Scompenso cardiaco sintomatico e asintomatico

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Dichiarazione dei conflitti d'interesse

Gianluca Perseghin dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Honorarium as a speaker in Scientific Events

AstraZeneca
Bayer
Boheringer Ingelheim
Daiichi Sankyo
Lilly
Menarini Diag
MSD
Novartis
Novo Nordisk
PikDare
Roche Diag
Sanofi
Servier

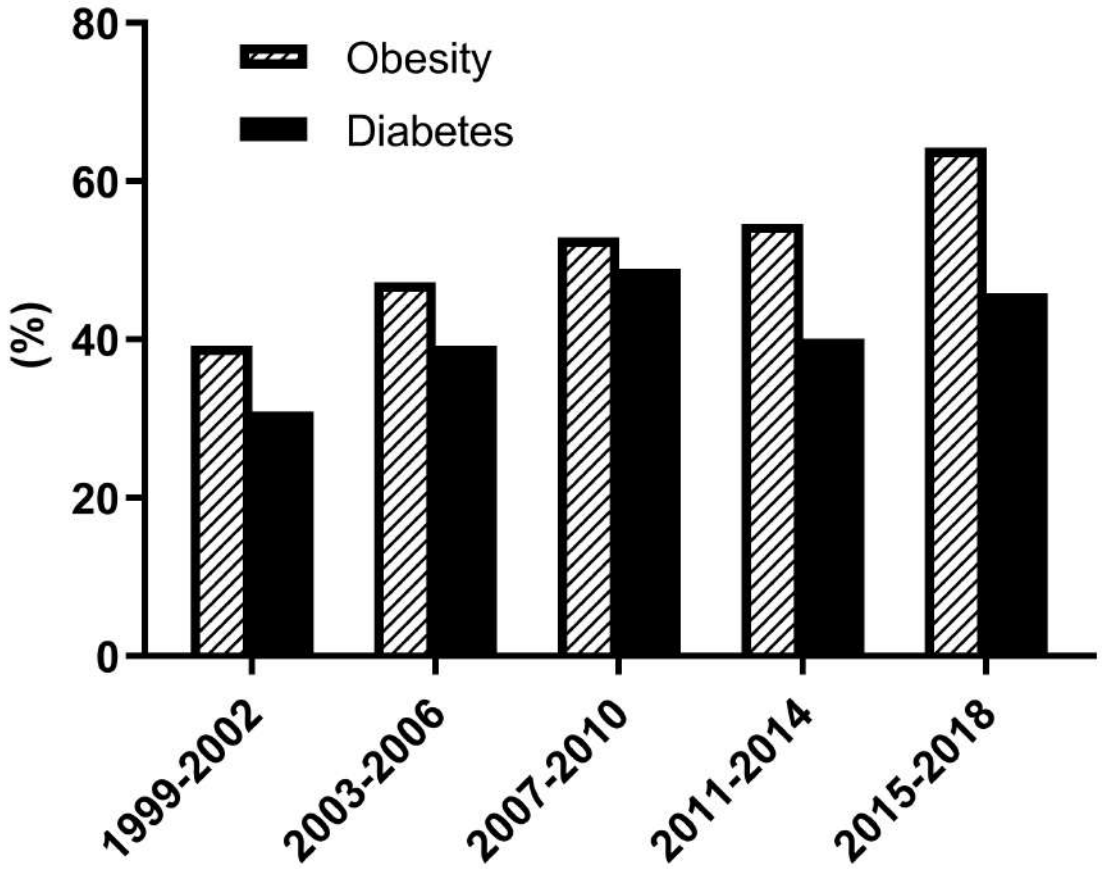
Scientific advisory boards

Lilly
Merck
Novartis
Novo Nordisk
Pfizer
PikDare
Sanofi

Topics

- **Relevance**
- **Natural history:** RFs, organ damage, symptoms
- **Action**: screening, therapy

Trend in HF in US NHANES 1999-2018



- Stable prevalence 3-4%
- **Increasing proportion of obesity and T2DM**

- Little improvement in BP
- Little improvement in HbA1c
- Improvement in the lipid profile up to 2010

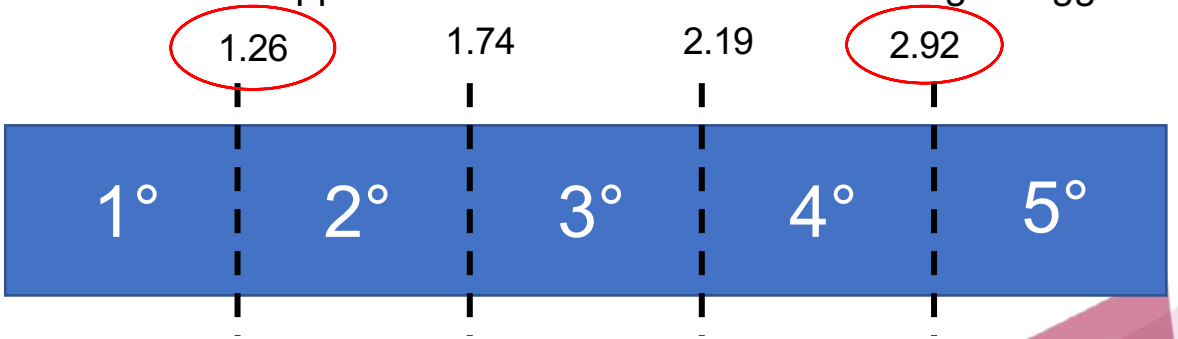
Ciardullo S et al, Int J Cardiol, 2022

Stima del rischio di SCC e di ASCVD nel T2DM in prevenzione CVD primaria

Rischio medio di SCC (QDiabetes) e di ASCVD a 10 anni			
N	1089	F = 532	M = 557
QDIABETES [%]	10.54 ± 7.45	10.77 ± 7.62	10.33 ± 7.29
ASCVD [%]	20.83 ± 13.84	17.50 ± 13.41	24.01 ± 13.50

