UNIKLINIK RWTH AACHEN

Department of Cardiology, Pneumology and Vascular Medicine

Challenges to device therapy

Devices therapy in heart failure

is the party over or is it just the beginning of personalised care?

Do we still need….devices?

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NHS National Institute for Health Research

Heart Research UK

FMS Finapres Medical Systems

British Heart Foundation

Klaus Witte: conflicts of interest

Investigator-initiated research funding (charitable/NGO):

- HRUK New and Evolving Technologies grant to Dr John Gierula and Dr Klaus Witte
- NIHR funding for Dr John Gierula (Post-doctoral fellowship),
- NIHR funding for Dr Maria Paton (Post-doctoral fellowship)
- ESC Nursing Fellowship for Melanie McGinlay
- BHF PhD fellowship Dr Sam Straw

Investigator initiated research funding (commercial):

- Unrestircted research grant for MASTER-AF from Cardiac Dimensions (RWTH Aachen)
- Unrestricted research/training grant for a Fellowship Program to the University of Leeds from Medtronic UK
- Unrestricted Research funding to Dr John Gierula and Dr Klaus Witte from Medtronic UK
- Unrestricted research grant for a study in prognosis in HFrEF to the University of Leeds from Astra Zeneca UK

Speaker fees and direct financial support for educational meetings:

- Astra Zeneca, Pfizer, BMS, Napp Pharmaceuticals, Novartis, Bayer, Cardiac Dimensions, Abbott, Microport, Medtronic
- ‘Device Therapie am Dreilaendereck’ (01.06.2022)

Advisory Board activity:

- Astra Zeneca, Bayer, Cardiac Dimensions

Indirect editorial assistance for writing projects:

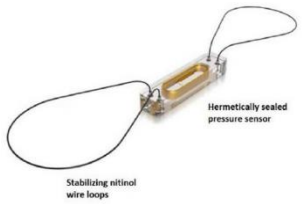
- Bayer, Medtronic

Commercially supported research activity:

- UK PI: TRANSITION (Novartis)
- UK PI: REDUCE-FMR (Cardiac Dimensions)
- UK PI and steering group: EMPOWER (Cardiac Dimensions)
- DSMB: RECOVER (Novartis)
- DSMB (Chair): ASTRAL (Microport)
- DE PI: CINCH (Cardiac Dimensions)
- DE PI: APOLLO (Microport)
- PI MASTER-AF (Cardiac Dimensions)

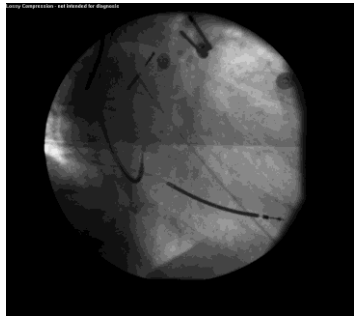
What do we mean?

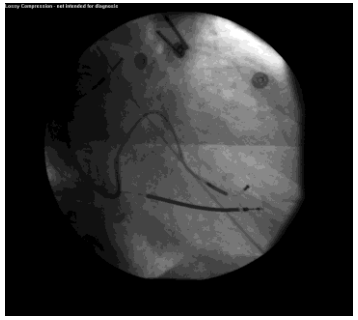
Monitoring



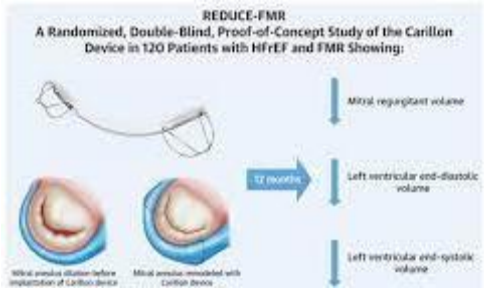
CRT-P

ICD / CRT-D





Valves

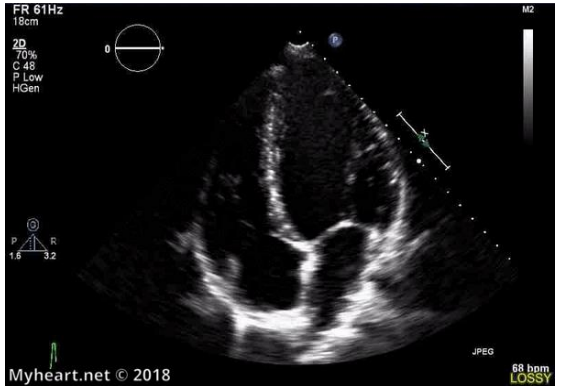


Chronic heart failure

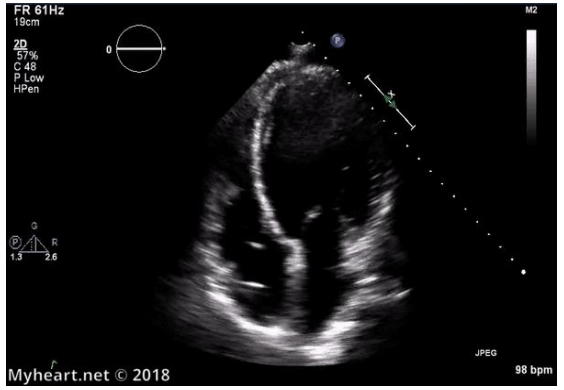
Chronic and persistent heart impairment:

- Symptoms of breathlessness, fatigue or congestion
- 500,000 people in the UK, 26 million across the globe
- High hospitalisation rate
- Shortened life expectancy
- Elevated risk of death due to
  - 1) arrhythmia
  - 2) deteriorating HF
  - 3) co-morbidities and frailty
- Proven medical and device treatment

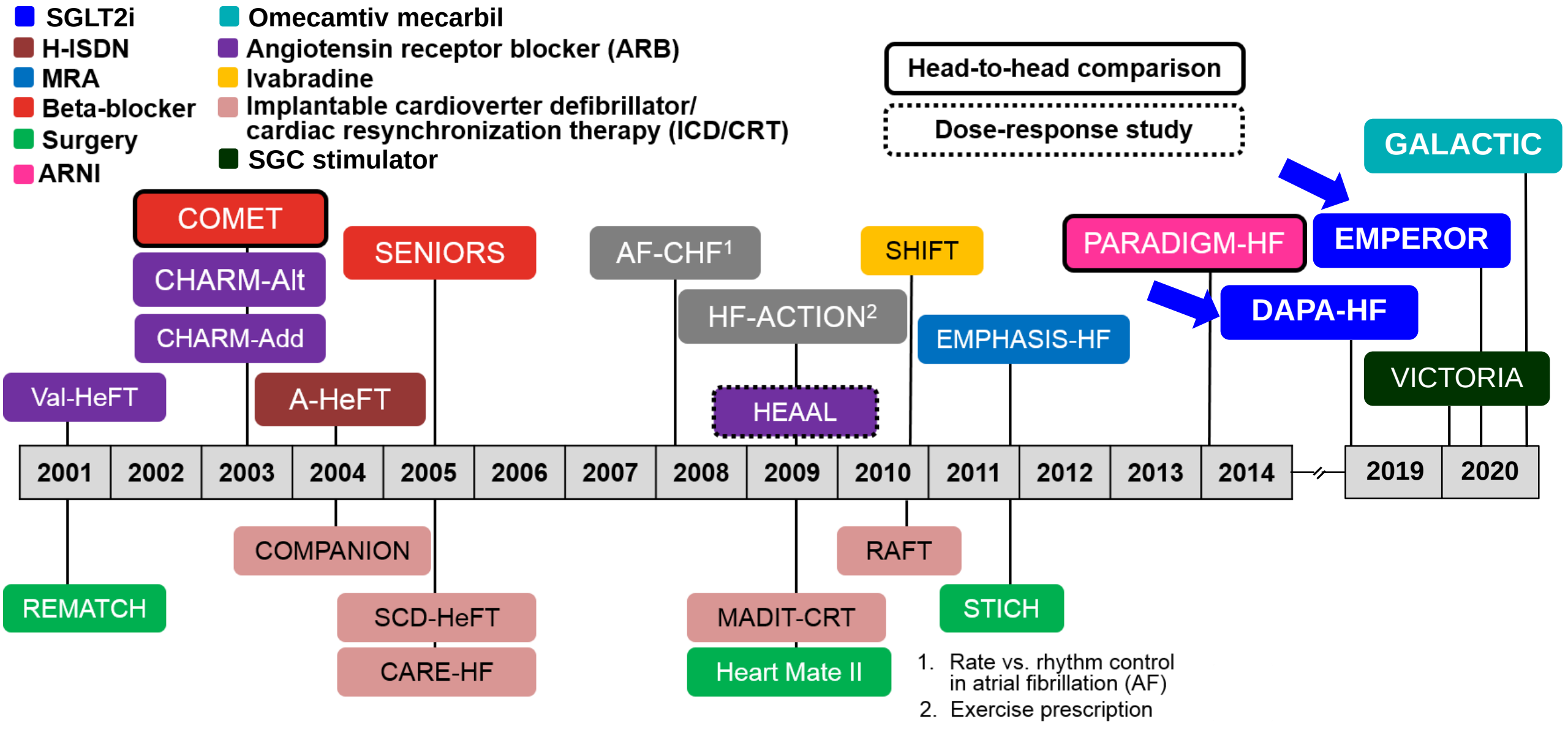
Normal EF

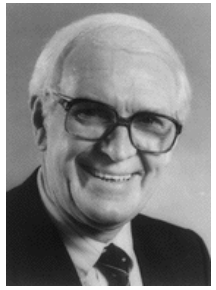


Reduced EF



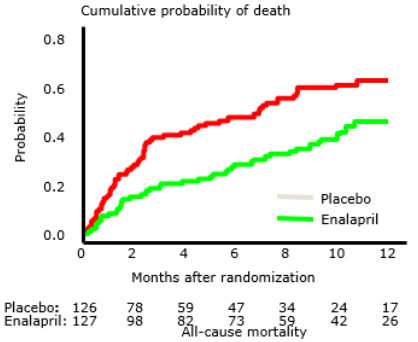
HFrEF: Positive trials 2001–2020



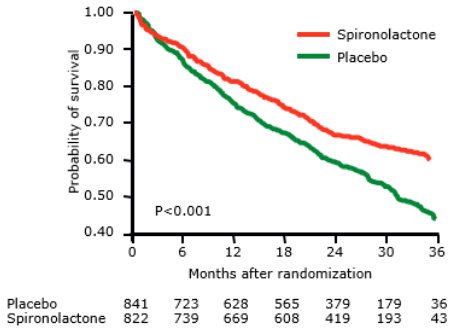


Established medical therapy improves prognosis

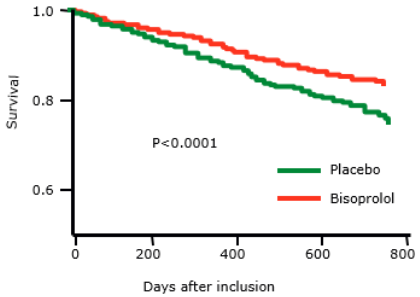
Invents propranolol (1962)
Invents cimetidine (1973)
Knighted 1981
Nobel Prize 1988



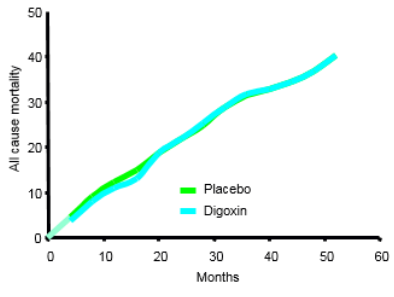
CONSENSUS Trial Study Group. *N Engl J Med* 1987;**316**:1429–35



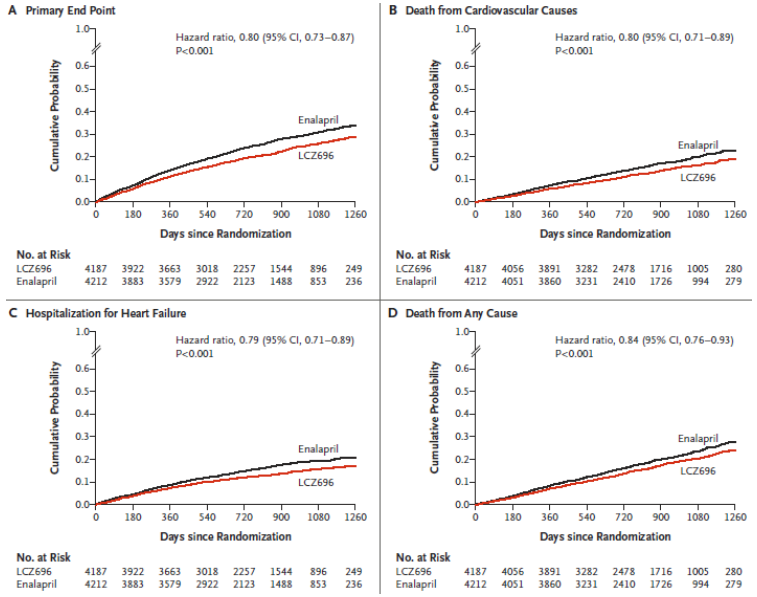
Pitt et al. *N Eng J Med* 1999; **341**: 709–17



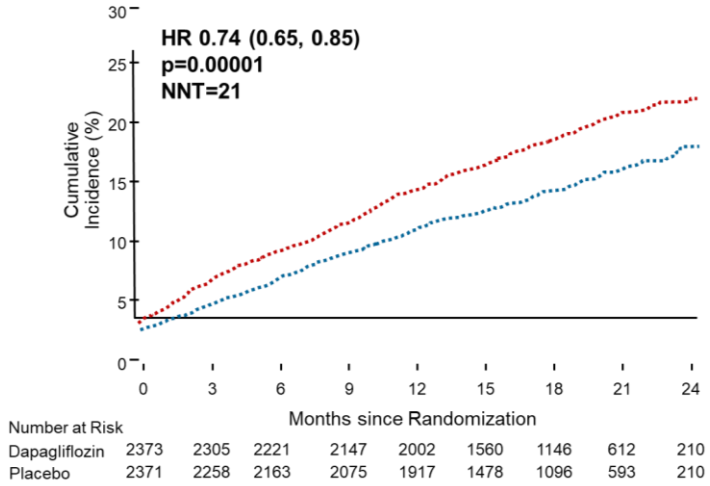
CIBIS-II Investigators and Committees. *Lancet* 1999; **353**:9–13



N Engl J Med 1997;**336**:525-33

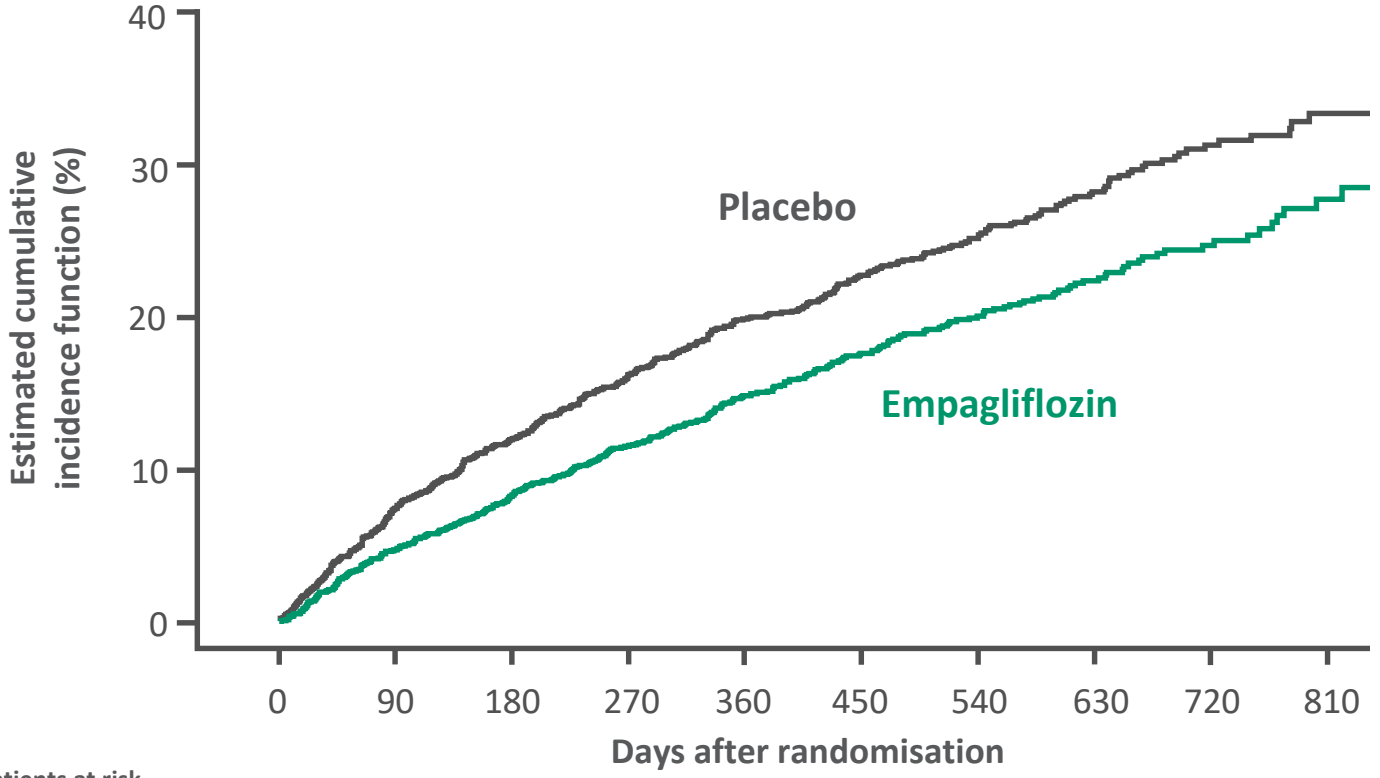


McMurray, et al. *N Engl J Med* 2014



McMurray JJV, et al. *N Engl J Med* 2019;381:1995–2008

SGLT2i improve cardiovascular death or hospitalisation for heart failure



Patients at risk										
Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

RRR 25% Relative risk reduction

ARR 5.2% Absolute risk reduction

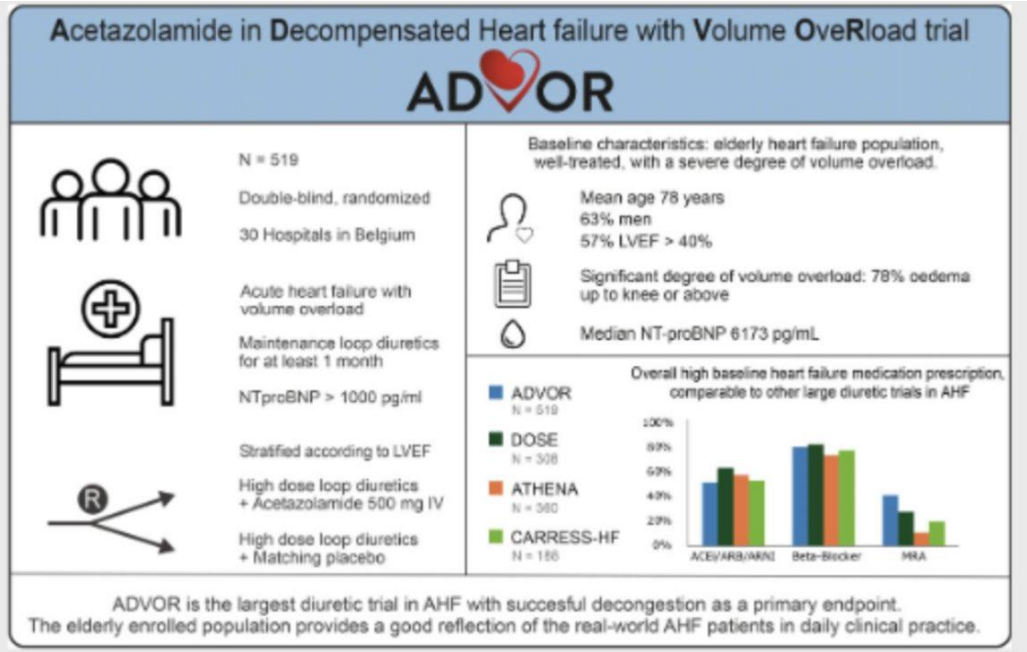
NNT=19*
(95% CI 13, 37)

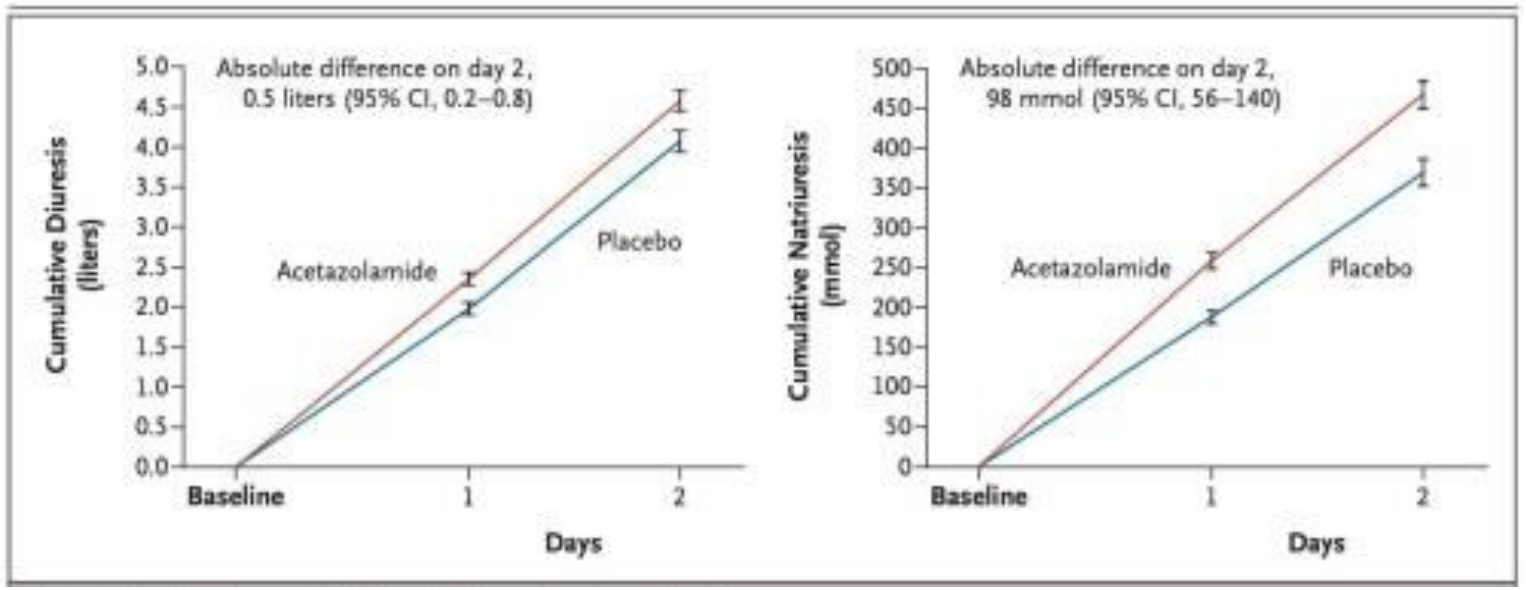
HR 0.75
(95% CI 0.65, 0.86)
P<0.0001

Empagliflozin significantly reduced the composite risk of cardiovascular death or hospitalisation for heart failure vs placebo

*Based on the 25% RRR (5.2% ARR) demonstrated for reduction in CV death or HHF, the patients who would need to have been treated with empagliflozin to prevent one primary event was 19 (95% CI, 13 to 37). Cox regression model including covariates age, baseline eGFR, geographic region, baseline diabetes status, sex, LVEF and treatment.

ARR: absolute risk reduction; CI: confidence interval; CV: cardiovascular; eGFR: estimated glomerular filtration rate; HR: hazard ratio; LVEF: left ventricular ejection fraction; NNT: number needed to treat; RRR: relative risk reduction Packer M *et al. N Engl J Med*. 2020;383:1413–1424.





