

Iron depletion in frequently donating whole blood donors

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Iron: relevance

- oxygen-transporting and storage proteins
 - hemoglobin and myoglobin
- iron-containing centers in many enzymes
 - mitochondrial respiratory chain
 - DNA-synthesis
- immune system: regulatory functions
 - immune cell proliferation
 - cytokine activities (e. g. IFN- γ effector pathway)

Depletion in storage iron

- Iron deficiency (ID)
 - Iron depletion phase (prelatent ID)
 - ♦ reduced iron stores
 - Iron deficient erythropoiesis (latent ID)
 - ♦ serum iron (functional department) decreased
 - ♦ iron deficient erythropoiesis, no anemia
 - Iron deficiency anaemia
 - ♦ $\text{Hb} < 12 \text{ g/dL}$ (♀), $< 13 \text{ g/dL}$ (♂) [WHO]

Iron deficiency: symptoms

- Iron deficiency anemia
 - Impaired physical capacity
 - ♦ reduced tissue oxygen
- Non anemia related symptoms
 - Impaired cognitive function
 - ♦ Impaired attention span
 - ♦ Decline of short term memory
 - ♦ Impaired learning ability
 - ♦ Impaired cognitive function
 - Impaired athletic performance

Iron loss from blood donation

- 1ml blood contains about 0,5 mg of iron
- Whole blood donation:
 - collection volume: 495 ml + 30 ml
 - loss of 220 - 290 mg iron,
corresponding to about 6% (male) and 10%
(females) of total body iron
- Plasmapheresis:
 - blood volume lost: 15 ml + 30 ml
 - loss of 20 - 25 mg iron

Iron balance

- dietary iron: 10 - 20 mg / day
 - only 20% of dietary iron is absorbed
 - maximum iron absorption: 3 – 4 mg/day
 - physiological iron loss:
 - ♦ 1 mg/day in men und postmenopausal women
 - ♦ additional 0,5 (- 1,2) mg/day in menstruating females

Compensating iron loss from blood donation

- iron compensation / donation interval:
 - 80 – 120 days (♂), 110 – 150 days (♀)
 - Minimum donation interval according to German guidelines: 2 months (♂) or 3 months (♀)
 - negative iron balance at more than 3 – 4 donations (♂) or 1 – 2 donations (♀) per year
- incidence of iron deficiency in regular blood donors:
 - up to 20% in male donors
 - up to 40% in female donors

Responsibilities of Transfusion Medicine

- sufficient blood supply
 - optimal „utilization“ of volunteers willing to give blood
- donor safety
 - determination of Hb prior to blood donation
 - deferral of donors with iron deficiency anemia
 - ♦ (permanent) loss of donors due to short term deferral
 - compensation of iron loss by supplementation
 - ♦ adverse effects of iron medication (GI-system 20%)
 - ♦ missing underlying disease (hemochromatosis, GI-bleeding)
 - ♦ change in blood center - donor relationship

