

ANEMIA MANAGEMENT IN THE ELDERLY CKD PATIENTS

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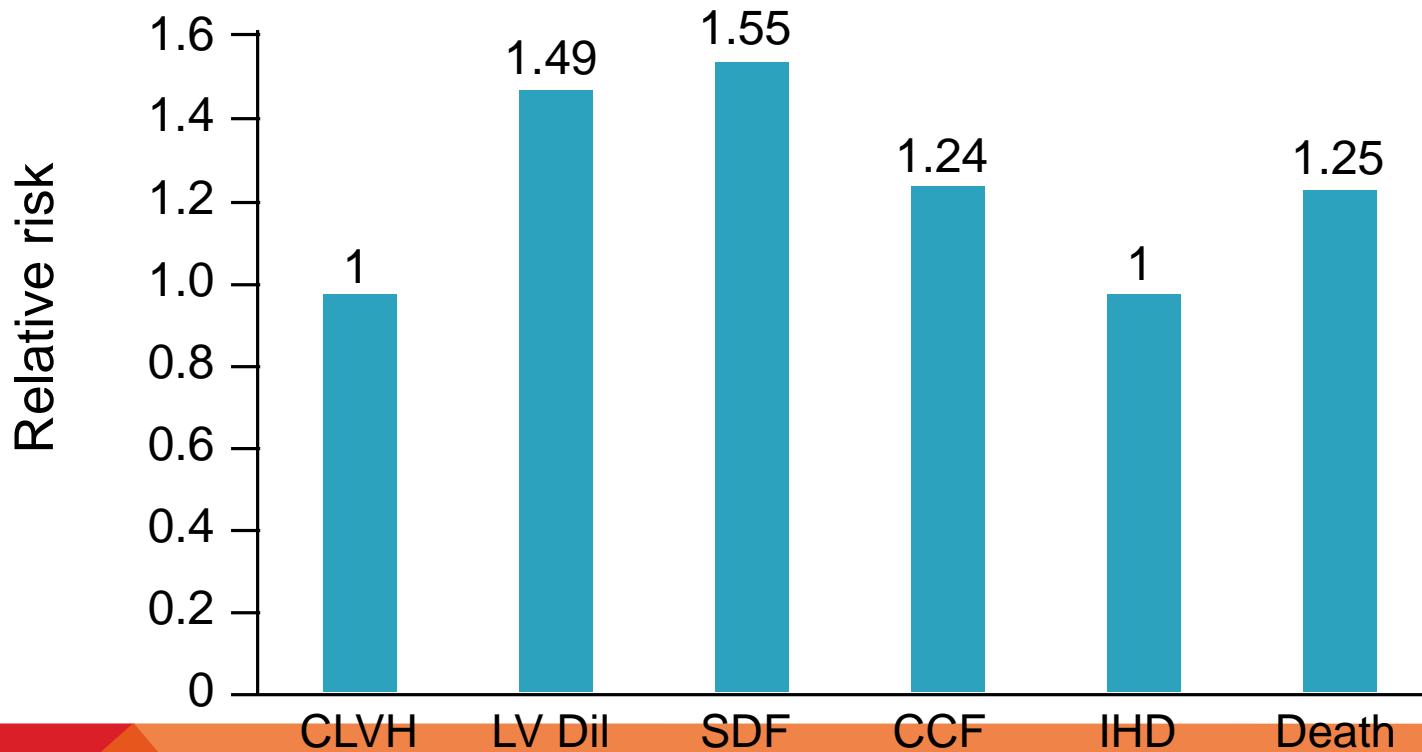
Head of internal medicine department

Sohag faculty of medicine

Historical background

- ◉ *Richard Bright (1836)*: first observed that anemia was a complication of renal failure.
- ◉ *Robert Christison*: further described renal anemia.
- ◉ *Miyake (1977)*: purified and identified Epo.
- ◉ *Eschbach (Dec 2, 1985)*: first human use of EPO

EFFECT OF 1 G/DL FALL IN HB



CLVH = concentric left ventricular hypertrophy


LV Dil = left ventricular dilatation

SDF = systolic dysfunction

CCF = chronic cardiac failure

IHD = ischaemic heart disease

OTHER EFFECTS OF ANEMIA IN CKD

- Acceleration of progression of kidney disease by oxygen deprivation.
 - Increased risk of bacteremia (11% increased risk for every 1g/dl fall in Hb)
 - Detrimental effects on brain and cognitive functions.
- 

