

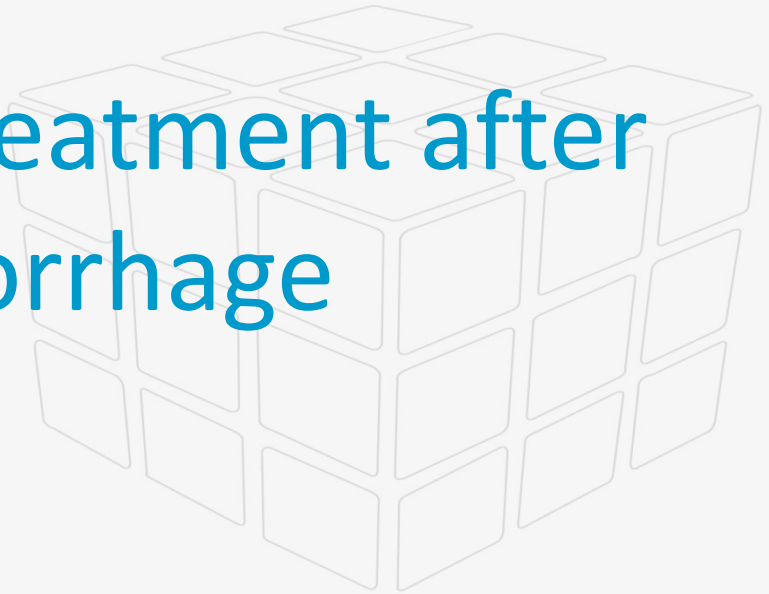
Intravenous iron treatment after postpartum haemorrhage

Charlotte Holm, MD, PhD

Department of Obstetrics

Rigshospitalet

Copenhagen, Denmark



Conflict of interest



Rigshospitalet

PHARMACOSMOS
Committed to Quality

UNIVERSITY OF
COPENHAGEN



FACULTY OF HEALTH AND MEDICAL SCIENCES



Innovation Fund Denmark
RESEARCH, TECHNOLOGY & GROWTH

Consequences of postpartum anaemia

- Fatigue and exhaustion
- Impaired quality of life
- Depression
- Breastfeeding duration
- Mother/child interaction



Exhausted Mother by Sylvestre Evrard

Bodnar LM *et al.* American Journal of Obstetrics and Gynecology. 2005
Lee KA, Zaffke ME. J Obstet Gynecol Neonatal Nurs. 1999
Rioux FM *et al.* Can J Diet Pract Res. 2006

Blood transfusion

2 % of Danish women receive blood transfusion at delivery¹

Side effects

- Adverse reactions
 - Fever, allergy, dyspnea, infection
 - Incorrect bloodtype
 - Viral transmission
- Alloimmunisation²
 - Future pregnancy
 - Future transfusion/transplantations



¹Holm C. *et al*, BJOG, 2012

²Pavord S. *et al*, Br J Haematol. 2012

Oral iron treatment

- Mild to moderate anaemia
- Low cost
- Long treatment period (months)¹
- Gastrointestinal side effects (10-30%)²
 - Constipation
 - Haemorrhoids



¹Camaschella C. Iron-deficiency anemia. N Engl J Med. 2015.

²Markova V *et al*, Treatment for women with postpartum iron deficiency anaemia, Cochrane Database Syst Rev. 2015.

Intravenous iron treatment

- Fast response
- High single dosing
- High cost
- Side effects¹
 - Hypersensitivity reactions
 - Anaphylaxis (very rare)

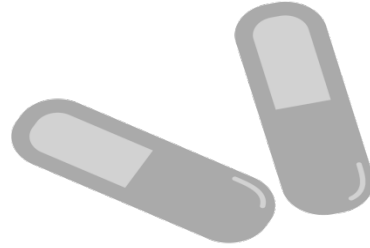


¹European Medicines Agency. Assessments Report for: Iron containing intravenous (IV) medicinal products, 2013.