- Suddivisione in quintili in base al rapporto tra rischio ASCVD e SCC di ogni soggetto

$$\frac{Rischio\ ASCVD\ [\%]}{Rischio\ SCC\ [\%]}$$



Cannistraci R tesi specializzazione 2022

Natural history of HF

Pop Busui R et al, Diabetes Care, 2022

HF: classification

HFrEF HFmrEF HFpEF

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

EF <40% EF 41-49% EF ≧ 50%

McDonagh TA et al. 2021 ESC HF Guidelines

Signs and symptoms

Classical

Dyspnea
Orthopnea

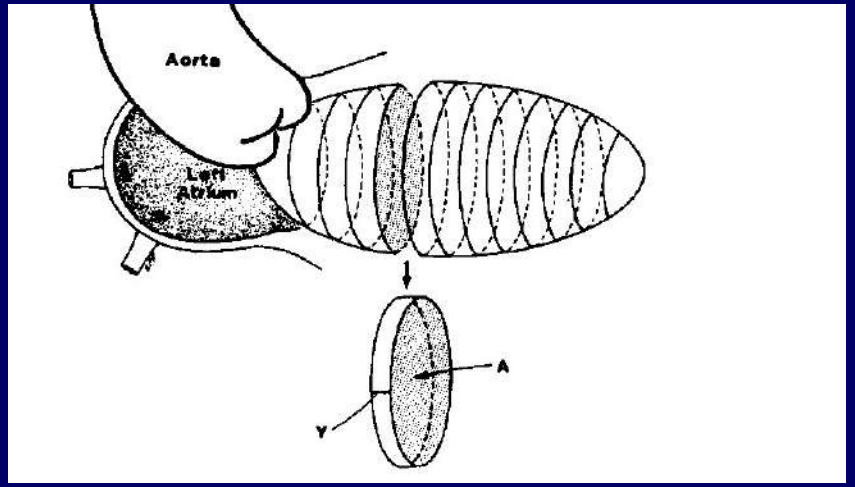
Reduced tolerance to physicl exercise
Weakness

Ankle edema

Less frequent

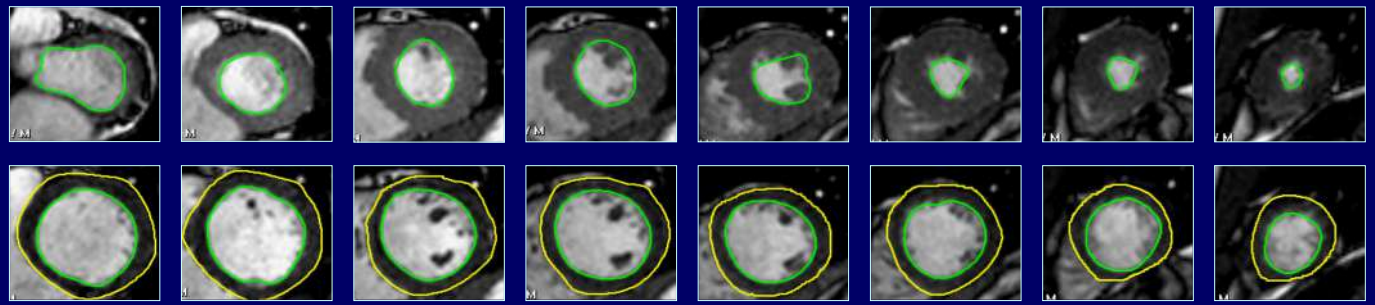
Night cough
Breath shorteness
Body weight reduction
Confusion/depression
Palpitations
Dizziness
Bendopnea

Modello grafico
(cine-RM)



