



Anemia in the Elderly

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National Anemia Action Council

www.anemia.org

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NAAC Mission



The National Anemia Action Council, Inc. (NAAC) is dedicated to raising the awareness of health care professionals and the public regarding the prevalence, symptoms, consequences, and treatment options of anemia.

NAAC is a 501(c)(3) nonprofit organization

NAAC's Online Resources for Medical Professionals



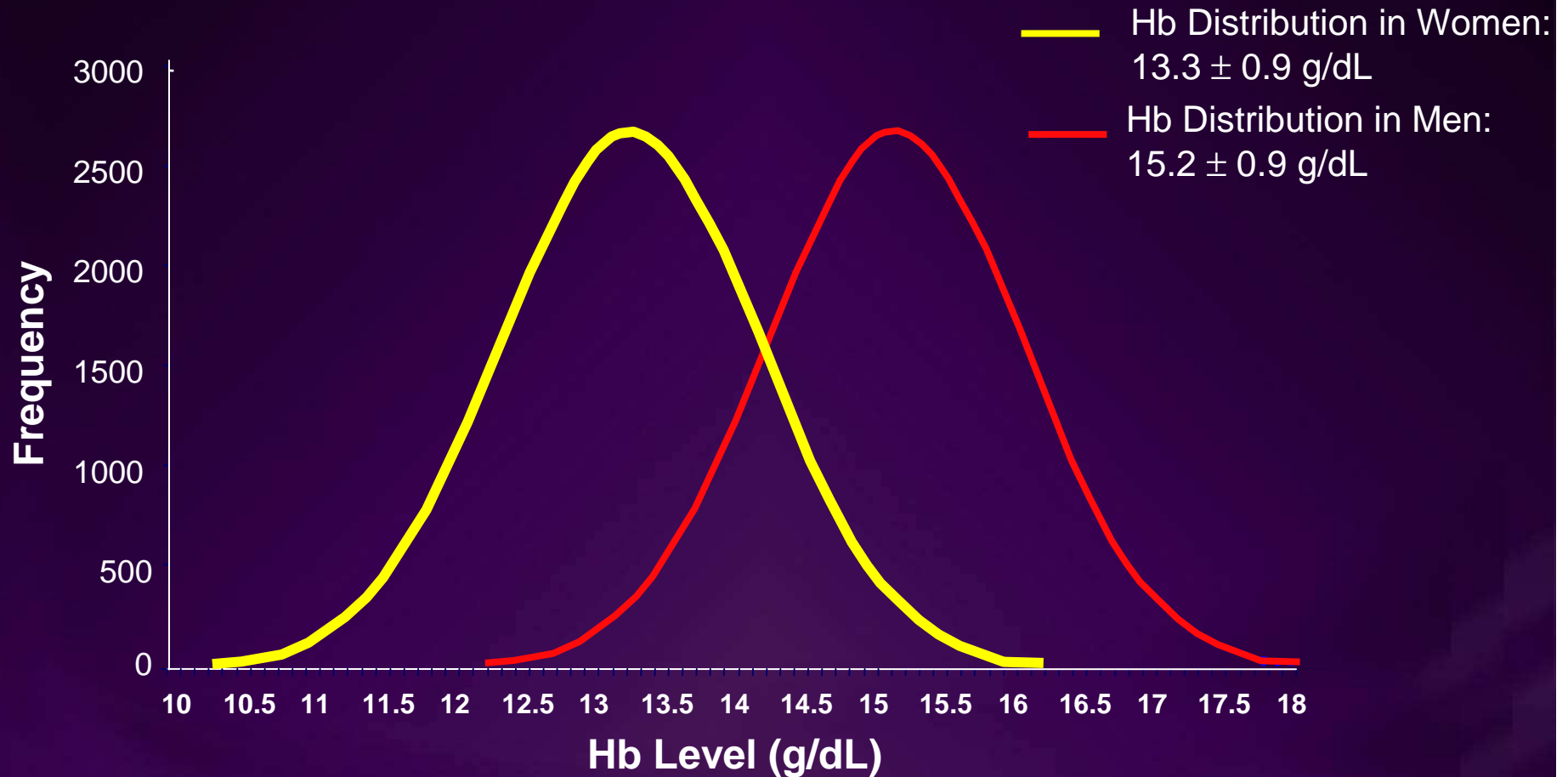
- Research Reviews - Recent clinical trials reviewed
- Ask the Expert - Your anemia questions answered
- Monograph - In-office handbook on anemia
- Feature Articles - Anemia related news and research
- Anemia Alert - Free monthly e-newsletter
- Slide Sets - Educational presentations about anemia
- We have materials for your patients too!

Key Points



- Anemia in the elderly is more commonly observed than appreciated and is often multifactorial
- Failure to evaluate anemia in the elderly could lead to delayed diagnosis of potentially treatable conditions
- Untreated geriatric anemia is associated with greater risk of death, greater risk of certain comorbidities, and impaired functional status
- Treatment of anemia in the elderly can improve healthcare outcomes

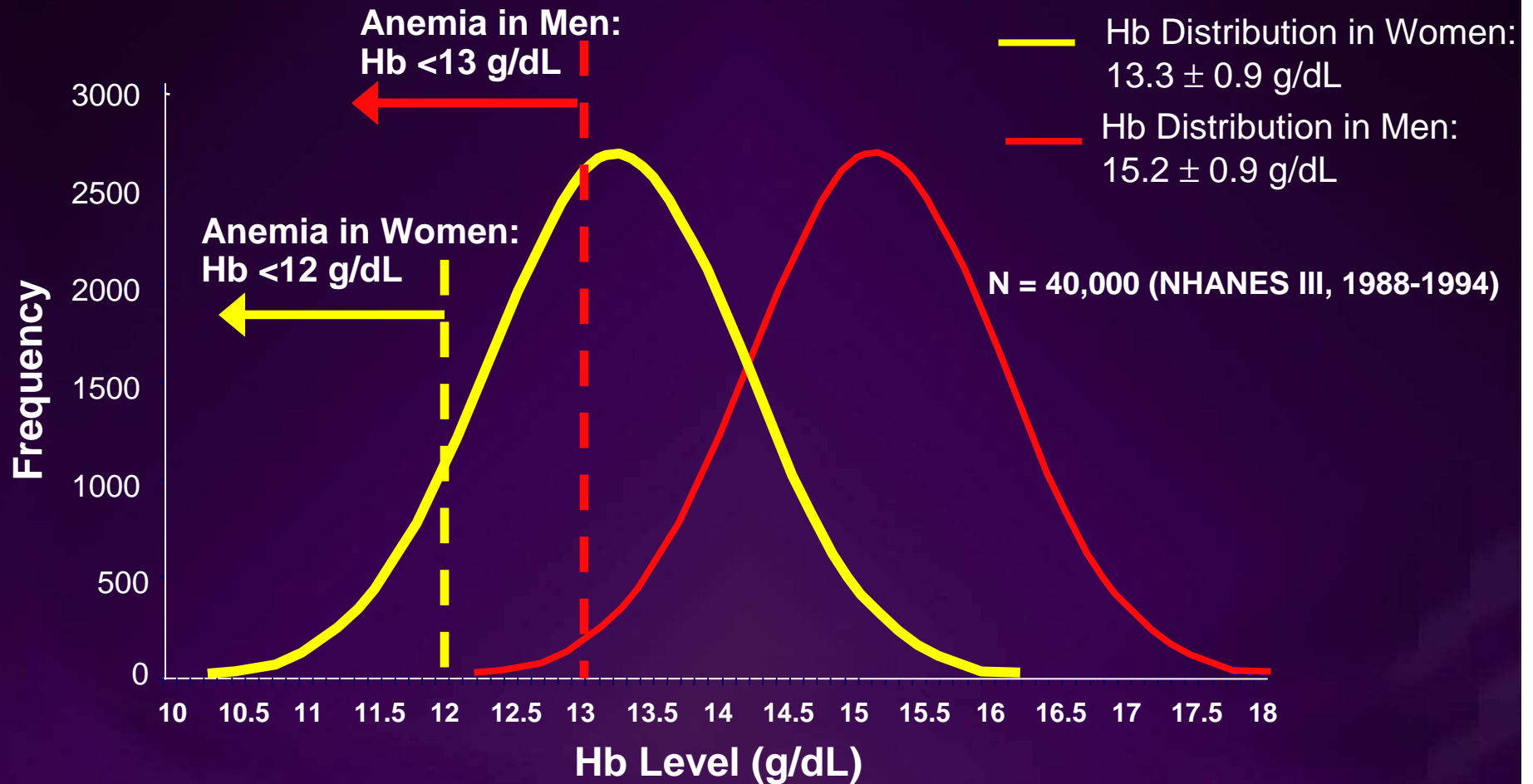
Hemoglobin (Hb) Distribution in the General Population



N = 40,000 (NHANES III, 1988-1994)

Dallman PR, et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74.

WHO Definition of Anemia vs. Hb Distribution in General Population



World Health Organization. Geneva, Switzerland; 2001.

Dallman PR, et al. In: *Iron Nutrition in Health and Disease*. London, UK: John Libbey & Co; 1996:65-74.

Laboratory Reference Ranges



Parameter	Male	Female
Hb (g/dL)	14.0 – 17.4	12.3 – 15.3
Hct (%)	41.5 – 50.4	36.0 – 45.0
RBC count ($10^6/\mu\text{L}$)	4.5 – 5.9	4.5 – 5.1
Reticulocyte count (% of RBC count)	0.5 – 2.5	
Mean corpuscular volume (fL)	80 – 96	
Mean corpuscular Hb (MCH) (pg)	27.5 – 33.2	
MCH concentration (g/dL)	33.4 – 35.5	

Hb = hemoglobin; Hct = hematocrit; RBC = red blood cell

Perkins S. In: Lee G, et al, eds. *Wintrobe's Clinical Hematology*. Vol 2. 10th ed. Baltimore, Md: Lippincott, Williams & Wilkins; 1998:2738.