Mullens et al *NEJM* 2022

openheart

The Four Pillars of Heart Failure

A new approach

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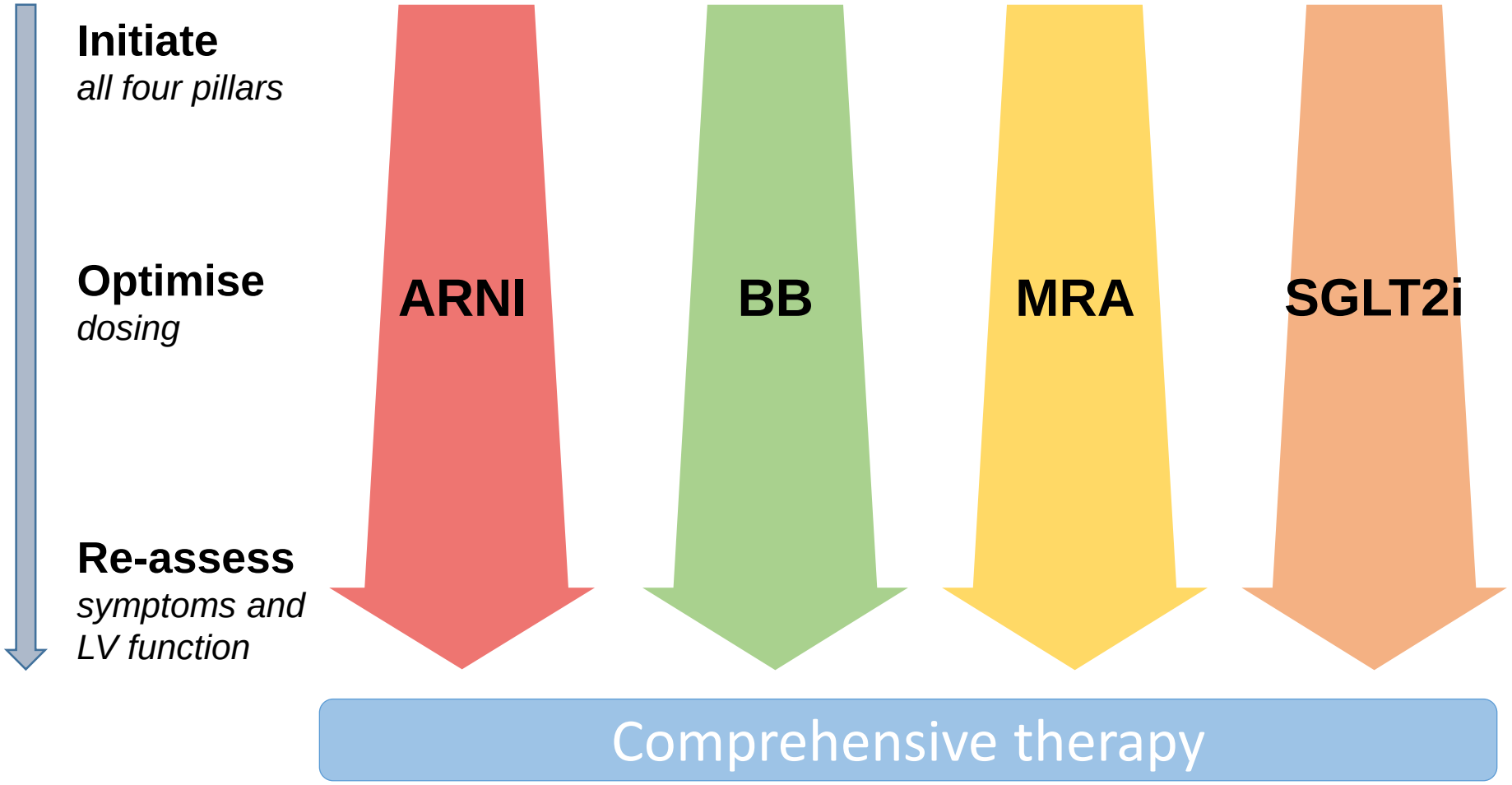
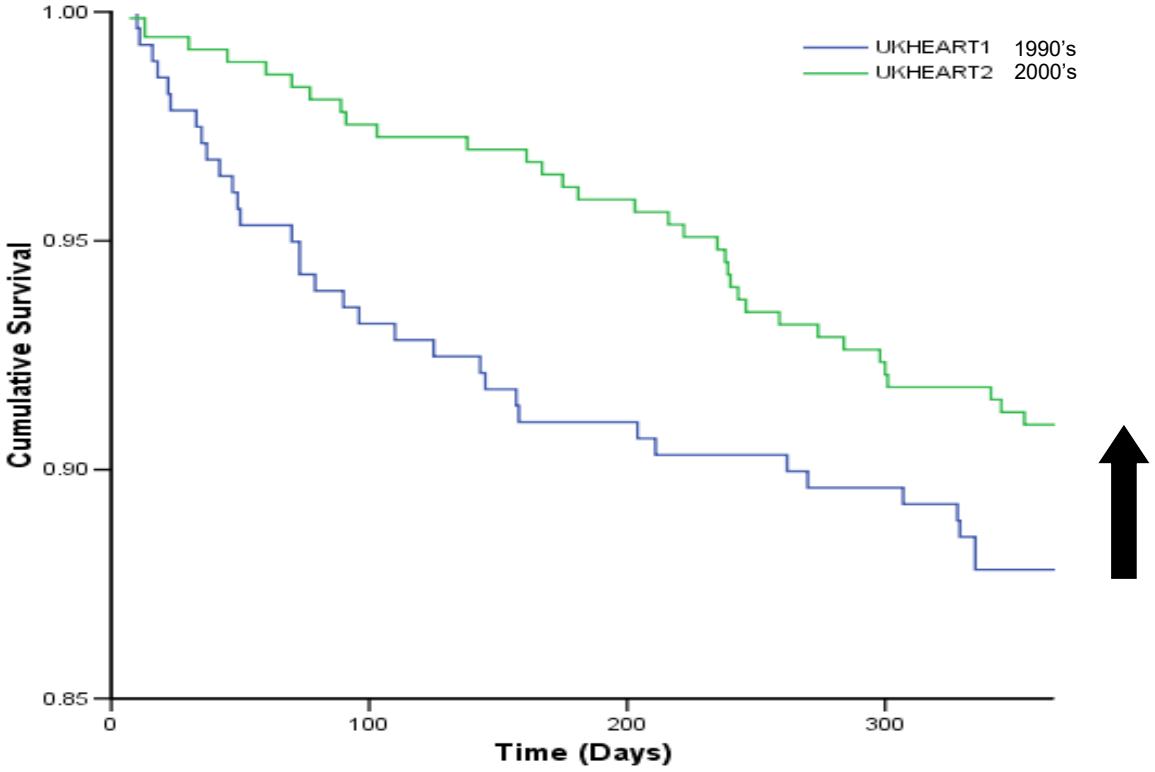


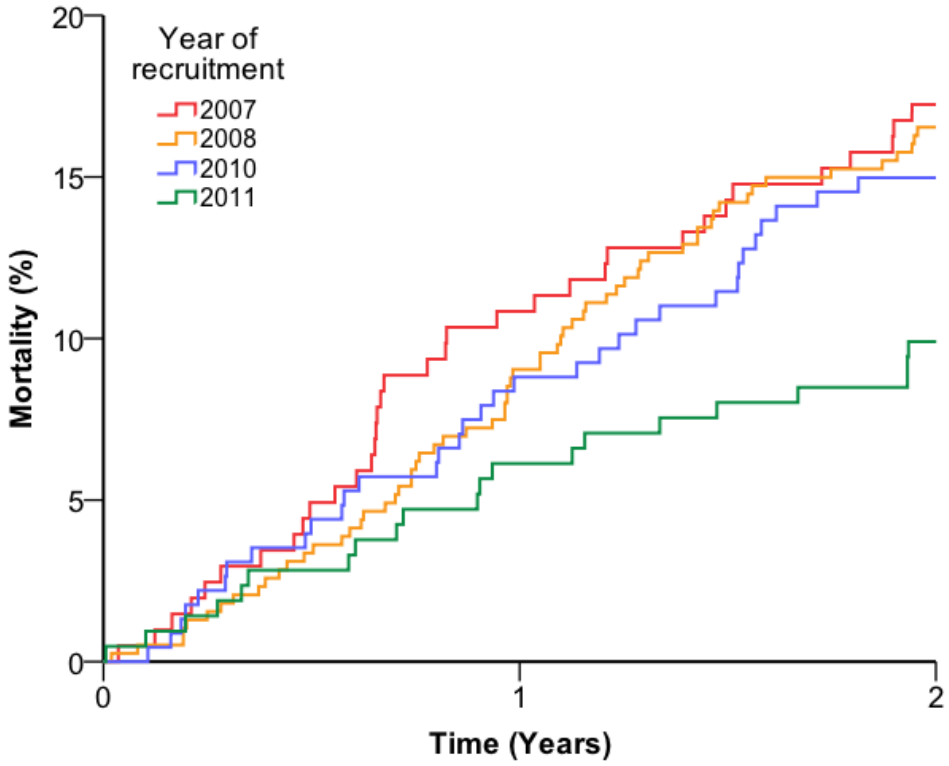
*For **every** patient*

Adapted from: Four Pillars of Heart Failure. Straw et al. 2021

Survival at 1 year has improved

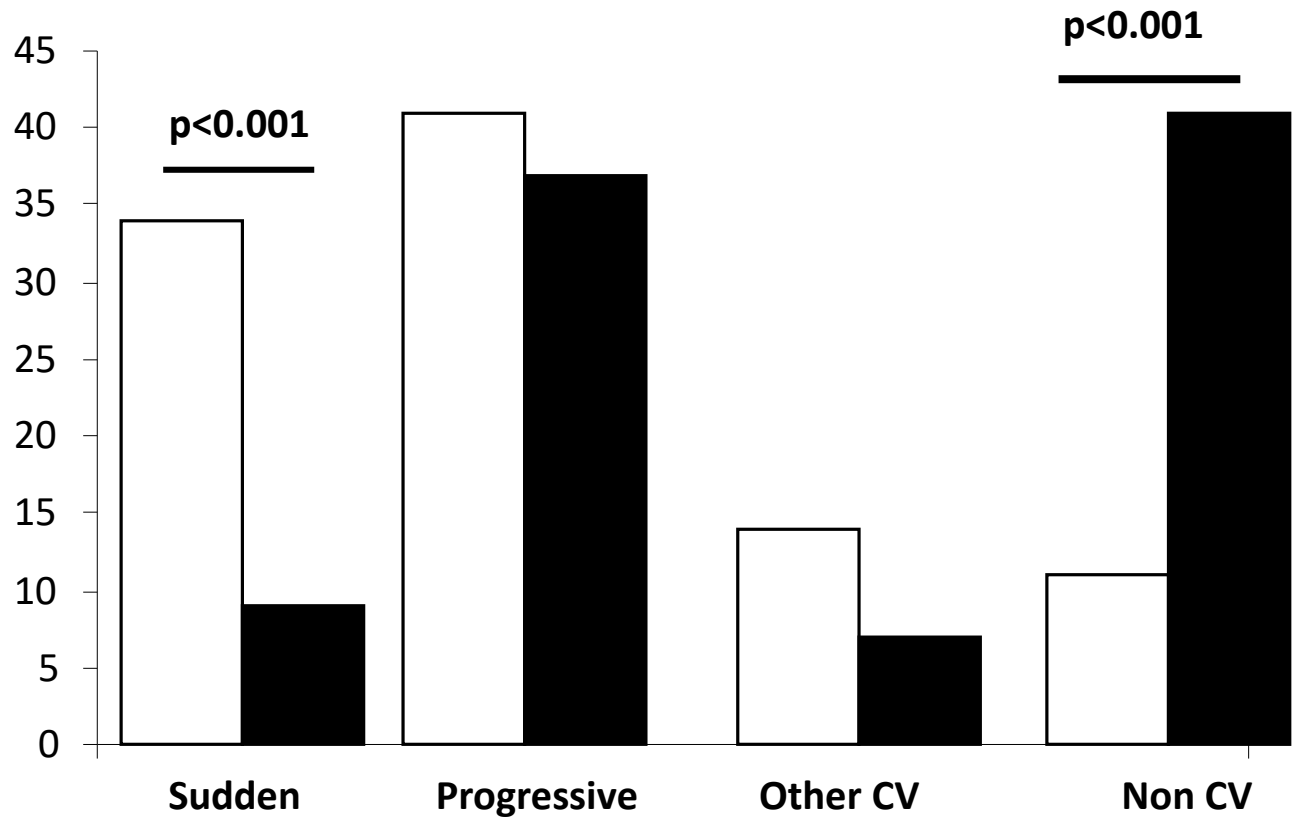


UK Heart 2



Cubbon et al *Circ Heart Fail* 2011

Challenge: Mode of death in CHF 2006-2009 (ICD recipients excluded)



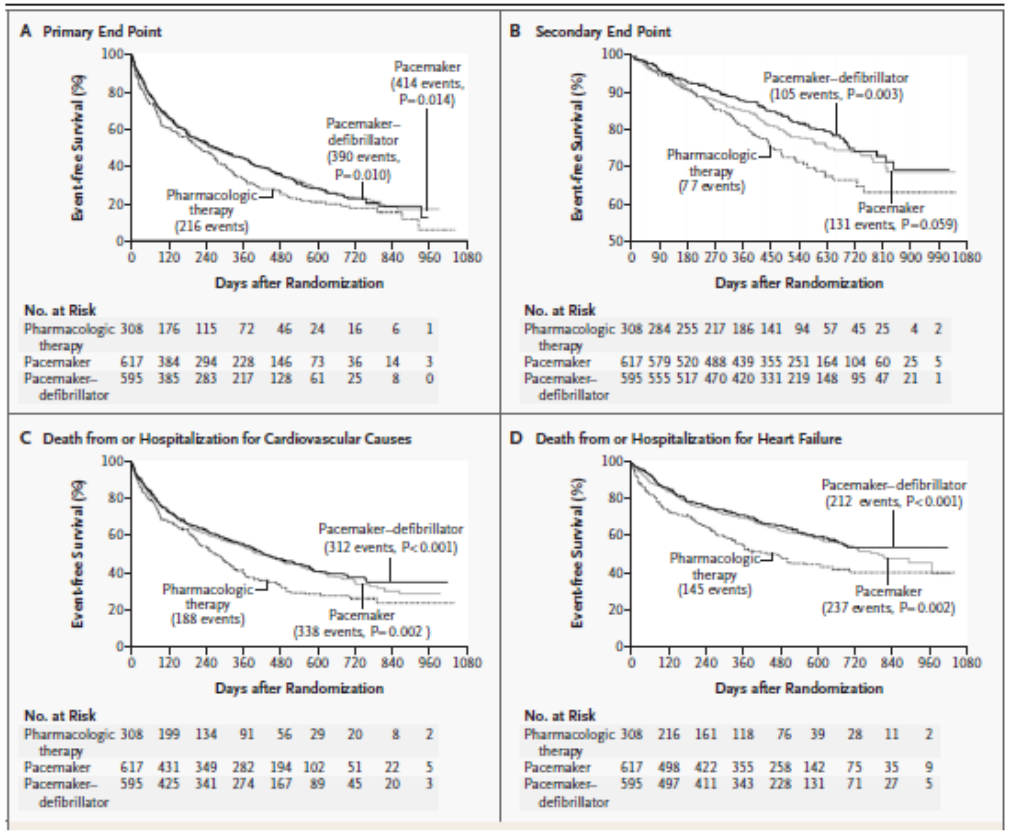
Cubbon et al *Circ HF* 2010

Challenge: CRT-D v CRT-P

COMPANION

- 600 CRT-P / 600 CRT-D / 300 OPT

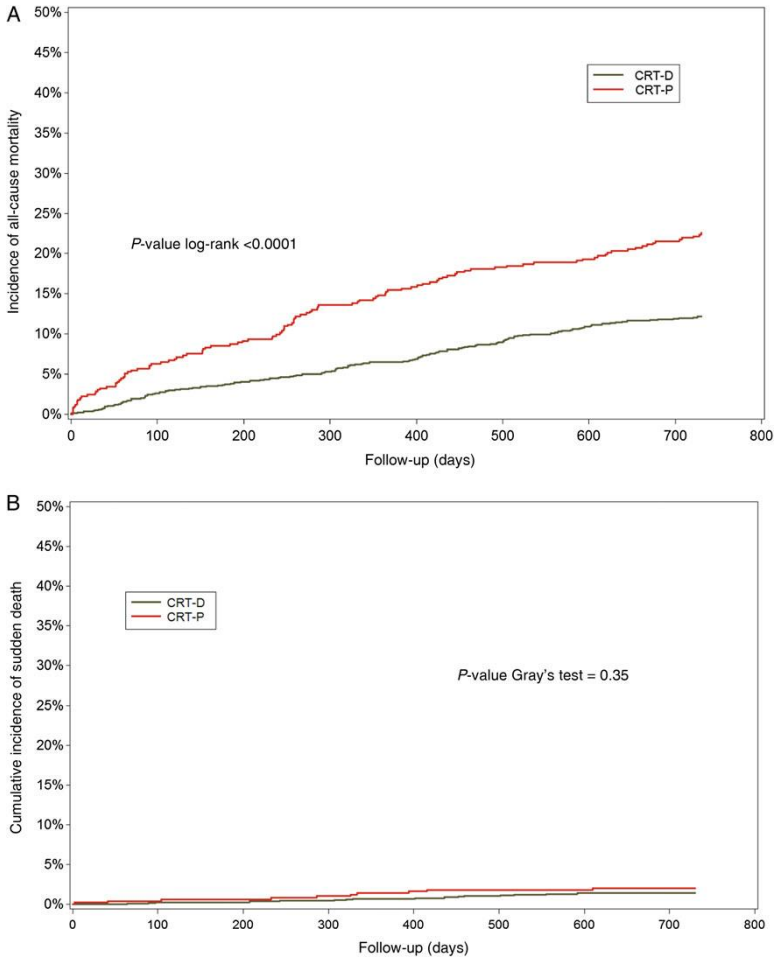
- QRS >120ms
- EF<35%
- NYHA class III / IV
- Hosp previous 12/12



Bristow et al: many many many years ago (B.C.)

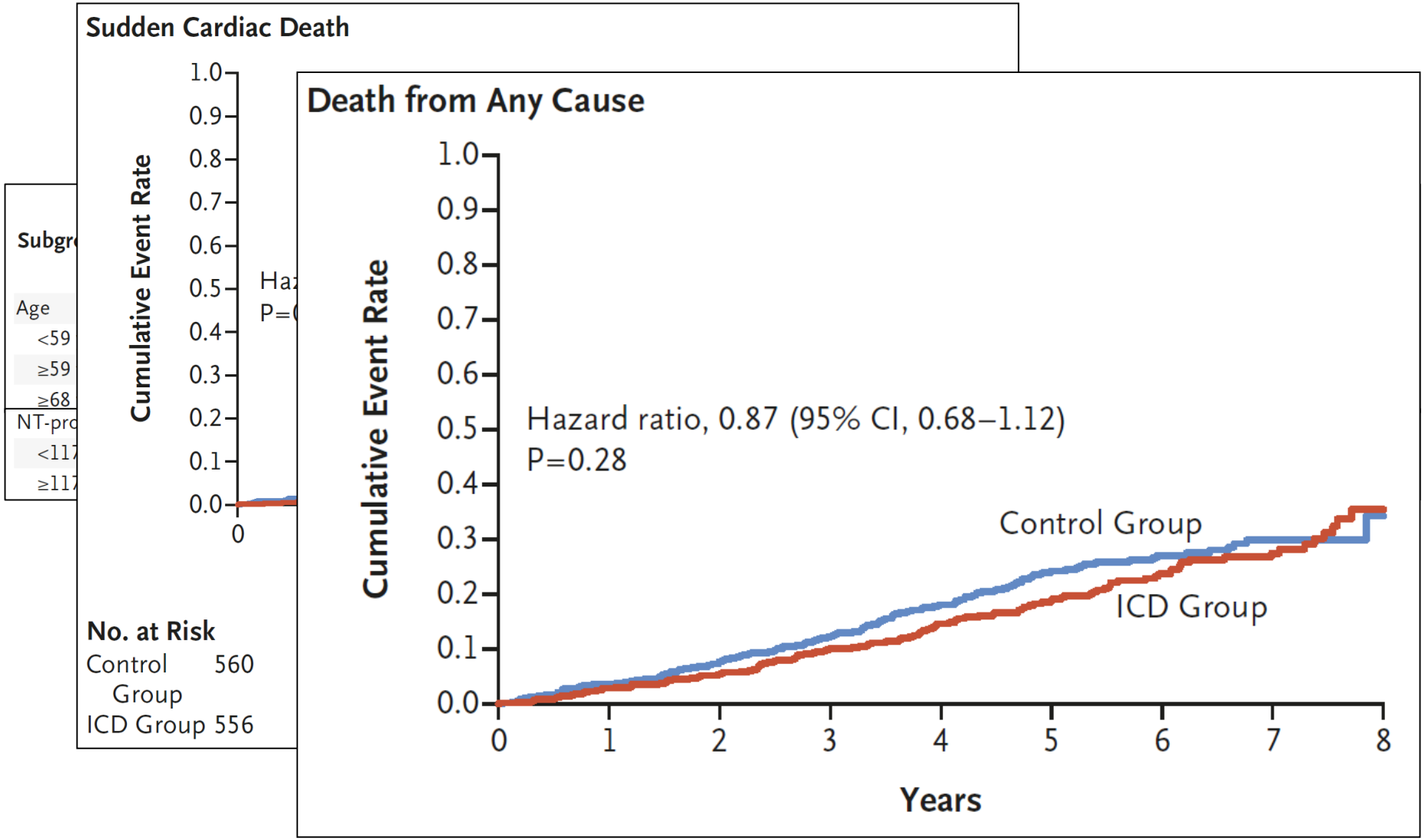
Challenge: CERTITUDE (CRT-P v CRT-D)

- Prospective, multicentre cohort study, 1705 patients
- CRT-P patients were older, with more advanced HF, and co-morbidities when compared with CRT-D recipients.
- At 2-years, CRT-P patients had 2-fold higher mortality than CRT-D
- Excess mortality among CRT-P subjects was almost entirely related to non-SCD
- Limited benefit from a defibrillator.



Marijon et al *EHJ* 2015

Challenge: DANISH trial

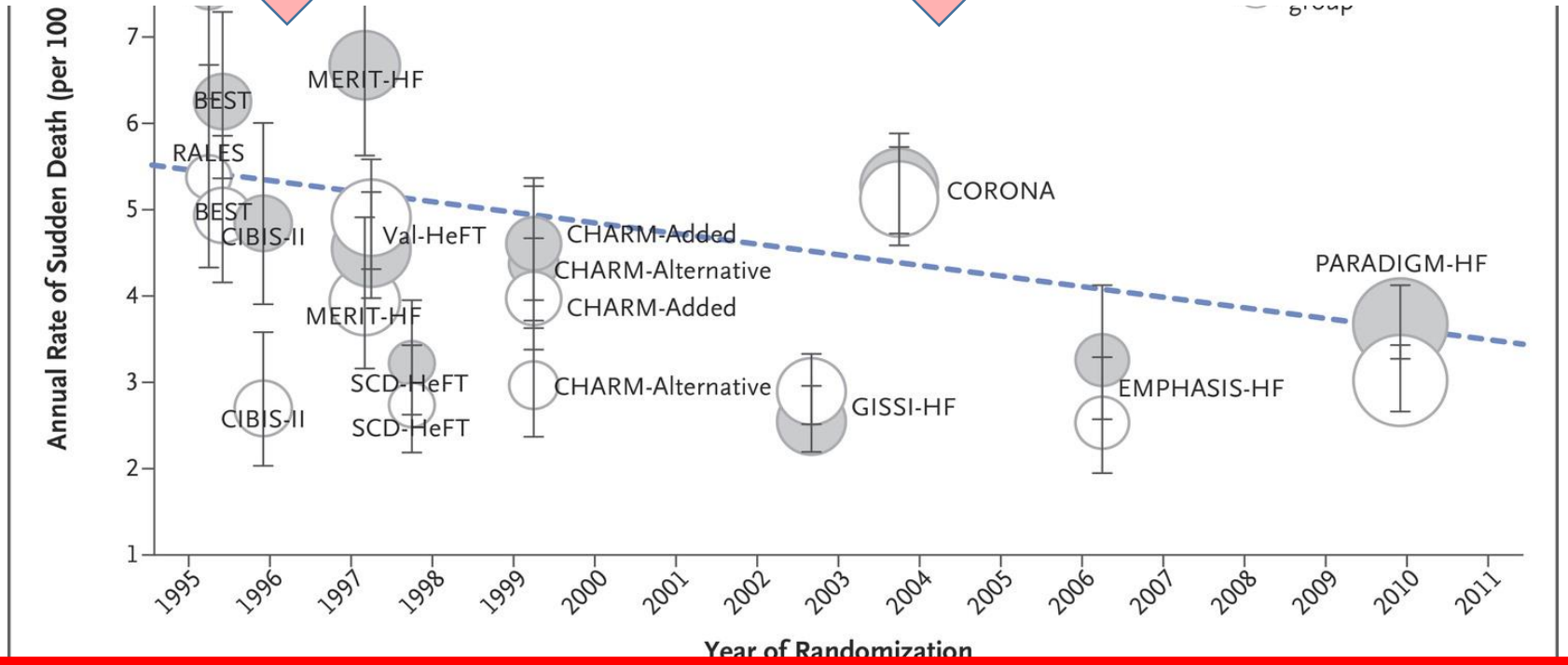


Kober et al. *NEJM* 2016

Challenge: SCD and Total Mortality in HFrEF

Table 2 Rates of therapy and all-cause mortality in treatment arm of selected RCTs and the Israeli ICD registry

Trial	Year	Average duration (mo)	Average annual rate of appropriate shock, %	1-Year all-cause mortality, %
MADIT II	2002	24	17	9
SCD-HeFT	2005	45.5	5	6
PREPARE	2008	12	5.4	4.9
MADIT-RIT	2012	16	3	3
ICD Registry	2014	20	1	6



SCD risk is reducing....

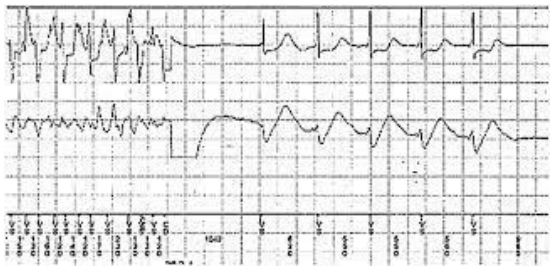
Things have changed in heart failure…

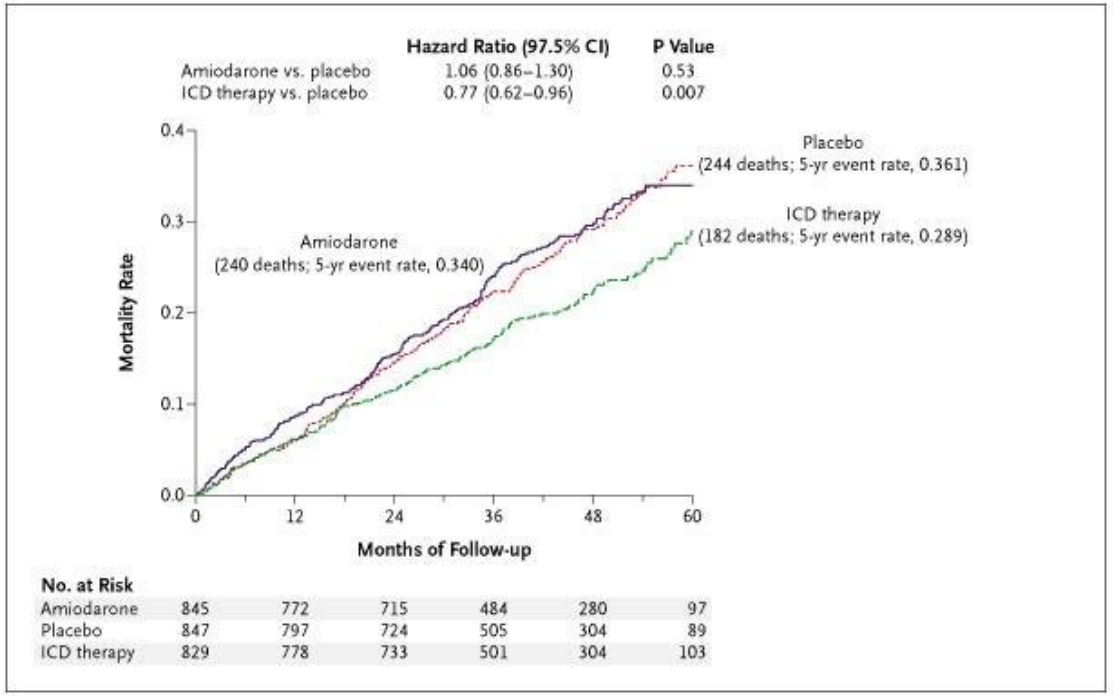
Do we still need: defibrillators?

Insurance covers unexpected and unpredictable events:

if they were expected or predictable we wouldn’t need insurance

Preventing arrhythmic death in HFrEF





The reality….

