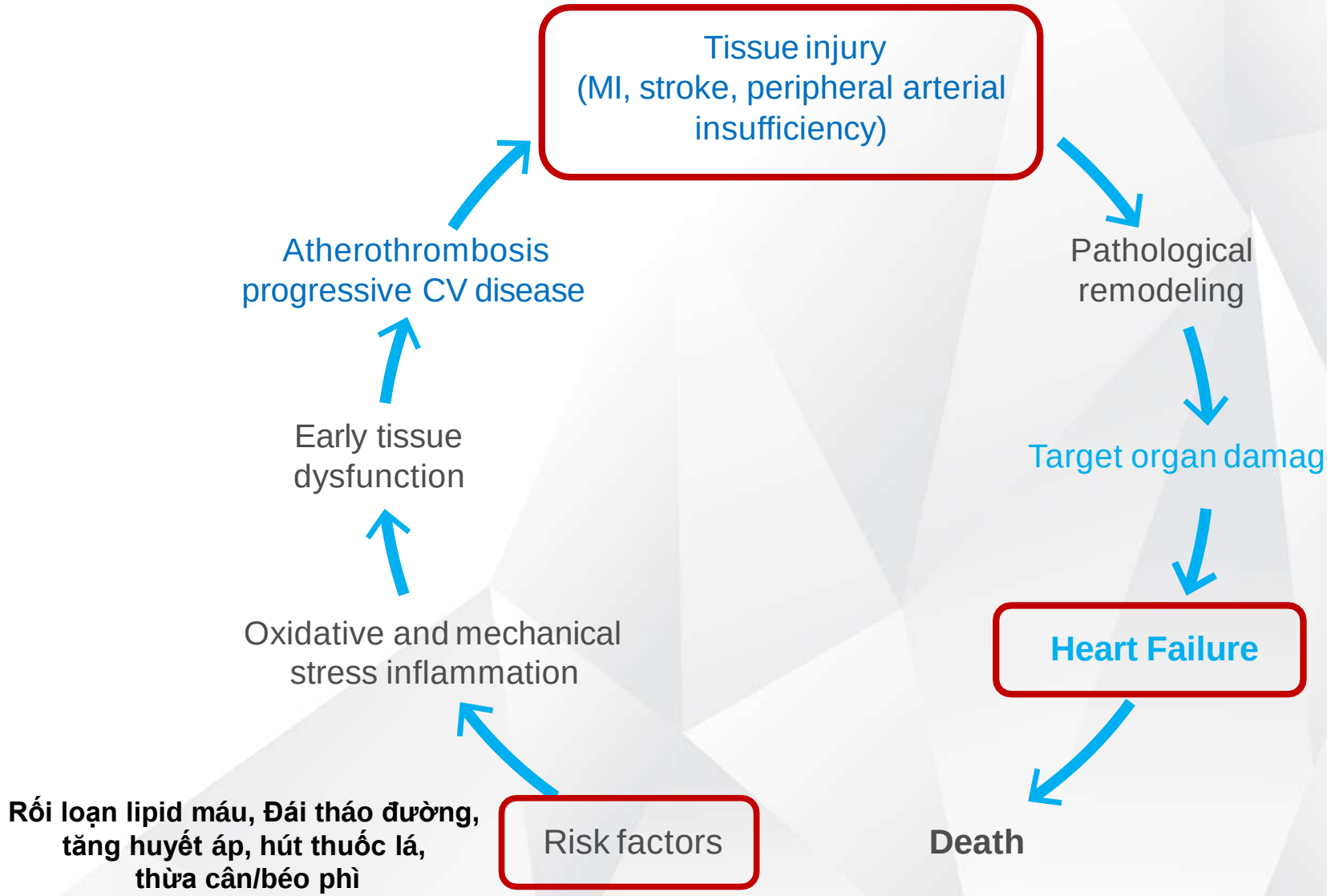
Tiếp cận cá thể hóa điều trị bệnh nhân suy tim phân suất tống máu giảm: Từ khuyến cáo đến thực hành lâm sàng

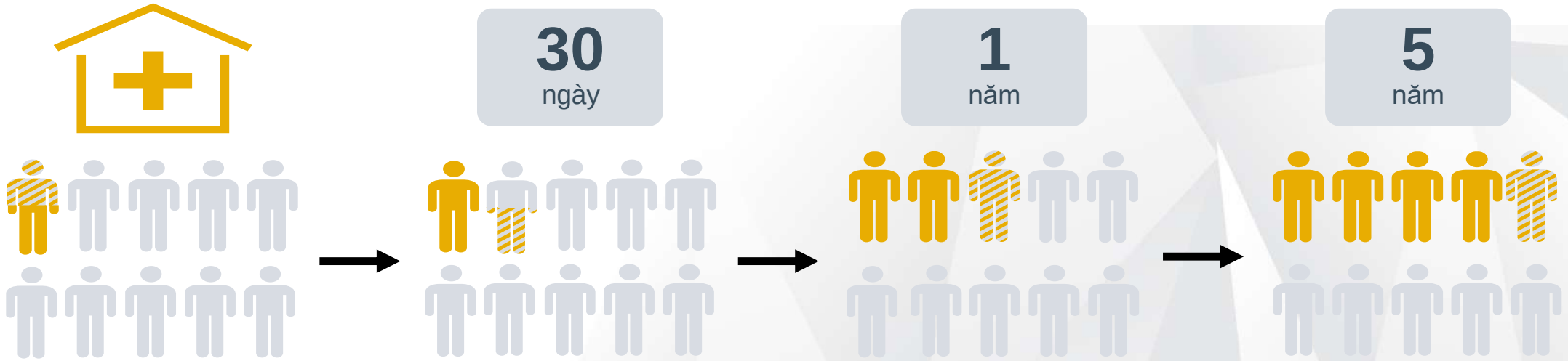
ThS. BSCKII Lý Văn Chiêu
Phó khoa Nội tim mạch,
Phó giám đốc Trung tâm tim mạch, Bệnh viện Chợ Rẫy
SERV-CARD-24-06-2023

SUY TIM: đích đến cuối cùng chuỗi bệnh lý tim mạch-chuyển hóa



Circulation
Volume 114, Issue 25, 19 December 2006, Pages 2850-2870

BN suy tim phân suất tống máu giảm có nguy cơ nhập viện và tử vong cao



~50% tử vong là đột tử [6]

*Dữ liệu nghiên cứu dựa trên 105.388 bệnh nhân Hoa Kì, nhập viện từ 1997 đến 2004 do suy tim trong nghiên cứu Acute Decompensated Heart Failure National Registry
HFrEF=Suy tim có phân suất tống máu giảm

1. Adams et al. Am Heart J 2005;149:209–16; 2. National HF audit 2013/14: www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/hfannual13-14.pdf;
3. Loehr et al. Am J Cardiol 2008;101:1016–22; 4. Chen et al. JAMA 2011;306:1669–78; 5. Roger et al. Circulation 2012;125:e2–220; 6. McMurray et al.. Eur Heart J 2012;33:1787–847