Benefits of anemia Control

↑ **Quality-of-life**

↑ **Exercise capacity**

↓ **cardiac output**

↓ **Angina**

↓ **LVH**

↓ **Bleeding tendency**

↑ **Brain / cognitive function**

↑ **Sexual function**

↑ **Endocrine function**

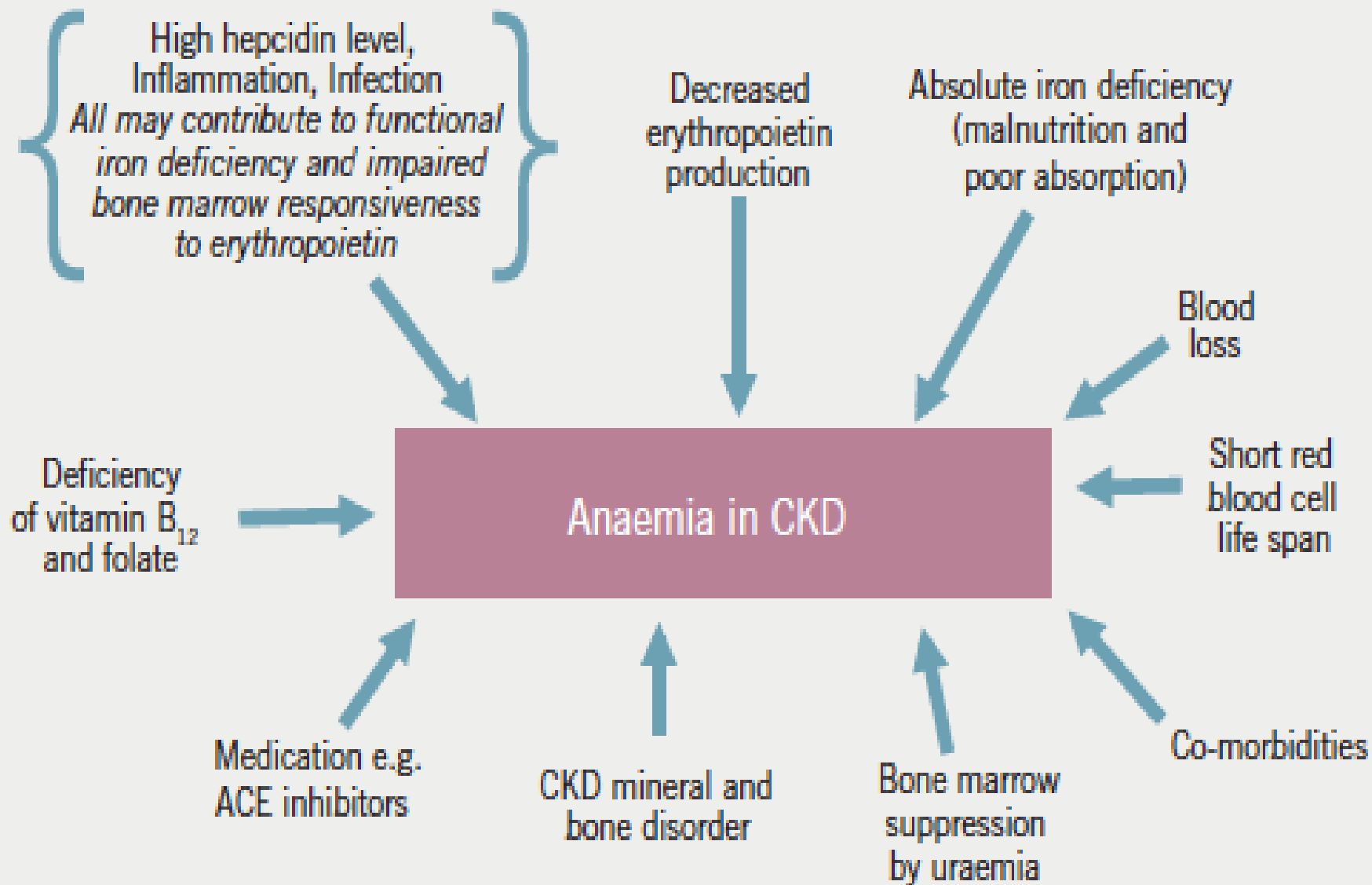
↑ **Immune function**

↑ **Muscle metabolism**

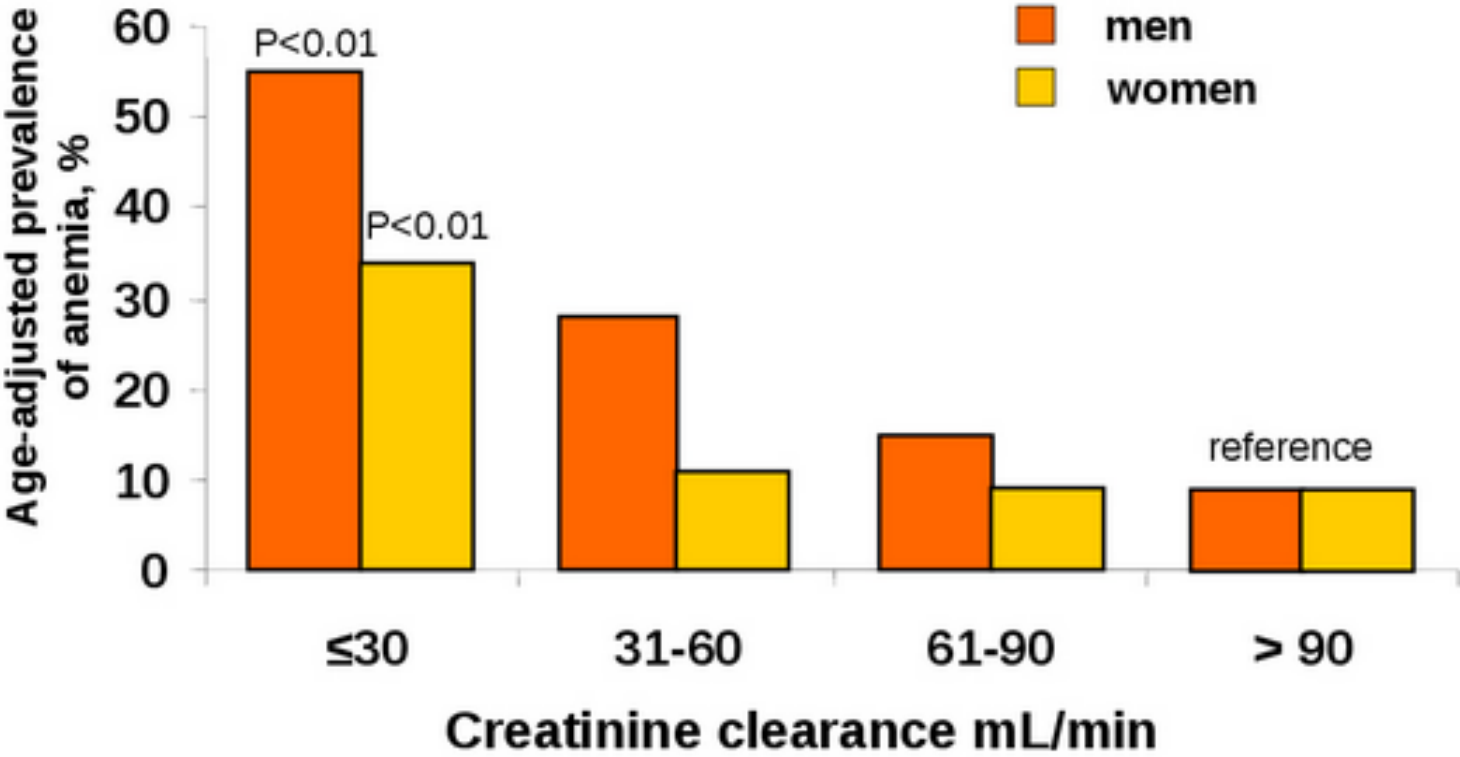
↓ **Hospitalizations**

↓ **Transfusions**

↑ **Nutrition**



Prevalence of anemia according to GFR in the elderly - *InCHIANTI study*



1005 participants ≥ 65 yrs

Ble A. Arch Intern Med 2005