After 7 years of ARNi
Do we still need devices?
(even in a well organised/funded healthcare system)

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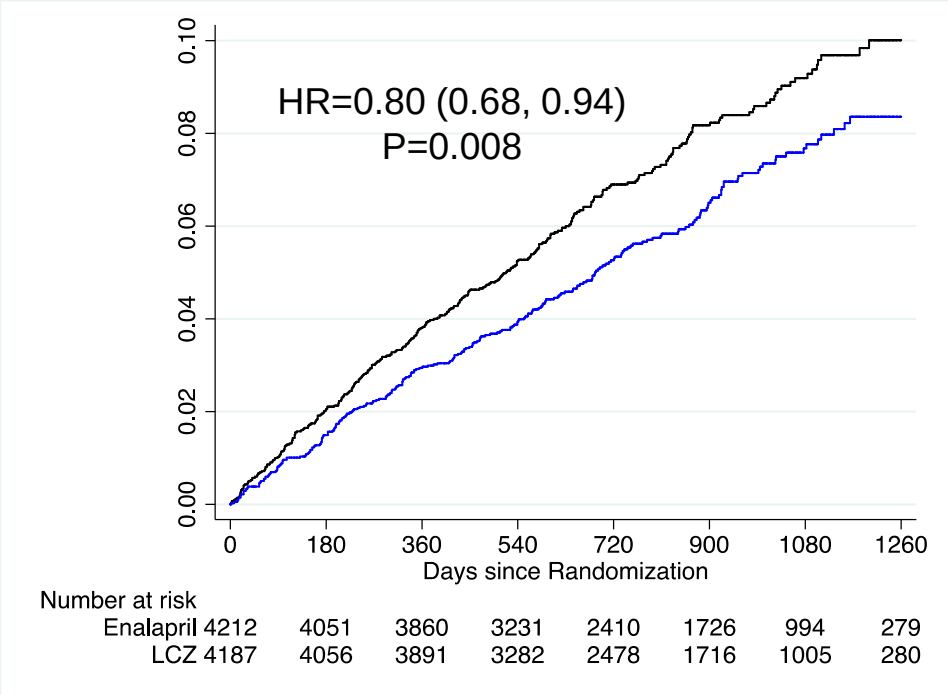
Persistent risk

Even with Sac/Val, the risk of mortality (and hospitlaisation) persists



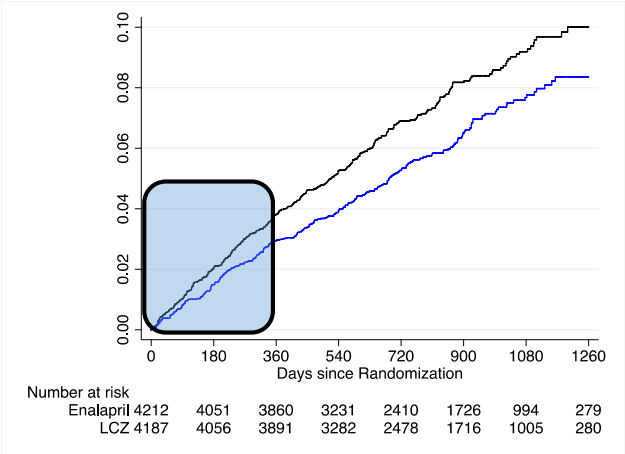
!

Several other issues to consider

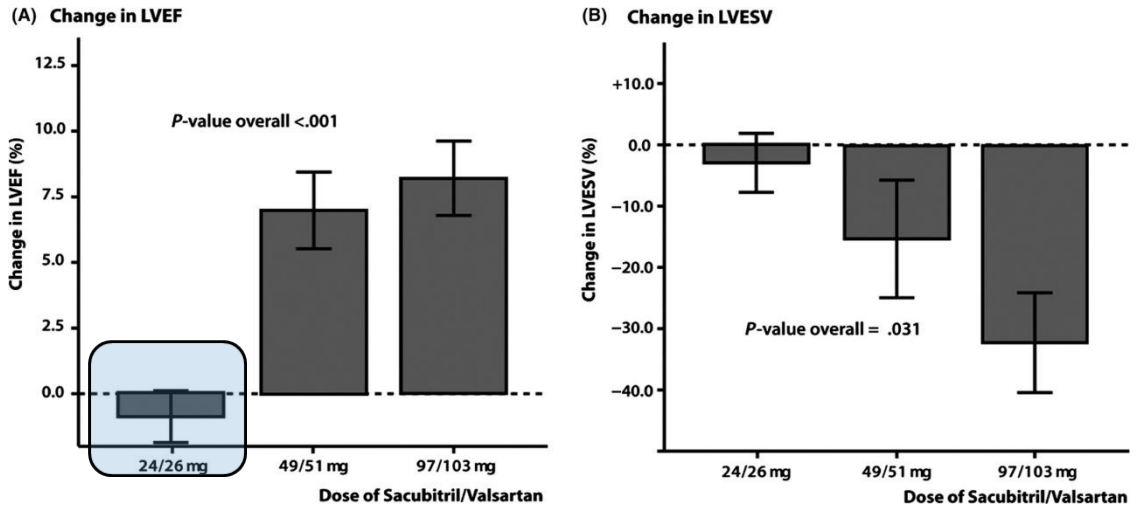
(even in a well organised/funded healthcare system)

Time

Tolerability



Immediate protection

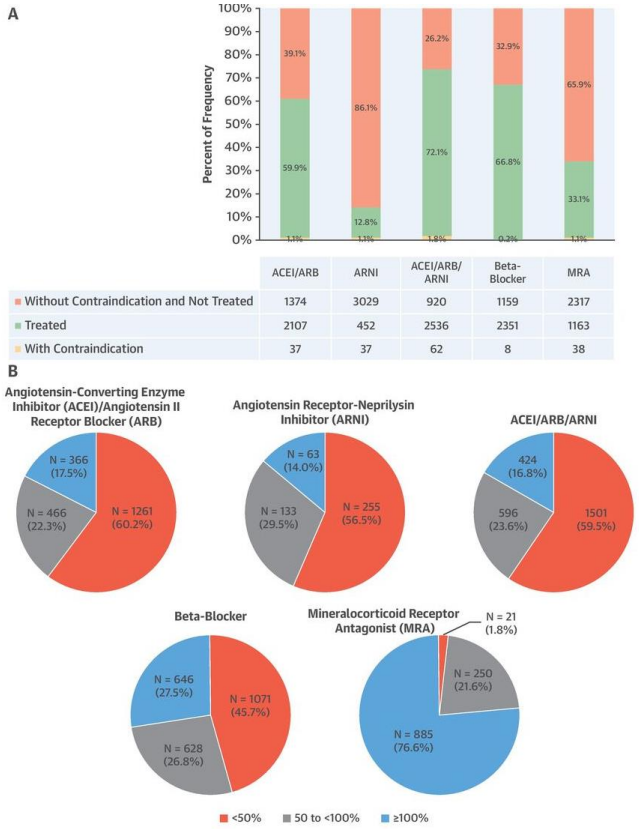


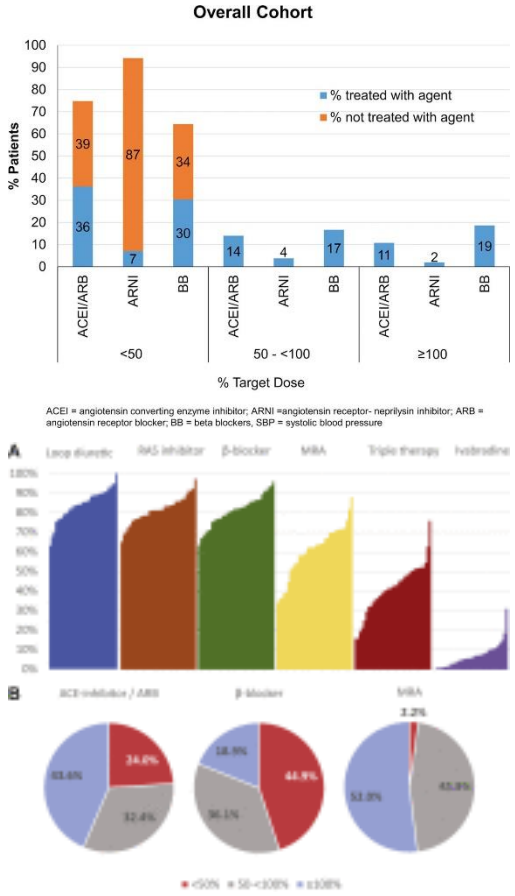
n=141 patients (5 died and 4 stopped taking the drug over 118 days)
100% on ACEi/ARB at outset (mean 57% of target)
65% on >100mgBD (mean dose 53% of target: 35% on a dose associated with progression)

Martens et al. *CV Therap* 2018

We consistently don’t get the drugs right

US and Netherlands: CHAMP-HF (>3500 patients) and CHECK-HF (>10,000)

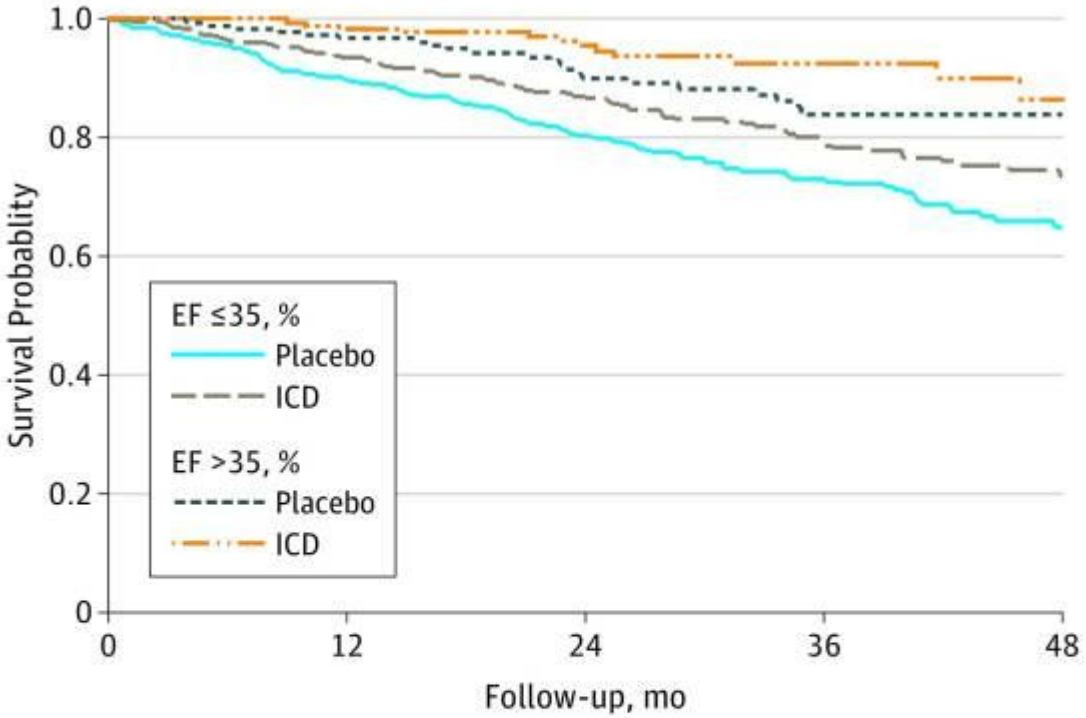




Greene et al; *JACC* 2019

Brunner La-Rocca et al; *JACC-HF* 2019

…robust benefit from ICDs in the remodelled cohort in SCDHeFT

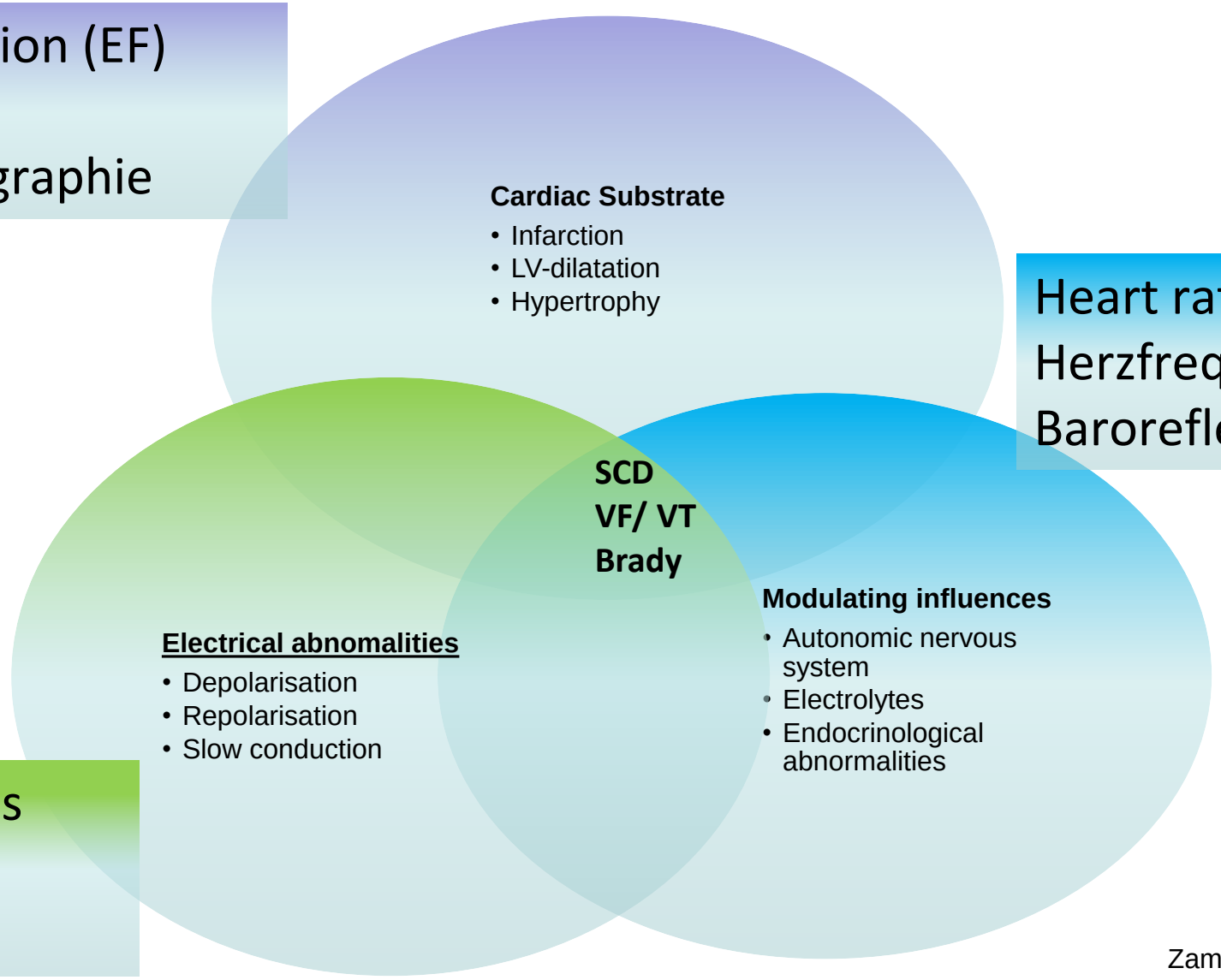


No. at risk					
EF ≤35, %					
Placebo	464	402	295	171	62
ICD	438	404	291	168	66
EF >35, %					
Placebo	185	173	121	72	23
ICD	186	176	120	62	21

Adabag et al; *JAMA-Cardiol* 2017

Risk Factors for SCD

LV-Pumpfunction (EF)
Stresstest
Koronarangiographie



Heart rate turbulence
Herzfrequenzvariabilität
Baroreflex-Sensitivität

T-Wellen-Alternans
Spätpotential
QT-Dispersion

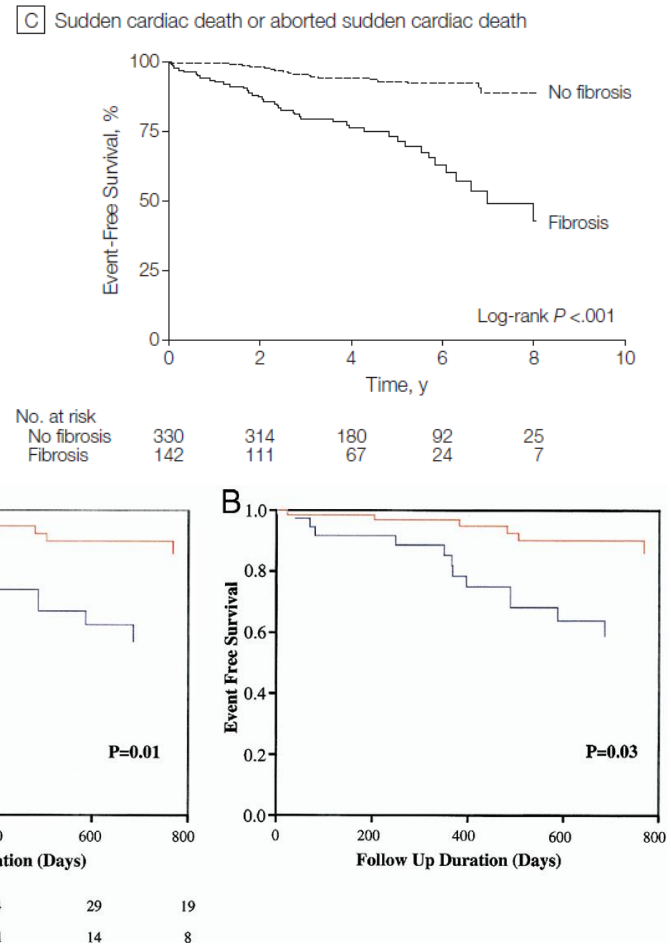
Zaman et al., Heart lung circ, 2019
Akhtar et al., Curr cardiol report, 2019

What about other contributors? - scar / fibrosis?

Why are we relying on LVEF?

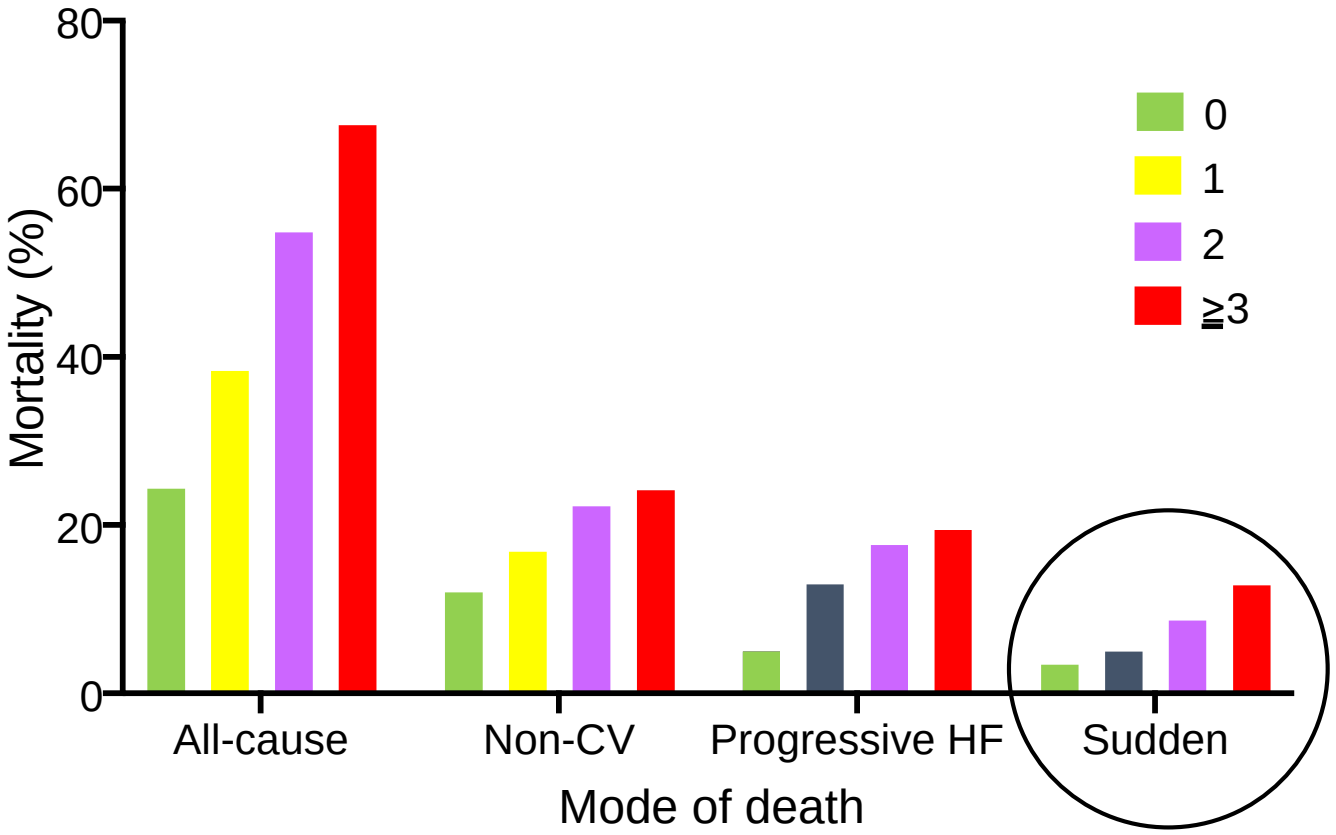
Because it's fairly good and easy

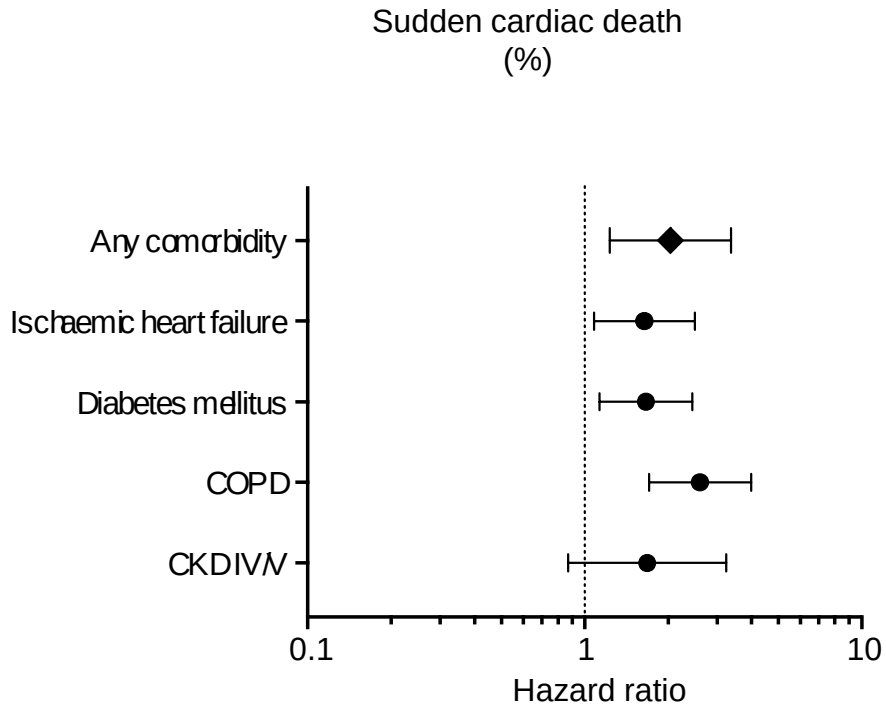
- n=472,
- mean EF 37%
- midwall fibrosis +/-
- LVEF falls out in multivariable analysis



Gulati et al. *JAMA* 2013
Assomull et al *JACC* 2006

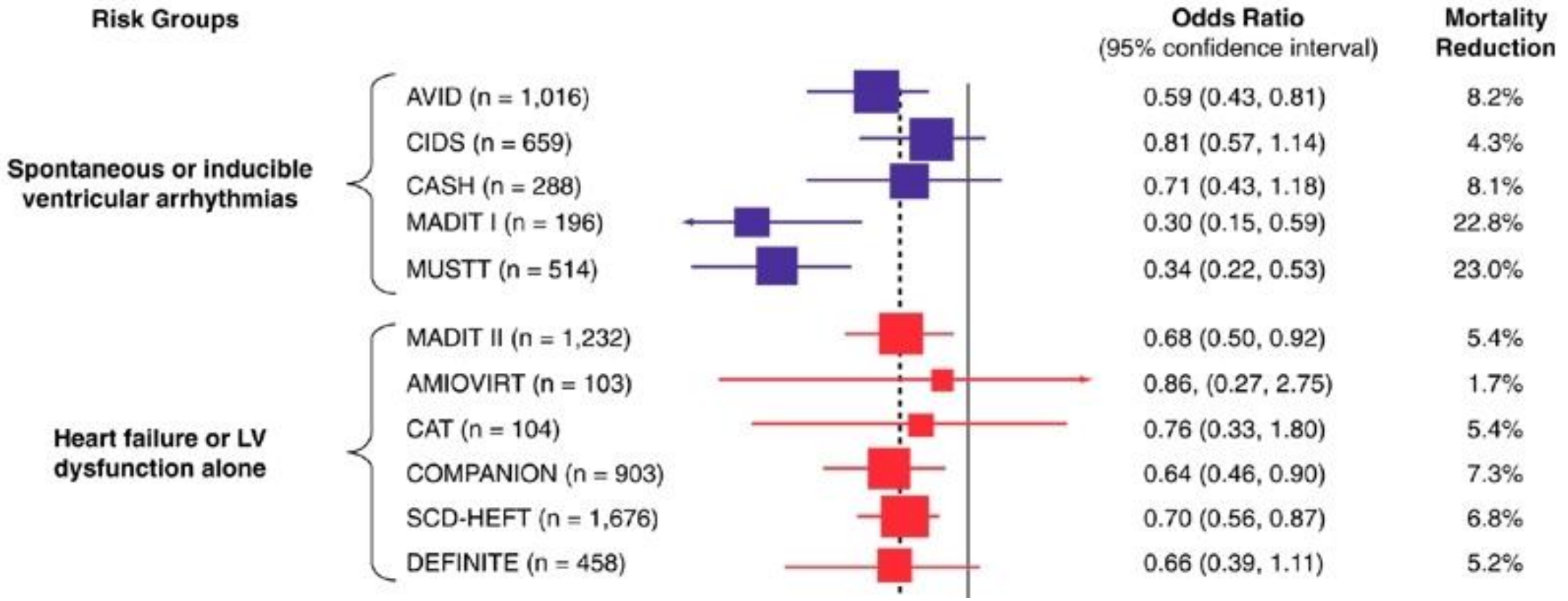
Sudden death persists especially in those with co-morbidities





Straw et al; *ESC-HF* 2020

Are we casting aside a generation of data?