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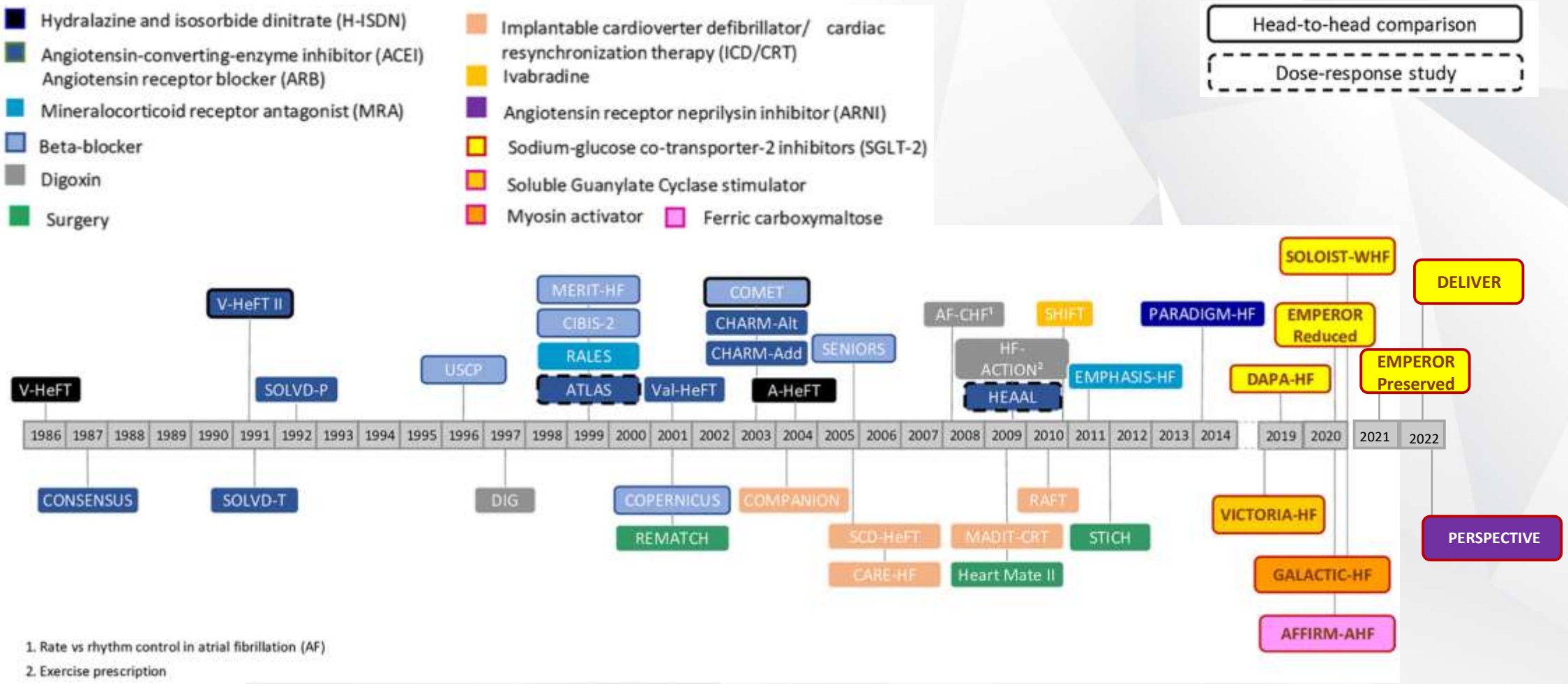
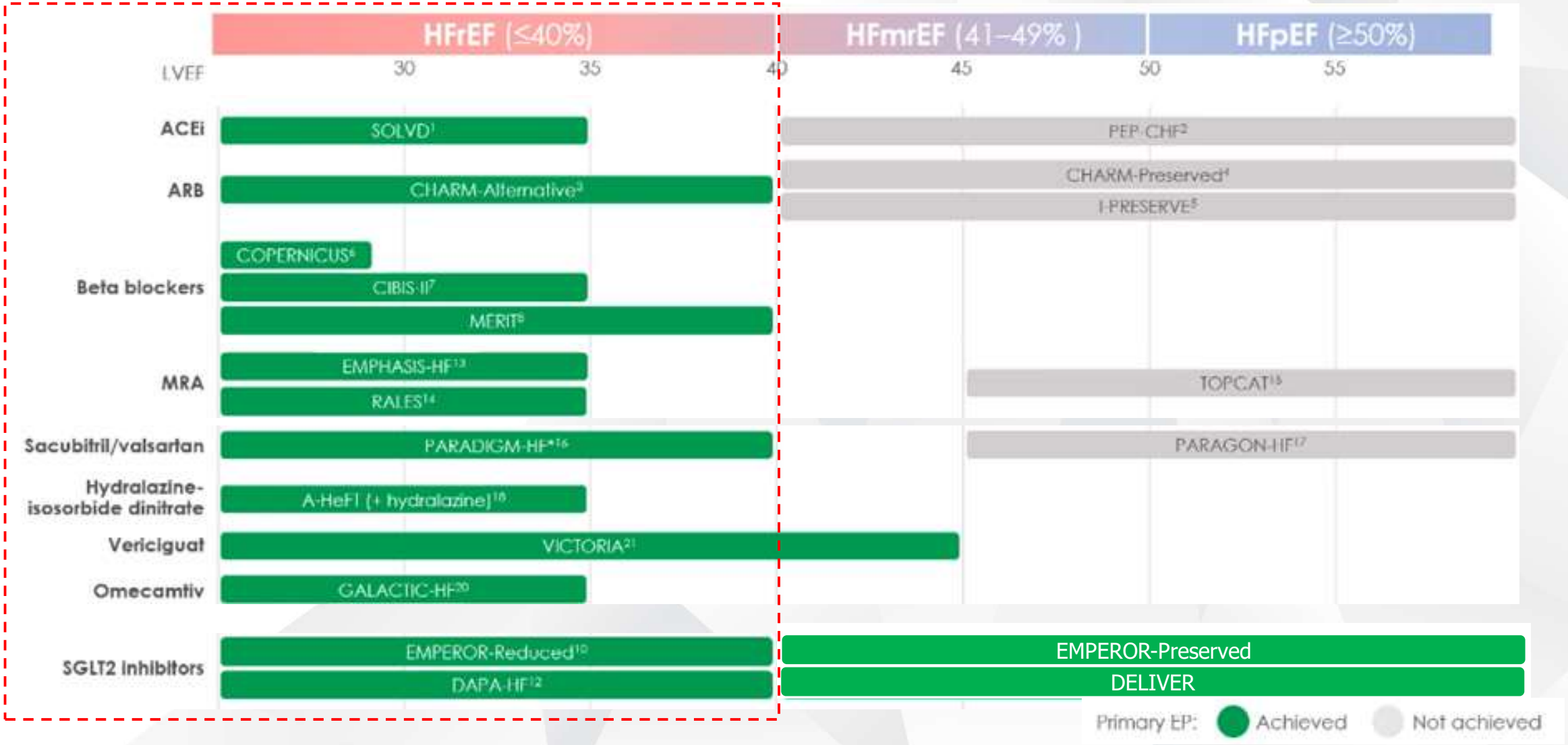
Các nghiên cứu suy tim nổi bật thập niên 1980s – 2020s



Positive trials in the treatment of heart failure with reduced ejection fraction from 1986 to 2020. Modified from McMurray

ESC Heart Failure2020;7:3505–3530. Published online in Wiley Online Library (wileyonlinelibrary.com)DOI:10.1002/ehf2.13124

Các thử nghiệm lâm sàng của các nhóm thuốc điều trị suy tim theo phân nhóm EF



Anker S *et al. N Engl J Med*. 2021;XX:XXX.

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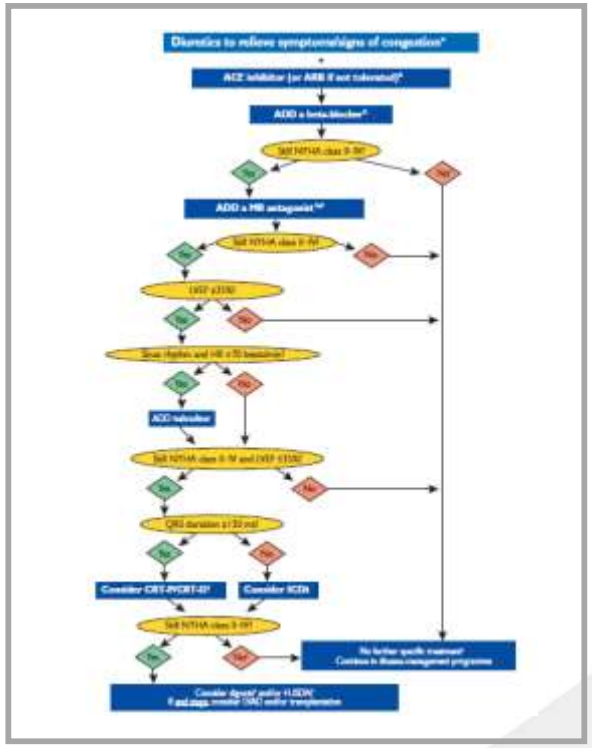
10 năm chuyển mình trong Khuyến cáo điều trị Suy tim