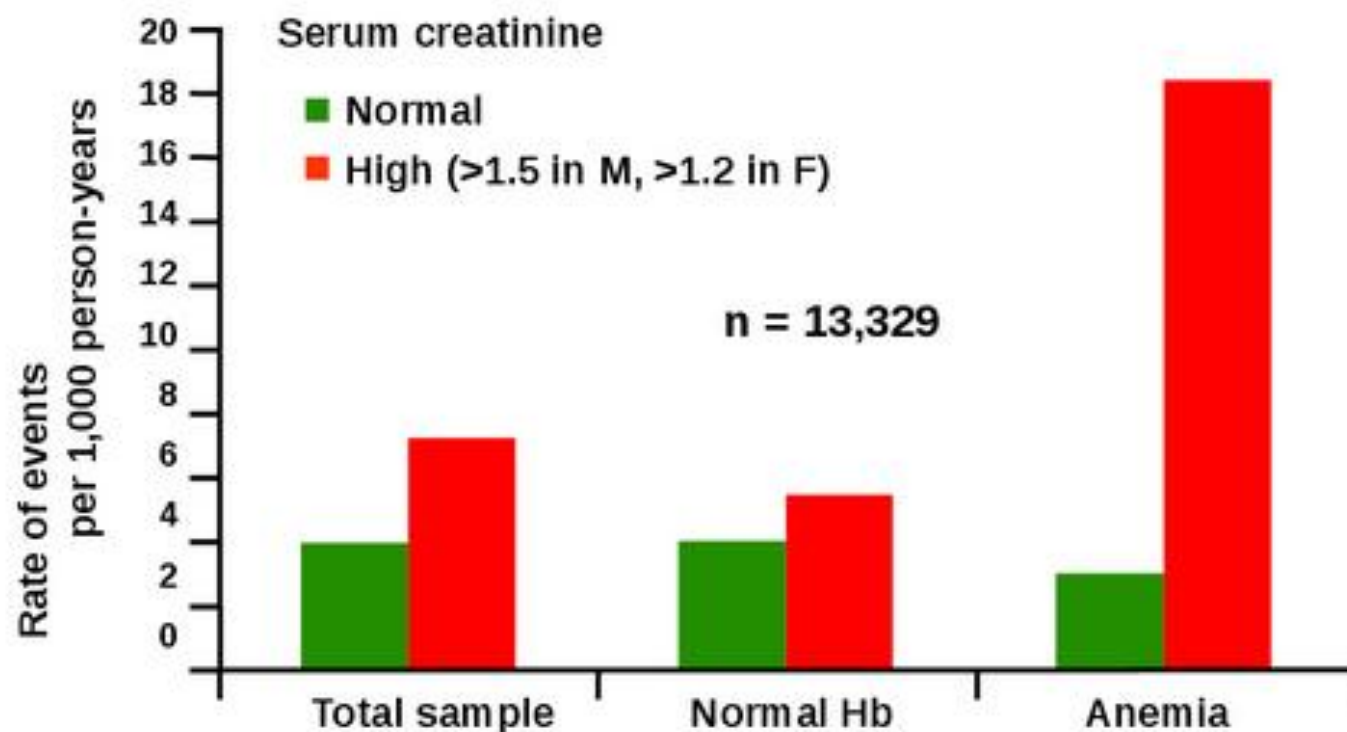


**There is a clear
relationship between
anaemia and outcome**



Anaemia increases risk of coronary heart disease (CHD) in patients with CKD

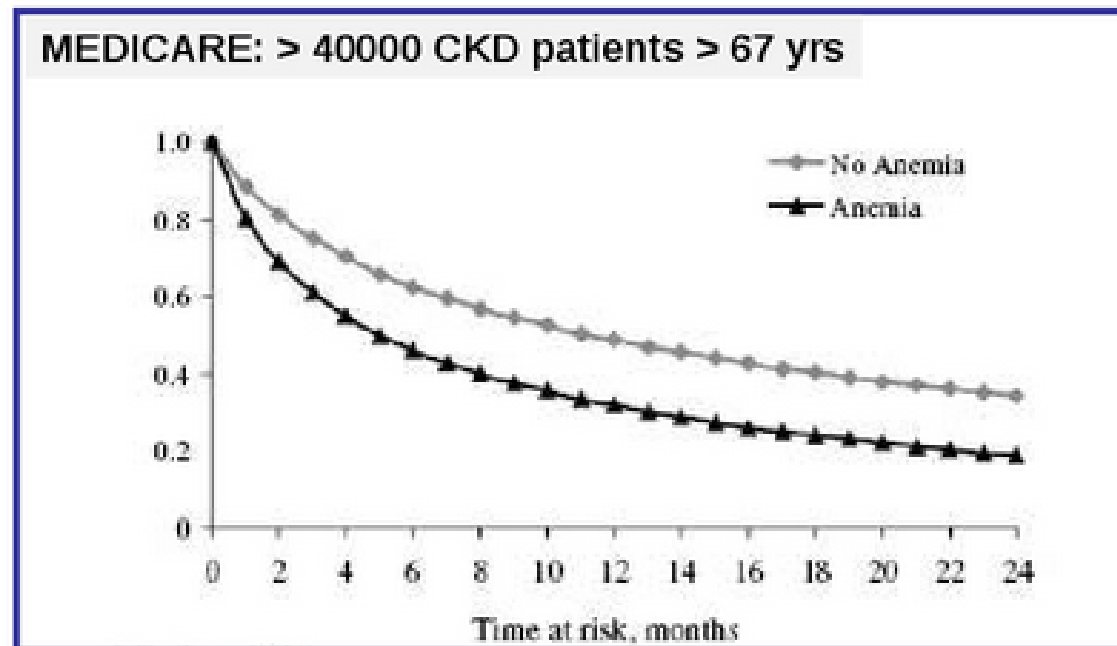
Atherosclerosis Risk In Communities (ARIC) study



Jurkovitz CT et al. J Am Soc Nephrol 2003; 14: 2919-2925

Anemia and CVD, Hospitalization, ESRD, and Death in Older Patients with CKD

Survival estimates: time to the combined endpoint of atherosclerotic vascular disease, CHF, RRT, death



Li S et al. Int Urol Nephrol 2005; 37:395-402

REVIEW ARTICLE

Anaemia and cognitive performances in the elderly: a systematic review

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- **Five observational studies and six prospective cohort studies were included in the analysis**
- **Patients older than 65 years.**

“A significant positive association was shown between anaemia and global cognitive decline as well as the incidence of dementia”



**Anaemia in the Ederly with CKD:
Which target?**



Do we have strong evidence suggesting that the Hb target of the elderly CKD patient should be different from that of young CKD patient ?