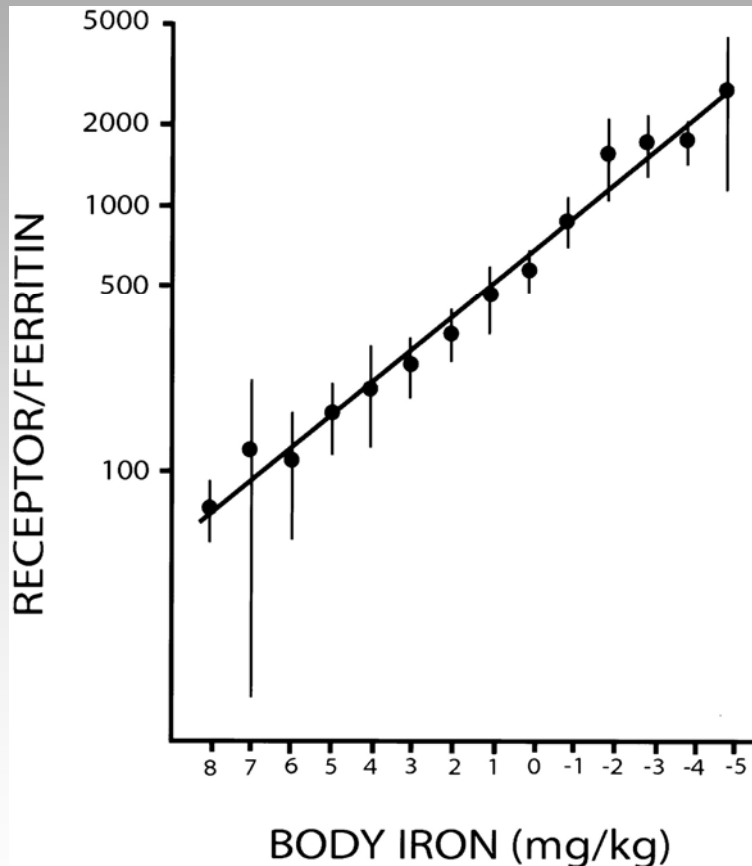
Prevention of iron deficiency by iron supplementation

- studies on menstruating women:
 - administration of 39 mg of elemental iron daily allowed menstruating woman to donate every 8 weeks without significant iron depletion (Simon et al. 1984)
- iron compensation with a lower dose possible?
- can donation frequency or volume be increased?

Laboratory evaluation of body iron

- Serum Ferritin
 - intracellular iron storage protein
 - Serum ferritin level correlates with body iron stores
 - ♦ 1 µg/l equivalent to 8 -10 mg of storage iron
 - ♦ Ferritin < 12 µg/l: indicate complete depletion of iron stores
 - acute phase reactant: false high values in malignancies, infections, liver disease
- Serum Transferrin Receptor (TfR)
 - proportional to cellular expression of the transferrin receptor
 - reflects functional iron compartment / iron-deficient erythropoiesis
 - assay is not standardized!

$$\log(\text{TfR}/\text{F})$$



- quantitative phlebotomy
- inverse linear relationship between logarithm of the ratio of the soluble transferrin receptor to ferritin concentration (TfR/F) and body iron