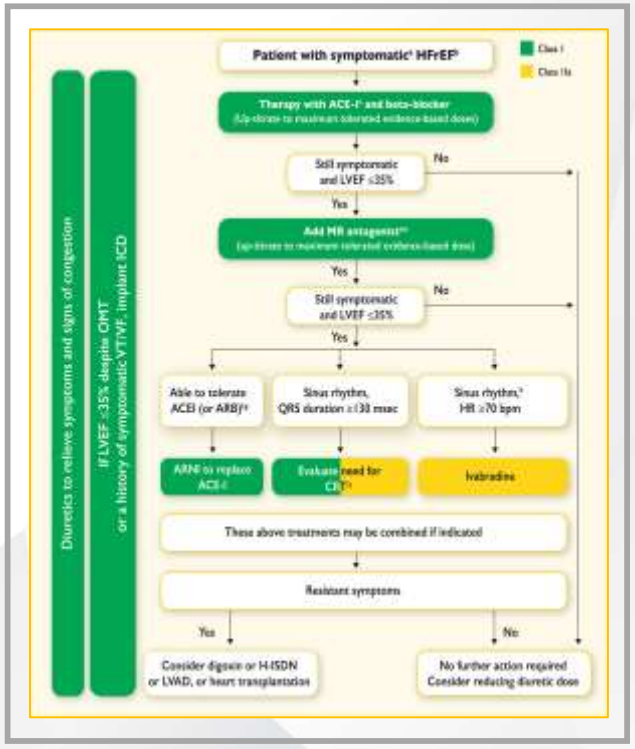
Từ khởi trị từ từ từng bước đến chăm sóc cá thể với khởi trị tích cực, nhanh

➢ 2012



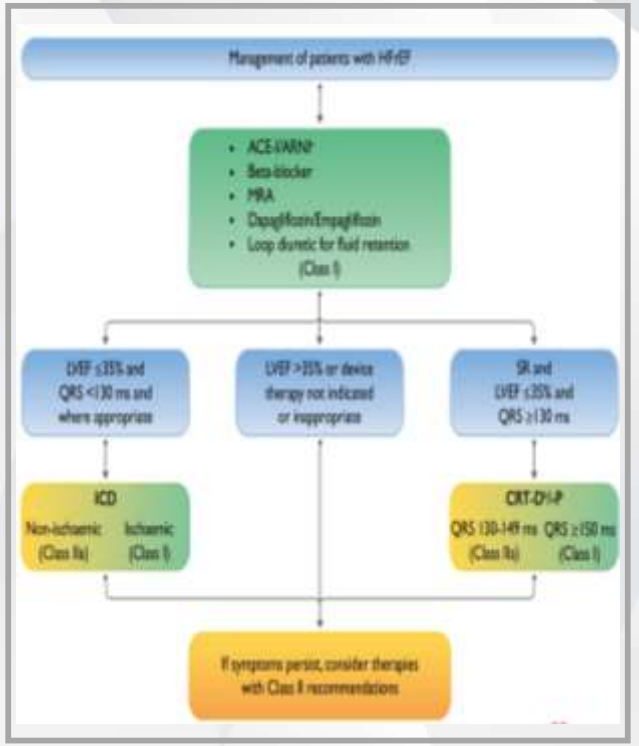
New indication for Ivabradine

➢ 2016



HF mid-range ejection fraction
New indication for ARNIs

➢ 2021



HF with mildly reduced EF
New recommendations for SGLT-2

1. European Heart Journal (2012) 33, 1787–1847; doi:10.1093/eurheartj/ehs104
2. European Heart Journal (2016) 37(27), 2129-2200, https://doi.org/10.1093/eurheartj/ehw128
3. European Heart Journal (2021) 42(36), 3599–3726, https://doi.org/10.1093/eurheartj/ehab368

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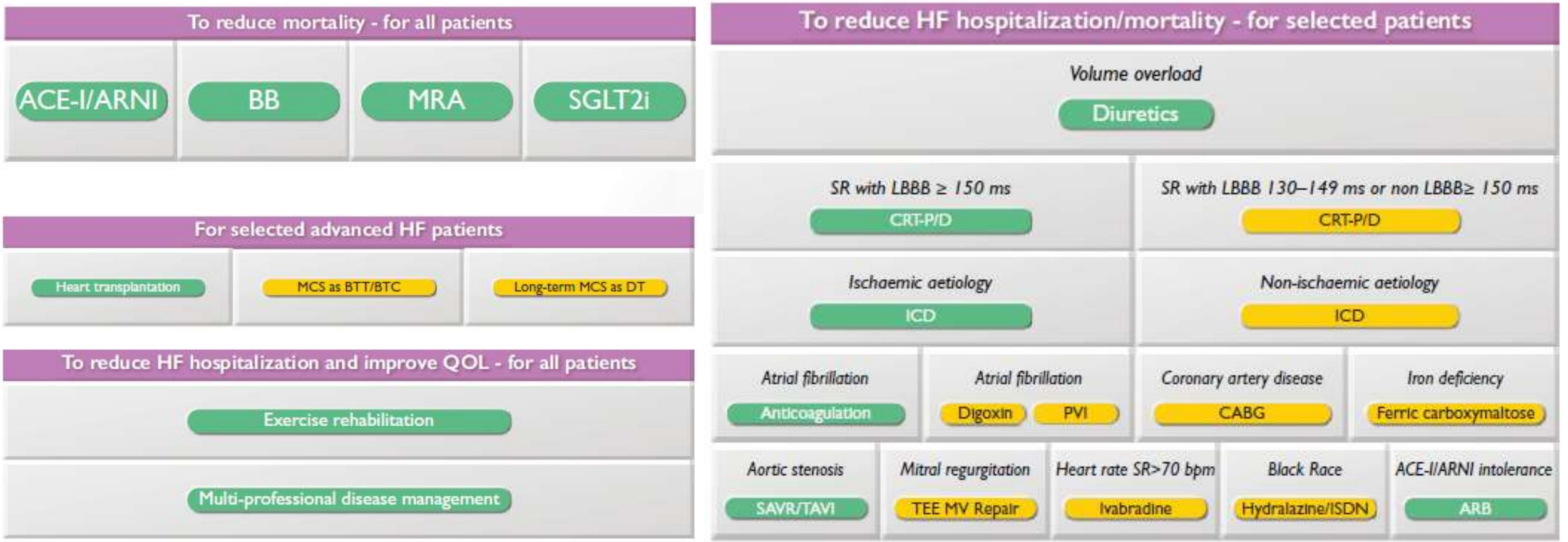
10 năm chuyển mình trong Khuyến cáo điều trị Suy tim

Từ khởi trị từ từ từng bước đến chăm sóc cá thể với khởi trị tích cực, nhanh



European Heart Journal (2021) 00, 1128 doi:10.1093/eurheartj/ehab368

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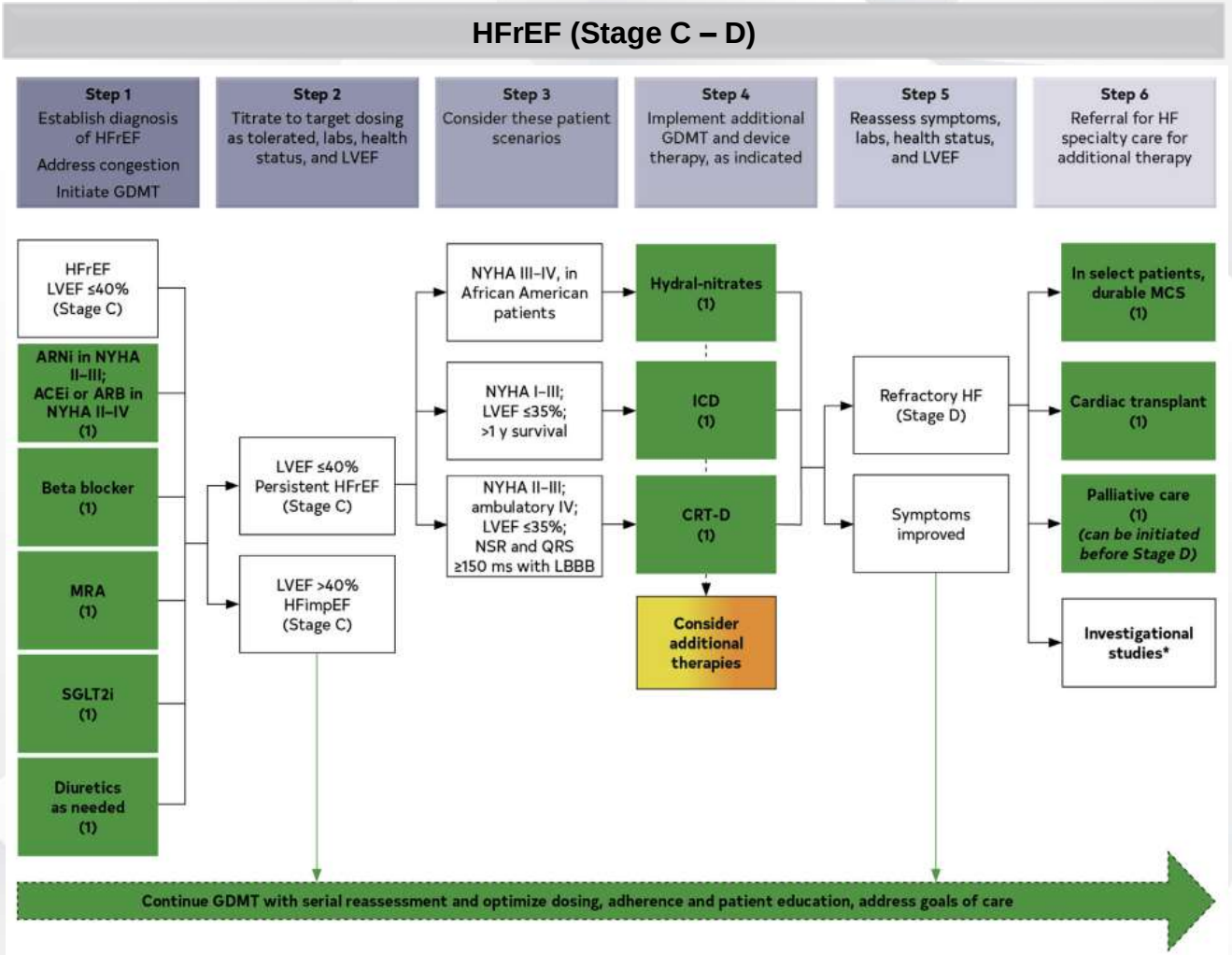
Khuyến cáo điều trị Suy tim – ACC 2022

