

The poster features a colorful, abstract background with a woman in a blue and white polka-dot dress riding a bicycle through a forest. The text is overlaid on the top and bottom of the image.

# 67° CONGRESSO NAZIONALE SIGG

PROGRAMMA DEFINITIVO

LA LONGEVITÀ DECLINATA AL FEMMINILE

  
SOCIETÀ ITALIANA  
DI GERONTOLOGIA  
E GERIATRIA

Roma, 30 novembre - 3 dicembre 2022  
UNIVERSITÀ CATTOLICA DEL SACRO CUORE



## Le anemie nell'anziano

Giovambattista Desideri  
UO Geriatria e Lungodegenza  
Dipartimento MESVA  
Università degli Studi di L'Aquila



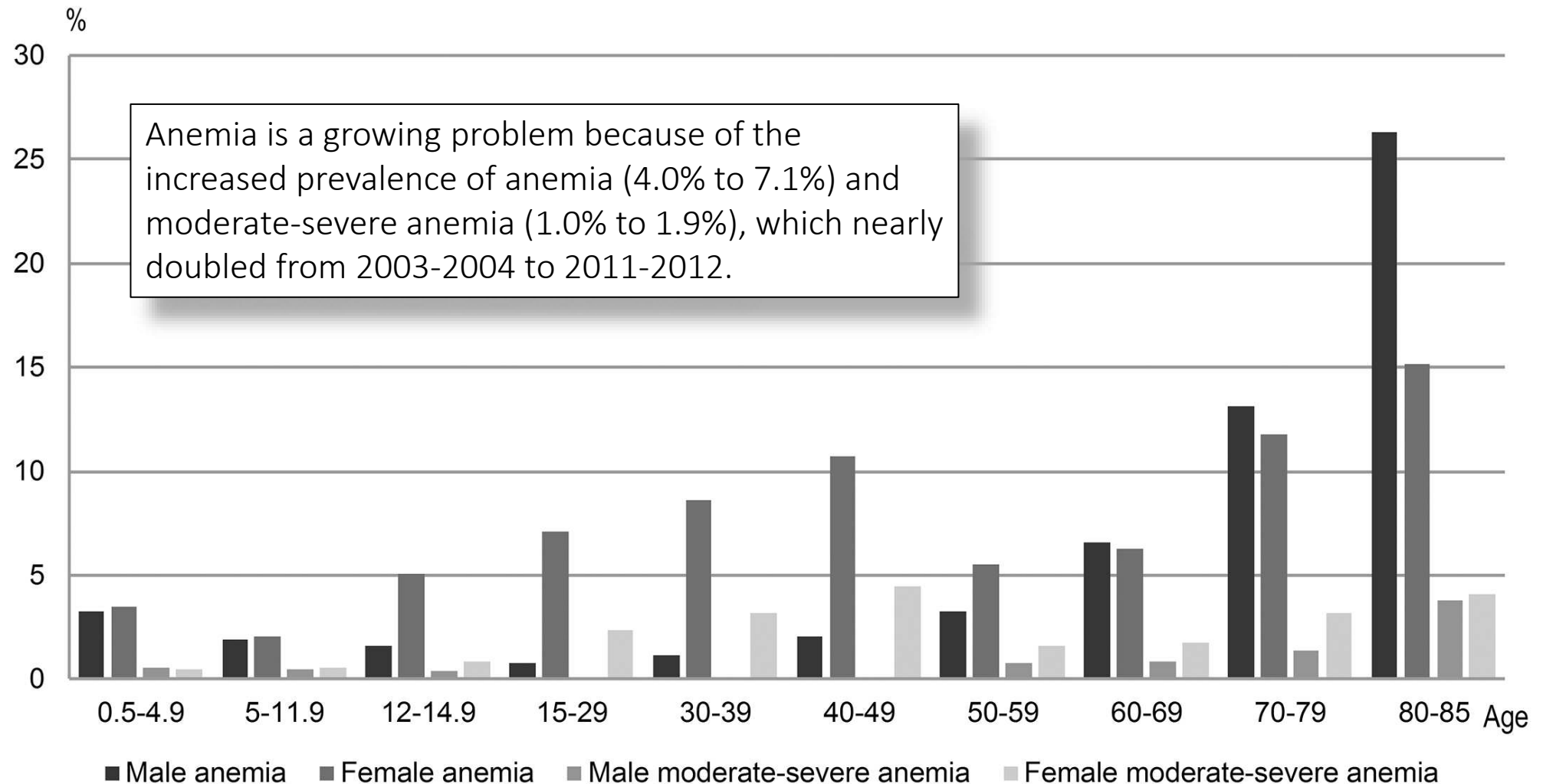


# Le anemie nel paziente anziano

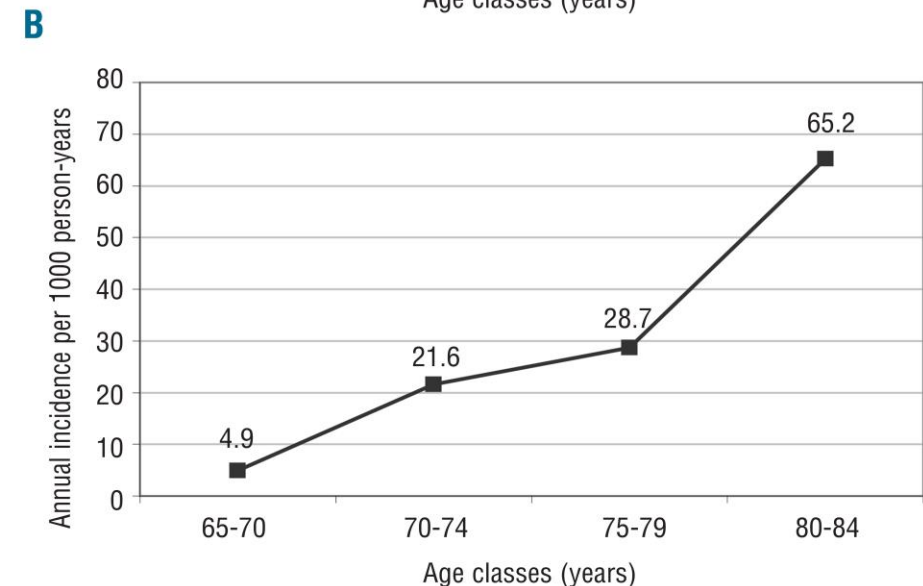
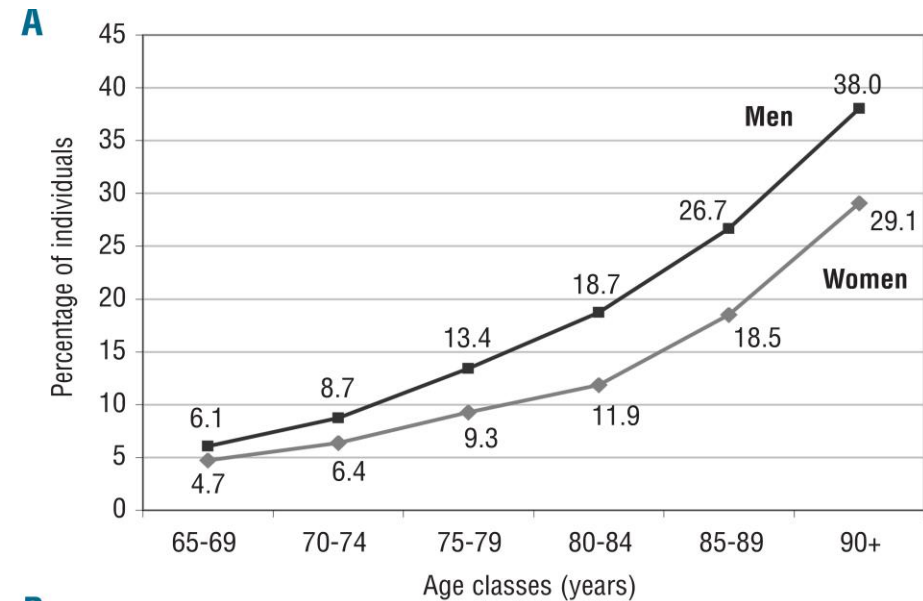


1. Quanto è frequente?

# The Prevalence of Anemia and Moderate-Severe Anemia in the US Population (NHANES 2003-2012)



# Prevalence, incidence and types of mild anemia in the elderly: the “Health and Anemia” population-based study



# Prevalence of anemia in hospitalized patients

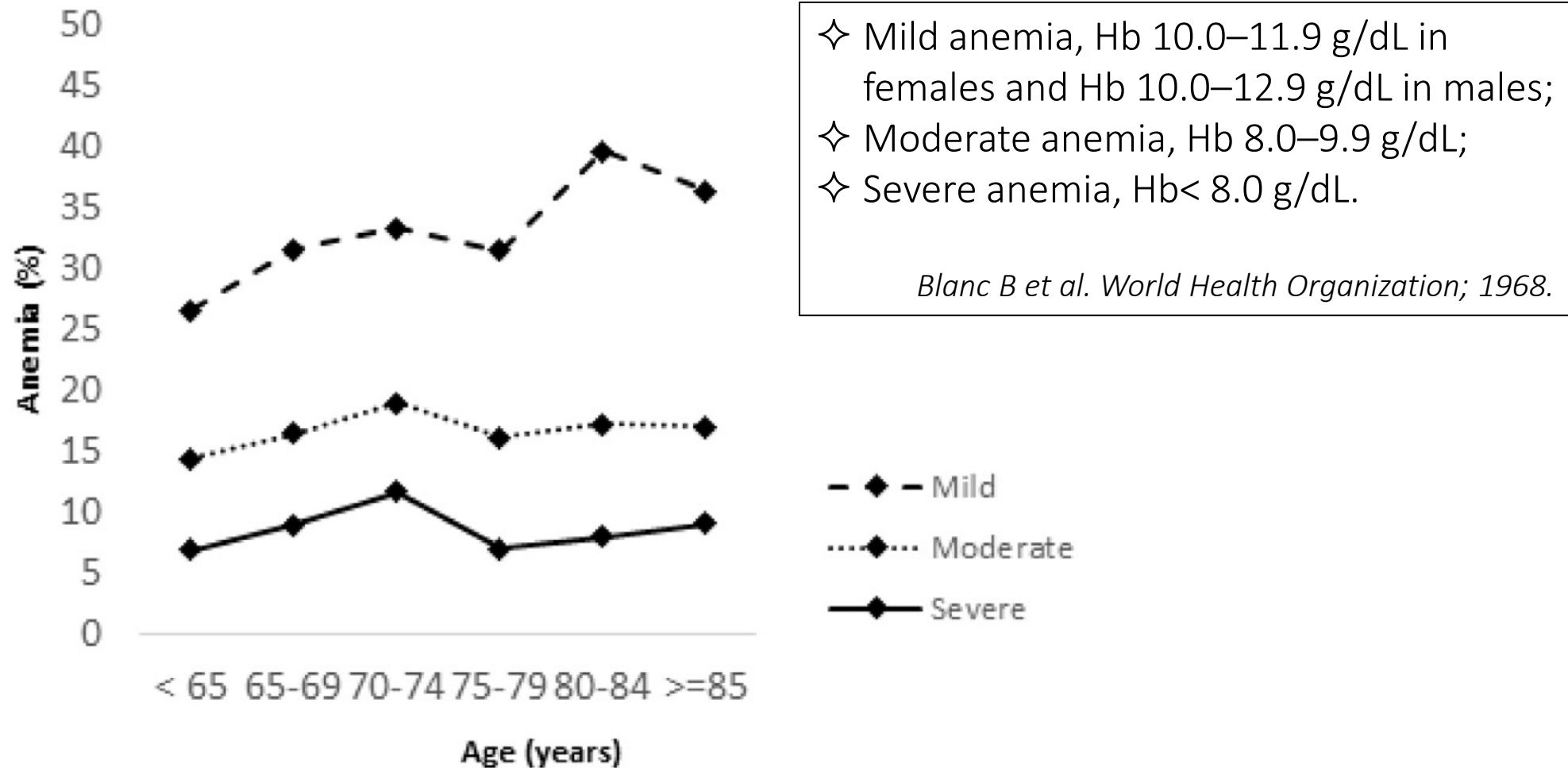


Age group years	Total population		
	n	Anemia prevalence, %	95% CI
Any	856	58.4	55.0 to 61.7
< 65	173	48.0	40.3 to 55.7
≥ 65	683	61.0	57.3 to 64.7
65–69	60	55.0	41.6 to 67.9
70–74	103	65.0	55.0 to 74.2
75–79	137	53.3	44.6 to 61.8
80–84	171	62.6	54.9 to 69.8
≥ 85	212	64.6	57.8 to 71.0

58.4%

Age group years	Male			Female		
	n	Anemia prevalence, %	95% CI	n	Anemia prevalence, %	95% CI
Any	439	57.9	53.1 to 62.5	417	59.0	54.1 to 63.7
< 65	102	44.1	34.3 to 54.3	71	53.5	41.3 to 65.4
≥ 65	337	62.0	56.7 to 67.2	346	60.1	54.7 to 65.3
65–69	37	54.0	39.9 to 70.5	23	56.5	34.5 to 76.8
70–74	54	70.4	56.4 to 82.0	49	59.2	44.2 to 73.0
75–79	74	54.0	42.1 to 65.7	63	52.4	39.4 to 65.1
80–84	83	67.5	56.3 to 77.3	88	57.9	46.9 to 68.4
≥ 85	89	61.8	50.9 to 71.9	123	66.7	57.6 to 74.9

