



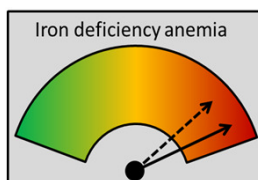
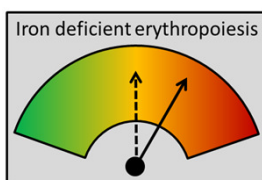
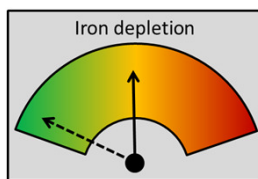
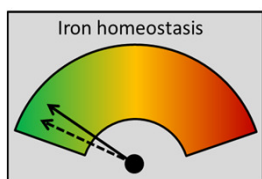
Iron monitoring and Hb deferrals

Can we do more?

Saurabh Zalpuri
Donor Studies
s.zalpuri@sanquin.nl



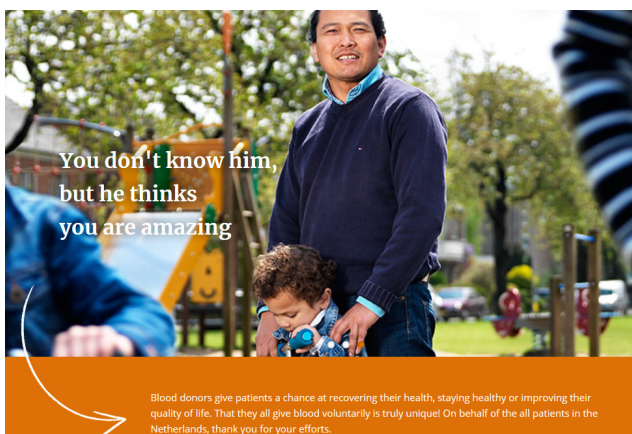
Iron depletion



↑ Iron stores
↑ Haemoglobin



Together with the donor, we ensure a better life for patients



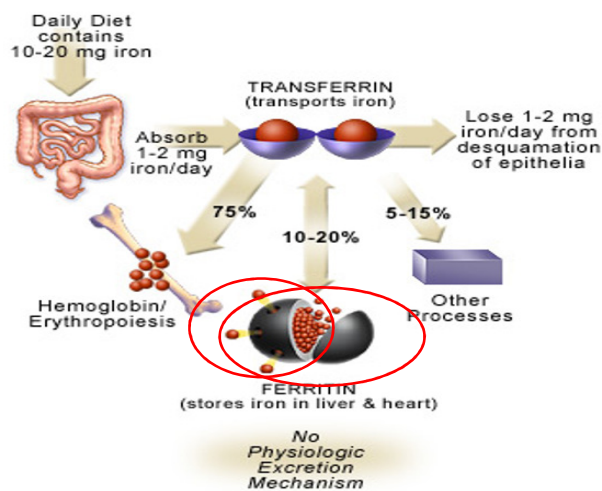
You don't know him,
but he thinks
you are amazing

Blood donors give patients a chance at recovering their health, staying healthy or improving their quality of life. That they all give blood voluntarily is truly unique! On behalf of the all patients in the Netherlands, thank you for your efforts.

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ZPP and Ferritin



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Donor InSight

- Cohort study on donor base characteristics, health and motivation
- Follow-ups:
 - DIS-I: 2007-2009 baseline questionnaire (n=31,338),
 - DIS-II: 2012-2013 questionnaire (n=34,823 (22,132 from DIS-I))
 - **DIS-III: 2015 questionnaire, genetics and blood sampling (n=3,000)**
- Study population:
 - Whole blood donors
 - < 70 years old
 - Minimum one follow up donation/ attempt
 - Zinc Protoporphyrin (ZPP) and Ferritin measurements



Added value of Ferritin and ZPP to Hb screening.

Outcome: Low Hb deferrals.