NO



Partial anemia correction improves outcome





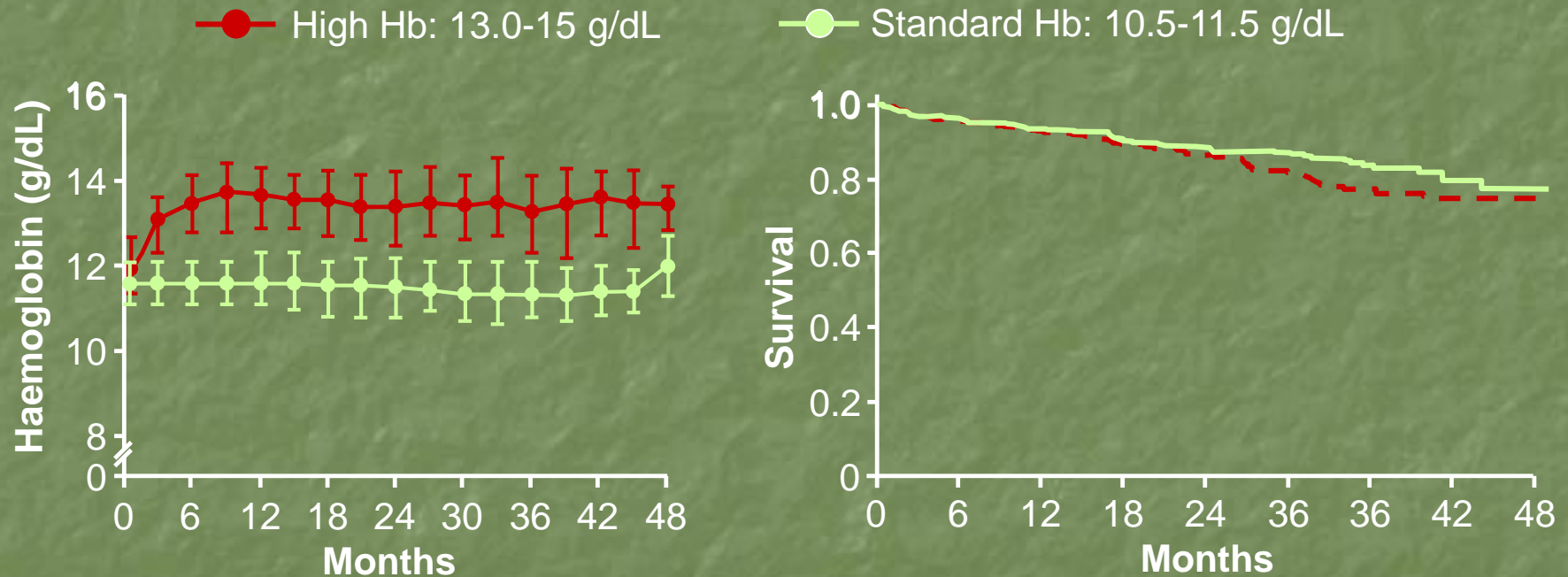
HOWEVER

***Interventional trials of
complete anaemia correction
did not give the expected results***

CREATE: In patients with CKD early and complete correction of anaemia did not reduce the risk of CV events

- Primary endpoint: Time to first CV event
Hazard ratio: 0.78; 95% CI, 0.53–1.14; p=0.20)

