



Faculty of Health Sciences



# *Improving T-cell assays for the diagnosis of active and latent TB infection using IP-10*

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**Conflict of interest statement:  
Hvidovre Hospital has applied for a patent  
disclosing IP-10 as a diagnostic marker for TB**





Cytokines  
e.g. IFN- $\gamma$

T-cell

monocyte

Chemokines  
e.g. IP-10

Ruhwald et al. M&I 2007

Ruhwald et al. BMC resc. notes 2009

2 Hoff S, submitted



# Developing a diagnostic algorithm for IP-10

**Aim:** Estimate cut off points for positive/negative test

## Material

Cases            80 TB patients

Controls        86 High School students

## Biomarkers

IP-10, IFN- $\gamma$

## Method

ROC curve analysis

Poster: Ruhwald et al. #1  
at 18.00 p.m. today



## Estimation of cut-offs



**Positive**

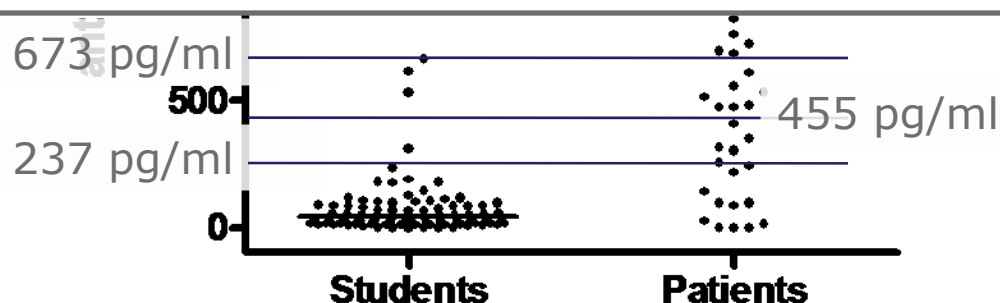
Ag response  $\geq 455$  pg/ml

**Negative**

Ag response  $< 455$  pg/ml

**Indeterminate**

Mitogen  $< 200$  pg/ml



## A first clinical evaluation: TB patients vs healthy controls – preliminary results

**Aim:** Estimate sensitivity and specificity of the IP-10 test

### Material

Patients	112 TB patients with confirmed TB
Controls	98 healthy controls with no history of exposure

