8th Annual Emirates Cardiac Society Conference

ACC Middle East Conference 2017

DUBAI

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ACC Middle East
Conference 2017

Important Comorbidities in Heart Failure Management

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Jeddah, Saudi Arabia

No Disclosures

Outline

Epidemiology & Mechanisms

Obesity

Sleep Apnea

Anemia

Diabetes

Hypertension

Comorbidities in HF

HF

Comorbidities in HF

Lipids

CAD

HTN

HF

Stroke
Psych

Afib

Comorbidities in HF

Lipids

CAD

CKD

Frailty

HTN

HF

DM

COPD
SDB

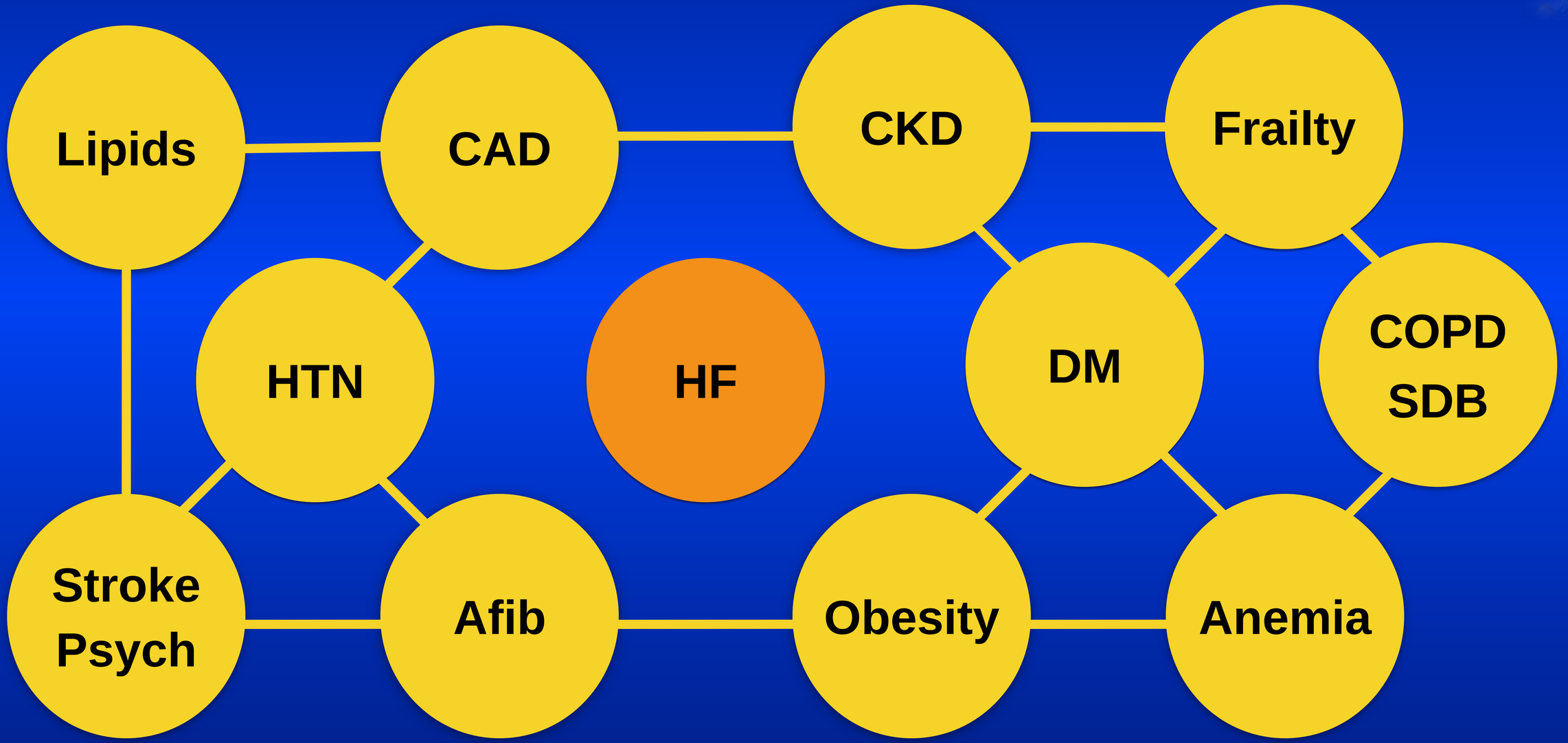
Stroke
Psych

Afib

Obesity

Anemia

Comorbidities in HF



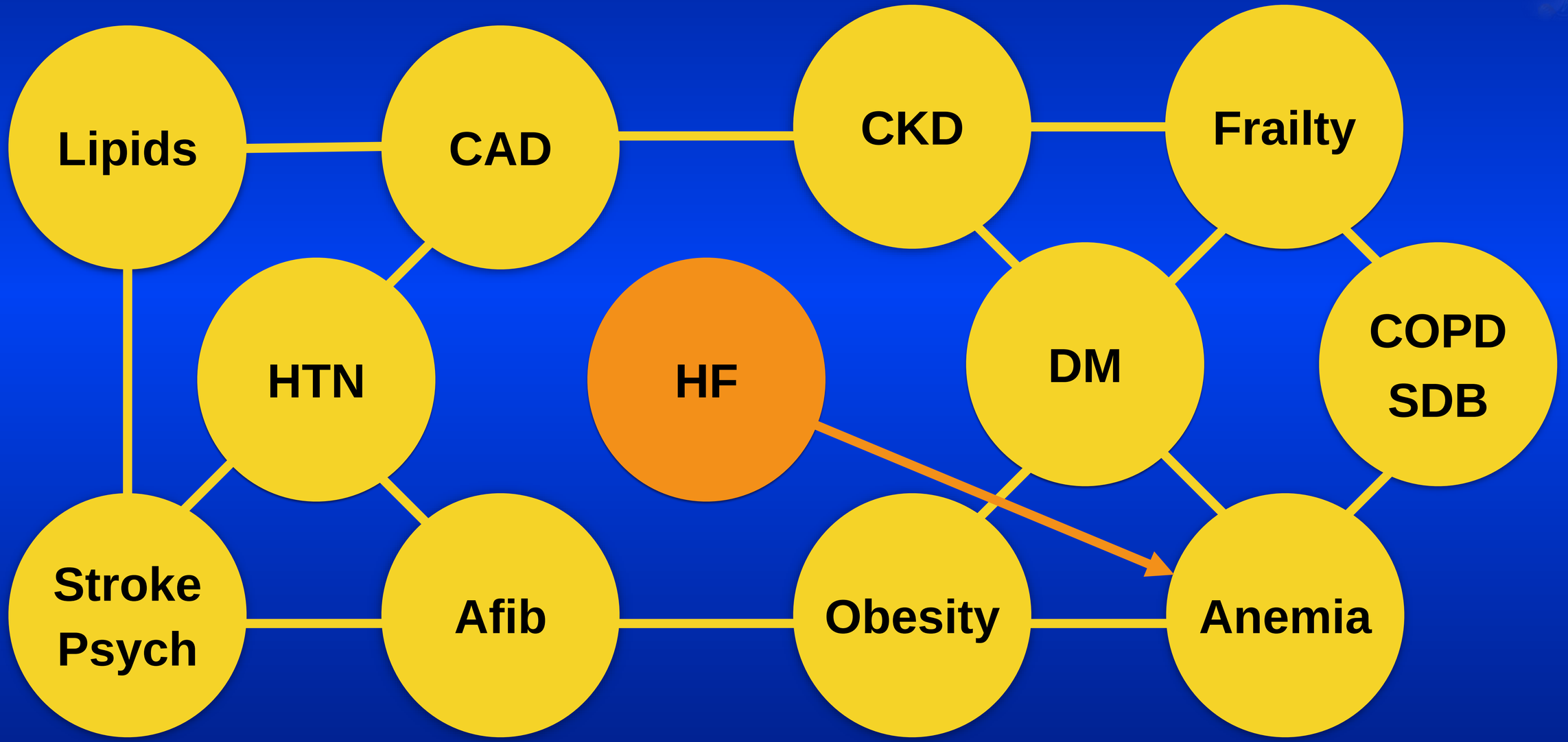
Comorbidities in HF

Beneficiary Age > 65 (N=4,376,150)

	N	%
HTN	3,685,373	84.2
CAD	3,145,718	71.9
Anemia	2,200,674	50.3
Diabetes	2,027,875	46.3
CKD	1,851,812	42.3
COPD	1,311,118	30

Most Common Co-Occurring Chronic Conditions Among Medicare Beneficiaries With HF, 2011

Comorbidities in HF



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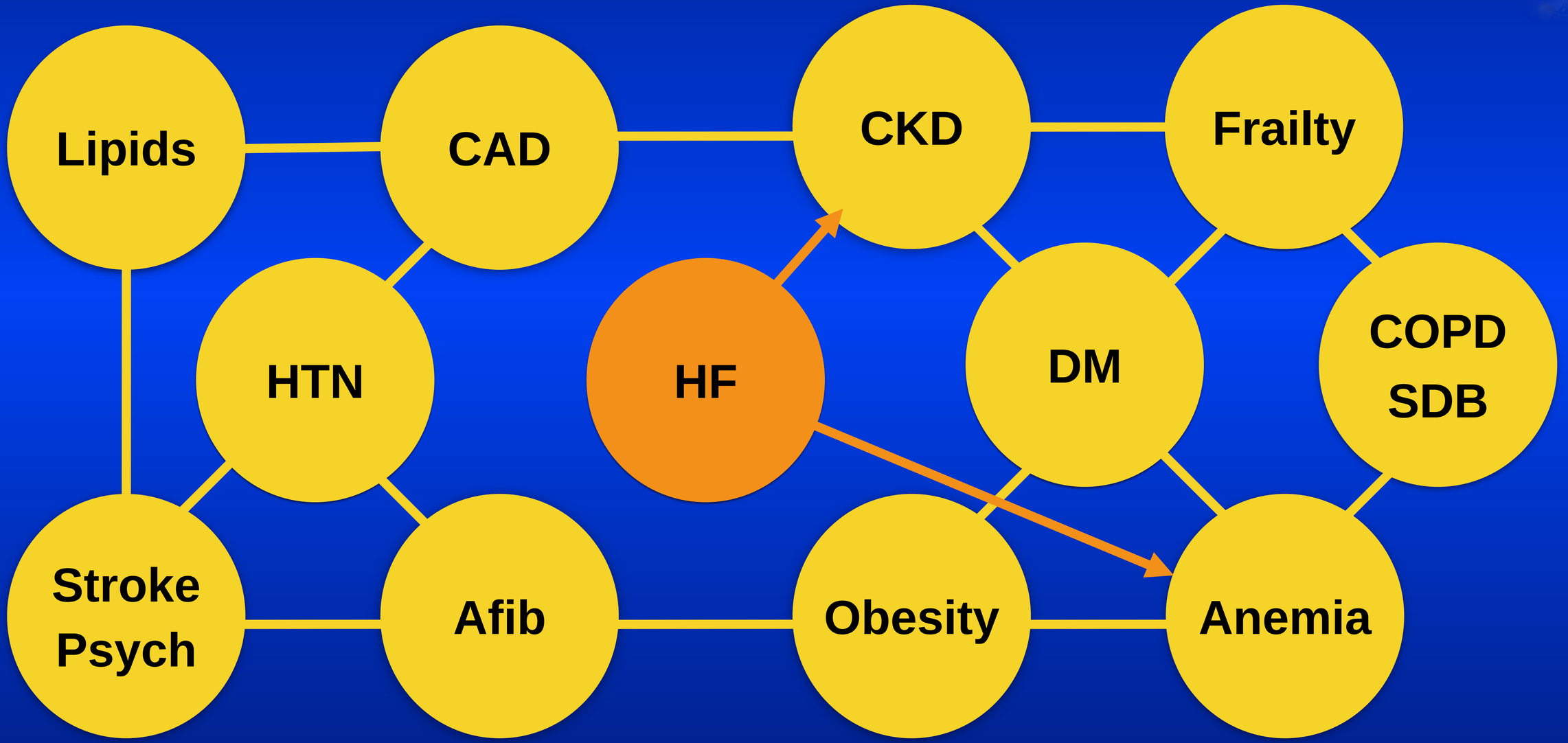

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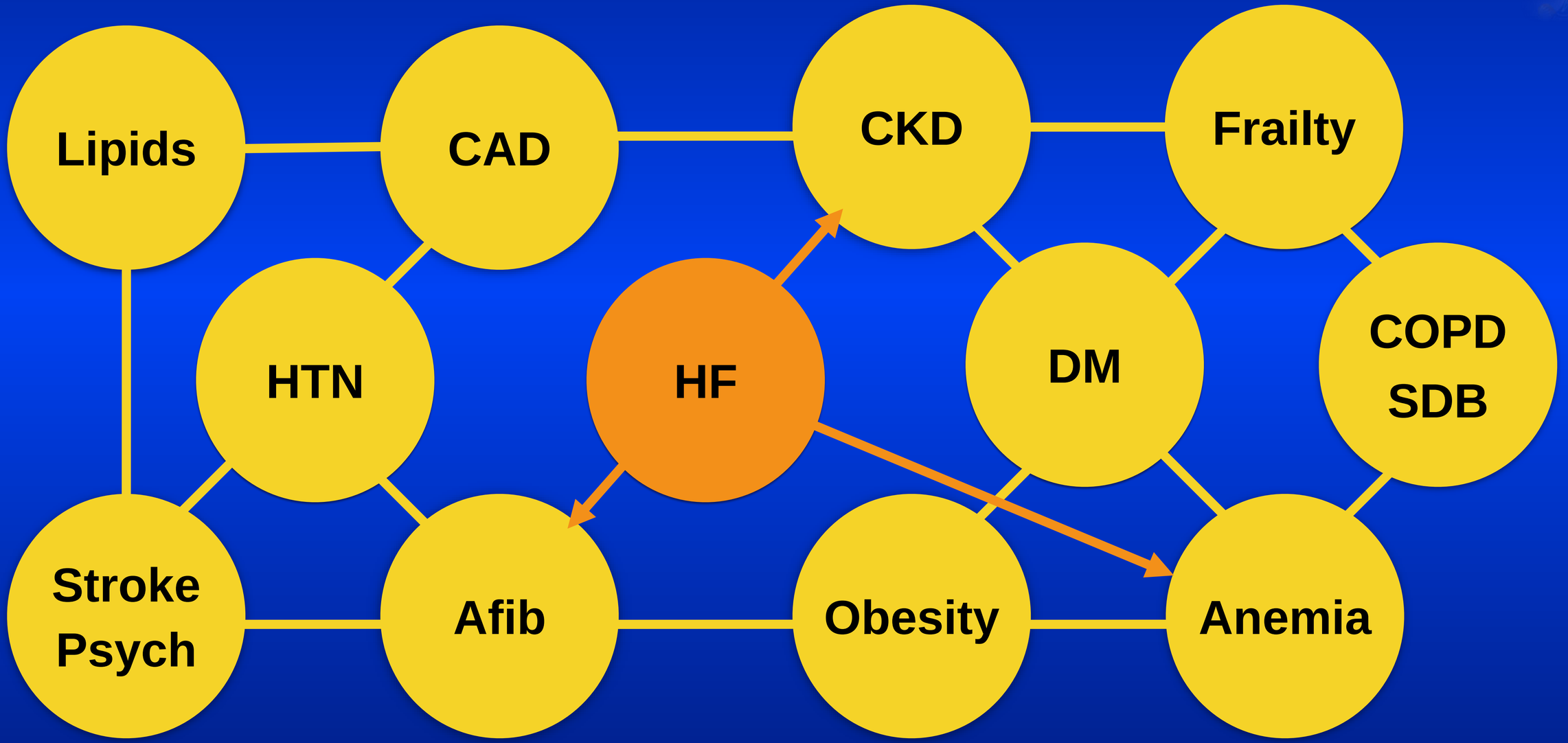

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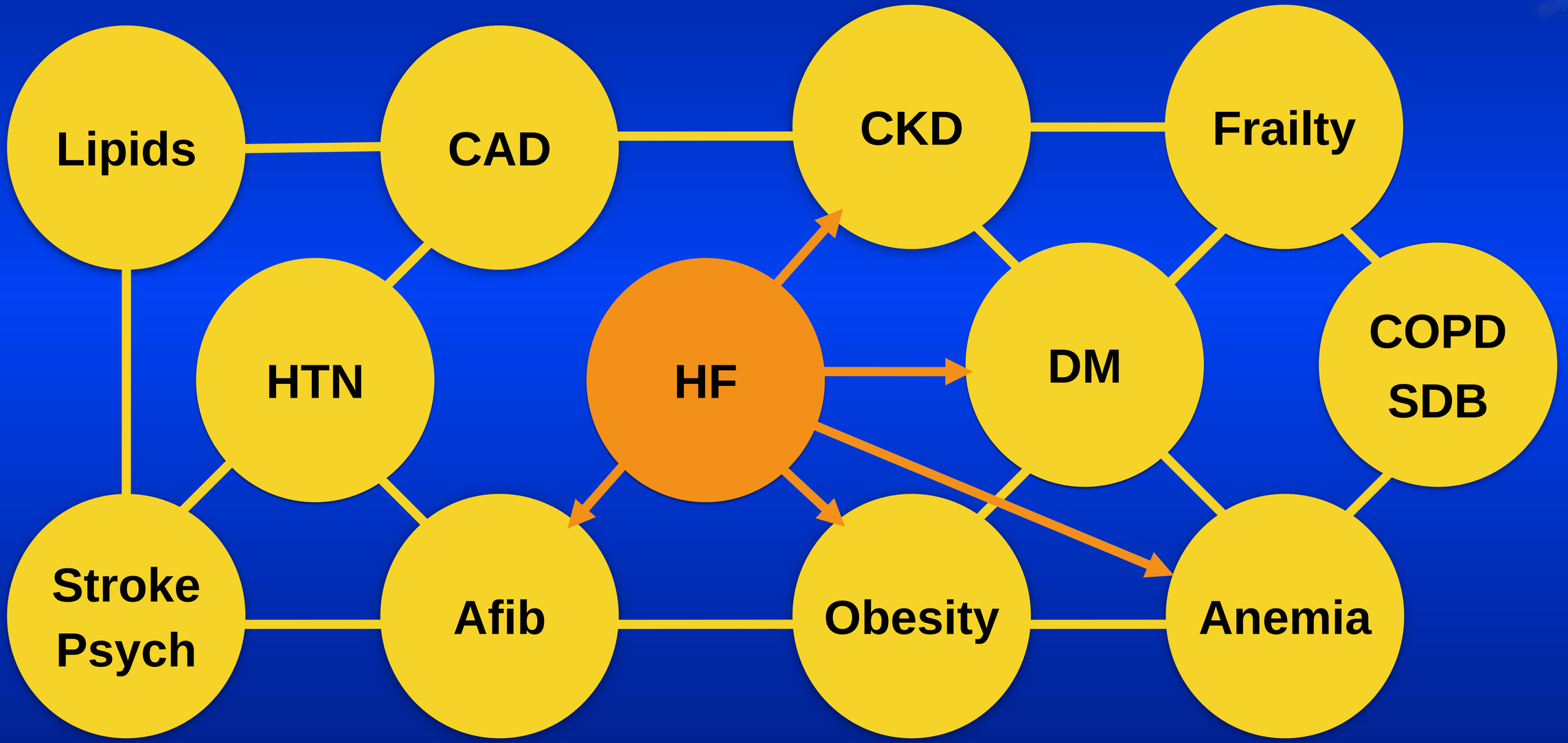