ESC Heart Failure Guidelines 2021

Primary prevention		
An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of an ischaemic aetiology (unless they have had a MI in the prior 40 days—see below), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.[161,165]	I	A
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of a non-ischaemic aetiology, and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.[161,166,167]	IIa	A

Consistent in 2016

Baseline risk in the NICM cohort in 2017 meta-analysis was 5.4% with a RRR of 0.76 for ICD (Shun-shin *EHJ* 2017)

Step down in recommendation in NICM

Cave:

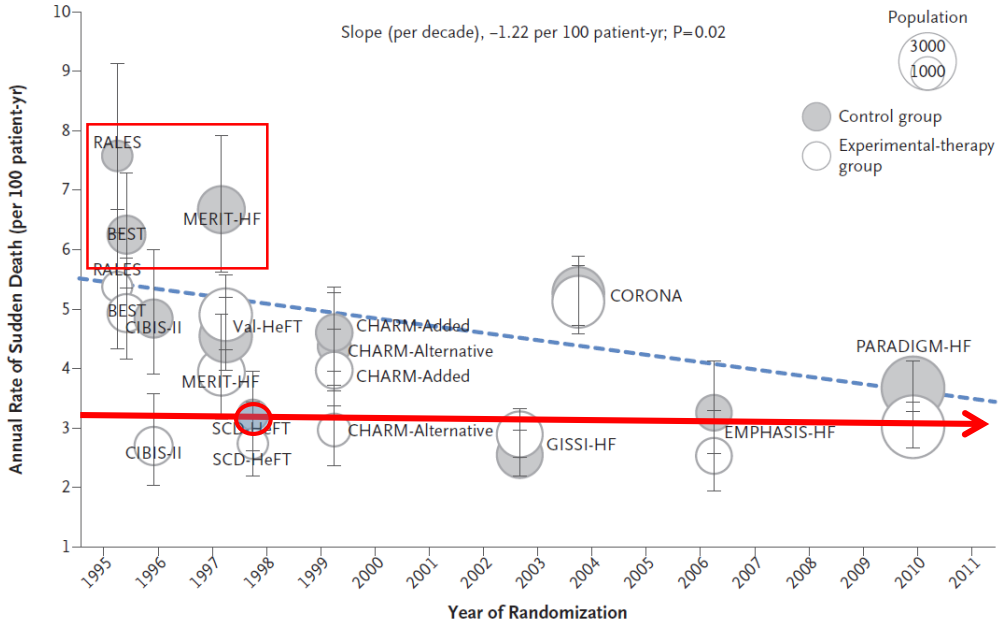
- DANISH: duration of HF was 20mths by enrolmment
- NICM is heterogenous illness (Fibrosis, Genetics,…)

Eur Heart J, Volume 42, Issue 36, 21 September 2021, Pages 3599–3726, https://doi.org/10.1093/eurheartj/ehab368

Trends in Sudden Cardiac Death

RALES: no. (%)

NYHA II	7	(0.4)
NYHA III	1,173	(70.5)
NYHA IV	483	(29.1)



PARADIGM-HF: no. (%)

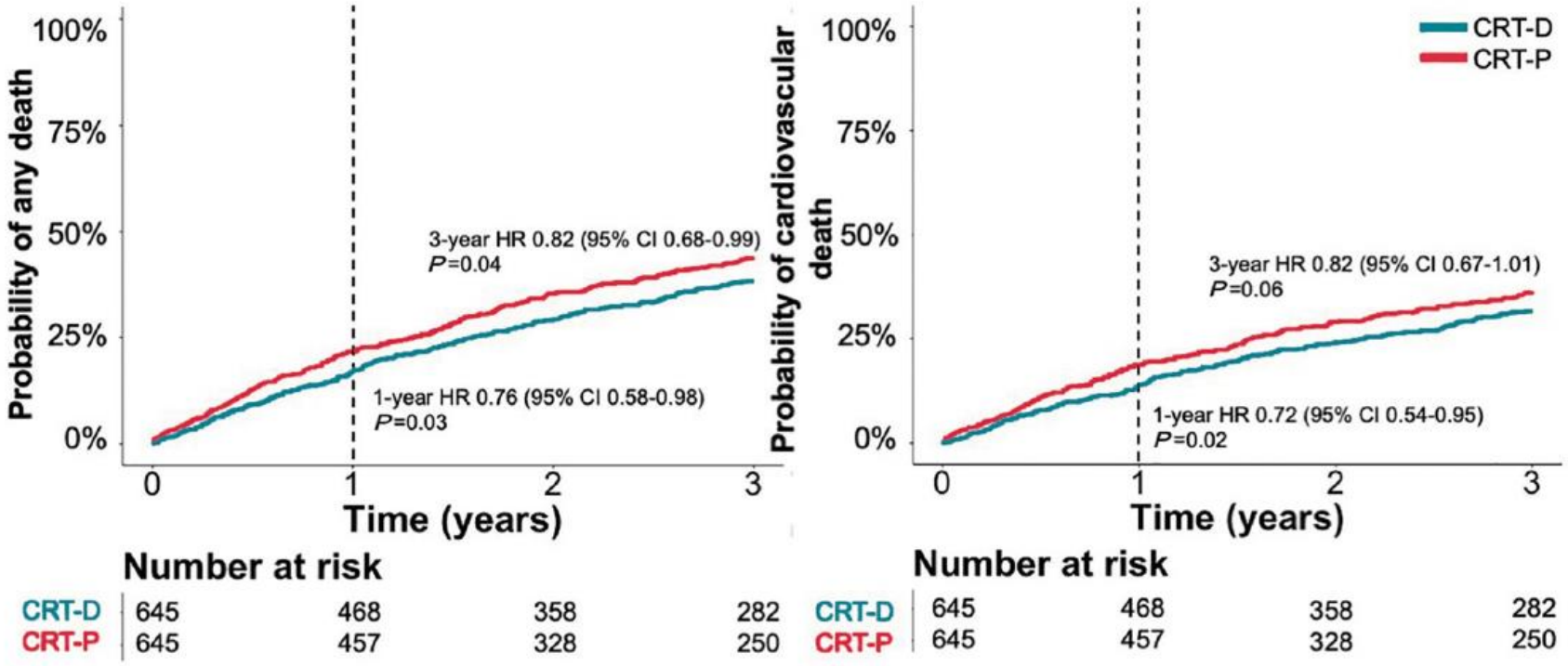
NYHA I	389	(4.6)
NYHA II	5,919	(70.6)
NYHA III	2,018	(24.1)
NYHA IV	60	(0.7)

1: Without control groups from RALES, BEST, and MERIT-HF the line is relatively flat
2: The SCD-HeFT control mortality is equivalent to the PARADIGM therapy group
3. 80% of people in SCDHeFT were on a beta-blocker

Shen L *NEJM* 2017
(Courtesy Dr Meine Utrecht)

SWEDE-HF

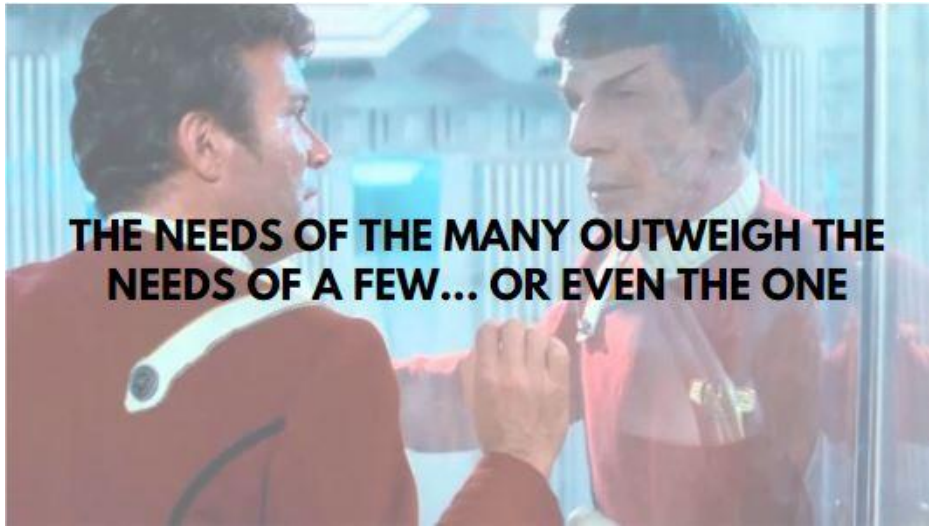
CRT-D v CRT-P
1 yr ACM 16.9% v 21.6%
1 yr CV mortality 13.8% v 18.7%



Courtesy Benedikt Schräge

Why the argument – just give everyone CRT-D!

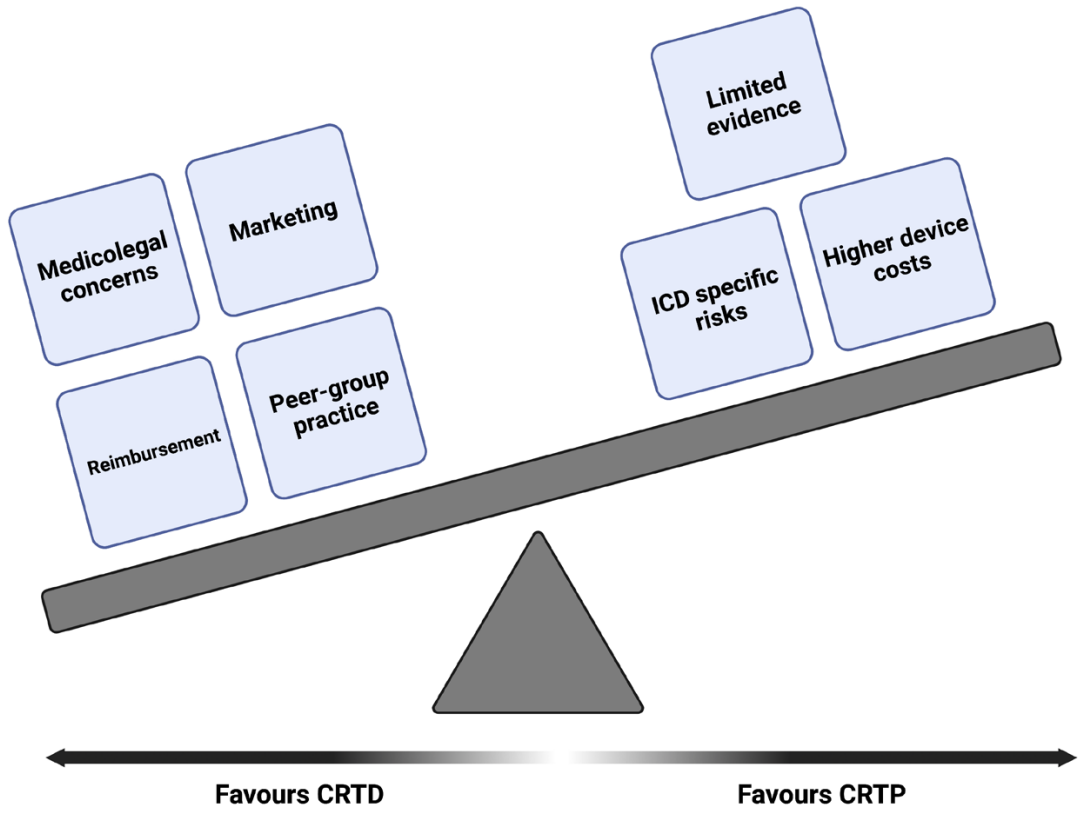
- Complications
- Battery life
- False shocks
- Inappropriate shocks
- Complications



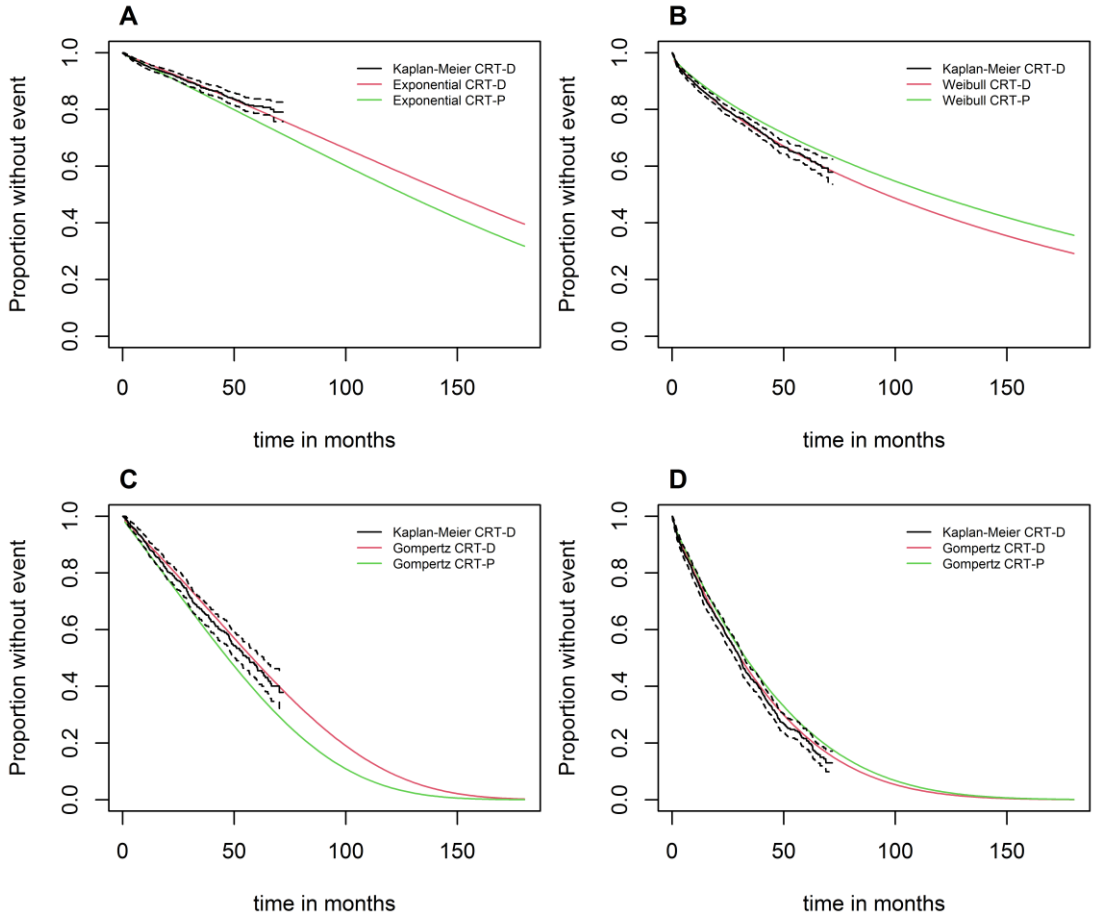
Cost Effectiveness – optimizing care for society

Balancing personalised care with societal care

Cost effectiveness of CRT-D v CRT-P in Germany



Straw, Mullens, Witte *Heart* 2022

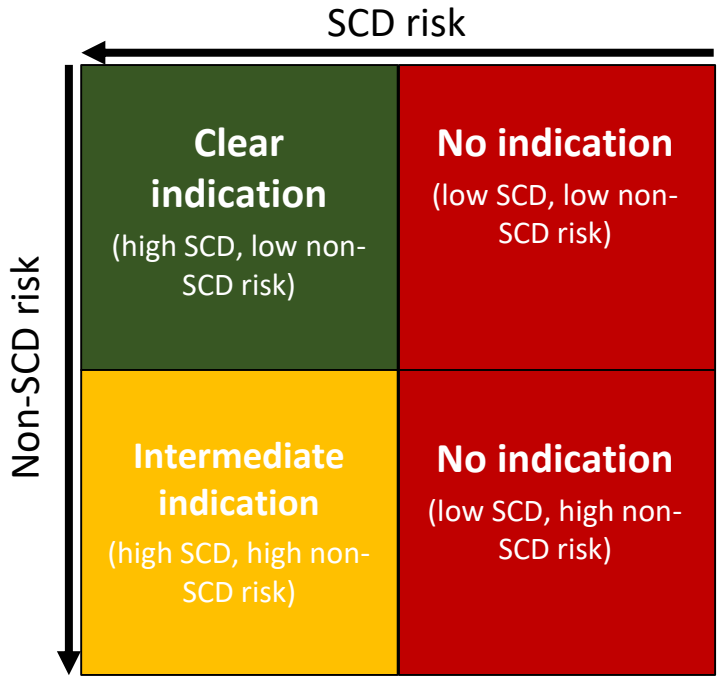


Hadwiger et al *EHJ* 2022

Prediction of SCD and total mortality – ‘benefit of ICD’

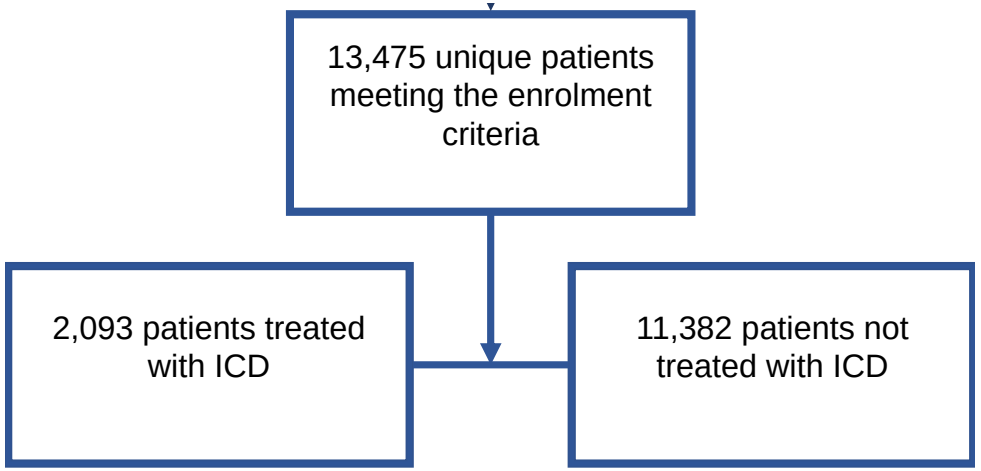
Towards personalised care:

Can we discern people at higher risk of SCD and lower risk of NCD or HF death?



Courtesy Benedikt Schräge

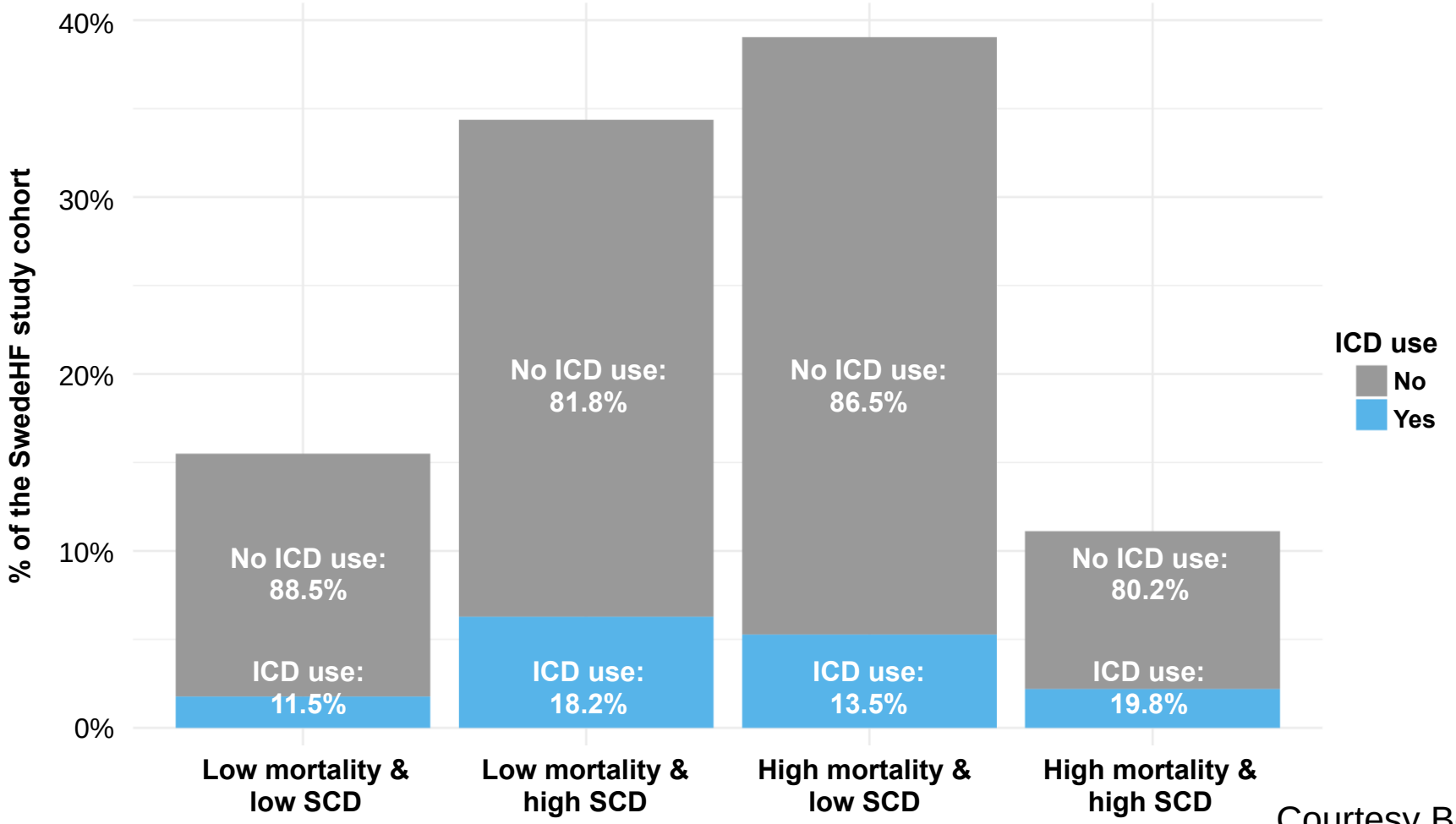
Prediction of SCD and total mortality – ‘benefit of ICD’



- Multiple imputation with chained equation to handle missing data
- Patients were stratified in 4 risk groups based on predicted all-cause mortality risk and predicted proportion of SCD
  - The *Seattle Heart Failure Model* was used to predict the mortality risk (above vs. below/equal to median)
  - The *Seattle Proportional Risk Model* was used to predict the proportion of SCD (above vs. below/equal to 45%)
- Logistic regression model to evaluate predictors of ICD use
- Cox regression model for outcome
  - Primary endpoint: 3-year all-cause mortality
  - Secondary endpoint: 3-year cardiovascular mortality

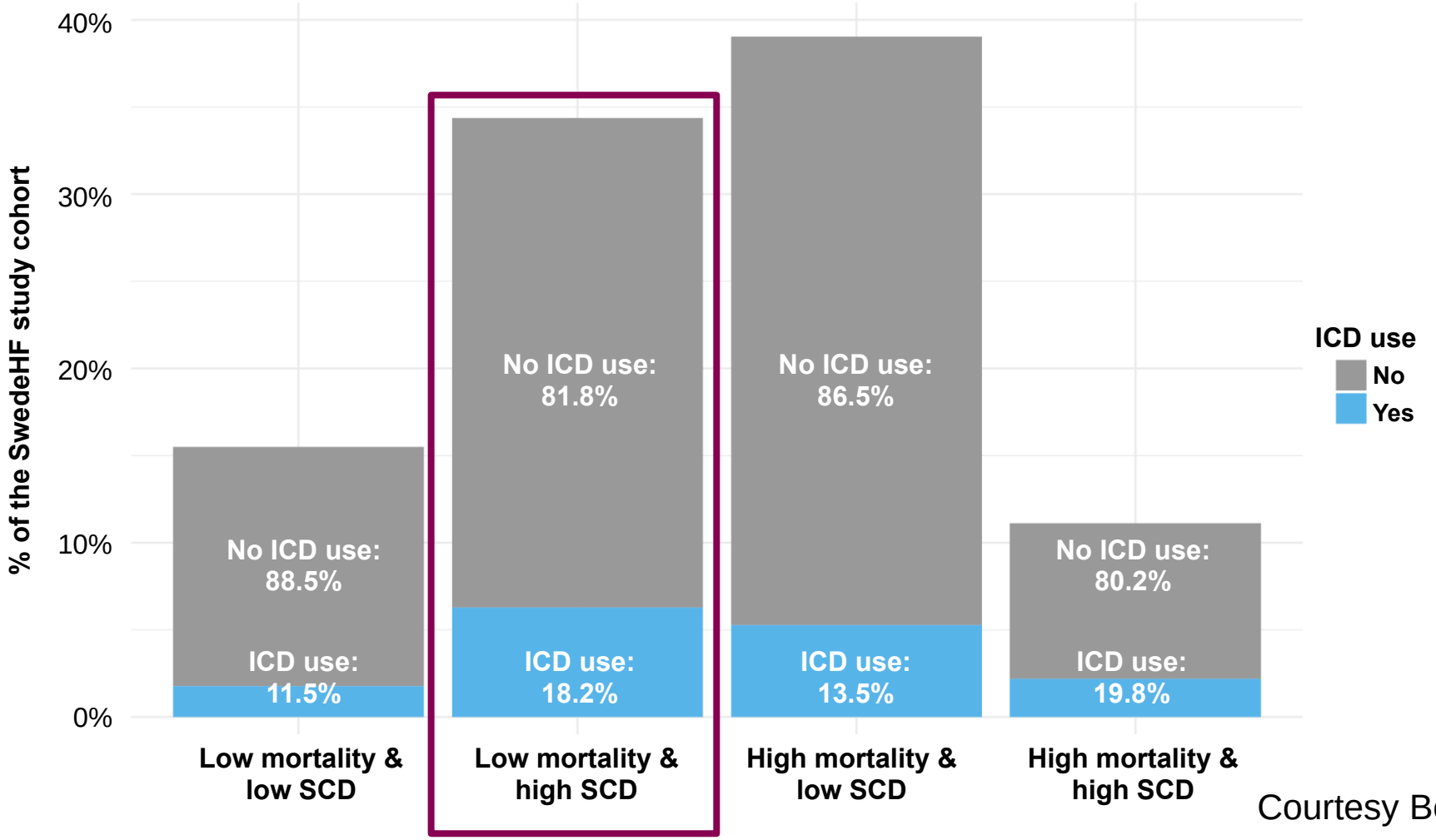
Courtesy Benedikt Schräge

Prediction of SCD and total mortality – ‘benefit of ICD’



Courtesy Benedikt Schräge

Prediction of SCD and total mortality – ‘benefit of ICD’



Courtesy Benedikt Schräge

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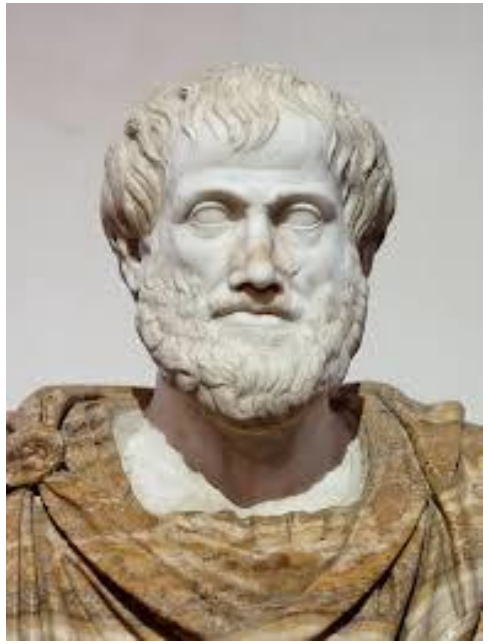
RESET CRT