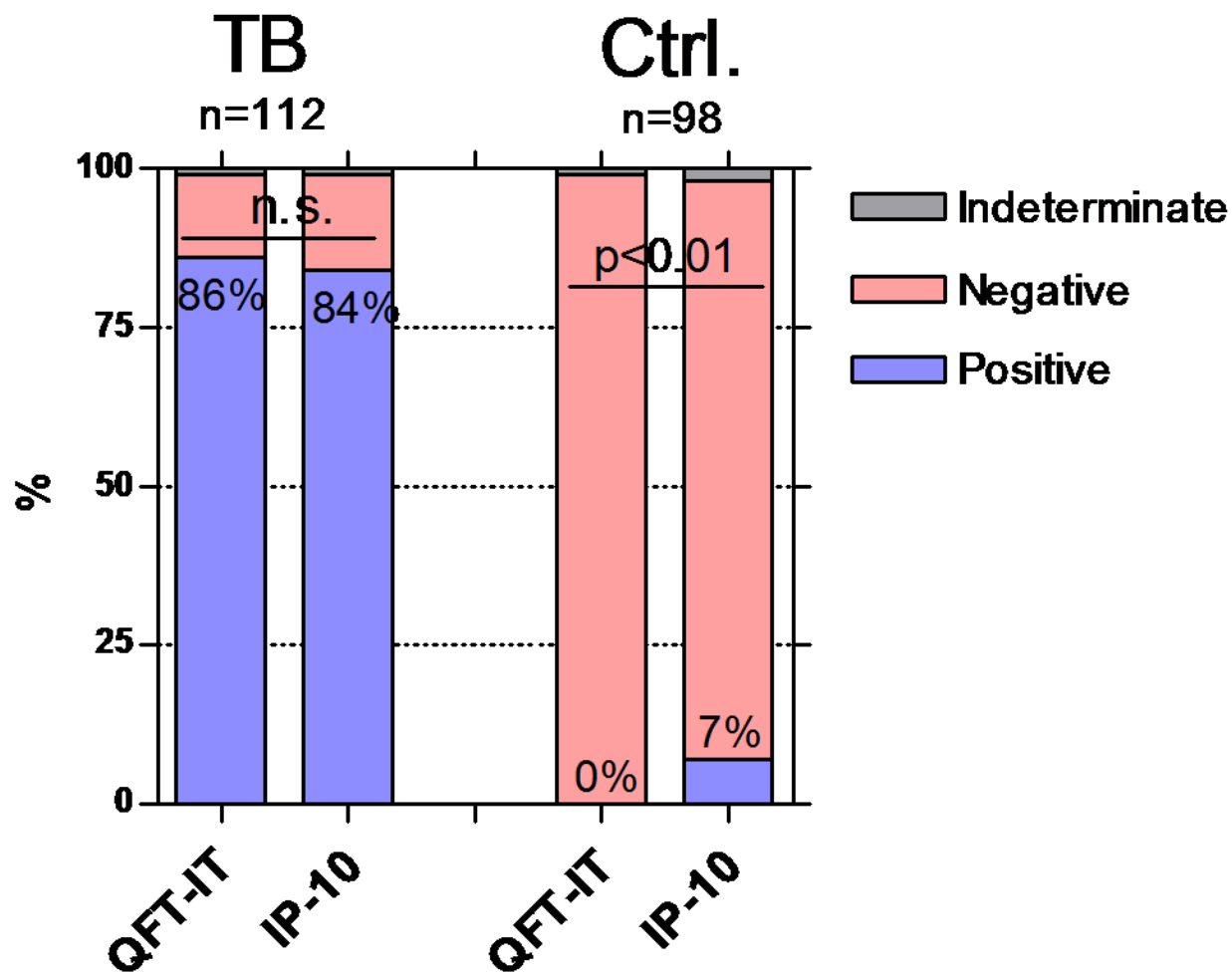
### Method

IP-10 test vs QFT-IT test

Poster: Ruhwald et al. #1  
at 18.00 p.m. today



# Sensitivity and specificity of IP-10



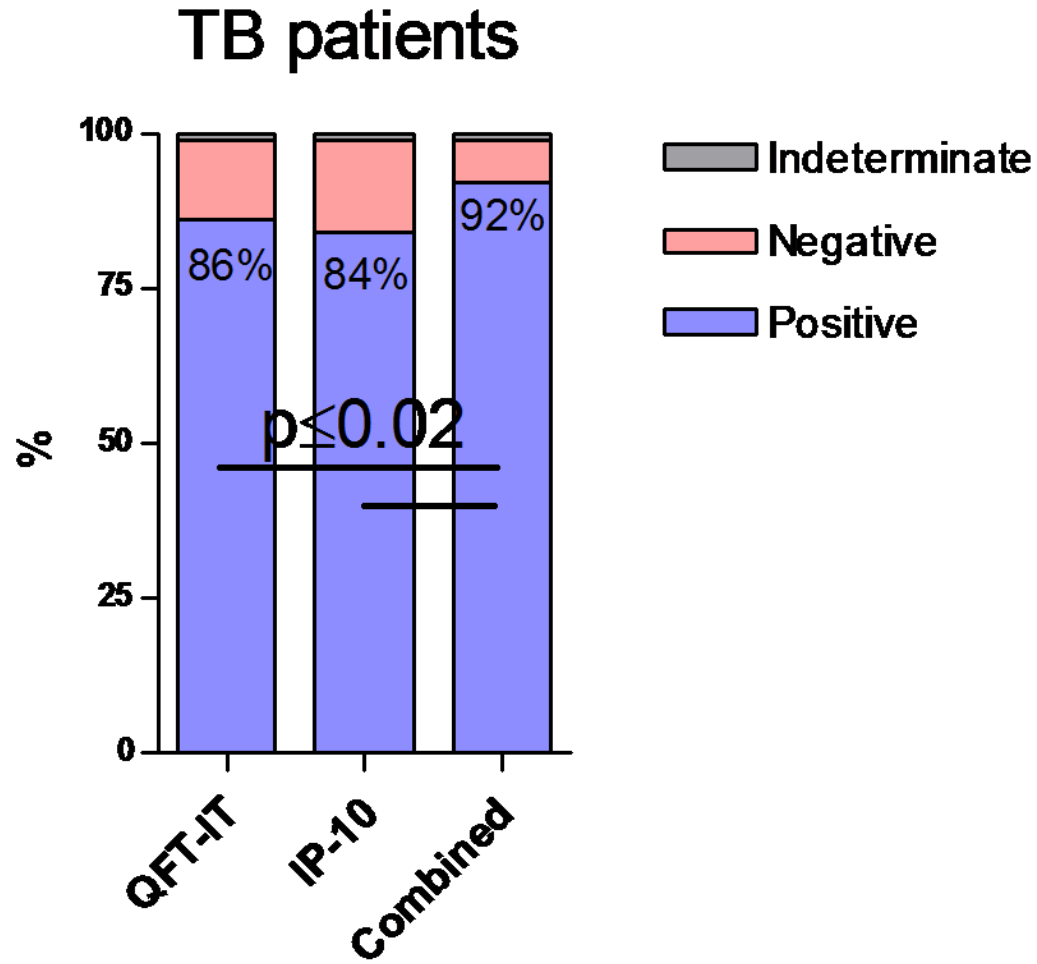