# Distribution of the prevalence of anemia by level in the elderly: the “Health and Anemia” population-based study





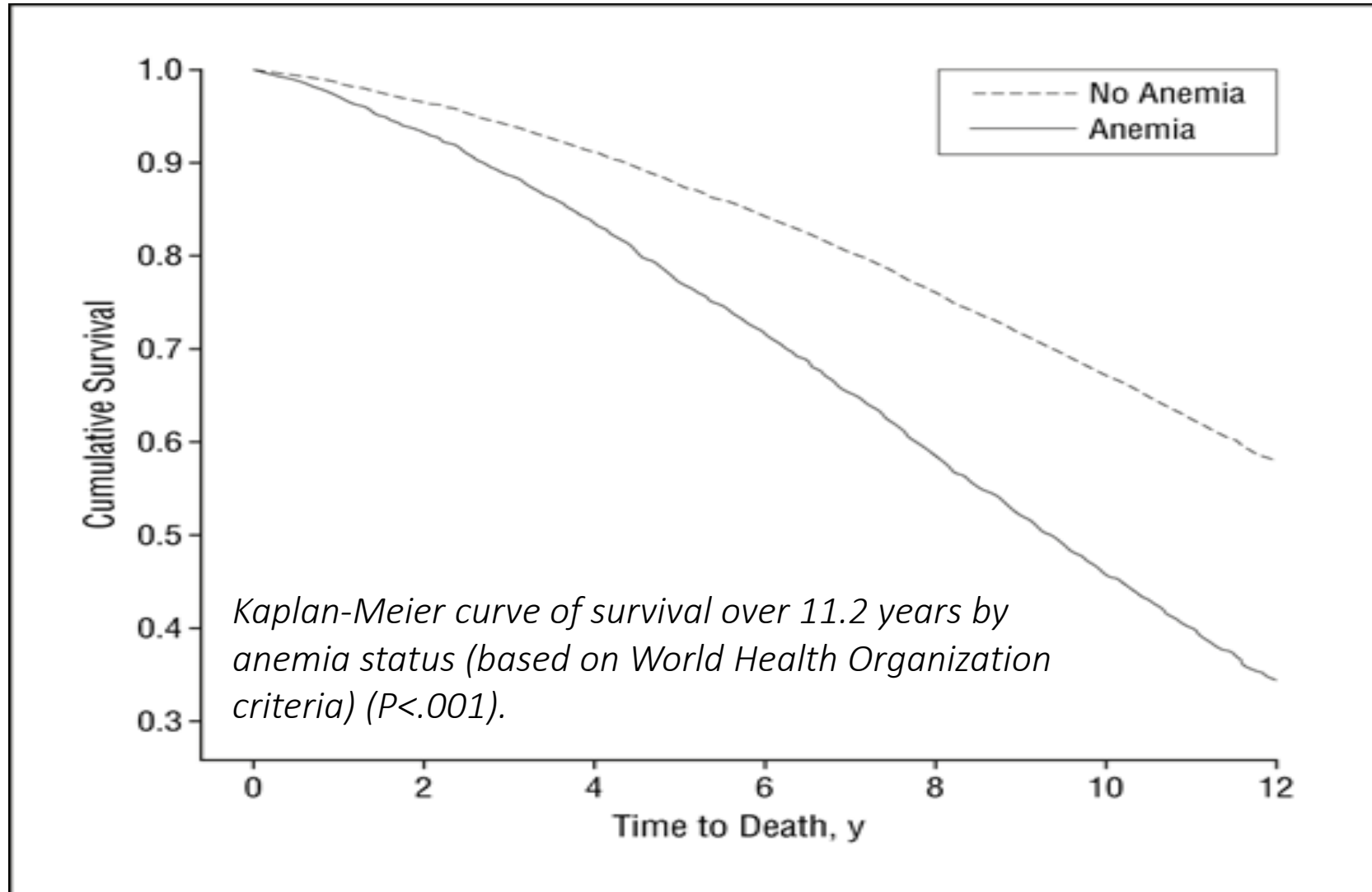
# Le anemie nel paziente anziano



1. Quanto è frequente?

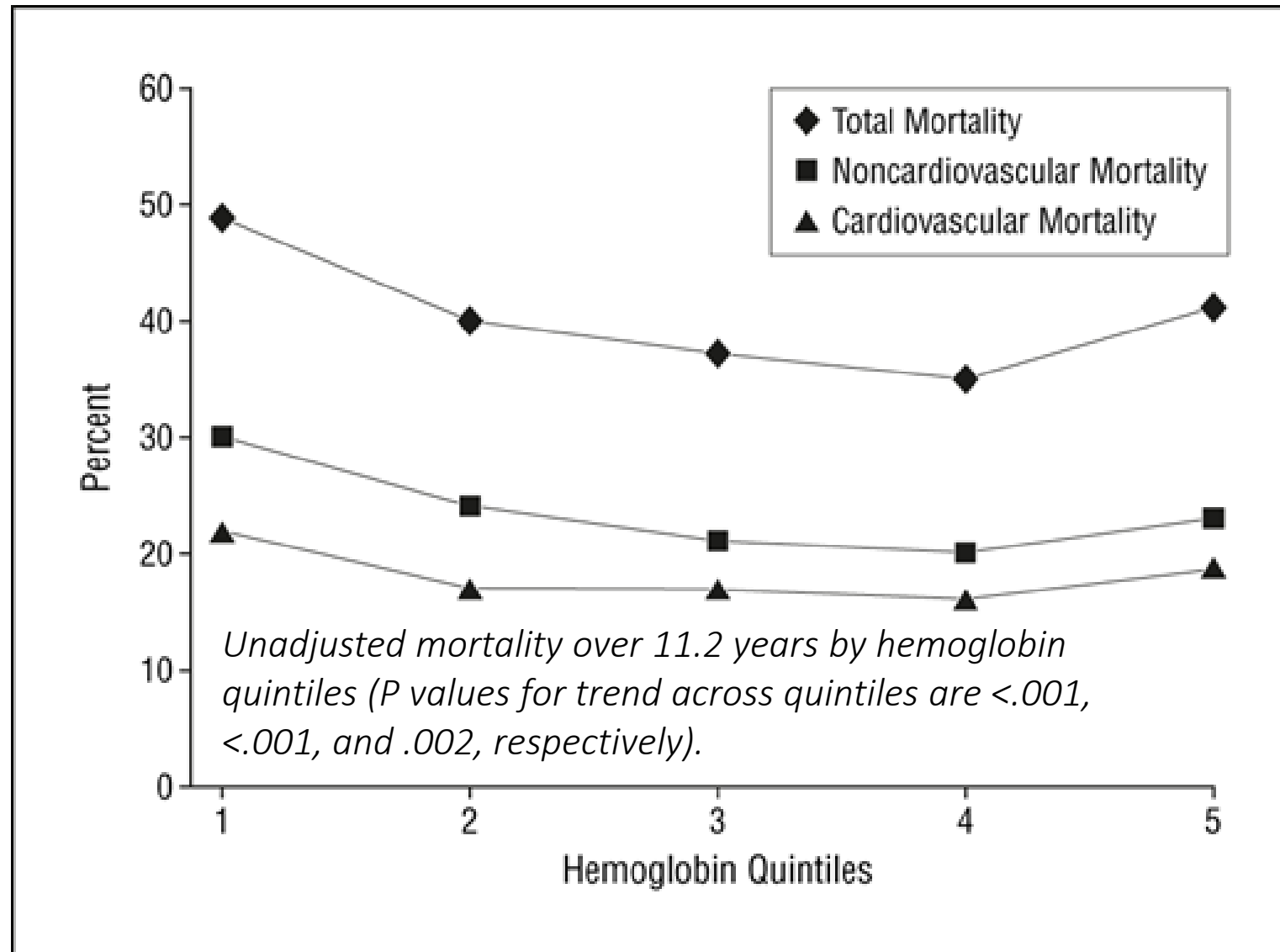
1.1 Molto, quindi... pensiamoci!

# A Prospective Study of Anemia Status, Hemoglobin Concentration, and Mortality in an Elderly Cohort - The Cardiovascular Health Study

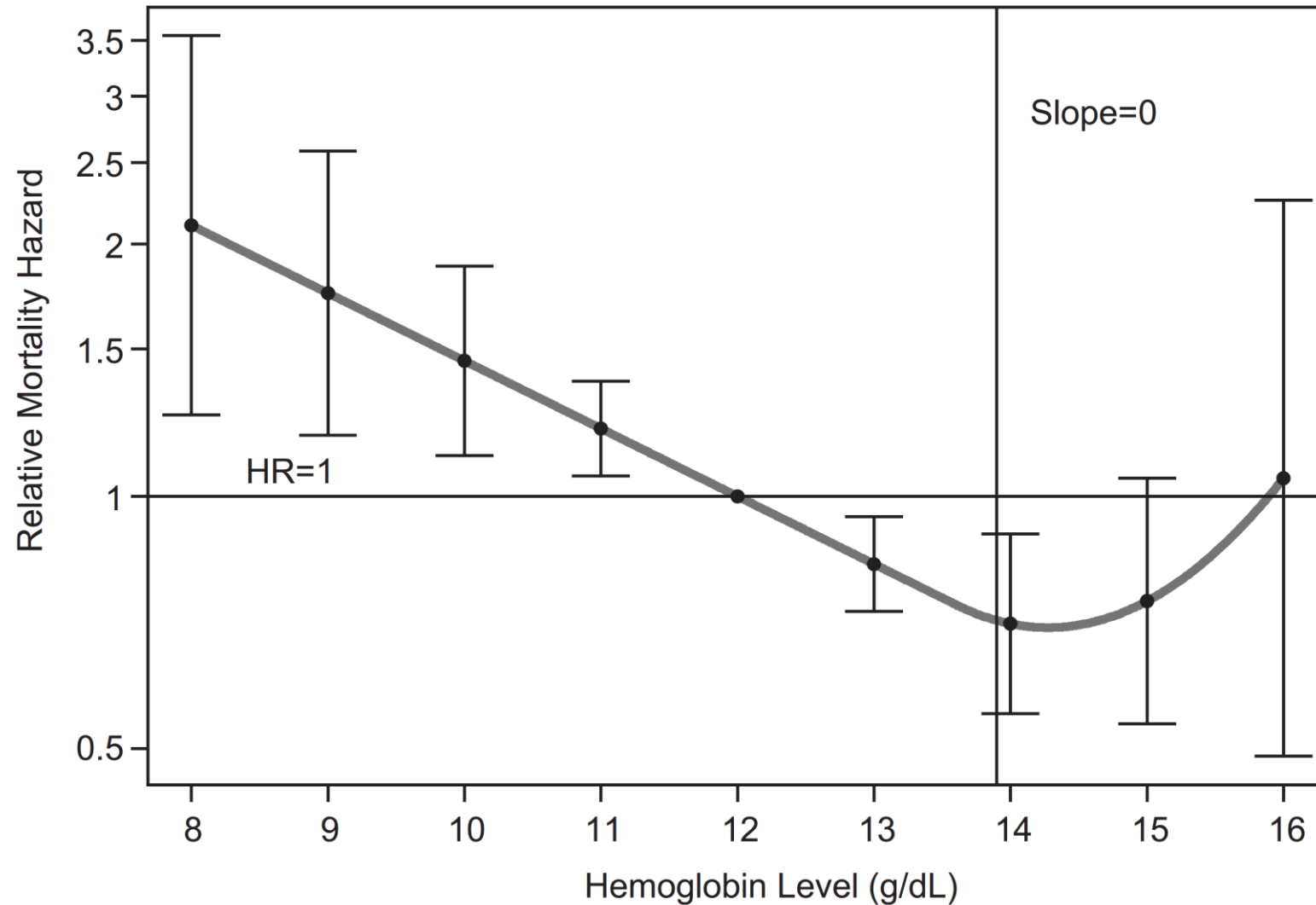




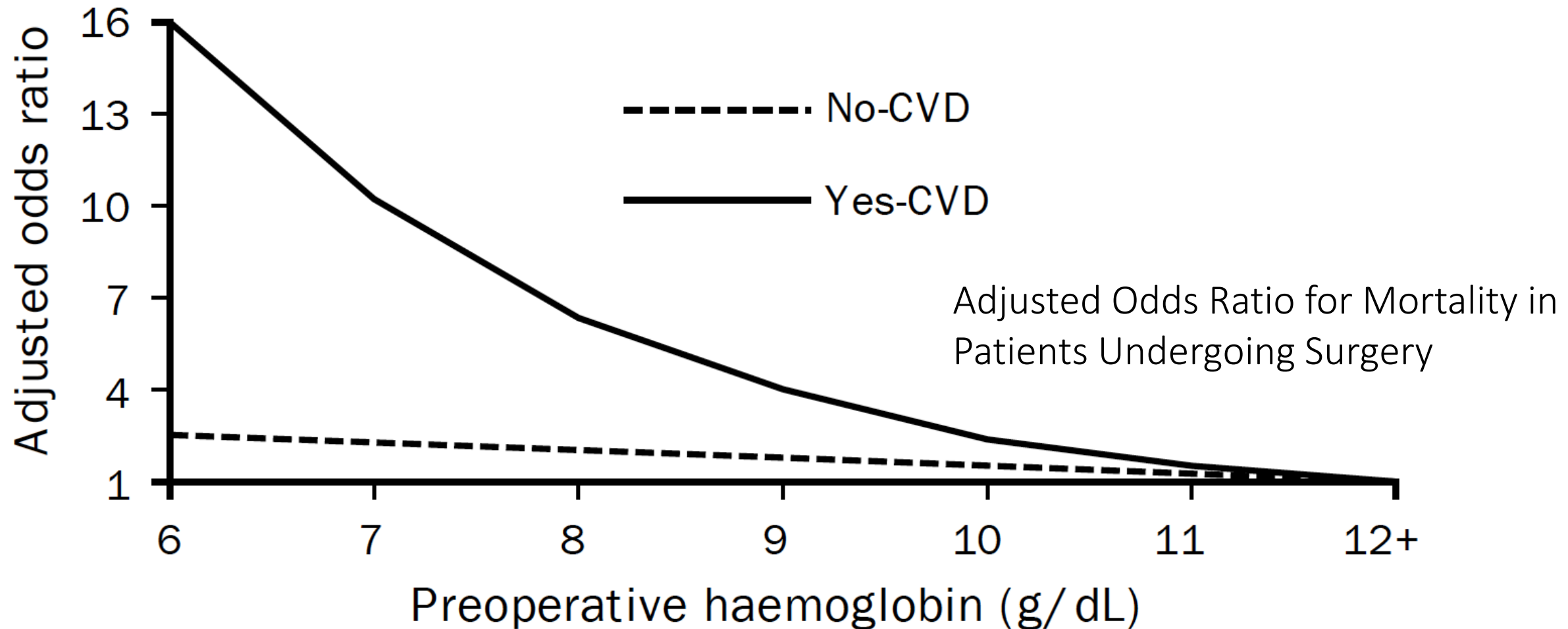
# A Prospective Study of Anemia Status, Hemoglobin Concentration, and Mortality in an Elderly Cohort - The Cardiovascular Health Study



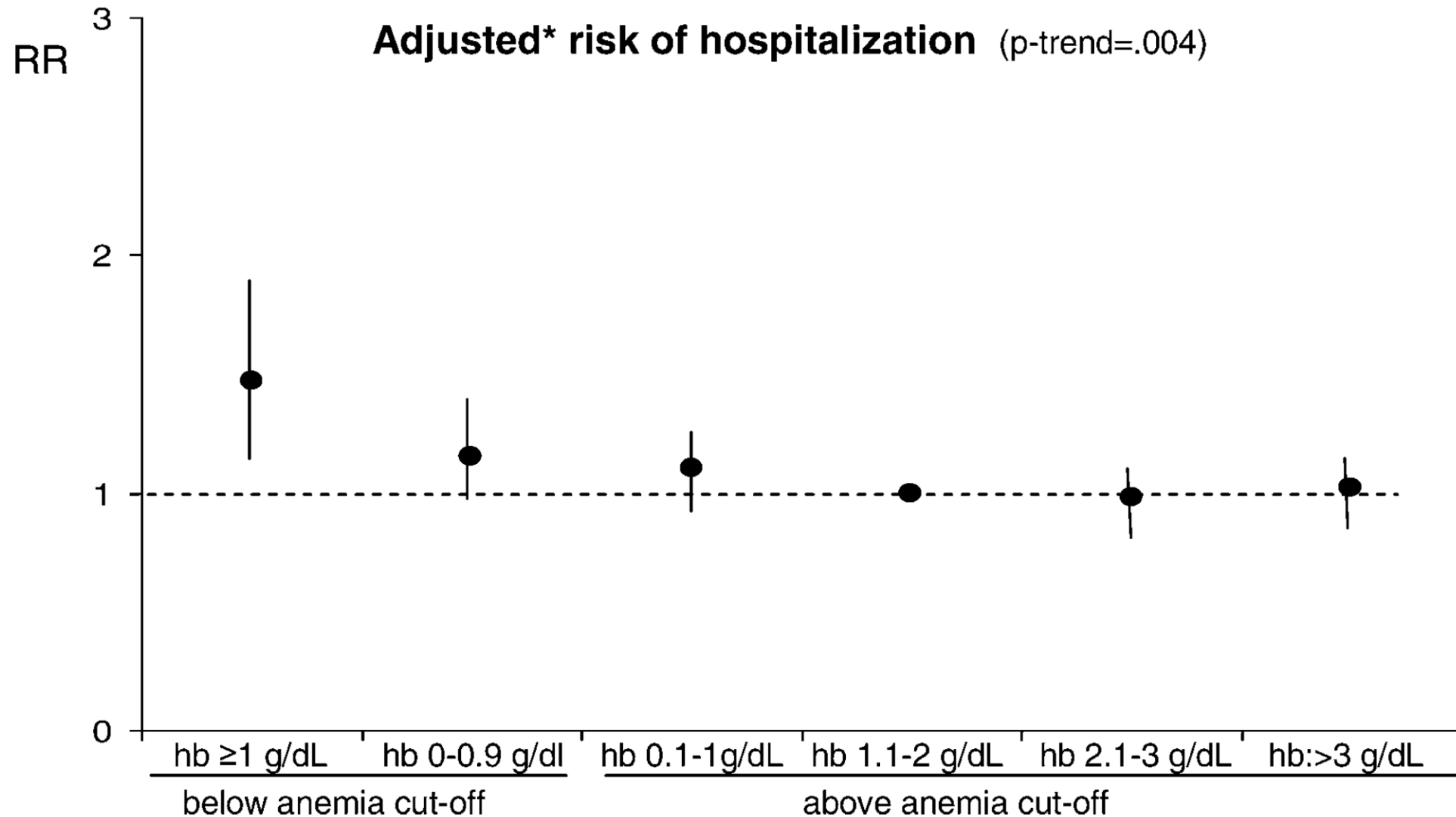
# Relationship between hemoglobin (Hb) concentration and 5-year all-cause mortality in community-dwelling, disabled older women