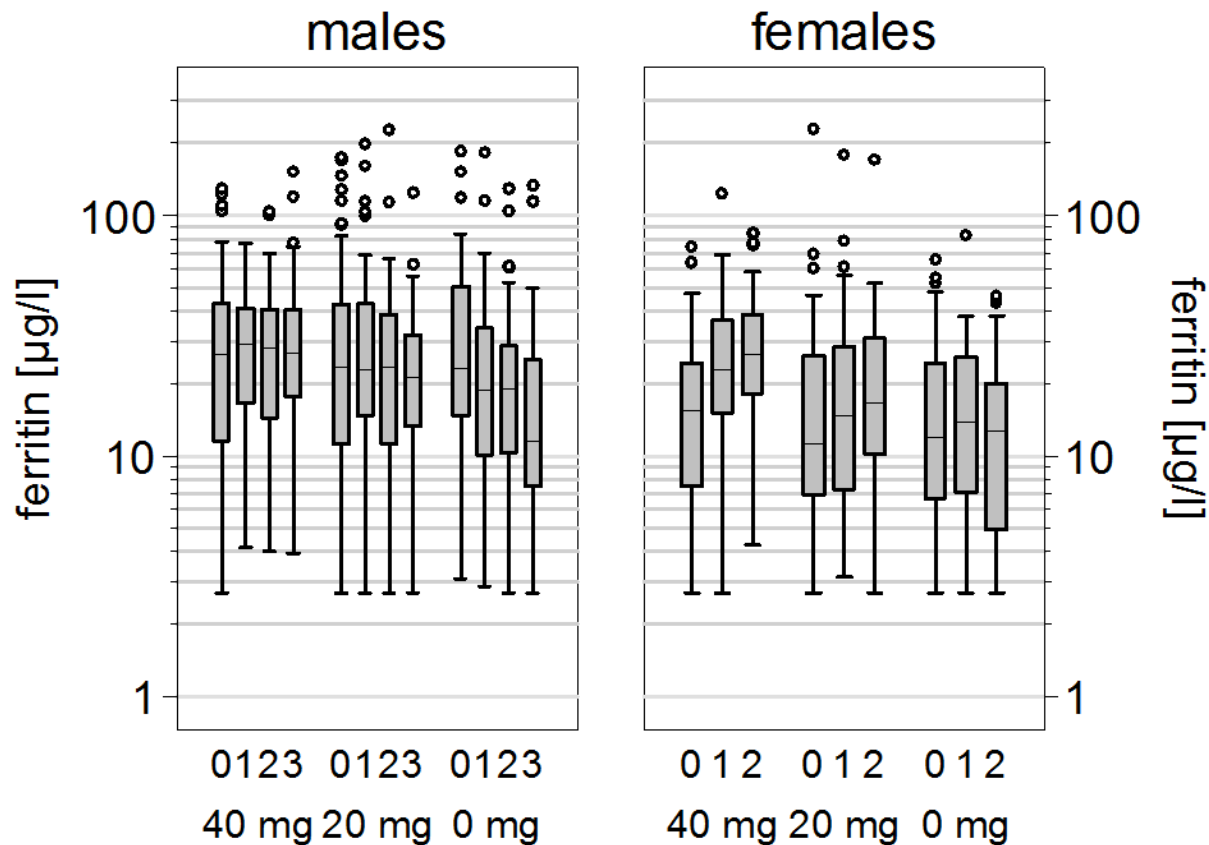
Iron supplementation in blood donors (1)

study design

- placebo-controlled, double-blind study
526 regular blood donors (289 ♂, 237 ♀)
 - iron supplementation:
 - ♦ 40 mg, 20 mg or 0 mg per day of elemental iron (ferrous-gluconate)
 - ♦ ascorbic acid and other vitamins
 - whole blood donation:
 - ♦ 4 donations every 8 weeks (♂)
 - ♦ 3 donations every 12 weeks (♀)
 - ♦ deferral if Hb < 13,5 mg/dL (♂), < 12,5 mg/dL (♀)
 - 237 drop outs (45%)