Study population

	Women (n= 593)	Men (n= 600)
Age, in years	47.7 (12.1)	49.5 (11.8)
Hb (mmol/L)	8.5 (0.5)	9.4 (0.6)
Zinc Protoporphyrin (µmol/mol)	68.2 (24.8)	61.4 (19.9)
Ferritin (µg/L)	37.6 (27.7)	51.2 (51.1)

All variables presented as means and standard deviations unless otherwise indicated.

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Predictive value of Ferritin and ZPP?

	OR (95% CI)	AUC		OR (95% CI)	AUC		OR (95% CI)	AUC
Hb			Hb + Ferritin		0.80	Hb + ZPP + Ferritin		
Women	0.08 (0.03- 0.18)	0.79	Women			Women		0.80
Men	0.14 (0.05- 0.41)	0.76	Hb	0.11 (0.04- 0.26)		Hb	0.13 (0.05- 0.32)	
			Ferritin	0.97 (0.95- 0.99)	0.77	Ferritin	0.98 (0.96-1.0009)	
			Men			ZPP	1.009 (0.99- 1.02)	
			Hb	0.17 (0.06- 0.48)		Men		0.76
			Ferritin	0.97 (0.95- 0.99)		Hb	0.18 (0.06- 0.51)	
Ferritin						Ferritin	0.97 (0.95- 1.002)	
Women	0.96 (0.93- 0.97)	0.72	Hb + ZPP			ZPP	1.009 (0.99- 1.02)	
Men	0.96 (0.94- 0.99)	0.71	Women		0.79	Hb		
			Hb	0.11 (0.04- 0.26)		Ferritin		
			ZPP	1.01 (1.002-1.02)		ZPP		
			Men		0.77	Hb		
			Hb	0.16 (0.06- 0.46)		Ferritin		
ZPP			ZPP	1.01 (1.0005-1.03)		ZPP	1.009 (0.99- 1.02)	
Women	1.02 (1.01- 1.03)	0.66						
Men	1.02 (1.006-1.03)	0.60						

Hb + Ferritin predicts deferral better than Hb alone

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Any other variables of interest?

Full model: Hb, ZPP, Ferritin, donations 2-yr prior to the study, age, BMI, low Hb deferral at last donation, season and blood group O negative

	OR (95% CI)	AUC
Women		0.80
Hb	0.12 (0.05- 0.29)	
Ferritin	0.97 (0.95- 0.99)	
Prior donations	0.80 (0.66- 0.97)	
Men		0.80
Hb	0.16 (0.05- 0.49)	
Ferritin	0.96 (0.93- 0.98)	
Prior donations	0.75 (0.63- 0.90)	
Age	1.05 (1.006- 1.09)	

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In this study, based on low Hb deferral...

- Ferritin and ZPP do not predict Hb deferral much better than just Hb.
- Ferritin + Hb predicts Hb deferral slightly better than just Hb.
- The existing standard practice is based upon Hb deferral and *not* Ferritin deferral.
- Important to know that a clear picture of donor deferral would not emerge unless deferral practices (*include ferritin*) are modified too.
- Ferritin may predict a low Hb deferral 4-5 donations down the line but who knows...

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ZINC Study

- Whole blood donors cohort
- First-time and repeat donors (8000 +/- donors)
- Follow-up 2009-2014
 - Repeated ZPP measurements
- Analysis
 - Linear mixed models
 - Number of donations as time-varying covariate