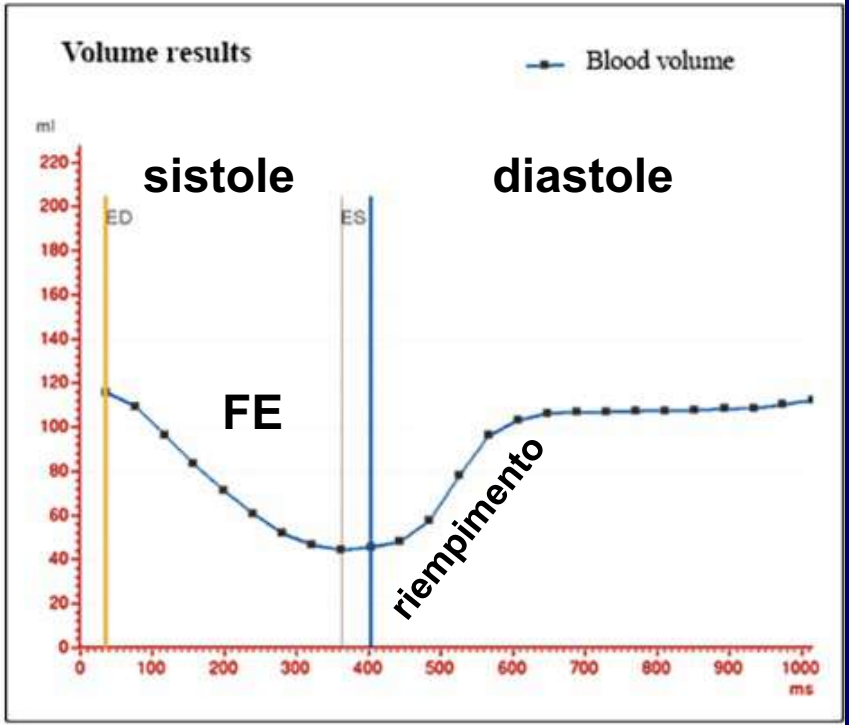
ES

ED



Volumi

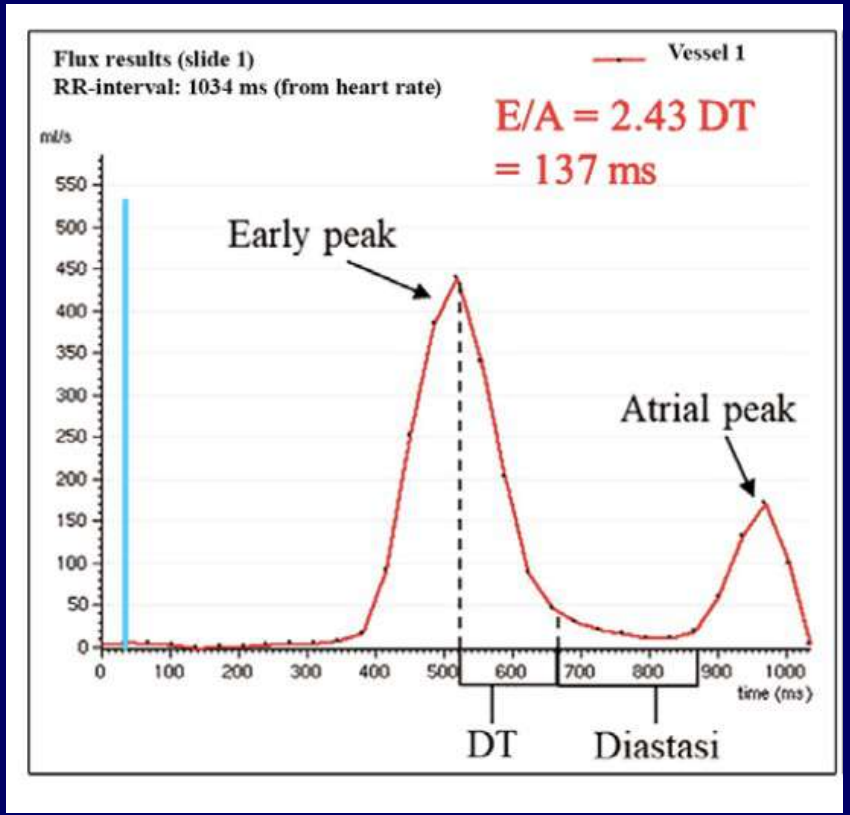
Healthy volunteer



Perseghin G, Il Diabete, 2022

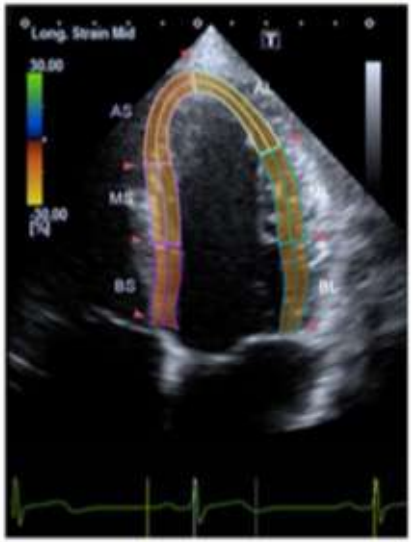
Flussi

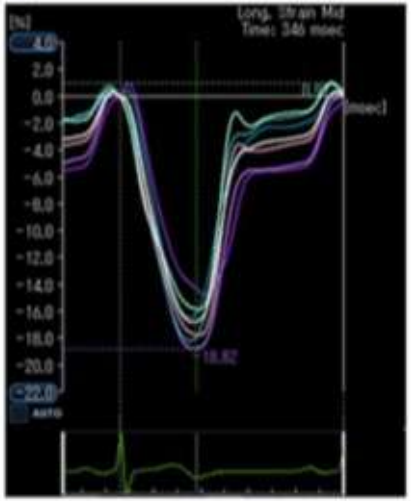
Healthy volunteer

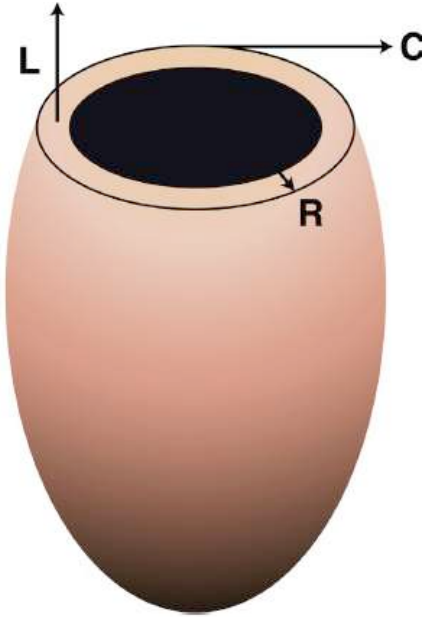


Perseghin G, Il Diabete, 2022

Global longitudinal strain (GLS)







- Longitudinal
- Radial
- Circumpherential

EF

Diastolic function

Filling pressure

Cardiac geometry

Perseghin G, Il Diabete, 2022

Abnormal Left Ventricular Energy Metabolism in Obese Men With Preserved Systolic and Diastolic Functions Is Associated With Insulin Resistance

STAGE B
Structural disorder

- LV systolic dysfunction
- LV diastolic dysfunction
- LV hypertrophy
- Chamber enlargement
- Valvular disease
- Increased filling pressures OR Elevated biomarkers

Table 2—*Morphologic parameters and functional features of study subjects stratified for quartiles of BMI (kg/m²)*

	Quartile I	Quartile II	Quartile III	Quartile IV
	21.7 ± 1.3 (18.5–23.2)	24.6 ± 0.7 (23.3–25.5)	26.9 ± 0.9 (25.5–29.0)	32.0 ± 1.7 (30.0–35.3)
Heart rate (beats/min)	63 ± 13	63 ± 9	63 ± 10	65 ± 9
Morphologic features				
End diastolic volume (ml)	143 ± 22	141 ± 21	148 ± 33	144 ± 28
End systolic volume (ml)	56 ± 14	55 ± 13	56 ± 16	[illegible]
End diastolic wall mass (g)	138 ± 24	133 ± 21	145 ± 17	157 ± 19*
End diastolic wall mass/volume ratio (g/ml)	0.97 ± 0.16	0.94 ± 0.10	1.02 ± 0.18	1.12 ± 0.19*
Systolic function				
Stroke volume (ml)	87 ± 13	86 ± 11	92 ± 19	93 ± 16
Cardiac output (l/min)	5.4 ± 1.4	5.4 ± 0.9	5.6 ± 1.0	6.0 ± 1.2
Ejection fraction (%)	61 ± 5	62 ± 5	62 ± 4	65 ± 4
Diastolic function				
Early PFR (ml/s)	464 ± 78	475 ± 74	432 ± 92	469 ± 96
Atrial PFR (ml/s)	213 ± 54	219 ± 42	238 ± 84	261 ± 64
E/A peak flow	2.31 ± 0.69	2.24 ± 0.49	1.99 ± 0.70	1.88 ± 0.49
Deceleration time (ms)	176 ± 26	183 ± 34	197 ± 39	183 ± 35

Data are means ± SD (BMI range) from two-tailed, independent-Samples *t* test. †$P < 0.05$ vs. quartiles I and II in one-way ANOVA and Bonferroni post hoc analysis.
PFR: peak filling rate