Anemia Signs and Symptoms



Central nervous system

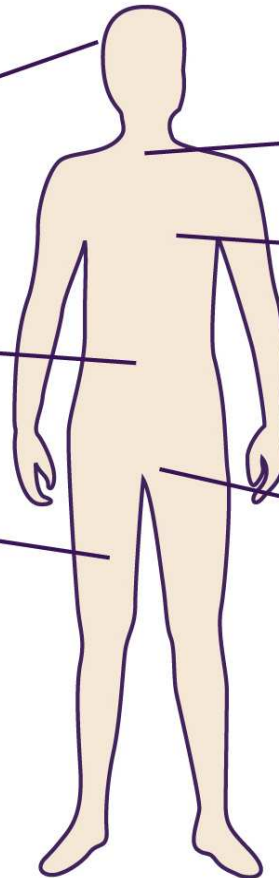
- Fatigue
- Depression
- Impaired cognitive function

Gastrointestinal system

- Anorexia
- Nausea

Vascular system

- Low skin temperature
- Pallor of skin, mucous membranes, and conjunctivae



Immune system

- Impaired T-cell and macrophage function

Cardiorespiratory system

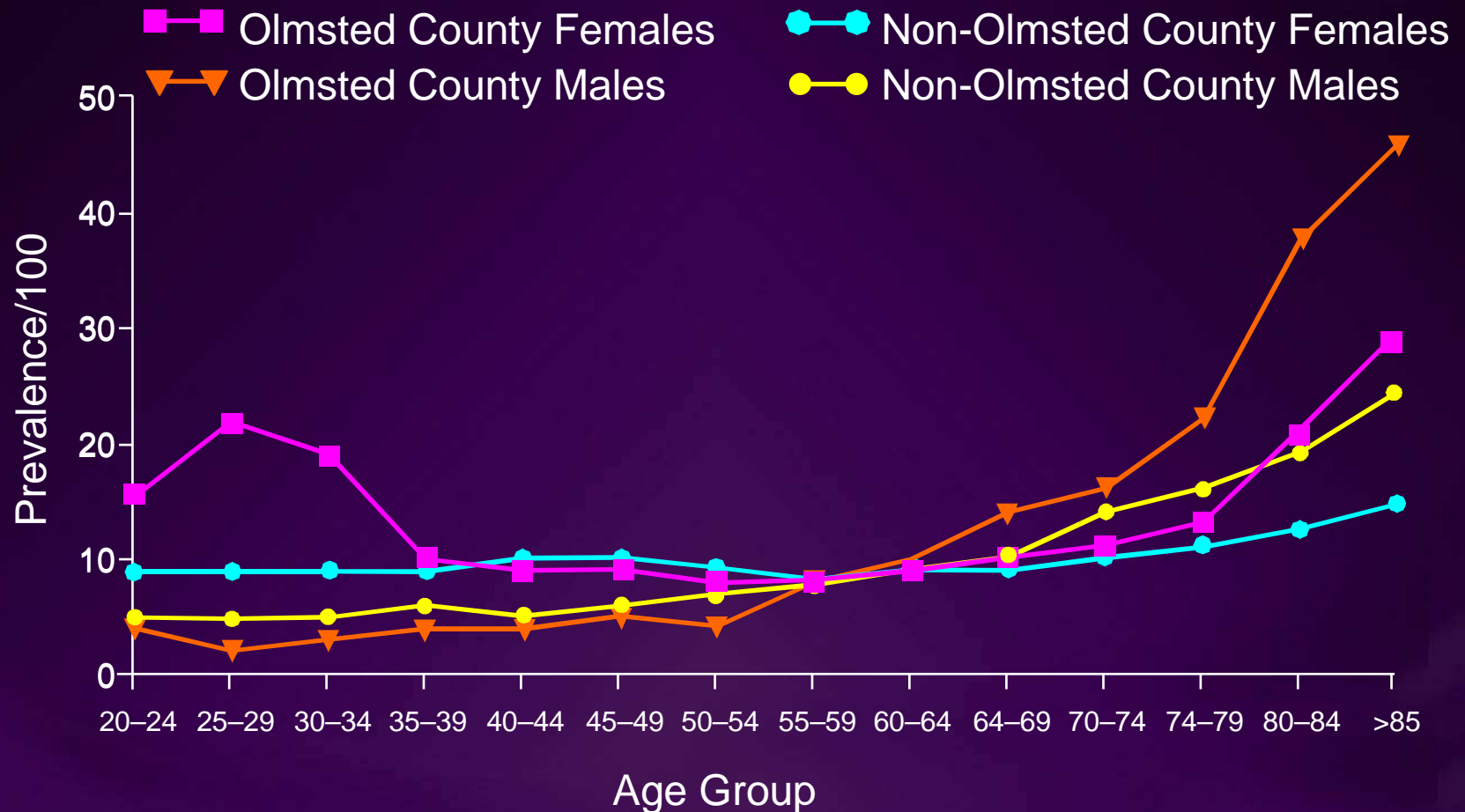
- Exertional dyspnea
- Tachycardia, palpitations
- Cardiac enlargement, hypertrophy
- Increased pulse pressure, systolic ejection murmur
- Risk of cardiac failure

Genital Tract

- Menstrual problems
- Loss of libido

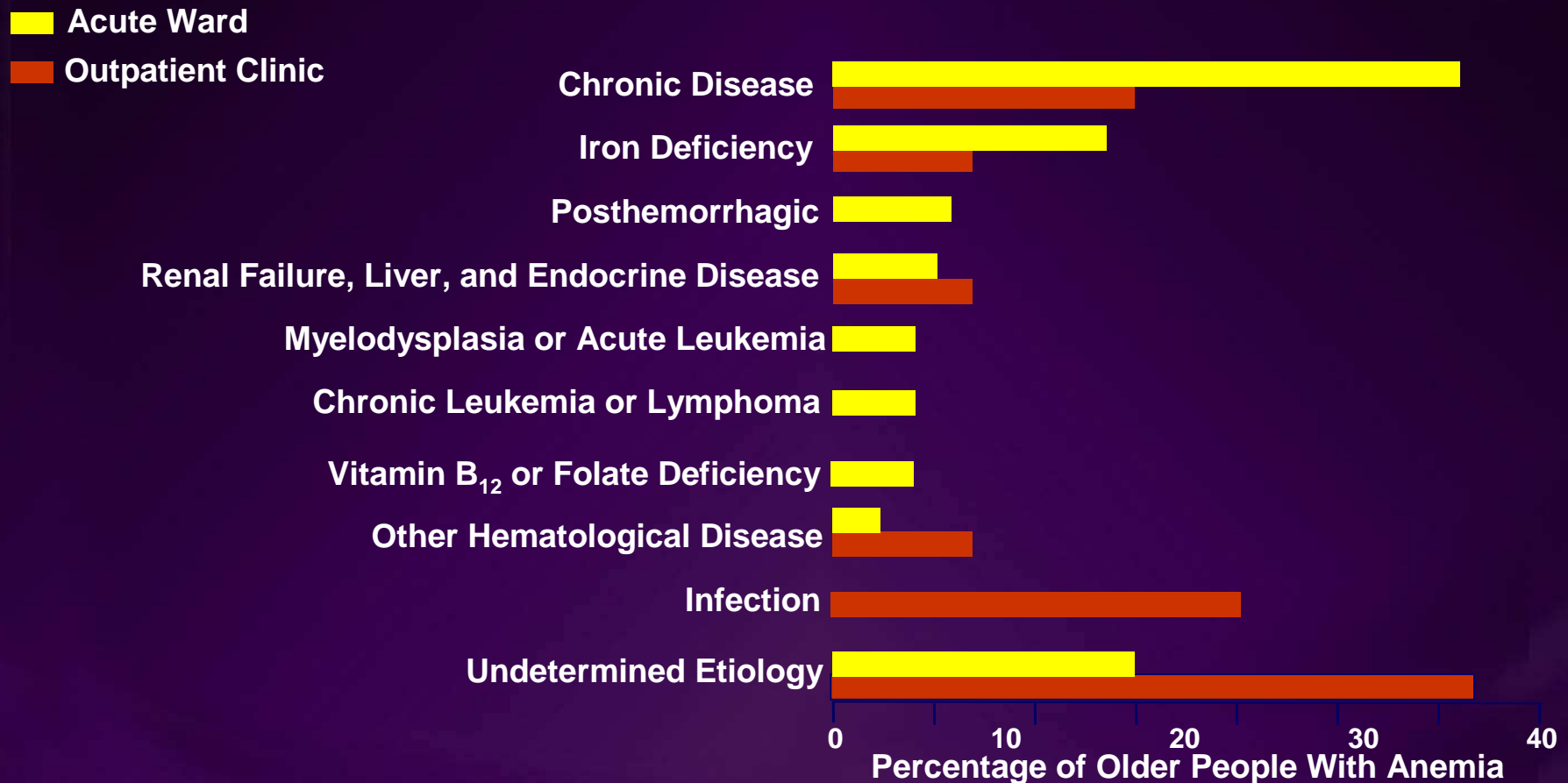
Adapted from Ludwig H, et al. *Semin Oncol.* 2001;28(suppl 8):7-14.

Age-Specific Prevalence of Anemia



Anía B, et al. *Mayo Clin Proc.* 1994;69:730-735.

Etiology of Anemia in the Elderly



Balducci L. *J Am Geriatr Soc*, 2003;51(suppl):S2-S9.

Joosten E, et al. *Gerontology*. 1992;38:111-117.

Anía B, et al. *J Am Geriatr Soc*. 1997;45:825-831.