# Concordance

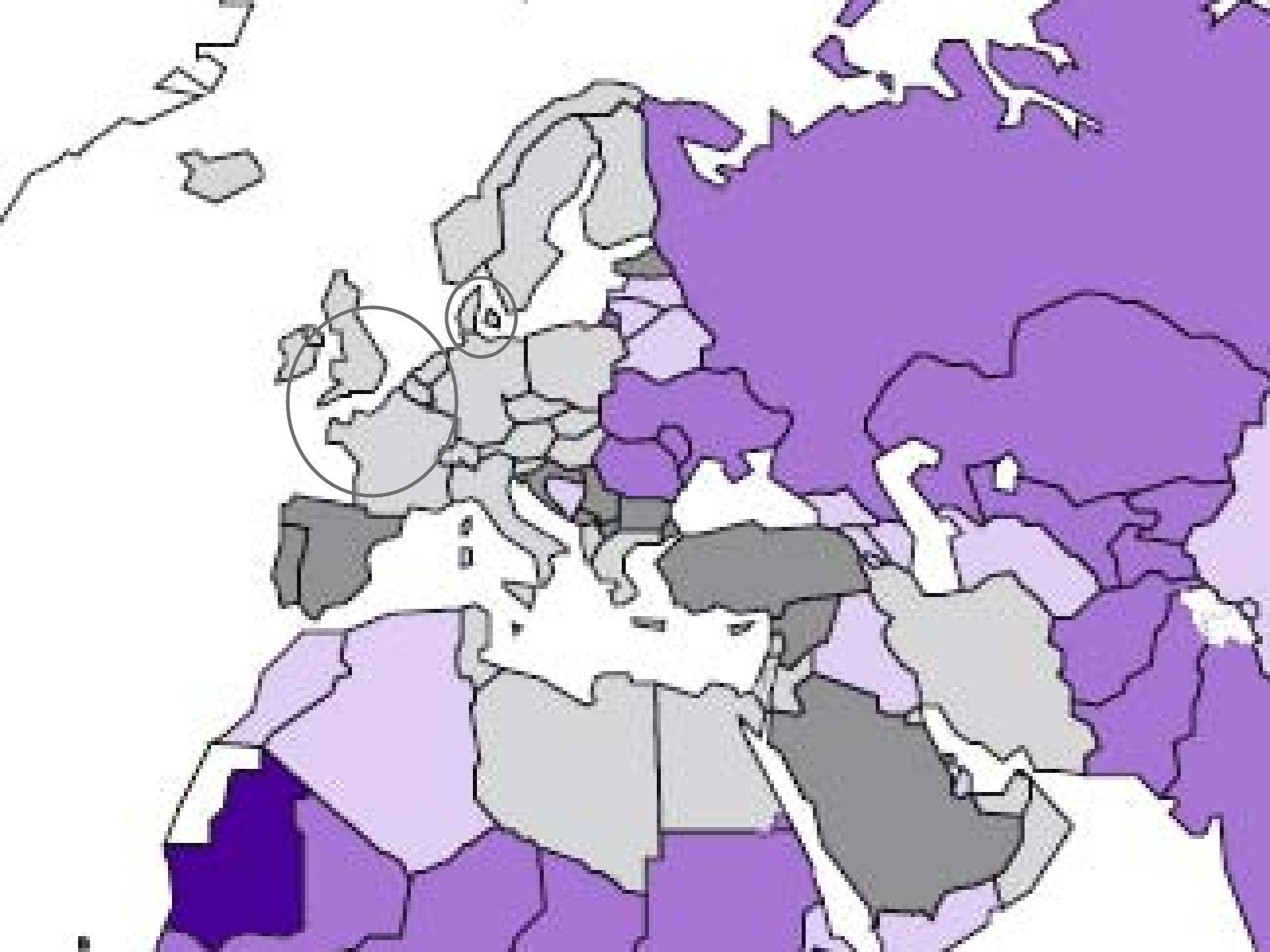
		Controls			$\Sigma$
		IFN- $\gamma$ (QFT-IT)			
IP-10		+	-	Indet	
	+	<b>0</b>	7	0	7
	-	0	<b>89</b>	0	89
	Indet	0	1	<b>1</b>	2
$\Sigma$	0	97	1	<b>98</b>	

		TB patients			$\Sigma$
		IFN- $\gamma$ (QFT-IT)			
IP-10		+	-	Indet	
	+	<b>87</b>	7	0	94
	-	8	<b>8</b>	1	17
	Indet	1	0	<b>0</b>	1
$\Sigma$	96	15	1	<b>112</b>	