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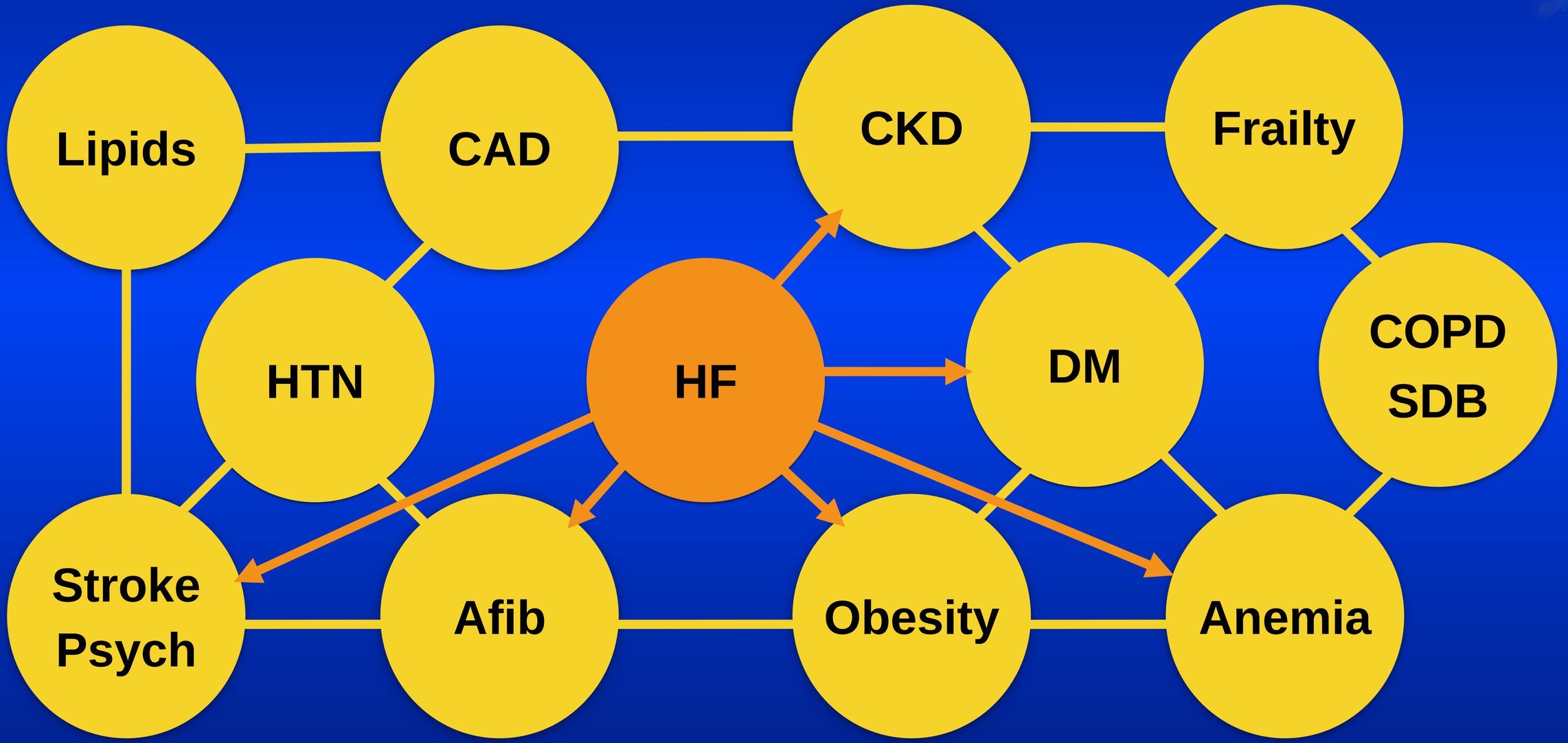

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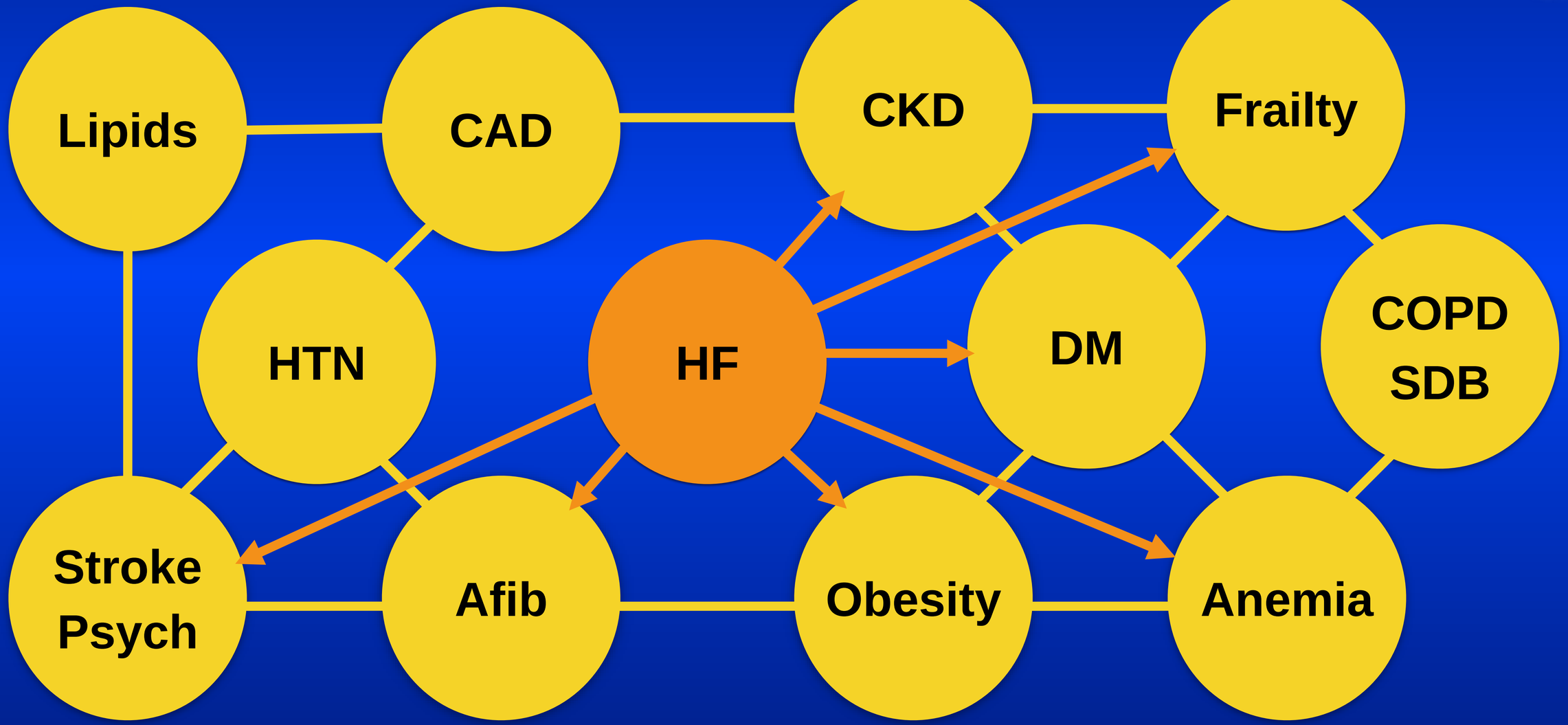

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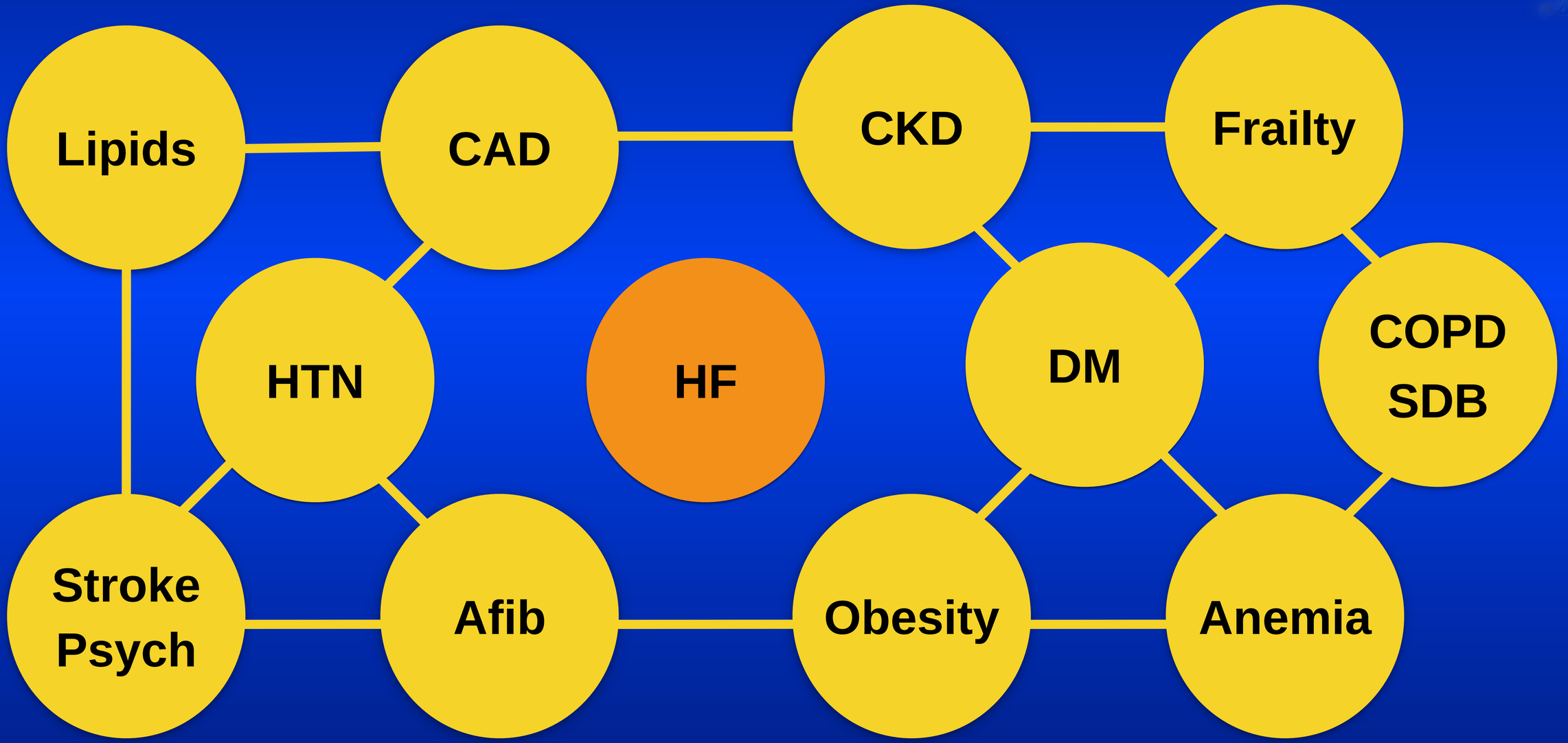

Impact of Comorbidities

Clinical assessment of HF

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Clinical assessment of HF

Adherence and response to HF meds

Impact of Comorbidities

Clinical assessment of HF

Adherence and response to HF meds

Polypharmacy

Impact of Comorbidities

Clinical assessment of HF

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Prognosis

Impact of Comorbidities

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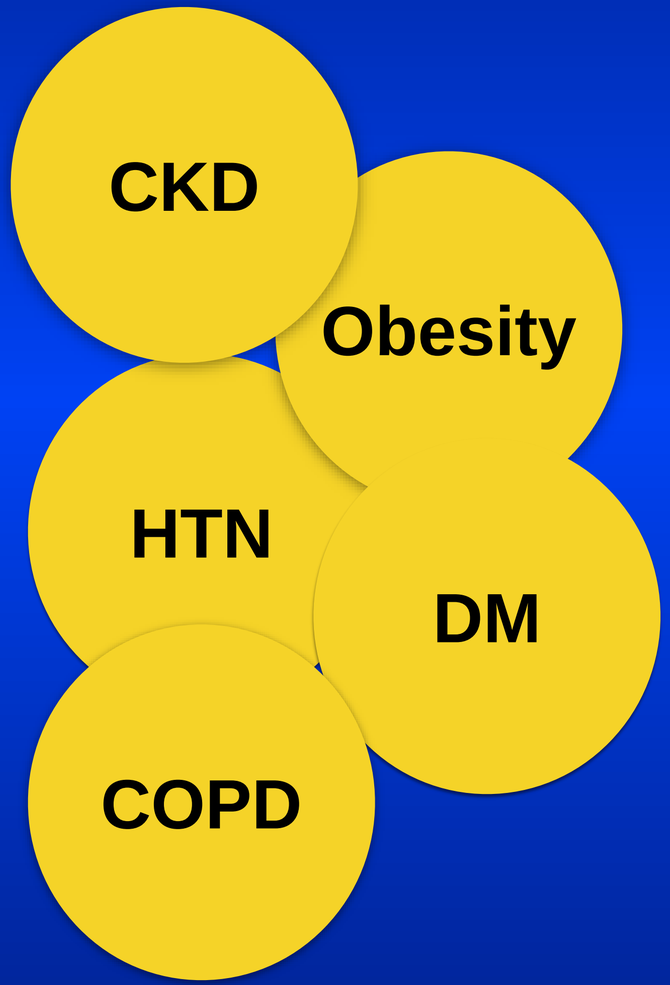
Development of HF

Not a Bystander: Pathophysiologic Links to HFpEF



Paulus WJ, et al. J Am Coll Cardiol 2013;62:263–71

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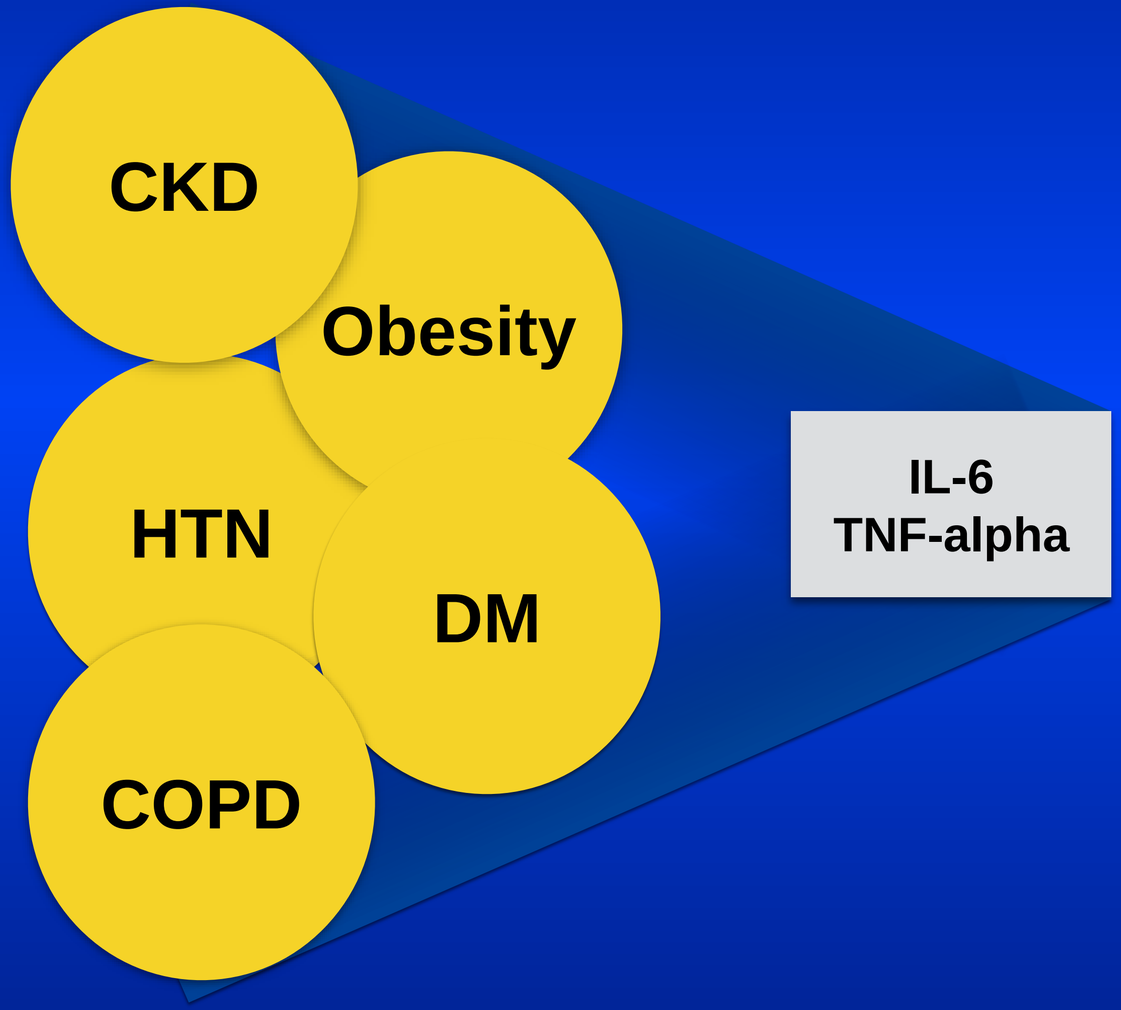

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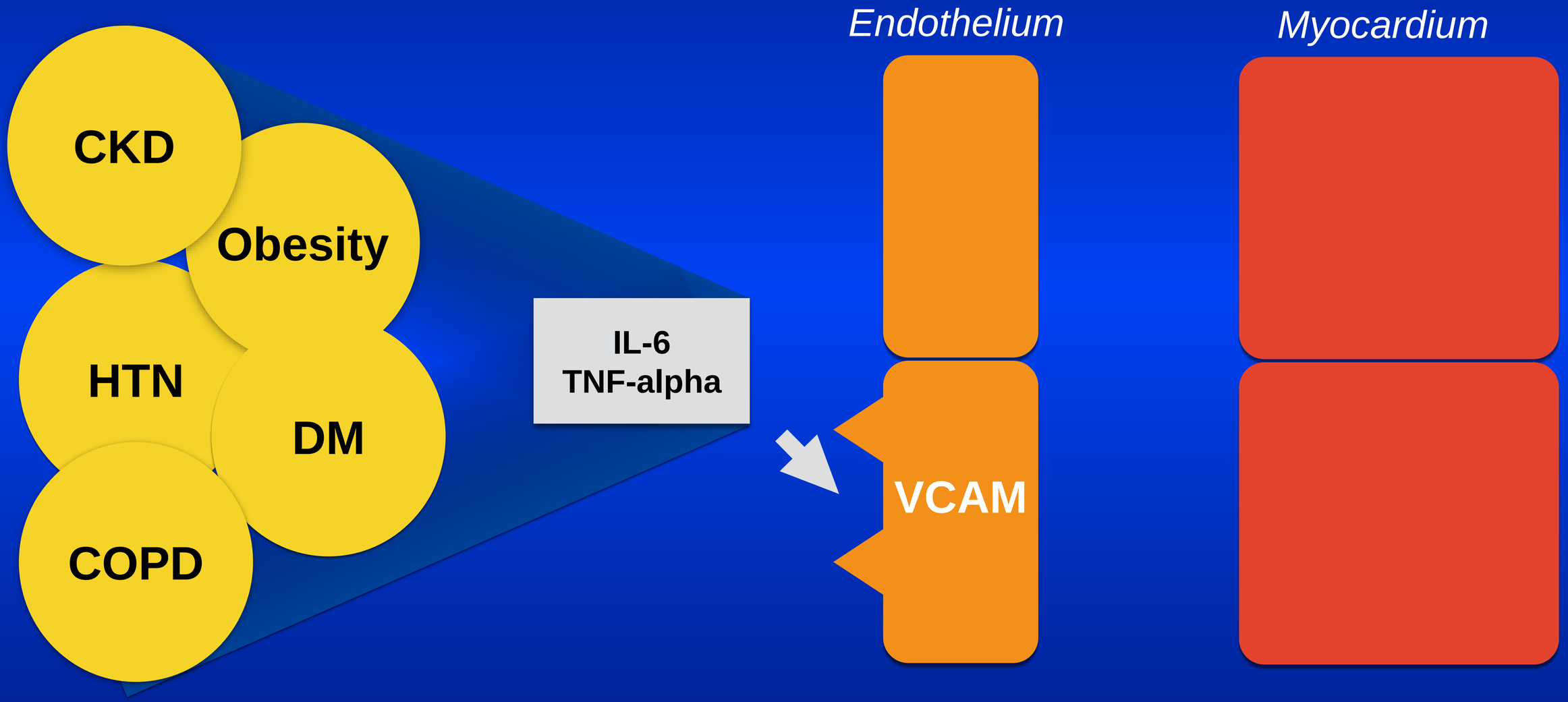