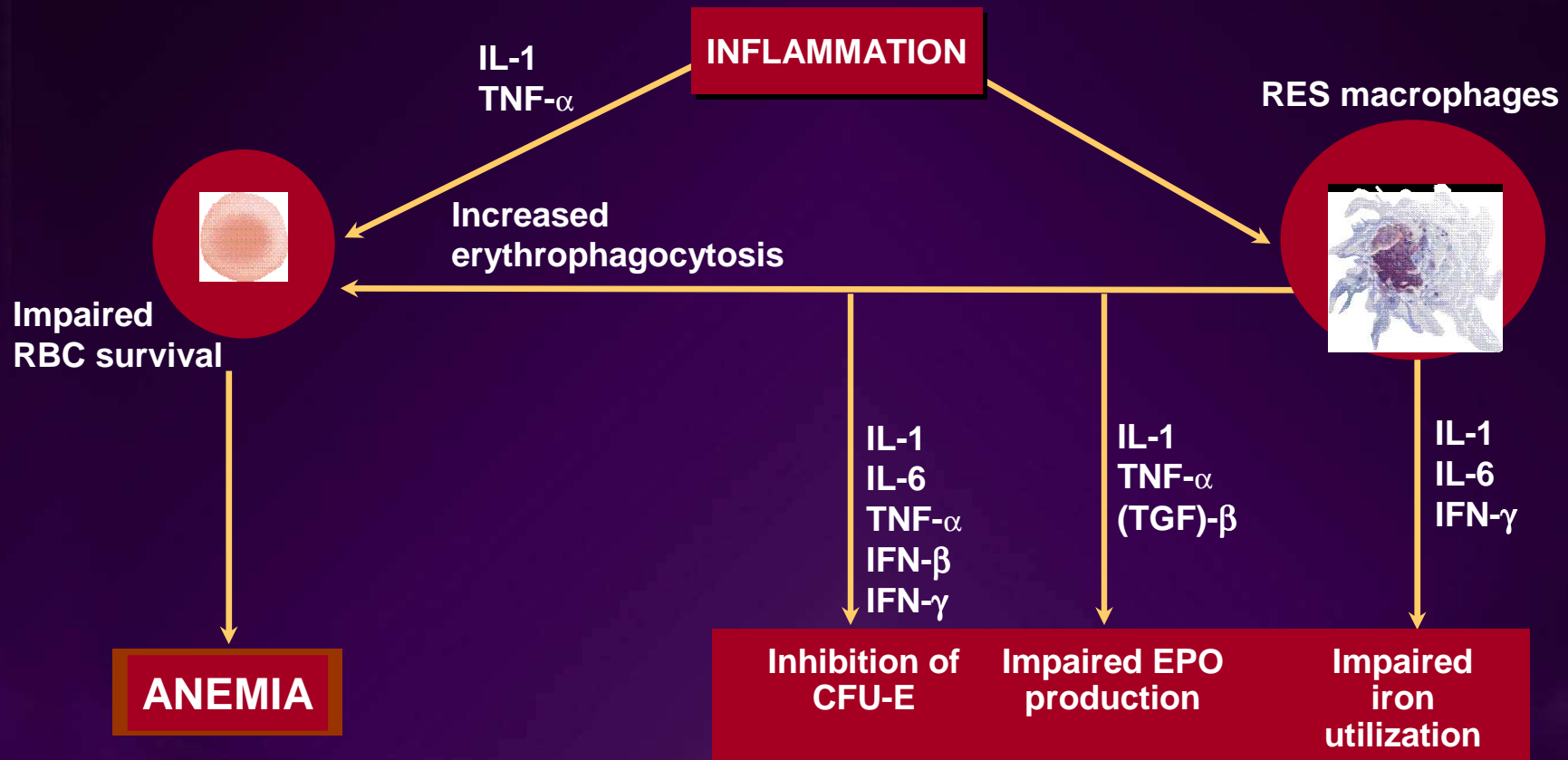
Anemia of Chronic Disease (ACD)



- Can be caused by cancer, infection, or chronic inflammatory diseases
- Severity of anemia correlates with severity of underlying disease
- Often coexists with other causes of anemia, especially iron deficiency

Balducci L. *J Am Geriatr Soc.* 2003;51:S2-S9.

Etiology of the Anemia of Chronic Disease



Jurado RI. *Clin Infect Dis*. 1997;35:888-895.

Means RT. *Int J Hematol*. 1999;70:7-12.

Weiss G. *Kidney Int*. 1999;55(suppl):S12-S17.

Iron Deficiency Anemia (IDA)



- Common causes: chronic blood loss, gastrointestinal ulcers, colon cancer, diverticula, or angiodysplasia¹⁻³
- More likely to coexist with ACD in older patients than in younger ones
- Sign of chronic blood loss until proven otherwise⁴

1. Smith DL. *Am Fam Physician*. 2000;62:1565-1572.

2. Chiari MM, et al. *J Am Geriatr Soc*. 1995;43:767-771.

3. Murphy PT, et al.. *Drugs Aging*. 1994;4:113-127.

4. Balducci L. *J Am Geriatr Soc*. 2003;51:S2-S9.

Distinguishing ACD From IDA



Blood test	Result in:		
	ACD	IDA	ACD + IDA
Iron	↓	↓	↓
Iron-binding capacity (IBC)	↓	↑	LN or ↓
% saturation of IBC	↓ or N	↓	↓
Ferritin	↑	↓	↓ or N
Soluble transferrin receptor	N	↑	↑

LN = low normal, N = normal

Smith DL. *Am Fam Physician*. 2000;62:1565-1572.

Murphy PT, et al.. *Drugs Aging*. 1994;4:113-127.

Abramson SD, et al. *Am Fam Physician*. 1999;59:851-858.

Balducci L. *J Am Geriatr Soc*. 2003;51:S2-S9.

Carmel R. *Blood Rev*. 2001;15:9-18.

Vitamin B₁₂ Deficiency



- Most common causes:
 - Reduced intestinal absorption (gastric achylia, pernicious anemia, gastrectomy)
 - Small-bowel disease, including bacterial overgrowth
 - Vegan diet: inadequate nutrient intake
- 60% of affected patients are anemic
- Neurological symptoms may occur before anemia
 - If no apparent cause for disorders such as cognitive dysfunction or peripheral neuropathy, vitamin B₁₂ deficiency should be considered

Smith D. *Am Fam Physician*. 2000;62:1565-1572.

Carmel R. *Blood Rev*. 2001;15:9-18.

Balducci L. *J Am Geriatr Soc*. 2003;51(suppl):S2-S9.

Folate Deficiency



- Deficiency usually due to inadequate dietary intake
- Other causes:
 - Excess use (hematopoiesis, marrow filtration, etc.)
 - Increased loss (liver disease, dialysis, CHF)
 - Malabsorption (celiac diseases)
 - Drugs (alcohol, anticonvulsants)

Balducci L. *J Am Geriatr Soc.* 2003;51(suppl):S2-S9.

Smith D. *Am Fam Physician.* 2000;62:1565-1572.

Myelodysplastic Syndromes (MDS)



- Acquired clonal hematopoietic disorders
- Characterized by:
 - Anemia and other cytopenias
 - Impaired blood cell production (WBC, RBC, platelets)
 - Propensity to develop leukemia (~19% of patients)
- Caused by hematopoietic stress impairing DNA repair
 - Risk factors include aging, chemotherapy, radiation, benzene

Rothstein G. *J Am Geriatr Soc.* 2003;51(suppl):S22-S26.

Idiopathic Anemia



- Studied nursing home population yields 45% idiopathic anemia
- Possible explanations
 - Inadequate evaluation
 - Anemia of aging

Artz AS, Fergusson D, Drinka P, et al. *J Am Geriatr Soc.* 2004;52(3):423-427
Balducci L. *J Am Geriatr Soc.* 2003;51(suppl):S2-S9.
Joosten E, et al. *Gerontology.* 1992;38:111-117.

Anía B, et al. *J Am Geriatr Soc.* 1997;45:825-831.
Carmel R. *Blood Rev.* 2001;15:9-18.
Rothstein G. *Blood.* 1993;82:2601-2604.

Is There an “Anemia of Aging”?



- In all previous series of geriatric patients with anemia, there is a component that defies classification
- Question whether this component reflects hematopoietic changes that take place concurrently with “normal aging”
 - Renal changes with aging
 - Blunted production of erythropoietin (EPO)
 - Dysregulated cytokine production
 - IL-6 changes with aging

Kario K, et al. *Am J Hematol.* 1992;41:252-257.

Carpenter MA, et al. *Eur J Haematol.* 1992;49:119-121.

Joosten E, et al. *J Am Geriatr Soc.* 1993;41:1301-1304.

Nafziger J, et al. *Am J Hematol.* 1993;43:172-176.

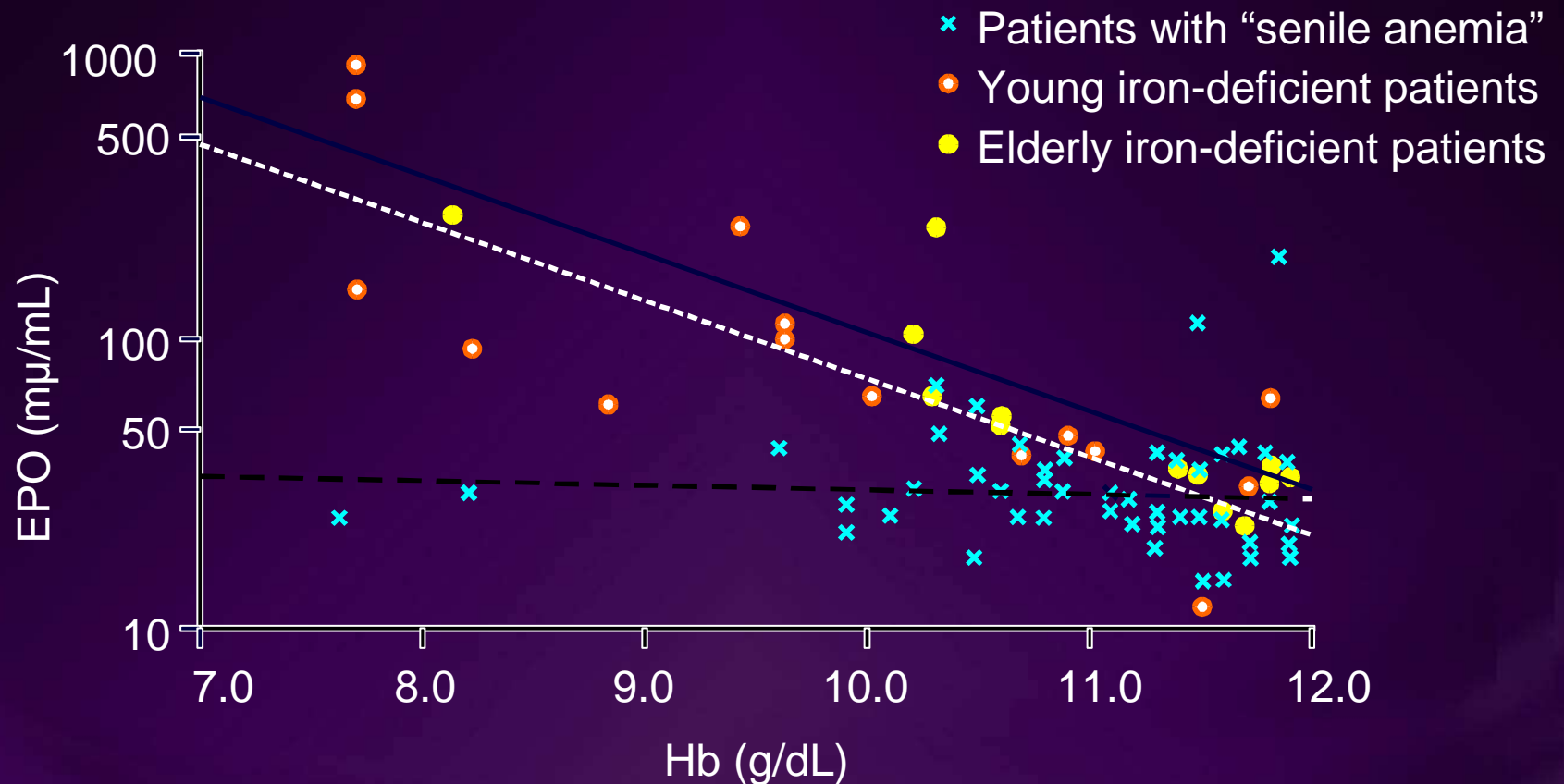
Ershler W. *J Am Geriatr Soc.* 2003;51(suppl):S18-S22.