Table 2. Treatment recommendations for patients with HFrEF are displayed. Step 1 medications may be started simultaneously at initial (low) doses recommended for HFrEF. Alternatively, these medications may be started sequentially, with sequence guided by clinical or other factors, without need to achieve target dosing before initiating next medication. Medication doses should be increased to target as tolerated.

RECOMMENDATIONS
1. In patients with HFrEF, titration of guideline-directed medication dosing to achieve target doses showed to be efficacious in RCTs is recommended, to reduce cardiovascular mortality and HF hospitalizations, unless not well tolerated (1-10).
2. In patients with HFrEF, titration and optimization of guideline-directed medications as frequently as every 1 to 2 weeks depending on the patient's symptoms, vital signs, and laboratory findings can be useful to optimize management.



Heidenreich et al JACC VOL. 79, NO. 17, 2022 2022 AHA/ACC/HFSA Heart Failure Guideline MAY 3, 2022:e263 – e421

Điều trị nội khoa tối ưu ở bệnh nhân suy tim: Kỳ vọng & thực tế !!!

Tỉ lệ bệnh nhân đạt liều đích của thuốc theo khuyến cáo

NGAY CẢ TRONG CÁC NGHIÊN CỨU RCT còn rất thấp

Table 1: Current Usage Rates of Guideline-Directed Medical Therapy and Comprehensive Disease Modifying Medical Therapy

	Percentage of Patients on Treatment					Percentage at ≥50% target					Percentage at target				
GDMT/ CDMMT	CHAMP-HF 2018[7]	PINNACLE 2020[8]	QUALIFY 2016[20]	ESC-HF 2013[21]	BIOSTAT-CHF 2017[7]	Savarese et al. 2021[23]	CHAMP-HF 2017[6*]	BIOSTAT-CHF 2017[22†]	QUALIFY 2016[20*]	Savarese et al. 2021[23†]	CHAMP-HF 2017[6*]	QUALIFY 2016[20*]	ESC-HF 2013[21*]	BIOSTAT-CHF 2017[22†]	Savarese et al. 2021[23†]
ACEI/ARB/ARNI	72.1%	78.0%					40.4%				16.8%				
ARNI	12.8%	8.5%				73%	43.5%			53%	14.0%				30%
ACEI/ARB	59.9%			92.2%	85%		39.8%	53%			17.5%			22%	
ACEI		54.8%	65.7%	70.7%		45%			63.3%	28%		27.9%	29.3%	27%	15%
ARB		27.8%	21.5%	23.5%		67%			39.5%	19%		6.9%	24.1%	20%	10%
β-blocker	66.8%	74.6%	86.7%	92.7%	90%	76%	54.3%	40%	51.8%	30%	27.5%	14.8%	17.5%	12%	12%
MRA	33.1%		69.3%	67%		60%	98.2%		99.1%	60%	76.6%	70.8%	30.5%		60%

% of patients on medication. †% of all study patients. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; CDMMT = comprehensive disease modifying medical therapy; GDMT = guideline-directed medical therapy; MRA = mineralocorticoid receptor antagonist.

Nicholas K Brownell, et al. Cardiac Failure Review (2021);7:e18

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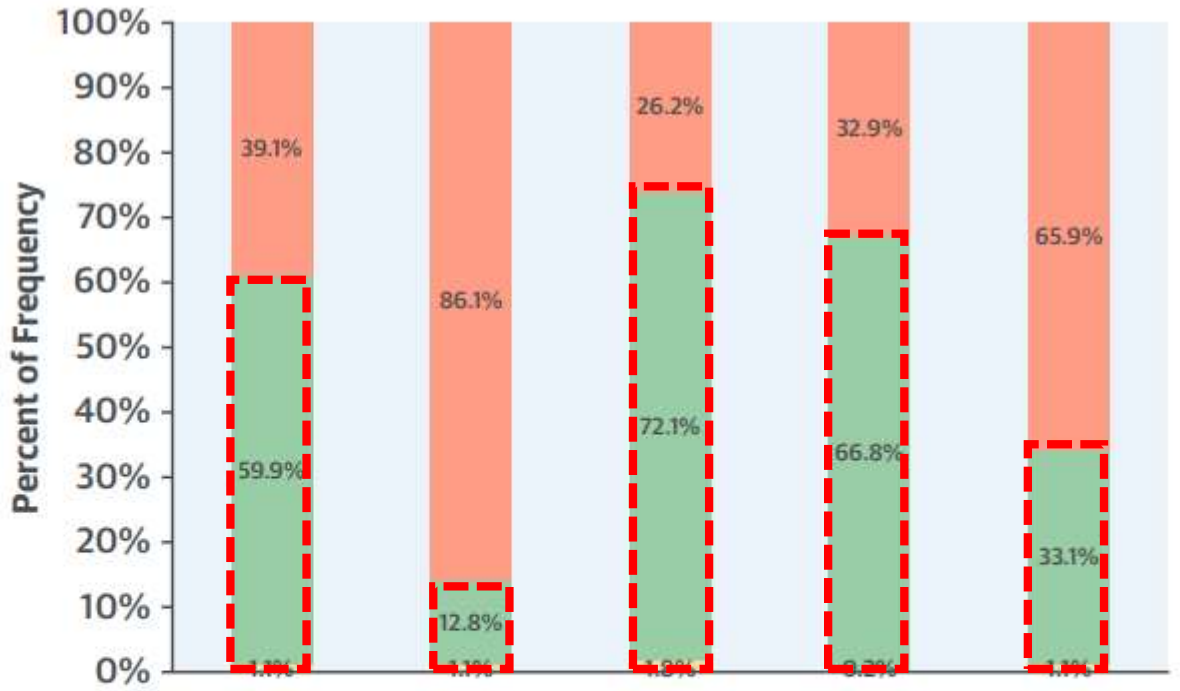
Thực tế, tỉ lệ BN được điều trị nội khoa tối ưu cũng còn thấp
Kết quả từ NC sổ bộ CHAMP-HF trên BN suy tim PSTM giảm



	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38
Tỉ lệ BN đạt liều đích	**17%**	**14%**		**28%**	**77%**
Tỉ lệ BN đạt <50% liều đích	**60.2%**	**56.5%**	**59.5%**	**45.7%**	**1.8%**

Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351–66.