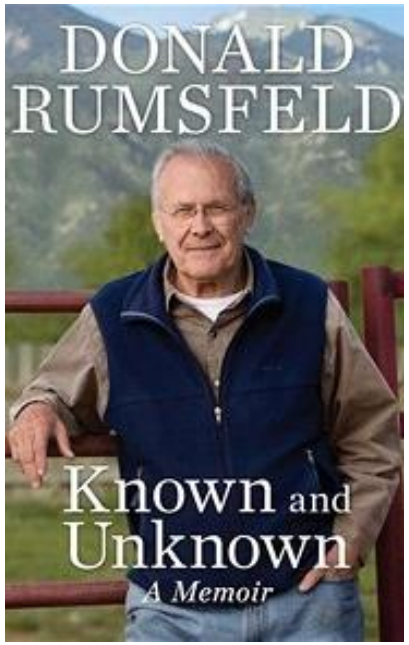
RCT of CRT-P v CRT-D (2018 with follow-up until 2024)

Target 1356 patients, currently 836 recruited



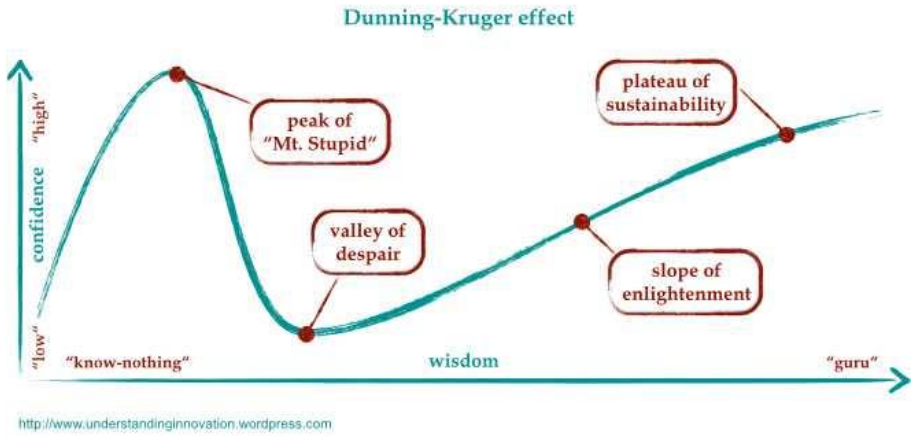
Aristotle

384-322 BC

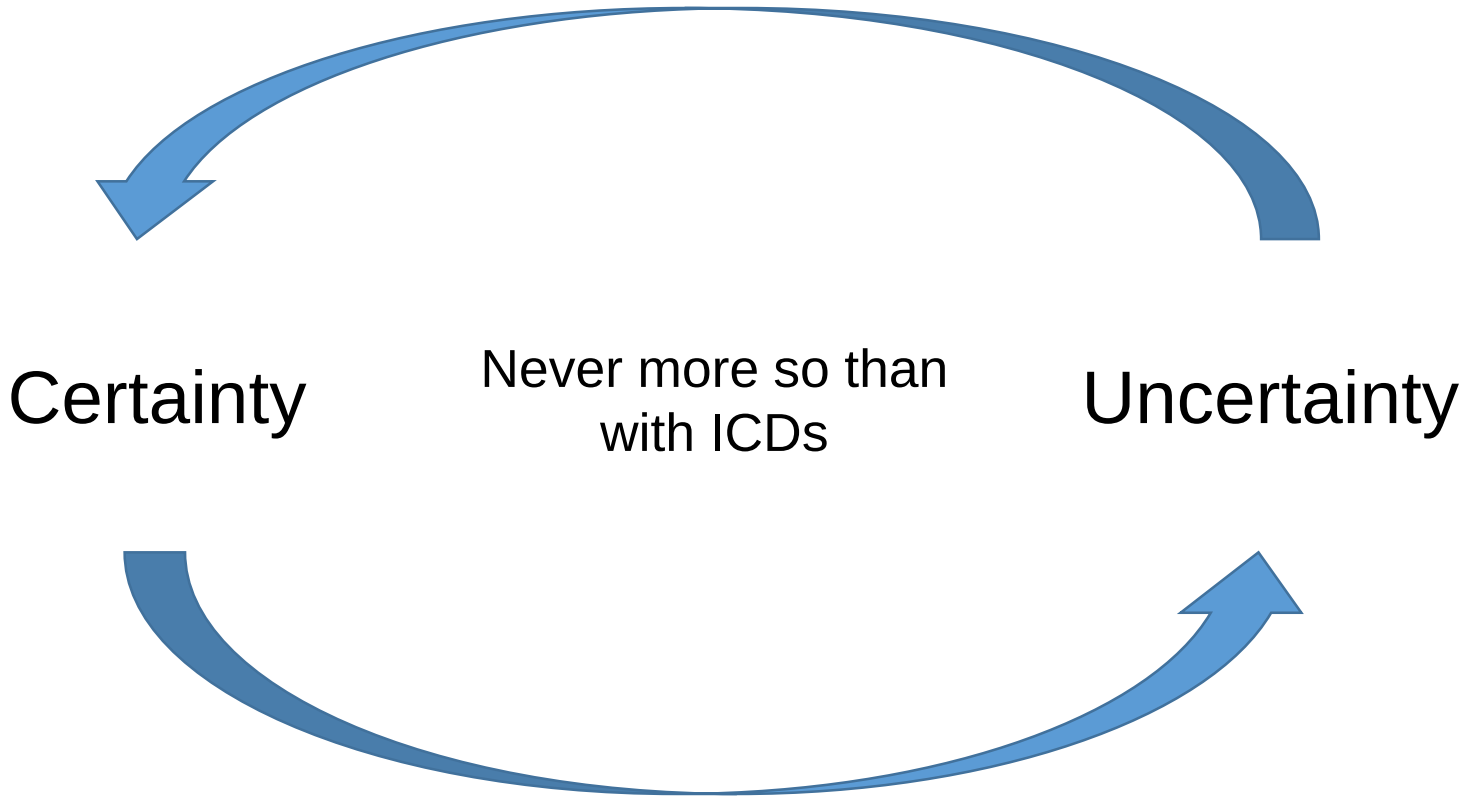


Donald Rumsfeld

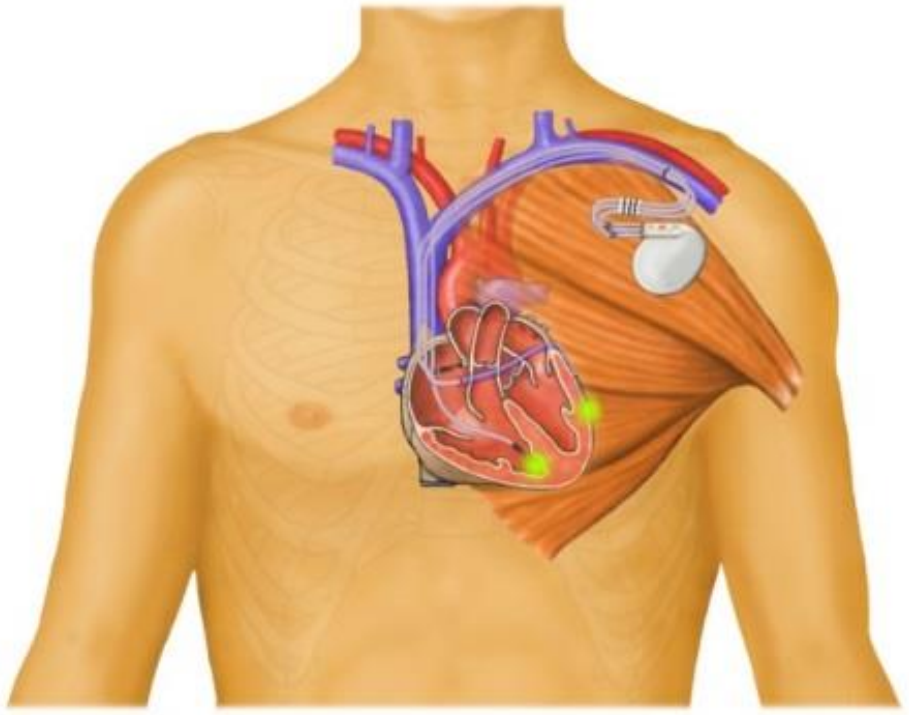
1932-2021 AD

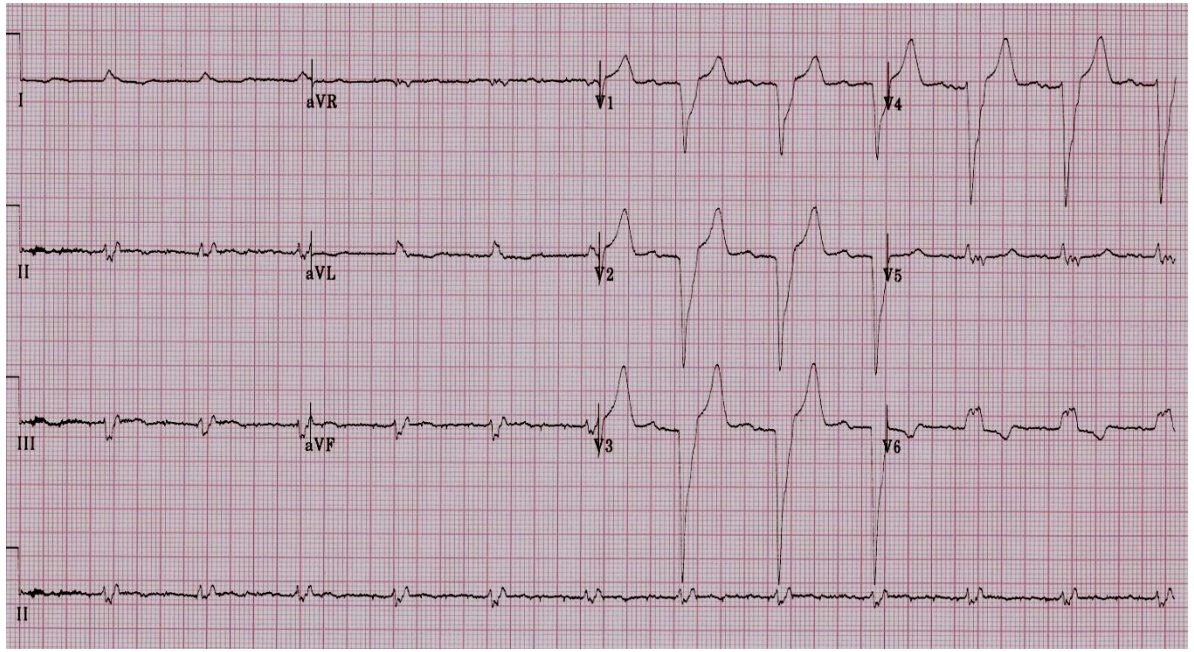


The more you know, the more you realize how much you don't know

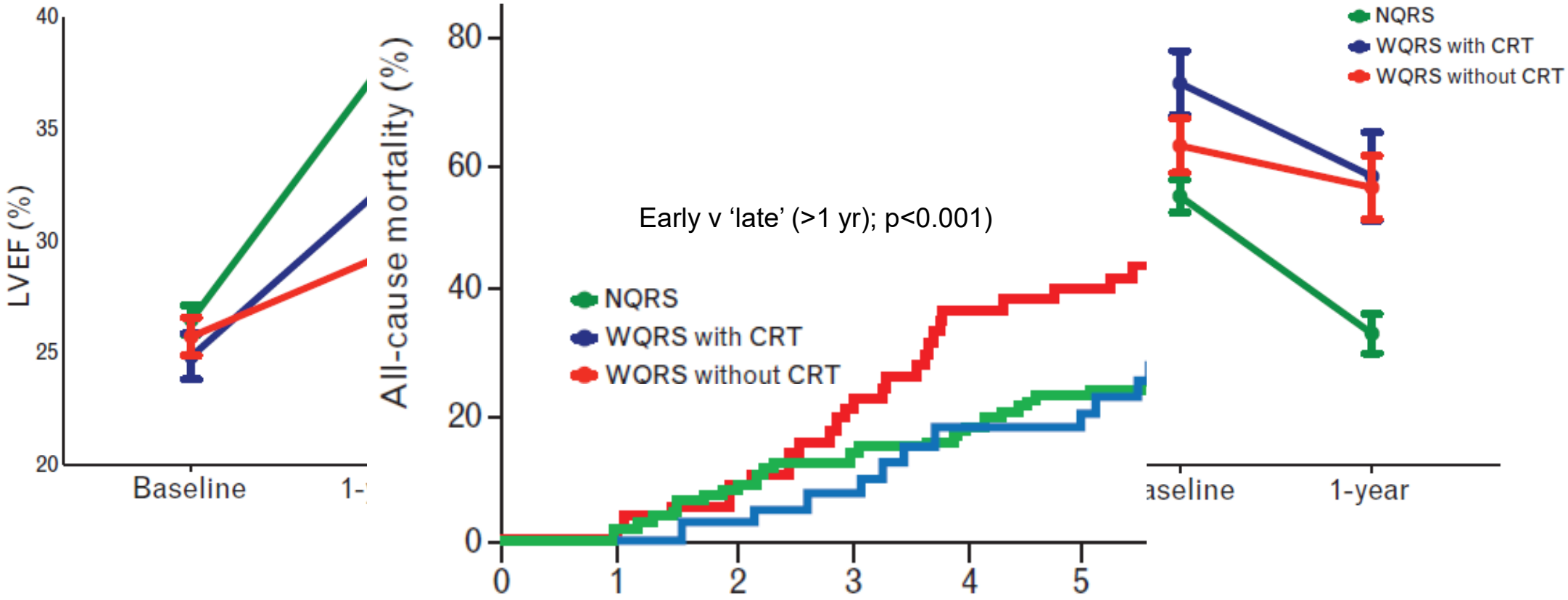


Do we still need:
Cardiac resynchronisation therapy (CRT)?





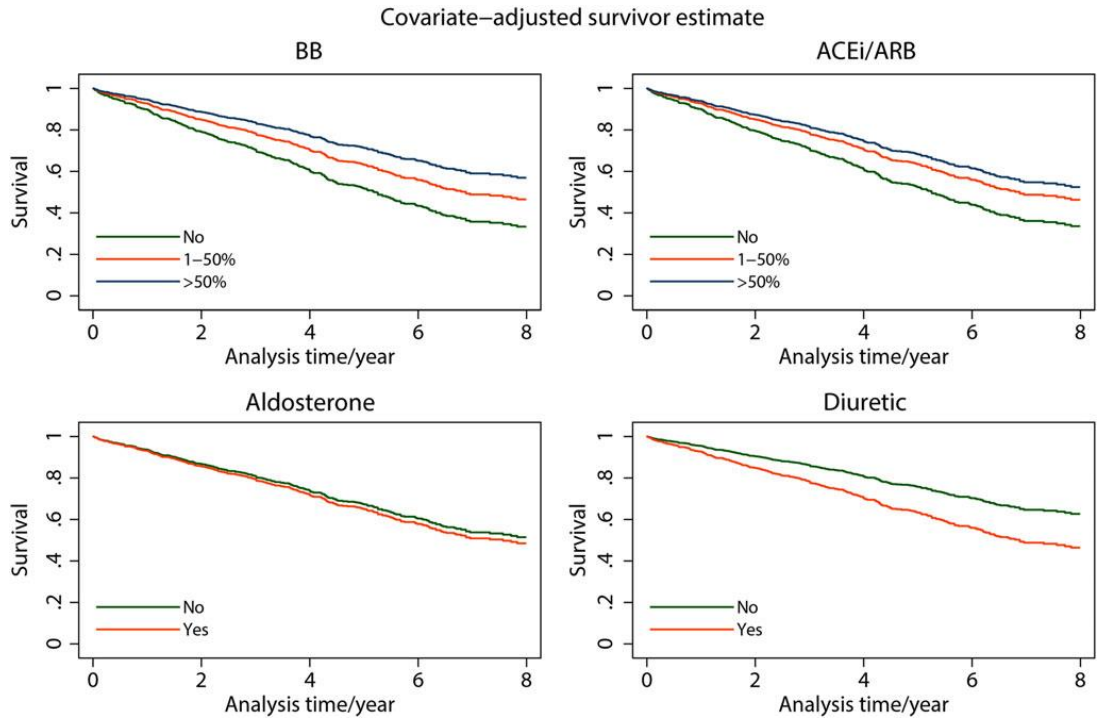
Do we still need: CRT?



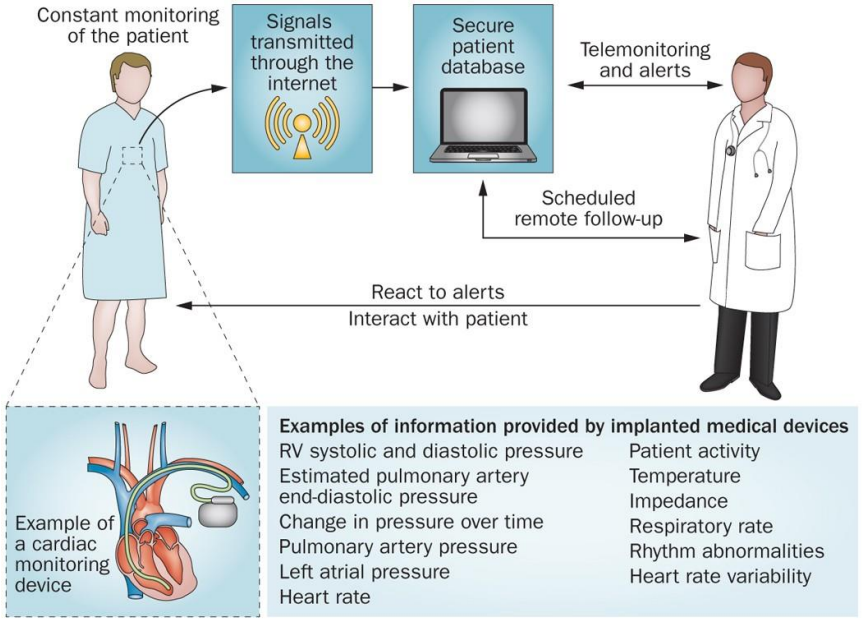
Maartens P et al. *Cardiovasc Ther* 2018
Straw S et al. *J Cardiovasc Med* 2021

Drug optimisation is facilitated

	Patients, *n* (%)			Daily dose (% of target)		
	Implantation	6 months	*P*-Value	Implantation	6 months	*P*-Value
BB	620 (75)	724 (88)	<0.001	43 (22–75)	53 (27–90)	<0.001
ACEi/ARB	747 (90)	753 (91)	0.51	74 (44–97)	78 (45–100)	0.02
Aldosterone antagonists	475 (58)	490 (59)	0.28	51 (38–65)	49 (36–58)	0.46
Loop diuretic	654 (79)	676 (82)	0.05	80 (40–120)	80 (40–140)	0.22



Witt et al *EHJ-Cardiovascular Pharmacotherapy* 2015



Do we still need: (Remote) Monitoring?

Critical points in the trajectory of a person with heart failure

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Primary Care

Symptoms

Attendance

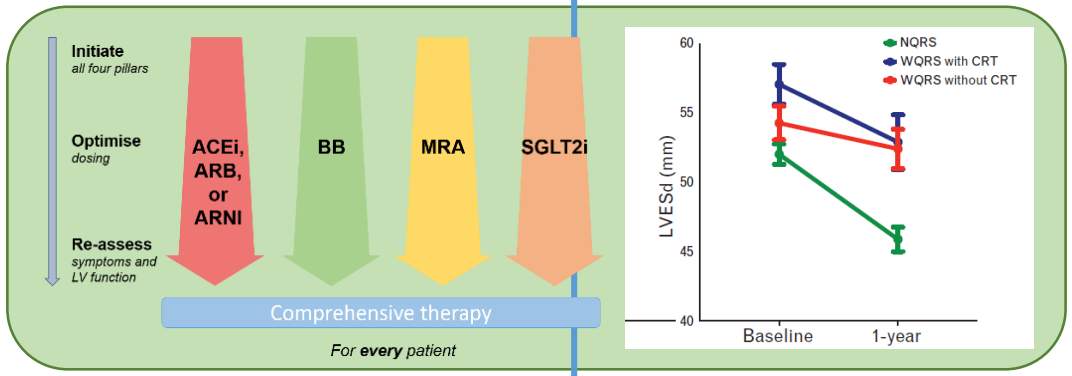
Referral

Diagnosis

HFpEF

HFrEF

Diuretics +/- SGLT2i



Progression ?

Valvular

LV function

Arrhythmia

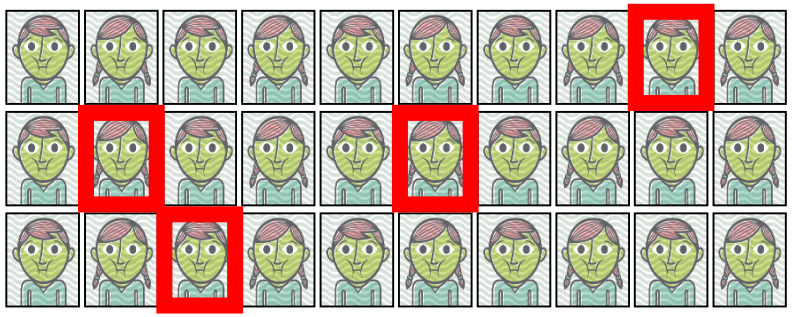
Ischaemia

Co-morbidities

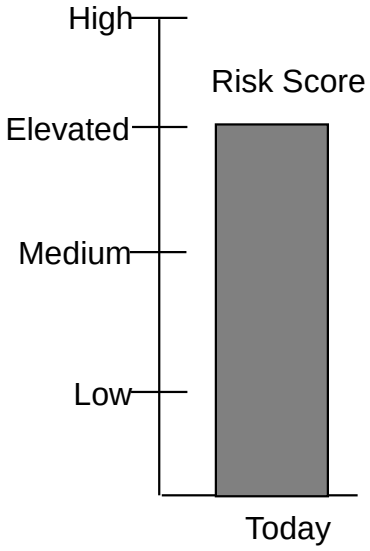
Advanced Heart Failure ?

Monitoring: who, when, what, why … ACTION

Identify



Risk of Heart Failure Event in Next 30 days



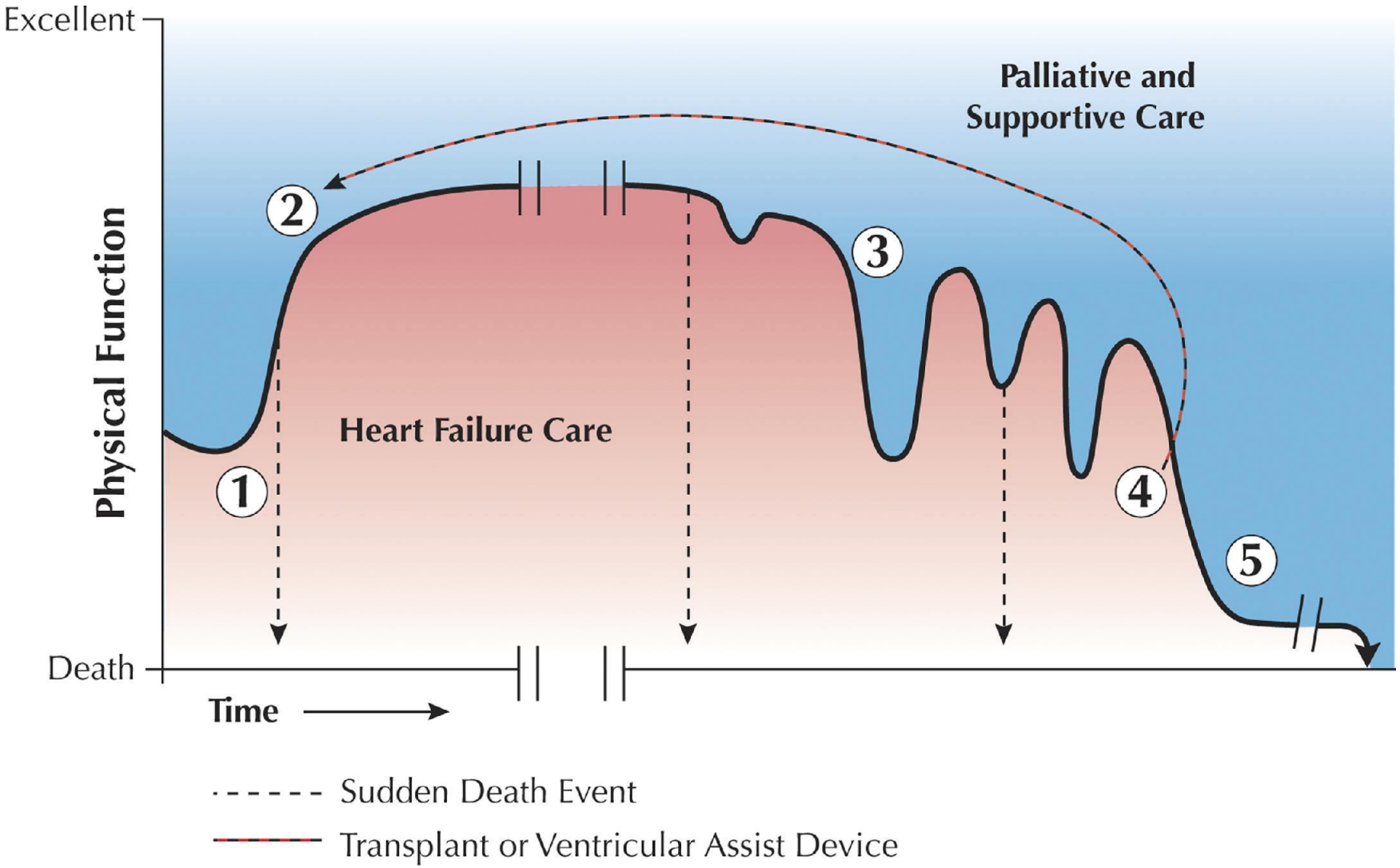
Decide

None ?? ?? ??