Leng S, et al. *J Am Geriatr Soc.* 2002;50:1268-1271.

Morra L, et al. *Ann Hematol.* 1994;68:67-71.

Ershler W, et al. *Annu Rev Med.* 2000;51:245-270.

“Anemia of Aging” Blunted EPO Production



Kario K, et al. *Am J Hematol.* 1992;41:252-257.

“Anemia of Aging” Cytokine Dysregulation



- Proinflammatory cytokine levels (eg, IL-6, TNF- α) increase in healthy older individuals¹⁻³
- Anemia may occur as a result of¹
 - Direct inhibition of erythropoietin
 - Interference of normal iron metabolism

1. Ershler W. *J Am Geriatr Soc.* 2003;51(suppl):S18-S22.

2. Leng S, et al. *J Am Geriatr Soc.* 2002;50:1268-1271.

3. Ershler W, et al. *Annu Rev Med.* 2000;51:245-270.



Anemia in Older People

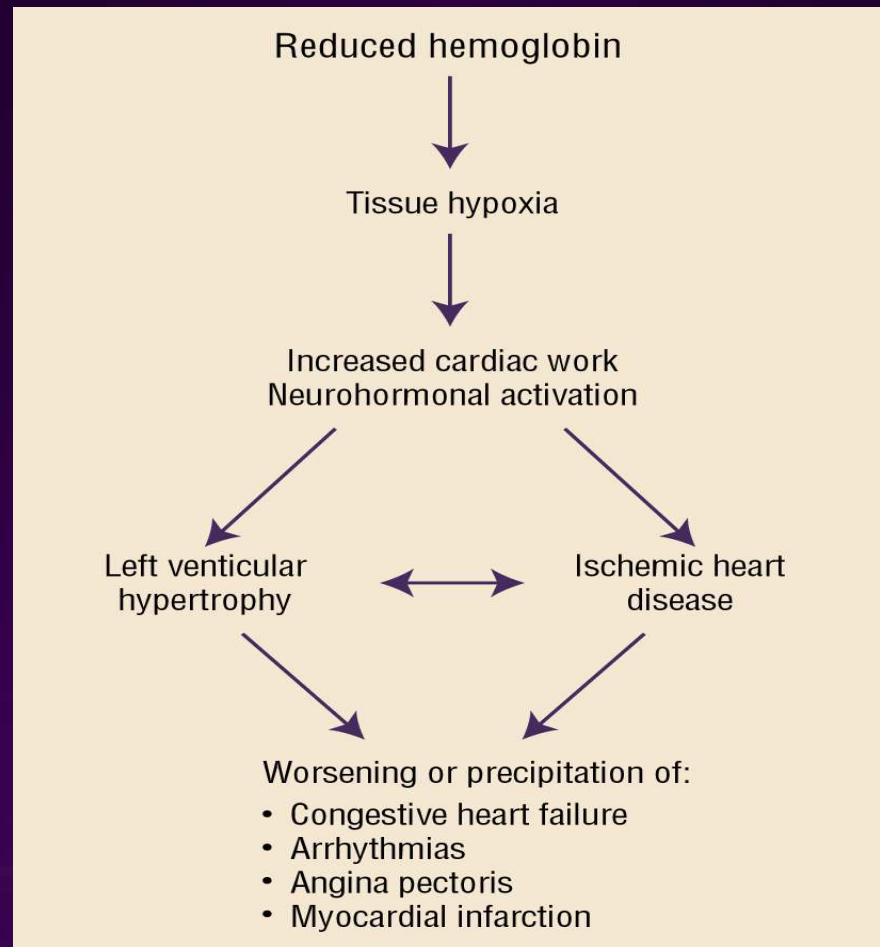
Associated Morbidities

Anemia-Associated Morbidity



- Cardiovascular disease
- Falls
- Functional impairment
- Cognitive and mood dysfunction

Anemia and Cardiovascular Disease



National Anemia Action Council. *Anemia: A Hidden Epidemic*. Los Angeles, CA: HealthVizion Communications, Inc.; 2002. 20.

Heart Failure (HF) in the Elderly

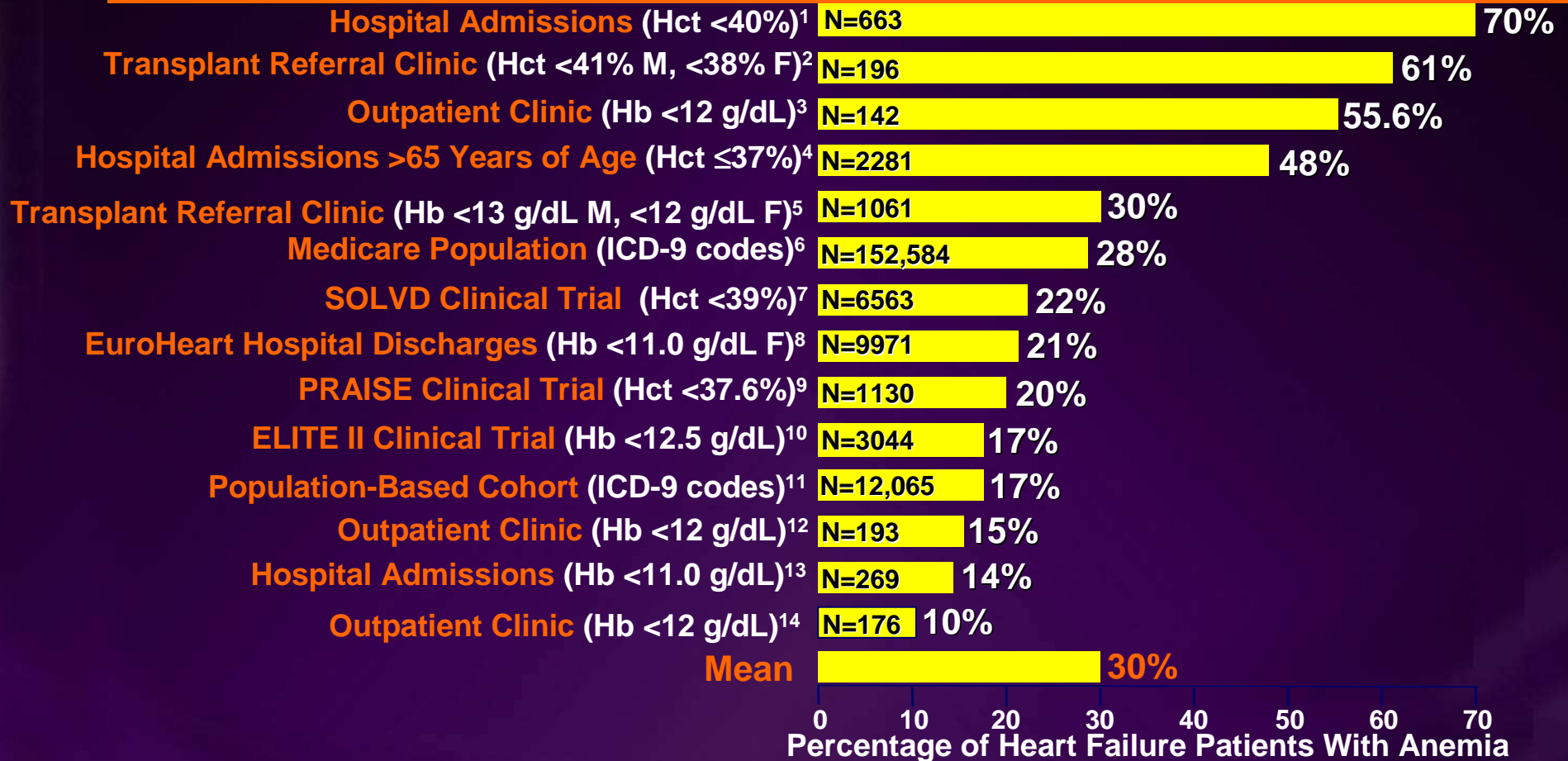


- Leading cause of hospitalization for people ≥ 65 years¹
- Affects 4.8 million Americans¹
- About 550,000 new cases occur each year²