IV IRON VERSUS ORAL IRON



VS



Holm C, Thomsen LL, Norgaard A, Langhoff-Roos J, Single-dose intravenous iron infusion or oral iron for treatment of fatigue after postpartum haemorrhage: a randomised controlled trial



Background



- Previous trials with a primary focus on haematological improvement of postpartum anaemia
- A recent Cochrane review recommends randomised controlled trials with clinical outcomes¹

¹ Markova V *et al*, Treatment for women with postpartum iron deficiency anaemia, Cochrane Database Syst Rev. 2015.

Aim



- To compare IV iron with oral iron after postpartum haemorrhage in a randomised controlled trial
- We hypothesised that IV iron is superior to currently used oral iron as measured primarily by aggregated patient-reported physical fatigue within 12 weeks

Multidimensional Fatigue Inventory



Five dimensions of fatigue

General

Physical

Mental

Reduced motivation

Reduced activity

Physical fatigue - 16 point scale

Minimal clinical relevant difference: 1.8

A hand holding a black pen with gold accents is shown filling out a form. The form is titled 'Instructions:' and contains text about the purpose of the inventory. It lists five statements for rating, each with a 16-point scale (yes, that is true to no, that is not true). The hand is currently writing on the first statement's scale.

Instructions:

By means of the following statements we would like to get an idea of how you have been feeling lately. There is, for example, the statement:

... is entirely true ... feeling relaxed lately, please place ... that is not true

The more you disagree with a statement, the more X's you should place next to each statement.

1. I feel fit	yes, that is true	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	no, that is not true
2. Physically I feel only able to do a little	yes, that is true	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	no, that is not true
3. I feel very active	yes, that is true	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	no, that is not true
4. I feel like doing all sorts of nice things	yes, that is true	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	no, that is not true
5. I feel tired	yes, that is true	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	no, that is not true



Study design

WOMEN \leq 48 HRS AFTER DELIVERY

PPH \geq 700 mL or
PPH $>$ 1000 mL
+ Hb $>$ 6.5 g/dL
(4.0 mmol/L)

IV IRON

1200 mg iron
isomaltoside
(n=100)