600



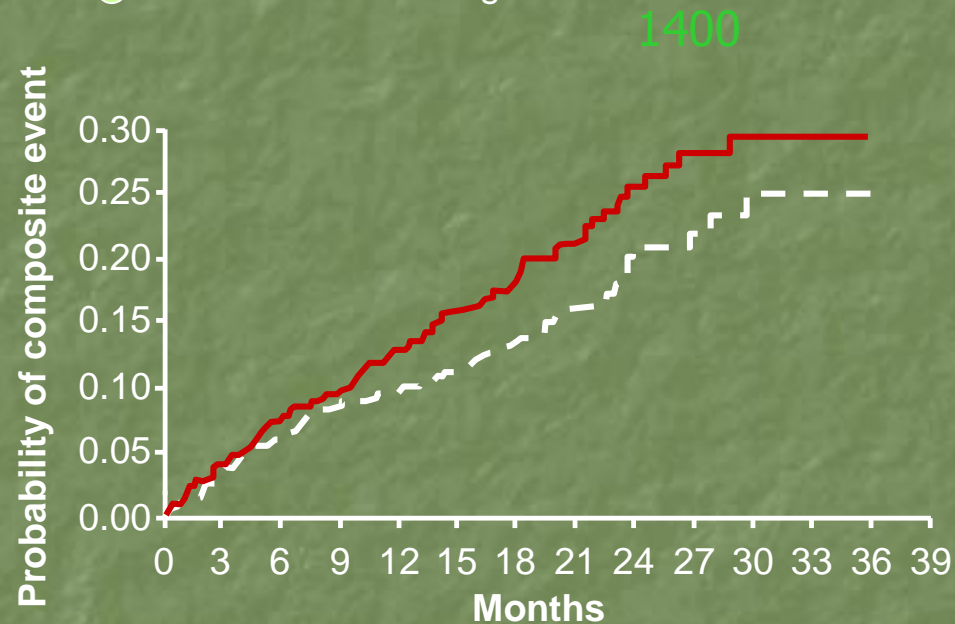
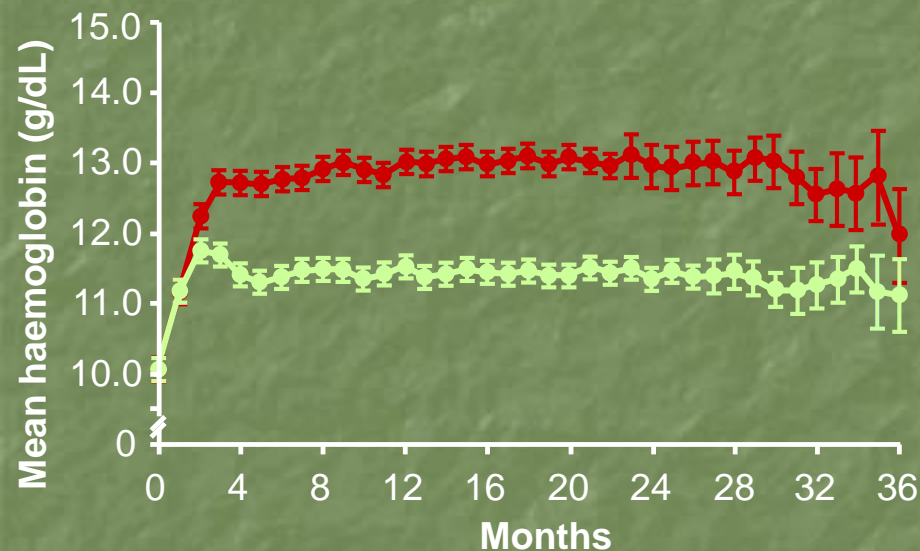
>> 58 events (high Hb, n=301) vs 47 events (low Hb, n=302)

CREATE, Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta

CHOIR: The use of a high target Hb level was associated with increased cardiovascular risk

- Primary endpoint: Time to death or CV event
Hazard ratio: 1.34; 95% CI, 1.03–1.74; p=0.03

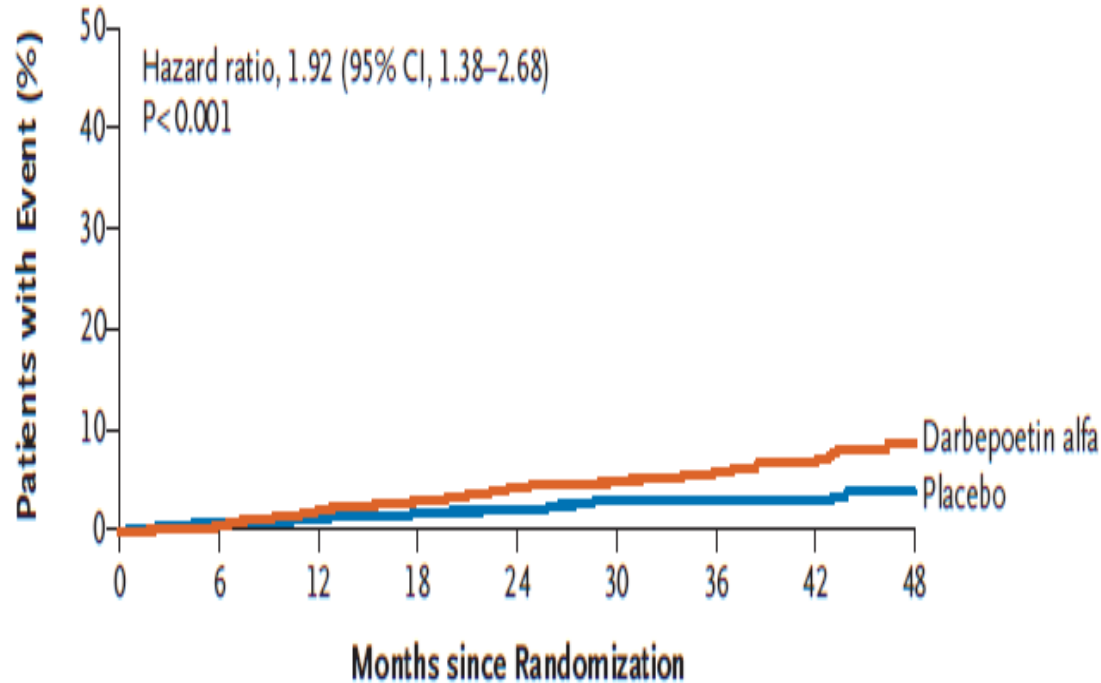
● High Hb: 13.5 g/dL ● Standard Hb: 11.3 g/dL