1. Lloyd-Jones DM, et al. *Circulation*. 2002;106:3068-3072.

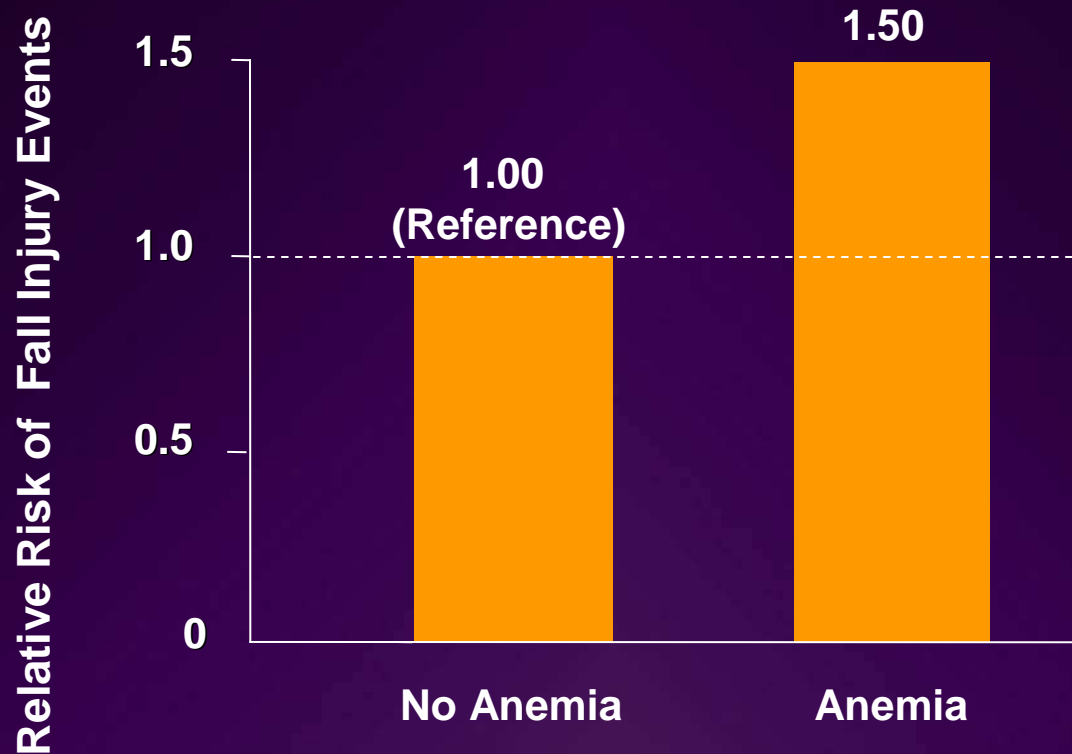
2. Levy D, et al. *N Engl J Med*. 2002;347:1397-1402.

Prevalence of Anemia in Heart Failure Patients



1. McClellan WM, et al. *J Am Soc Nephrol.* 2002;13:1928-1936. 2. Androne AS, et al. *Circulation.* 2003;107:226-229. 3. Silverberg DS, et al. *J Am Coll Cardiol.* 2000;35:1737-1744. 4. Kosiborod M, et al. *Am J Med.* 2003;114:112-119. 5. Horwich TB, et al. *J Am Coll Cardiol.* 2002;39:1780-1786. 6. Herzog CA, et al. *J Card Fail.* 2002;8(suppl):S63. Abstract 228. 7. Al-Ahmad A, et al. *J Am Coll Cardiol.* 2001;38:955-962. 8. Cleland JG, et al. *Eur Heart J.* 2003;24:442-463. 9. Mozaffarian D, et al. *J Am Coll Cardiol.* 2003;41:1933-1939. 10. Anker SD, et al. *Circulation.* 2002;106(suppl):472. Abstract 2335. 11. Ezekowitz JA, et al. *Circulation.* 2003;107:223-225. 12. Tanner H, et al. *Int J Cardiol.* 2002;86:115-121. 13. Cromie N, et al. *Heart.* 2002;87:377-378. 14. Szachniewicz J, et al. *Int J Cardiol.* 2003 Aug;90(2-3):303-308.

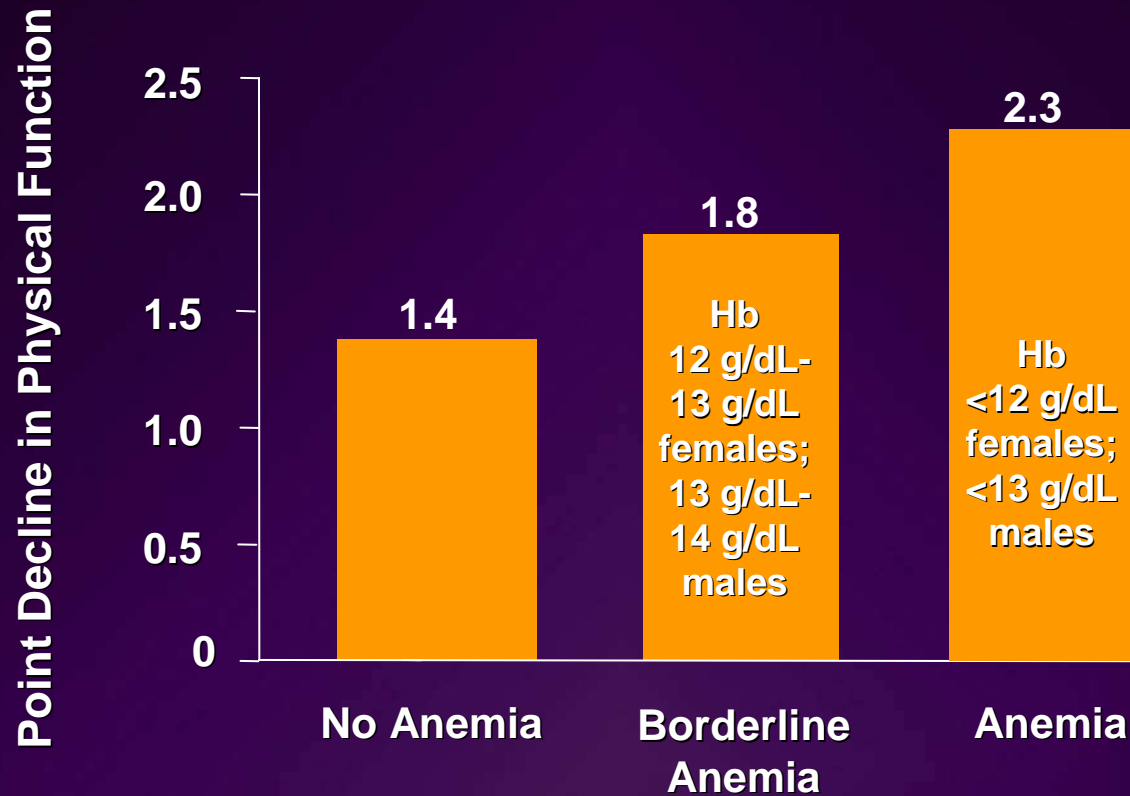
Anemia Increases Risk of Falls in Elderly



N = 1158

Herdon J, et al. *J Am Geriatr Soc.* 1997;45:739-743.

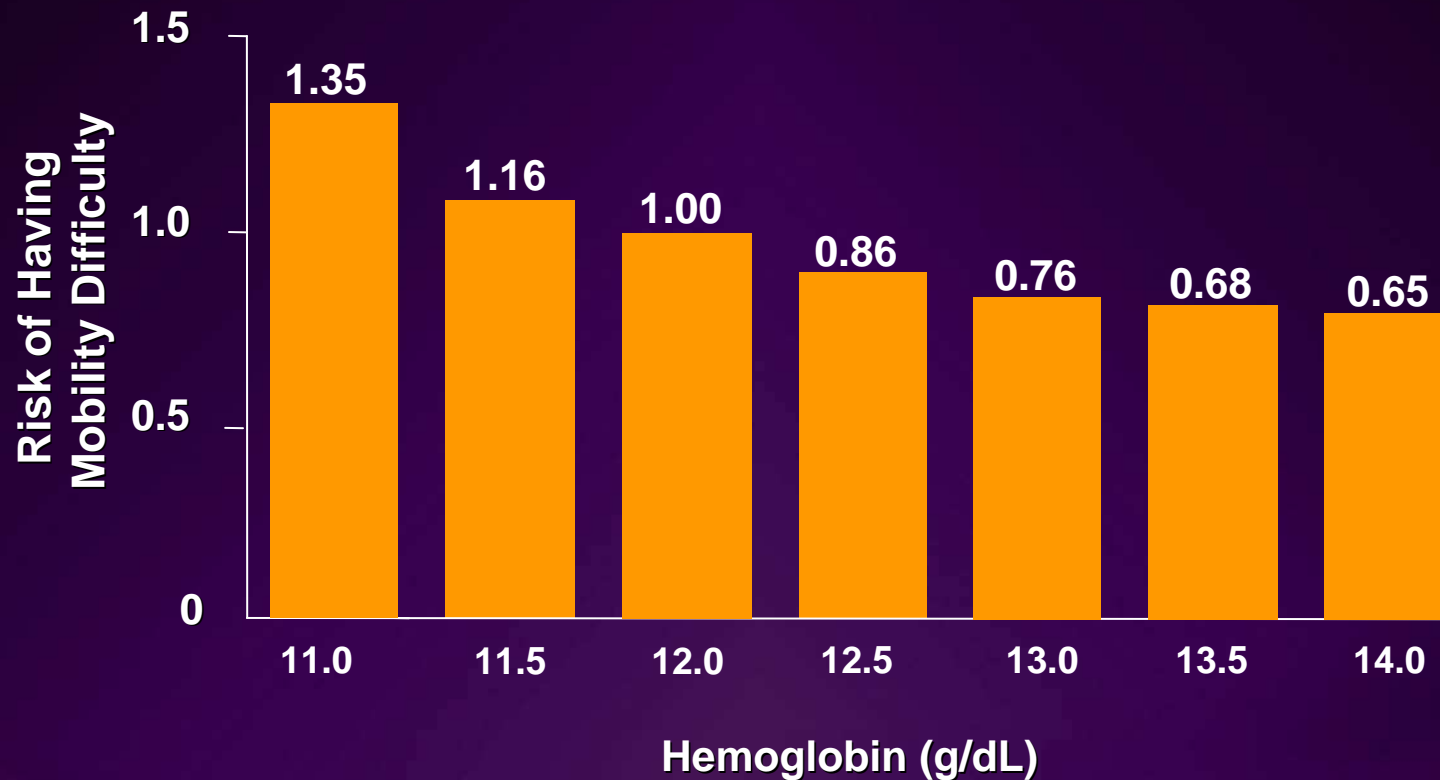
Even Mild Anemia Impacts Physical Performance



N = 1146 \geq 71 years of age

Pennix WJH, et al. *Am J Med.* 2003;115:104-110.