# Added sensitivity by combination?





# HIV and TB co-infected adult patients

**Aim:** Study the impact of HIV infection on IP-10 test performance

## Material

157 patients with culture+ pulm. TB from Mwanza Tz  
92 HIV-  
65 HIV+

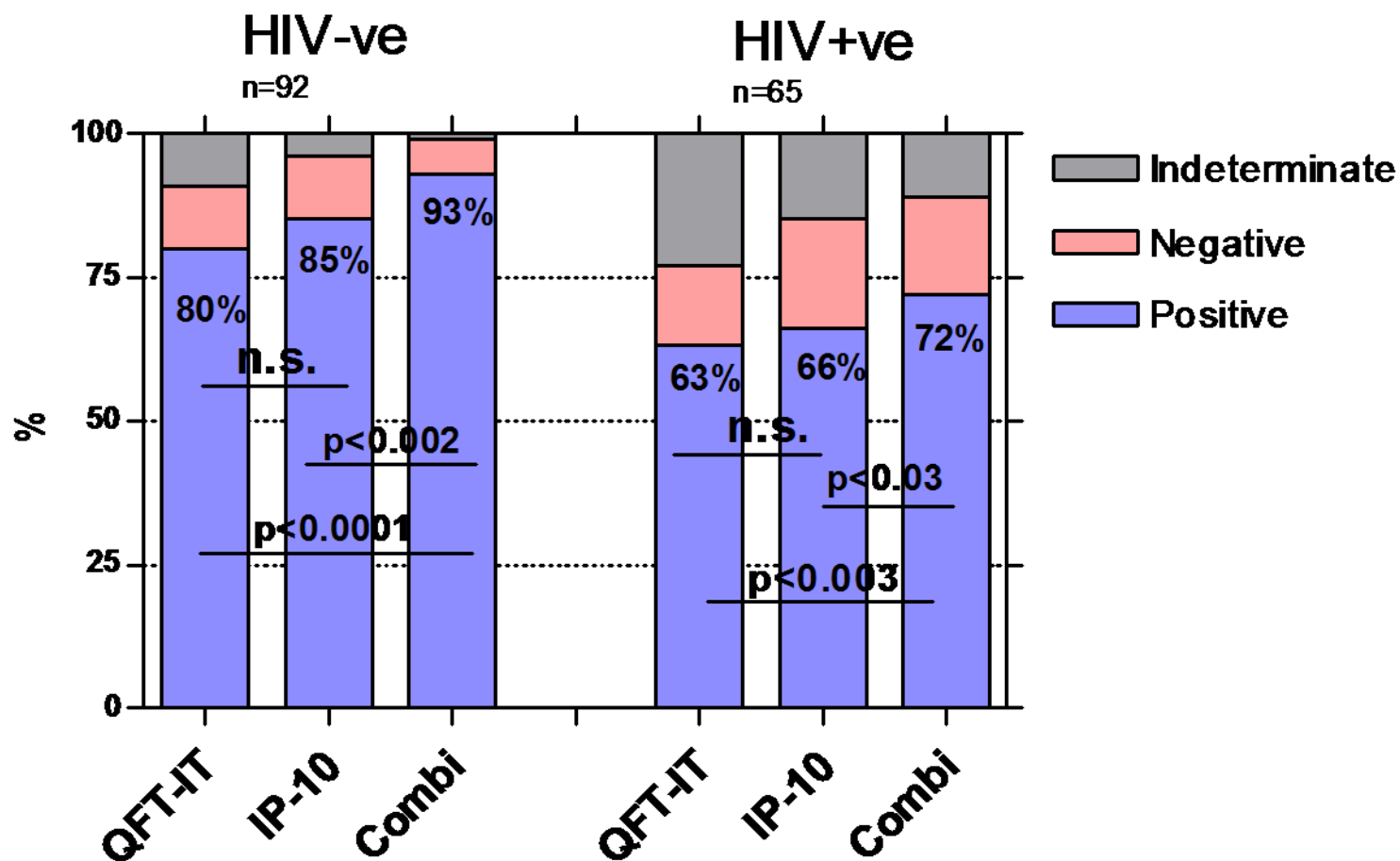
## Method

IP-10 test vs QFT-IT

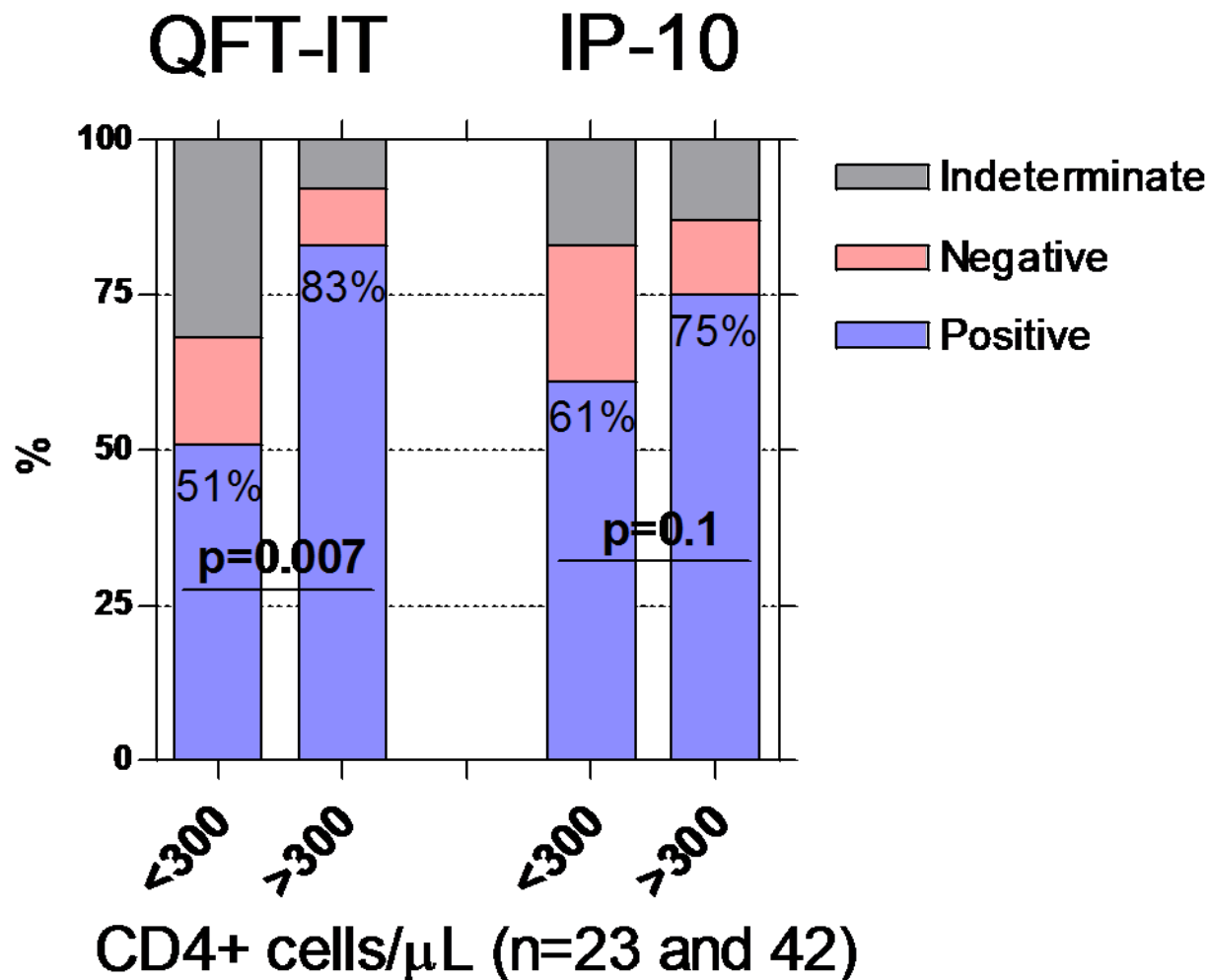
Poster: Aabye et al.  
at 18.00 p.m. today