**Added value of ZPP to Hb screening.
Outcome: Future Hb levels.**



Study Population

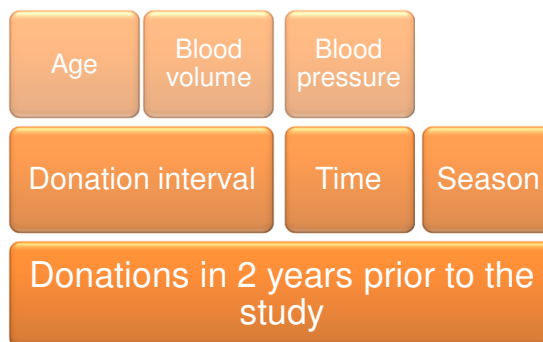
	Women (n= 5162)	Men (n= 3005)
Age (years)	37.9 (13.9)	41.9 (14.4)
Blood volume (L)	4.3 (0.5)	5.6 (0.5)
Number of donations	2.3 (2.3)	2.9 (3.6)
Number of donations in 2 years prior to the study	5.5 (5.3)	6.7 (7.1)
Hb (mmol/L)	8.7 (0.7)	9.1 (0.8)
ZPP (μmol/mol)	66.49 (26.4)	59.1 (22.5)
New donors	3182 (61.6%)	1664 (55.4%)
Repeat donors	1980 (38.4%)	1341 (44.6%)

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Does ZPP predict future Hb levels?

Hb level at the next donation				
	Women	p-value	Men	p-value
	Coefficient (95% CI)		Coefficient (95% CI)	
Univariate model				
Log of ZPP at previous donation	-0.17 (-0.22; -0.11)	<0.001	-0.07 (-0.14; -0.007)	0.03
AIC	-8964.8		7778.3	
Hb level at the next donation				
	Women	p-value	Men	p-value
	Coefficient (95% CI)		Coefficient (95% CI)	
Full model				
Log of ZPP at previous donation	-0.16 (-0.22; -0.11)	<0.001	-0.09 (-0.16; -0.02)	0.007
AIC	8977.1		7809.7	



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New and Repeat donors

	Hb level at the next donation Coefficient (95% CI), p-value			
	Women		Men	
	New	Repeat	New	Repeat
Log of ZPP at previous donation	-0.08 (-0.16; -0.02) 0.04	-0.25 (-0.32; -0.18) <0.001	-0.02 (-0.12; 0.08) 0.7	-0.10 (-0.19; -0.01) 0.02

	Hb level at the next donation Coefficient (95% CI), p-value	
	Pre-Menopausal women	Post-Menopausal women
Log of ZPP at previous donation	-0.19 (-0.26; -0.12) <0.001	-0.10 (-0.19; -0.02) 0.01

ZPP predicts Hb levels in new and repeat female donors

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Sensitivity analysis

Hb^{alt} = Hemoglobin measurement from a venous sample

$$ZPP^{alt} = ZPP * Hb^{alt}$$

	Women	Men
	Hb ^{alt} level at the next donation Coefficient (95% CI), p-value	
Log of ZPP at previous donation	-0.22 (-0.28; -0.16) <0.001	-0.03 (-0.10; 0.02) 0.09
	Hb level at the next donation	
Log of ZPP ^{alt} at previous donation	-0.11 (-0.16; -0.06) <0.001	-0.01 (-0.07; 0.05) 0.7
	Hb ^{alt} level at the next donation	
Log of ZPP ^{alt} at previous donation	-0.17 (-0.23; -0.11) <0.001	-0.11 (-0.16; -0.05) <0.001

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In this study, based on subsequent Hb levels...

- With every unit increase in ZPP, Hb at the next donation decreased.
 - Among new and repeat female donors.
 - Statistically significant
- Effect estimate (regression coefficient) were very small.
- Clinically relevant?
- What next?

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Ferritin screening **IN** Donors - iron **M**onitoring to prevent iron deficiency and low haemoglobin (**FIND'M**)

- **Intervention: Ferritin screening 1st visit; and every 5th donation subsequently**
- Staggered implementation
- Cluster randomization

Steps	One-month pilot	Time					
		0-4 months	4-8 months	8-12 months	12-16 months	16-20 months	24 months
1	0	1	1	1	1	1	Follow-up
2	0	0	1	1	1	1	Follow-up
3	0	0	0	1	1	1	Follow-up
4	0	0	0	0	1	1	Follow-up

0= No ferritin screening; 1= Ferritin screening initiated

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