CONTROL

Current treatment
practice with oral iron
(n=100)
e.g. 100 mg daily

FOLLOW-UP VISITS

Questionnaires

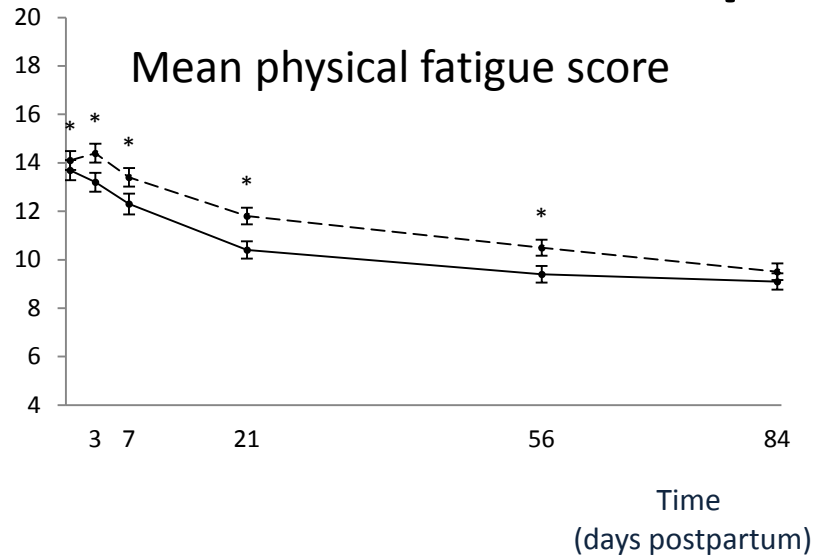
- MFI
- EPDS

Blood sample

- Red blood count
- Iron status



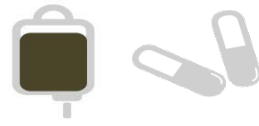
Results – primary outcome



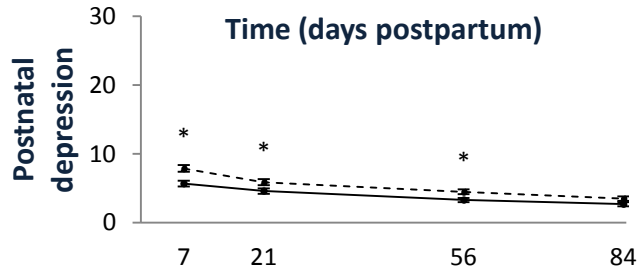
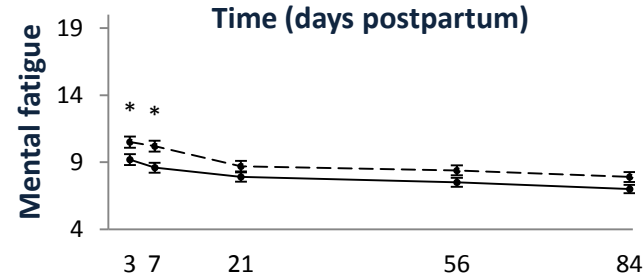
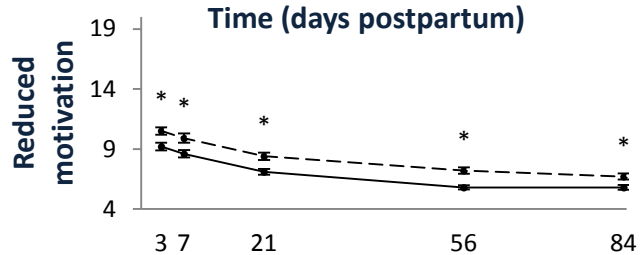
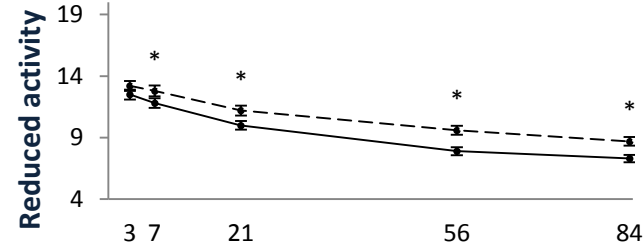
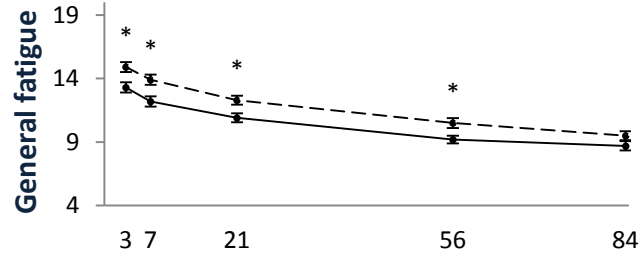
IV iron: —
Oral iron: - - -

* $P < 0.05$

IV iron group vs Oral iron group				
	n	LsMean	Estimate (95% CI)	P value
FULL ANALYSIS SET				
Intravenous iron	97	-3.60	-0.97 (-1.65; -0.28)	0.006
Oral iron	99	-2.63		