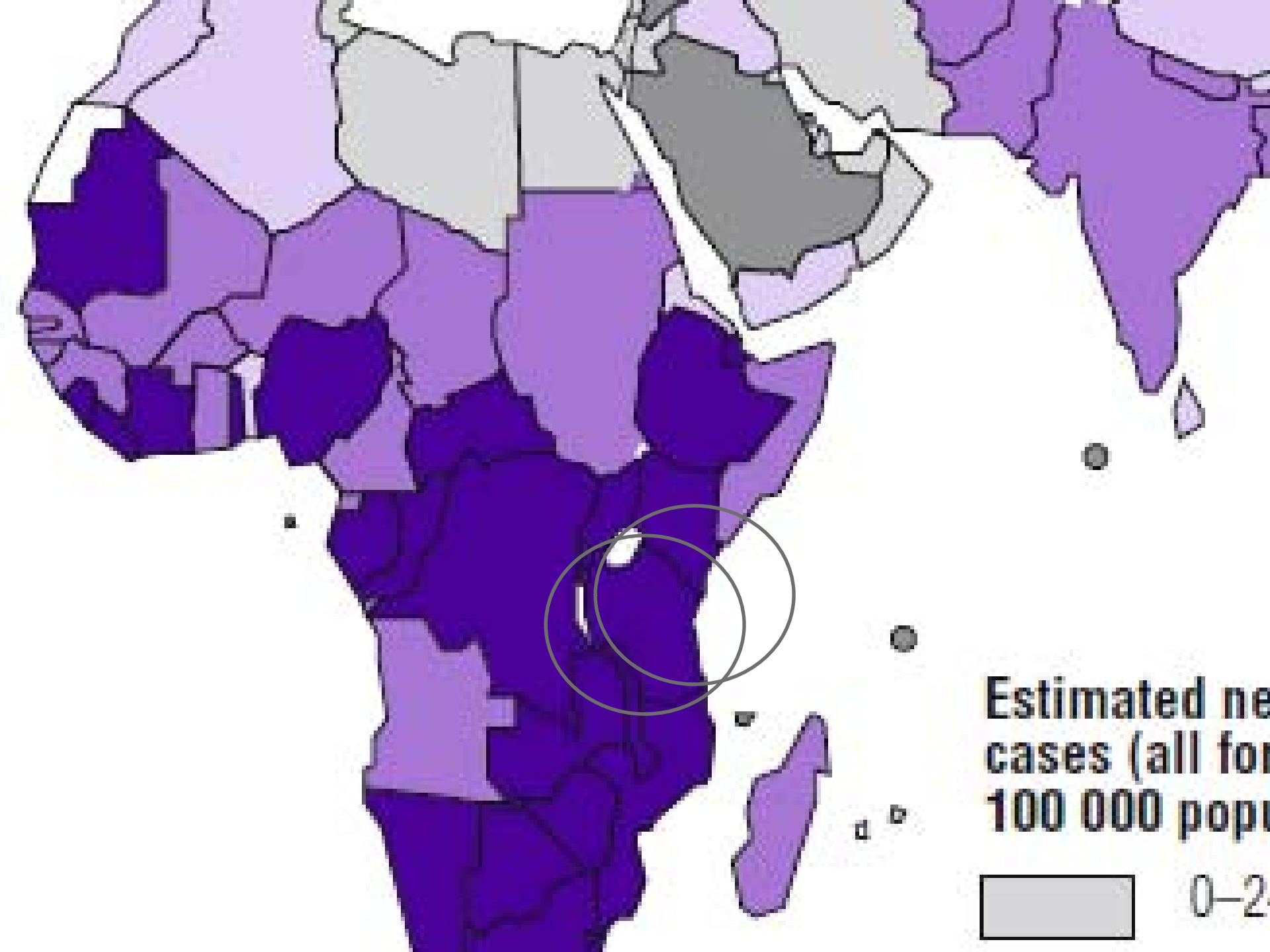


# QFT-IT and IP-10 performance is influenced by HIV-infection, but sensitivity improves by combination



# IP-10 test appears less influenced by CD4 count in HIV+ patients





# Test performance in exposed children in high endemic setting

**Aim:** To compare the performance of IP-10 test to QFT-IT and TST in recently exposed children in a high endemic setting

## Material

120 children (1-14yrs) from Abuja Nigeria

59 High risk of TB infection (SS+)

61 Low risk

38 household contact to smear-ve TB patient (SS-)

23 community controls (CC)