Today's Risk Factors

- AF burden ☒
- Ventricular rate during AF ☐
- Patient activity ☒
- Night heart rate ☐
- Heart rate variability ☐

Identify those requiring more care early

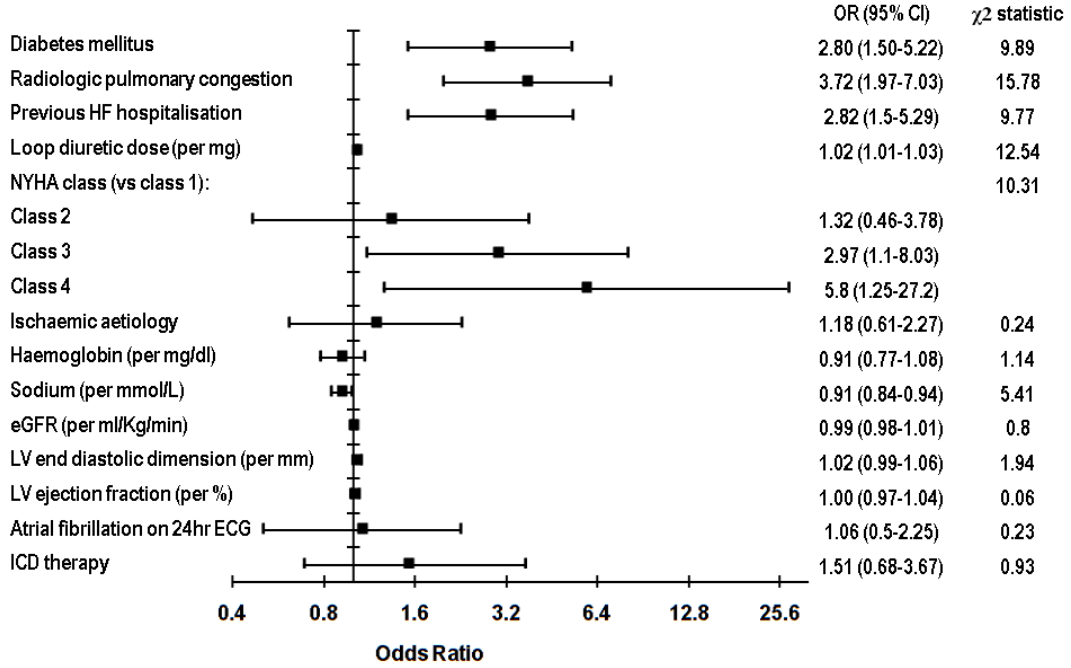


Goodlin, *JACC* 2009

Remote monitoring in heart failure

Our monitoring comfort zone….

We know who to monitor…..



Cubbon et al *Heart* 2013

…and we know (sort of) what to monitor

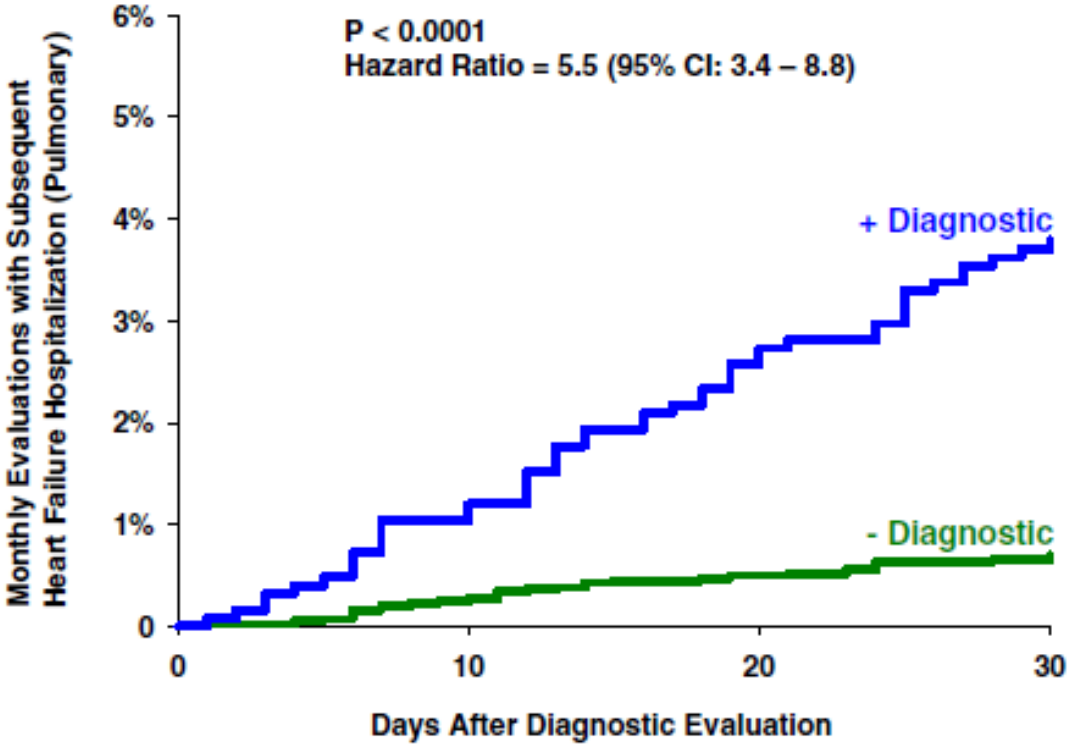
- Partners-HF
  - 694 patients with CRT-D
  - Series of variables collected monthly
  - 11.7 months (2)
  - 90 patients with 141 hospitalisations
  - Binary code requiring 2 criteria (of 8)

AF duration
Ventricular rate during AF
Fluid index
Patient activity
Night heart rate
Heart rate variability
%CRT pacing
ICD shock

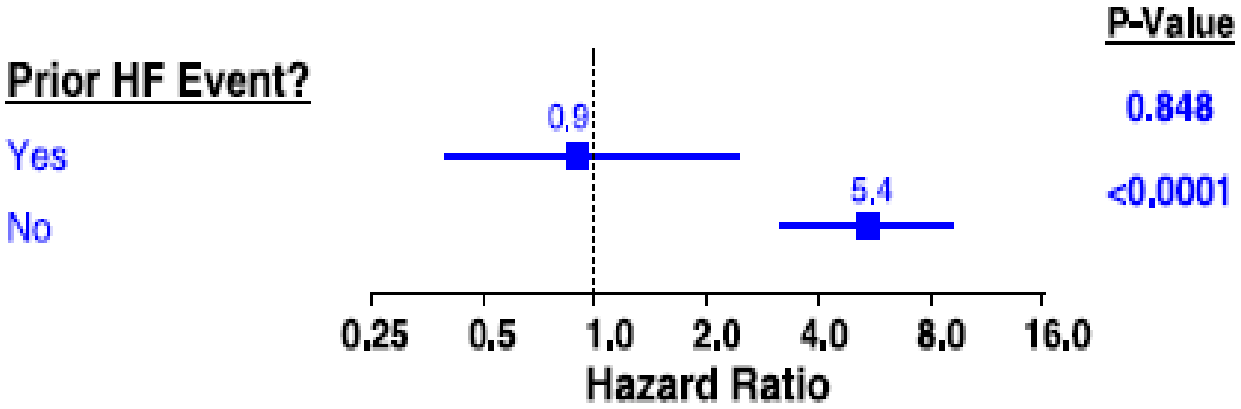
Whellan et al *JACC* 2010

…and we know that we can (sort of) predict:

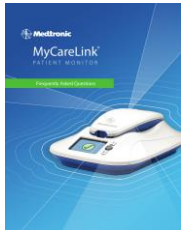
HF hospitalisation



HF re-hospitalisation



Whellan et al *JACC* 2010

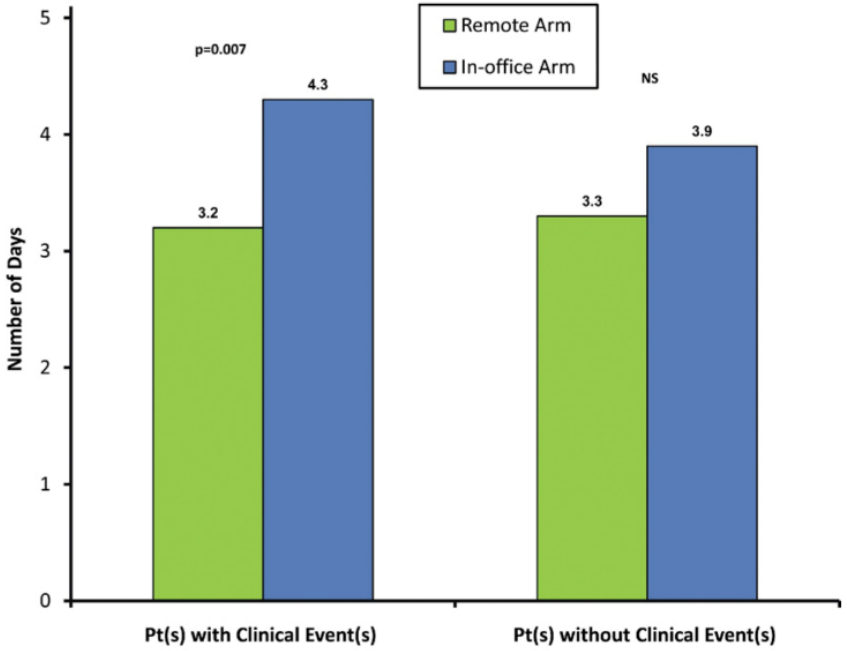


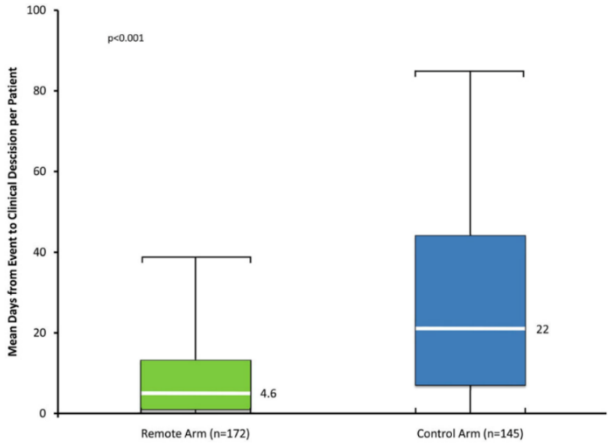
…and we think we can reduce decision time

CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) Trial

Table 1 Protocol Required Alert Programming (Clinical Events)

Alert/Clinical Event	Remote Arm	In-Office Arm
Medtronic CareLink Home Monitor	Yes	No (not provided)
Clinical management alerts		
AT/AF daily burden	Automatic clinician alert (12 h/day)	Off
Ventricular rate during AT/AF	Automatic clinician alert (120 beats/min for ≥6 h AT/AF per day)	Off
Number of shocks delivered	Automatic clinician alert (2 shocks)	Off
All therapies exhausted in a zone	Automatic clinician alert (on)	Off
Lead/device integrity alerts		
Lead impedance out of range	Automatic clinician alert + audible patient alert (nominal ranges)	Audible patient alert (nominal ranges)
VF detection/therapy off	Automatic clinician alert + audible patient alert (nominal ranges)	Audible patient alert (nominal ranges)
Low battery voltage RRT	Automatic clinician alert + audible patient alert (nominal ranges)	Audible patient alert (nominal ranges)
Excessive charge time EOS	Automatic clinician alert + audible patient alert (nominal ranges)	Audible patient alert (nominal ranges)





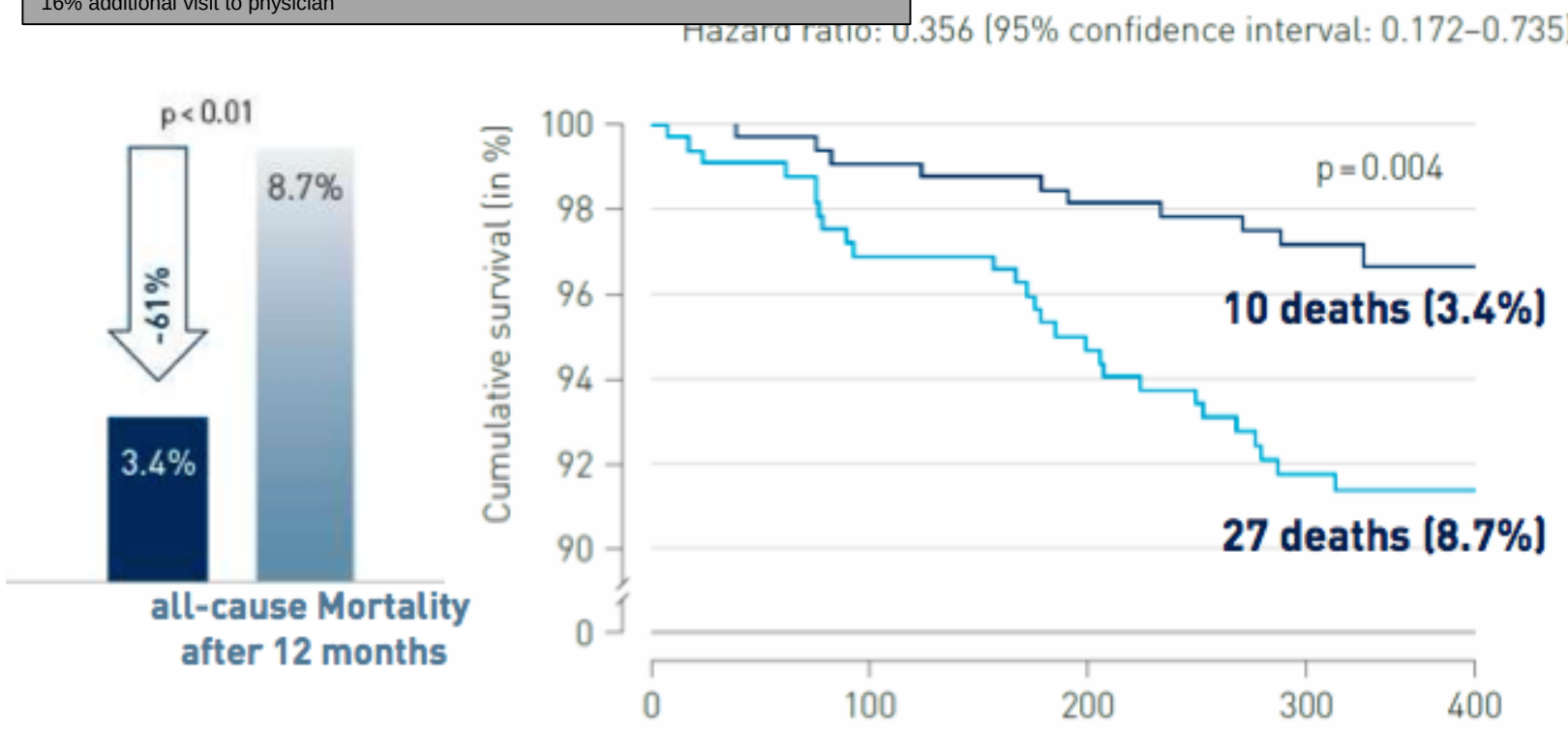
'Automatic clinician alerts were determined by clinicians to be meaningful in 62% while only 24% of routine in-office device follow-ups provided new and meaningful information'

Crossley G et al. J Am Coll Cardiol 2011;57:1181–9)

Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial

*Gerhard Hindricks, Milos Taborsky, Michael Glikson, Ullus Heinrich, Burghard Schumacher, Amos Katz, Johannes Brachmann, Thorsten Lewalter, Andreas Goette, Michael Block, Josef Kautzner, Stefan Sack, Daniela Husser, Christopher Piorkowski, Peter Søgaard, for the IN-TIME study group**

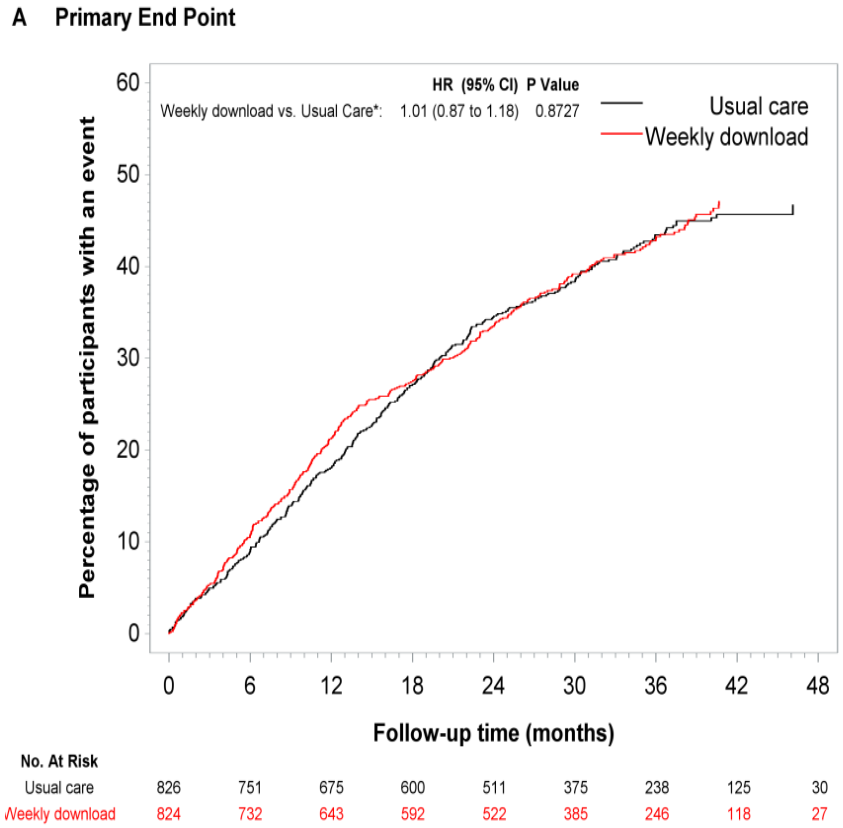
2,27 patient contacts / year
1.4 clinical events / year (AF / < 80% CRT / VT-shock / other)
13% drug incompliance
16% additional visit to physician



Hindricks G. et al Lancet 2014;384:583-90

Despite this background: REM-HF study

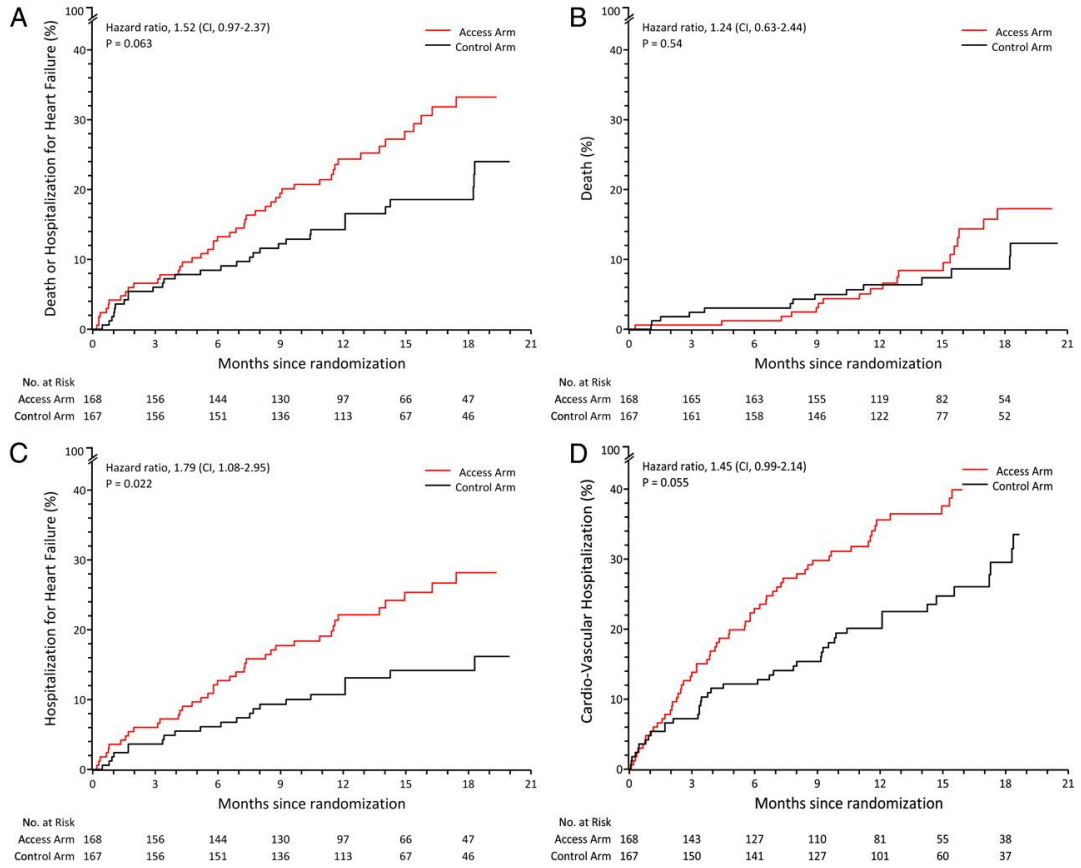
	RM N=824	Usual care N=826
Age (mean ± SD) years	69.5±10.3	69.5±10.0
Male %	86	86
NYHA Class II III IV	 585 (71%) 238 (29%) 1 (0.1%)	 561 (68%) 263 (32%) 2 (0.2%)
LVEF (mean ± SD)(%)	29.9 ± 10.2	30.0 ± 9.8
Documented coronary artery disease	563 (69%)	548 (67%)
Diabetes mellitus	208 (25%)	225 (27%)
History of atrial fibrillation	339 (41%)	338 (41%)
Type of CIED ICD CRT-D CRT-P	 275 (33%) 442 (54%) 107 (13%)	 276 (33%) 438 (53% 112 (14%)



Morgan et al; *Eur Heart J* 2017

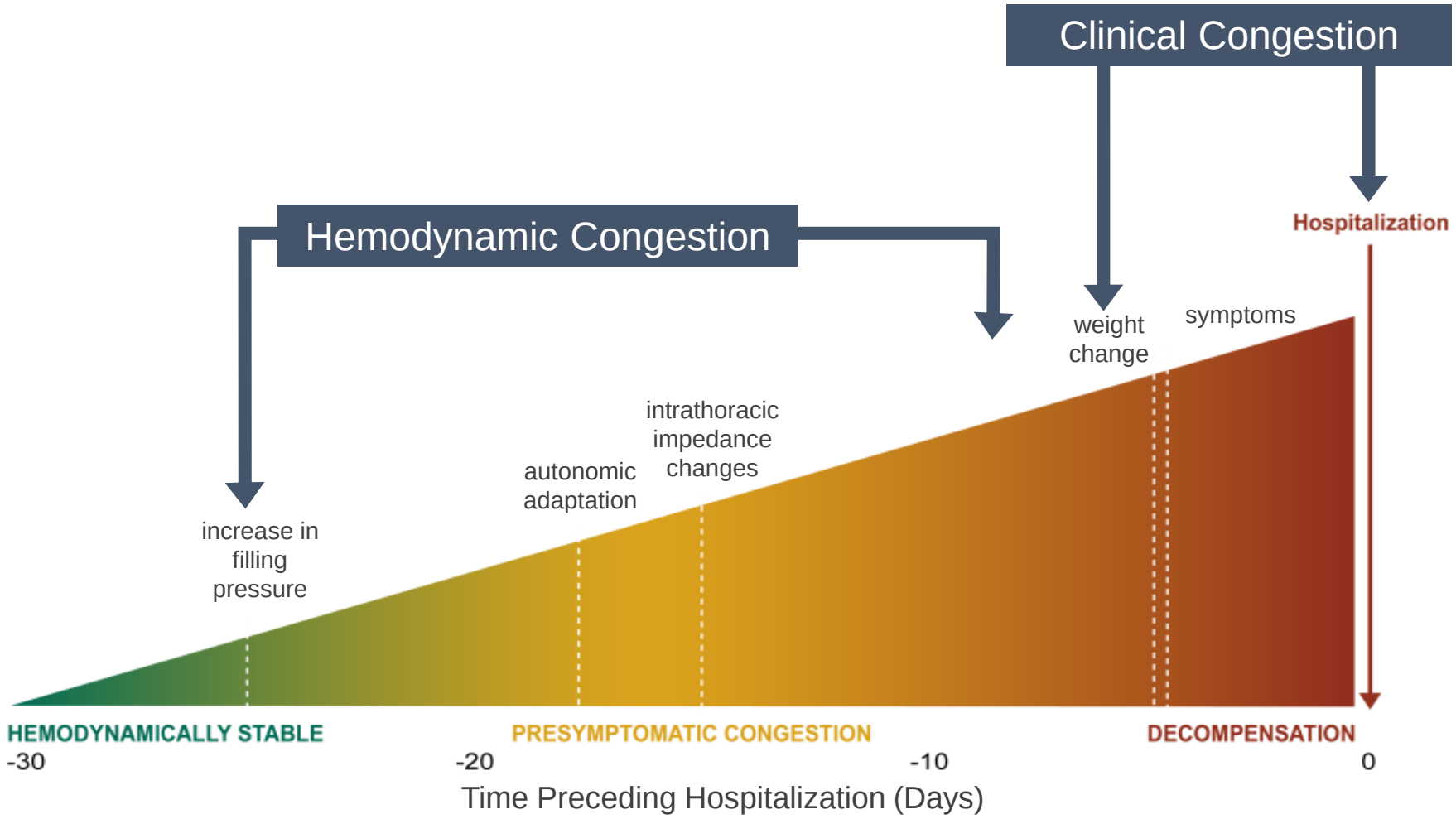
Not without harm

- DOT-HF
  - 335 patients
  - Implanted devices, free 100% monitoring
  - Intrathoracic impedance and other variables with audible alert
  - Increased hospitalisations and out-patient visits,
  - No difference in outcome



Van Veldhuisen et al *Circ* 2011

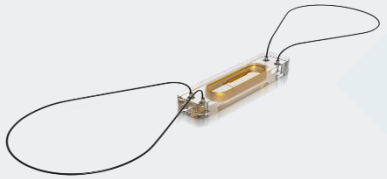
Maybe it’s not enough time or enough certainty? How to buy even more time or more certainty



* Graph adapted from Adamson, P. B. (2009). Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: New insights from continuous monitoring devices. Current Heart Failure Reports, 6(4), 287-92. https://www.ncbi.nlm.nih.gov/pubmed/19948098

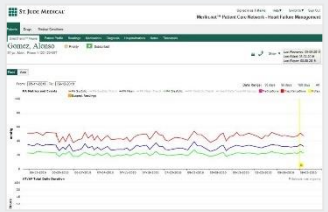
CardioMEMS™ HF System for the Management of HF