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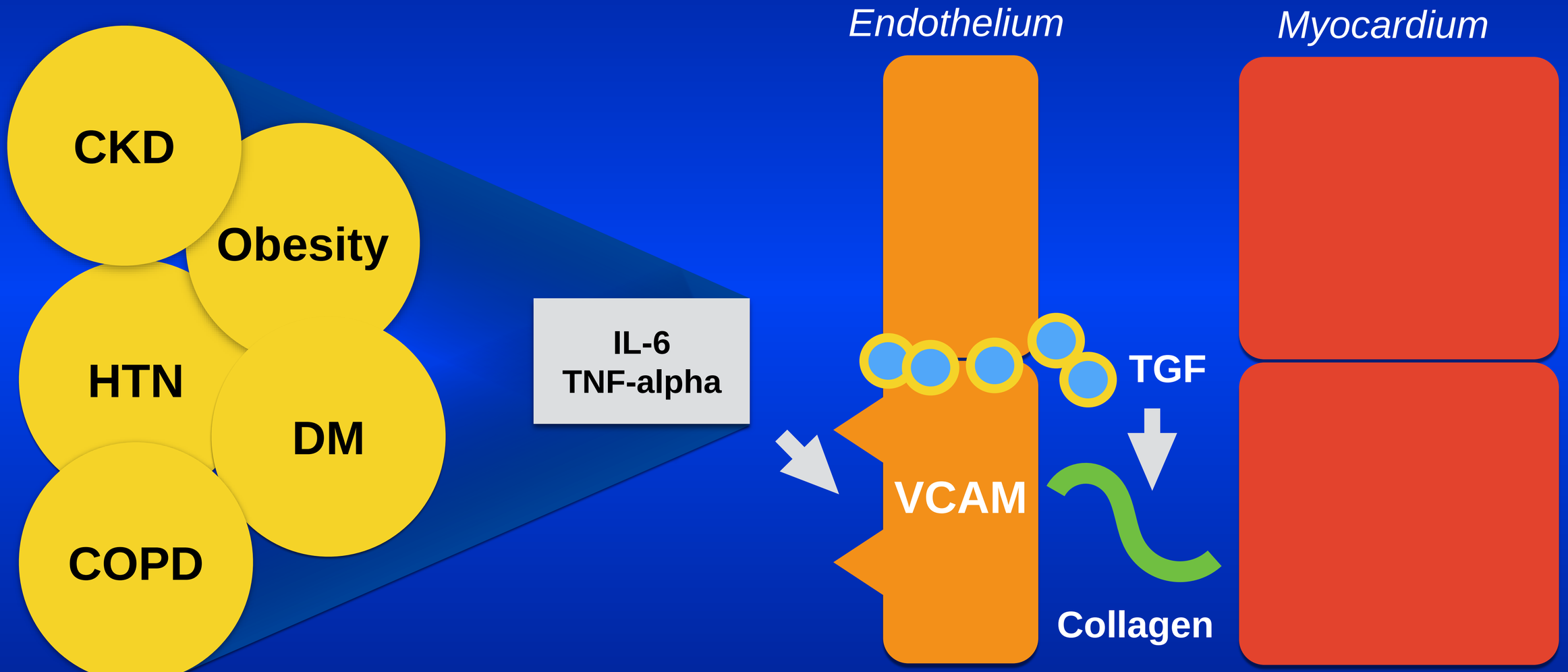

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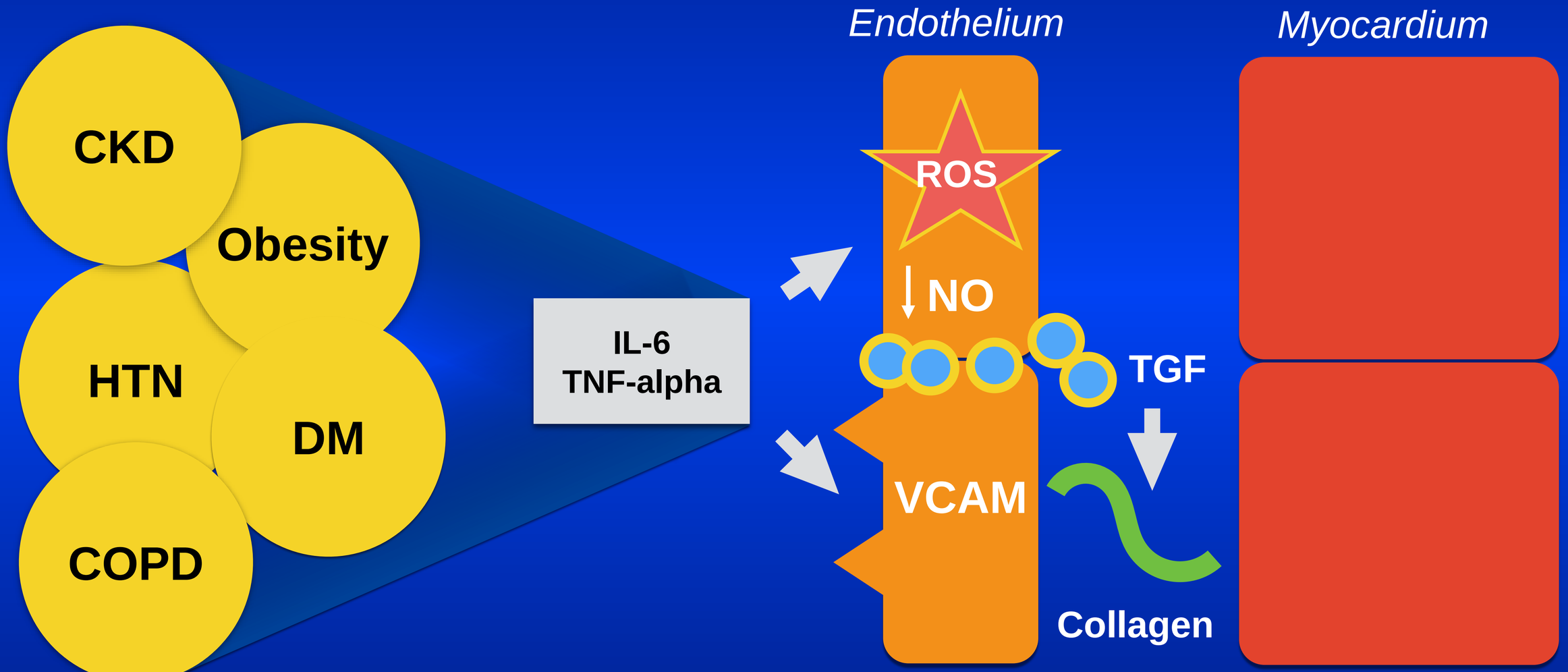

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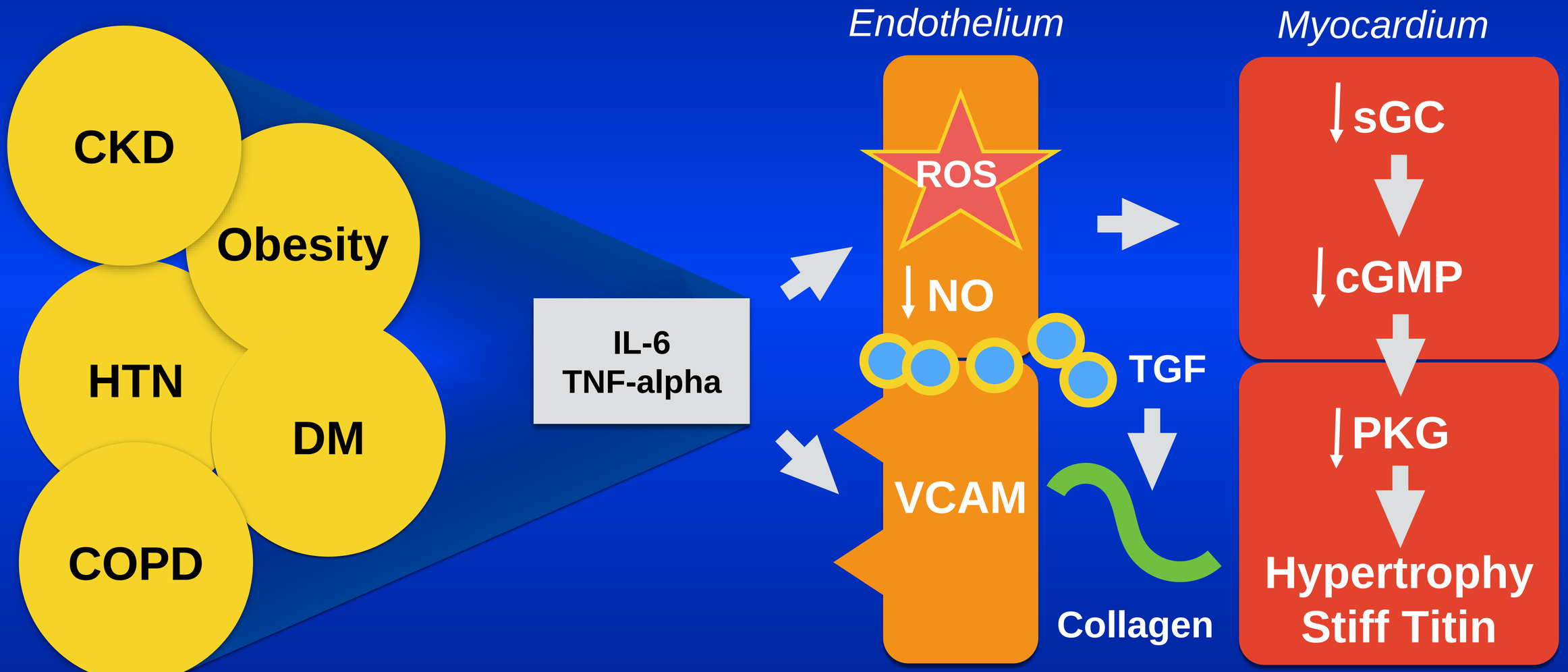

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Outline

Epidemiology & Mechanisms

Obesity

Sleep Apnea

Anemia

Diabetes

Hypertension

Global Burden of Obesity

Estimated global burden in 2015*

Adults	**603.7 million**	**(12%)**
Children	**107.7 million**	**(5%)**

Prevalance in Arabian Gulf

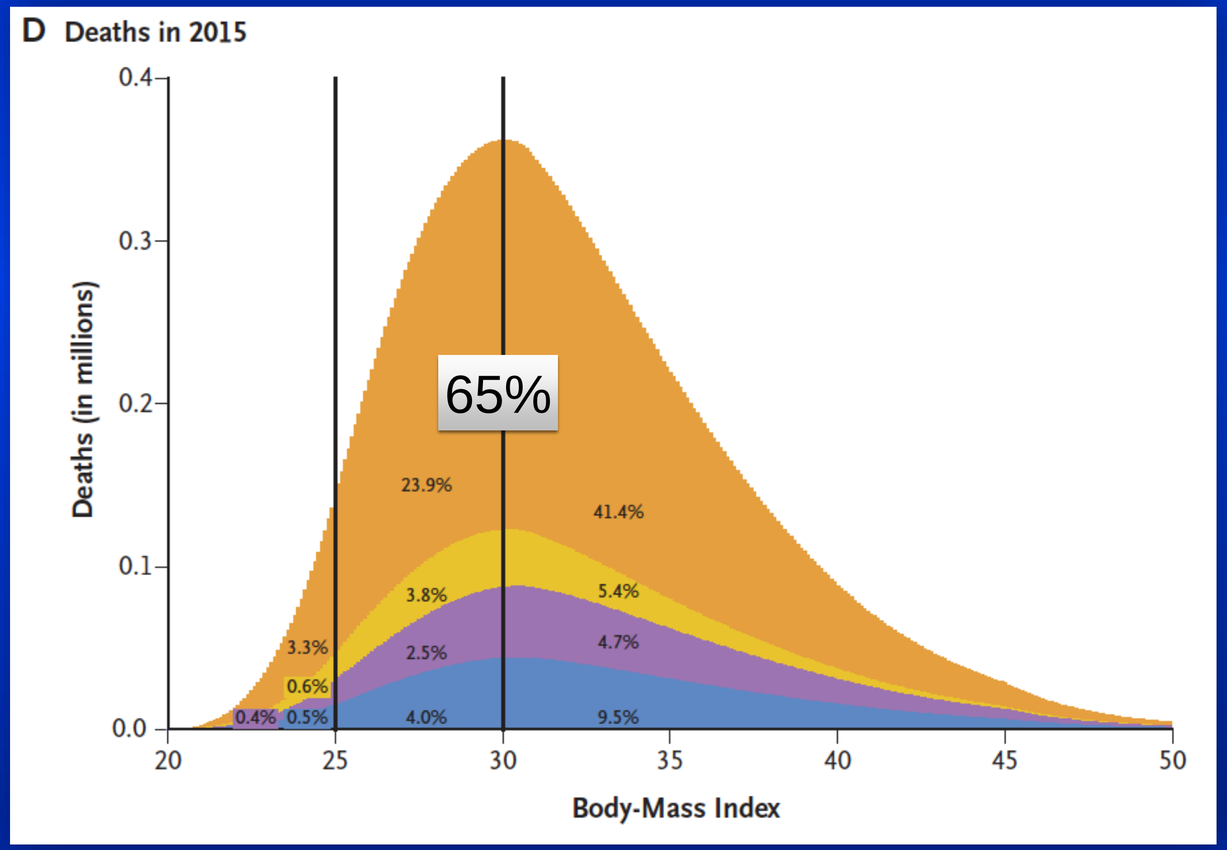
Females	**> 35%**
Men	**25-29%**

Normal	**BMI**	**18.5 - 24.99 kg/m^2**
Overweight	**BMI**	**25-29.99 kg/m^2**
Obese	**BMI**	**≥ 30 kg/m^2**

*Source: Global Burden of Disease 2015 Obesity Collaborators (N Engl J Med 2017;377:13-27)

Obesity-Associated Mortality

Deaths attributable to high BMI in 2015: 4 million (7.1%)

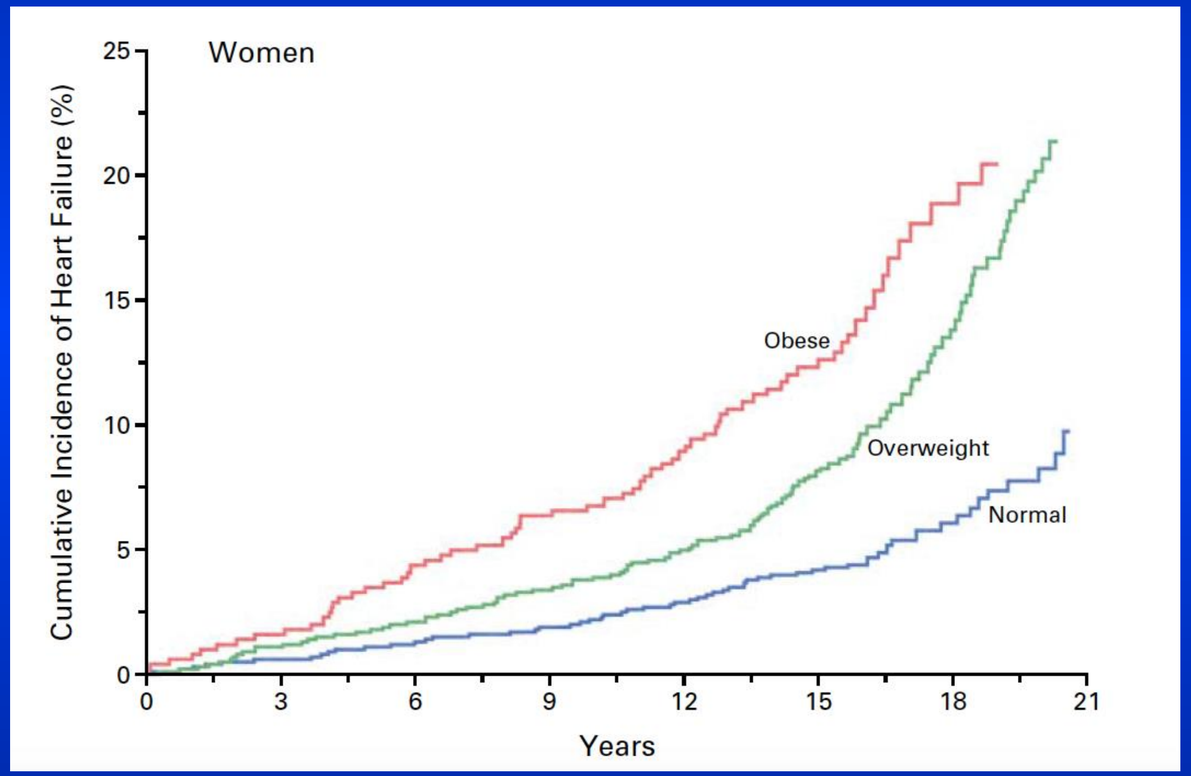


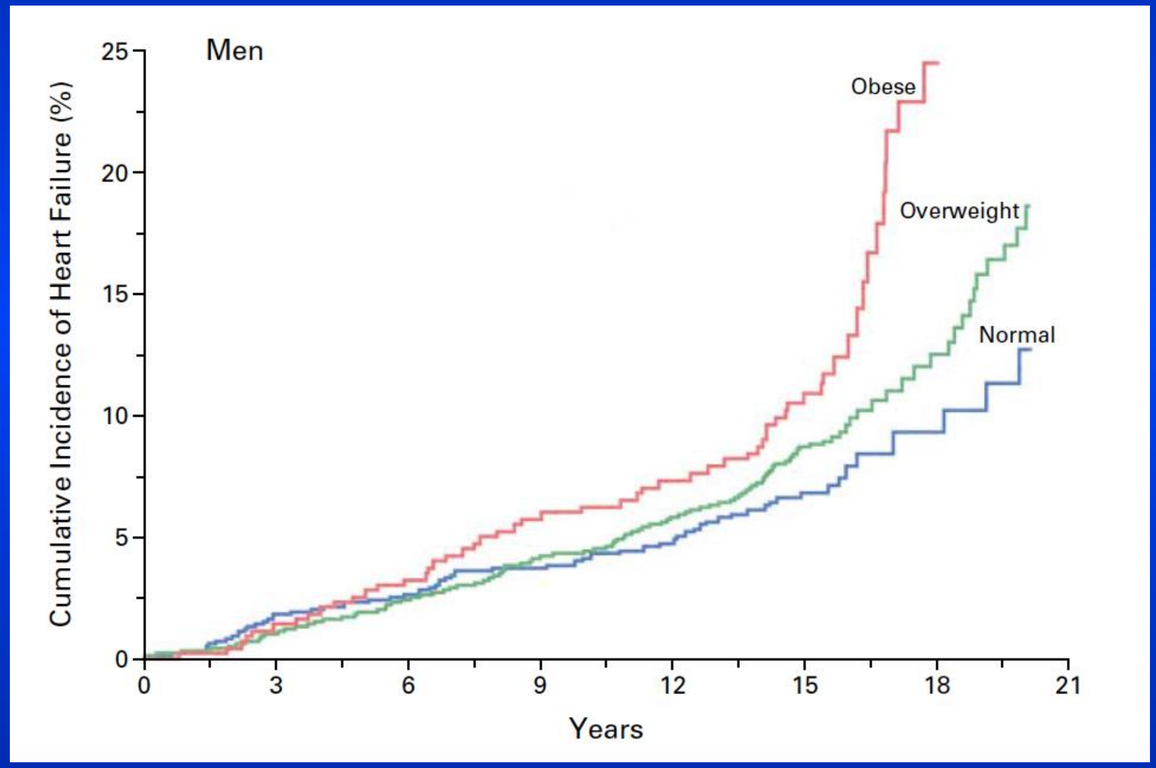
- CV Diseases
- Cancers
- CKD
- Diabetes Mellitus