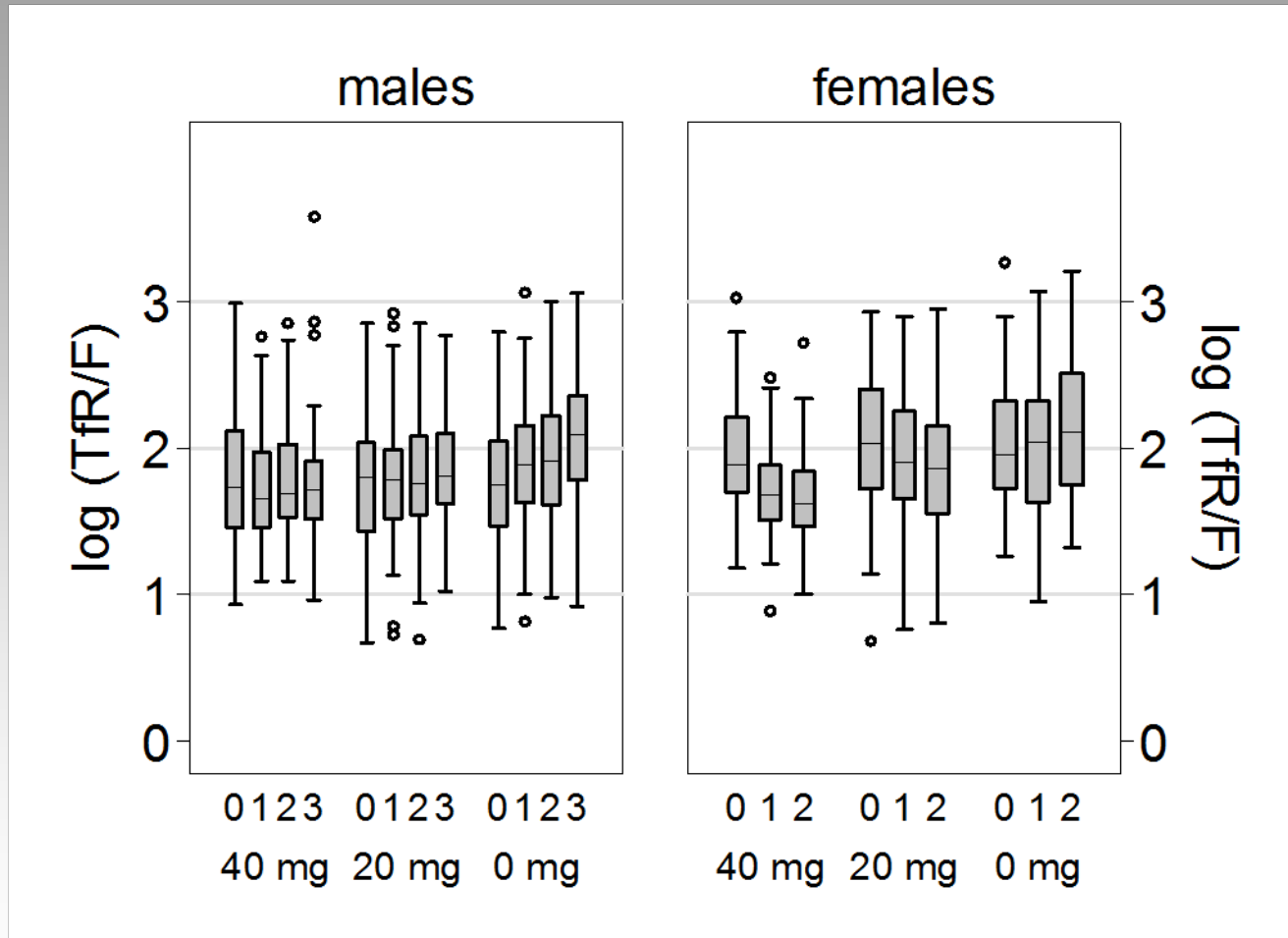
Iron supplementation in blood donors (1)

serum ferritin



Iron supplementation in blood donors (1)

$\log(\text{TfR}/F)$



deferral (Hb): $n = 3$ vs. 2 vs. 9 ; $p = 0,022$ $n = 1$ vs. 2 vs. 10 ; $p = 0,001$

Iron supplementation in blood donors (1)

frequency of adverse effects

adverse effect	40 mg iron	20 mg iron	Placebo only
gastrointestinal complaints	9,4 %	10,7 %	8,4 %
signs of anemia	1,7 %	1,1 %	2,2 %
other symptoms	13,3 %	6,2 %	8,4 %