PULMONARY ARTERY PRESSURE SENSOR



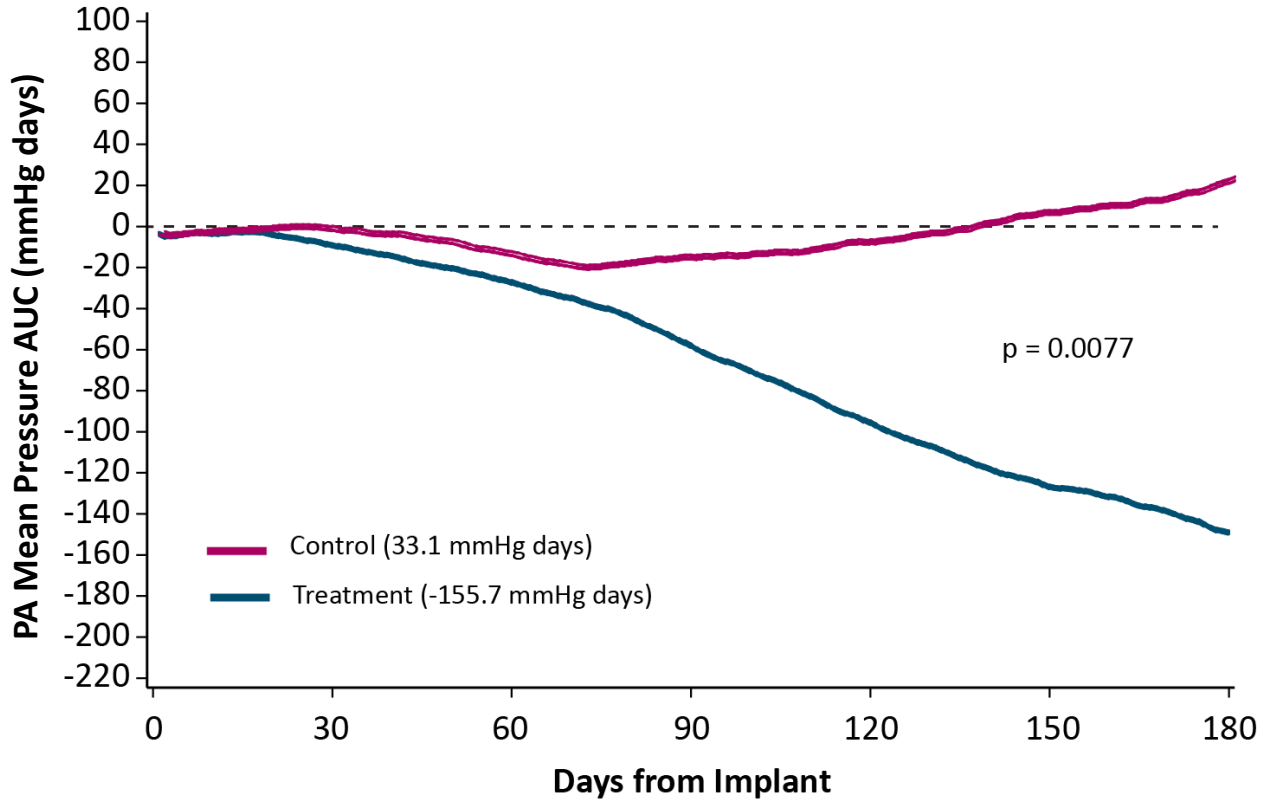
PATIENT ELECTRONICS SYSTEM

MERLIN.NET™ PCN



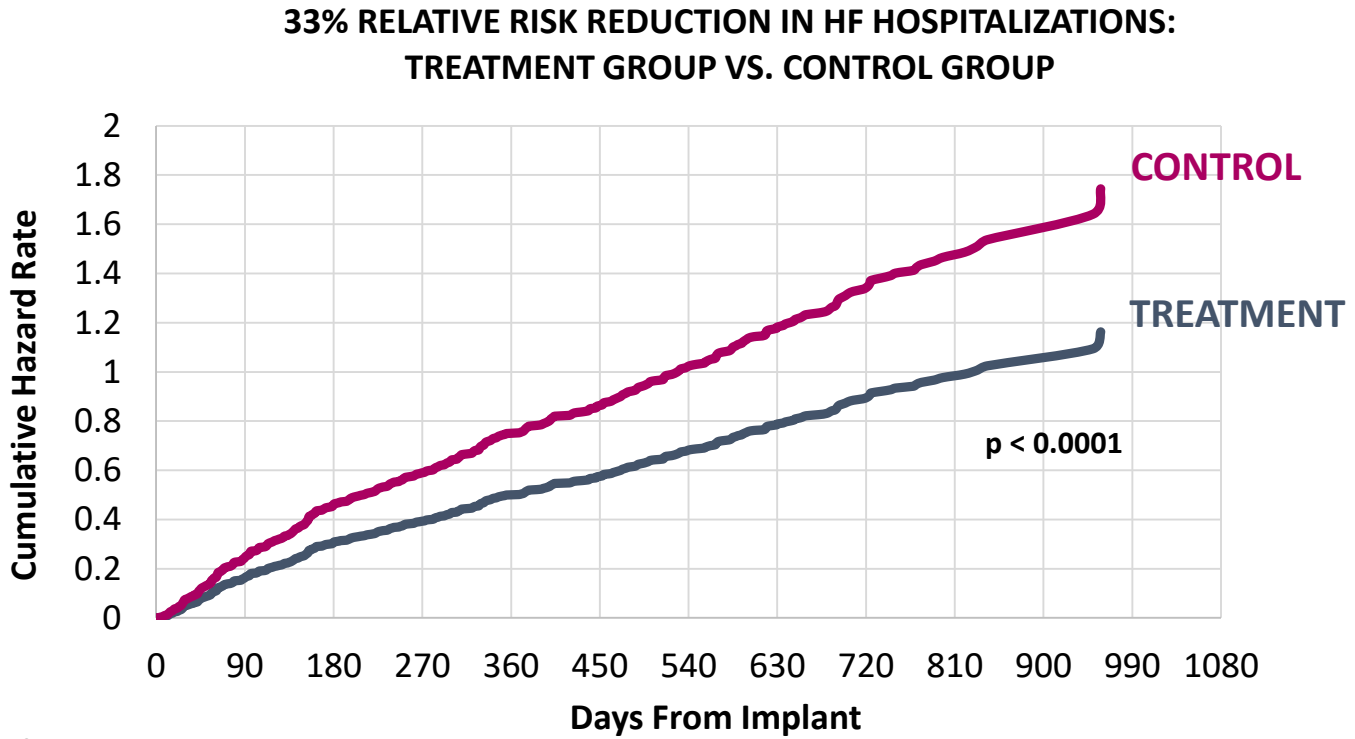
TARGET LOCATION FOR PA PRESSURE SENSOR

Monitoring with CardioMEMS™ HF System Leads to Reduction in Mean PA Pressure from Baseline



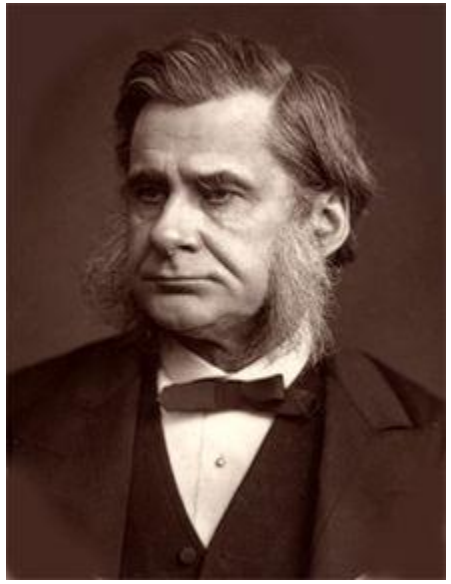
SECONDARY ENDPOINT: Targeting PA pressures and titrating medications results in reduction of mean PA pressure over time.

Primary Efficacy Endpoint Met with Significantly Reduced Heart Failure Hospitalization



No. at Risk												
CONTROL	280	267	254	241	210	175	131	101	62	27	12	5	0
TREATMENT	270	262	246	235	197	164	125	105	75	38	8	3	0

Abraham W, et al. *Lancet*, 2016



Thomas Huxley 1825-1895

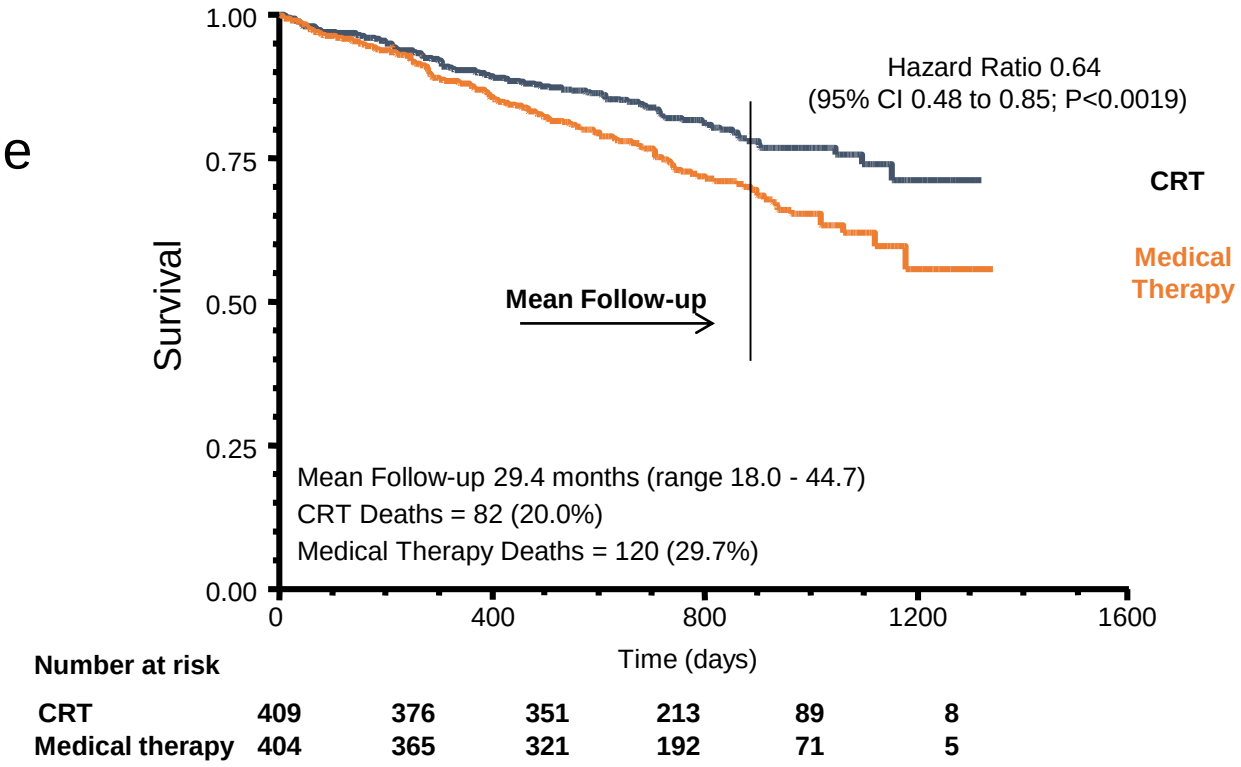
‘the deepest sin against the human mind is to believe things without evidence’

Do we still need:

‘Response’

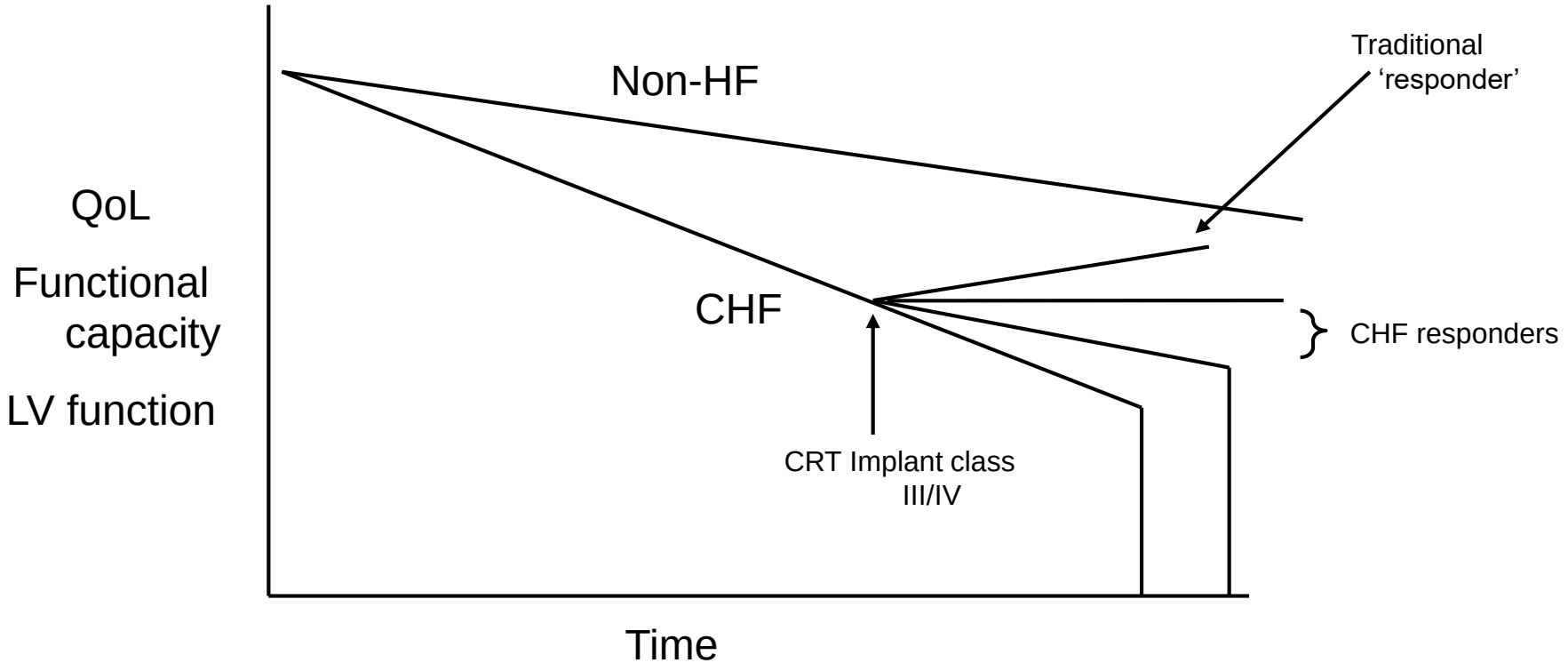
Population level ‘response’

- QRS >150ms (or 120ms with simple dyssynchrony)
- EF<35%
- NYHA class III / IV



Cleland et al. *NEJM* 2005

Challenges of individual ‘response’: the ‘Disease Modification’ approach



Cubbon and Witte *BMJ 2009*
Mullens *et al EJHF* 2021

So… why do we care about response?

Decision regarding indication?

ESC European Society of Cardiology
European Heart Journal (2021) **00**, 1–94
doi:10.1093/eurheartj/ehab364

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2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

Developed by the Task Force on cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology (ESC)

With the special contribution of the European Heart Rhythm Association (EHRA)

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Eur Heart J 2021; **12:**1-94

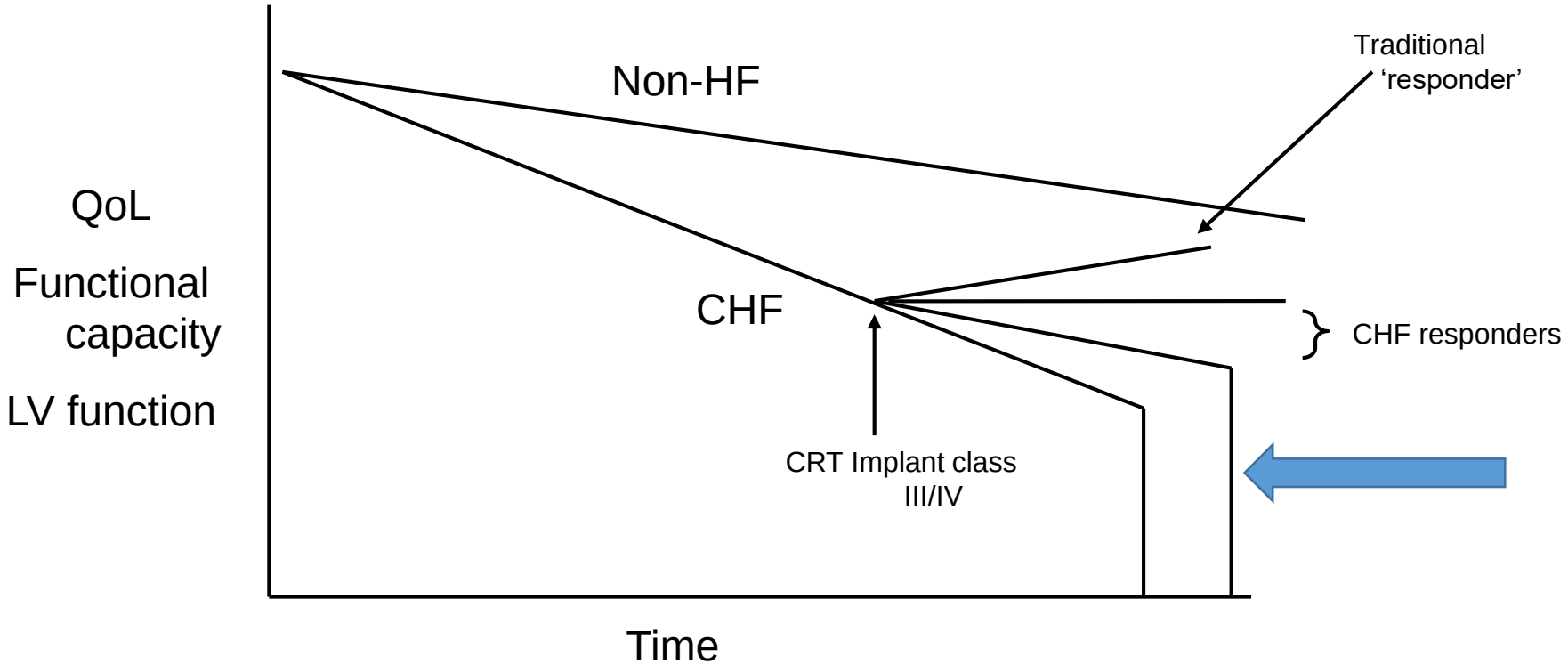
Recommendations	Class	Level
LBBB QRS morphology		
CRT is recommended for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.	I	A
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.	IIa	B
Non-LBBB QRS morphology		
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.	IIa	B
CRT may be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.	IIb	B
QRS duration		
CRT is not indicated in patients with HF and QRS duration <130 ms without an indication for RV pacing.	III	A

So… why do we care about response?

Decision regarding indication?

Decision regarding post implant management

Challenges of individual ‘response’: the ‘Disease Modification’ approach



Cubbon and Witte *BMJ 2009*
Mullens *et al EJHF* 2021

Critical points in the trajectory of a person with heart failure

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Primary Care

Symptoms

Attendance

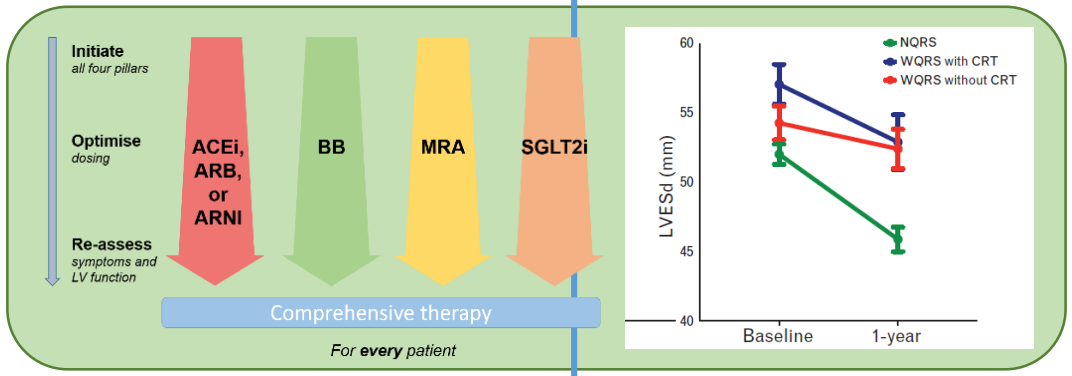
Referral

Diagnosis

HFpEF

HFrEF

Diuretics +/- SGLT2i



Progression ?

Valvular

LV function

Arrhythmia

Ischaemia

Co-morbidities

Advanced Heart Failure ?

What is advanced heart failure and how do we spot it?

All of the following:

1. Severe and persistent symptoms of heart failure (NYHA III)
2. Severe cardiac dysfunction (one of)
    - LVEF≤30%
    - RV failure
    - Severe non-operable valve or congenital abnormalities or congenital
    - Persistently high NT-pro-BNP
3. Functional evidence of cardiac dysfunction (one of)
    - Recurrent congestion or pulmonary oedema requiring i.v. diuretics
    - Low output state requiring positive inotropes
    - Malignant arrhythmia causing >1 unplanned hospital visit in 12 months
4. Severe impairment of exercise capacity (<300m or <12ml/kg/min or <50% expected)

McDonagh T et al. *EHJ* 2021;**42:**3599–3726

So… we ***do*** care about response

(but not for decision to implant)

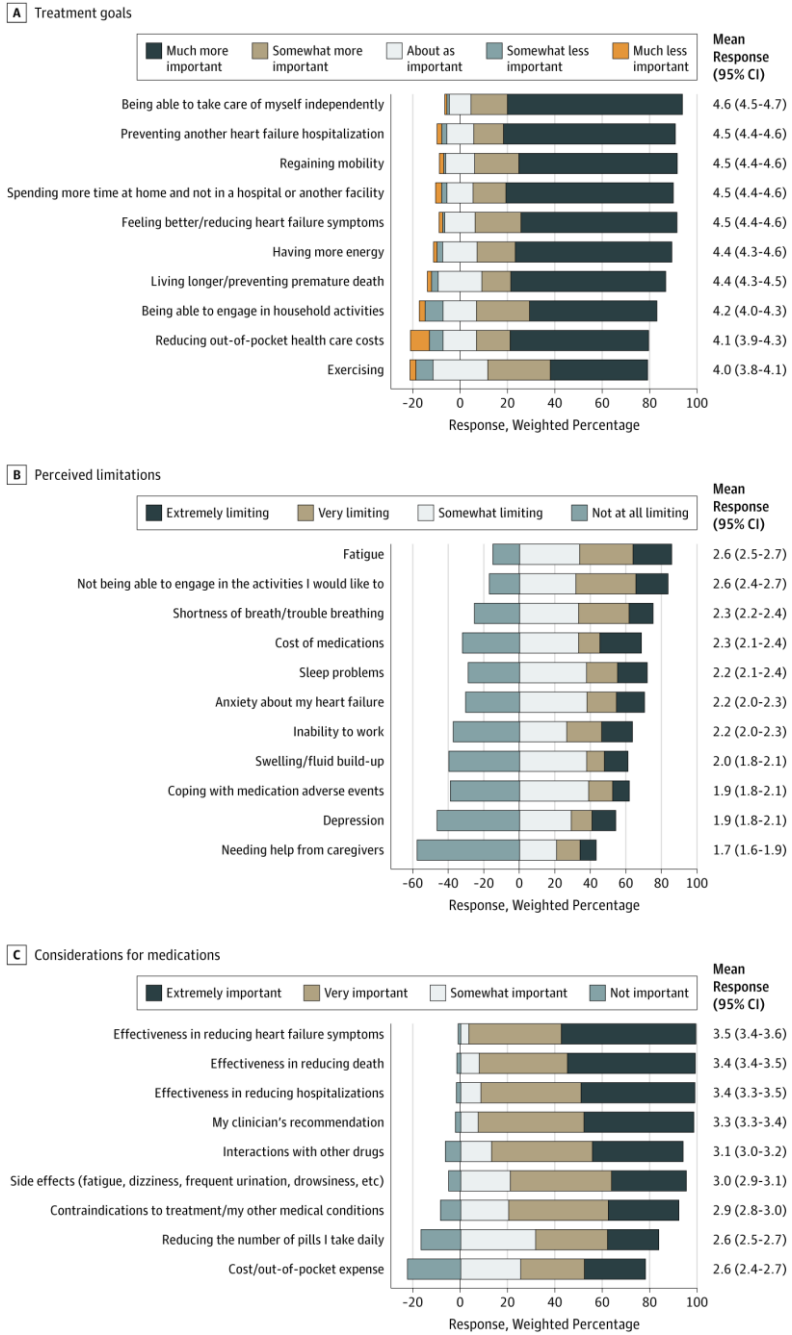
Decision regarding post implant management

- When and what do we assess?
- When do we do what to whom?

Assessing response *following CRT*

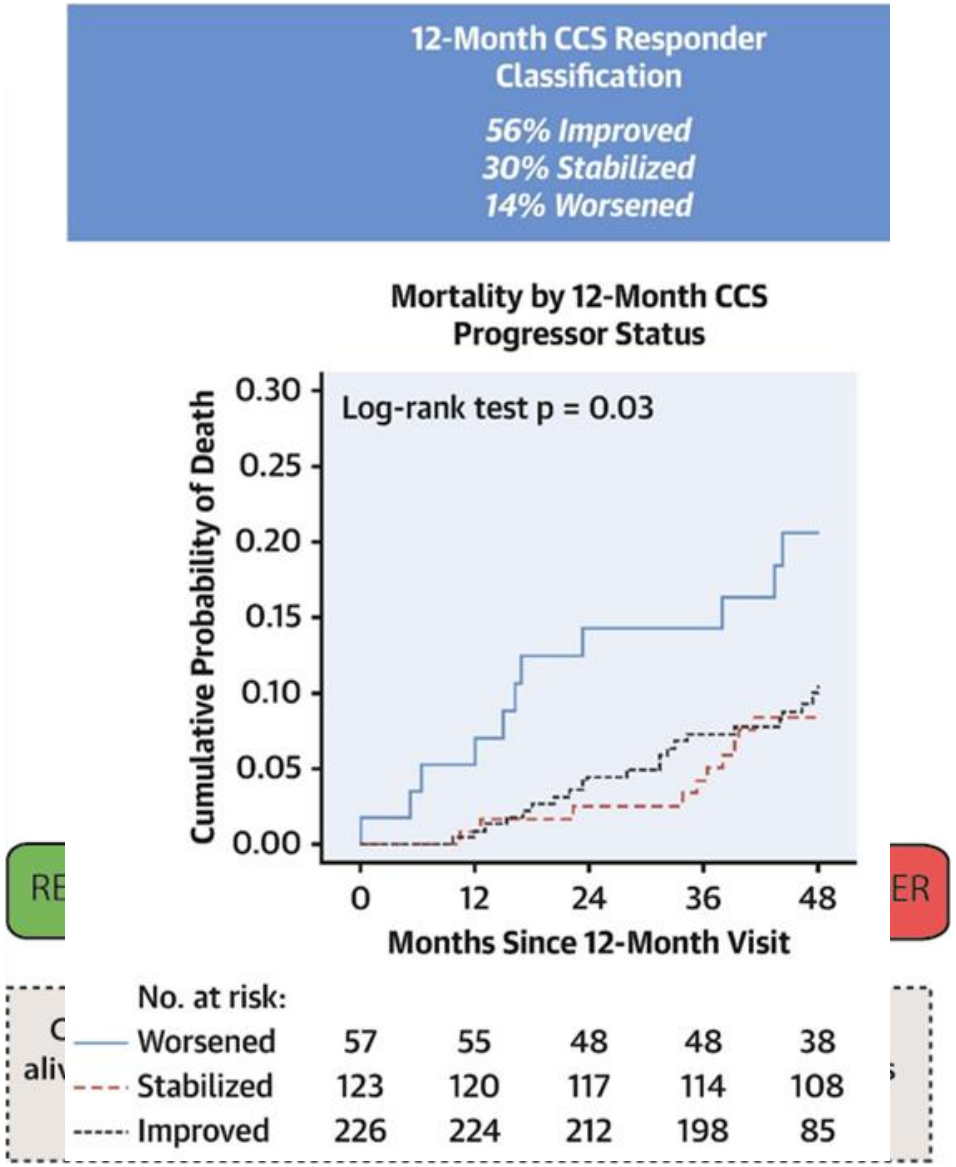
Systems/payers/doctors	**Patients/doctors**
Death	Symptoms
Hospitalisation	Quality of life
LV structure and function	Functional capacity
	Hospitalisation
Cost effectiveness	Clinical effectiveness

Symptom control consistently features more highly than survival



Stansky et al. *JAMA Cardiol* 2019

Response to CRT: a hierarchical set of clinical criteria

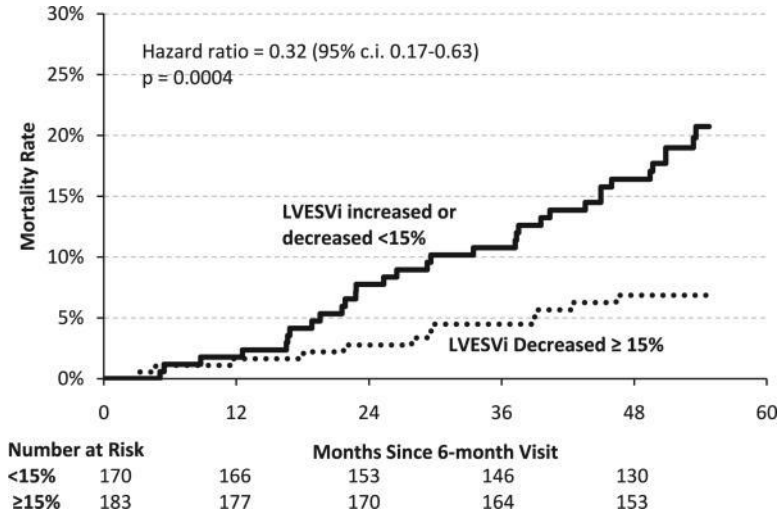


CLINICAL RESPONSE TO CRT

A responder is defined as a patient who at one year is still alive, is free from any HF event, and who ***improves*** NYHA class, global patient assessment or Quality of Life.