Source: Global Burden of Disease 2015 Obesity Collaborators (N Engl J Med 2017;377:13-27)

Risk of HF in the Obese Population

Mean follow - up : 14 years (up to 21 years)





Women: 7% risk with each increment of 1 BMI

Men: 5% risk with each increment of 1 BMI

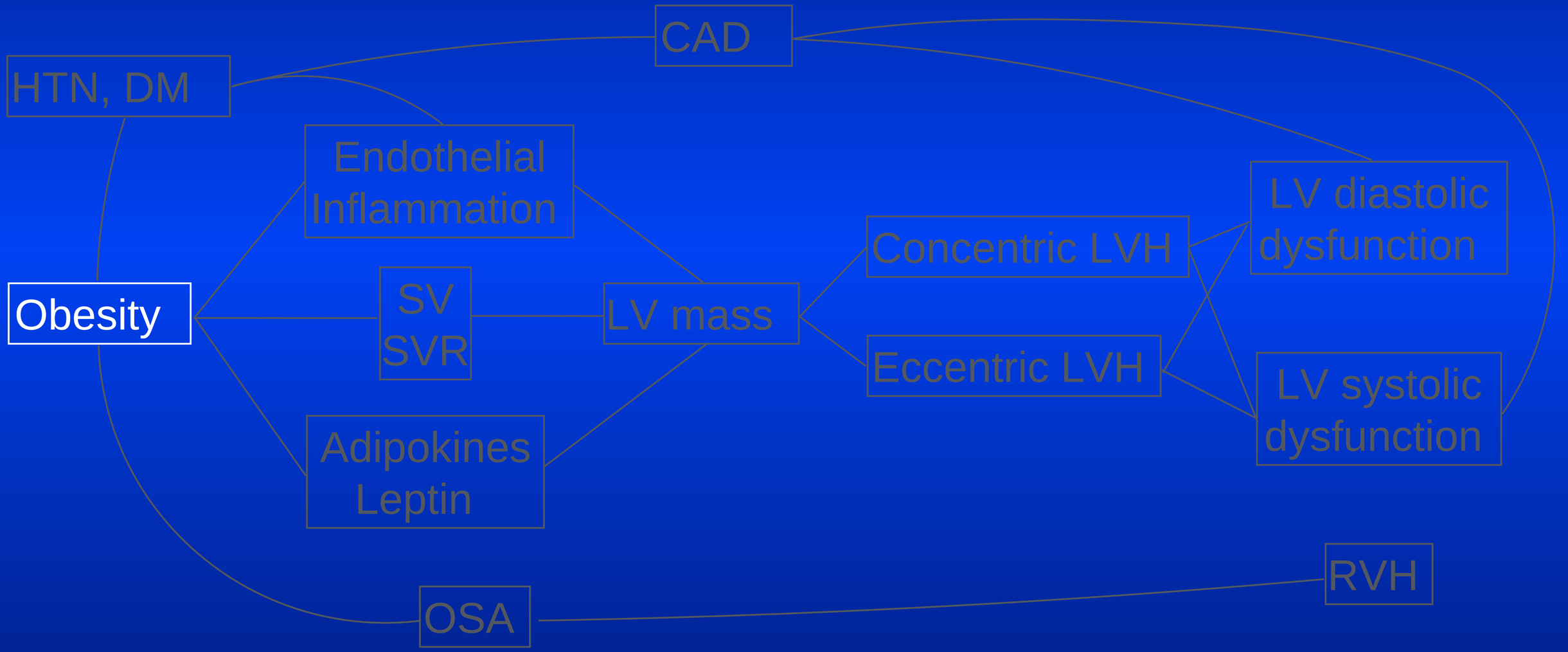
Kanchaiah S, et al. N Engl J Med 2002; 347:305-13

Obesity Rates in HF Population

Characteristic	Reduced Ejection Fraction (N=2429)	Preserved Ejection Fraction (N=2167)	P Value
Age (yr)	71.7±12.1	74.4±14.4	<0.001
Male sex (% of patients)	65.4	44.3	<0.001
Body-mass index‡	28.6±7.0	29.7±7.8	0.002
Obesity (% of patients)‡§	35.5	41.4	0.007

Owan T, et al. N Engl J Med 2006;355:251-9

HF in Obesity



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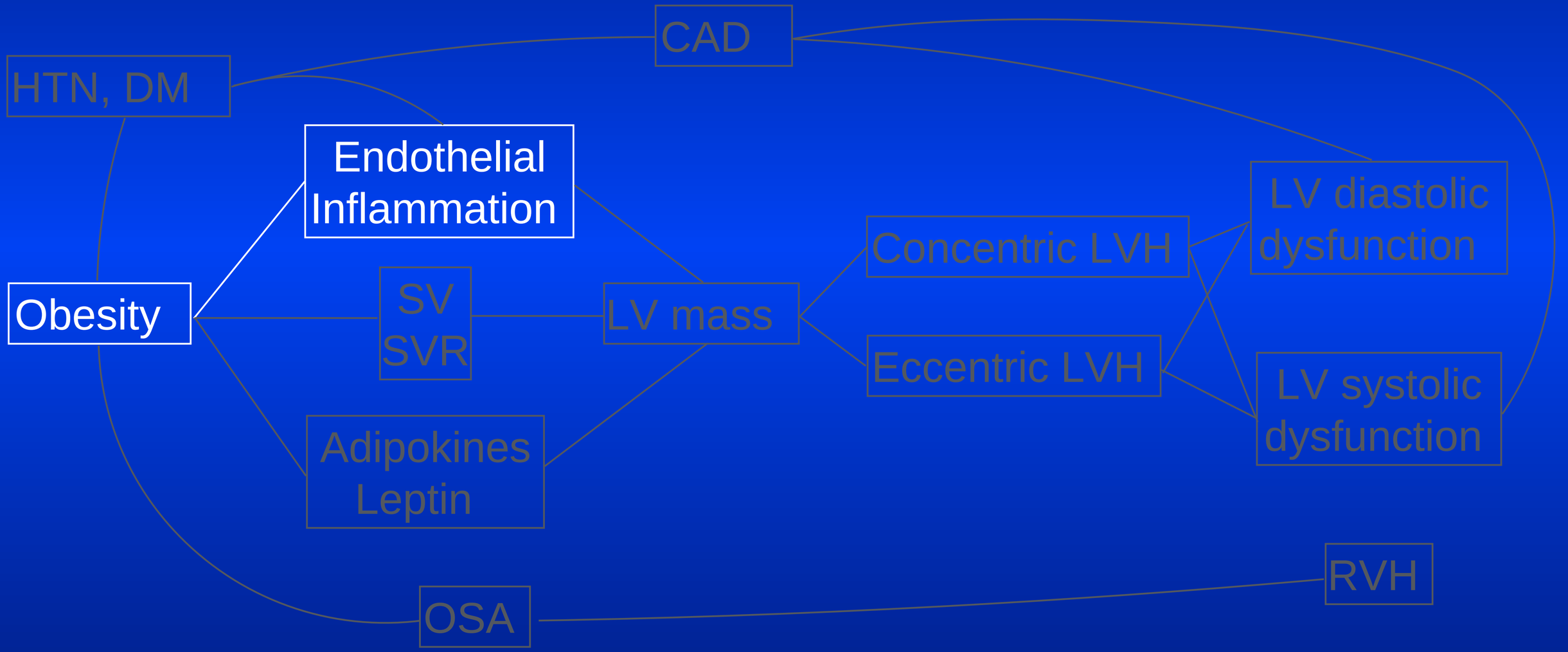

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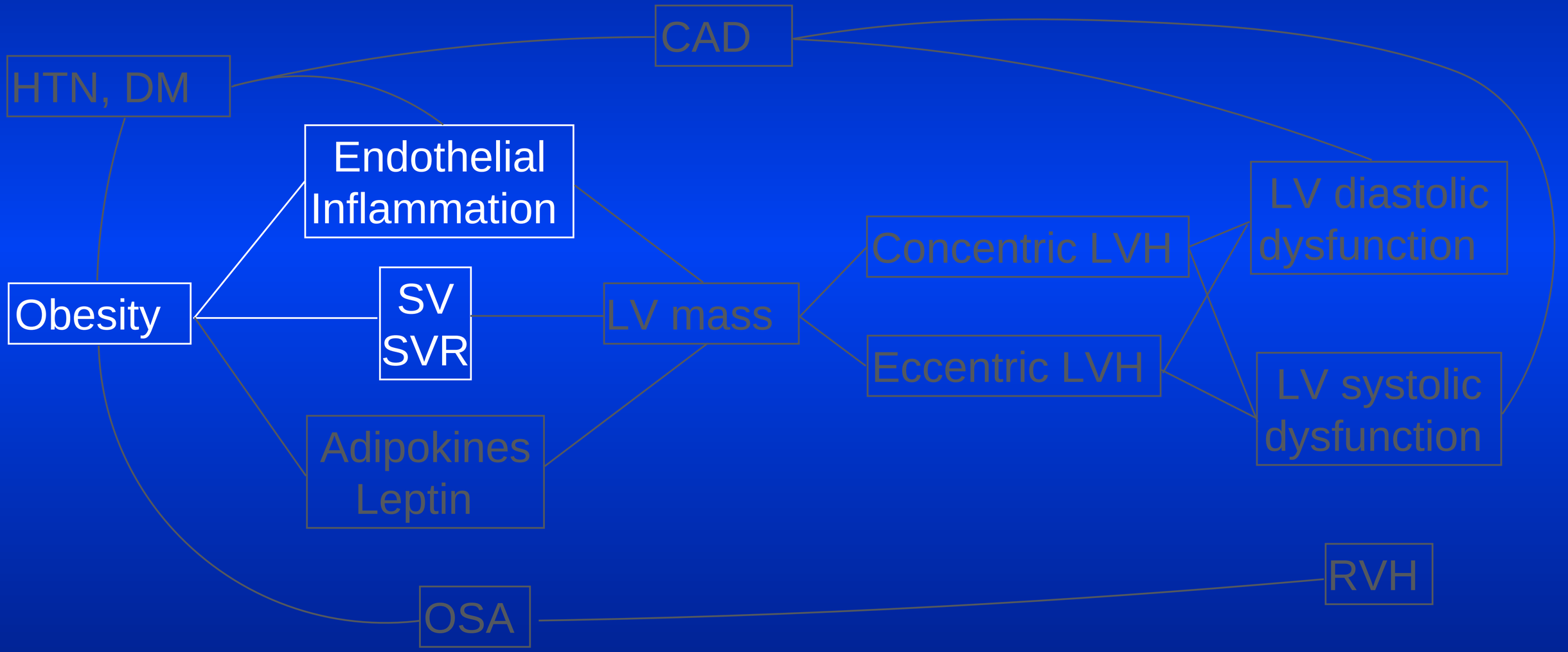

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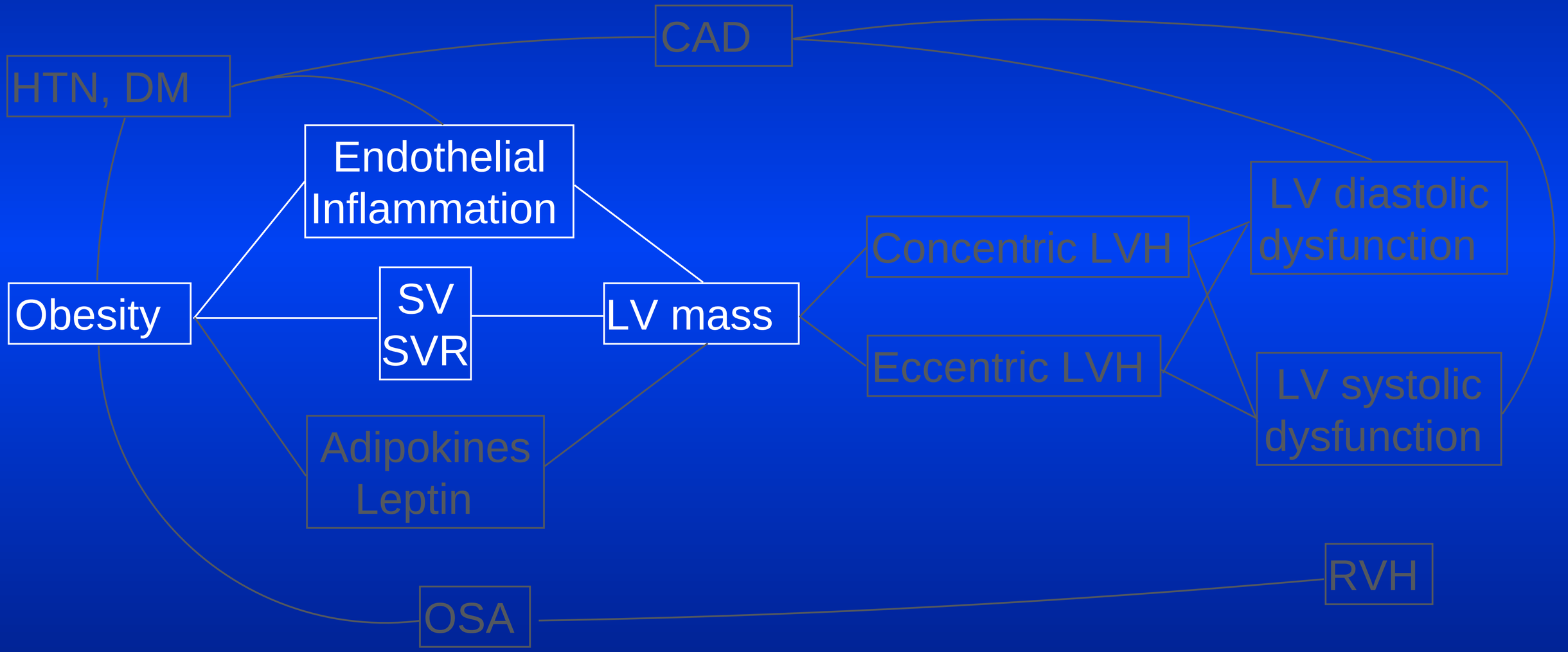

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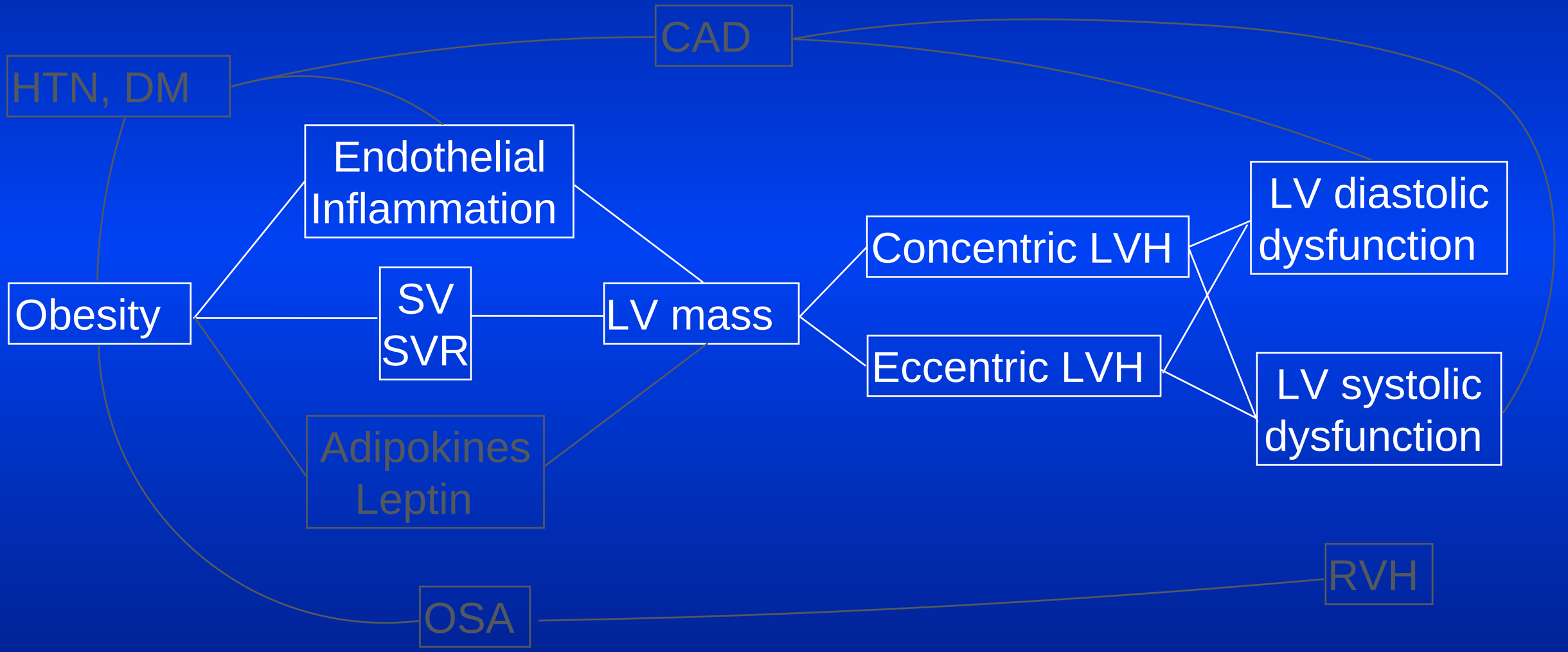