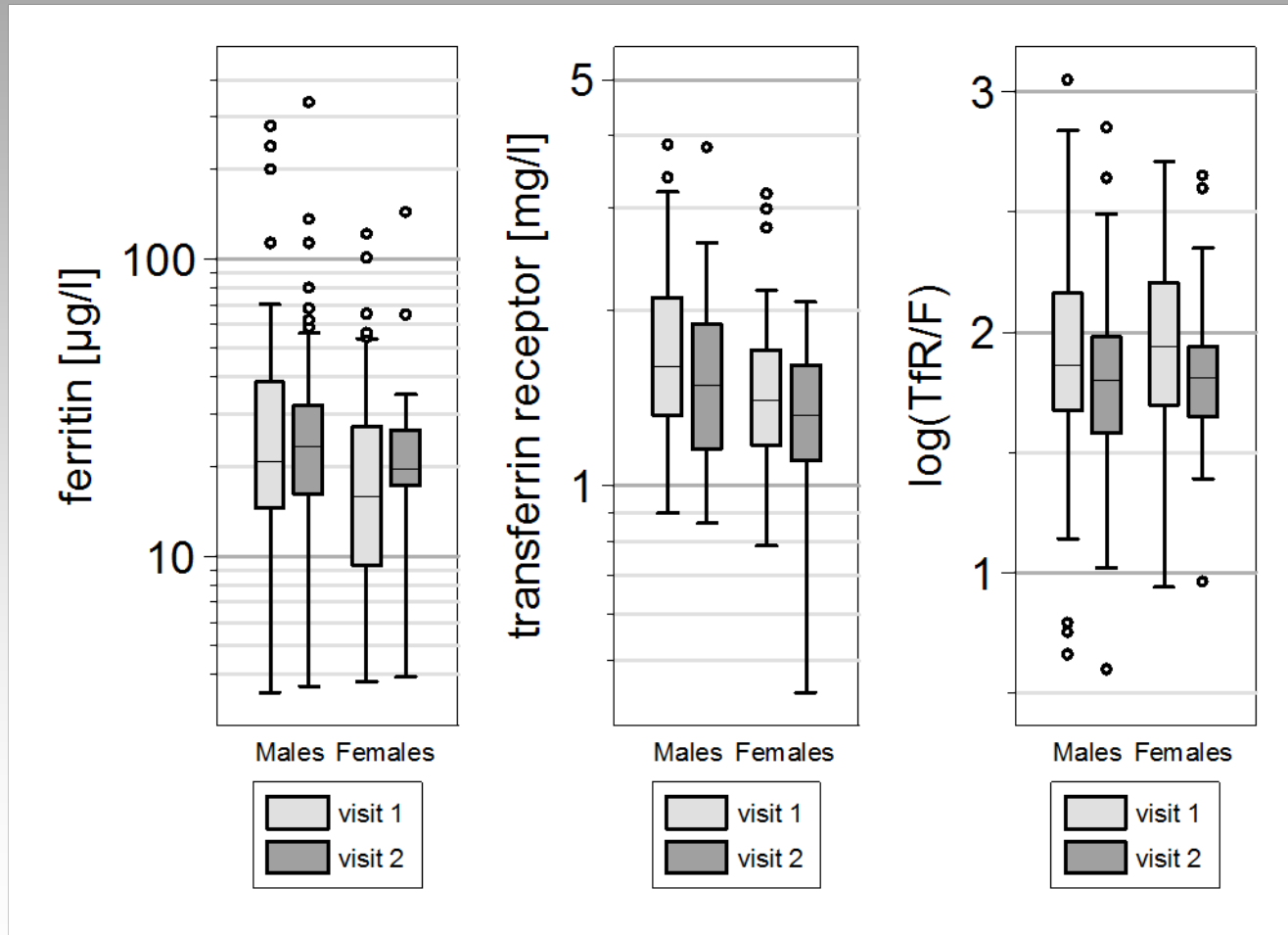
No significant difference between groups

Iron supplementation in blood donors (2)

study design

- open study:
 - 165 regular blood donors (83 ♂, 82 ♀)
 - whole blood donation on day 0
 - ♦ follow-up after two months (♂)
 - ♦ follow-up after three months (♀)
 - iron supplementation:
 - ♦ 20 mg per day of elemental iron (ferrous-gluconate) for 30 days (total dose 600 mg)
 - ♦ ascorbic acid and other vitamins
 - 66 drop outs (40%)

Iron supplementation in blood donors (2)

