# Donor health studies

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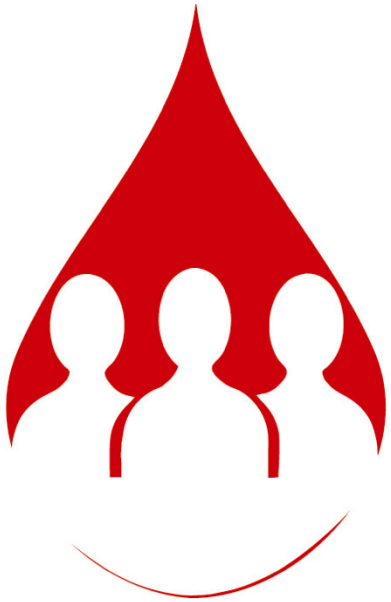


# Zika risk assessment:
# Incidence of transfusion during pregnancy

Zika infection in 1st and 2nd trimester associated with microcephaly
Zika infection in 3rd trimester associated with late-onset microcephaly?

In non-endemic areas:
What is the risk of donation from an infectious donor?
What is the risk of transfusing that unit to a pregnant woman?

# Transfusion of pregnant women in Denmark and Sweden

## Denmark – pregnancies and transfusions 2000-2008

| Year | Births | Number of transfusions | | | Total transfusions in Denmark | % units transfused to pregnant women | % units transfused to women in 1st and 2nd trimester | Units per 1,000 births |
|---|---|---|---|---|---|---|---|---|
| | | 1st trimester | 2nd trimester | 3rd trimester | | | | |
| 2000 | 66,651 | 33 | 47 | 143 | 426,208 | 0.052 | 0.019 | 3.3 |
| 2001 | 64,698 | 33 | 49 | 116 | 458,452 | 0.043 | 0.018 | 3.1 |
| 2002 | 63,382 | 54 | 37 | 222 | 501,407 | 0.062 | 0.018 | 4.9 |
| 2003 | 63,868 | 23 | 49 | 220 | 490,803 | 0.059 | 0.015 | 4.6 |
| 2004 | 63,918 | 30 | 29 | 156 | 449,405 | 0.048 | 0.013 | 3.4 |
| 2005 | 63,512 | 45 | 38 | 169 | 444,289 | 0.057 | 0.019 | 4.0 |
| 2006 | 64,226 | 33 | 52 | 159 | 451,685 | 0.054 | 0.019 | 3.8 |
| 2007 | 63,928 | 24 | 50 | 198 | 450,716 | 0.060 | 0.016 | 4.3 |
| 2008 | 64,211 | 17 | 35 | 149 | 442,264 | 0.045 | 0.012 | 3.1 |
| Sum/mean | 578,394 | 292 | 386 | 1,532 | 4,115,229 | 0.054 | 0.016 | 3.8 |

# Transfusion of pregnant women in Denmark and Sweden

## Sweden – pregnancies and transfusions 2000-2010

| Year | Births | Number of transfusions | | | Total transfusions in Sweden | % units transfused to pregnant women | % units transfused to women in 1st and 2nd trimester | Units per 1,000 births |
|---|---|---|---|---|---|---|---|---|
| | | 1st trimester | 2nd trimester | 3rd trimester | | | | |
| 2000 | 87,250 | 48 | 68 | 437 | 624,154 | 0.089 | 0.019 | 6.3 |
| 2001 | 87,926 | 34 | 45 | 380 | 592,107 | 0.078 | 0.013 | 5.2 |
| 2002 | 92,152 | 46 | 79 | 283 | 576,704 | 0.071 | 0.022 | 4.4 |
| 2003 | 94,604 | 71 | 43 | 394 | 672,820 | 0.076 | 0.017 | 5.4 |
| 2004 | 95,101 | 170 | 96 | 367 | 672,614 | 0.094 | 0.040 | 6.7 |
| 2005 | 94,627 | 97 | 62 | 570 | 678,802 | 0.107 | 0.023 | 7.7 |
| 2006 | 97,226 | 123 | 154 | 637 | 691,146 | 0.132 | 0.040 | 9.4 |
| 2007 | 97,536 | 73 | 90 | 325 | 714,968 | 0.068 | 0.023 | 5.0 |
| 2008 | 98,659 | 57 | 80 | 424 | 723,143 | 0.078 | 0.019 | 5.7 |
| 2009 | 99,372 | 73 | 108 | 590 | 743,006 | 0.104 | 0.024 | 7.8 |
| 2010 | 103,814 | 55 | 234 | 658 | 720,608 | 0.131 | 0.040 | 9.1 |
| Sum/mean | 1,048,267 | 847 | 1,059 | 5,065 | 7,410,072 | 0.094 | 0.026 | 6.7 |

# Transfusion of pregnant women in Denmark and Sweden

- 11,525,301 units and 1,626,661 pregnancies
- percentage of products used for pregnant women was low but much higher in Sweden than in DK (0.094% vs. 0.054%)
- The number of units used per pregnancy is about 75% higher in Sweden (6.7 vs. 3.8 units/1,000 pregnancies)
- 1-2 women per 1,000 pregnancies require transfusion