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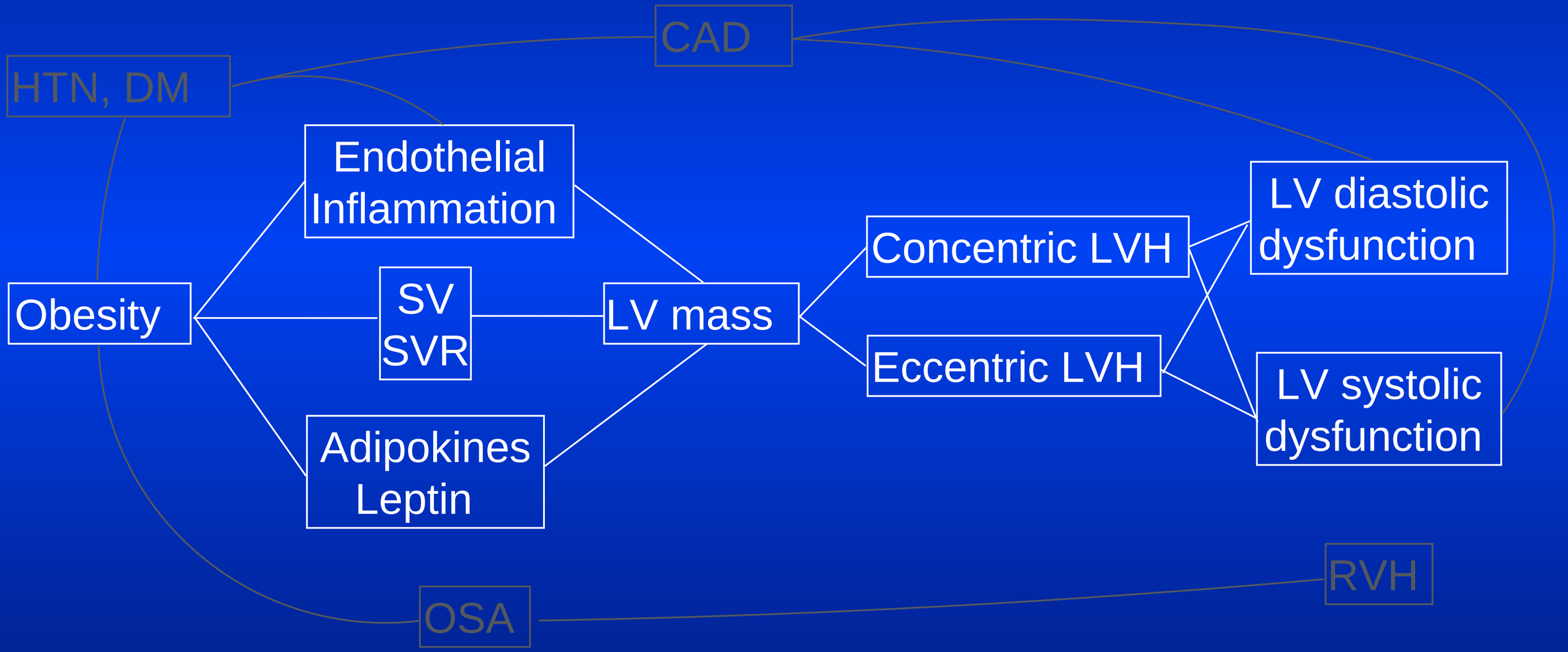

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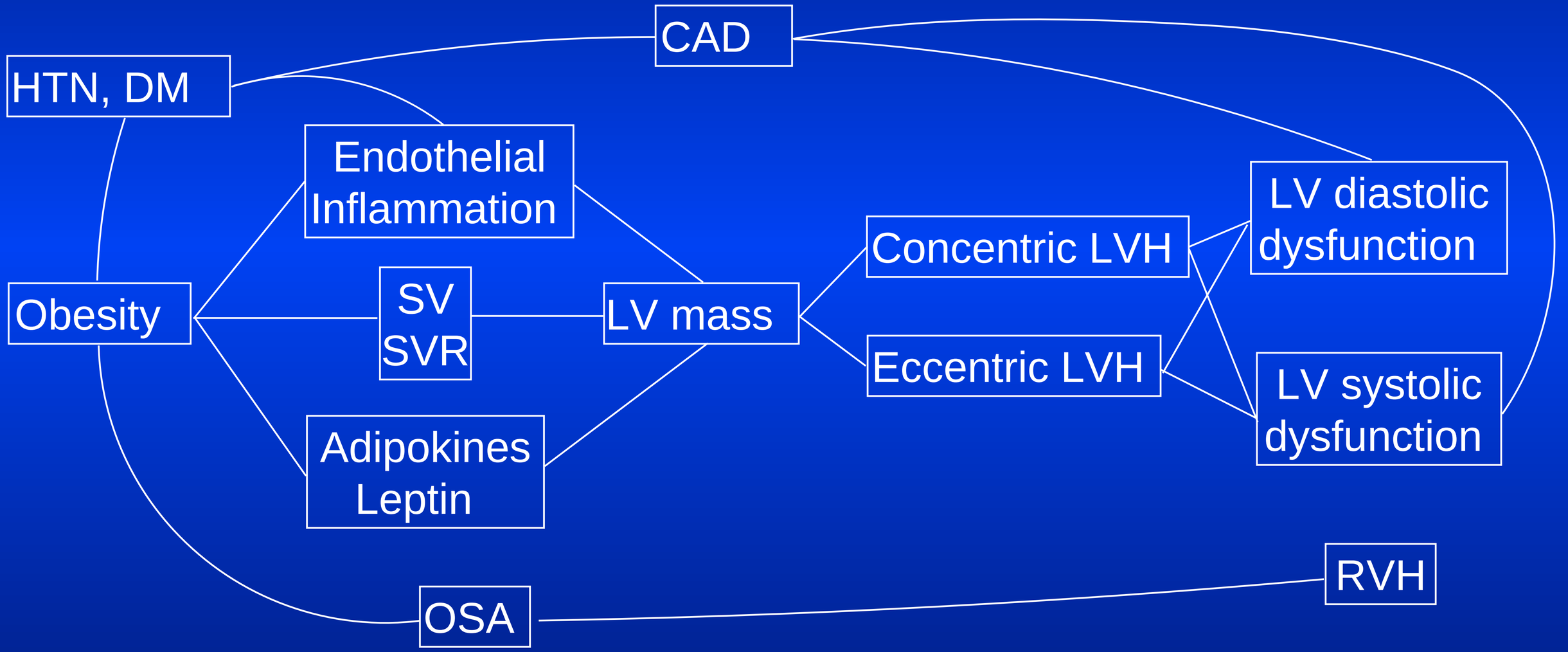

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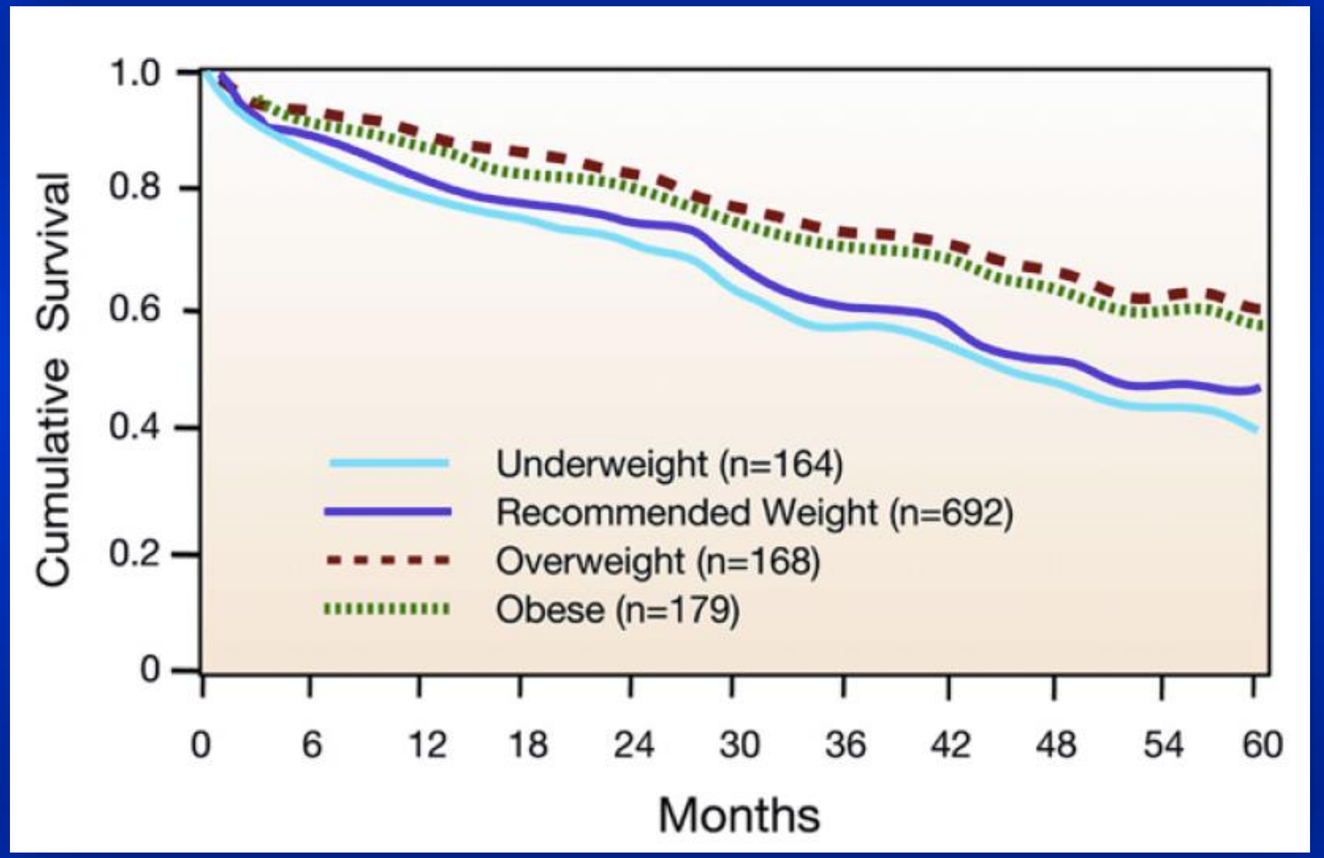
Obesity and HF: The Paradox



n = 1203

Horwich TB, et al. J Am Coll Cardiol 2001;38:789 –95

Obesity and HF: Weight Loss Therapy

Obesity and HF: Weight Loss Therapy

- **Retrospective analysis of bariatric surgery at the Cleveland Clinic (2004-2013)**

	Active comparator	Clinical comparison group	Echo comparison group
N	**42**	**2588**	**38**
Patients	**LVEF< 50% (EF 38%, BMI 47%, MI 24%)**	**Non-HF**	**HF non surgical (BMI 38)**

Vest A, et al Circ Heart Fail. 2016

Obesity and HF: Weight Loss Therapy

	N = 42	N = 2588	p
% Weight loss	22.6 ± 12	28.1 ± 11	0.011
Post op HF	4 (10%)	4 (0.2%)	< 0.001
Post op MI	1 (2%)	1 (0.04%)	0.032
1 year mortality	0 (0%)	27 (1%)	NS

- Post op LVEF (+5.1%, p 0.005 vs. +3.4%, p = 0.052)
- 11/47 (23%) LVEF > 10%

Vest A, et al Circ Heart Fail. 2016

Obesity and HF:
Guideline Recommendations

- ACC 2013 HF Guidelines: U-shaped relationship, no BMI cutoff
- ACC 2017 HF Guidelines Update: no update

Obesity and HF: Guideline Recommendations

- ACC 2013 HF Guidelines: U-shaped relationship, no BMI cutoff
- ACC 2017 HF Guidelines Update: no update
- ESC 2016 HF Guidelines:

  Wight loss if BMI ≥ 35 for symptom relief and risk factor control

  No prospective data on safety or benefit of weight loss

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Sleep Apnea

Anemia

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Hypertension

Sleep Apnea and HF

Reduced brainstem output to upper airways

Altered brainstem output to thoracic pump muscles

Obstructive Sleep Apnea

Central Sleep Apnea

Javaheri S, et al. J Am Coll Cardiol. 2017 Feb 21;69(7):841-858

Sleep Apnea and HF

Reduced brainstem output to upper airways

Altered brainstem output to thoracic pump muscles

Obesity

Short neck

Retrognathism

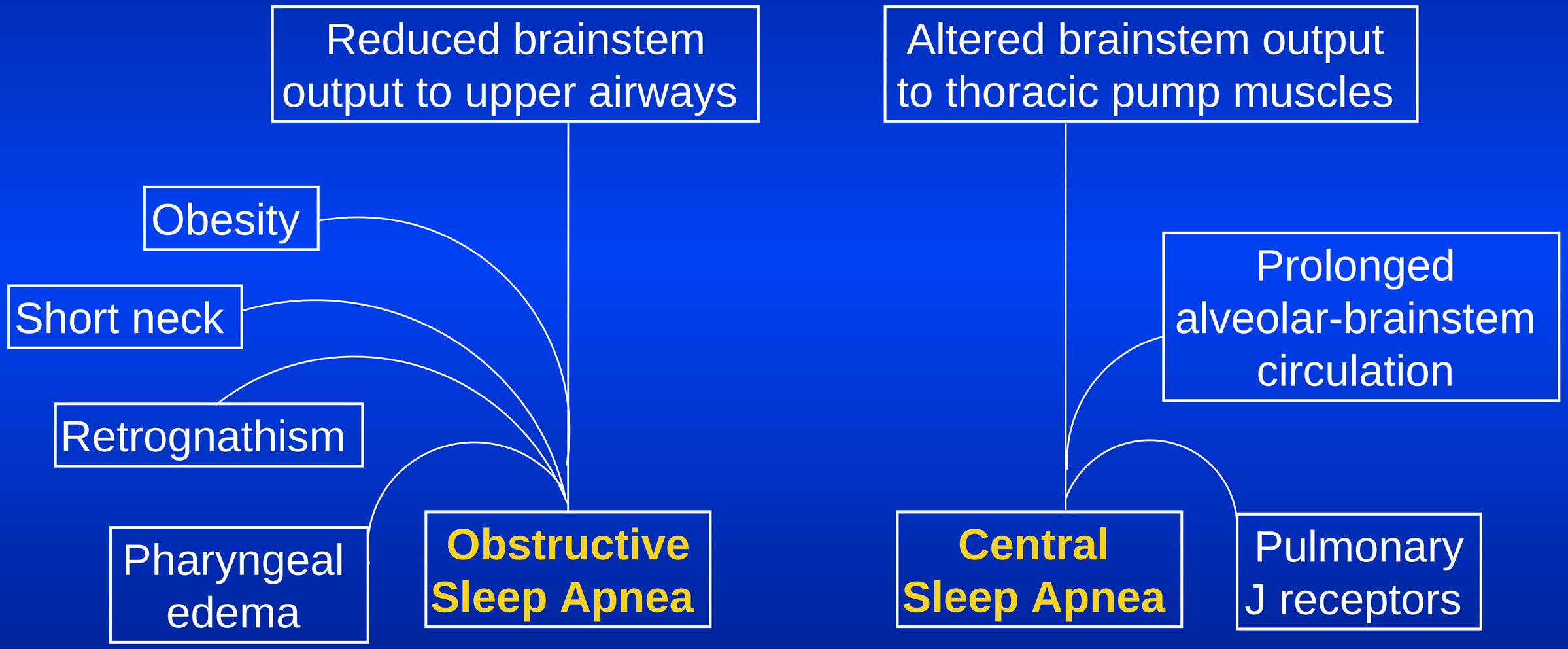
Pharyngeal edema

Obstructive Sleep Apnea

Central Sleep Apnea

Javaheri S, et al. J Am Coll Cardiol. 2017 Feb 21;69(7):841-858

Sleep Apnea and HF



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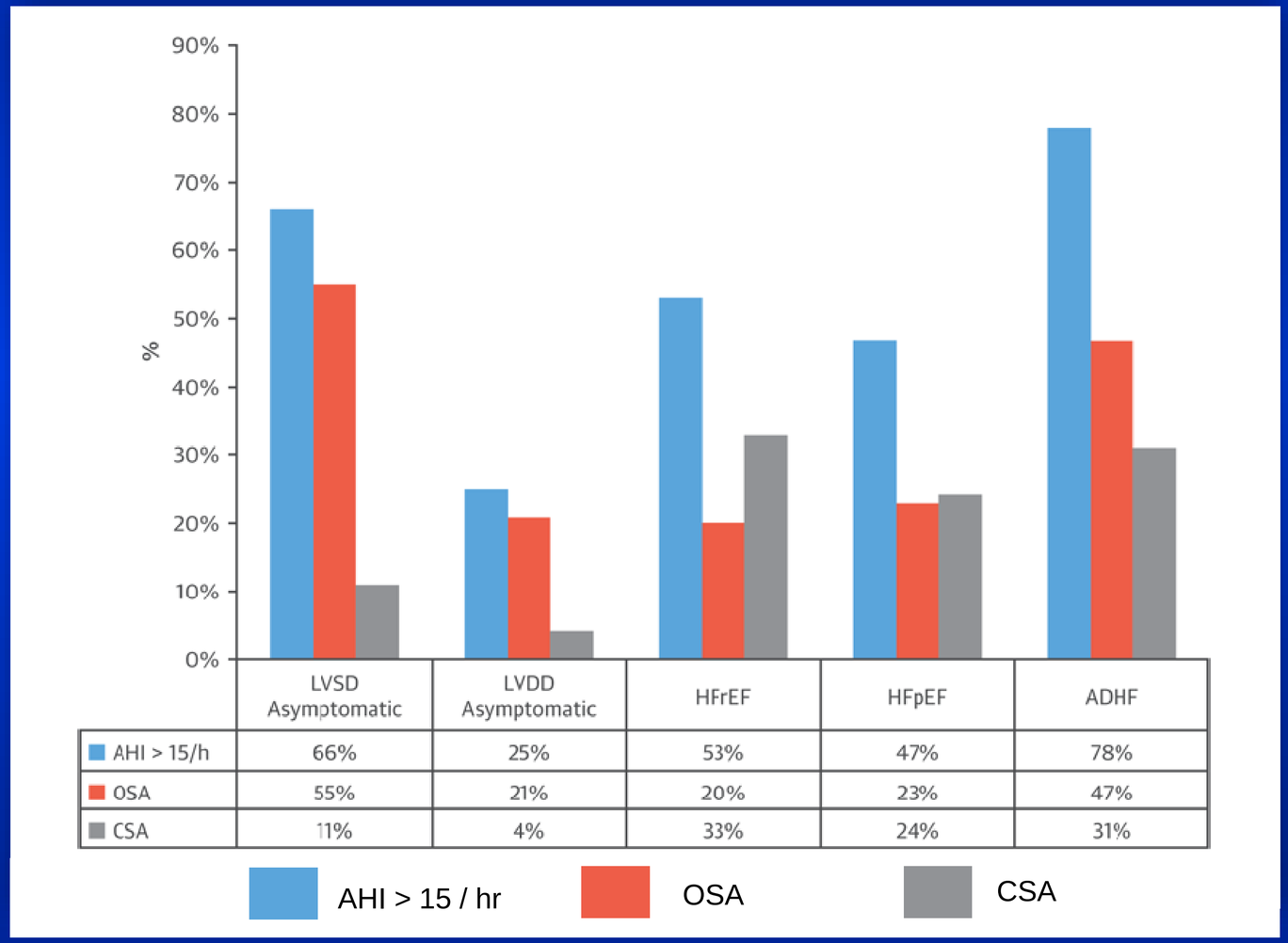
Sleep Apnea and HF: Epidemiology



	LVSD Asymptomatic	LVDD Asymptomatic	HFrEF	HFpEF	ADHF
AHI > 15/h	66%	25%	53%	47%	78%
OSA	55%	21%	20%	23%	47%
CSA	11%	4%	33%	24%	31%