# Effect of anaemia and cardiovascular disease on surgical mortality and morbidity

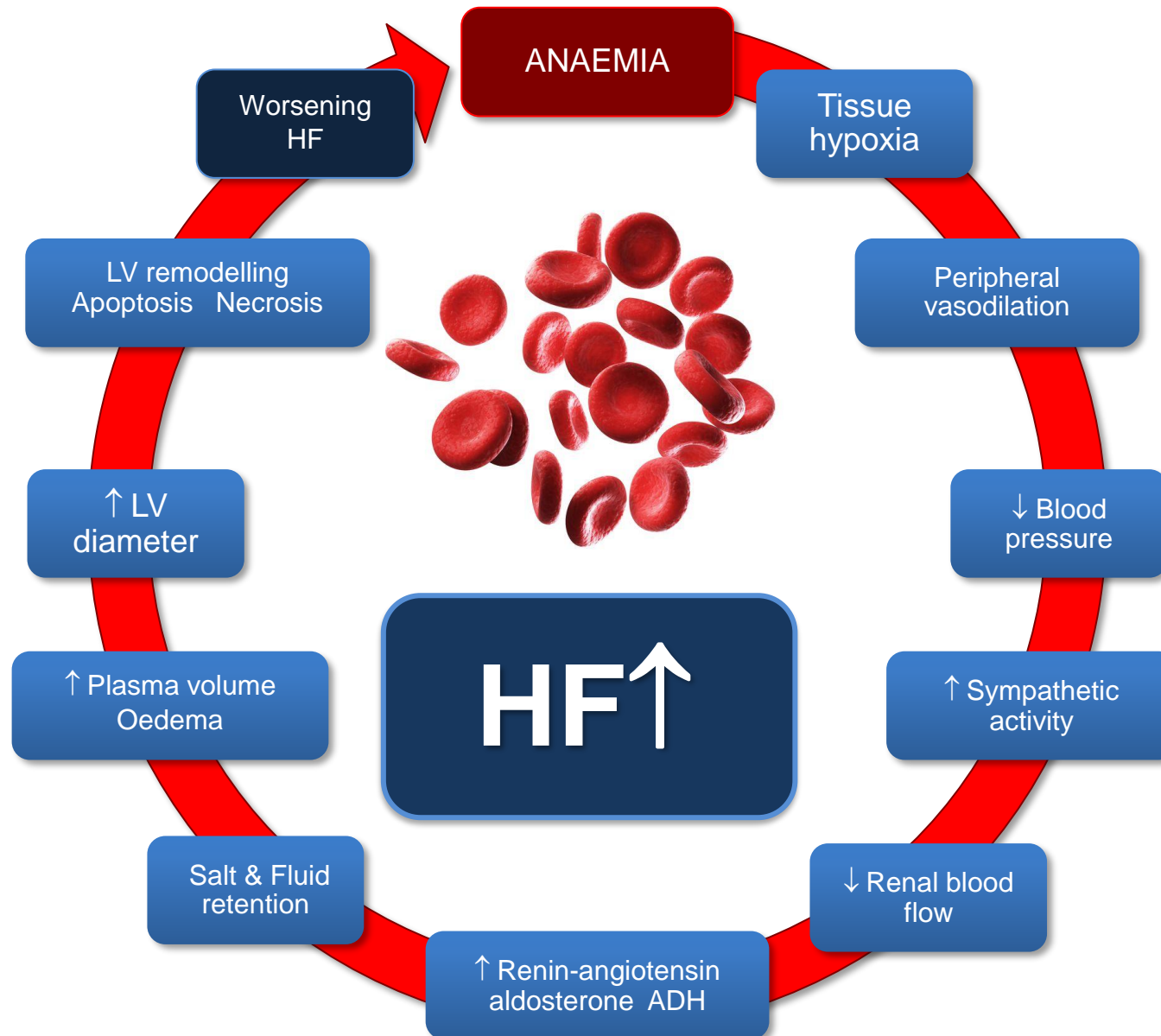


# Anemia in Old Age Is Associated With Increased Hospitalization

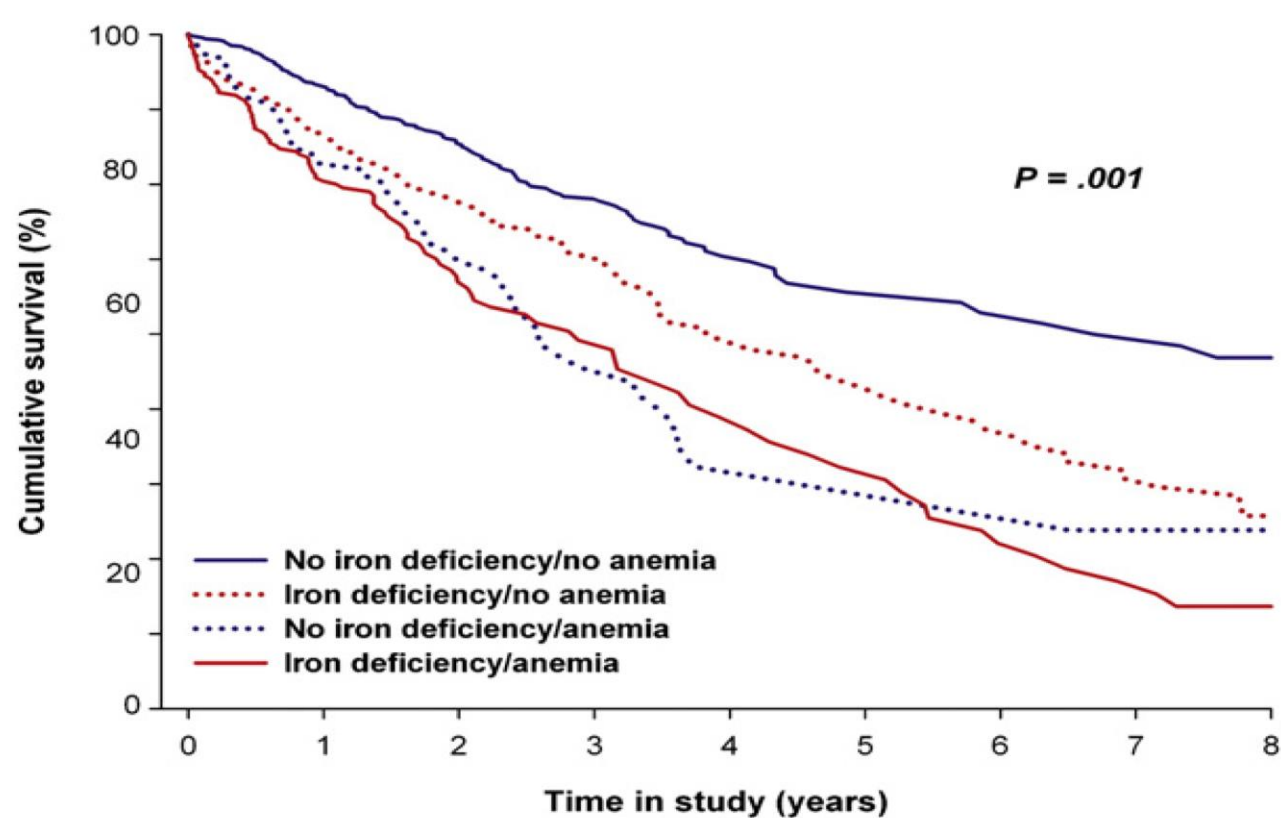




# Vicious circle of Anemia and HF

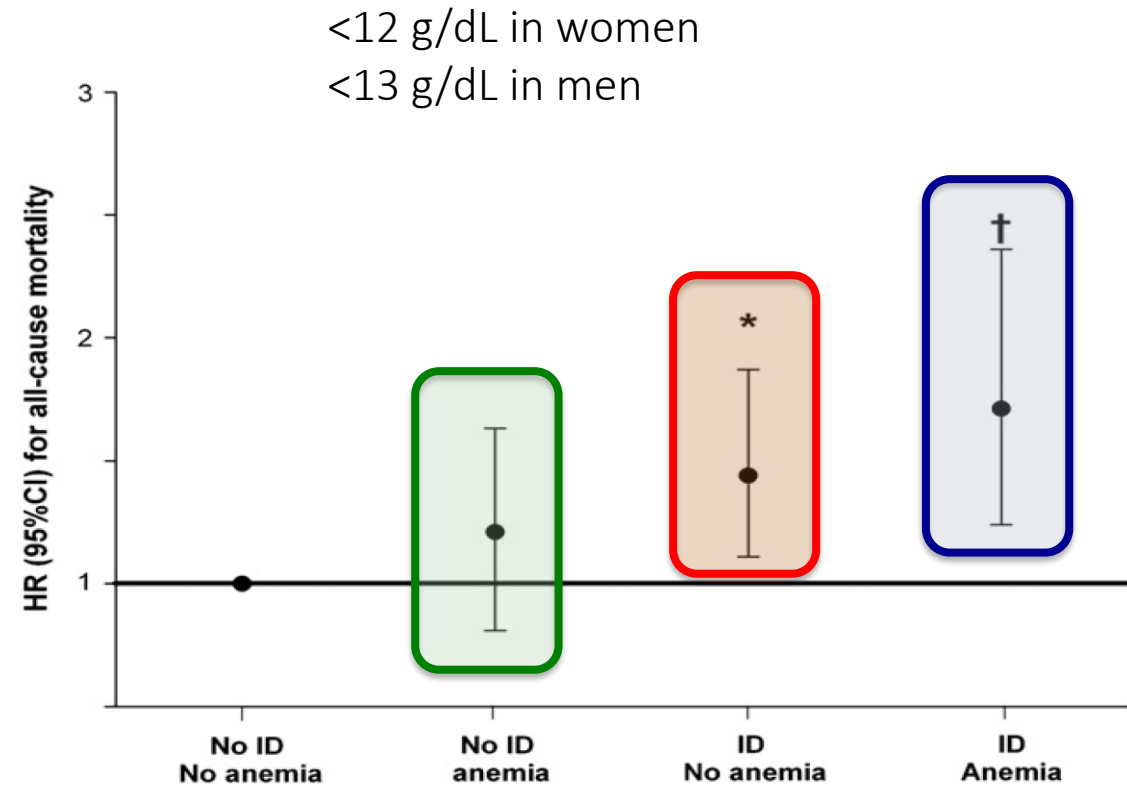


# Difference in **event-free survival** rates between iron-deficient and non-iron-deficient patients with HF with or without anemia



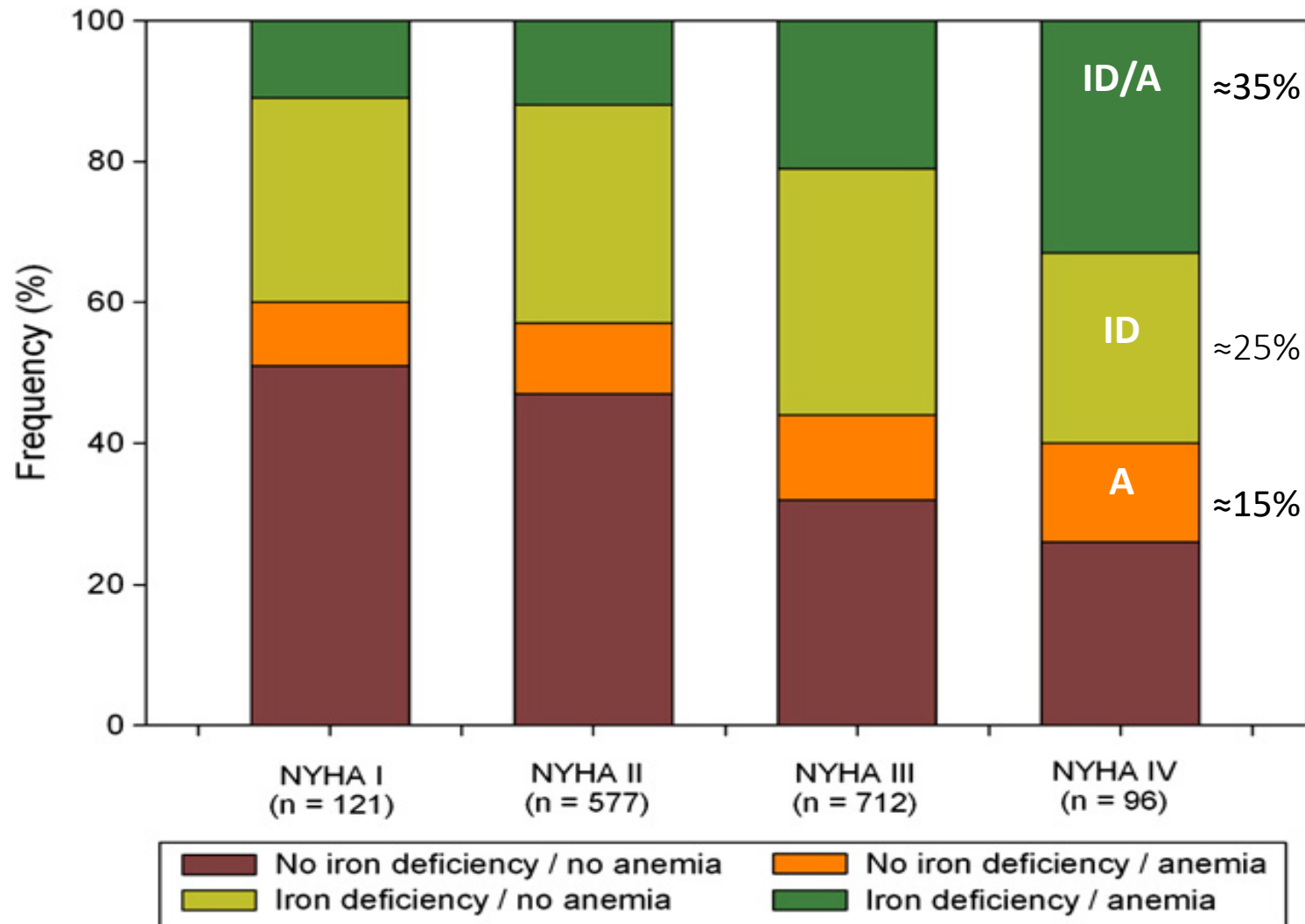
## Numbers at risk:

No ID/no anemia	589	328	86	38	31
ID/no anemia	492	256	76	50	26
No ID/anemia	164	58	18	11	9
ID/anemia	261	87	24	13	7



# Iron deficiency and/or anemia stratified by NYHA functional class.

## Prevalence of ID and/or anemia per NYHA functional class.



**ID commonly occurs even without anaemia in HF**

➤ ID (with or without anaemia) is present in 50% of HF patients

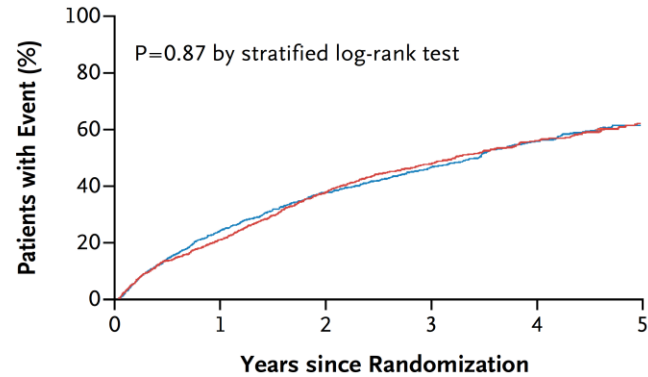


**Iron deficiency definition used:**

- Serum ferritin <100 µg/L or
- Serum ferritin <299 µg/L if TSAT <20%

# Treatment of Anemia with Darbepoetin Alfa in Systolic Heart Failure – RED HF study

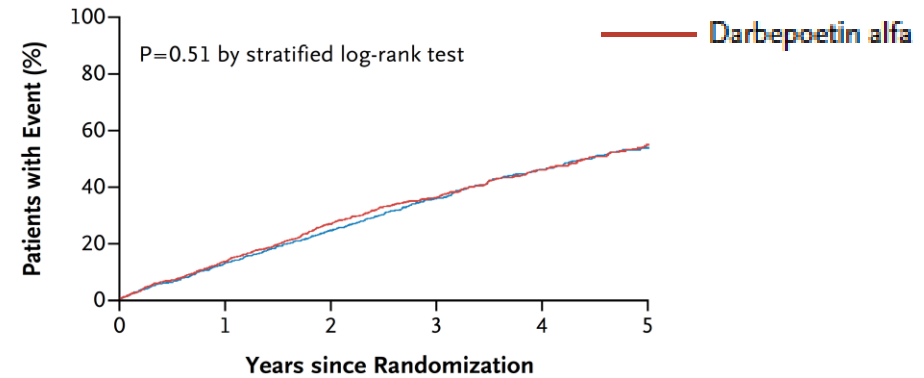
**A Primary Composite Outcome**



**No. at Risk**

Placebo	1142	956	818	695	591	497	395	290	211	154	92
Darbepoetin alfa	1136	975	855	712	581	473	385	281	212	161	101

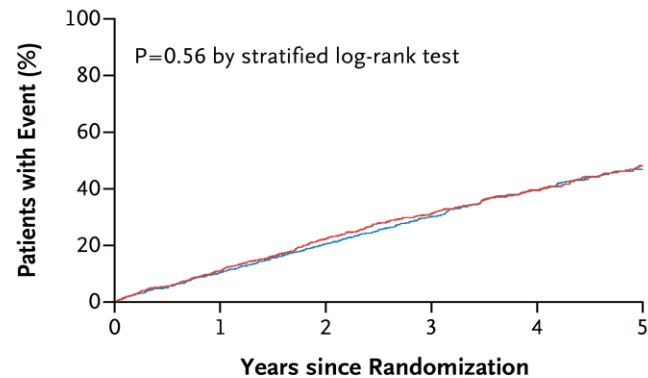
**B Death from Any Cause**



**No. at Risk**

Placebo	1142	1055	942	824	715	599	481	352	264	192	118
Darbepoetin alfa	1136	1053	940	816	687	573	474	351	272	201	124

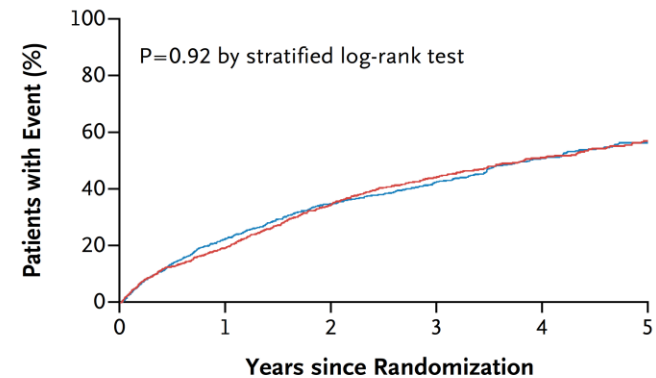
**C Death from Cardiovascular Causes**



**No. at Risk**

Placebo	1142	1055	942	824	715	599	481	352	264	192	118
Darbepoetin alfa	1136	1053	940	816	687	573	474	351	272	201	124

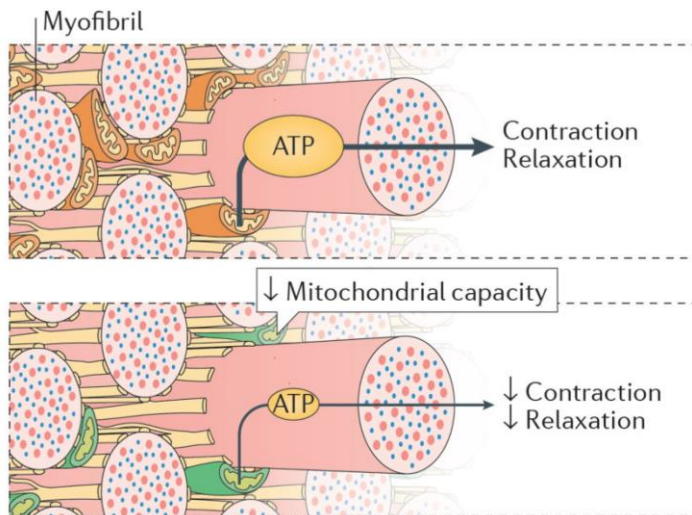
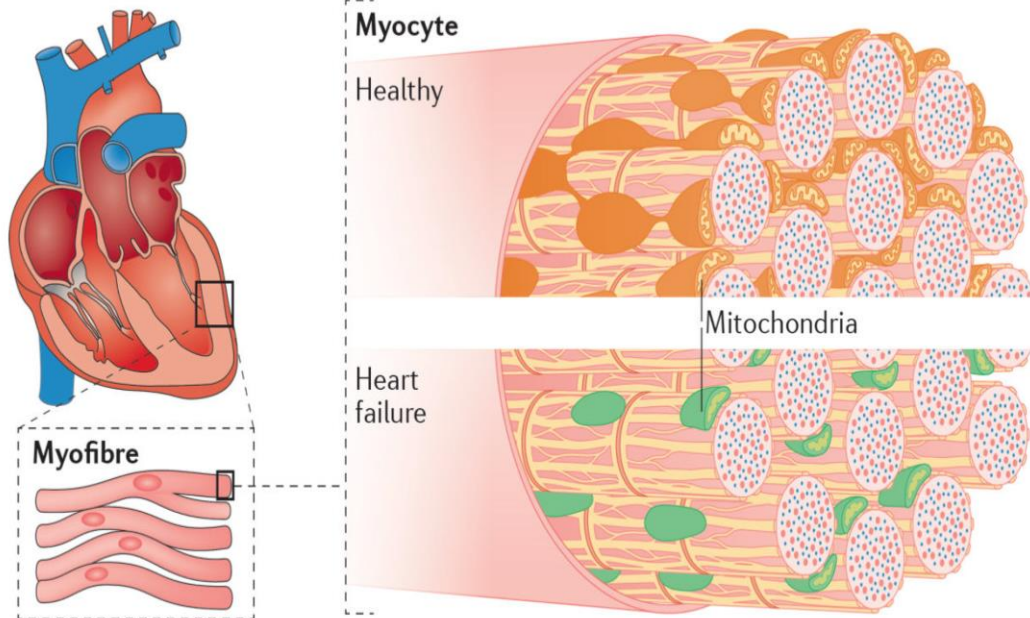
**D Death from Cardiovascular Causes or First Hospitalization for Worsening Heart Failure**



**No. at Risk**

Placebo	1142	956	818	695	591	497	395	290	211	154	92
Darbepoetin alfa	1136	975	855	712	581	473	385	281	212	161	101





The numbers of the heart:

- ✧ 100.800 beats/day
- ✧ 5-6 kg ATP/day
- ✧ mitochondria: 40% cell volume

As a vigorously metabolically active tissue, the heart is a primary tissue target of iron delivery<sup>1</sup>



➤ **Iron Deficiency is associated with energy deficiency**  
 ⇒ Reduced activity of respiratory complexes at the mitochondrial level

- The heart requires robust levels of ATP to sustain continuous contractions  
 ⇒ **Cardiomyocytes are highly mitochondria-dense**
- Iron is required for iron/sulphur cluster protein and heme-containing cytochrome components of the electron transport chain complexes I-IV  
 ⇒ **ATP synthase within the mitochondria**

ATP, Adenosine Tri-Phosphate; ADP, Adenosine Diphosphate; CHF, Chronic heart failure; Fe, iron

## Recommendations

Class<sup>a</sup>

Level<sup>b</sup>



ESC

European Society  
of Cardiology

European Heart Journal (2021) 42, 3599–3726  
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

It is recommended that all patients with HF be periodically screened for anaemia and iron deficiency with a full blood count, serum ferritin concentration, and TSAT.