Perseghin G et al Diabetes Care, 2007

Diagnostic algorithm

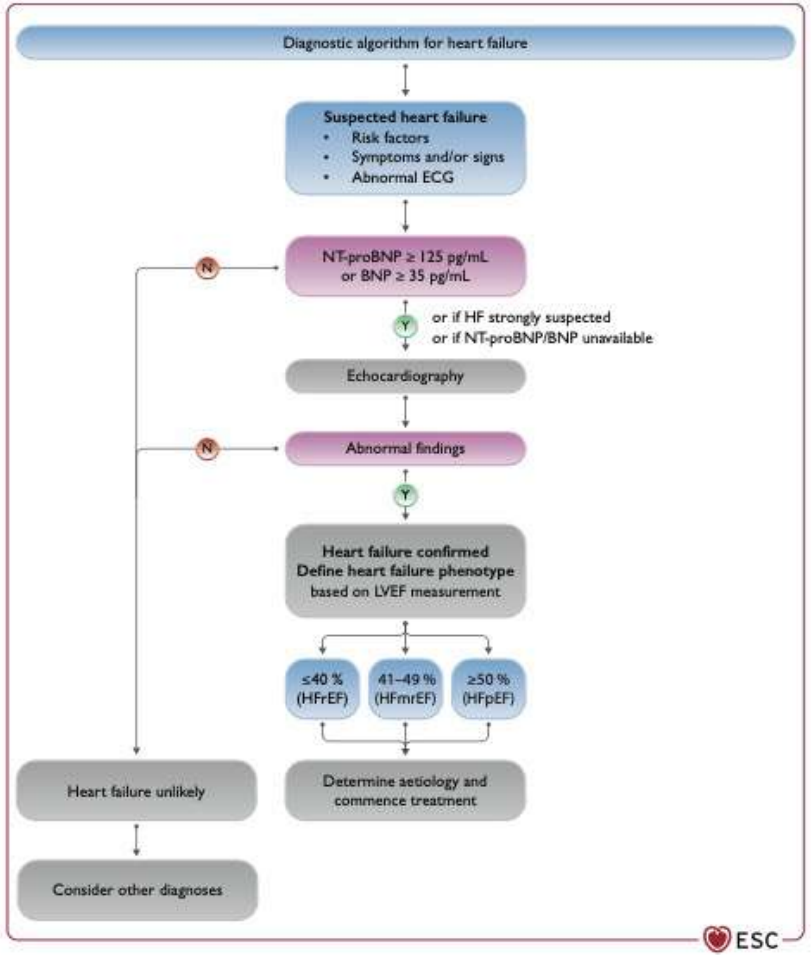


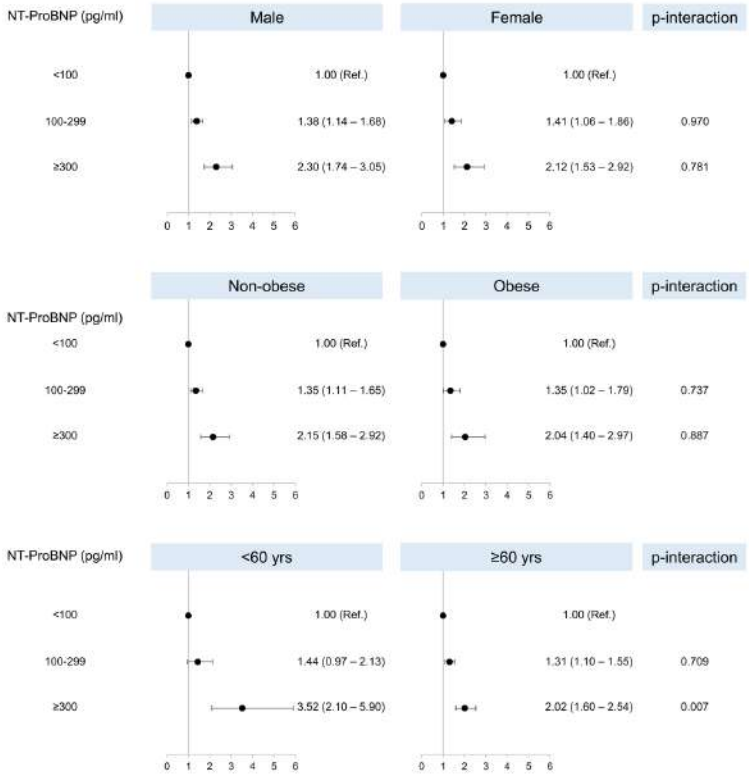
Figure 1 The diagnostic algorithm for heart failure. BNP = B-type natriuretic peptide; ECG = electrocardiogram; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B type natriuretic peptide. The abnormal echocardiographic findings are described in more detail in the respective sections on HFrEF (section 5), HFmrEF (section 7), and HFpEF (section 8).

Eur Heart J, 2021

NT-ProBNP in T2DM (NHANES 1999-2004 through 2015)

Across the spectrum of glucose tolerance

	NT-ProBNP (pg/ml)			
	All-cause mortality		Cardiovascular mortality	
	Events (n/N)	Incidence rate per 1000 person-years (95% CI)	Events (n/N)	Incidence rate per 1000 person-years (95% CI)
Entire cohort				
<100	655/3446	14.8 (13.7-15.9)	123/3446	2.8 (2.3-3.3)
100-299	499/1462	29.0 (26.6-31.7)	116/1462	6.7 (5.6-8.1)
≥300	355/585	64.2 (57.8-71.2)	91/585	16.5 (13.4-20.2)
HbA1c<5.7%				
<100	323/2144	11.5 (10.3-12.9)	59/2144	2.1 (1.6-2.7)
100-299	284/925	25.3 (22.6-28.5)	53/925	4.7 (3.6-6.2)
≥300	169/305	55.6 (47.8-64.6)	33/305	10.8 (7.7-15.3)
HbA1c 5.7-6.4%				
<100	151/727	16.5 (14.0-19.3)	24/727	2.6 (1.8-3.9)
100-299	92/280	28.4 (23.1-34.7)	27/280	8.3 (5.7-12.2)
≥300	75/116	69.9 (55.7-87.6)	22/116	20.5 (13.5-31.1)
Diabetes				
<100	181/575	25.7 (22.2-29.8)	40/575	5.7 (4.2-7.8)
100-299	123/257	44.7 (37.5-53.3)	36/257	13.1 (9.4-18.1)
≥300	111/164	78.4 (65.1-94.4)	36/164	25.4 (18.3-35.2)



Ciardullo S et al
Cardiovasc Diabetol, 2022

STAGE C/D
Symptoms of HF

- Exertional dyspnea
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Weakness/fatigue
- Weight gain