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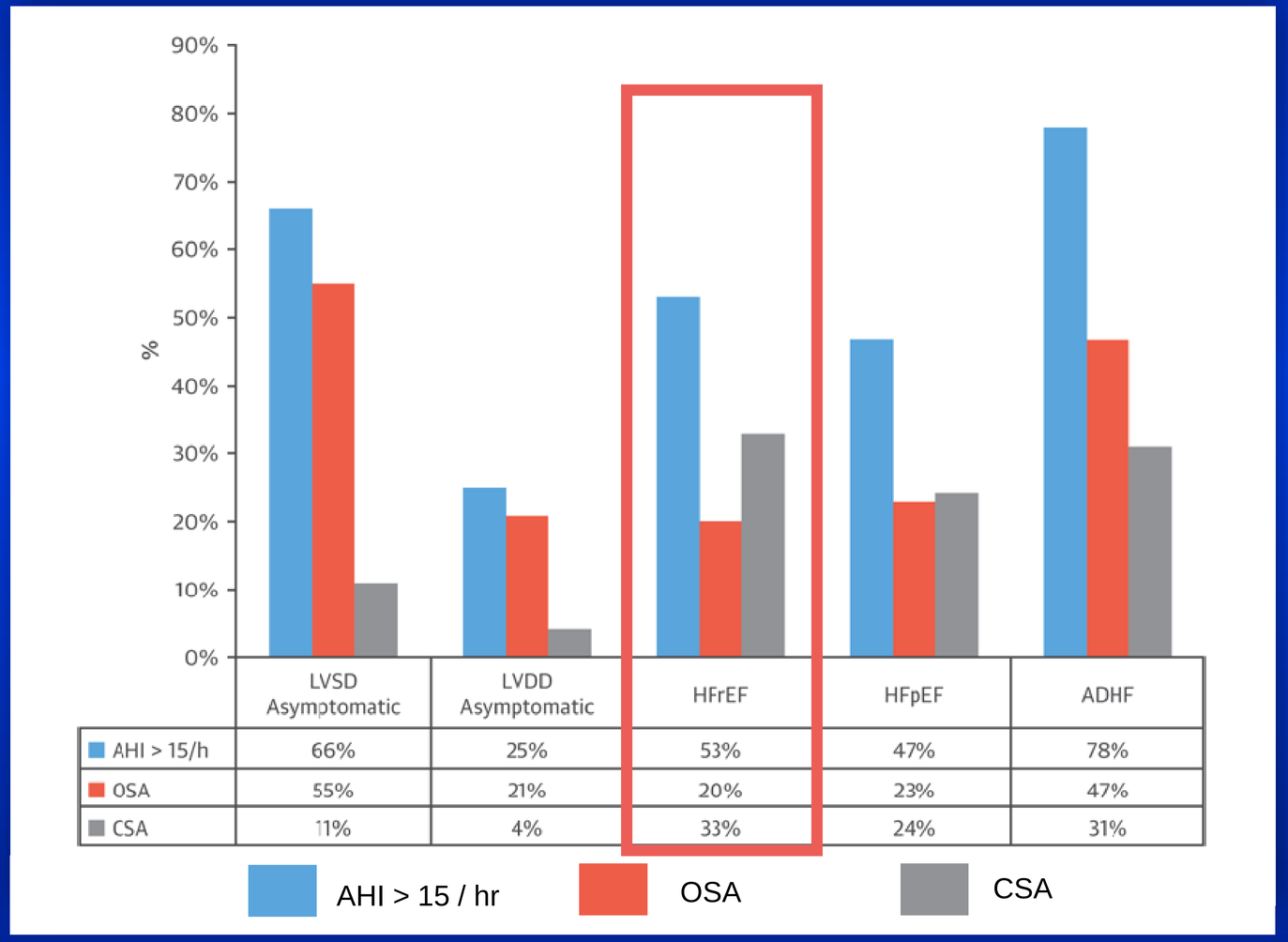

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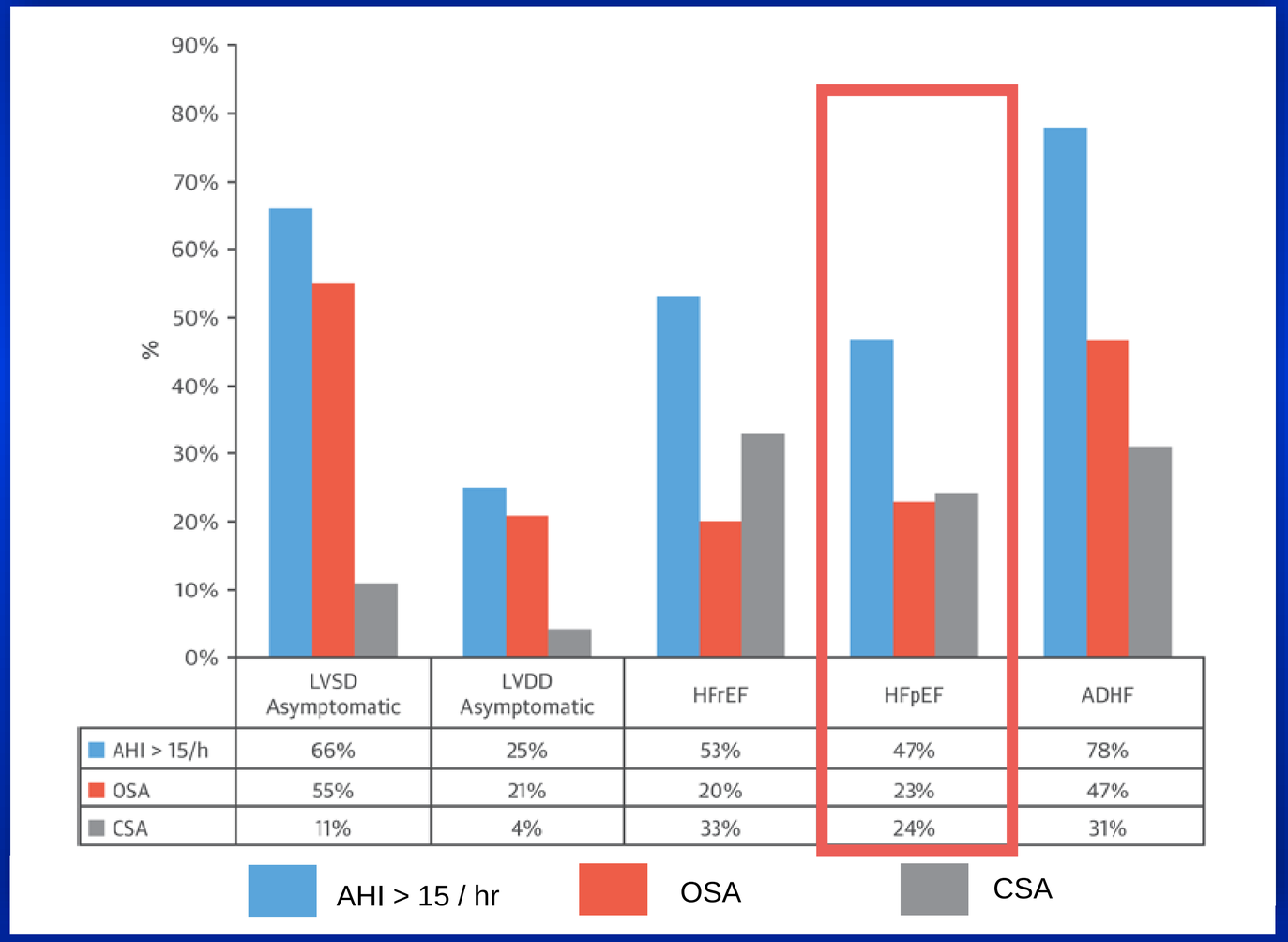

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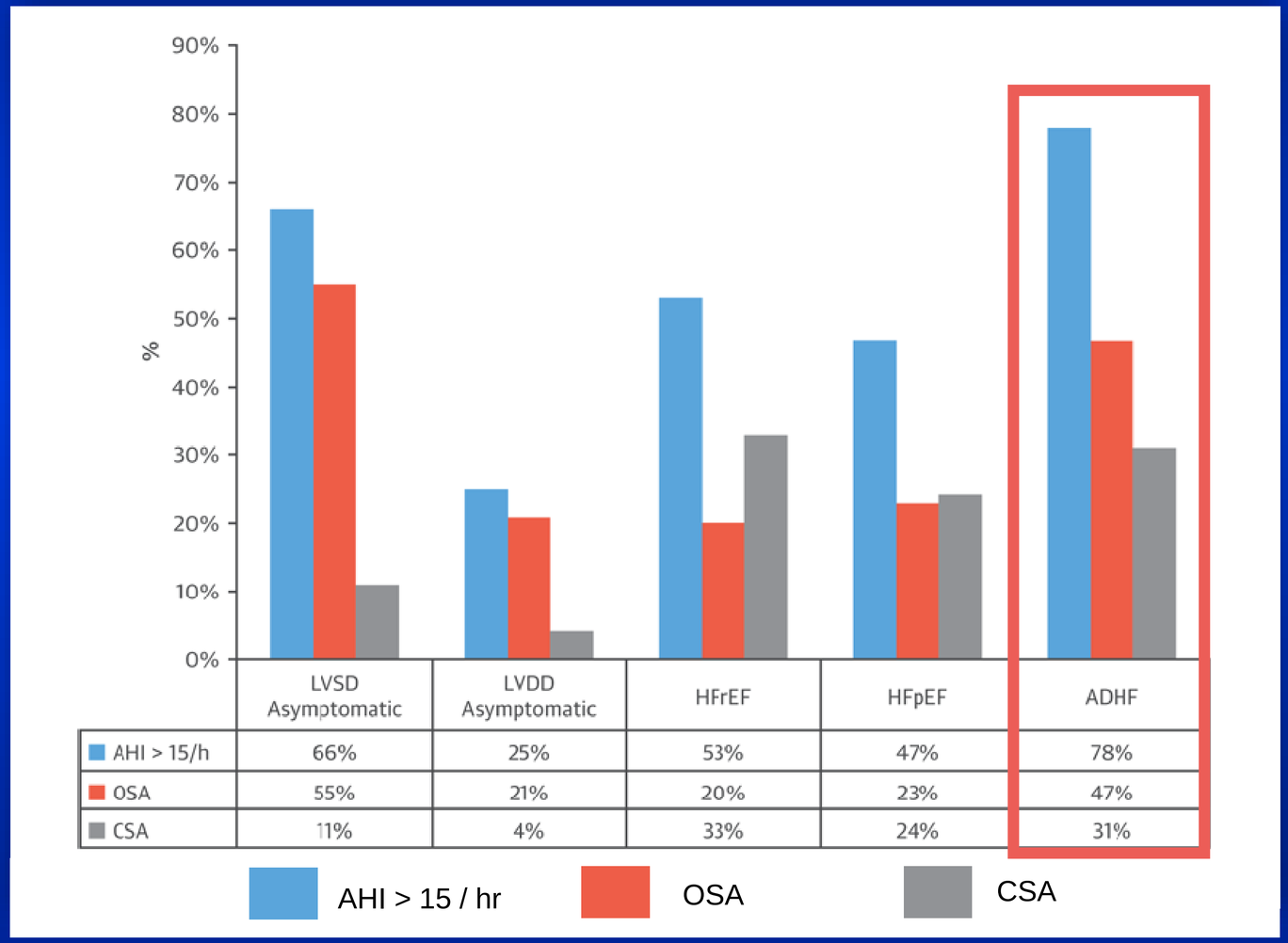

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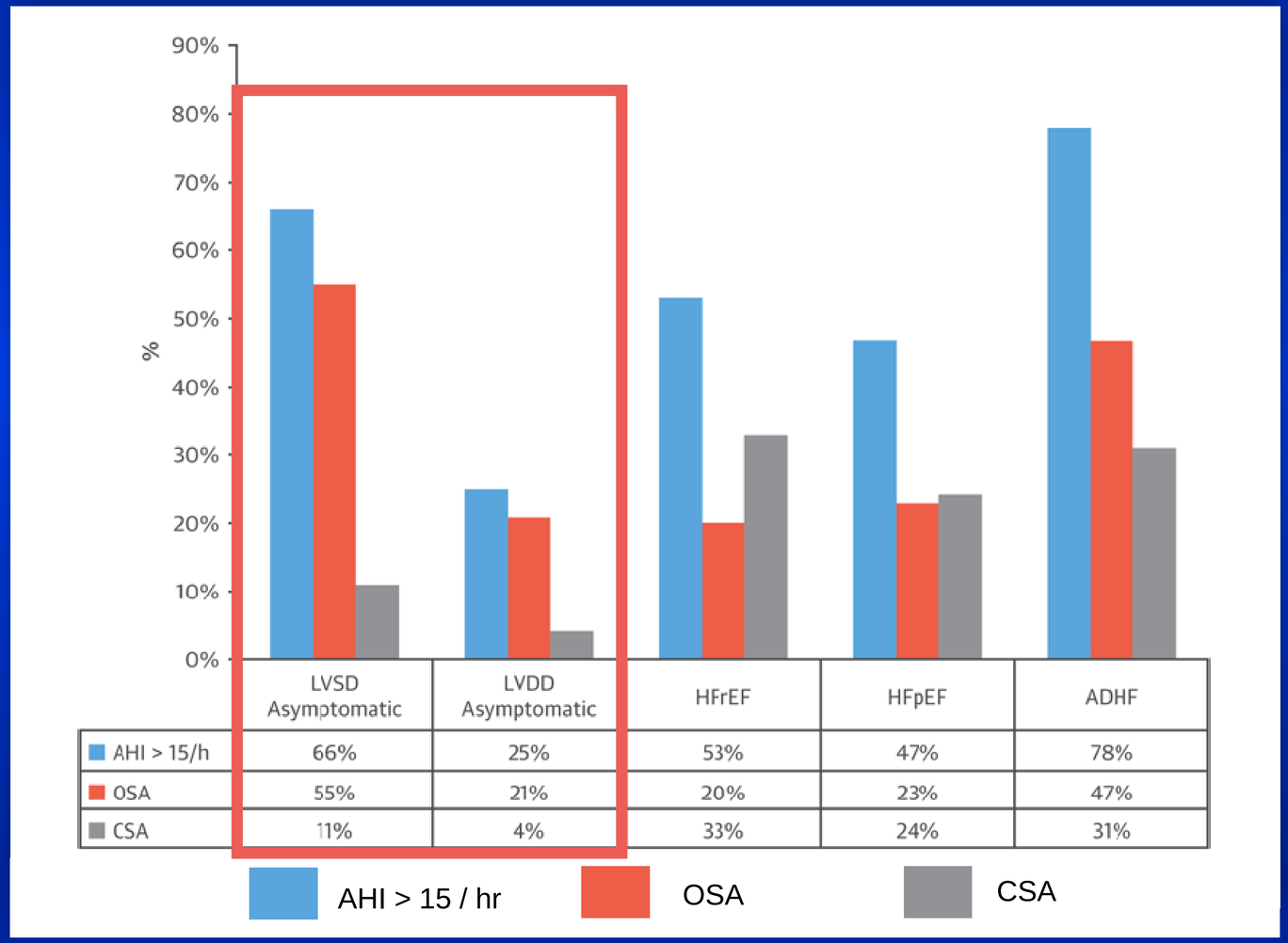

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CV Effects of OSA and CSA

Intermittent hypoxemia / reoxygenation

Decreased parasympathetic and increased sympathetic activity

Large negative intrathoracic pressure swings

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CV Effects of OSA and CSA

Intermittent hypoxemia / reoxygenation

(Oxidative stress, inflammation, pulm vasoconstriction)

Decreased parasympathetic and increased sympathetic activity

(Elevated BP, HR, arrhythmia risk)

Large negative intrathoracic pressure swings

(chamber overload, afterload)

Javaheri S, et al. J Am Coll Cardiol. 2017 Feb 21;69(7):841-858

OSA Therapy: CPAP in Secondary Prevention

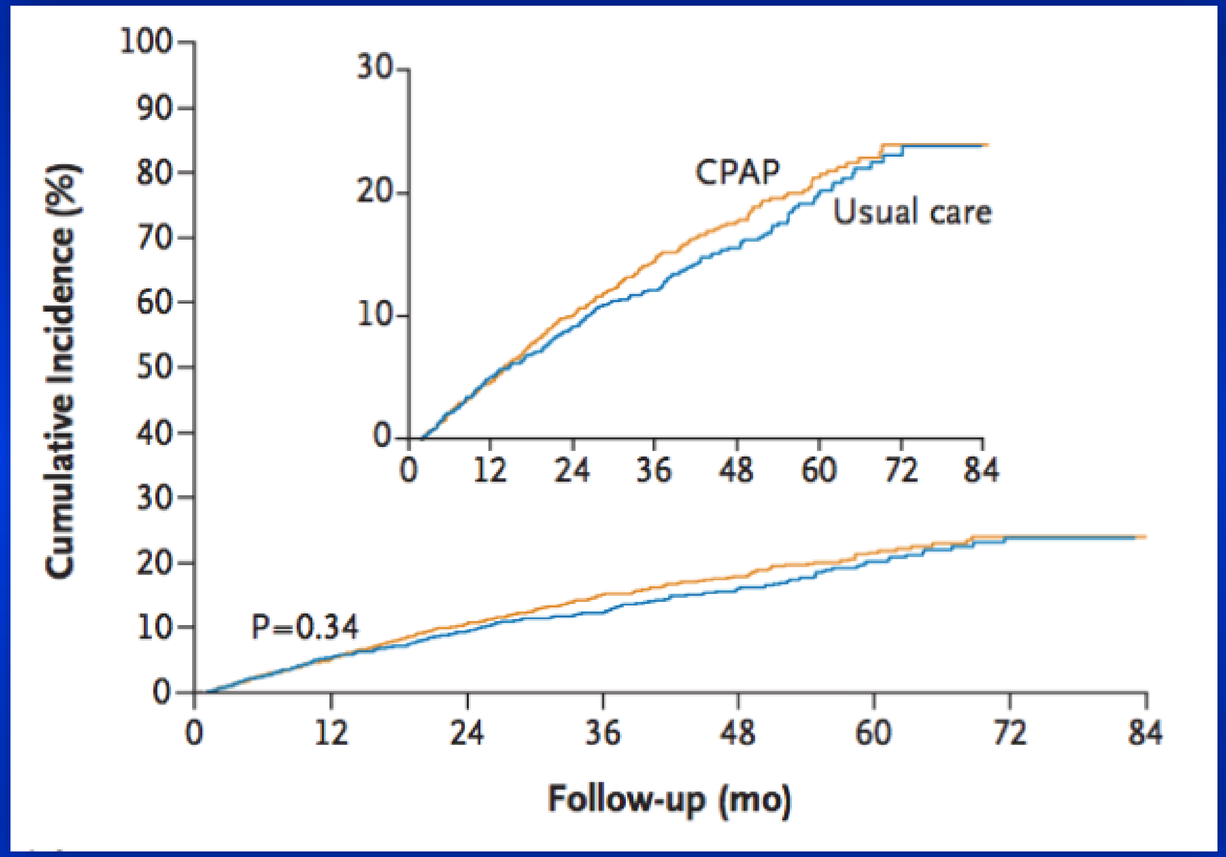
SAVE Trial

N = 2717

Patients: moderate-severe sleep apnea and coronary artery or ceberovascular disease

(CAD 51%, CVA 49%, HTN 79%)