**I**

**C**

Intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic patients with LVEF <45% and iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to alleviate HF symptoms, improve exercise capacity and QOL.<sup>720,722,724</sup>

**IIa**

**A**

Intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic HF patients recently hospitalized for HF and with LVEF <50% and iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to reduce the risk of HF hospitalization.<sup>512</sup>

**IIa**

**B**

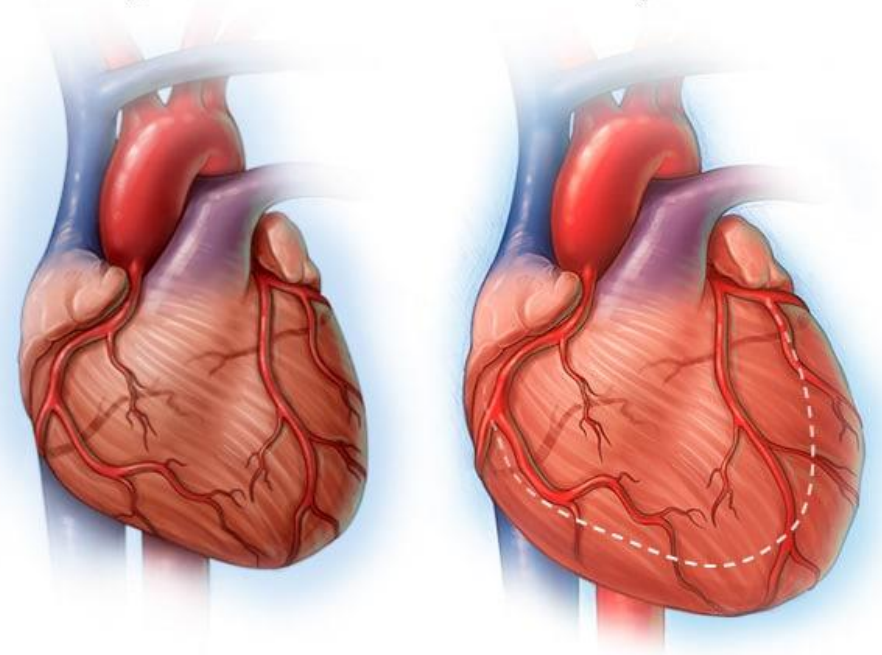
## 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

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

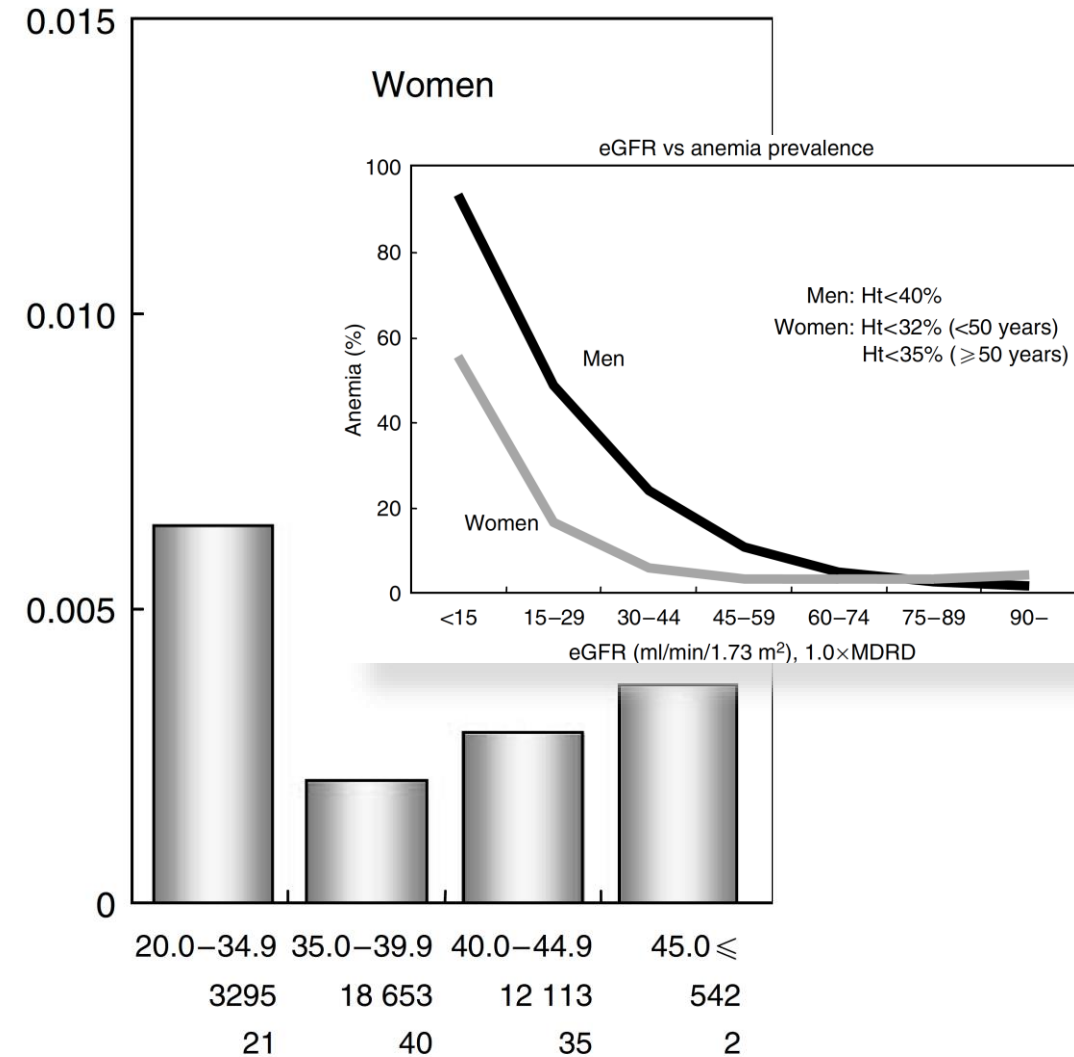
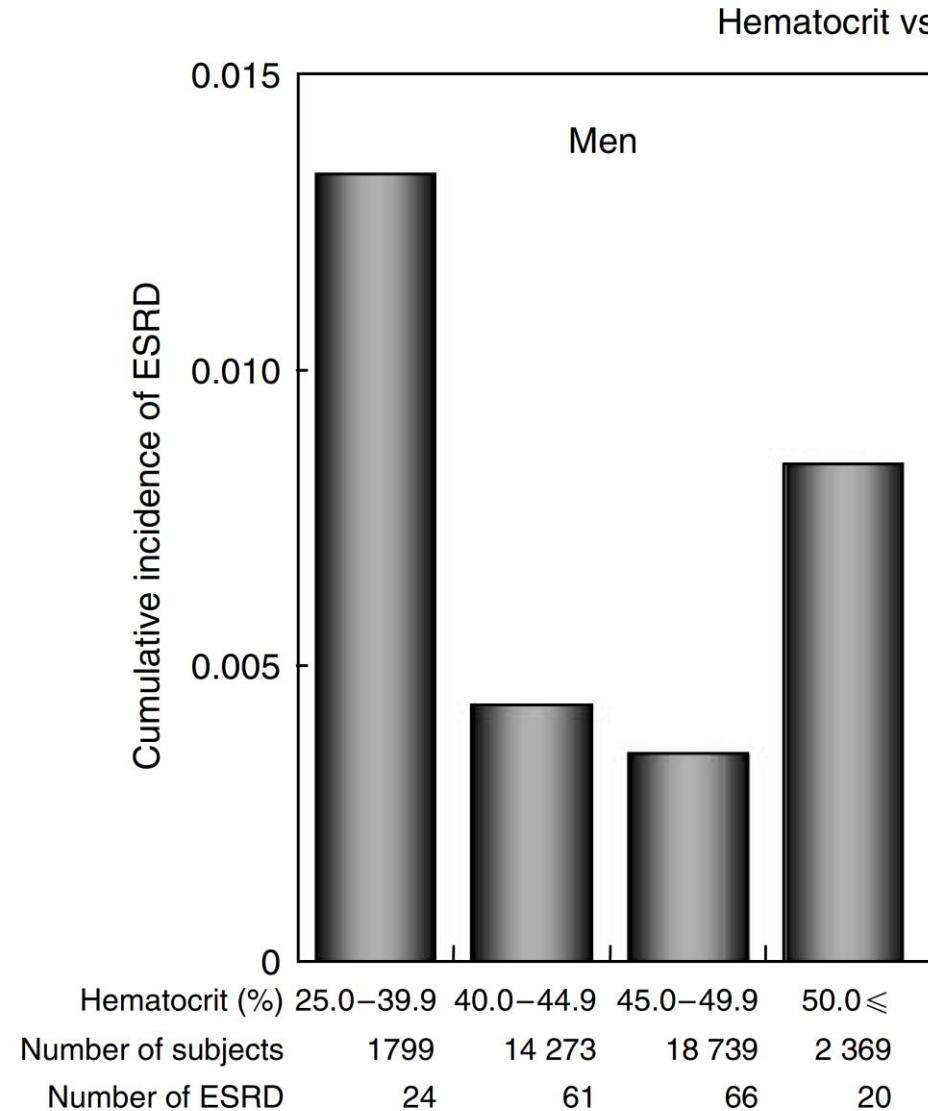
With the special contribution of the Heart Failure Association (HFA) of the ESC

Typical heart

Enlarged heart

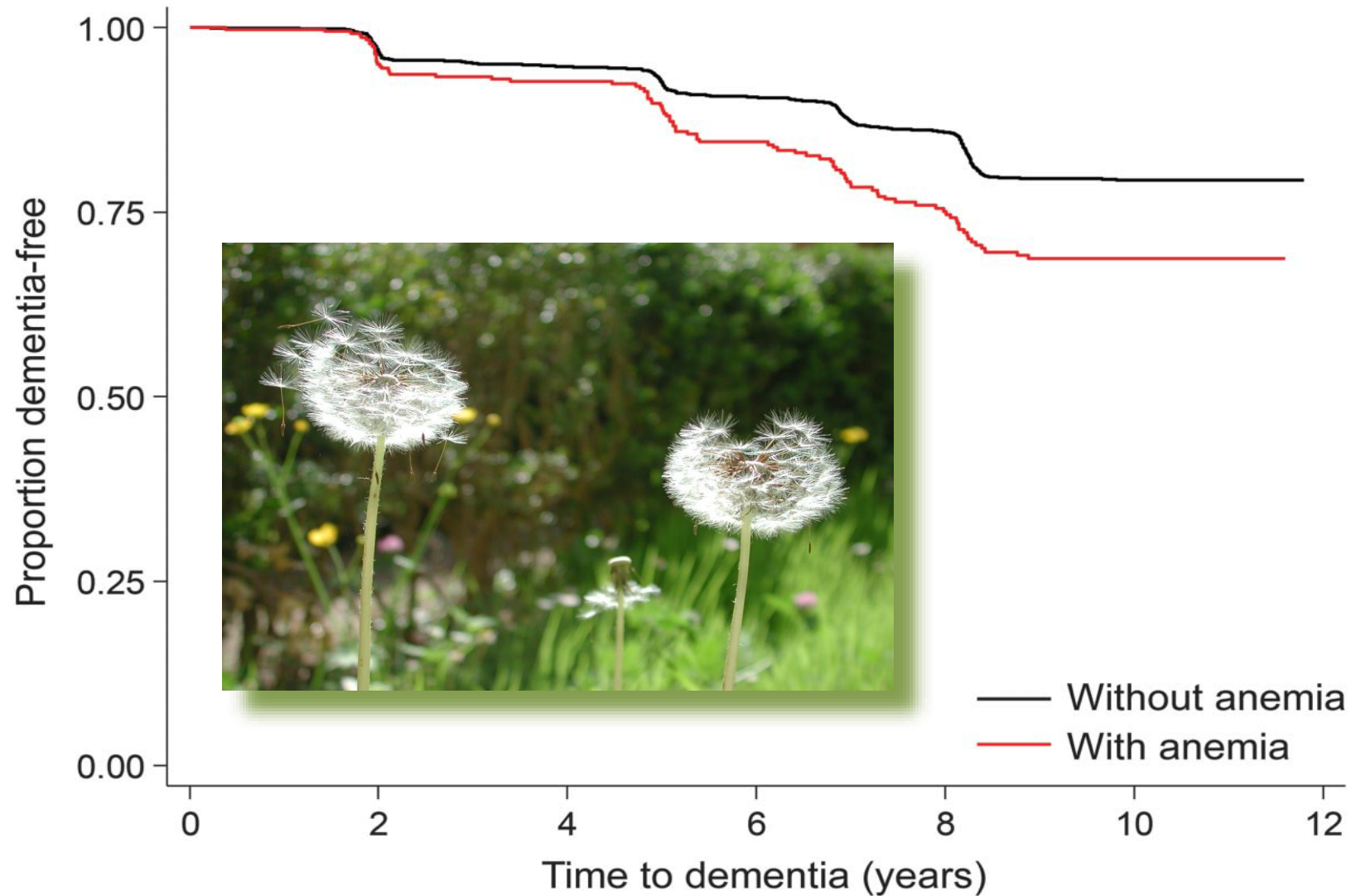


# Relationship between the baseline levels of Hct and the cumulative incidence of ESRD



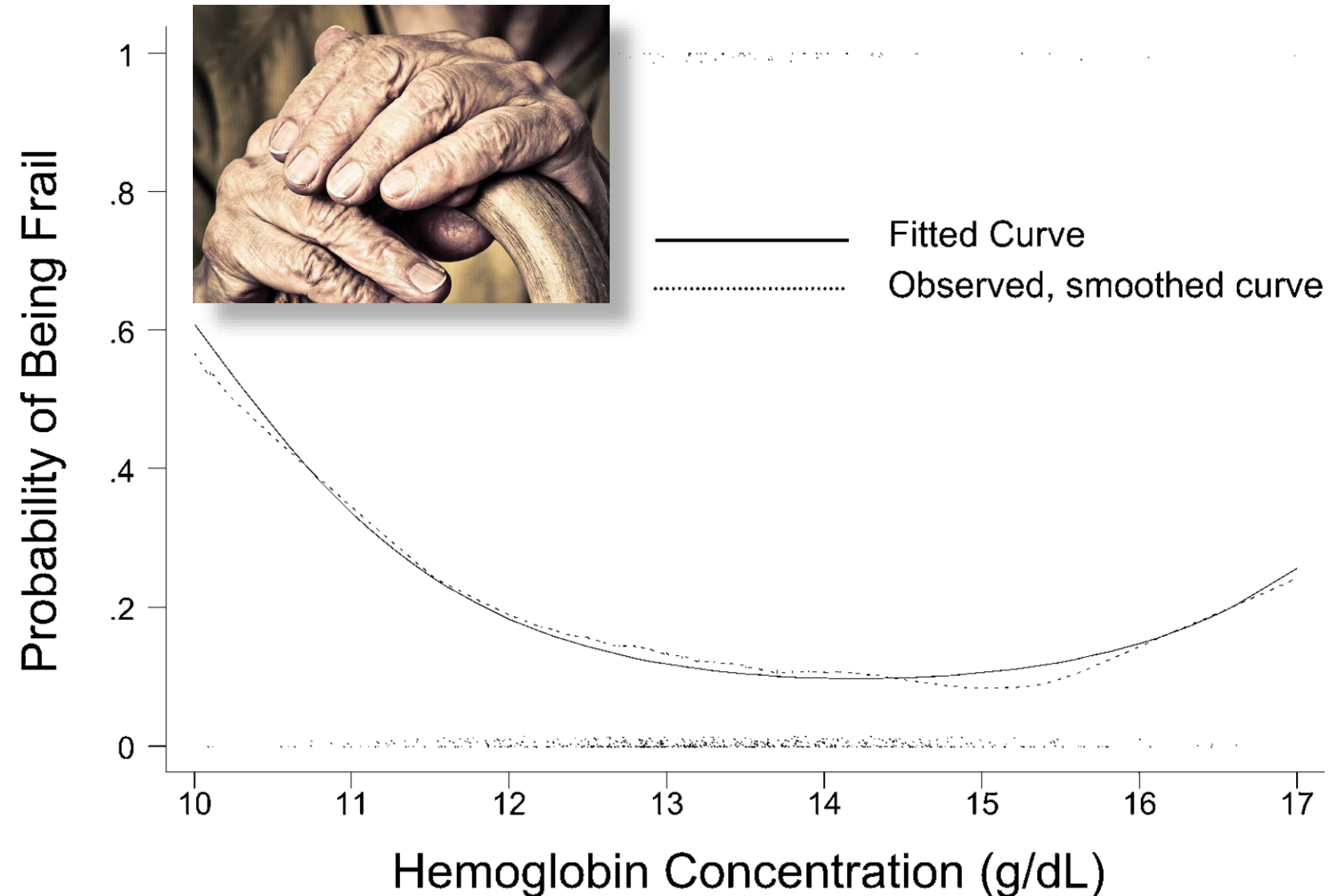


# Kaplan-Meier survival function of time to dementia diagnosis by baseline anemia





Cross-sectional relationship between Hb concentration and prevalent frailty status, Women's Health and Aging Studies I and II, 1992–1996.