## Conclusion

- 5-9 per 10,000 units of blood are transfused to pregnant women

# Low hemoglobin and risk of infection

- Low Hb is associated with poor general health and linked to anemia of chronic disease
  => increased risk of infection?
- Iron is needed by replicating microorganisms
  => decreased risk of infection?
- Association between Hb and risk of infection among healthy individuals not yet investigated.
- 1998-2012: 497,390 donors; 5,458,499 donations; window: 3 months after each donation; 1,339,362 person years of observation

# Low hemoglobin and prescriptions of anti-microbials

| | Pre-menopausal women | | | | Post-menopausal women | | | | Men | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Events | Person years at risk | HR | 95%CI | Events | Person years at risk | HR | 95%CI | Events | Person years at risk | HR | 95%CI |
| Deferral <12.6/13.6 g/dL | **29,539** | **74,158** | **0.92** | **0.91-0.93** | **3,741** | **11,858** | **0.93** | **0.89-0.97** | **5,994** | **28,903** | **0.91** | **0.88-0.94** |
| No deferral (reference) | 159,025 | 375,022 | 1 | | 41,685 | 122,975 | 1 | | 174,135 | 746,528 | 1 | |
| Very low Hb <0.1% | **167** | **517** | **0.8** | **0.67-0.93** | **46** | **232** | **0.67** | **0.45-1.00** | 329 | 1,502 | 1.06 | 0.89-1.25 |
| No very low Hb (reference) | 188,397 | 448,663 | 1 | | 45,380 | 134,601 | 1 | | 179,800 | 773,928 | 1 | |

Adjusted for age, similar when stratified for previous year donation frequency

# Low hemoglobin and risk of infection

Conclusions:

- Hb below deferral guidelines was not associated with risk of hospital contact due to infection.
- Hb below deferral guidelines was associated with a slightly reduced risk of filling a prescription for anti-microbials:
  HR: 0.91-0.93

(Kotze et al, in revision)

Upcoming: Nation-wide pseudo-cluster-randomised trial of ferritin-guided iron supplementation:
Does iron supplementation affect risk of infection?

# The Danish Blood Donor Study - Status

Initiated March 2010

110,000 blood donors have been included

Work dataset: 92,000 participants; 350,000 person-years of follow-up by June 2015

All baseline samples transferred to automated sample management system

DNA purified from 55,000 samples

>600,000 plasma archive samples from every donation available for research

# *S. aureus* colonisation among healthy individuals

- A nasal swab has been obtained from 2,500 donors; aim 10,000
- Primary aim: to study the associations of *S. aureus* colonisation with morbidity (infections, metabolic disorders, autoimmune diseases)
- Secondary aims:
  Nasal microbiome and donor morbidity
  *S. aureus*/nasal microbiome and recipient outcome

# Nasal *S. aureus* colonisation among healthy individuals

| | Women | | | | | Men | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Total** | ***S. aureus* positive** | | ***S. aureus* negative** | | **Total** | ***S. aureus* positive** | | ***S. aureus* negative** | |
| | **n** | **n** | **%** | **n** | **%** | **n** | **n** | **%** | **n** | **%** |
| **Number of participants:** | 758 | 246 | 32 | 512 | 68 | 1141 | 516 | 45 | 625 | 55 |
| Age<25: | 144 | 58 | 40 | 86 | 60 | 141 | 71 | 50 | 70 | 50 |
| 25≤age<35: | 198 | 74 | 37 | 124 | 63 | 325 | 146 | 45 | 179 | 55 |
| 35≤age<45: | 129 | 41 | 32 | 88 | 68 | 248 | 120 | 48 | 128 | 52 |
| 45≤age<55: | 155 | 39 | 25 | 116 | 75 | 221 | 97 | 44 | 124 | 56 |
| Age≥55: | 132 | 34 | 26 | 98 | 74 | 206 | 82 | 40 | 124 | 60 |
| **BMI, kg/m2** | 26.8 (25.1-28.6) | 24.4 (23.9-24.9) | | 24.7 (24.4-25.1) | | 25.7 (25.4-26.1) | 25.6 (25.3-25.9) | | 25.3 (25.1-25.6) | |
| **Current smoker (%)** | 10.2 | 6.4 | | 12.1 | | 9.2 | 6.5 | | 11.4 | |

*S. aureus* colonisation: lower with age (OR=0.85 with 10 year older), smoking (OR=0.51) and female sex (OR=0.60)

Enhancement broth: more S. aureus than previously thought

Women have lower concentrations of bacteria than men

Decreasing smoking prevalence: the reason for the increasing prevalence of *S. aureus* colonisation?

Colonisation and transfusion risk?