Primary outcome: CV death, MI, stroke, HF hospitalization, ACS, or TIA



Significant reductions in Epworth Sleepiness score, anxiety, and depression

McEvoy RD, et al. N Engl J Med 2016;375:919-31

Therapy for CSA

SERVE-HF Trial

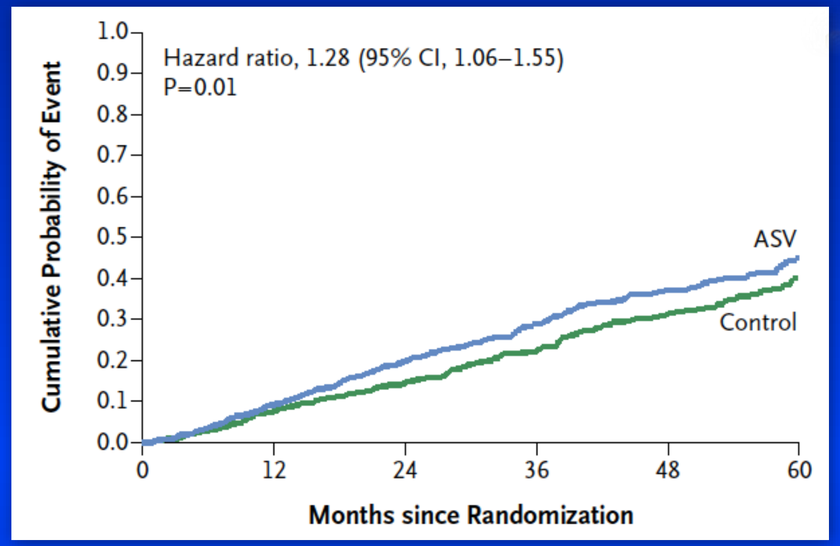
N = 1325

Patients: LVEF ≤ 45%, ambulatory NYHA II or more, AHI ≥ 15 events / hr

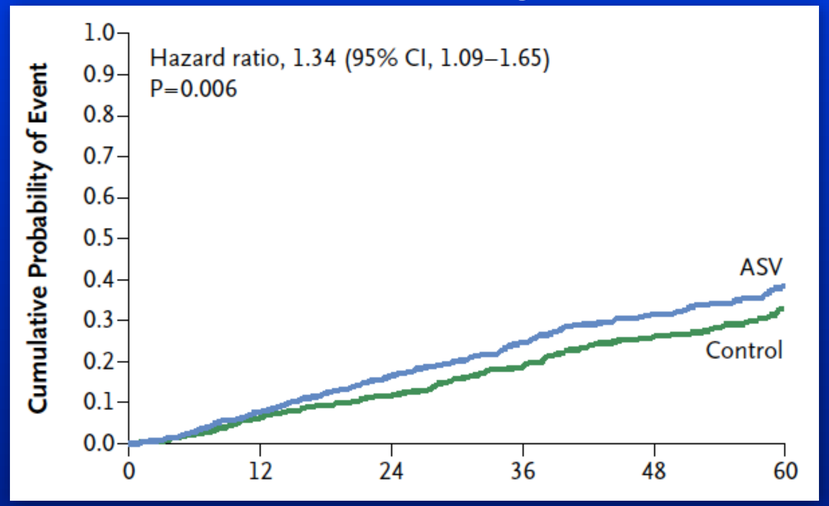
Intervention: Adaptive servo ventilation to target AHI < 10 / hr

Outcome: All-cause death, life-saving cardiac intervention, HF hospitalization

All-cause mortality



CV mortality



Cowie MR, et al. N Engl J Med 2015;373:1095-105

Therapy for CSA

Trial	#pts	LVEF	Intervention	Baseline AHI	F/u AHI	Primary Outcome	Comments
CANPAP 2005	258	25%	CPAP	40	19	Neutral	Suspended
SERVE-HF 2015	1325	32%	ASV	31.2	6.6	Neutral	↑CV and all-cause mortality
CAT-HF 2017	126 (hosp)	32%	ASV	35.7	2.1	Neutral	Suspended
ADVENT-HF 2018*	850	<45%	ASV	AHI >15	TBD	TBD	In progress

Sleep Apnea in HF: Guideline Recommendations

COR, LOE	ACC 2017 Update of ACC 2013 HF Guidelines
Class IIa, LOE B	In patients with NYHA class II–IV HF and suspicion of sleep-disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable
Class IIb, LOE B	In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness
Class III, LOE B	In patients with NYHA class II–IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm

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Class IIa, LOE B	In patients with NYHA class II–IV HF and suspicion of sleep-disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable
Class IIb, LOE B	In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness
Class III, LOE B	In patients with NYHA class II–IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm

Sleep Apnea in HF: Guideline Recommendations

COR, LOE	ESC 2016 HF Guidelines
Class III, LOE B	Adaptive servo-ventilation is not recommended in patients with HFrEF and a predominant central sleep apnoea because of an increased all-cause and cardiovascular mortality

Outline

Epidemiology & Mechanisms

Obesity

Sleep Apnea

Anemia

Diabetes

Hypertension

Iron Deficiency and Anemia in HF

Anemia in HF

50% of Medicare beneficiaries with HF > 65 yrs

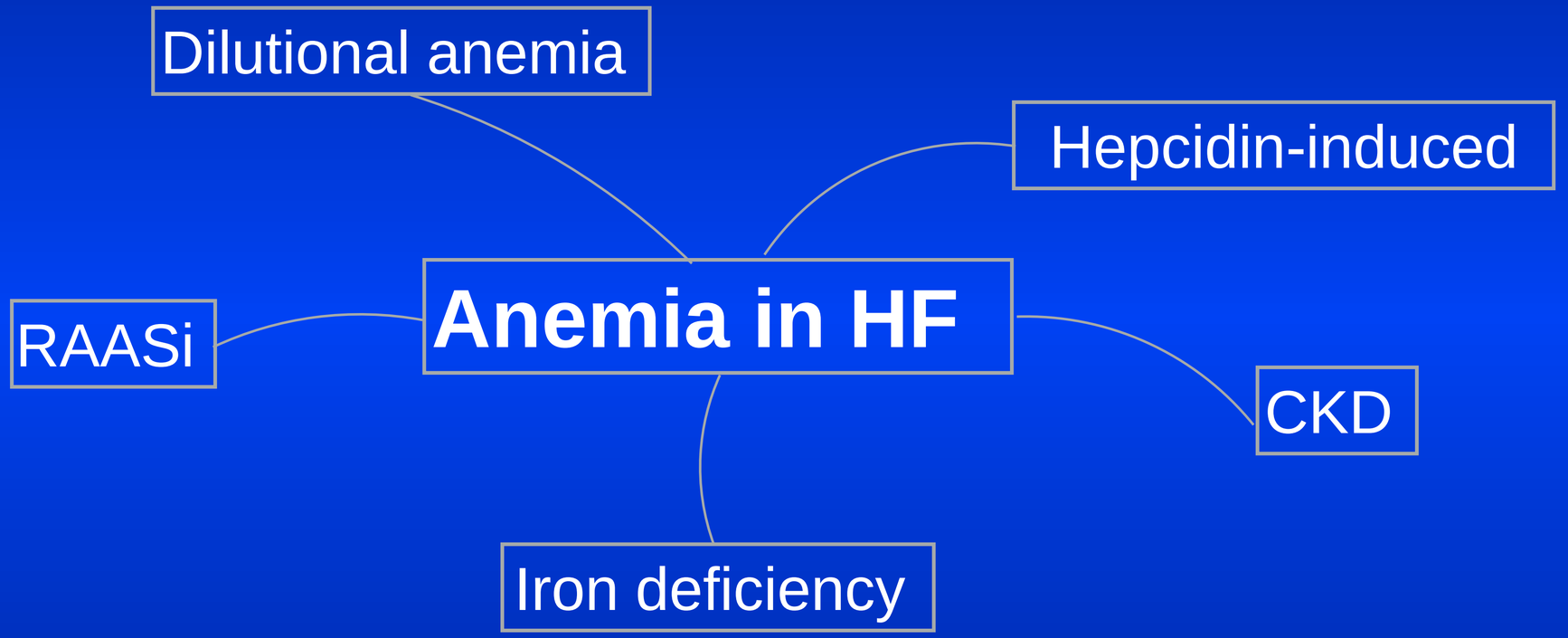
SOLVD trial: 22% Hct < 40*

HB < 10 g/dl 9.9% HFrEF vs. 21.1% HFpEF, p < 0.001^

*Al-Ahmad A, et al. J Am Coll Cardiol. 2001;38(4):955

^Bhatia RS, et al. N Engl J Med 2006;355:260-9

Iron Deficiency and Anemia in HF



Iron Deficiency and Anemia in HF

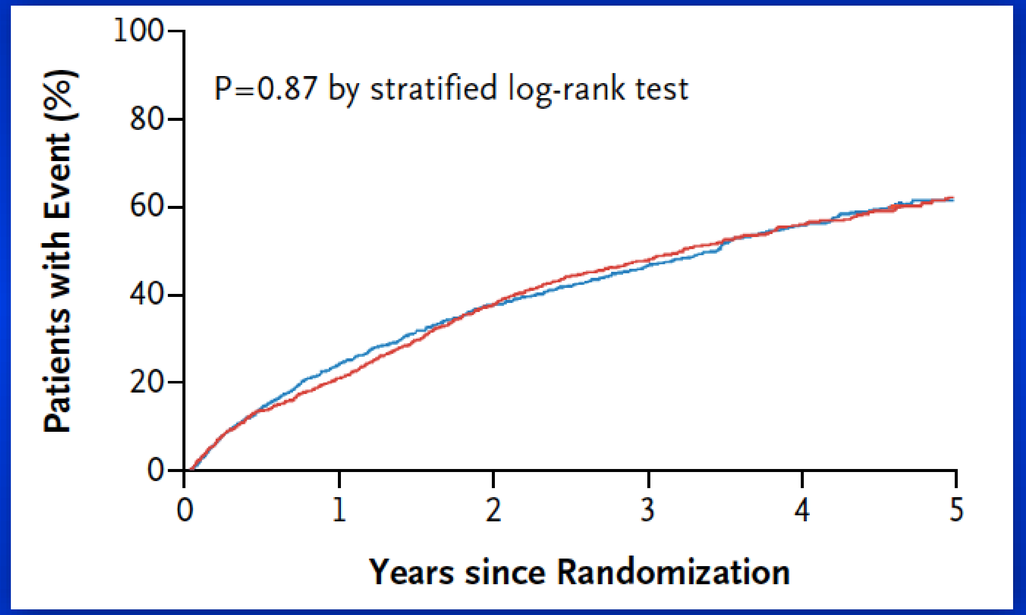
RED-HF

N = 2278

Patients: HB 9 - 12 g/dl, LVEF ≤ 40%, NYHA ≥ II

Intervention: darbapoetin alfa 0.75 mcg / kg weekly to HB > 13 then monthly

Outcome: All-cause mortality or first HF hospitalization



Any thombo-embolic event
4.5% vs 2.4%, p = 0.005

Swedberg K, et al. N Engl J Med 2013;368:1210-9

Iron Deficiency and Anemia in HF

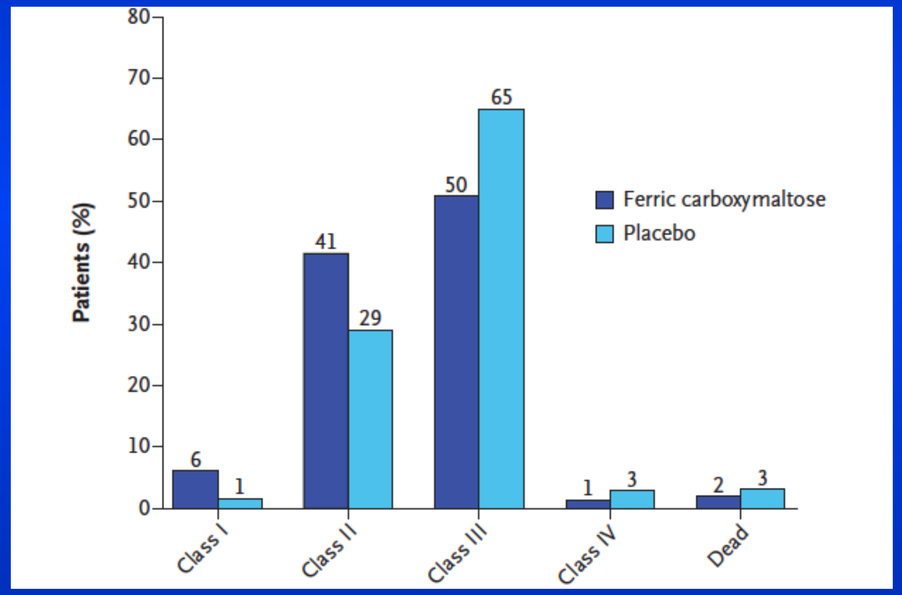
	FAIR-HF (NEJM 2009)	CONFIRM-HF (EHJ 2015)
N	459 (2:1)	304 (1:1)
Patients	NYHA II/III, LVEF < 45, Ferritin <100 ng/ml or 100-299 + Tsat <20%	NYHA II/III, LVEF < 45, BNP> 100 pg/ml (NT-PBNP >400), Ferritin <100 ng/ml or 100-299 + Tsat <20%, HB <15 g/dl
Intervention	IV Ferric Carboxymaltose (correction + maintenance)	IV Ferric Carboxymaltose (correction + maintenance)
Outcome	Week 24 NYHA class, Patient Global Assessment	Primary: 6MWT distance at 24 wks Sec: NYHA, Patient Global Assessment

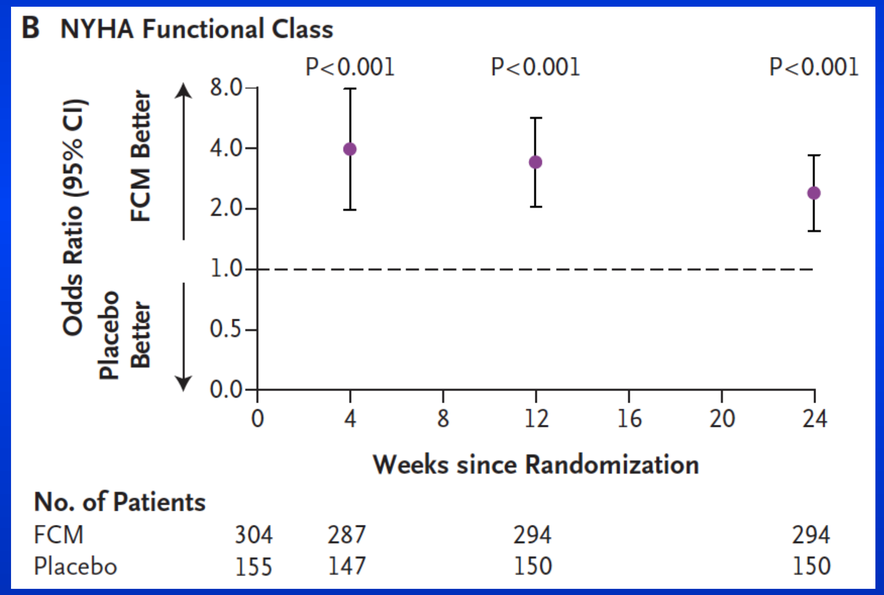
Total Iron Deficit (Ganzoni's formula) = Weight x (Target Hb in g/dL - Actual Hb in g/dL) x 2.4 + Iron Stores

Anker SD, et al. N Engl J Med 2009;361:2436-48

Ponikowski P, et al. Eur Heart J. 2015 Mar 14;36(11):657-68

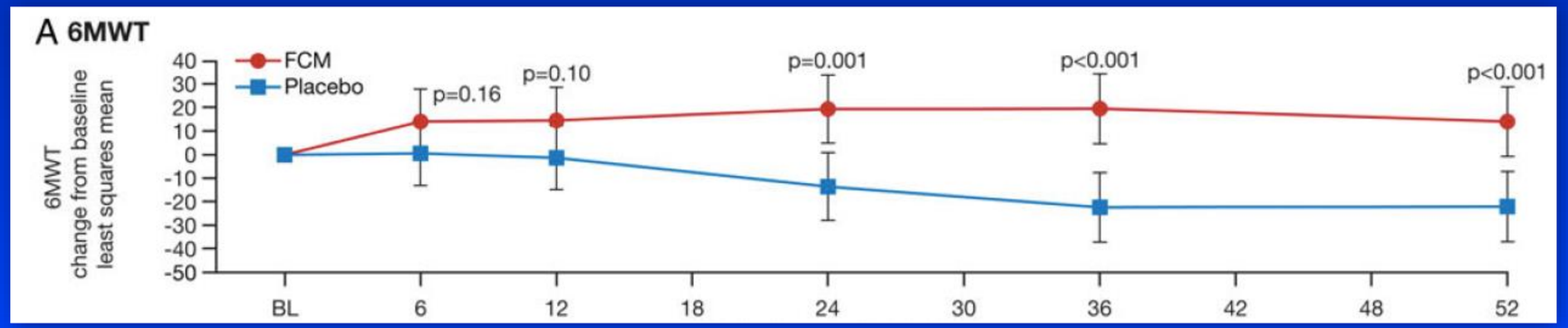
Iron Deficiency and Anemia in HF

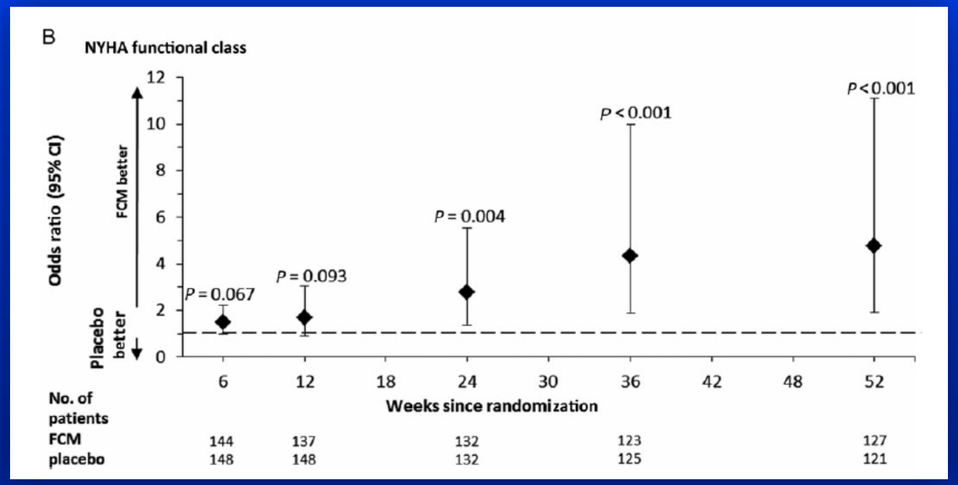




Anker SD, et al. N Engl J Med 2009;361:2436-48

Iron Deficiency and Anemia in HF





Ponikowski P, et al. Eur Heart J. 2015 Mar 14;36(11):657-68

Iron Deficiency and Anemia in HF: Guideline Recommendations

COR, LOE	ACC 2017 Update of ACC 2013 HF Guidelines
Class IIb, LOE B	In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL
Class III, LOE B	In patients with HF and anemia, erythropoietin stimulating agents should not be used to improve morbidity and mortality

Iron Deficiency and Anemia in HF: Guideline Recommendations

COR, LOE	ESC 2016 HF Guideilnes
Class IIa, LOE A	Intravenous FCM should be considered in symptomatic patients (serum ferritin <100 µg/L, or ferritin between 100–299 µg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life