# Le anemie nel paziente anziano



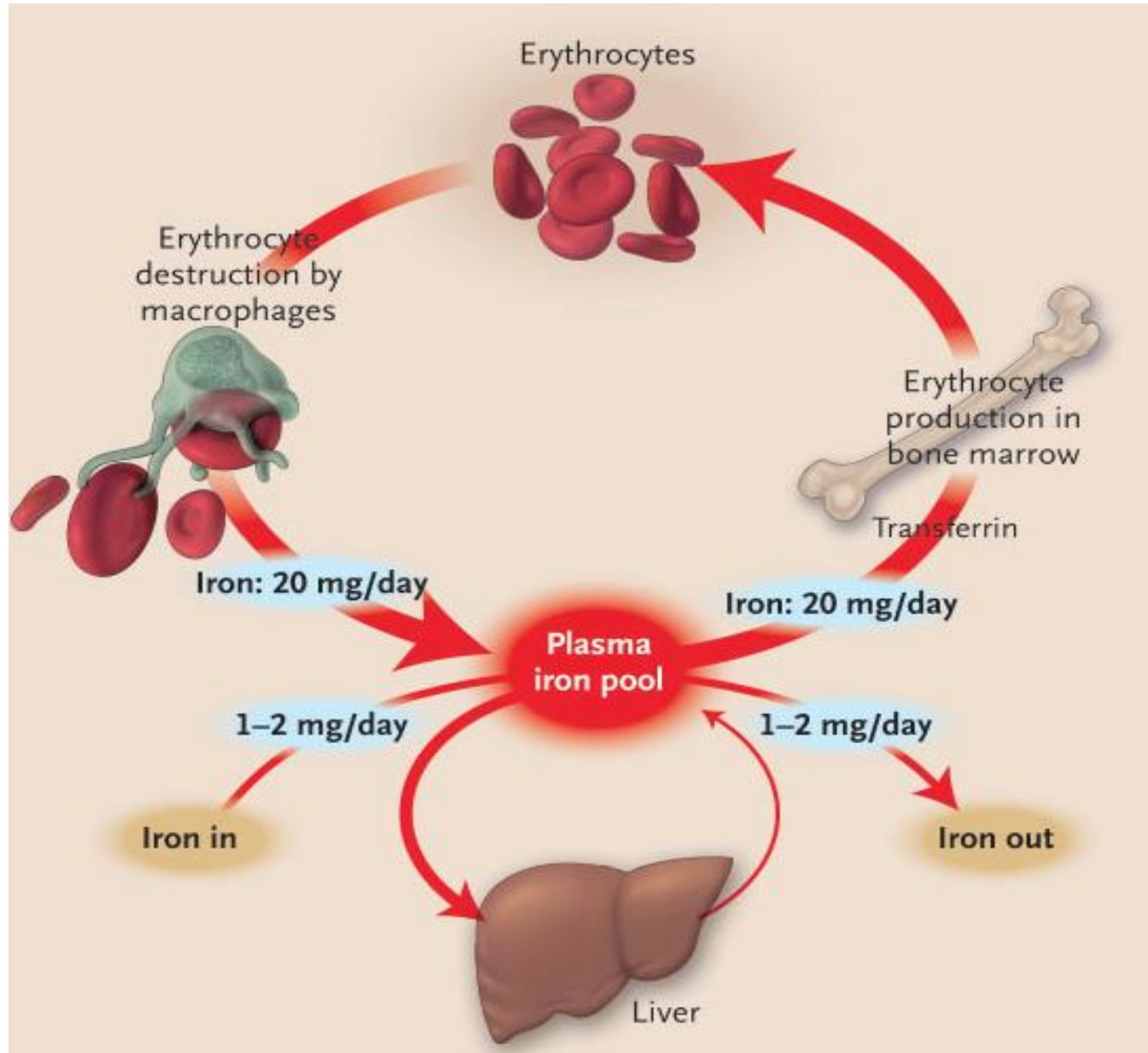
3. A cosa è dovuta?

# Types of anemia and mild anemia in the elderly population

	Anemic elderly			Mildly anemic elderly		
	n	%	%	n	%	%
Thalassemia trait	71	14.4		67	15.4	
Thalassemia			11.2			12.0
Thalassemia + low B <sub>12</sub> or folate			3.2			3.4
Vitamin B <sub>12</sub> or folate deficiency	50	10.1		44	10.1	
Low vitamin B <sub>12</sub> and MCV higher than 95 fL			3.9			4.2
Low folate and MCV higher than 95 fL			4.2			4.1
Low vitamin B <sub>12</sub> + low folate and MCV higher than 95 fL			2.0			1.8
Iron deficiency anemia (IDA)	79	16.0		54	12.4	
IDA			9.5			7.1
IDA + low vitamin B <sub>12</sub> and/or folate			6.5			5.3
Anemia of chronic disease (ACD)	86	17.4		80	18.4	
ACD			8.1			9.0
ACD + low vitamin B <sub>12</sub> or folate			3.7			4.1
ACD + IDA			2.4			2.8
ACD + IDA and/or low vitamin B <sub>12</sub> or folate			1.4			1.1
Hematologic malignancy			1.8			1.4
Renal insufficiency	74	15.0		63	14.5	
Renal insufficiency			9.7			10.0
Renal insufficiency + thalassemia			0.6			0.4
Renal insufficiency + IDA and/or low vitamin B <sub>12</sub> and/or low folate			4.7			4.1
Unexplained anemia	130	26.4		124	28.5	
Unexplained			18.3			20.0
Possible myelodysplastic syndromes <sup>a</sup>			8.1			8.5
Other types of anemia	3	0.6		3	0.7	
Total anemia types	493	100		435	100	
Insufficient laboratory data	33	6.3		30	6.4	
Total anemic subjects	526			465		

<sup>a</sup>Possible myelodysplastic syndromes: macrocytosis, leukopenia, or thrombocytopenia.

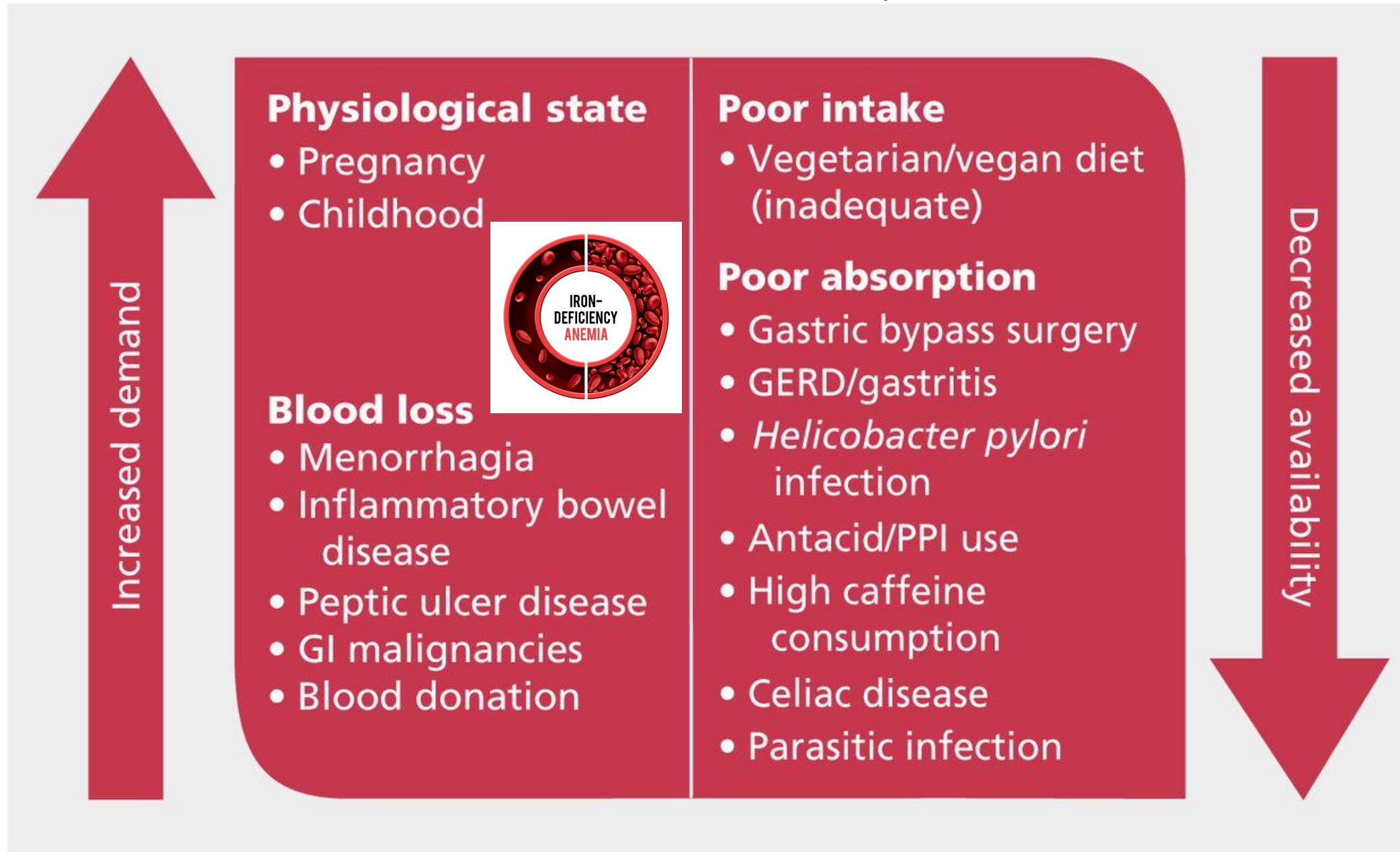
# Normal Iron Homeostasis in Humans



*Plasma levels of iron are closely regulated to ensure a daily supply of approximately 20 mg to the bone marrow for incorporation into hemoglobin in erythroid precursors and mature red cells*



# Causes of iron deficiency anemia

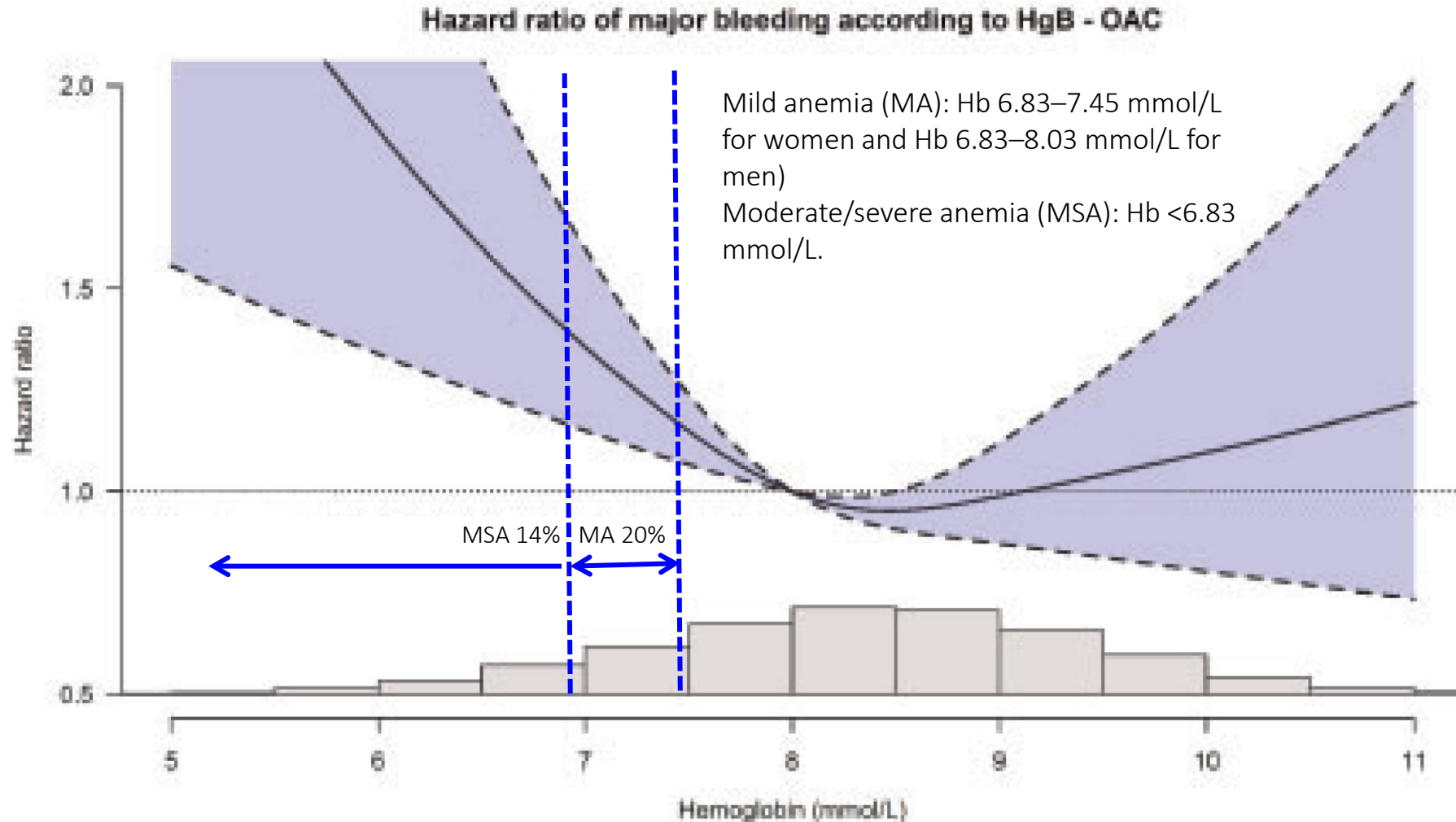


# Diagram summarising the NOACs RCT findings



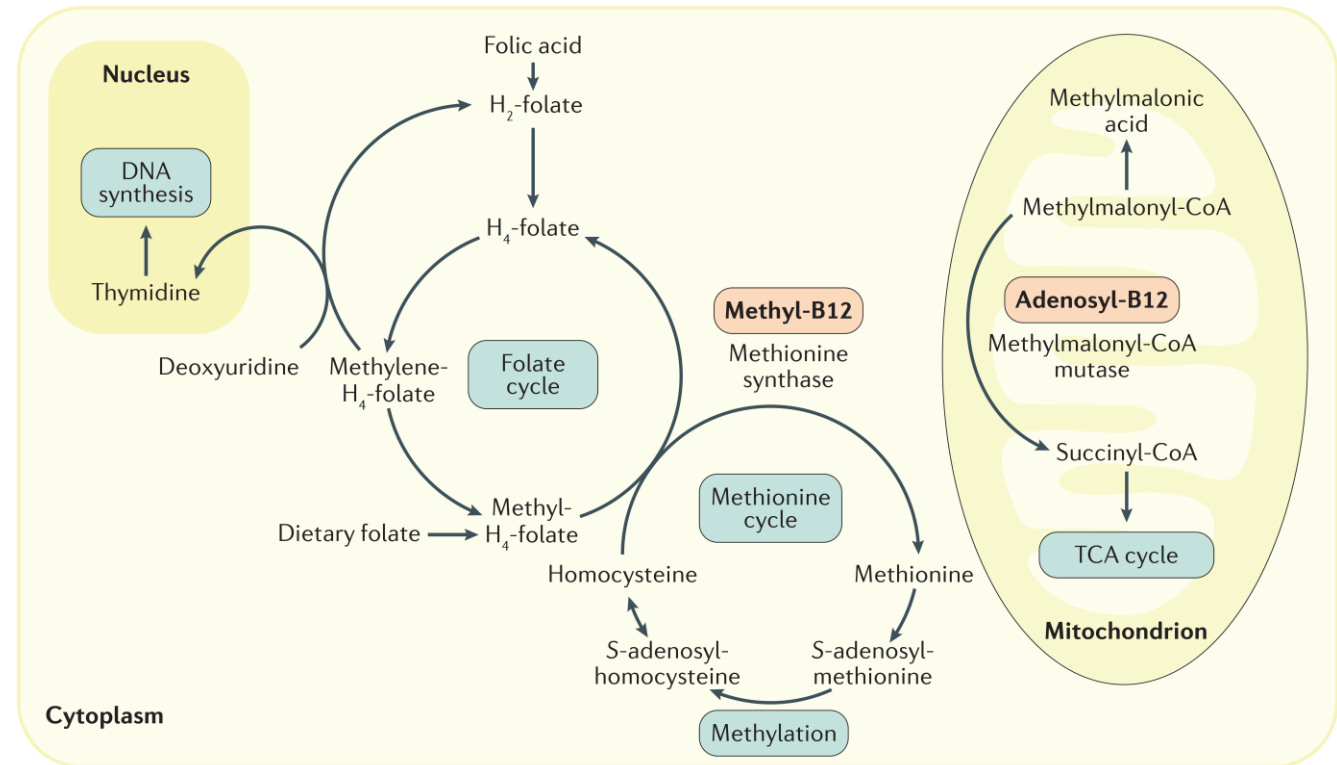
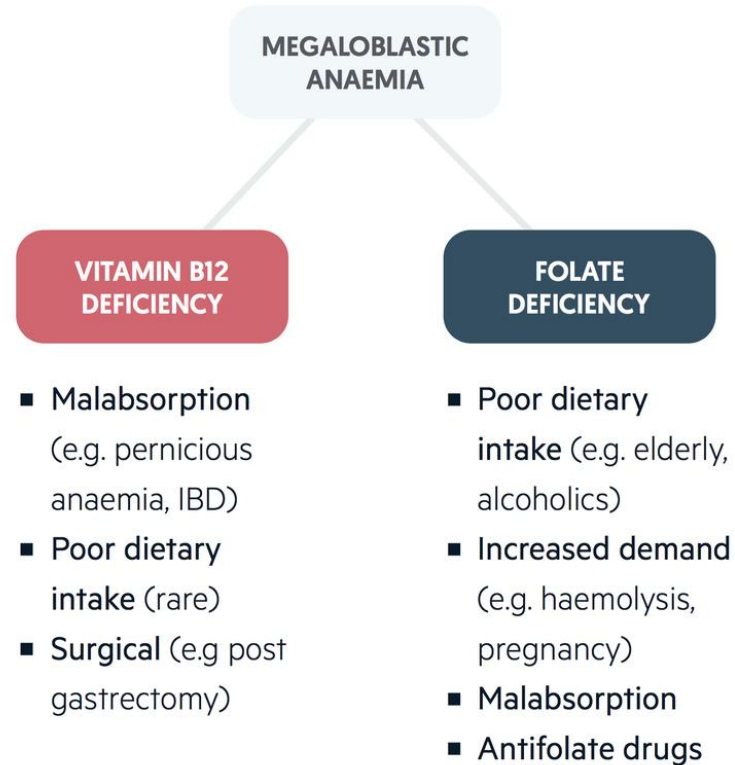
Outcome	Dabigatran (RE-LY)		Rivaroxaban (ROCKET-AF)	Apixaban (ARISTOTLE)	Edoxaban (ENGAGE – TIMI-AF) 60 mg
	110 mg	150 mg			
Intracranial bleeding	↓	↓	↓	↓	↓
Major bleeding	↓	↔	↔	↓	↓
GI bleeding	↔	↑	↑	↔	↑