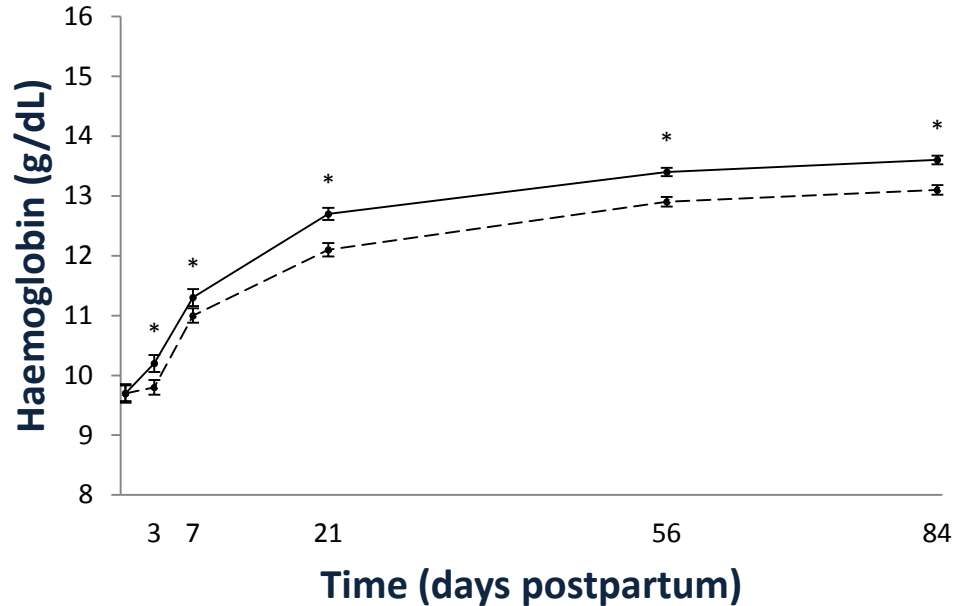
Fatigue and depression



IV iron: —
Oral iron: - - -

* $P < 0.05$ for change from baseline

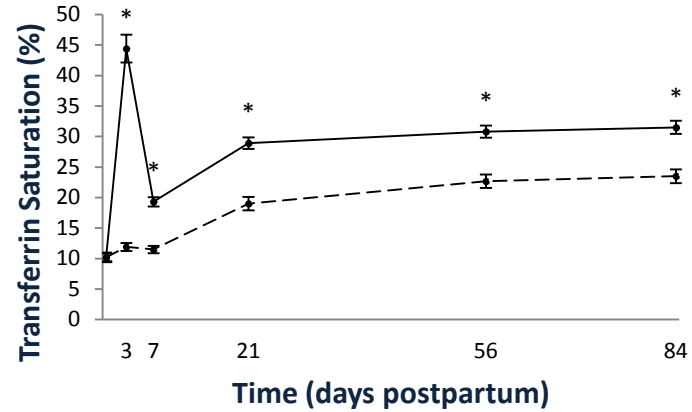
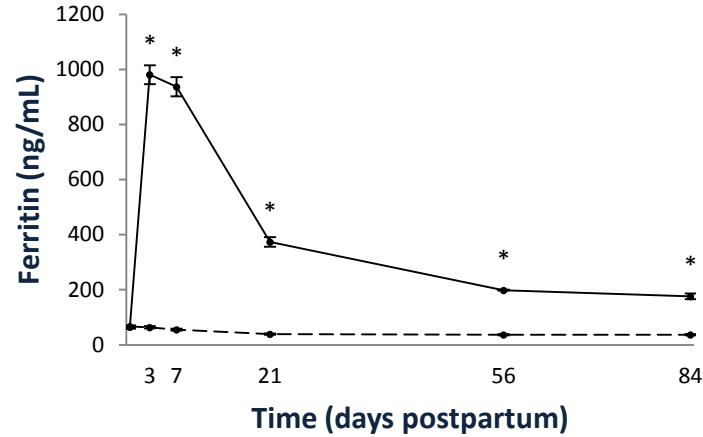
Haemoglobin response



IV iron: —
Oral iron: - - -

* $P < 0.05$ for change from baseline

Iron response



IV iron: —
Oral iron: - - - - -

* $P < 0.05$



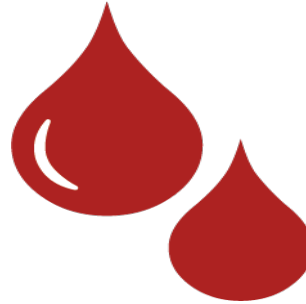
Conclusion

- The clinical efficacy of single-dose IV iron was not proven superior to the current treatment practice with oral iron, as the predefined change in physical fatigue score was not met.
- IV iron was associated with a statistically significant improvement in fatigue and depression scores, a significantly faster haematopoietic response and replenishment of iron stores.

IV IRON VERSUS BLOOD TRANSFUSION



VS



Holm C, Thomsen LL, Norgaard A, Langhoff-Roos J, Single-dose intravenous iron infusion versus red blood cell transfusion for treatment of severe postpartum anaemia: a randomised controlled pilot study

Background



- The Dutch WOMB study showed less fatigue in women treated with blood transfusion compared to expectant management¹
- In a French retrospective study in women with severe postpartum anaemia, administration of IV iron reduced the number of women receiving blood transfusions with 65%²

¹Prick BW, *et al.* BJOG. 2014.

²Broche DE, *et al.* Gynécologie Obstétrique & Fertilité. 2004.