Outline

Epidemiology & Mechanisms

Obesity

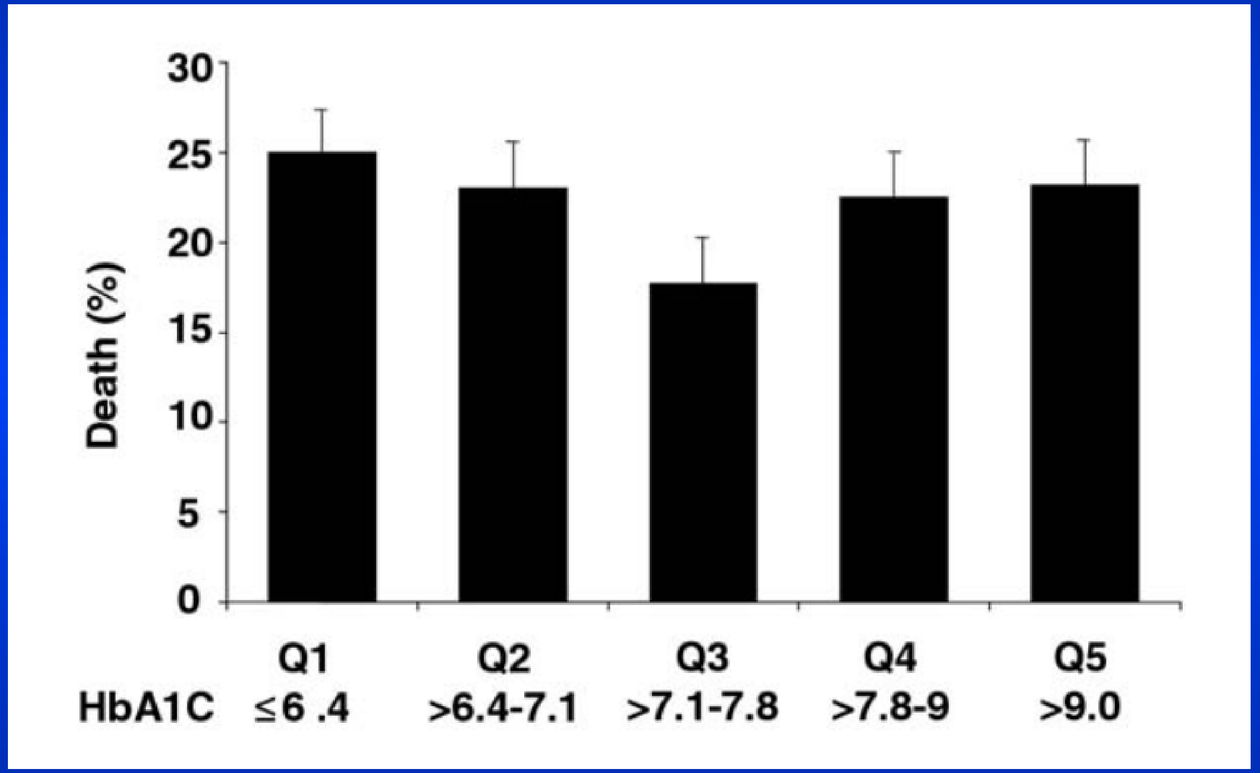
Sleep Apnea

Anemia

Diabetes

Hypertension

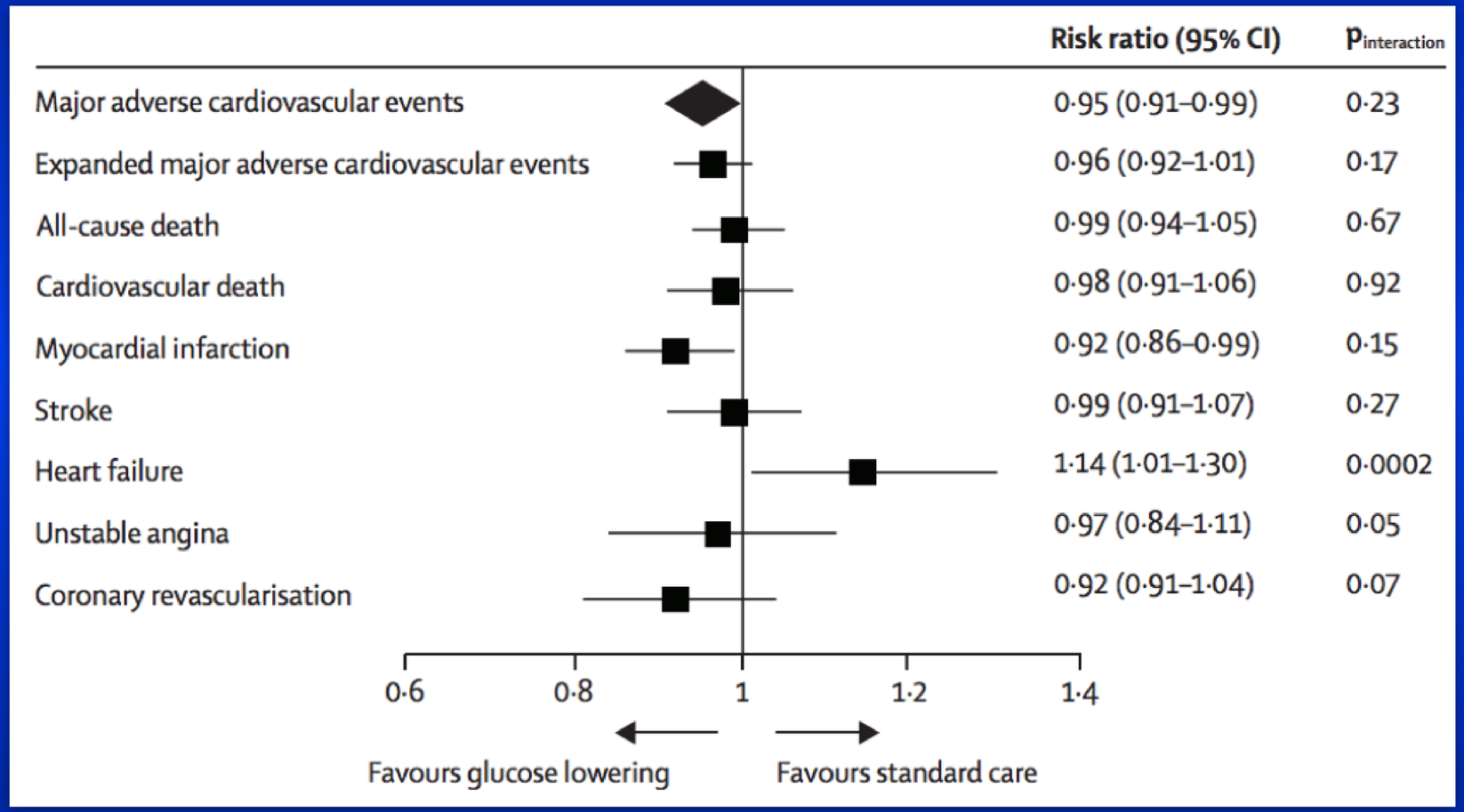
Glycemic Control Diabetes and HF



N = 5815 ambulatory patients with HF followed for 2 yrs

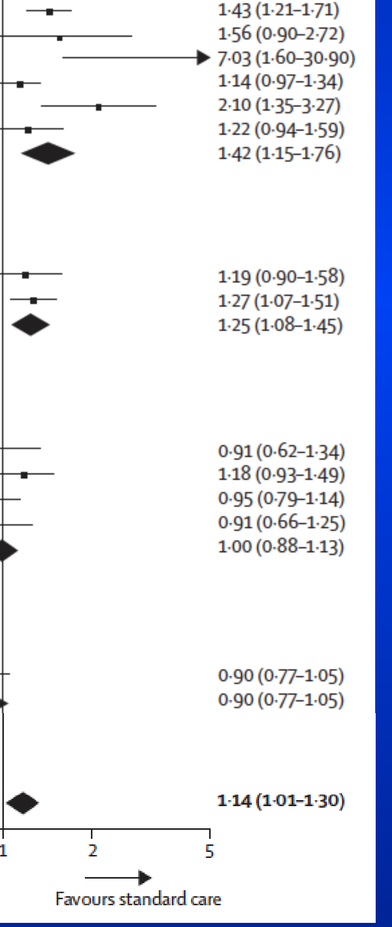
Aguilar D, et al. J Am Coll Cardiol 2009;54:422–8

Therapies in Diabetes and HF



Udell JA, et al. Lancet Diabetes Endocrinol. 2015 May;3(5):356-66

Therapies in Diabetes and HF



	More glucose control		Less glucose control		Weight	Heart failure risk ratio (95% CI)
	Events	Total	Events	Total		
PPAR agonists						
2005 PROactive[36]	281	2605	198	2633	9·5%	1·43 (1·21–1·71)
2006 ADOPT[37]	22	1456	28	2895	3·6%	1·56 (0·90–2·72)
2006 DREAM[38]	14	2635	2	2634	0·7%	7·03 (1·60–30·90)
2009 BARI2D[41]	248	1183	218	1185	9·7%	1·14 (0·97–1·34)
2009 RECORD[42]	61	2220	29	2227	4·8%	2·10 (1·35–3·27)
2014 AleCardio[46]	122	3616	100	3610	7·7%	1·22 (0·94–1·59)
Subtotal		13715		15184	35·9%	1·42 (1·15–1·76)
Heterogeneity: Tau^2=0·04; χ^2=13·82, df=5; p=0·017; I^2=64%						
Test for overall effect: Z=3·29; p=0·0010						
DPP-4 inhibitors						
2013 EXAMINE[16,17]	106	2701	89	2679	7·3%	1·19 (0·90–1·58)
2013 SAVOR-TIMI 53[15]	289	8280	228	8212	9·5%	1·27 (1·07–1·51)
Subtotal		10981		10891	16·8%	1·25 (1·08–1·45)
Heterogeneity: Tau^2=0·00; χ^2=0·15, df=1; p=0·70; I^2=0%						
Test for overall effect: Z=2·94; p=0·0033						
Intensive control						
1998 UK Prospective Diabetes Study[35]	80	2729	36	1138	5·5%	0·91 (0·62–1·34)
2008 ACCORD[39]	152	5128	124	5123	8·3%	1·18 (0·93–1·49)
2008 ADVANCE[40]	220	5571	231	5569	9·3%	0·95 (0·79–1·14)
2009 VADT[43]	76	892	82	899	6·7%	0·91 (0·66–1·25)
Subtotal		14320		12729	29·8%	1·00 (0·88–1·13)
Heterogeneity: Tau^2=0·00; χ^2=2·80, df=3; p=0·42; I^2=0%						
Test for overall effect: Z=0·01; p=0·99						
Insulin glargine						
2012 ORIGIN[44]	310	6264	343	6273	9·8%	0·90 (0·77–1·05)
Subtotal		6264		6273	9·8%	0·90 (0·77–1·05)
Heterogeneity: not applicable						
Test for overall effect: Z=1·67; p=0·10						
Total		**47850**		**47652**	**100%**	**1·14 (1·01–1·30)**
Heterogeneity: Tau^2=0·04; χ^2=45·56, df=13; p<0·0001; I^2=71%						
Test for overall effect: Z=2·04; p=0·041						
Test for subgroup differences: χ^2=21·85, df=4; p=0.00021, I^2=81·7%						

0·2 0·5 1 2 5

Favours glucose-lowering Favours standard care

Udell JA, et al. Lancet Diabetes Endocrinol. 2015 May;3(5):356-66

Diabetes and HF Therapies

EMPA-REG OUTCOME Trial

Empagliflozin: SGLT2 inhibitor

N = 7020

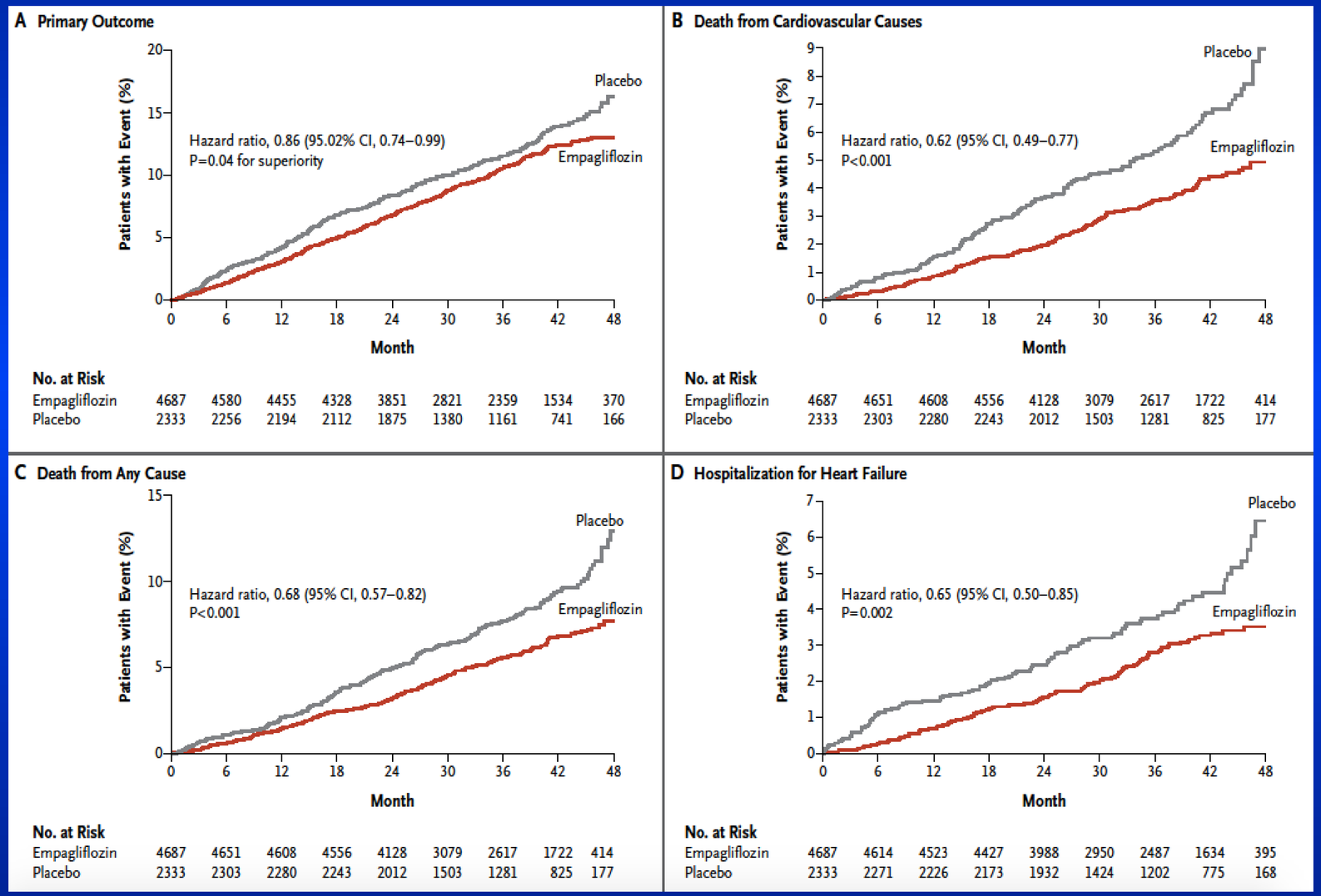
Patients: DM, HBA1c 7 - 9%, eGFR > 30 ml/min

Intervention: Empagliflozin 10 or 25 mg or placebo

Outcome: CV mortality, non-fatal MI, non-fatal stroke

Zinman B, et al. N Engl J Med 2015;373:2117-28

Diabetes and HF Therapies



Zinman B, et al. N Engl J Med 2015;373:2117-28

Diabetes and HF Therapies: Guideline Recommendations

COR, LOE	ESC 2016 Heart Failure Guidelines
Class IIa, LOE C	Metformin should be considered as control in patients with diabetes and HF, unless contra-indicated
Class III, LOE A	Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization

Outline

Epidemiology & Mechanisms

Obesity

Sleep Apnea

Anemia

Diabetes

Hypertension

HTN and HF

SPRINT Trial

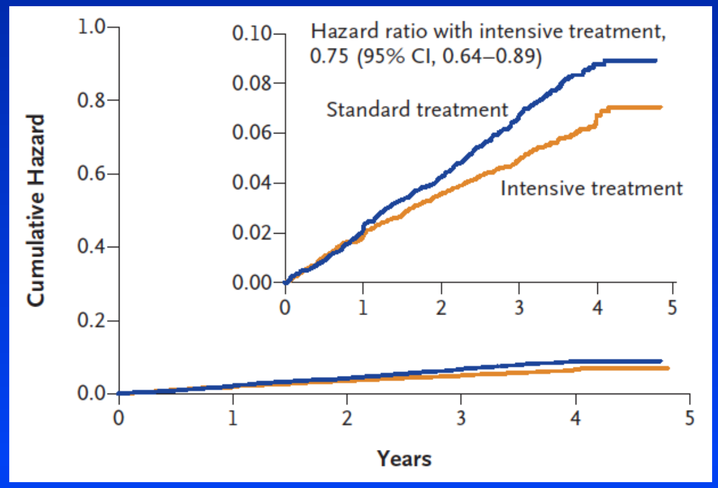
N = 9361

Patients: At least one of the following - established vascular disease, chronic renal disease, or a Framingham Risk Score >15%, age > 75

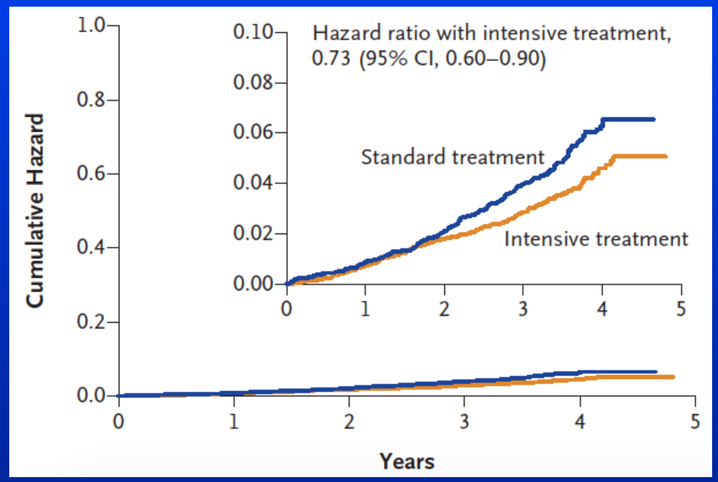
Intervention:
SBP < 140 mmHg vs. SBP < 120 mmHg

Outcome:
Composite ACS, stroke, ADHF, CV death

Primary end point



All-cause mortality



Wright JT, et al. Published online Nov 9, 2015 at NEJM.org

Heart Failure HR 0.62 (0.45 - 0.84, p = 0.002)

HTN in HF: Guideline Recommendations

COR, LOE	ACC 2017 Update of ACC 2013 HF Guidelines
Class I, LOE B	In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg
Class I, LOE C	Patients with HFrEF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg
Class I, LOE B	Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg

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Conclusion

- Comorbidities are highly prevalent in heart failure patients
- Novel mechanisms linking comorbidities to heart failure provide additional diagnostic and therapeutic opportunities
- Treating some comorbidities can lead to a heterogeneous impact on heart failure outcomes, as some comorbid conditions may represent adaptive responses and are only markers of poor prognosis
- Our understanding of comorbidities and therapeutic strategies continues to evolve