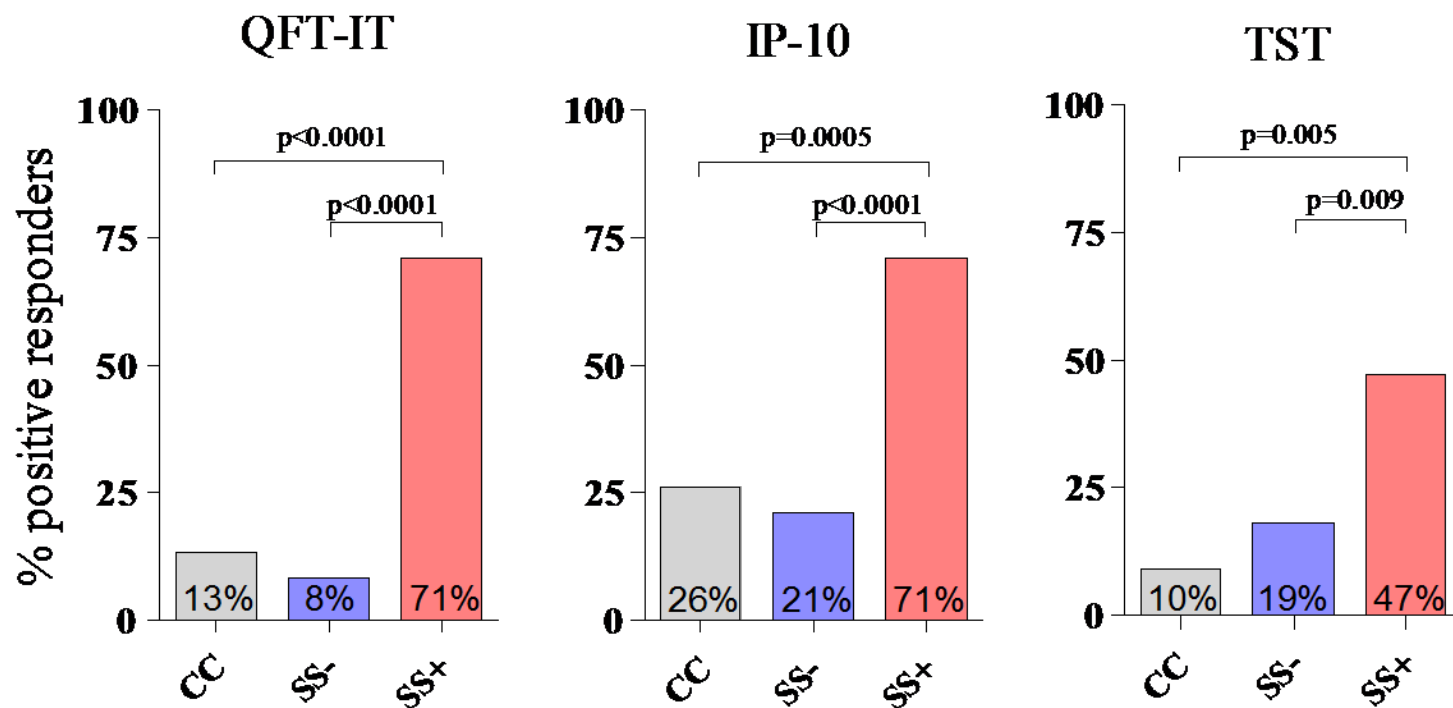
## Method

IP-10 test, QFT-IT, Tuberculin Skin Test

Poster: Ravn  
et al. at 18.00  
p.m. today



# Prevalence of latent TB determined by QFT-IT, IP-10 and TST



## Summary and conclusions

IP-10 is expressed in response to antigen stimulation in infected individuals

IP-10 is produced in high concentrations compared to INF- $\gamma$

The IP-10 test performed with comparable sensitivity and specificity as the QFT-IT

Combining IP-10 and QFT-IT significantly improves accuracy



## Perspectives

Exploring various cut off points and diagnostic algorithms

The high concentrations of IP-10 allows quantification on multiple platforms

Improving performance by combining multiple biomarkers



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