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	ACEI/ARB		ARNI		BB		MRA	
	<50% Target Dose (n = 1,261)	50% to <100% Target Dose (n = 466)	<50% Target Dose (n = 255)	50% to <100% Target Dose (n = 133)	<50% Target Dose (n = 1,071)	50% to <100% Target Dose (n = 628)	<50% Target Dose (n = 21)	50% to <100% Target Dose (n = 250)
Age, yrs	67 (58-75)	67 (58-75)	65 (55-73)	63 (54-71)	68 (59-76)	67 (58-74)	71 (64-76)	65 (56-74)
Female	359 (28.5)	133 (28.5)	68 (26.7)	47 (35.6)	305 (28.5)	167 (26.6)	7 (33.3)	62 (24.8)
Ejection fraction, %	30 (23-35)	31 (25-36)	27 (20-33)	28 (22-32)	28 (21-35)	30 (23-35)	32 (29-39)	30 (20-35)
NYHA functional class								

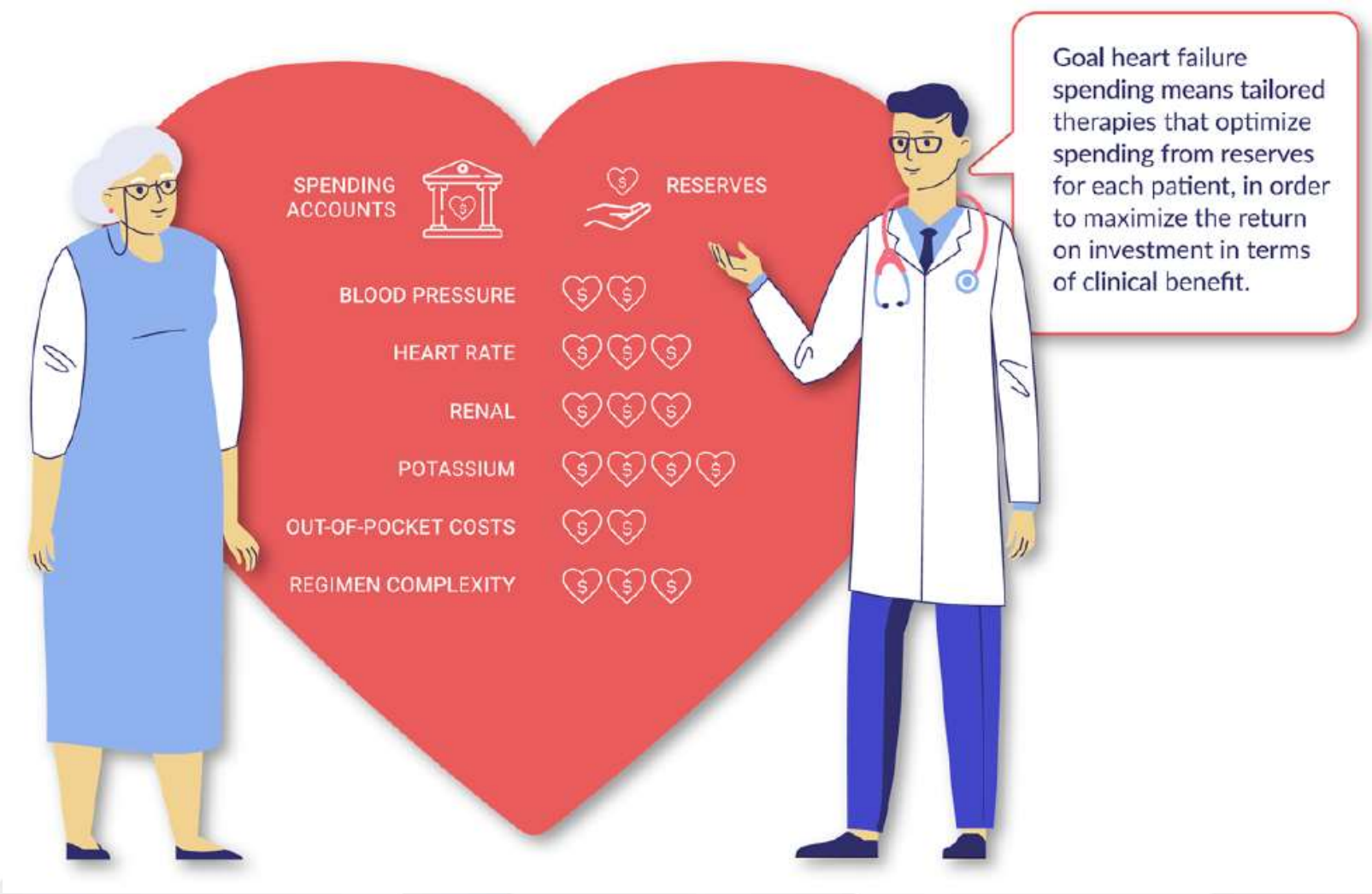
RESULTS Overall, 3,518 patients from 150 primary care and cardiology practices were included. Mean age was 66 ± 13 years, 29% were female, and mean EF was 29 ± 8%. Among eligible patients, 27%, 33%, and 67% were not prescribed ACEI/ARB/ARNI, beta-blocker, and MRA therapy, respectively. When medications were prescribed, few patients were receiving target doses of ACEI/ARB (17%), ARNI (14%), and beta-blocker (28%), whereas most patients were receiving target doses of MRA therapy (77%). Among patients eligible for all classes of medication, 1% were simultaneously receiving target doses of ACE/ARB/ARNI, beta-blocker, and MRA. In adjusted models, older age, lower blood pressure, more severe functional class, renal insufficiency, and recent HF hospitalization generally favored lower medication utilization or dose. Social and economic characteristics were not independently associated with medication use or dose.

CONCLUSIONS In this contemporary outpatient HFrEF registry, significant gaps in use and dose of guideline-directed medical therapy remain. Multiple clinical factors were associated with medication use and dose prescribed. Strategies to improve guideline-directed use of HFrEF medications remain urgently needed, and these findings may inform targeted approaches to optimize outpatient medical therapy. (J Am Coll Cardiol 2018;72:351-66)

Chronic renal insufficiency	208 (16.5)	79 (17.0)	42 (16.5)	17 (12.9)	216 (20.2)	128 (20.4)	4 (19.0)	39 (15.6)
Asthma/COPD	389 (30.9)	142 (30.5)	65 (25.6)	37 (28.0)	327 (30.6)	170 (27.2)	6 (28.6)	56 (22.4)
History of ventricular tachycardia/fibrillation	270 (21.4)	71 (15.3)	77 (30.2)	26 (19.5)	199 (18.6)	140 (22.3)	8 (38.1)	72 (28.8)
Depression	328 (26.1)	105 (22.6)	58 (22.8)	33 (25.0)	270 (25.2)	132 (21.1)	5 (23.8)	54 (21.6)
Active cigarette smoking	275 (21.8)	100 (21.5)	51 (20.1)	27 (20.5)	223 (20.8)	141 (22.5)	2 (9.5)	42 (16.8)

Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351–66.

A heart failure spending function – a conceptual framework for tailored intensification of GDMT



Allen A et al. Circulation: Heart Failure. 2022;15
https://doi.org/10.1161/CIRCHEARTFAILURE.121.008594

Đồng thuận suy tim 2021 ESC đưa ra các kiểu hình bệnh nhân suy tim
Cá thể hóa điều trị với khởi trị sớm, tích cực dựa trên 4 thông số nền tảng