Aim



- A pilot study to evaluate the feasibility of randomising women to blood transfusion or IV iron
- To describe patient-reported and haematological outcomes of IV iron compared with blood transfusion for the treatment of severe postpartum anaemia

Study design



WOMEN \leq 48 HRS AFTER DELIVERY

PPH > 1000 mL
AND
Hb 5.6 - 8.0 g/dL
(3.5-5.0 mmol/L)

IV IRON

1500 mg iron isomaltoside
(n=7)

BLOOD TRANSFUSION

Hb 5.6-6.3 g/dL - 2 units RBCs
Hb 6.4-8.1 g/dL - 1 unit RBCs
(n=6)

FOLLOW-UP VISITS

Questionnaires

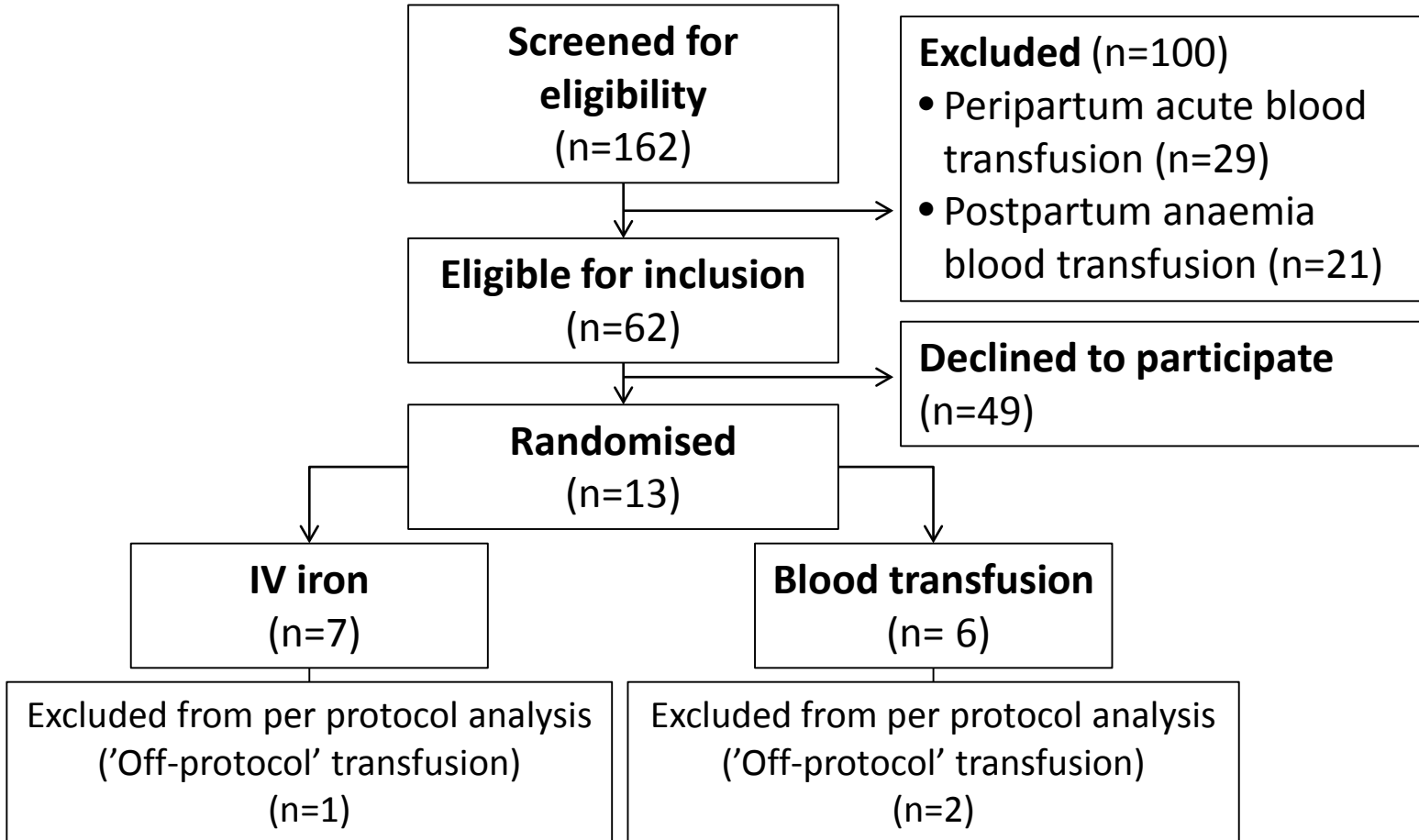
- MFI
- EPDS

Blood sample

- Red blood count
- Iron status



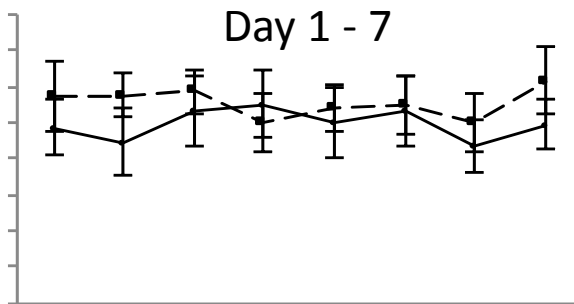
Flow chart