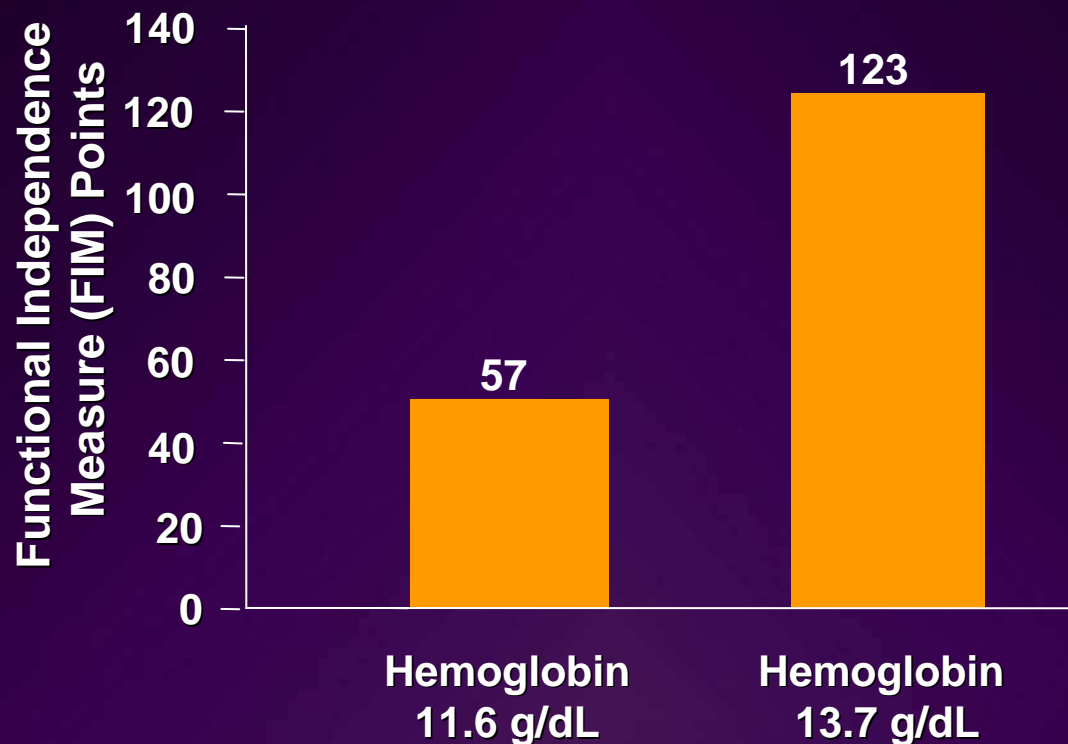
Declining Hemoglobin Linked to Mobility Difficulty



N = 673

Chaves PHM, et al. *J Am Geriatr Soc.* 2002;50:1257-1264.

Hemoglobin Levels and Functional Independence



N = 48

Kamenetz Y, et al. *Aging (Milano)*. 1998;10:32-38.

Anemia and Cognitive Function



- Anemia is associated with cognitive impairment^{1,2}
 - Concentration deficits
 - Depression
- Coexisting vascular dementia may be a factor³

1. Katz IR, et al. *J Geriatr Psychiatry Neurol.* 1993;6:161-169.

2. Argyriadou S, et al. *BMC Fam Pract.* 2001;2:5.

3. Milward E, et al. *NeuroReport.* 1999;10:2377-2381.



Anemia in Older People

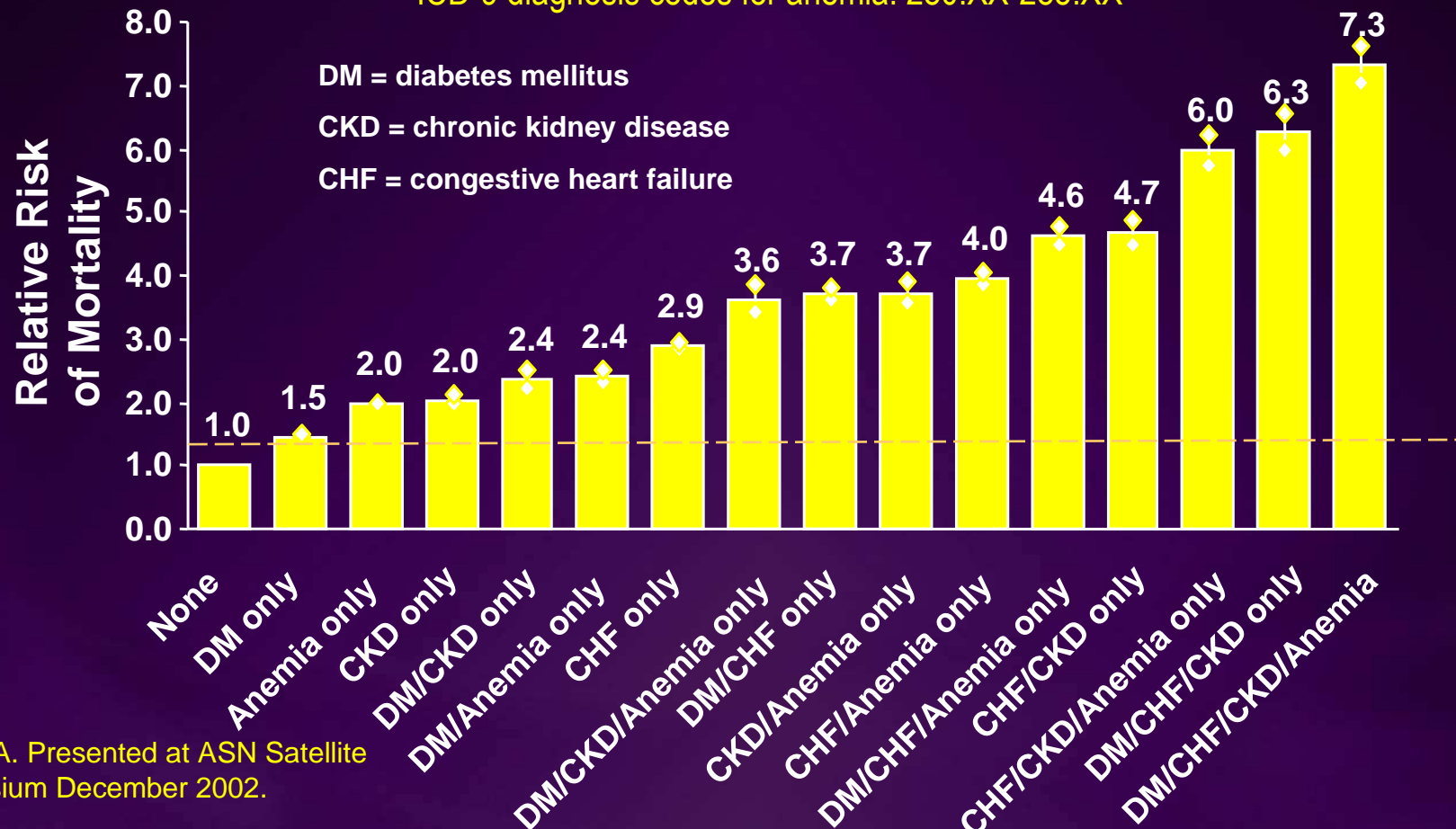
Increased Mortality Risk

Anemia Is a Mortality Risk Multiplier



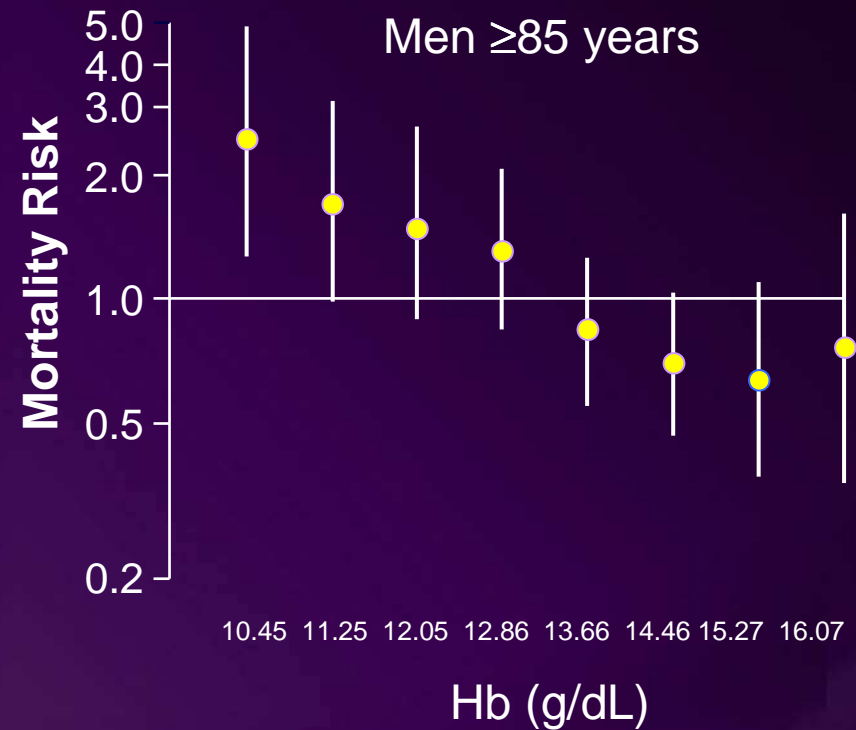
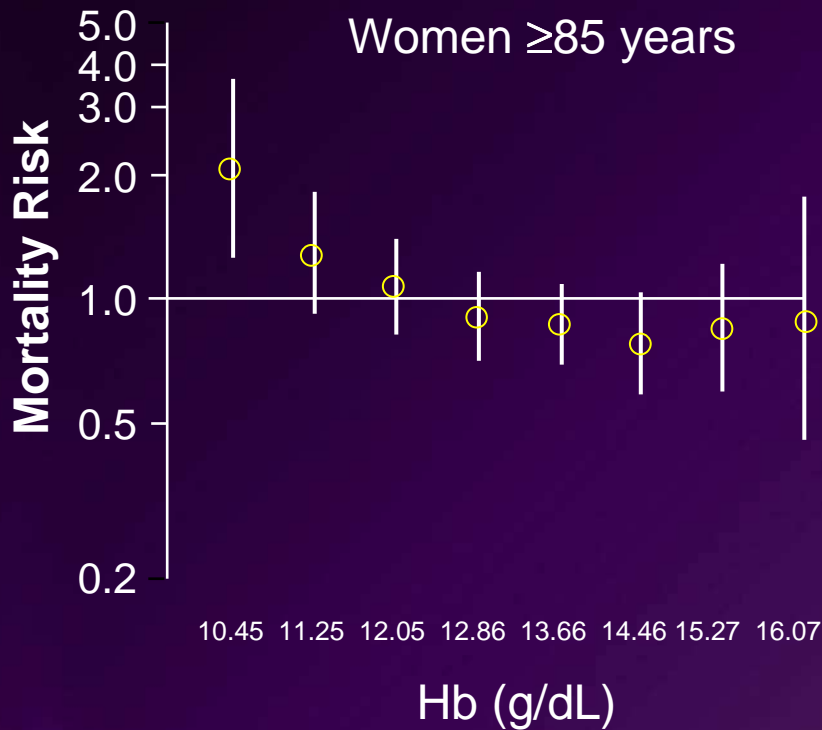
Likelihood for death before ESRD during 2-year follow-up in Medicare 5% Sample 1996-97

ICD-9 diagnosis codes for anemia: 280.XX-285.XX



Collins A. Presented at ASN Satellite Symposium December 2002.