CVOTs in HF

Table 2. Cardiovascular Outcome Trials Involving Patients with Heart Failure.*

Variable	DAPA-HF	EMPEROR-Reduced	EMPEROR-Preserved	SOLOIST-WHF
Drug	Dapagliflozin	Empagliflozin	Empagliflozin	Sotagliflozin
No. of patients	4744	3730	5988	1222
Type 2 diabetes — % of patients	41.7	49.8	49.1	100
LVEF — %	31.1	27.4	54.3	35
Median NT-proBNP — pg/ml	1437	1907	970	1864
Mean eGFR — ml/min/1.73 m^2	65.7	62.0	60.6	49.9
Outcomes — hazard ratio (95% CI)				
Cardiovascular death or hospitalization for heart failure	0.74 (0.65–0.85)	0.75 (0.68–0.86)	0.79 (0.69–0.90)	0.67 (0.52–0.85)
Hospitalization for heart failure	0.70 (0.59–0.83)	0.69 (0.59–0.81)	0.73 (0.61–0.88)	0.64 (0.49–0.83)

* Data sources for the trials are as follows: DAPA-HF, McMurray et al.[24]; EMPEROR-Reduced, Packer et al.[25]; EMPEROR-Preserved, Anker et al.[26]; SOLOIST-WHF, Bhatt et al.[27] The abbreviation eGFR denotes estimated glomerular filtration rate, LVEF left ventricular ejection fraction, and NT-proBNP N-terminal pro–B-type natriuretic peptide.

HF Trials
(+/- diabetes)

DAPA-HF
(Dapagliflozin NEJM 2020)

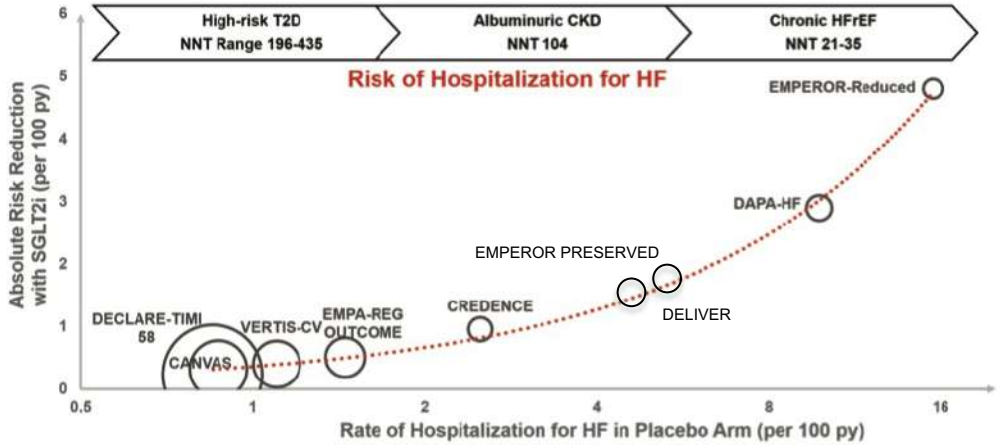
Emperor Reduced
(Empagliflozin NEJM 2020)

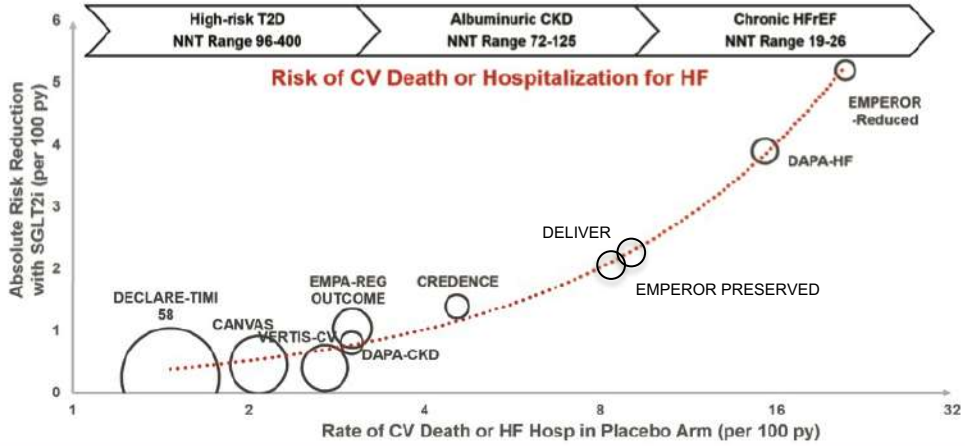
Emperor Preserved
(Empagliflozin NEJM 2021)

SOLOIST – WHF
(Sotagliflozin NEJM 2021)

DELIVER
(Dapagliflozin NEJM 2022)

Braunwald E, N Engl J Med, 2022





Risk/Benefit relationship

Bathia K et al, Eur J Heart Fail, 2021

hHF

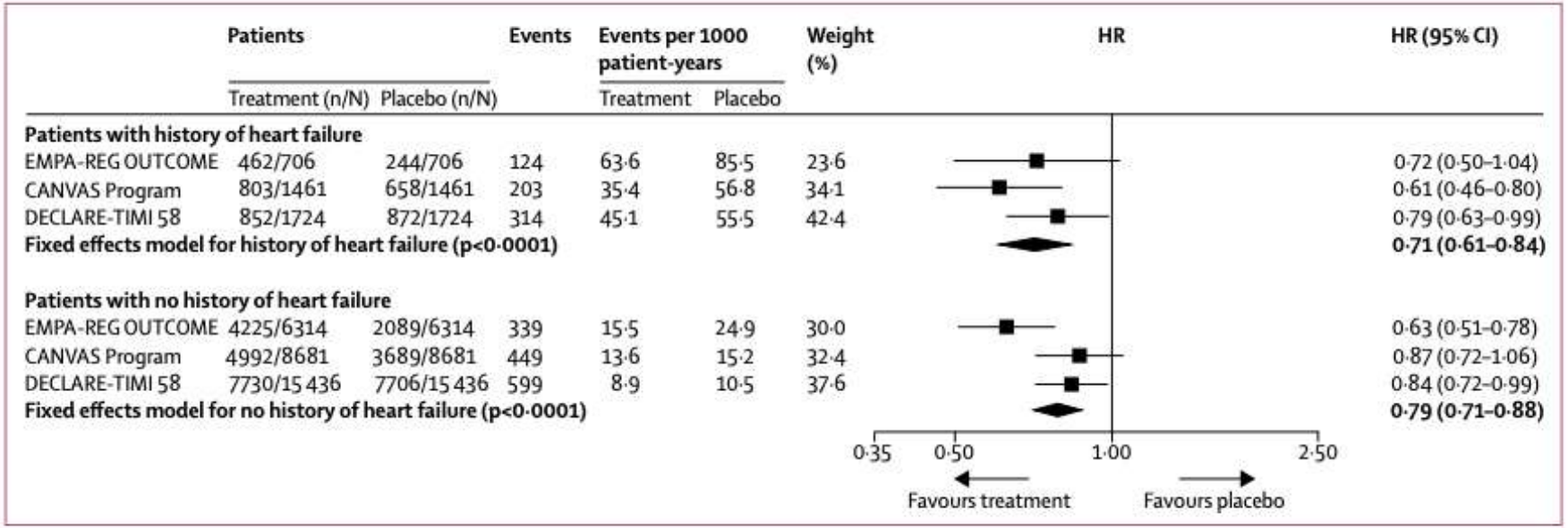
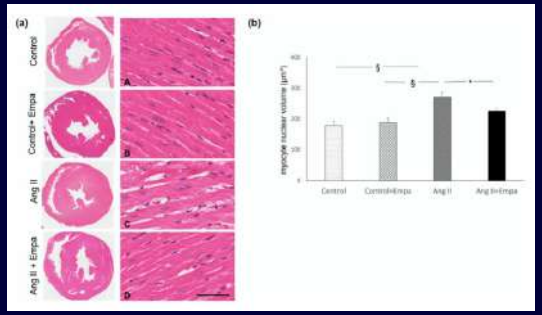