➤➤ 125 events (high Hb, n=715) versus 97 events (low Hb, n=717)

The TREAT study

E Fatal or Nonfatal Stroke



No. at Risk

Darbepoetin alfa	2012	1923	1787	1581	1247	863	590	341	141
Placebo	2026	1914	1783	1575	1262	886	561	338	132

Pfeffer et al, NEJM, 2010

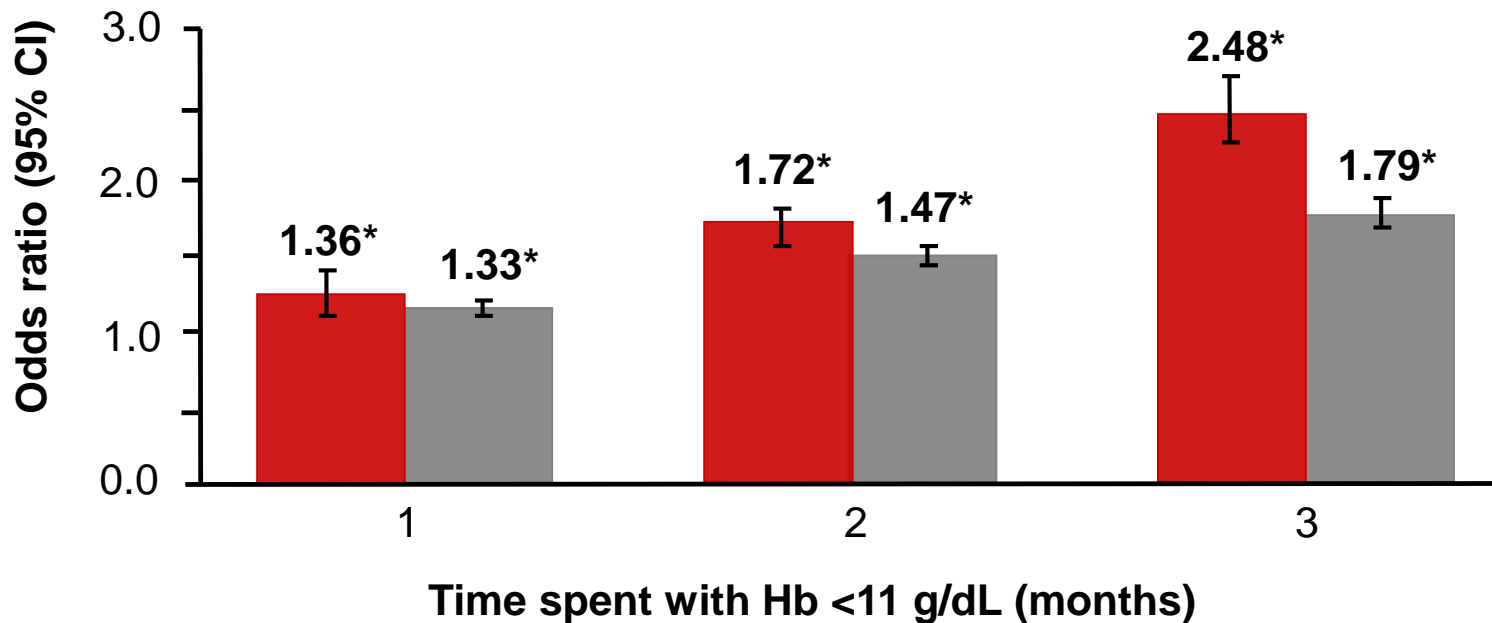
TREAT :increase strokes in higher hb gp (achieved 10.5 vs 12.5)

More time spent <11 g/dL was associated with increased risk of hospitalization and mortality

■ Death
■ Hospitalization

n = 54'328 dialysis patients

*p < 0.0001



CI, Confidence interval

“in fact, clinical guidelines are supposed to be guides, not rules, and tailoring of therapy is a critical aspect of management because *‘one size certainly does not fit all patients’*.”