# Oral anticoagulation among atrial fibrillation patients with anaemia: an observational cohort study

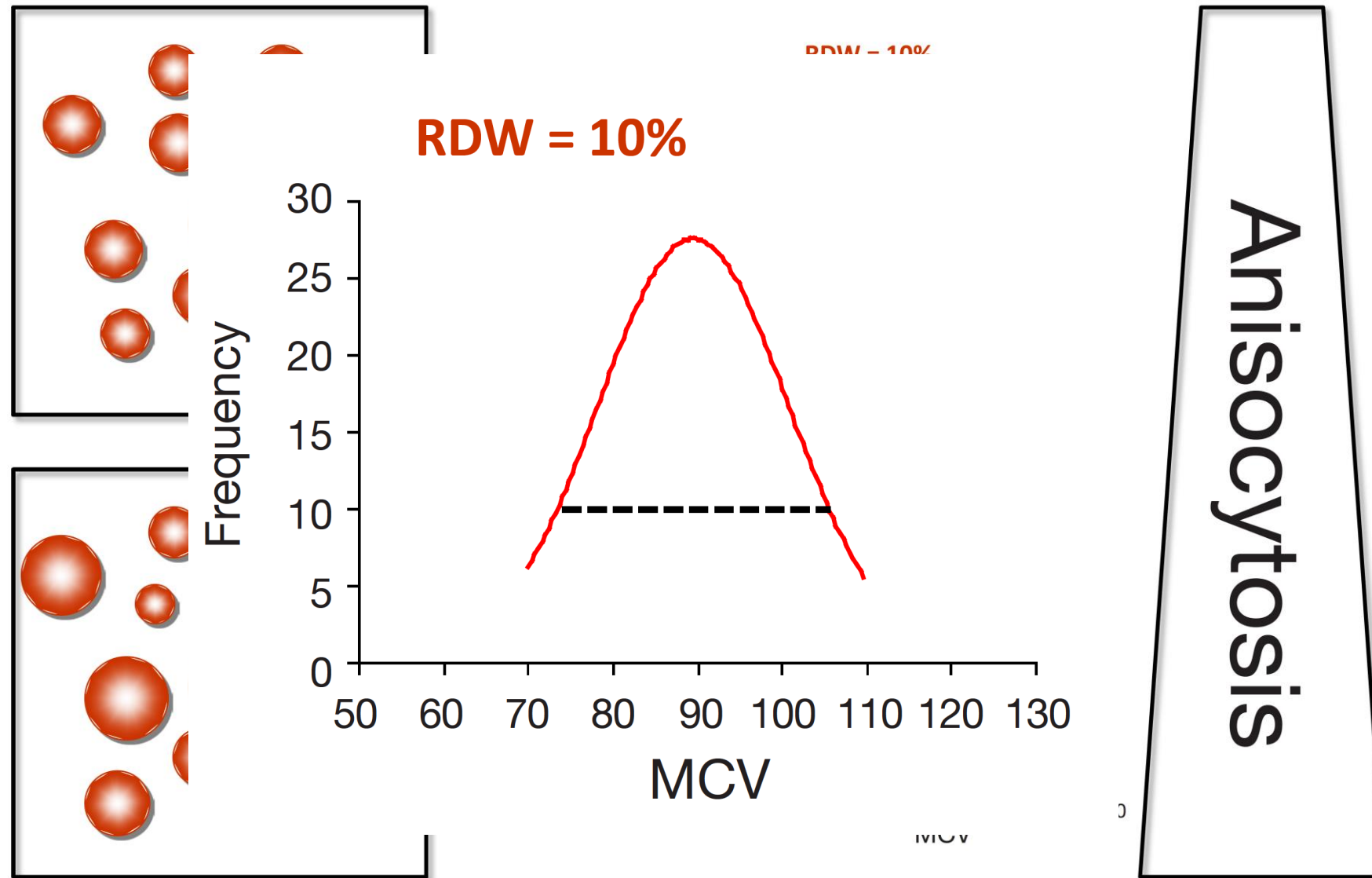


To covert mmol to mg:  $\times 1/0.6206$

# Vitamin B12 and folate metabolism and function.

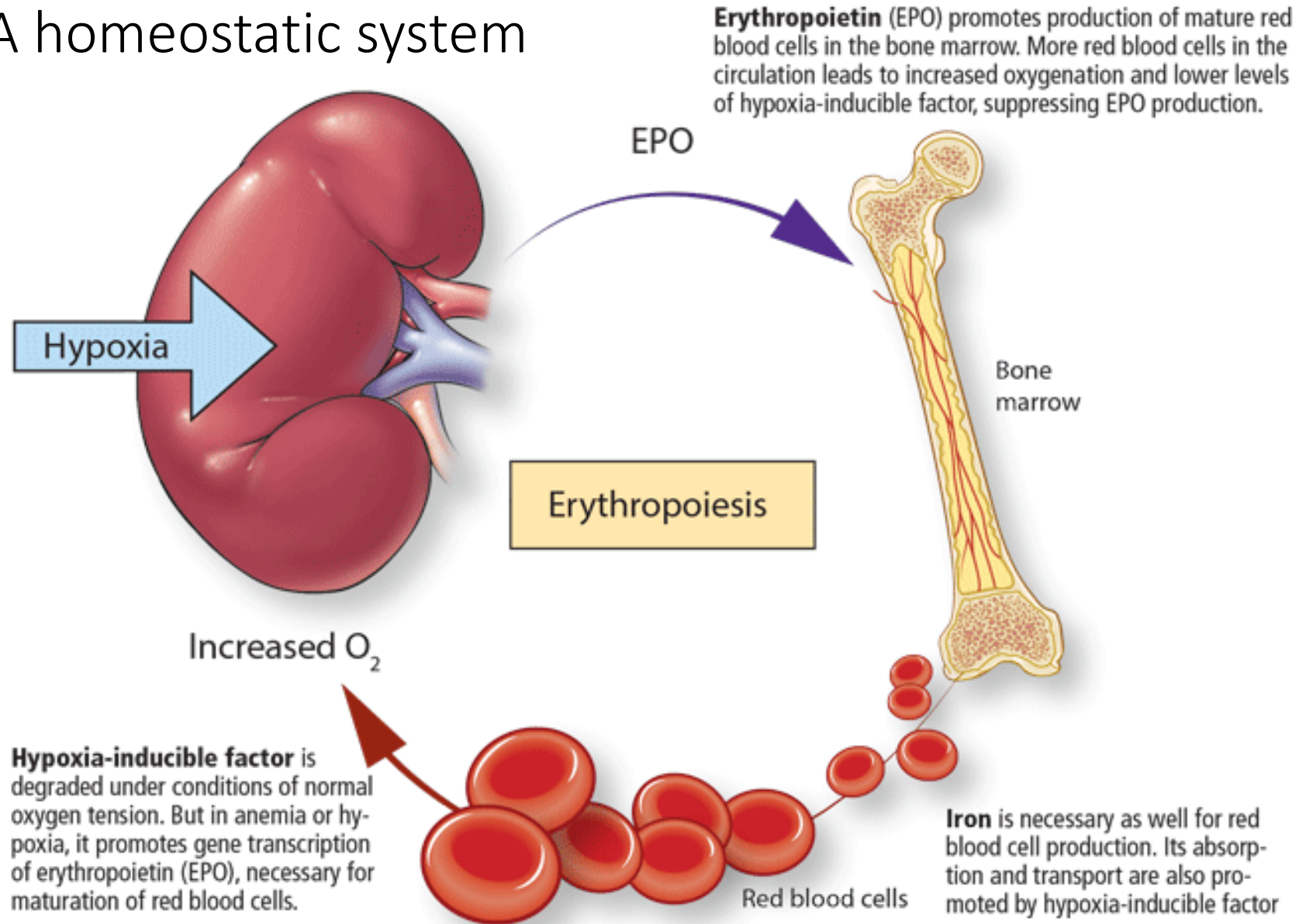


The relationship between distribution of mean corpuscular volume (MCV), anisocytosis and red blood cell distribution width (RDW).