Figure 3: **Meta-analysis of SGLT2i trials on hospitalisation for heart failure and cardiovascular death stratified by history of heart failure**

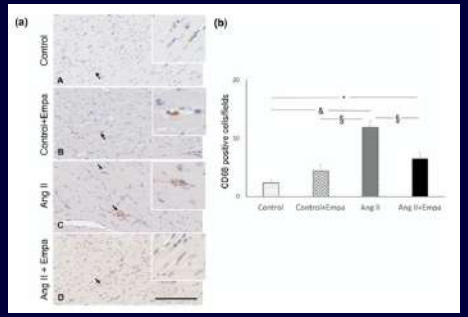
History of heart failure: Q statistic=2·02, p=0·37, I^2=0·8%; no history of heart failure: Q statistic=5·89, p=0·0527, I^2=66%. The p value for subgroup differences was 0·51. Tests for subgroup differences were based on F tests in a random effect meta-regression estimated using restricted maximum likelihood and Hartung Knapp adjustment. HR=hazard ratio. SGLT2i=sodium-glucose cotransporter-2 inhibitors.

Zelnicker TA et al, Lancet, 2019

Regardless glucose control

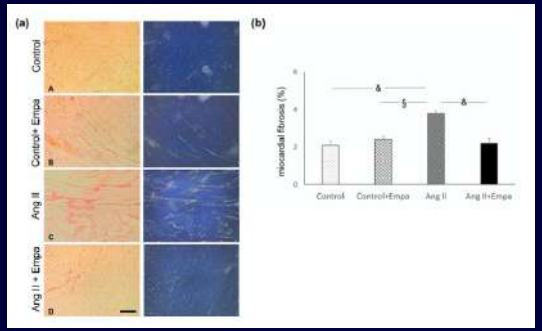


Hypertrophy

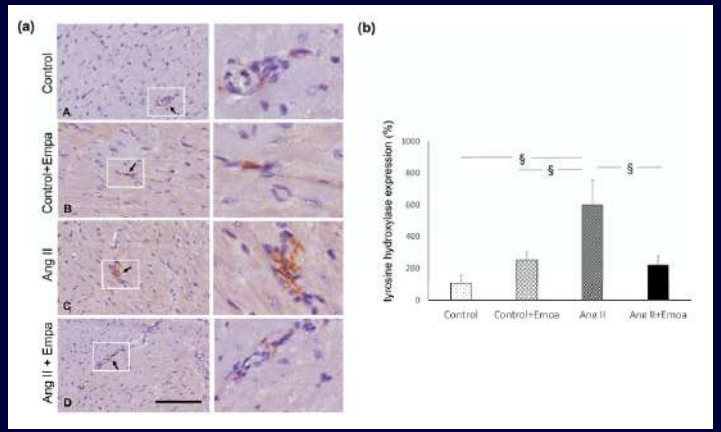


Inflammation

Non-diabetic
Hypertensive Sprague Dawley rats
(chronic angiotensin administration
using subcutaneously implanted
osmotic minipumps)



Fibrosis



Sympatetic
activity

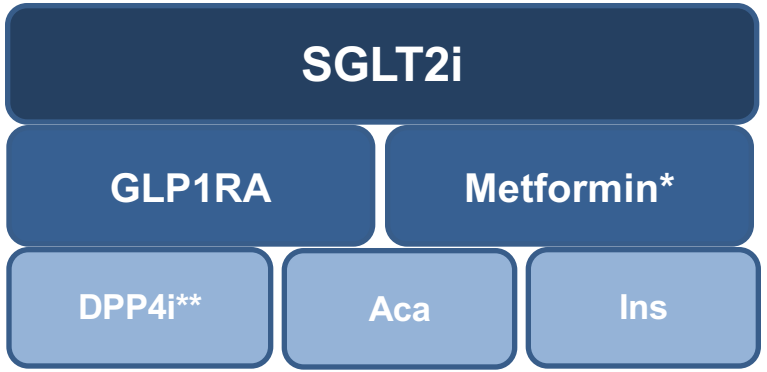
Castoldi G et al, Int J Mol Sci, 2023

Terapia Farmacologica

Quali sono i farmaci di prima, seconda e terza istanza da impiegare per il controllo della glicemia nei pazienti con diabete di tipo 2 con scompenso cardiaco?

Si raccomanda l'uso di SGLT-2i come farmaci di prima scelta per il trattamento a lungo termine di pazienti con diabete di tipo 2 con scompenso cardiaco.

I GLP-1 RA e metformina dovrebbero essere considerati come farmaci di seconda scelta, mentre DPP-4i, acarbosio ed insulina come farmaci di terza scelta.



*La metformina è controindicata in classe NYHA III-IV
**Saxagliptin è associato ad un aumento di ricoveri per scompenso cardiaco

Forza della raccomandazione: forte. Qualità delle prove: moderata.