# *S. aureus* colonisation and HLA

HLA-DR15 is associated with colonisation
Odds ratio for DR15 carrier: 1.84 (CI: 1.08-3.16)

Tendency for HLA-DQ6:
Odds ratio 1.55 (CI: 0.98-2.45)

Kotb et al, Nature Medicine 2012

Invasive group A streptococcal infections:

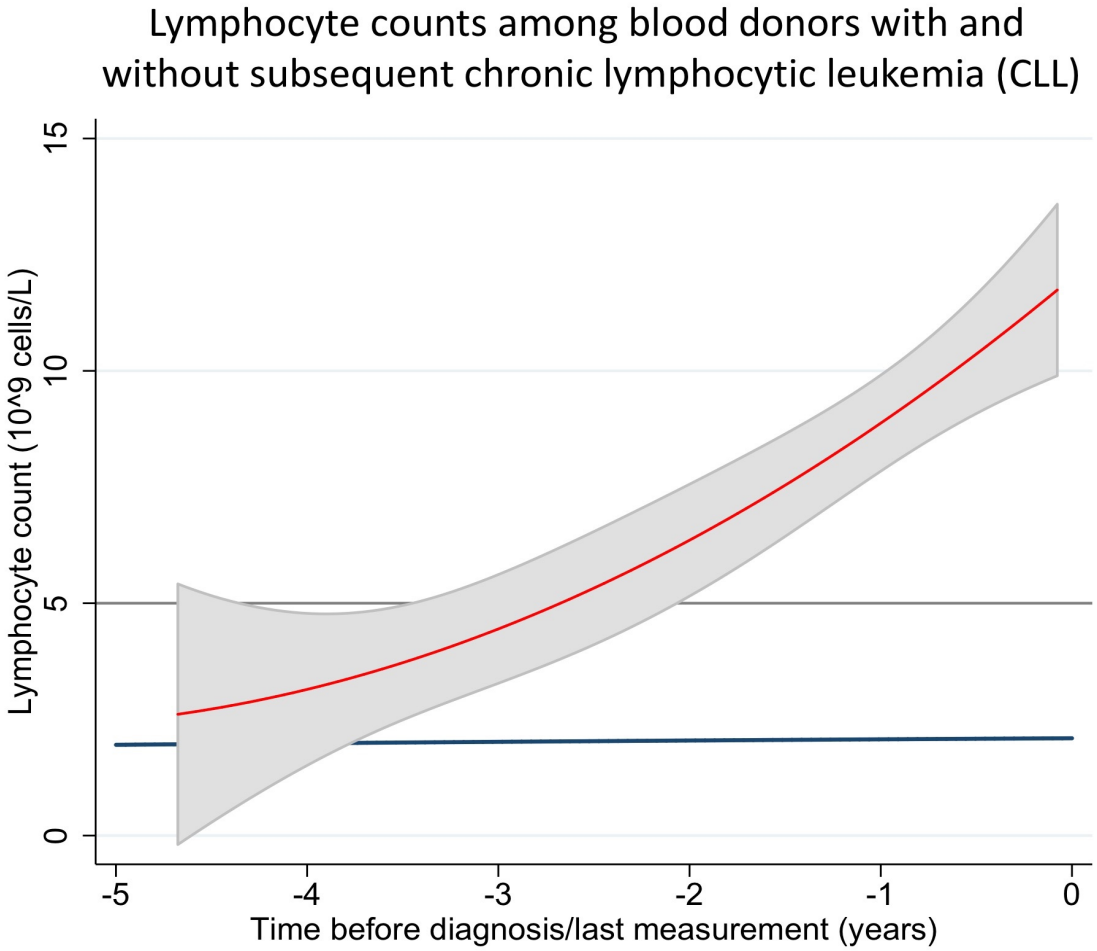
*Patients with the DRB1*1501/DQB1*0602 haplotype mounted significantly reduced responses and were less likely to develop severe systemic disease ($P < 0.0001$).*

# Risk assessment of donors using hematology analyzer data (unfortunately not infection-related...)
# Prediction of chronic lymphatic leukemia

- Sysmex and hemoglobin measurements:
  Full white cell differential: 65,000 measurements /y
  Red cell parameters: approx. 150,000 measurements /y

Proof of concept:

- One small donation facility: 118,430 lymphocyte measurements from 15,448 donors during 13 years
- 32 donors had 1 to several measurements of lymph.>5
- 7 donors subsequently diagnosed with CLL
- HR: 1499 (95% CI: 270-8317)




Criteria: age>40 years and lymph. >5 × $10^9$ cells/L
Sensitivity: 100% (59-100)
Specificity: 99,94% (99,89-99,97)
Positive predictive value: 41% (18-67)

# Conclusions

- We bleed donors with CLL

**No evidence of transmission of chronic lymphocytic leukemia through blood transfusion**

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(Blood 2015)

- Donors should be informed and offered counselling
- New medicine – early intervention may be feasible for some mutations
- Sysmex data – immense possibilities

# Upcoming:

Donor disclosure

- Collaboration with Brian Custer

GWAS

- 20,000 samples to be typed
- Collaboration with deCode
- Research and blood center operation:

  Blood types and HLA types to be imputed

# Donor disclosure

- 5,458,499 donations, 414,119 prescriptions for anti-microbials filled within 3 months of donation
- Incidence rate of 0.3 prescriptions/year
- 7.6% of our donors fill a prescription for an anti-microbial within 3 months of each donation

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- How many fill a prescription within 2 weeks of donation?
- Could some of the infections affect recipient health?

# The Danish Blood Donor Study

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Give blood, save lives, create knowledge