

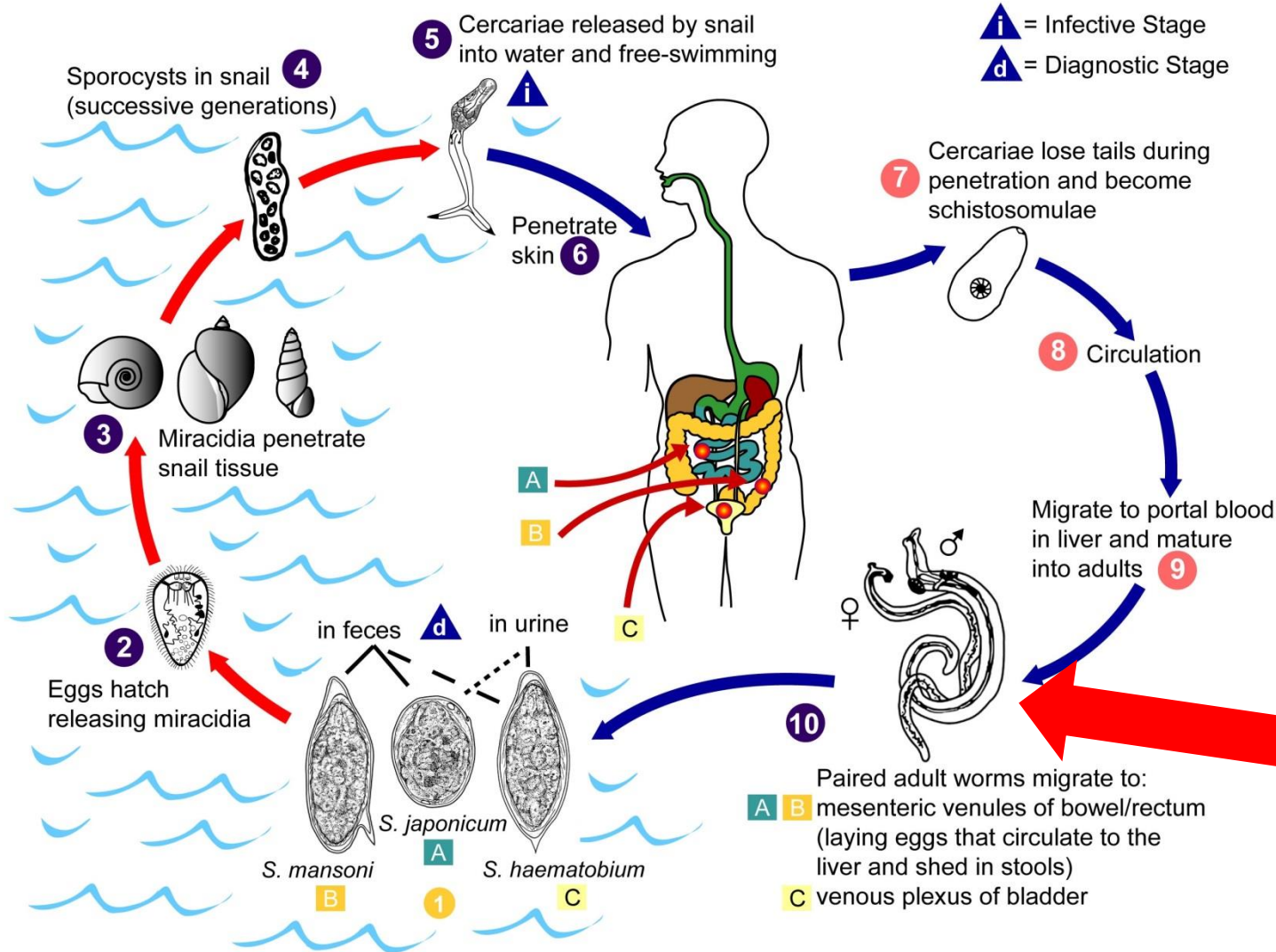
Diagnostiek van schistosomiasis door antigeen-detectie (CAA en CCA): op zoek naar die ene worm.

**Govert van Dam, Claudia de Dood, Djoeke Kornelis, Elisa
Tjon Kon Fat, Rebecca van Grootveld, Lisette van
Lieshout, Paul Corstjens**

Depts. of Parasitology and Molecular Cell Biology
Leiden University Medical Center, The Netherlands