Rosano GMC et al. *Eur J Heart Fail. 2021;23:872-81*

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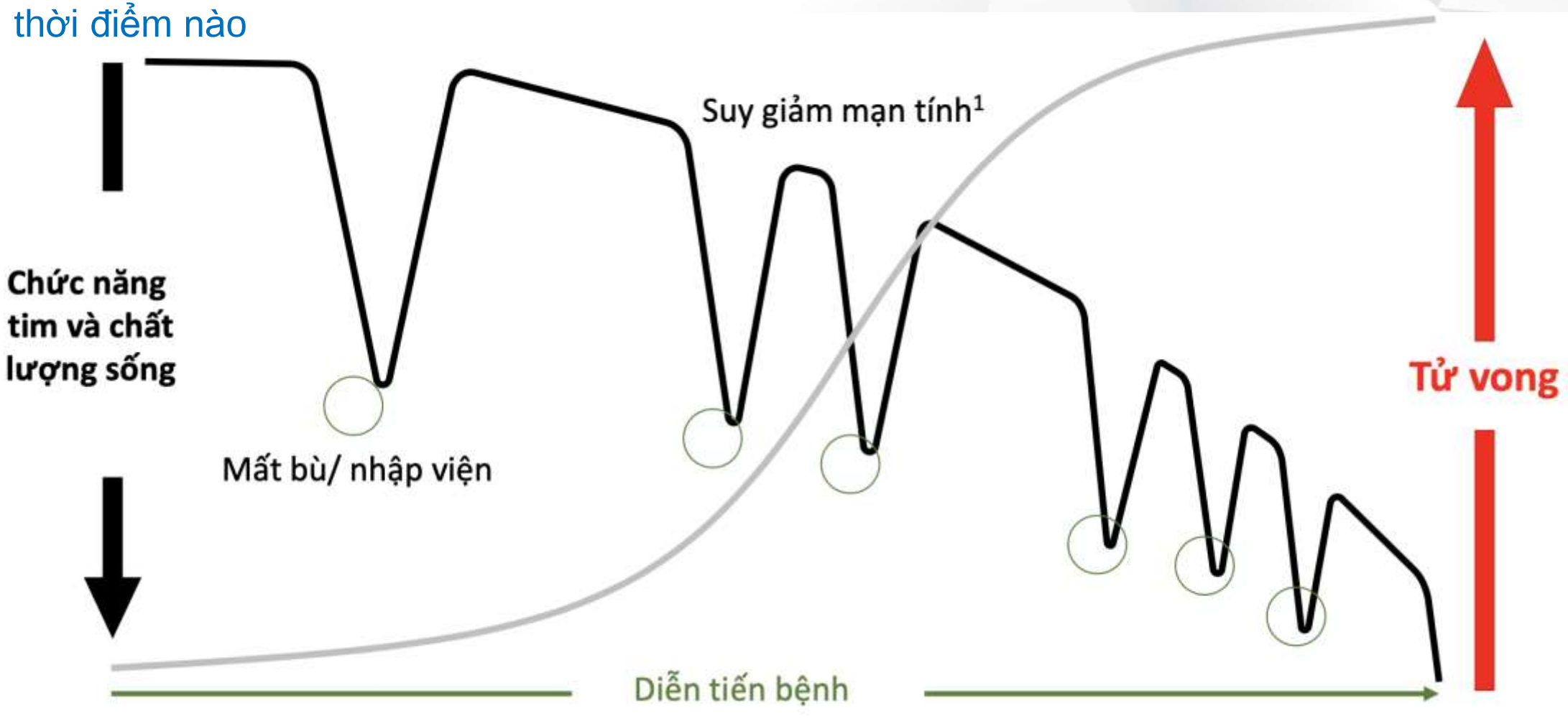
Bệnh nhân suy tim không thể được xem là "ổn định"

Tần suất mất bù và nguy cơ tử vong gia tăng[1-5] với những đợt cấp và đột tử xảy ra vào bất kì thời điểm nào



1. Adapted from Gheorghiade et al. Am J Cardiol 2005;96:11G–17G; 2. Ahmed et al. Am Heart J 2006;151:444–50; 3. Gheorghiade and Pang. J Am Coll Cardiol 2009;53:557–73; 4. Holland et al. J Card Fail 2010;16:150–6; 5. Muntwyler et al. Eur Heart J 2002;23:1861–6

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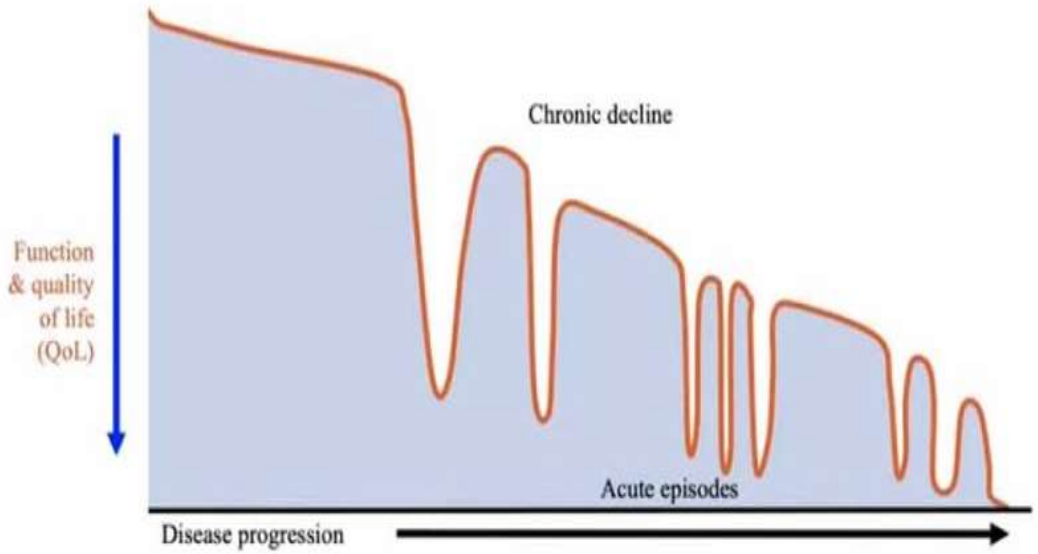
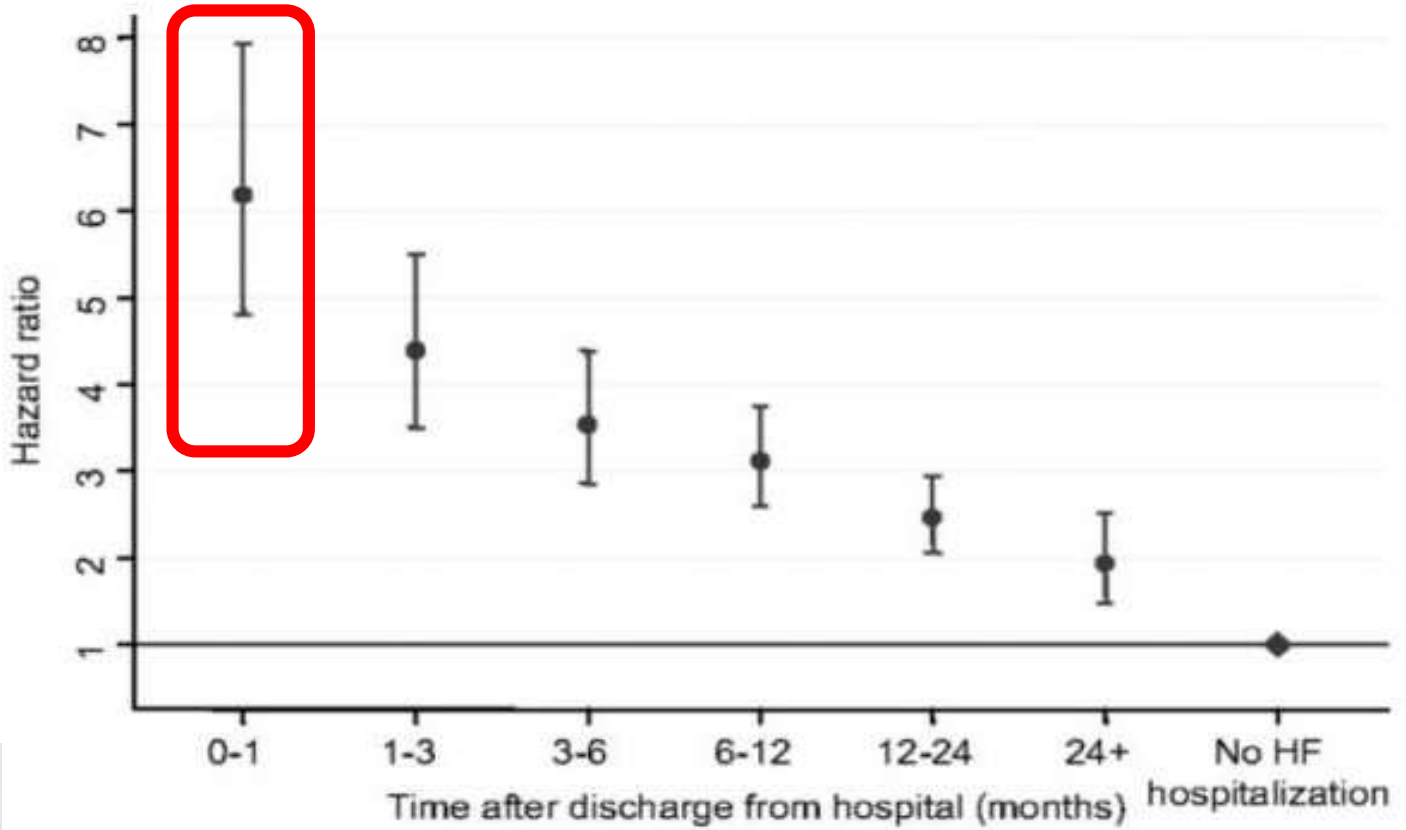
Tỷ lệ tái nhập viện cao nhất tại thời điểm 1 tháng ra viện