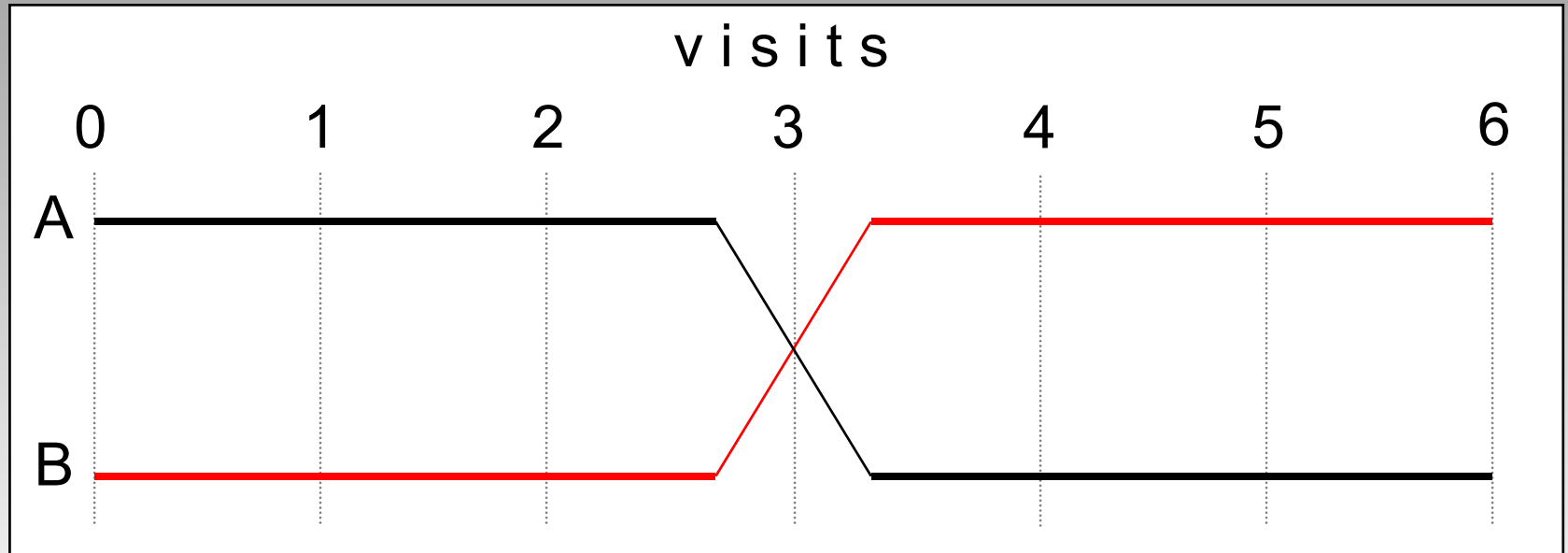


Increasing donation frequency

study design

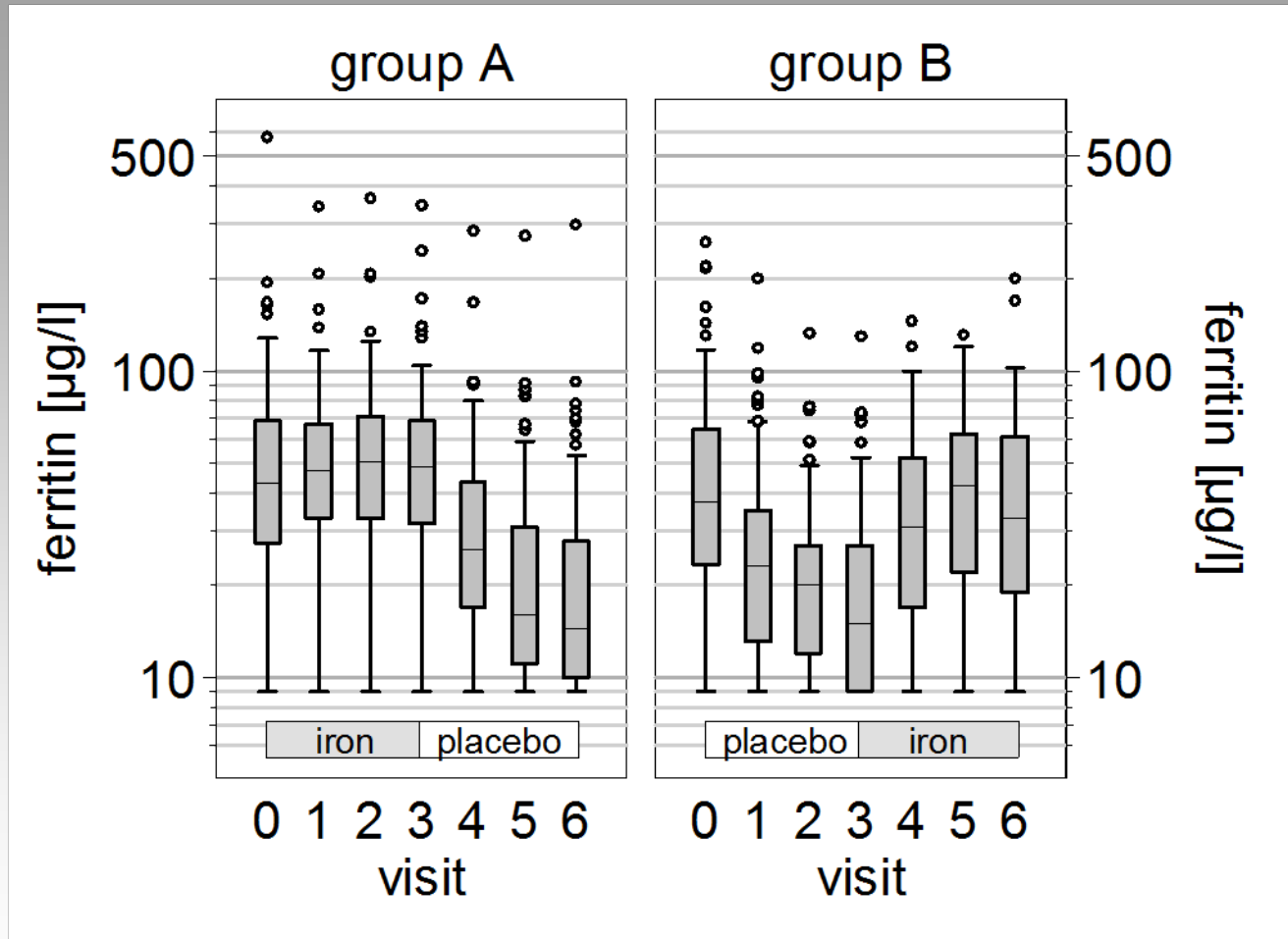
- placebo-controlled double-blind study:
260 participants (247 ♂, 3 ♀)
 - regular blood donors, body weight ≥ 68 kg,
Hb $\geq 14,5$ g/dl
 - 2-unit RBC apheresis at intervals of 8 - 10 weeks
 - ♦ Haemonetics MCS+, protocol SDR
 - iron supplementation: daily 100 mg of iron(II) or placebo, respectively

Increasing donation frequency study design



- Group A: iron from visit 0-3, placebo from visit 3-6, Group B: placebo from visit 0-3, iron from visit 3-6
- Deferral if Hb < 14 g/dl
- 66 dropouts (25%)

Increasing donation frequency serum ferritin



deferral (Hb): 18% of 1519 visits (placebo: 186, iron: 82; $p < 0,001$)

Increasing donation frequency

frequency of adverse effects

adverse effects	Iron treatment	Placebo treatment
gastrointestinal complaints	8,7%	5,2%
signs of anemia	3,9%	3,9%
other symptoms	5,7%	8,2%

No significant difference between groups

Conclusion

- 20 mg iron for 30 days (total dose 600 mg) adequately compensates for iron loss from whole blood donation
- 100 mg iron daily compensates a substantial increase in donation frequency
- tolerance of iron supplementation was good
- limited supplementation (study 2) less likely to obscure underlying disease
- the form of iron used (study 1,2) meets the European Community criteria for dietary foods for special medical purposes

Thank you