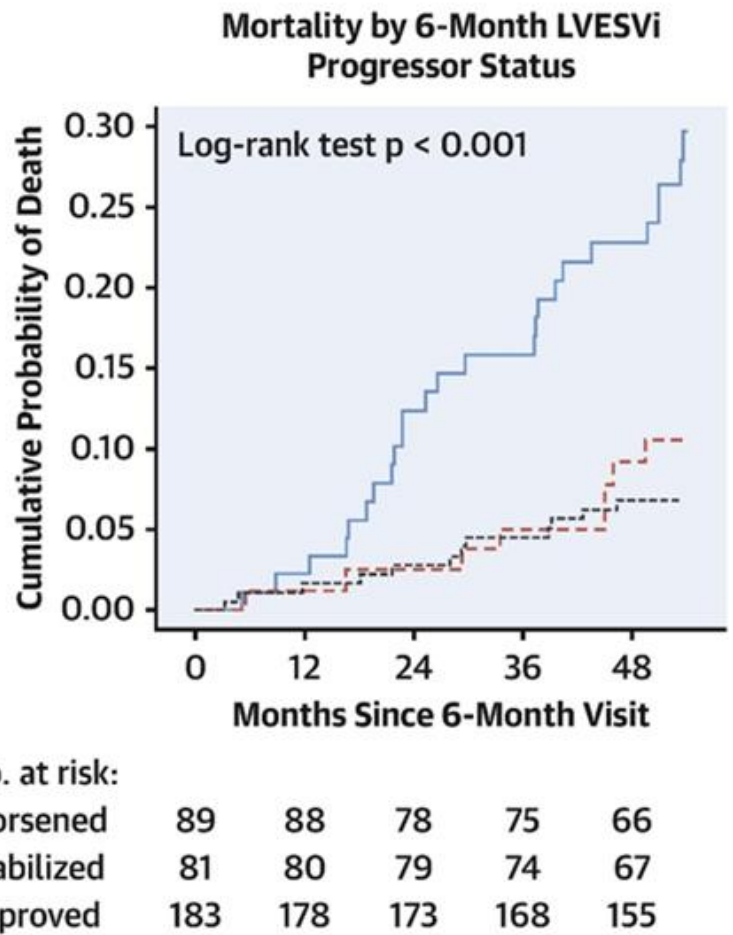
Mullens et al. *EJHF* 2020
Gold et al. *JACC EP* 2021

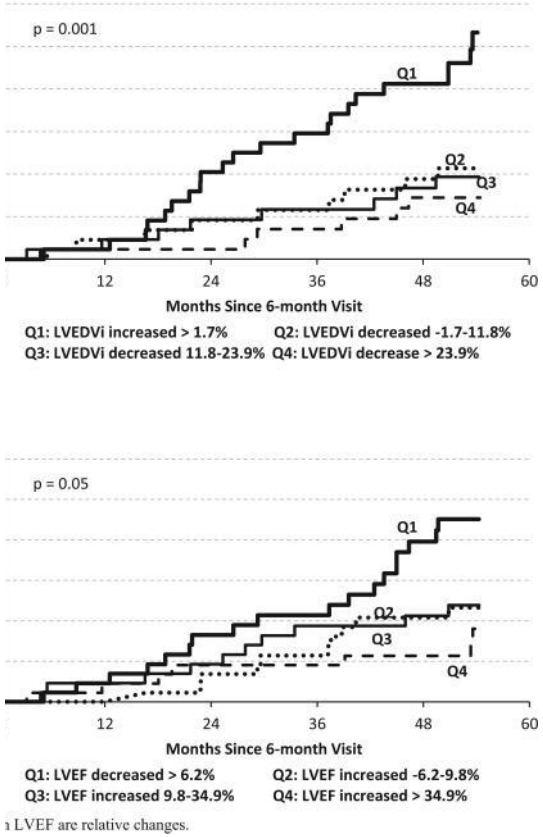
Remodelling (lack of it) at 6m predicts outcomes



6-Month LVESVi Responder Classification

52% Improved
23% Stabilized
25% Worsened





Gold et al. *Heart Rhythm* 2015
Gold et al. *JACC EP* 2021

Remodelling *or* symptoms?

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 74, NO. 21, 2019

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Evaluation, Management, and Outco[B] of Patients Poorly Responsive to Cardiac Resynchronization Device Th

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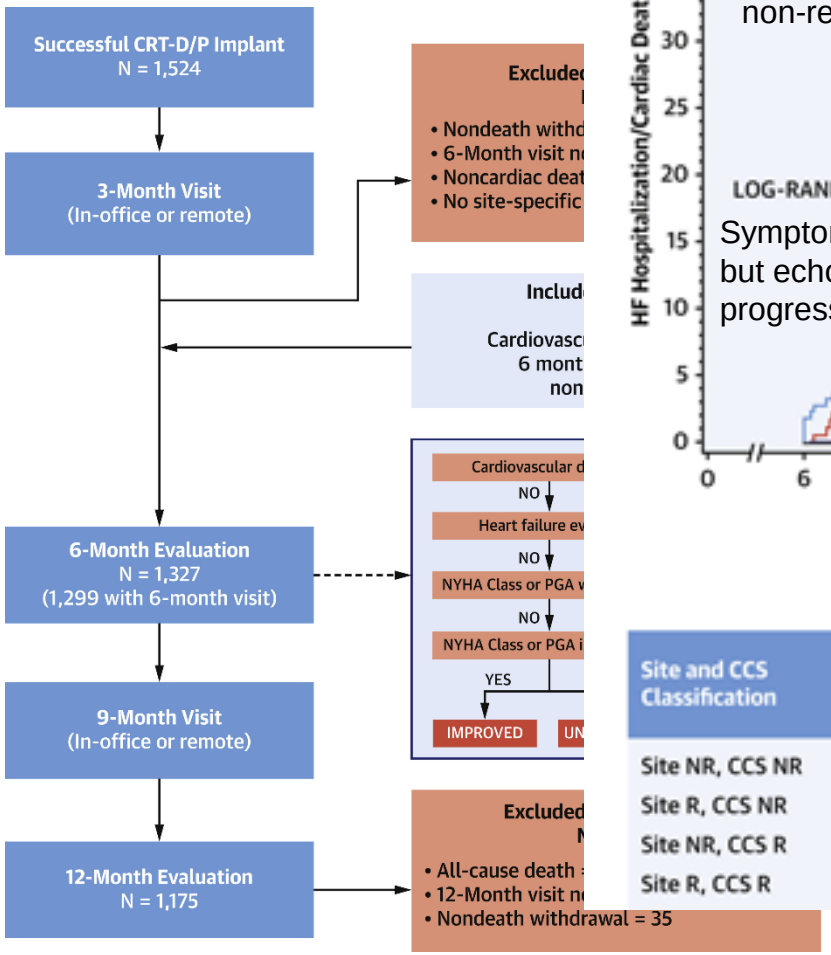
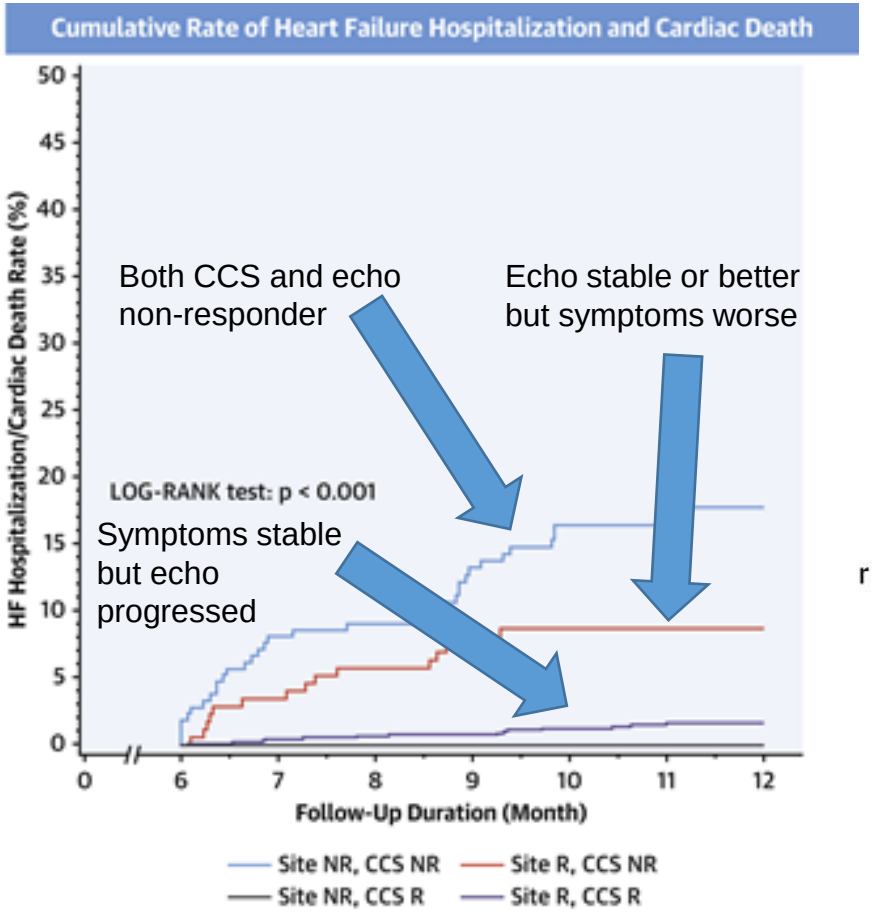
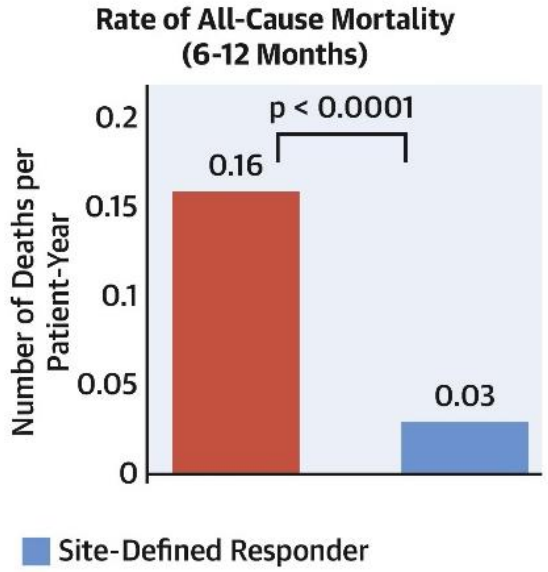
Mariarosa Costanzo, MD,[f] Anil Saxena, MD,[g] Lixian Sun, MS,[h] Michael R. Gold, MD, PhD,[i] Ja
John Gill, PhD,[h] Angelo Auricchio, MD, PhD[k]





Site and CCS Classification	6 Months n at Risk (n of events)	9 Months n at Risk (n of events)	12 Months n at Risk (n of events)
Site NR, CCS NR	210 (4)	166 (27)	79 (35)
Site R, CCS NR	175 (0)	156 (14)	77 (15)
Site NR, CCS R	28 (0)	28 (0)	16 (0)
Site R, CCS R	886 (0)	844 (7)	435 (14)



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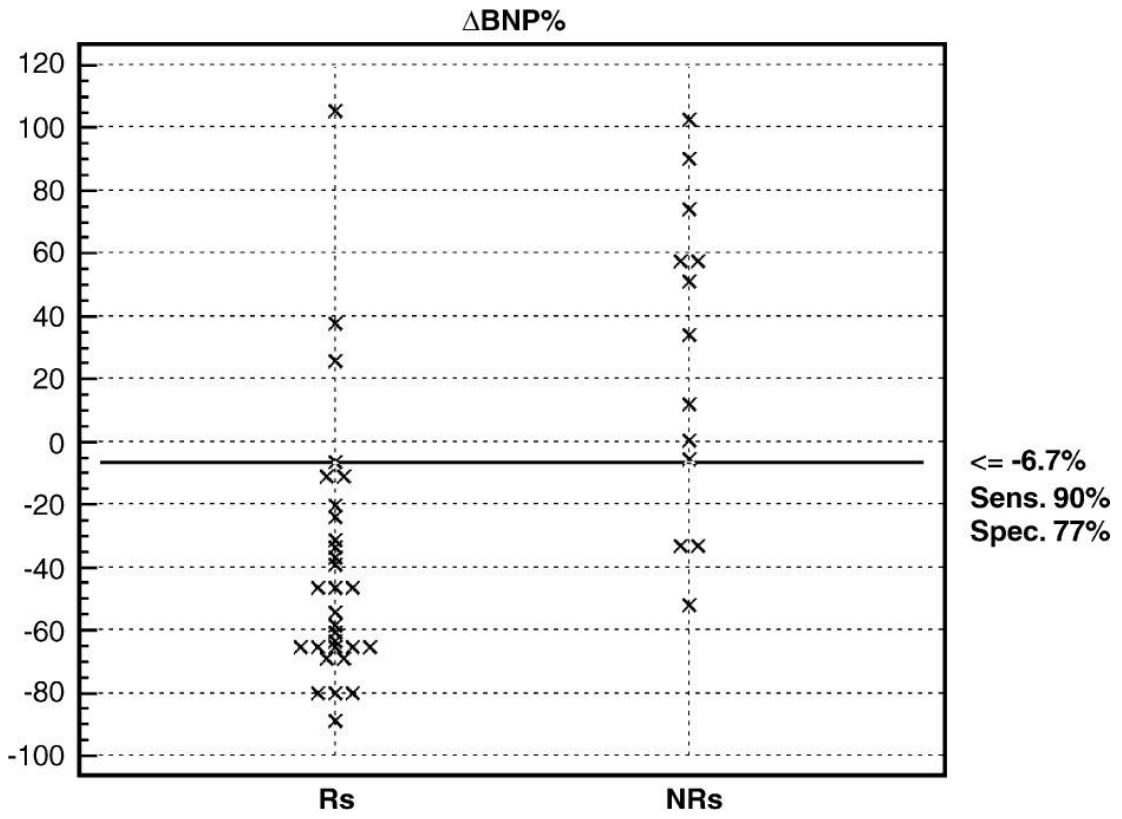
Interaction between echocardiography and clinical status

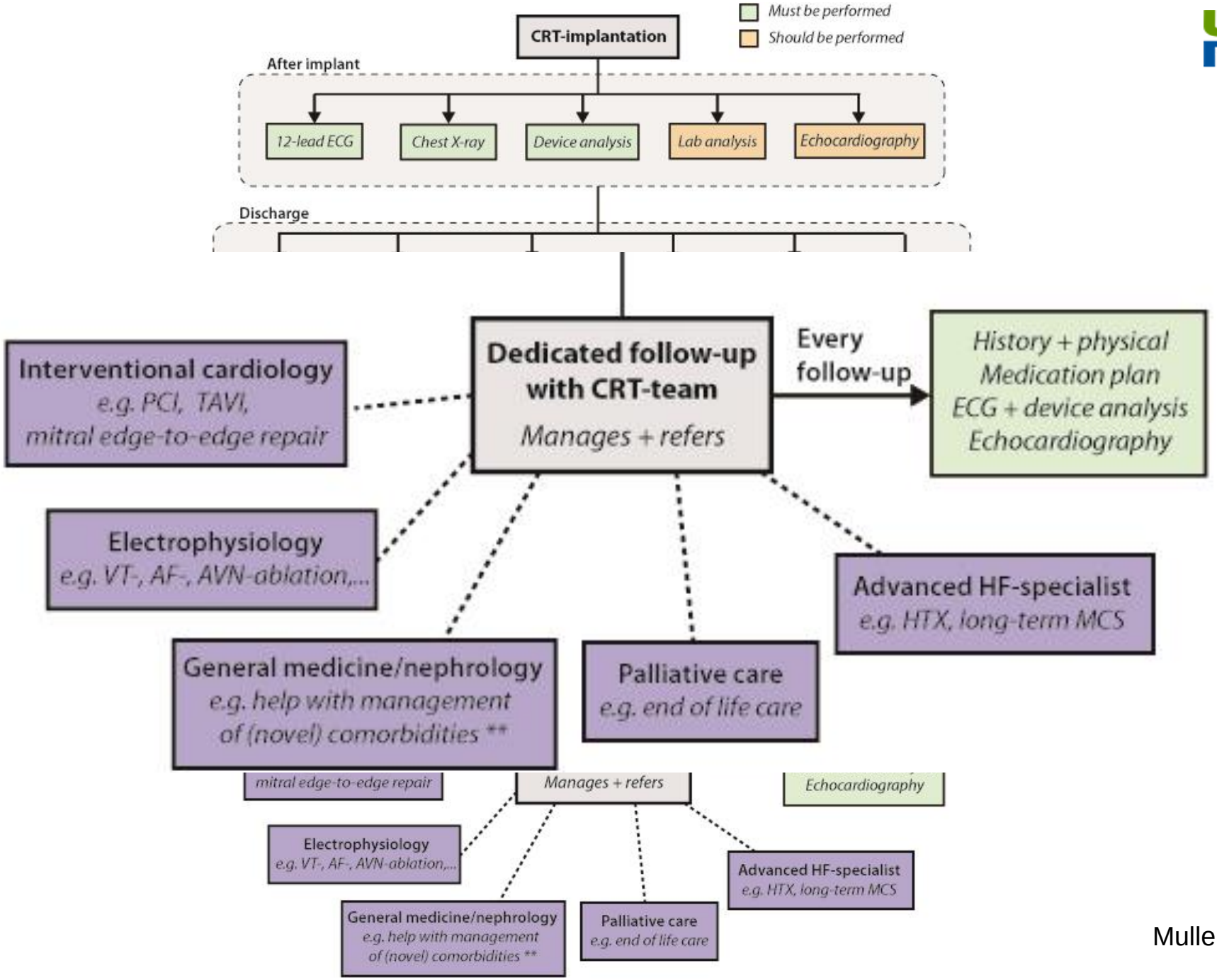
Varma *et al*. *JACC* 2009

What about BNP?

n=43
Change in BNP at three months predicted improvement at 12 and 24 months

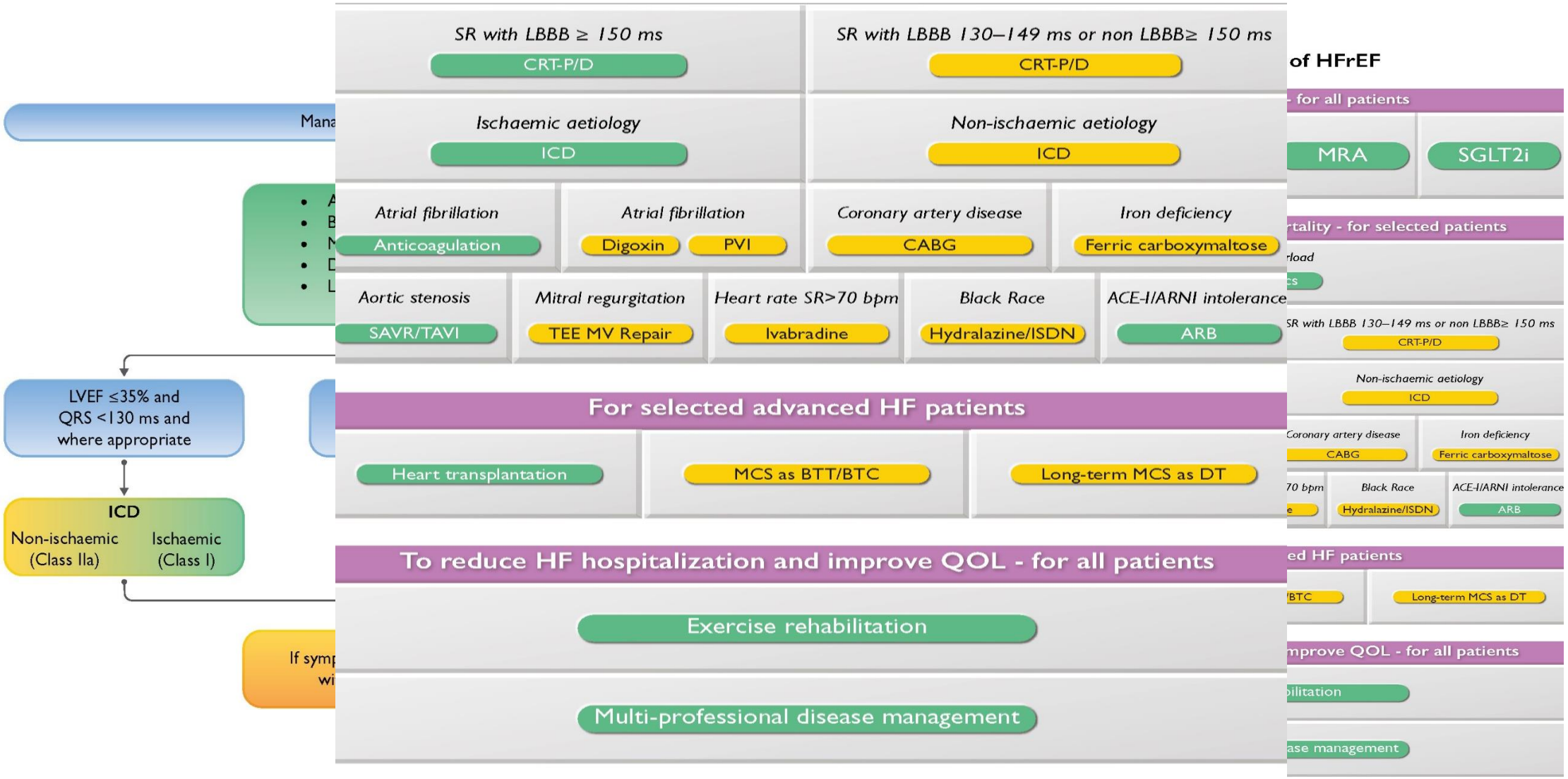


Kubanek et al. *EJHF* 2006

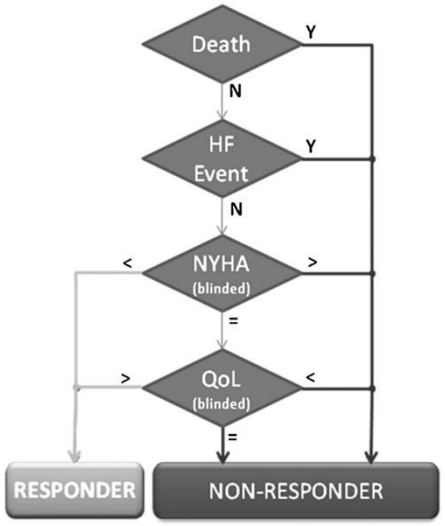


Mullens *et al*. *EJHF* 2020

Chronic heart failure



McDonagh T et al. *EHJ* 2021;**42:**3599–3726



Forget pre-implant predictors of non-response

(to determine indication for CRT implantation)

Focus on the prediction that non-response offers

(to determine post-CRT management)

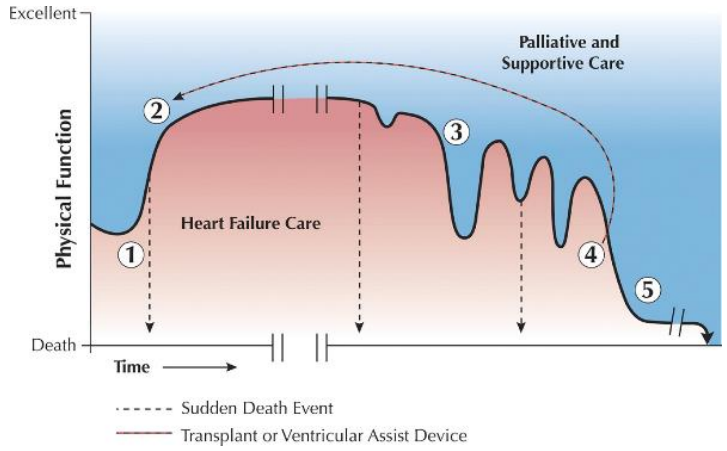
We still know too little

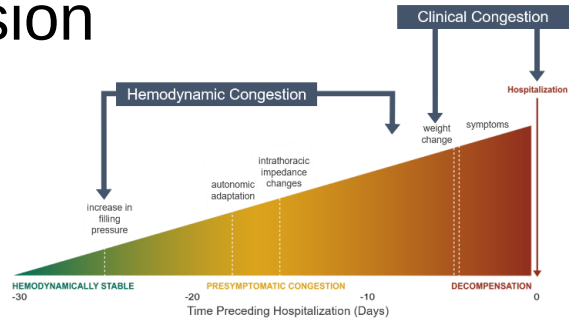
- Monitoring
- ICD v no ICD
- CRT-P v CRT-D
- Mitral interventions
- Balancing up society (achieving equity)

- Personalisation of device delivery would achieve all of these aims
- Requires:
  - An open mind
  - Good data
  - Lack of bias

Do we still need devices?

1) Decide on ICD or not – do not use anecdote
2) CRT early (even before or to facilitate OMT)
3) Monitor and optimise response to CRT in a dedicated clinic
4) Avoid or delay progression by actively managing contributors
5) Assess response to CRT at 3-6 months (symptoms)
6) Decide early and review patients progressing to advanced heart failure,
7) React rapidly (refer early) to early signs of progression
8) Move up to treatments for advanced HF early
9) Make early decision for palliative care



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