	26	0.44 (0.22–0.88)	0.03
Disabling stroke	13 (6.9)	15	9 (5.2)	11	1.25 (0.54–2.93)	0.66

LVAD problem

- Blödning
- Höger kammarsvikt
- Trombo-embolism
- Infektion

DT: Destinations behandling

- 2010 FDA godkänd med HM II
- 2012 40% av alla LVAD i USA



	2006	2007	2008	2009	2010	2011	2012
Cont Intra Pump	0	0	7	32	537	723	395
Puls Intra Pump	15	48	46	22	5	1	0

Slaughter MS et al NEJM 2009

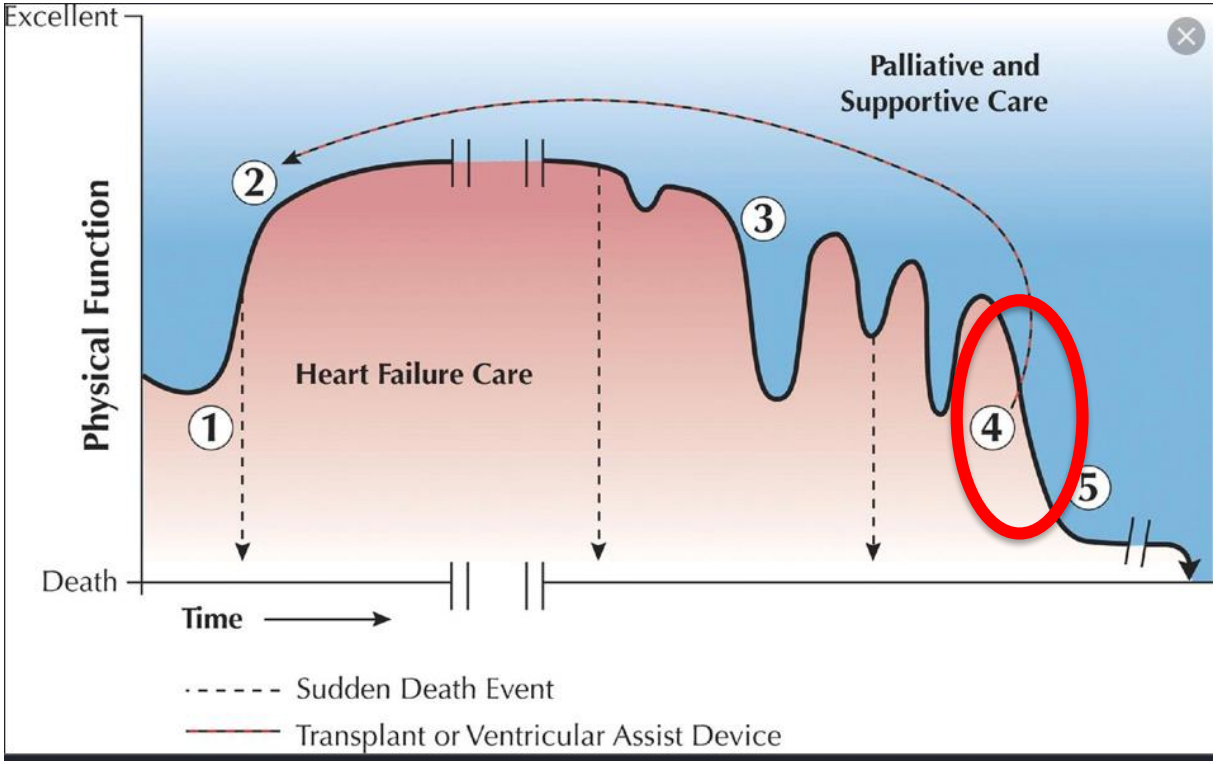
Region Östergötland

DT: Vem?

- Icke transplantationskandidat

- Hög risk för försämring/mortalitet:
  - Läkemedel intolerant
  - Återinläggning för hjärtsvikt
  - VO2 arbetstest < 14 ml/min x kg
  - Beroende av inotropi i.v.
  - CI < 2,0
  - Multiorgansvikt
  - Kardiell kakexi

DT: när?



Region Östergötland

SWEdish evaluation of left Ventricular Assist Device

- 80 pat med avancerad hjärtsvikt
- NYHA 3b/IV, INTERMACS 2-6.
- EF < 30%, NTproBNP > 2000
- 1:1 randomisering OMM vs LVAD (HM3)

- 37 pat inkluderade

- Kontakta gärna oss på US !!!

Region Östergötland