Diễn tiến của Suy tim





Sau mỗi lần nhập viện,
BN Suy tim lại càng gần với tử vong

Tỷ lệ tái nhập viện cao nhất
ở tháng đầu tiên sau xuất viện

Timing and Duration of Interventions in Clinical Trials for Hospitalized Heart Failure Patients. Marti NC et al, Circ Heart Fail. 2013 Sep 1; 6(5):

TẦN SỐ TIM CAO trước lúc xuất viện gia tăng tử vong & tái nhập viện trong giai đoạn mong manh (Vulnerable phase)

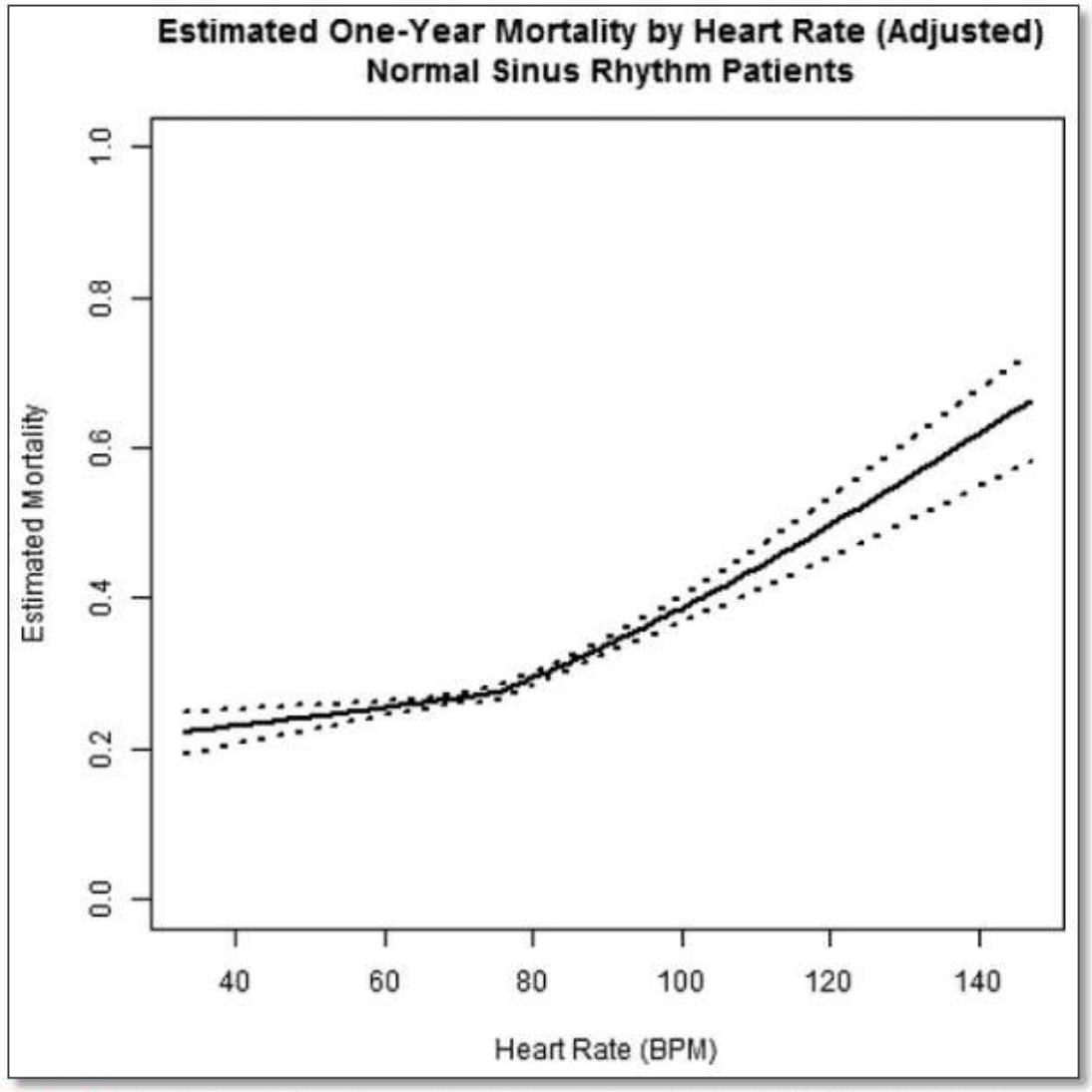


Figure 2. Estimated mortality at 1 year in patients with sinus rhythm (n=26 020). The inflection point represents a single linear spline at 75 bpm (see text for details). Risk of mortality rises steadily with heart rate. BPM indicates beats per minute.

J Am Heart Assoc. 2015;4:e001626. https://doi.org/10.1161/JAHA.114.001626

A retrospective cohort study from clinical registry data linked to medicare claims for 46 217 patients participating in get with the guidelines®–heart failure (2005 – 2011)

Outcome in patients with HR ≥ 75 bpm, sinus rhythm group (n = 26 020)	Adjusted Model (Patient and Hospital Characteristics)	
	HR for Heart Rate per 10 bpm	*P* Value
Mortality	***1.185***	*<0.0001*
[0,30] days	***1.300***	*<0.0001*
[31,365] days	***1.155***	*<0.0001*
All-cause readmission	***1.063***	*<0.0001*
[0,30] days	***1.128***	*<0.0001*
[31,365] days	***1.02***	*0.1872*
Composite readmission/mortality	***1.082***	*<0.0001*
[0,30] days	***1.148***	*<0.0001*
[31,365] days	***1.037***	*0.0125*