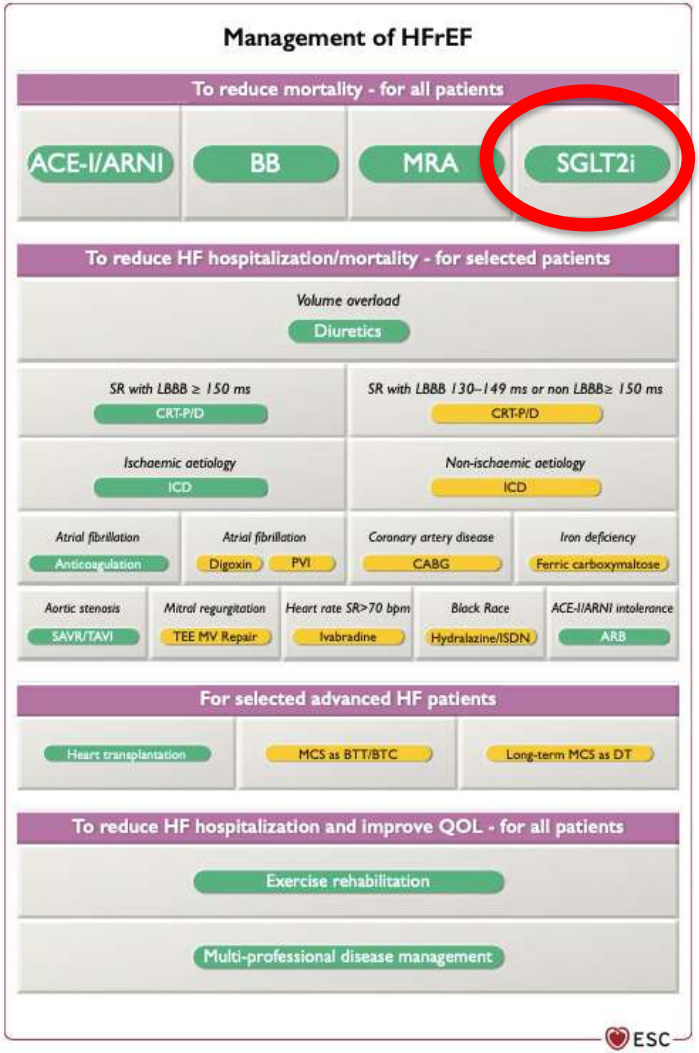
SISTEMA NAZIONALE LINEE GUIDA DELL'ISTITUTO SUPERIORE DI SANITÀ (6 luglio 2021)

ESC European Society of Cardiology
European Heart Journal (2021) **00**, 1–128
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

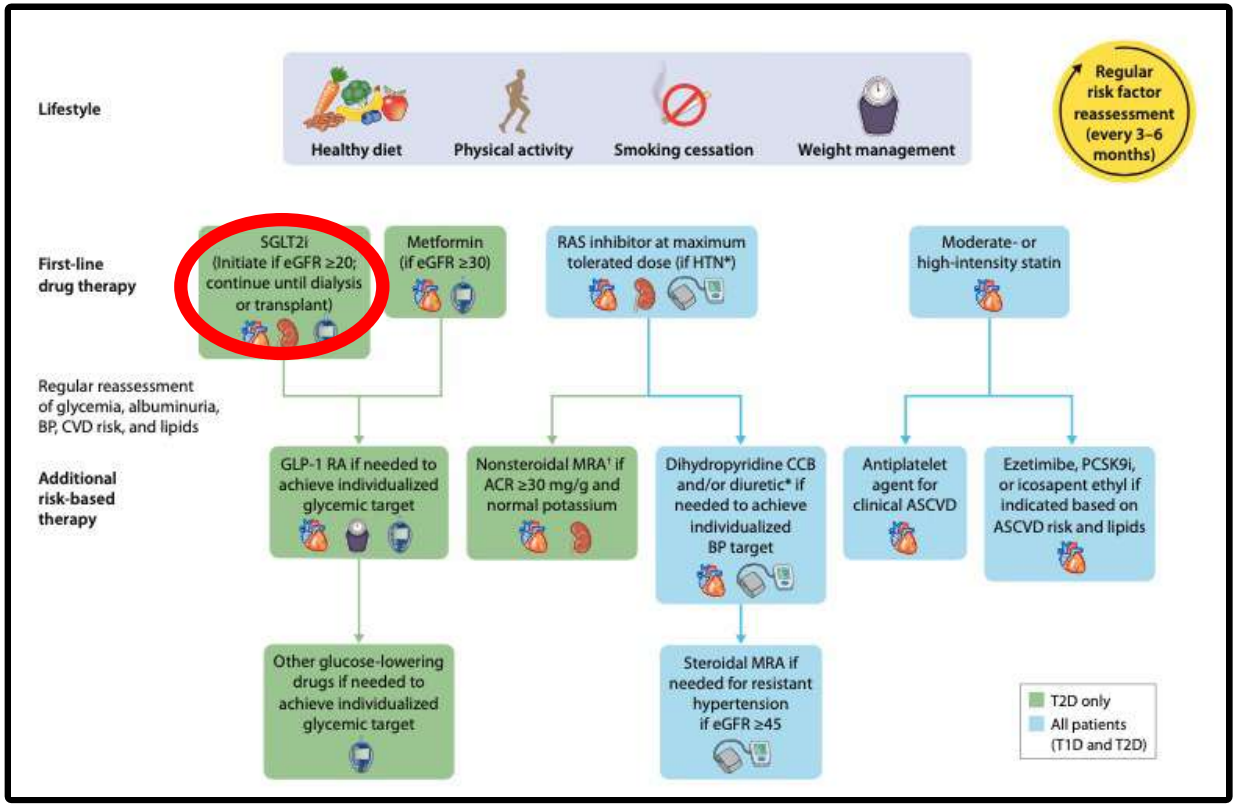
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)



Eur Heart J, 2021

Consensus ADA KDIGO

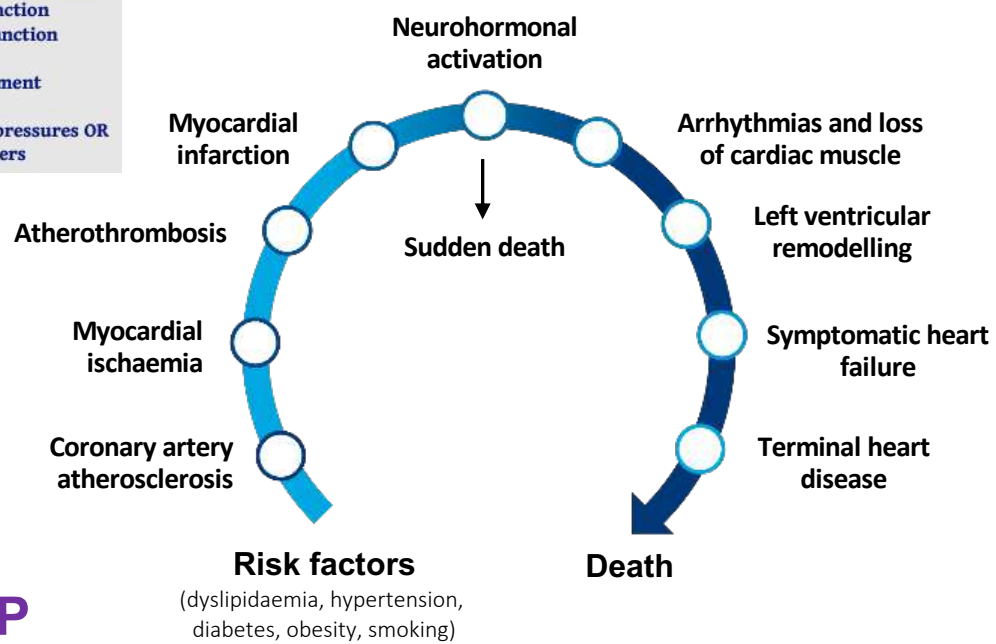


de Boer IH et al, Diabetes Care, 2022

What is the role of the HCPs?