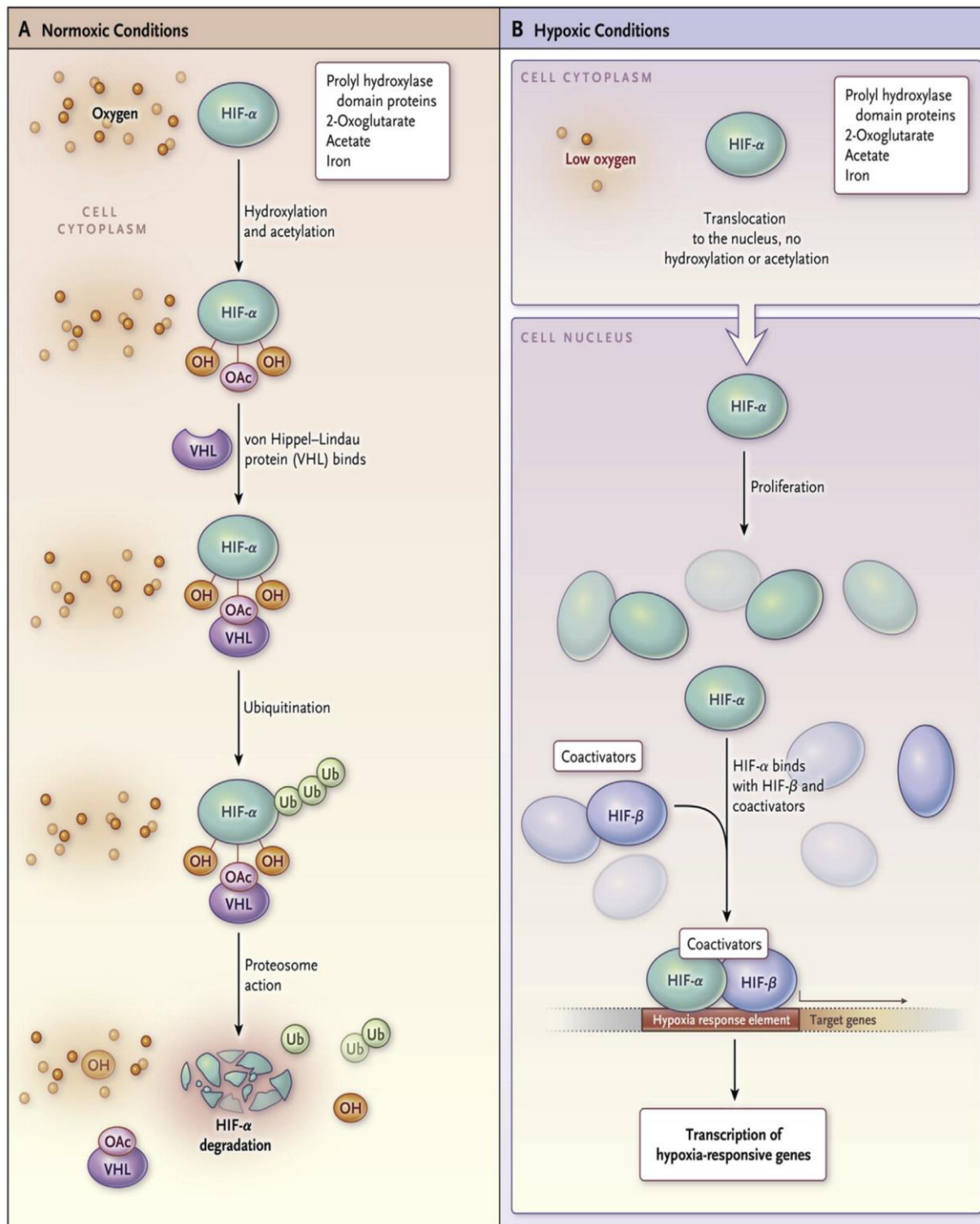




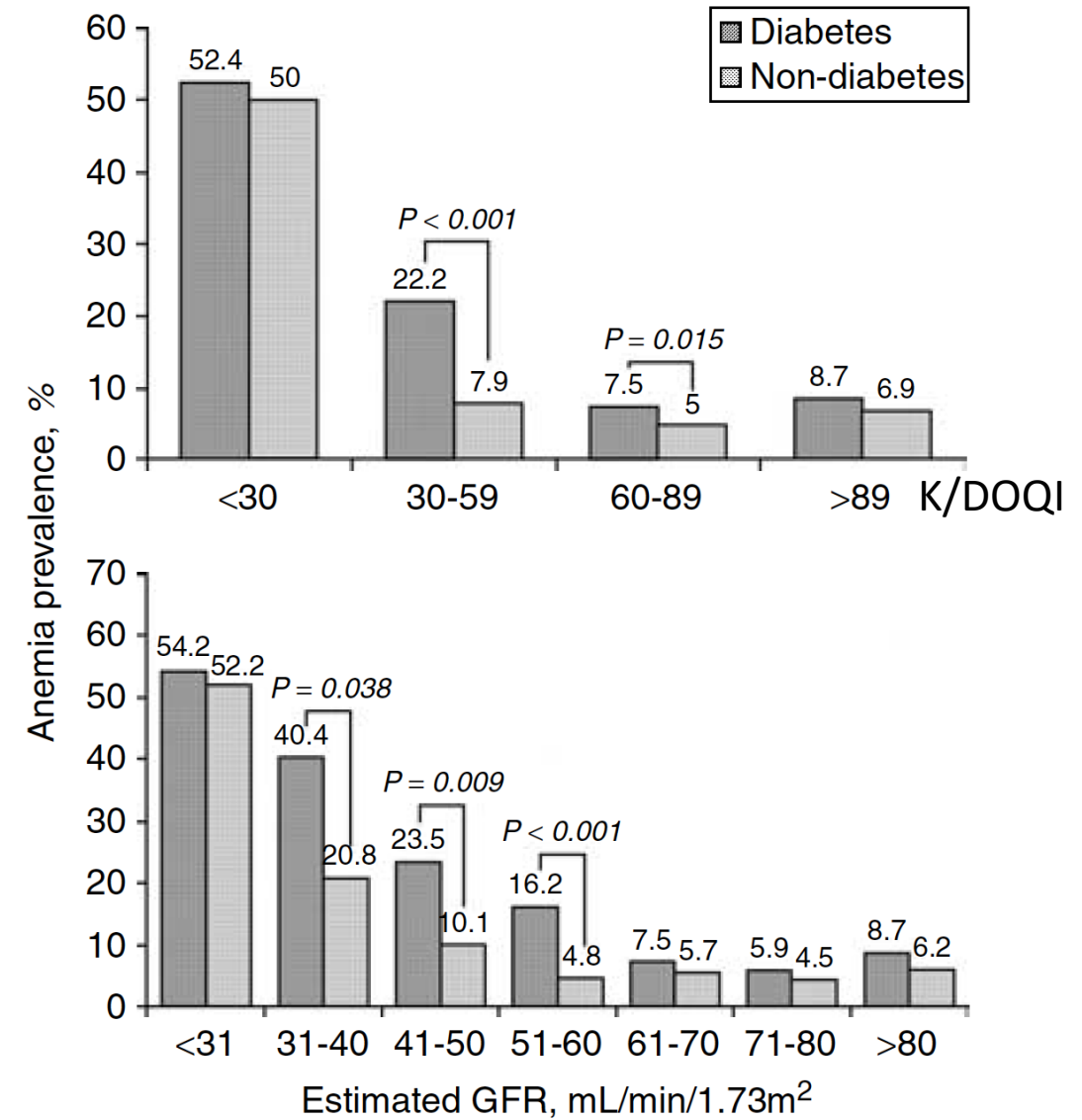
# Erythropoiesis: A homeostatic system

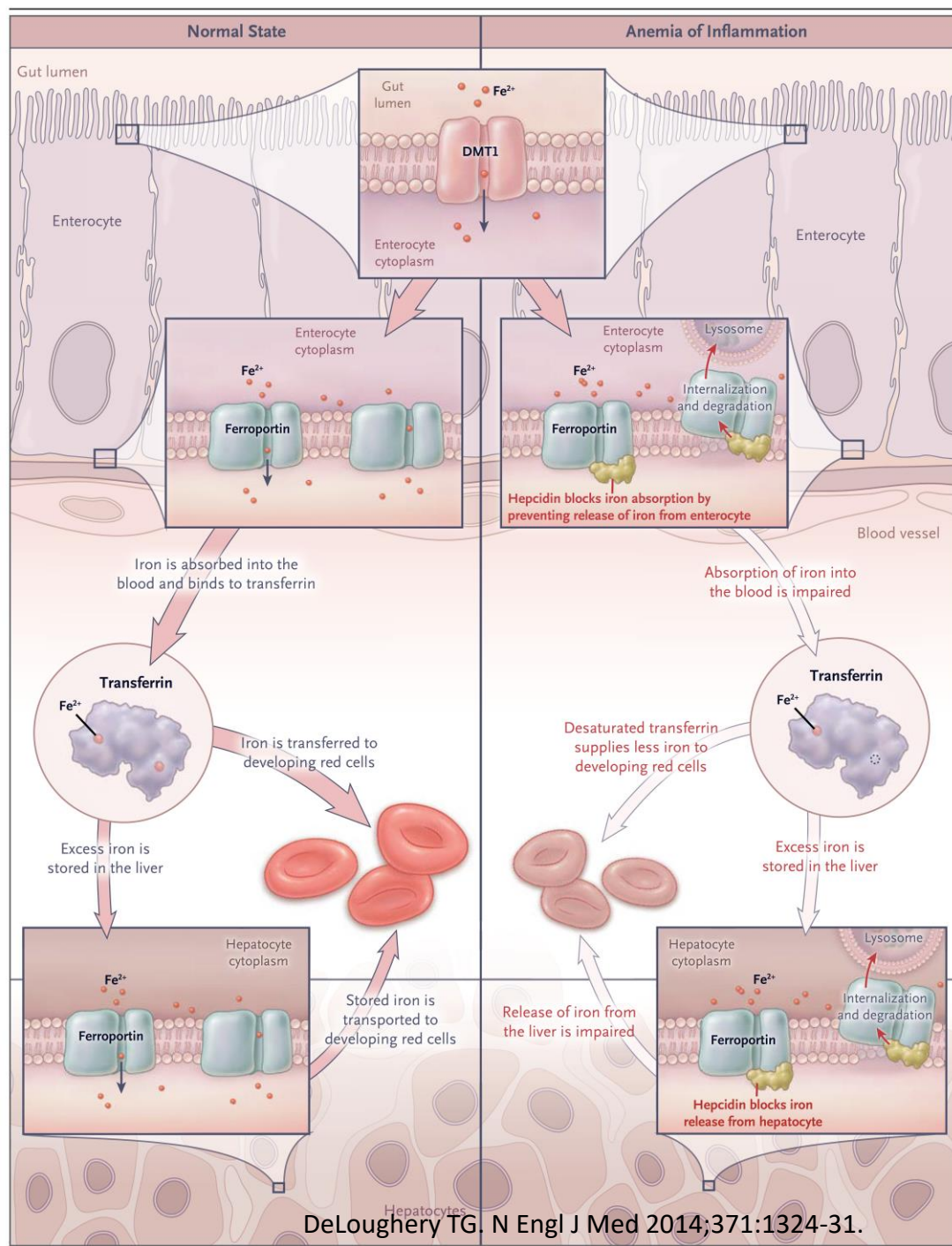




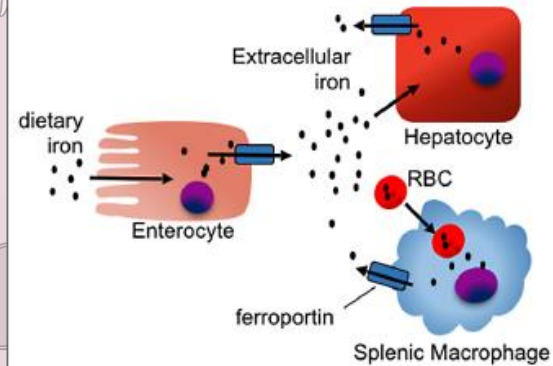


# Update on Anemia in ESRD and Earlier Stages of CKD:

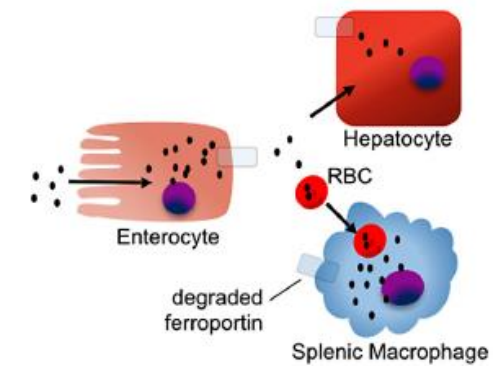




**Low hepcidin conditions:**  
Iron exported via ferroportin into extracellular space

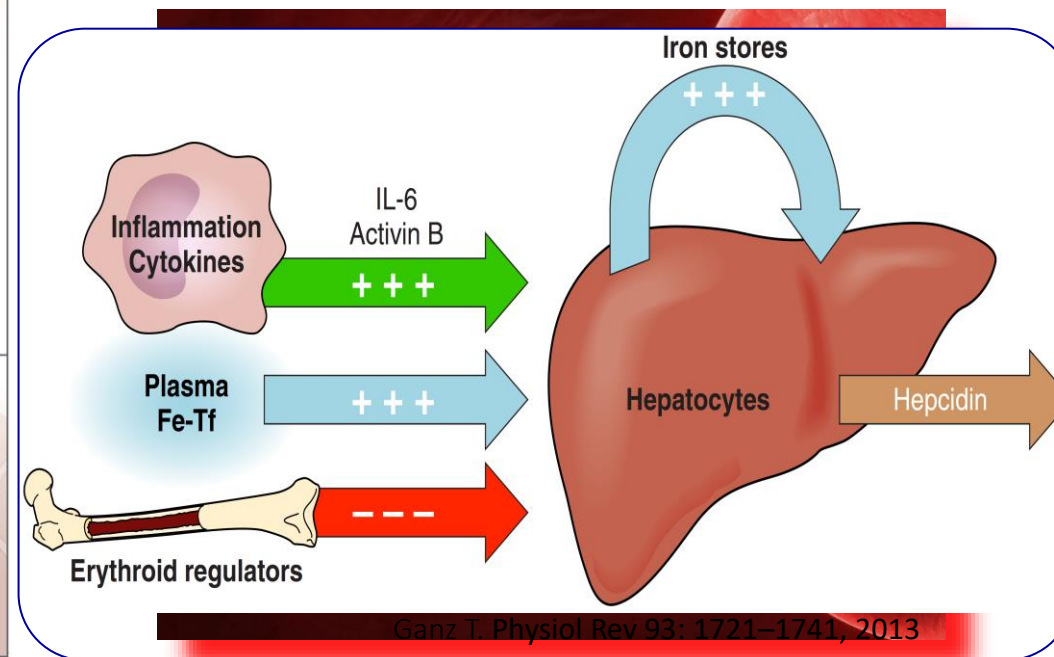


**High hepcidin conditions:**  
Ferroportin degraded, iron accumulates intracellularly



Michels K et al. PLoS Pathog. 2015 Aug; 11(8): e1004998

## Anemia of chronic disease



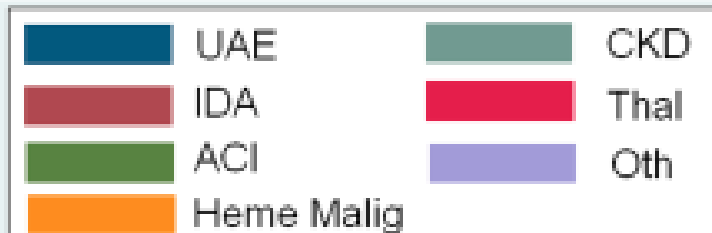
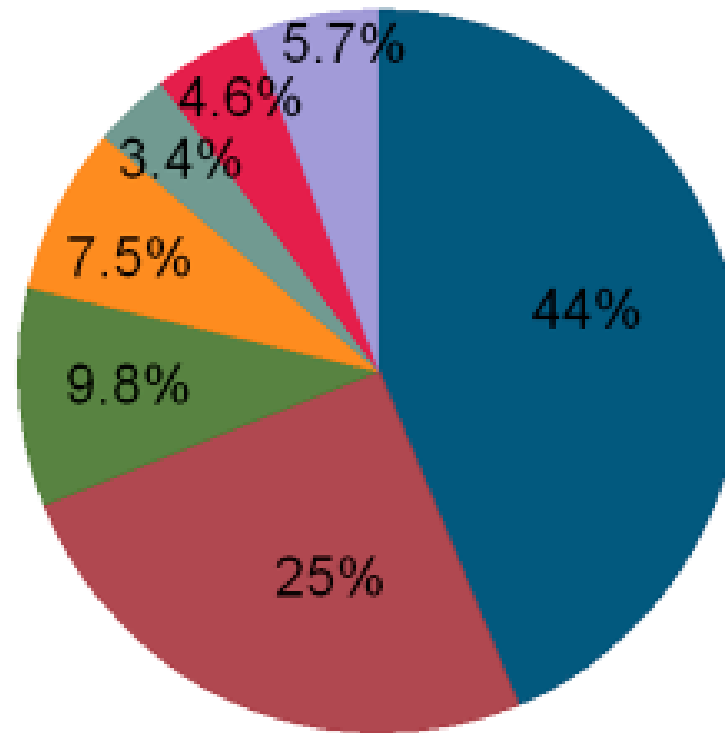
Ganz T. Physiol Rev 93: 1721-1741, 2013

# Unexplained Anemia Predominates Despite an Intensive Evaluation in a Racially Diverse Cohort of Older Adults From a Referral Anemia Clinic

Unexplained anemia of the elderly (UAE) is a real entity characterized by a **hypoproliferative normocytic anemia** that is not due to

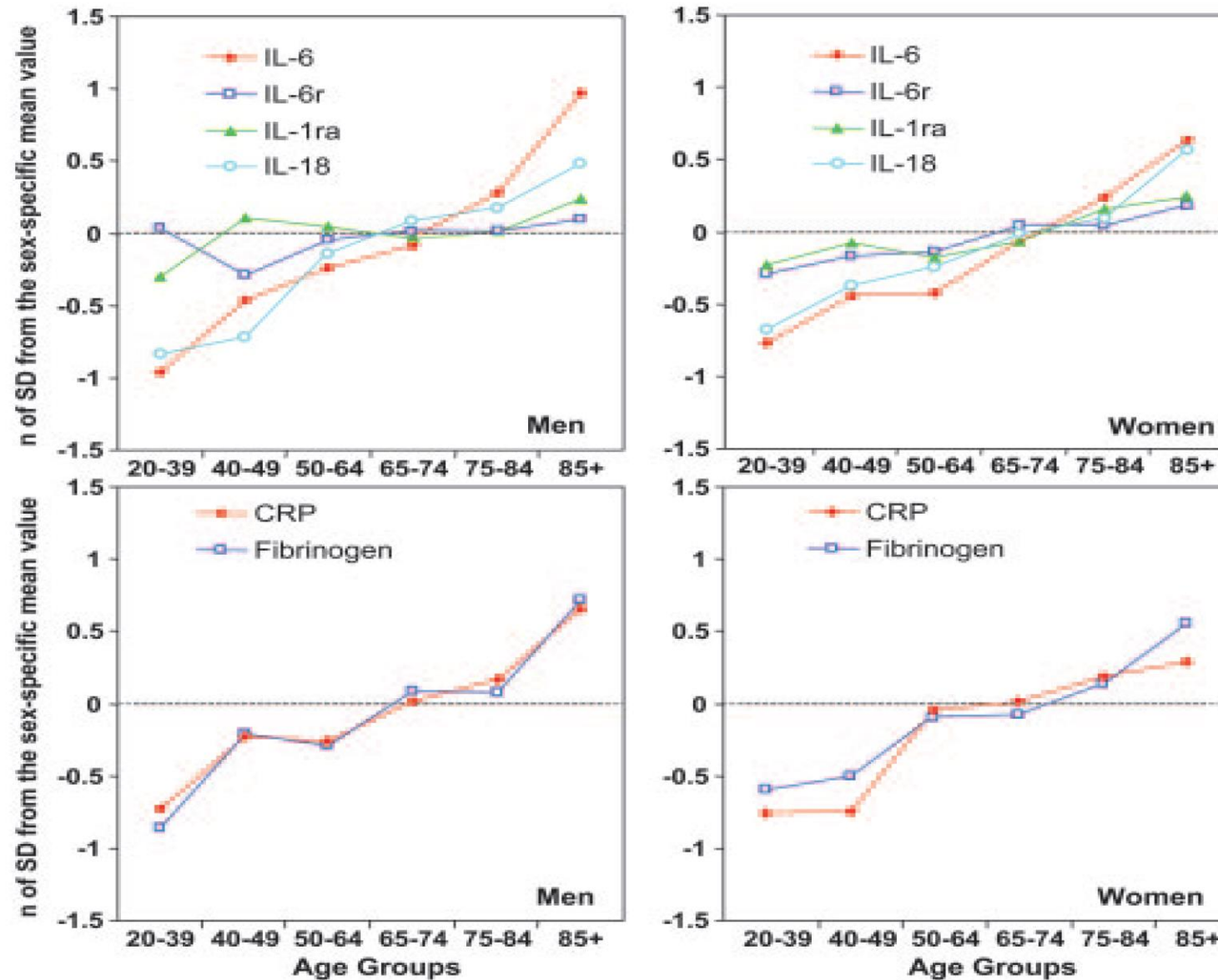
- ✧ *nutritional deficiency,*
- ✧ *CKD or*
- ✧ *inflammatory disease; and in which*
- ✧ *the erythropoietin response to anemia appears to be blunted.*

Prevalence of anemia by category

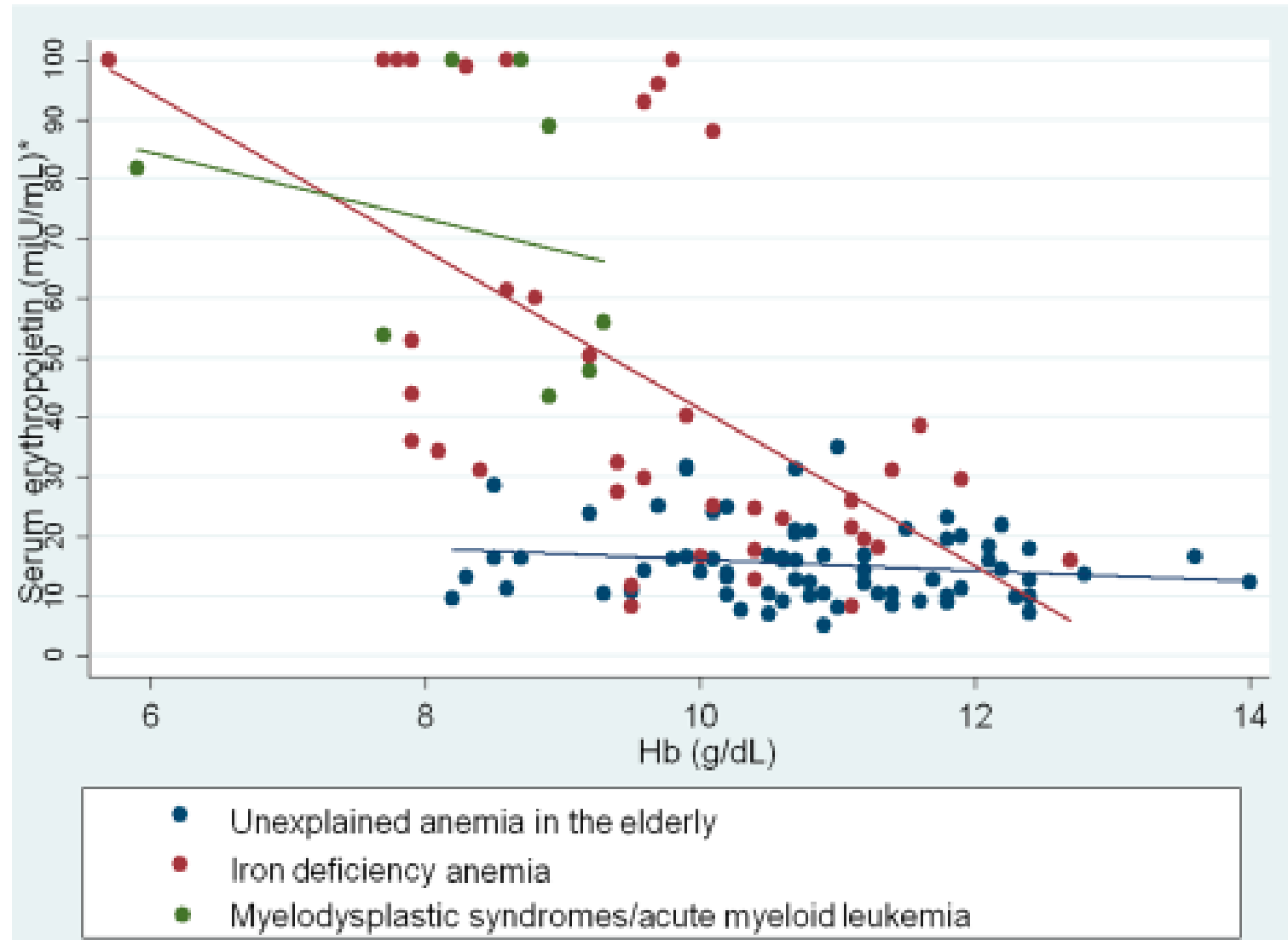




# The origins of age-related proinflammatory state



Serum erythropoietin (EPO) levels by hemoglobin concentration among iron deficiency anemia, unexplained anemia in the elderly, and myelodysplastic syndromes and acute myeloid leukemia.