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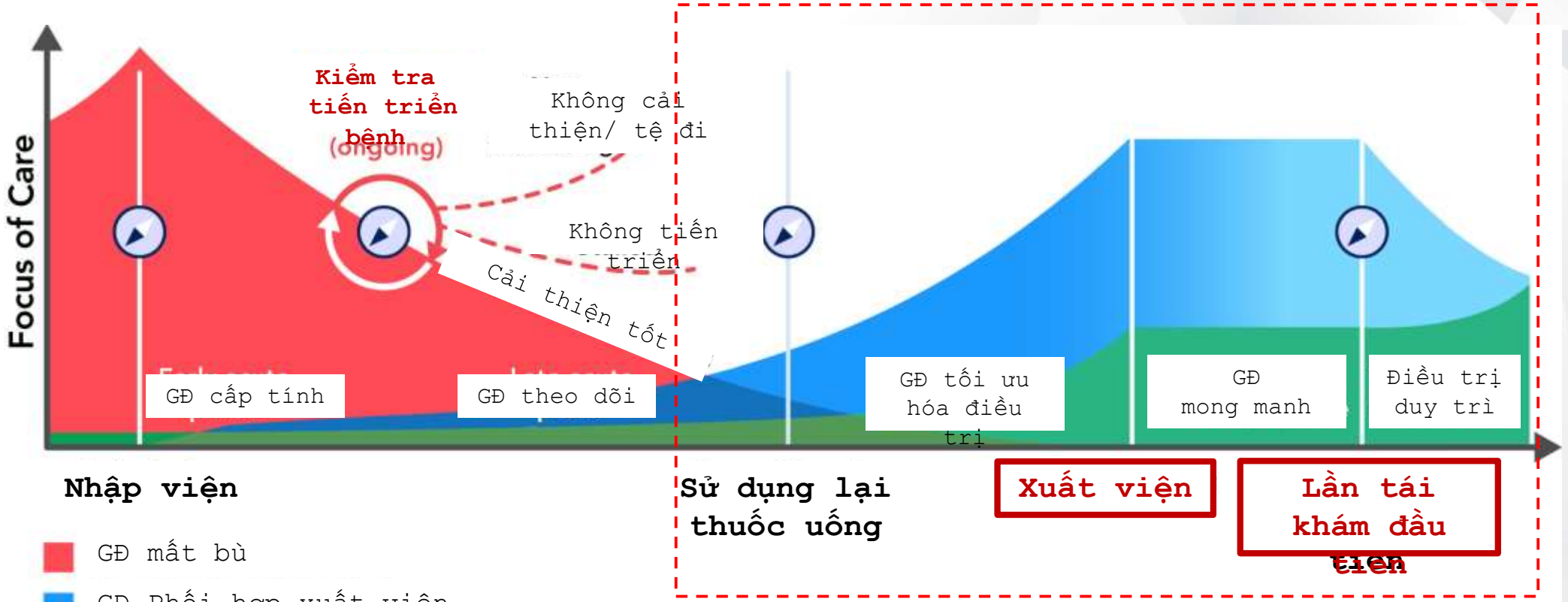
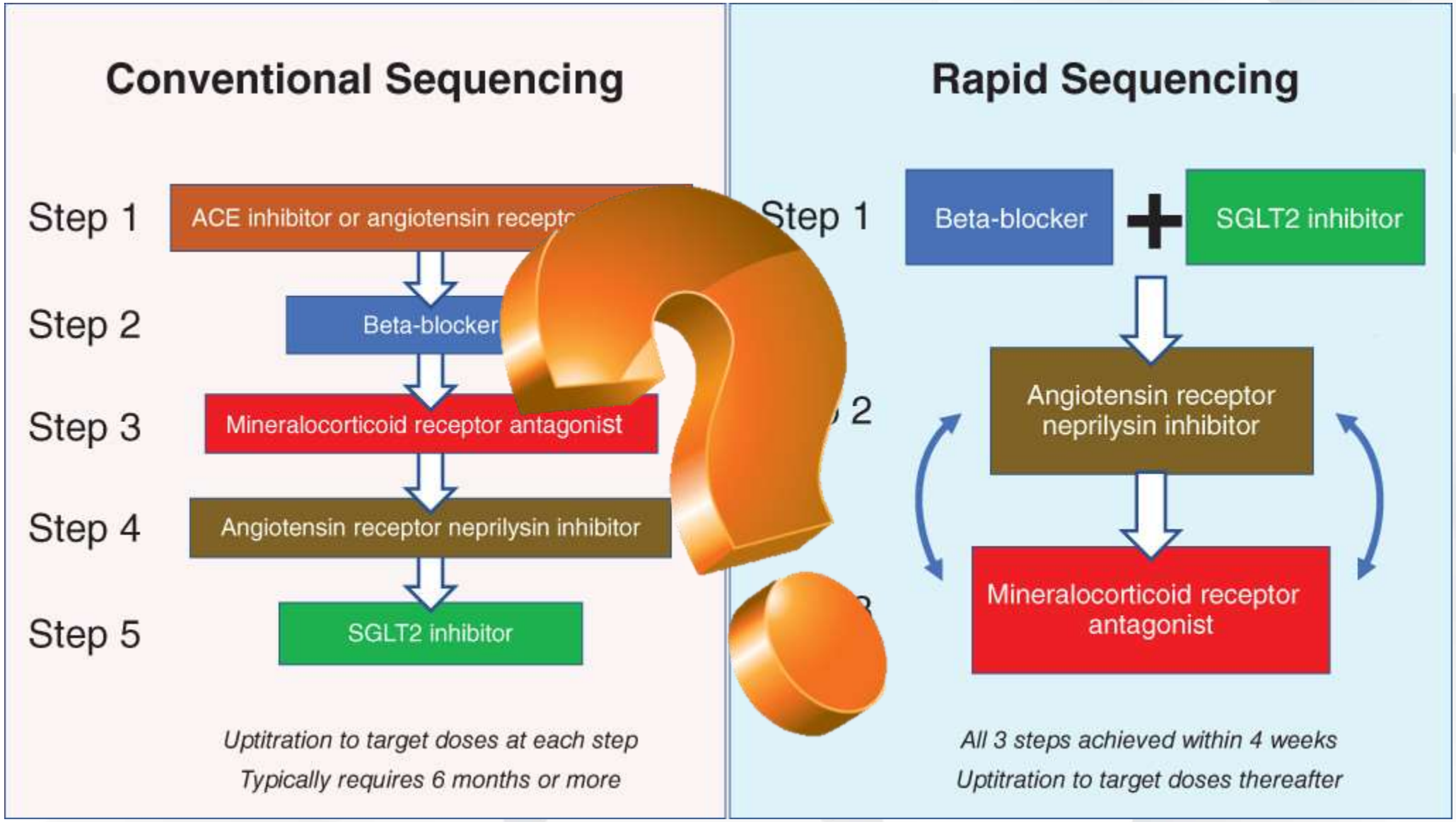
Thời điểm vàng để tối ưu hóa điều trị nội khoa & kiểm soát TST

Optimal moment



JACC, Volume 74, Issue 15, 15 October 2019, Pages 1966-2011; https://doi.org/10.1016/j.jacc.2019.08.001

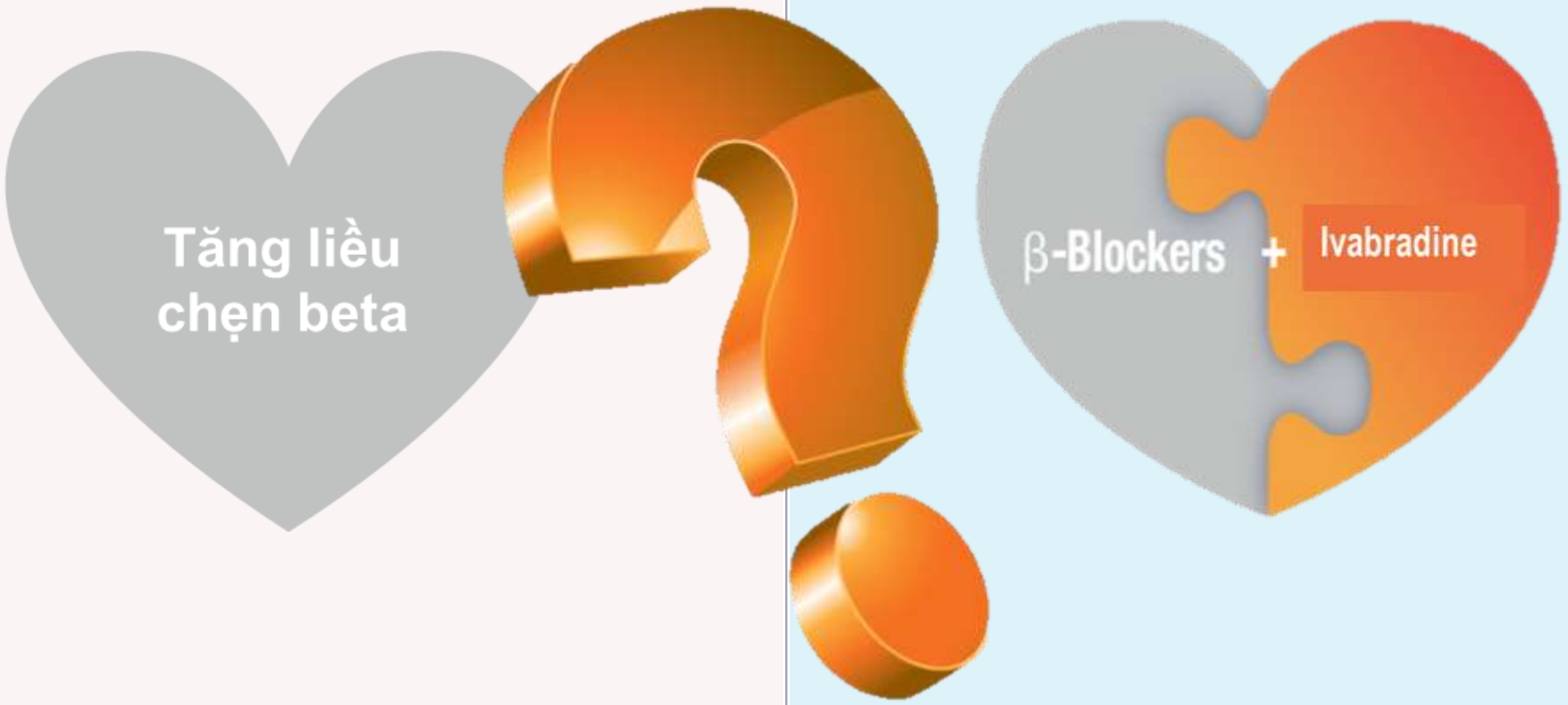
Thời gian của Bệnh nhân SUY TIM – KHÔNG CHỜ ĐỢI!



European Journal of Heart Failure (2021) 23, 882–894 REVIEW doi:10.1002/ejhf.2149

Thời gian của Bệnh nhân SUY TIM – KHÔNG CHỜ ĐỢI!

Kiểm soát TẦN SỐ TIM



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CHÂN THÀNH CẢM ƠN SỰ CHÚ Ý LẮNG NGHE CỦA QUÝ ĐỒNG NGHIỆP!