Summary, target

- **Targeting** 10 (10.5)-12g/dl is safe in dx and pre dx patients
- **Targeting** higher Hb is risky in older patients, diabetics, CVD and poor responders to ESA.
- Risks of higher Hb only refer to **TARGETING** higher levels using ESA
- Special considerations for healthier and younger as well as symptomatising patients

Managing Iron Needs

Diagnosing iron deficiency

- Absolute deficiency
 - TSat
 - Flaws related to nutritional transferrin deficiency
 - Ferritin
 - Flaws related to inflammation
 - Percentage microcytic cells
 - Flaws related to cell swelling
 - Reticulocyte Hb content

Diagnosing iron deficiency

- Functional deficiency
 - Pathophysiology
 - Inflammation, hepcidin, transferrin deficiency
 - Lab diagnosis
 - High ferritin, low TSAT
 - Clinical
 - Therapeutic testing

“Targets” of iron repletion

- Ferritin > 200 (Hdx)/100 (NDD and PD), up to 500
- TSat
 - 20-30

The ERBP position statement about KDIGO guidelines on anaemia

ESA INITIATION

- ◆ Hb values should not routinely be let to fall below 10 g/dl in all CKD patients

ESA MAINTENANCE THERAPY

- ✱ It is reasonable to use ESA therapy to generally maintain CKD patients with Hb values **ranging between 10 and 12 g/dl**
- ✱ Caution should be used in patients with specific risk factors especially among diabetics (symptomatic limb arteriopathy, stroke or **non-symptomatic ischaemic heart disease**, cancer or in those who are hyporesponsive to ESA treatment). In these patients, if ESA therapy is used, it seems wise to aim at the lower Hb levels of the suggested target range (10 – 12 g/dl).

A study of the response of elderly patients with ESRD to epoetin alfa or beta

- **An incident cohort (n=198) was used to compare the correction of anaemia in a population of elderly (≥ 65 years) and young dialysis patients**
- **Anaemia correction in the elderly was similar to the younger patients, with a median haemoglobin of 11.3 g/dL**
 - **The elderly patients maintained significantly higher serum ferritin levels throughout (median 209 microg/L) and required less epoetin alfa or beta (median 91.6 units/kg/wk)**

Darbepoetin Alfa Impact on Health Status in Diabetes Patients with Kidney Disease: A Randomized Trial

Clinically meaningful improvement in FACT-Fatigue scores

Hospitalization events and Hb 9 g/dl at any point were significantly associated with worse scores on all three HRQOL domains



Hemoglobin levels and health-related quality of life in young and elderly patients on specialized predialysis care

In the PREPARE-2 follow-up study, incident predialysis patients were included (2004-2011) when referred to one of the 25 participating Dutch outpatient.

No Therapy

Elderly patients (n=214) not prescribed ESA/iron and with a high Hb (≥ 13 vs. 11-12 g/dl) had a statistically significant ($p < 0.05$) and/or clinically relevant ($> 3-5$ points) higher physical (11.9, 95% CI 1.7;22.2) and mental (6.4, 95% CI -1.7;14.6) summary score

Therapy

High Hb was not associated with a higher HRQOL in 19 elderly patients who were prescribed ESA/iron.

Hb levels and health-related quality of life in young and elderly patients on specialized predialysis care

Editorial comment

The effect of quality of life in different age groups has been little studied previously, despite its possible important implication in everyday clinical practice.

“It is wrong to assume that all individuals would weigh the risks and benefits and arrive at the same risk-benefit calculation”



Adverse Effects of ESA Therapy

- Worsening of HTN
- Seizure
- Increased blood clotting
- Slight decrease of Kt/V
- Impaired phosphorus balance
- Hyperkalemia
- Expensive
- Pure Red cell aplasia (PRCA)

Hyporesponsiveness to ESA

- Inflammation (ferritin, CRP)
- Iron deficiency
- Under-dialysis
- Blood loss
- Malignancy, myeloma
- Drugs
- Hematological disease
- ?hyperparathyroidism
- Nutritional
- Aluminum

Conclusions

- A large majority of CKD patients are elderly but specific evaluation of their anaemia treatment needs are lacking
- No evidences are available suggesting different HB targets, response to ESA and type of ESA in the elderly
- Quality of life, independence, mental and physical performances should be taken into account in the elderly anemia treatment



THANK YOU