Anemia Increases Mortality Risk in the Elderly



N = 755

Izaks GJ, et al. *JAMA*. 1999;281:1714-1717.



Anemia in Older People

Management

The Cause of Anemia Directs Therapy



<u>Cause of Anemia</u>	<u>Therapy</u>
Chronic disease	ESPs ¹ or Transfusion ²
Iron deficiency	Iron ¹
Vitamin B ₁₂ deficiency	Vitamin B ₁₂ ¹
Folate deficiency	Folate ¹
MDS	ESPs + G-CSF or Transfusion ³
Anemia of aging	ESPs ^{4,5}

ESP = Erythropoietic stimulating protein

G-CSF = Granulocyte colony-stimulatory factor

MDS= Myelodysplastic syndrome

1. Smith D. *Am Fam Physician*. 2000;62:1565-1572.

2. Balducci L. *J Am Geriatr Soc*. 2003;51(suppl):S2-S9.

3. Rothstein G. *J Am Geriatr Soc*. 2003;51(suppl):S22-S26.

4. Matsuo T, et al. *Am J Hematol*. 1992;41:252-257.

5. Cohen H. *J Am Geriatr Soc*. 2003;51(suppl):S1.

Some Risks of Allogeneic Blood Transfusion¹



Blood Transfusion Risk	Estimated Frequency Per Unit
<i>VIRUS</i>	
Hepatitis B	1/60,000-1/200,000
Hepatitis C	1/800,000-1/1.6 x 10 ⁶
HIV	1/1.4-2.4 x 10 ⁶
<i>BACTERIA</i>	
Red cells	1/500,000
Platelets	1/2000
<i>ACUTE HEMOLYTIC REACTIONS</i>	1/250,000-1,000,000
<i>DELAYED HEMOLYTIC REACTIONS</i>	1/1000
<i>TRANSFUSION-RELATED ACUTE LUNG INJURY</i>	1/8000
<i>ABO CLERICAL ERROR²</i>	1/16,000

1. Modified with permission from Goodnough LT, et al. *N Engl J Med.* 1999;340:438-447.

2. Krombach J, et al. *Anesth Anal.* 2002;94:154-156.

Allogeneic Blood Transfusion Current Guidance



Red-cell containing components should not be used to treat anemia that can be corrected with specific medications such as iron, vitamin B12, folic acid, or recombinant erythropoietin, except when the patient's symptoms require immediate enhancement of oxygen-carrying capacity.

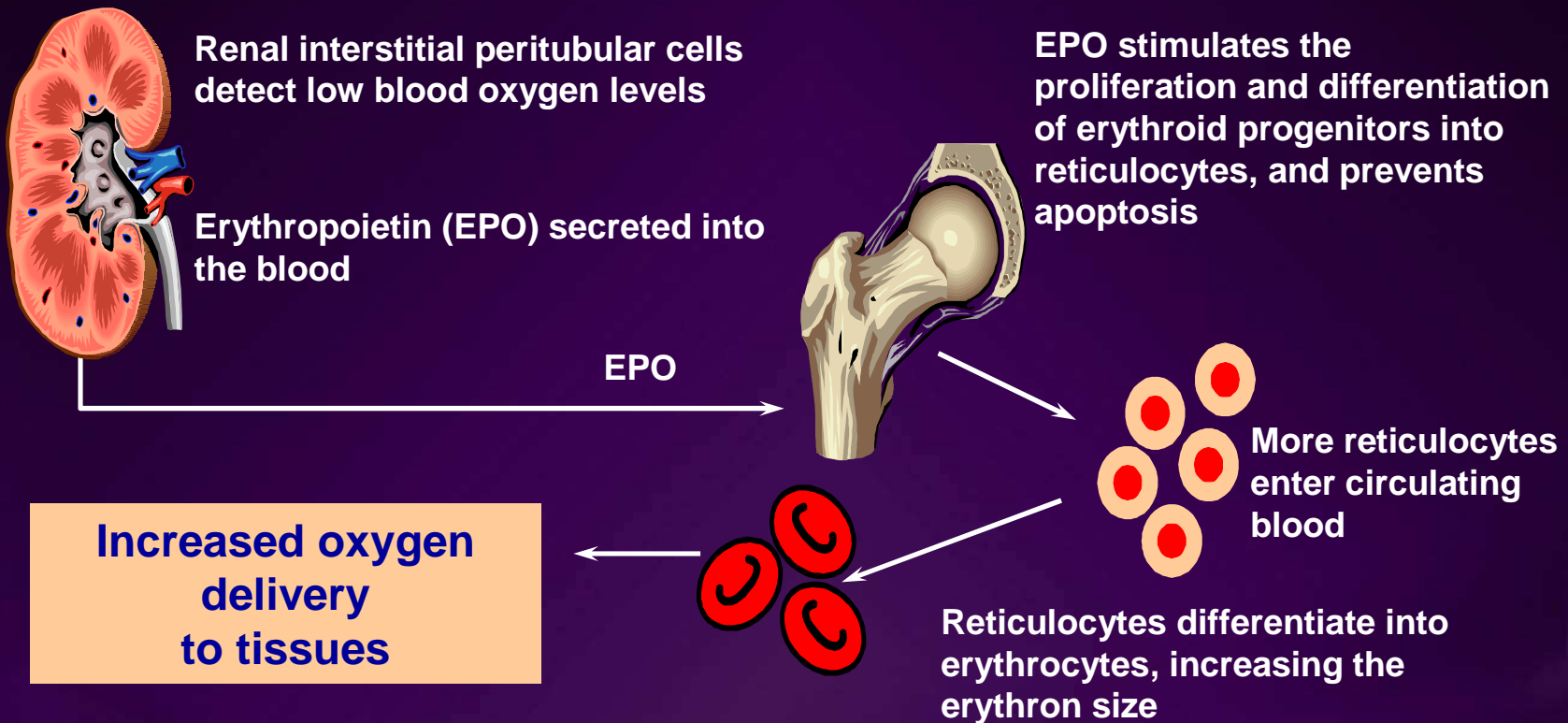
American Association of Blood Banks, America's Blood Centers, and the American Red Cross

Erythropoietic Stimulating Proteins (ESPs)



- Peptide hormones and their derivatives, manufactured by recombinant DNA technology, which stimulate the production of red blood cells
 - Recombinant human erythropoietin (rHuEPO)
 - eg, epoetin alfa, epoetin beta, epoetin omega
 - Darbepoetin alfa

Erythropoietin Regulates Red Blood Cell Production



1. Bunn H. In: Isselbacher K, et al, eds. *Harrison's Principles and Practice of Internal Medicine*. 13th ed. New York, NY: McGraw-Hill; 1994:1717–1721.
2. Dessypris E. In: Lee G, et al, eds. *Wintröbe's Clinical Hematology (Vol. 1)*. Baltimore: Lippincott, Williams & Wilkins; 1998:169–192.

Treatment Can Improve Outcomes in Anemic Patients



- Evidence from patients with CKD¹ and HF² shows improvements in:
 - Cardiac function²
 - Cognitive function^{1,3-5}
 - Exercise capacity²⁻⁵
 - Need for hospitalization²
 - Quality of life³⁻⁵