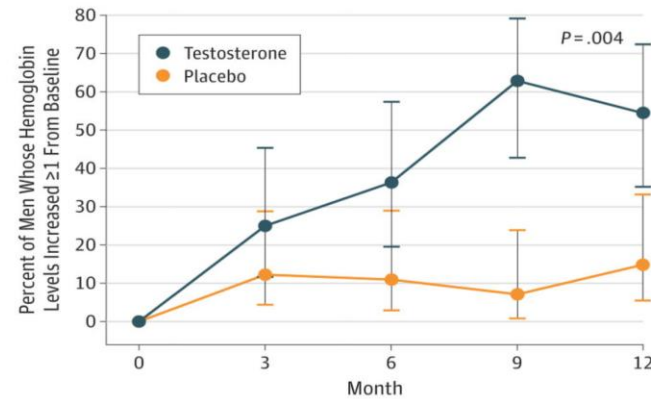
# Association of Testosterone Levels With Anemia in Older Men: A Controlled Clinical Trial

**788 elderly**  
**Testosterone  $\leq 275$  ng/dL.**

**16% with anemia**

- ✧ 6.3% myelodysplasia,
- ✧ 33.3% iron deficiency,
- ✧ 2.4% B12 deficiency
- ✧ 7.9% chronic inflammation or disease
- ✧ **49.2% unexplained anemia.**

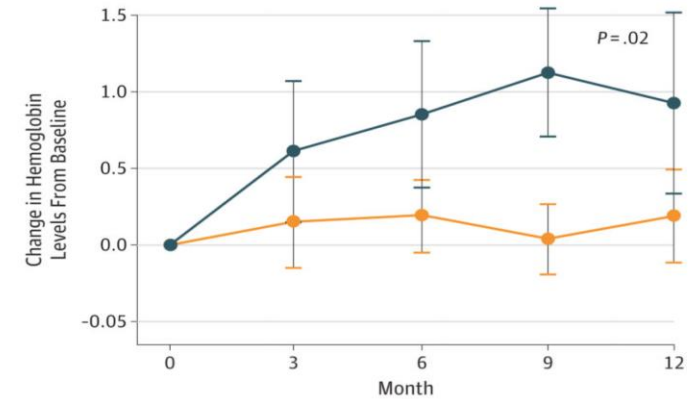
**A** Unexplained anemia at baseline



No. at risk  
Testosterone  
Placebo

27	24	22	24	24
35	32	27	28	27

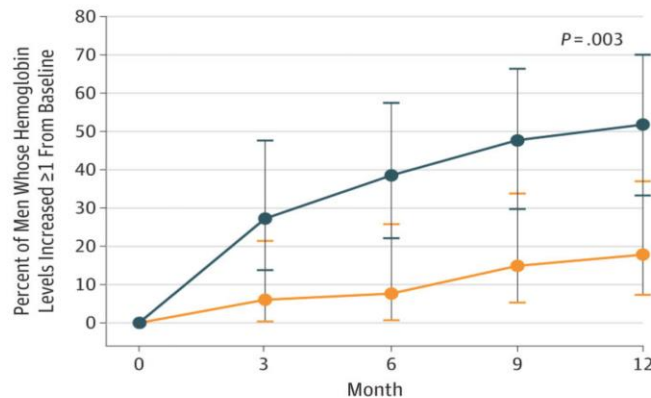
**B** Change in hemoglobin levels for unexplained anemia from baseline



No. at risk  
Testosterone  
Placebo

27	24	22	24	24
35	32	27	28	27

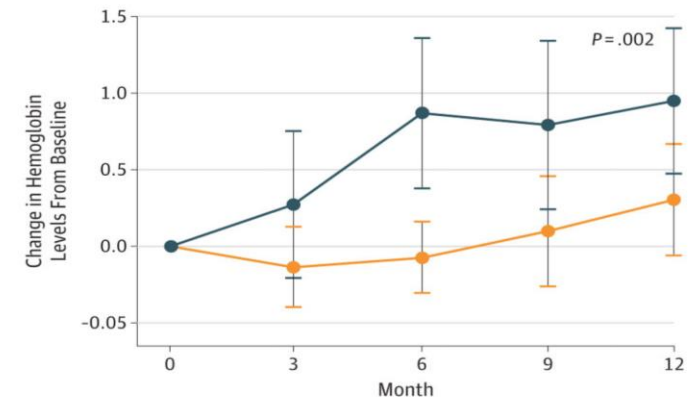
**C** Anemia of known cause at baseline



No. at risk  
Testosterone  
Placebo

29	25	26	25	25
35	31	25	26	27

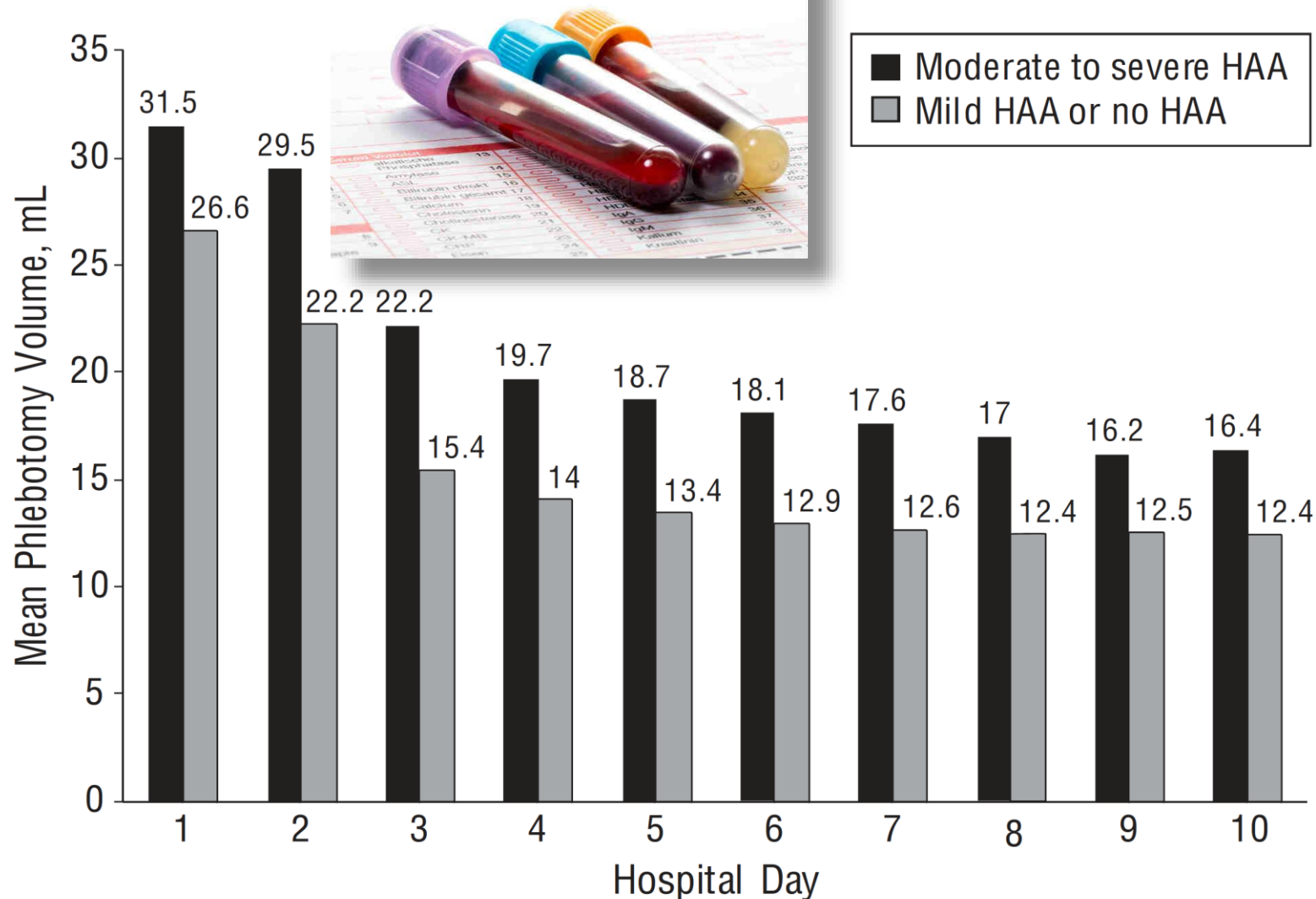
**D** Change in hemoglobin levels for anemia of known cause from baseline



No. at risk  
Testosterone  
Placebo

29	25	26	25	25
35	31	25	26	27

# Diagnostic Blood Loss From Phlebotomy and Hospital-Acquired Anemia During **Acute Myocardial Infarction**

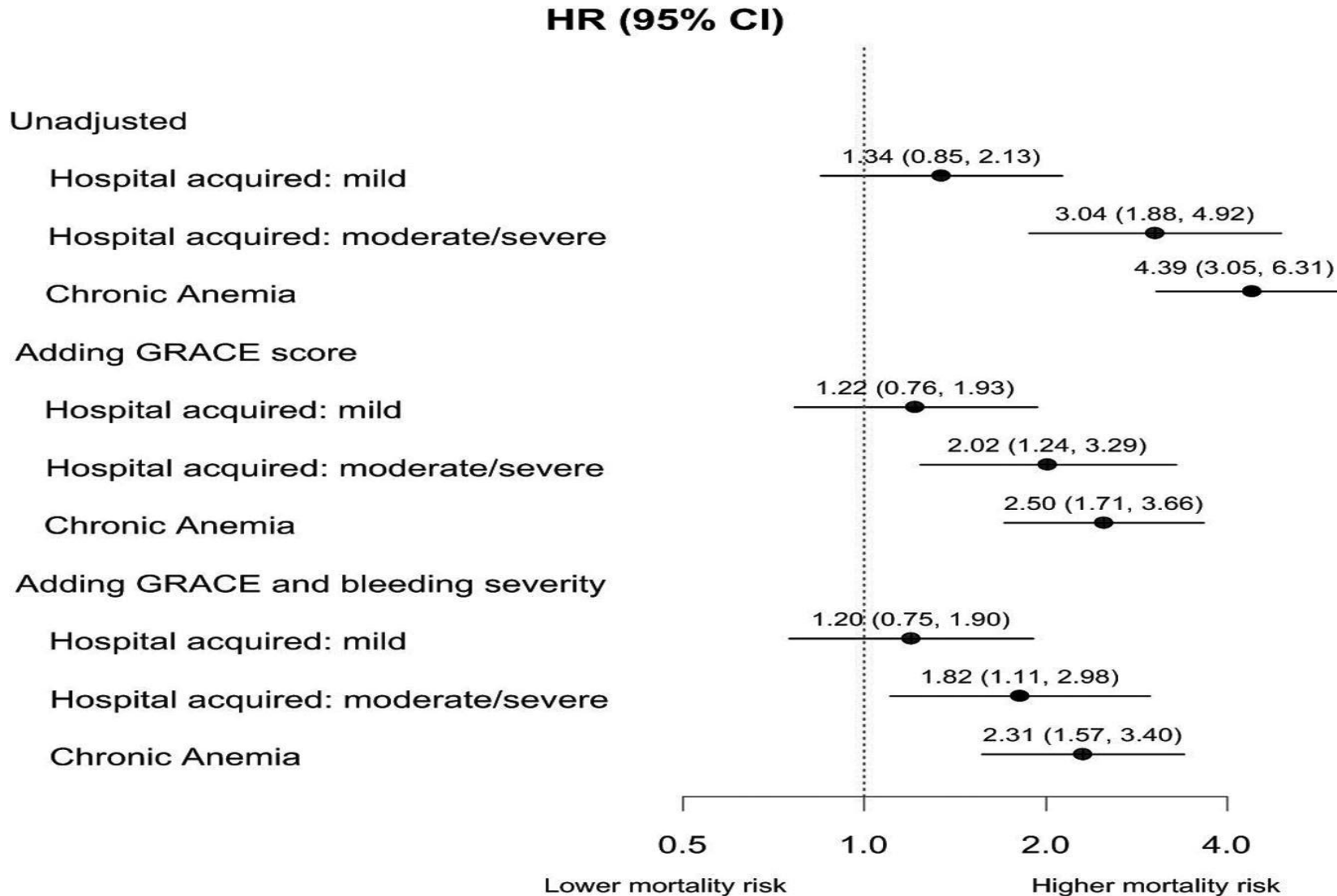


Moderate to severe HAA developed in 20% of patients.

The mean phlebotomy volume was higher in patients with HAA ( $173.8 \pm 139.3$  mL vs those without HAA ( $83.5 \pm 52.0$  mL;  $P.001$ ).

For every 50 mL of blood drawn, the risk of moderate to severe HAA increased by 18%,

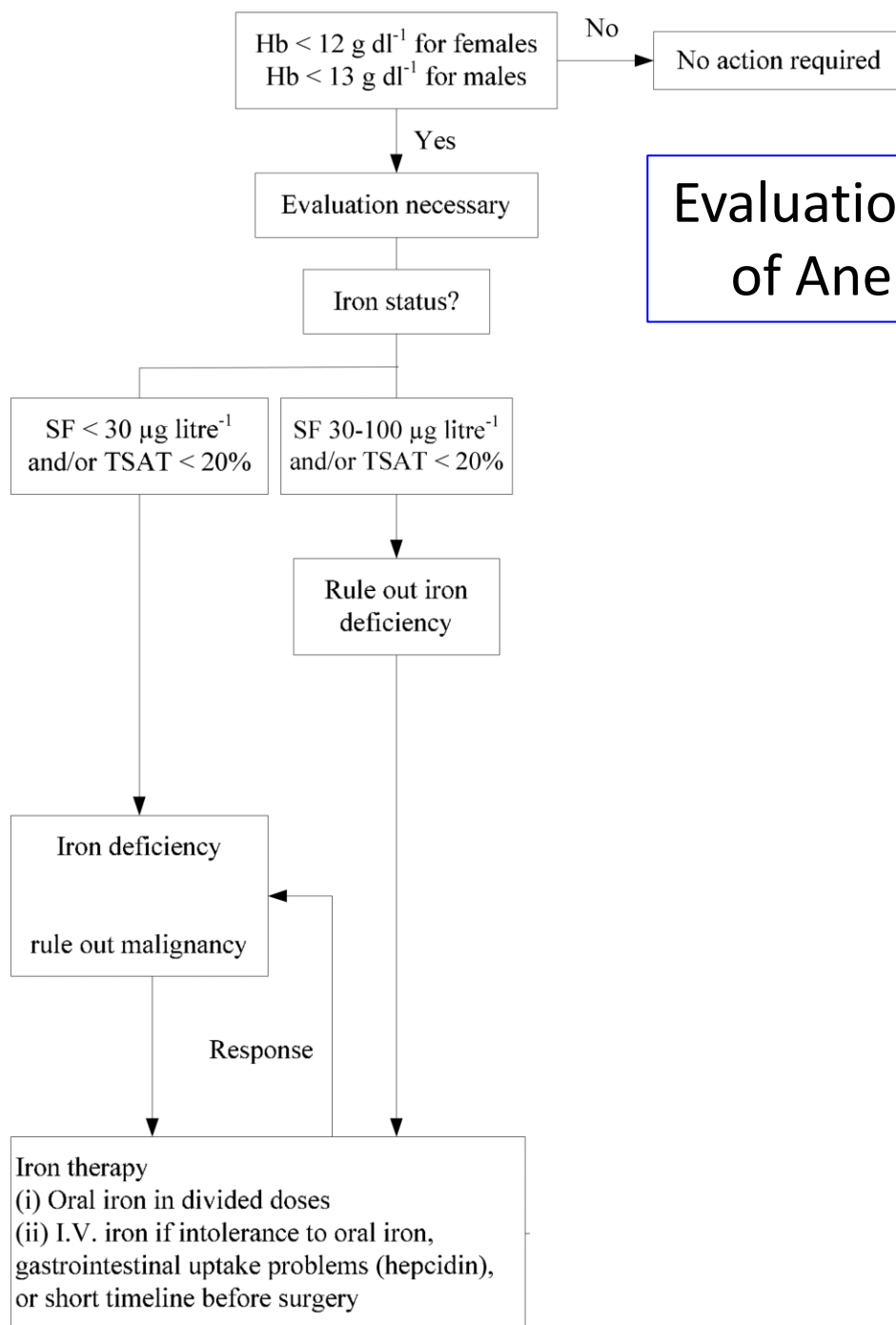
# Twelve-month mortality among patients with mild Hospital-Acquired Anemia (HAA), moderate-severe HAA, and chronic anemia and AMI.



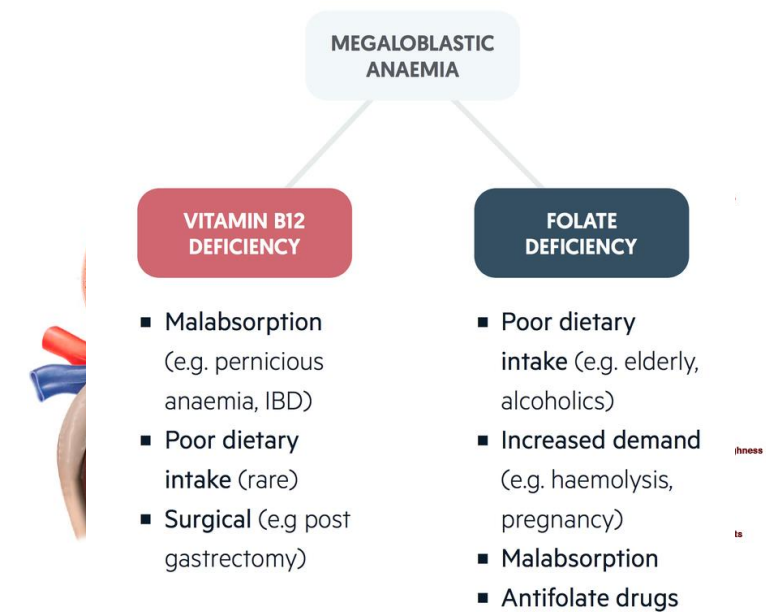
# Le anemie nel paziente anziano



4. Come gestirla?



## Evaluation and Management of Anemia in the Elderly





# Le anemie nel paziente anziano



4. Come gestirla?

4.1 Terapia mirata e.... follow-up!

# Le anemie nel paziente anziano

- E' frequente
  - ✧ ...pensiamoci