Patient-reported outcomes



Mean physical fatigue score

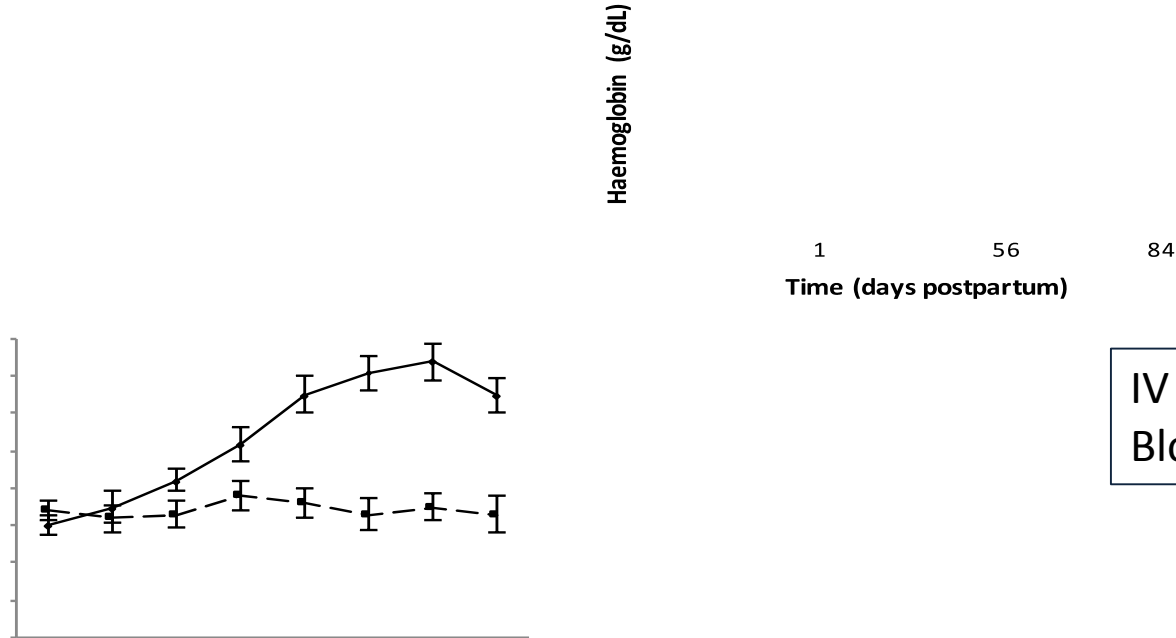


Week 1 - 12

artum)

IV iron:	_____
Blood transfusion:	-----

Haematological response



Conclusion



- A larger trial is feasible, but difficult and a multicentre trial is needed to confirm the findings

Clinical interpretation

IV iron is not a first choice for all women with postpartum haemorrhage

But an option in special cases such as:

- Excessive post partum bleeding
- Intolerance to oral iron
- Malabsorption of iron
- Need of fast correction of iron deficiency
- To avoid blood transfusion

THANK YOU

- Jens Langhoff-Roos
- Lars Lykke Thomsen
- Astrid Norgaard