1. Marsh JT, et al. *Kidney Int.* 1991;39:155-163.

2. Silverberg DS, et al. *J Am Coll Cardiol.* 2000;35:1737-1744.

3. Collins A, et al. *Semin Nephrol.* 2000;20:345-349.

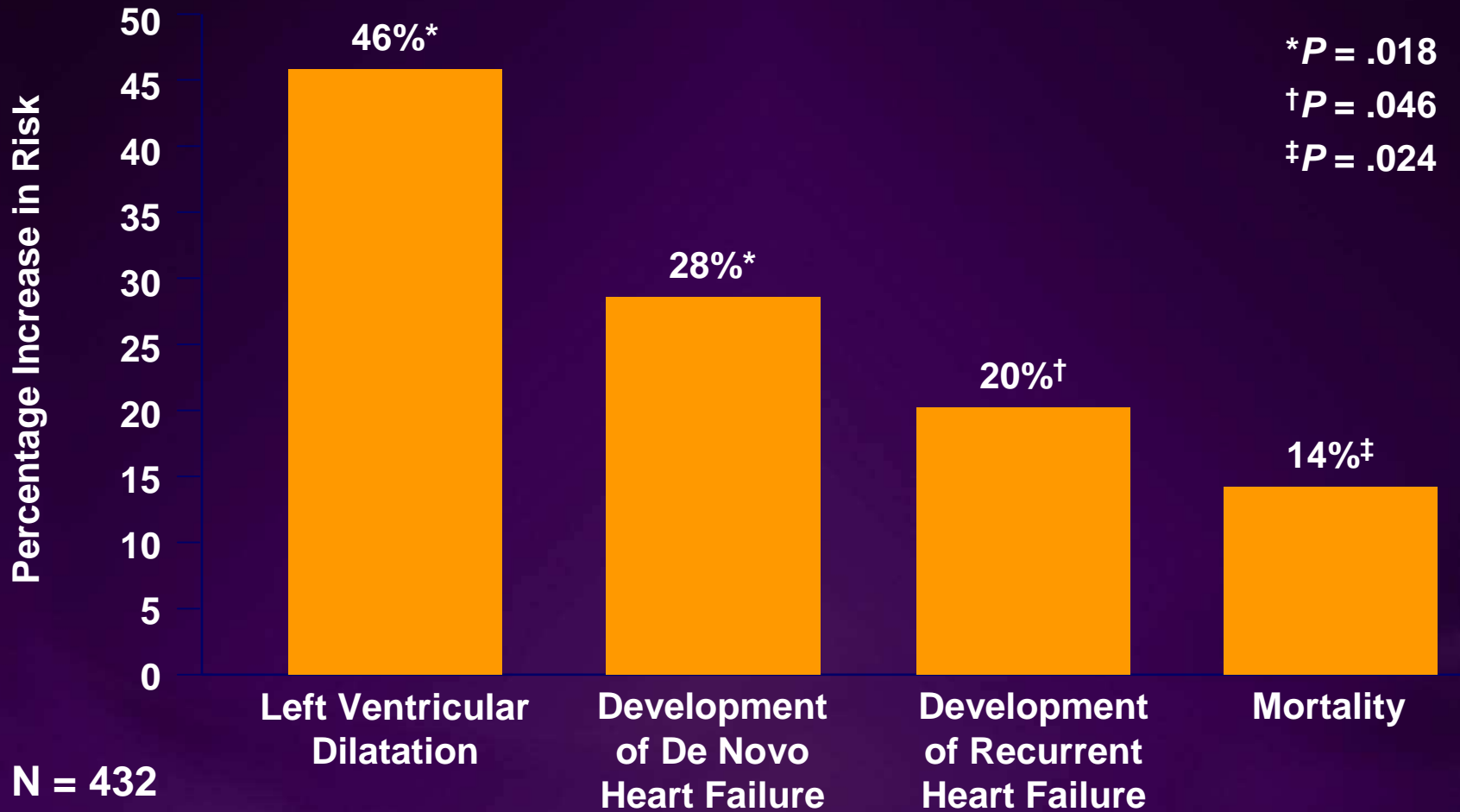
4. Pickett LI, et al. *Am J Kidney Dis.* 1999;33:1122-1130.

5. Valderabanno F, et al. *Am J Kidney Dis.* 2001;38:443-464.

Impact of Anemia on Cardiomyopathy and Mortality in Dialysis Patients

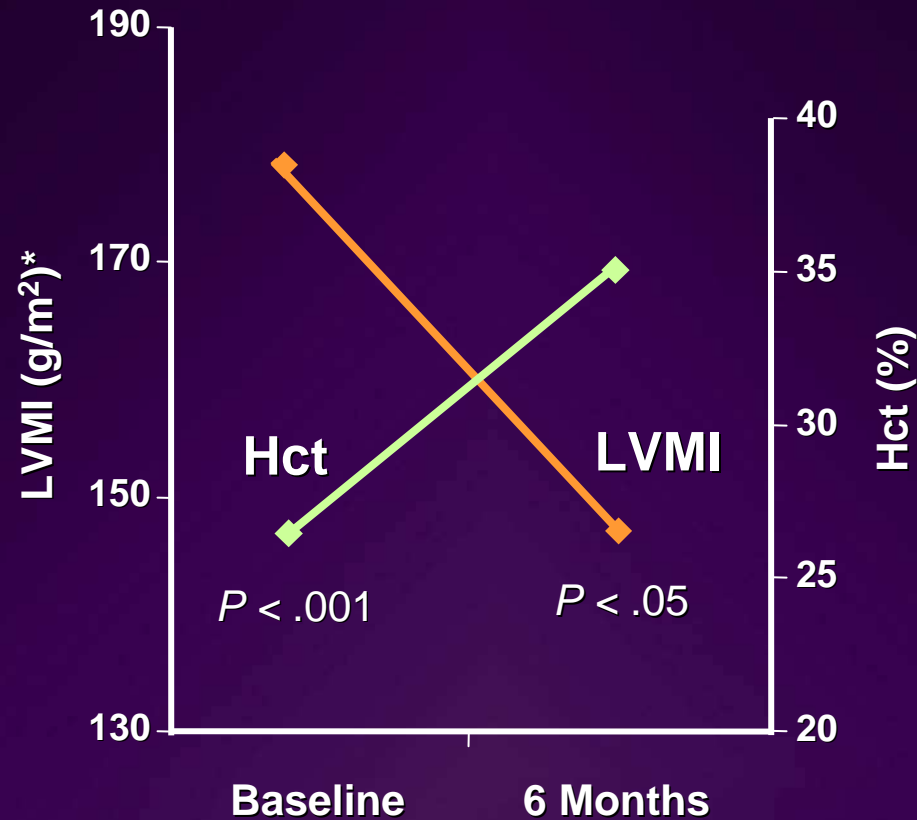


Increase in Risk for Each 1-g/dL Decrease in Mean Hemoglobin



Foley RN, et al. *Am J Kidney Dis.* 1996;28:53-61.

Anemia Treatment May Result in Partial Regression of LVH



N = 11
LVH = left ventricular hypertrophy
LVMI = left ventricular mass index

*Note: Normal LVMI² = 125 g/m²

1. Portoles J, et al. *Am J Kidney Dis.* 1997;29:541-548.
2. Casale PN, et al. *Ann Intern Med.* 1986;10:173-178.



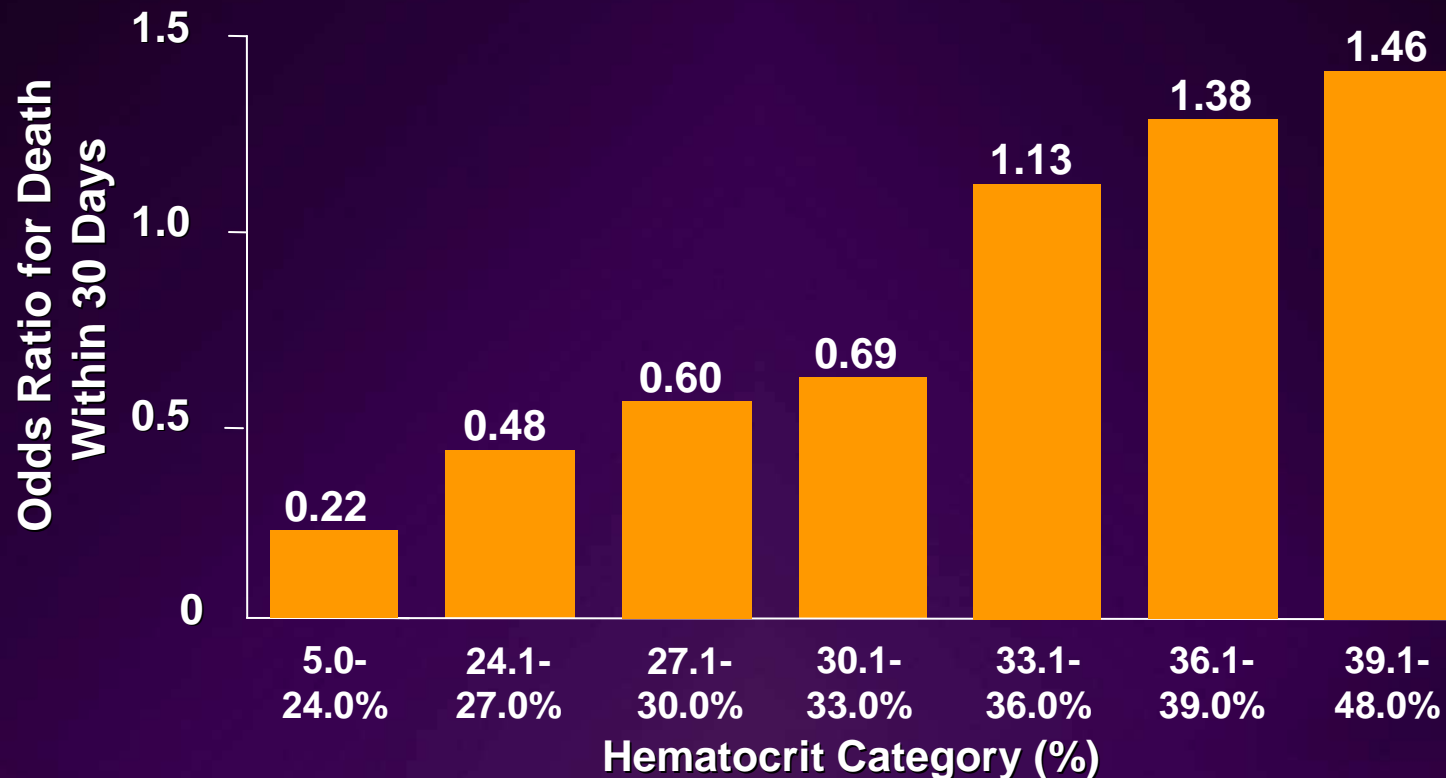
rHuEPO for the Elderly

- Elderly patients benefits equal those of the younger population
 - Increase in Hb/Hct^{1,2}
 - Decreased need for transfusion¹
 - Improved quality of life²

1. Cascinu S, et al. *Oncology*. 1995;52:422-426.

2. Moreno F, et al. *Am J Kidney Dis*. 1996;27:548-556.

Transfusion Associated With Lower 30-Day Mortality in Elderly AMI Patients With Severe Anemia



AMI = Acute Myocardial Infarction

N = 78,974 Medicare Recipients ≥ 65 Years of Age

Wu W-C, et al. N Eng J Med. 2001;345:1230-1236.

Summary



- Anemia in the elderly is more commonly observed than appreciated and is often multifactorial
- Anemia is unacceptable in the elderly, regardless of whether or not “anemia of aging” does exist
- Anemia can indicate serious pathology and should be evaluated in all patients with life expectancy >1 year
- Untreated anemia in the elderly is associated with increased risk of mortality and certain comorbidities, as well as impaired functional status
- Treatment of anemia in the elderly can improve outcomes

Please send feedback on this slide set to info@anemia.org