GP
Diab
Cardio
Nephro

STAGE B
Structural disorder
- LV systolic dysfunction
- LV diastolic dysfunction
- LV hypertrophy
- Chamber enlargement
- Valvular disease
- Increased filling pressures OR Elevated biomarkers



STAGE C/D
Symptoms of HF
- Exertional dyspnea
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Weakness/fatigue
- Weight gain

GP
Diab
Cardio
Nephro

STAGE A
High risk for HF
- Obesity
- Hypertension
- Hyperlipidemia
- DKD
- CAD
- Sex
- SDOH

GP
Diab

Dzau VJ et al Circulation, 2006

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Barbara Biffi

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Nephrology
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Giovanni Corrao

Papa Giovanni XXIII - BG UNIMIB
Roberto Trevisan

Clinical Utility of Cardiovascular Risk Scores for Identification of People With Type 2 Diabetes More Likely to Benefit From Either GLP-1 Receptor Agonist or SGLT2 Inhibitor Therapy

Julian W. Sacre,[1] Dianna J. Magliano,[2,3] and Jonathan E. Shaw[1]

Savor-TIMI
Declare
Empa-Reg

Diabetes Care 2022;45:1900–1906 | https://doi.org/10.2337/dc21-1929

CONCLUSIONS

A greater increase in the rate of HHF relative to MACE was observed with progressively higher cardiovascular risk, regardless of the risk score applied. Consequently, SGLT2is may offer greater overall cardiovascular protection in those at highest MACE risk, not just those at highest HHF risk.

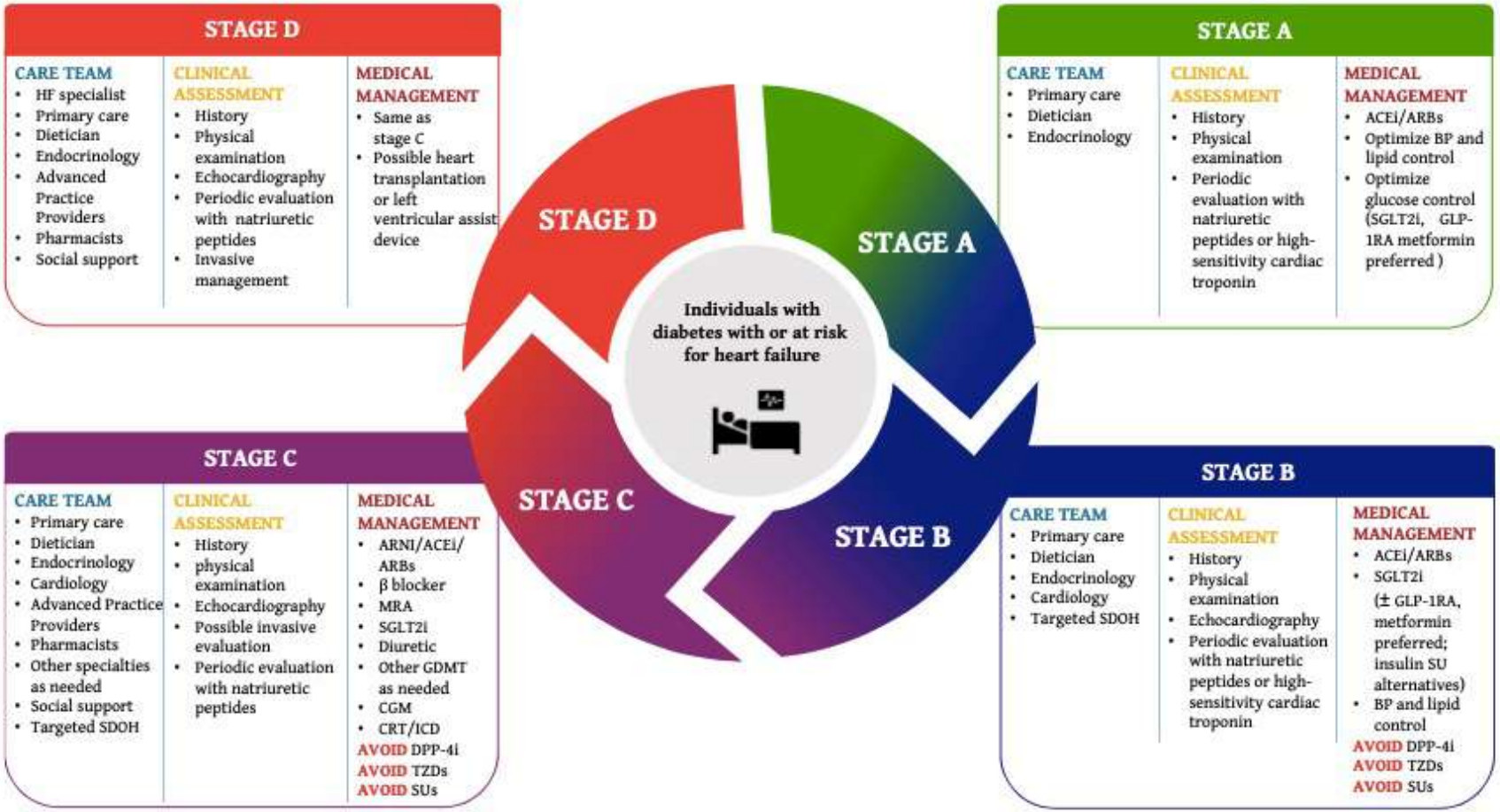

Figure 2—Multidisciplinary personalized care for in individuals with HF and diabetes. DPP-4i, DPP-4 inhibitors; SUs, sulfonylureas.