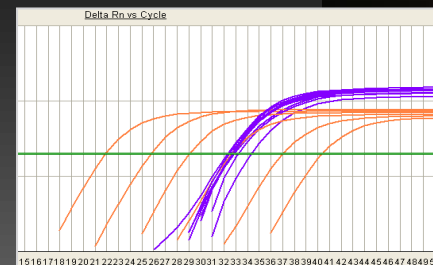
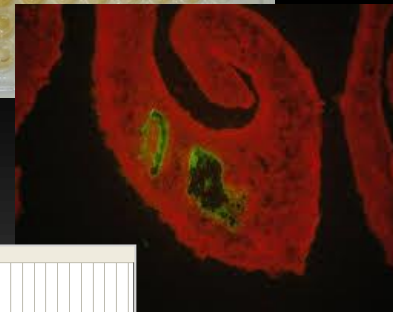
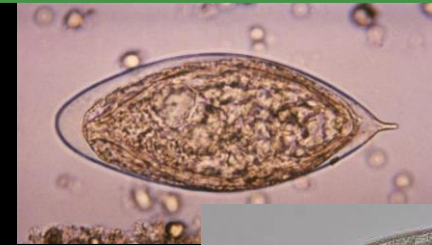
Schistosomiasis

Schistosomiasis

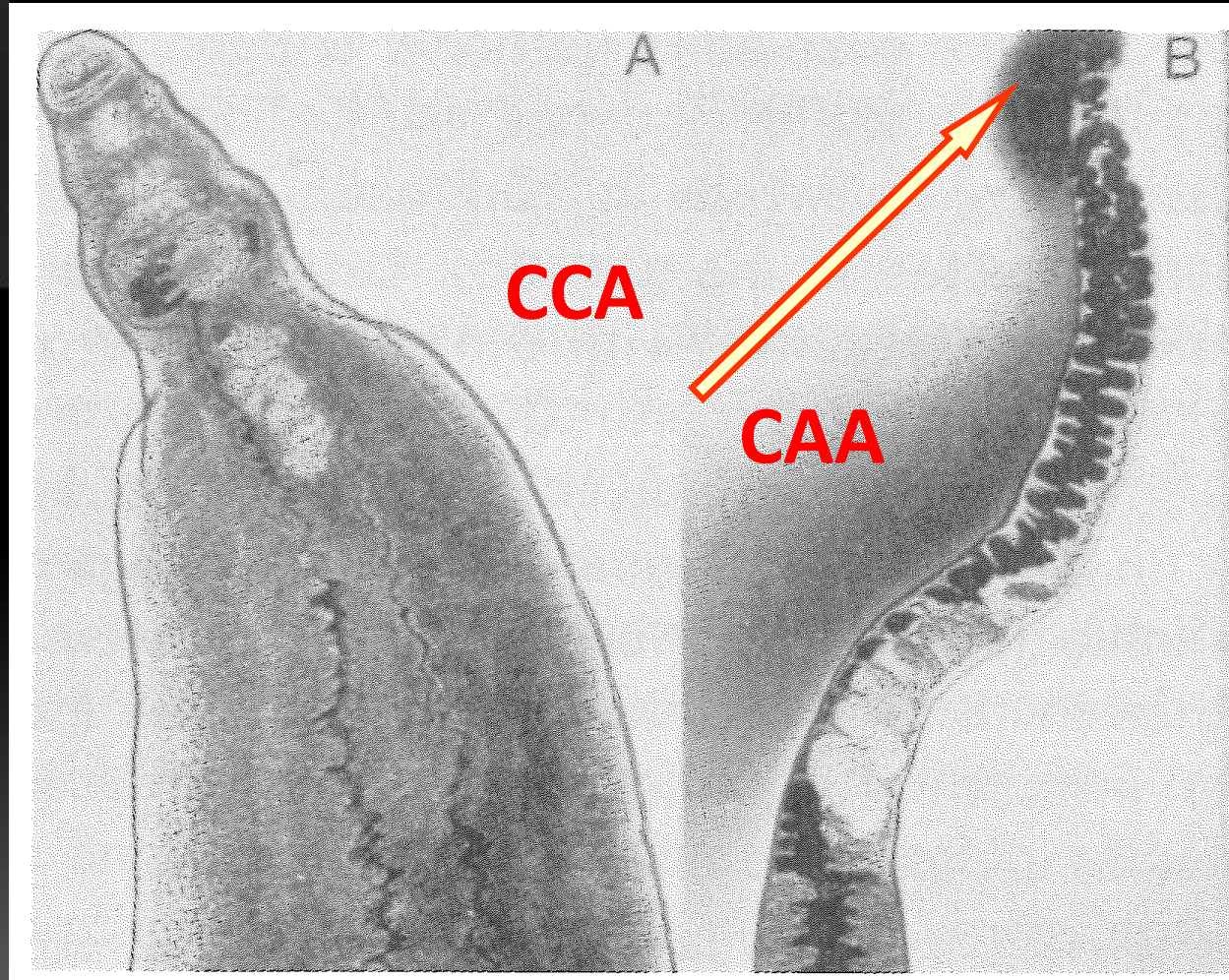


Current diagnostics

- Traditional / field: microscopy (Kato-Katz, urine filtration, Flotac)
- Field rapid test: POC-CCA
- Laboratory diagnosis (LUMC): antibody detection, ELISA & IFA
- Novel laboratory techniques: PCR, UCP-LF CAA assay

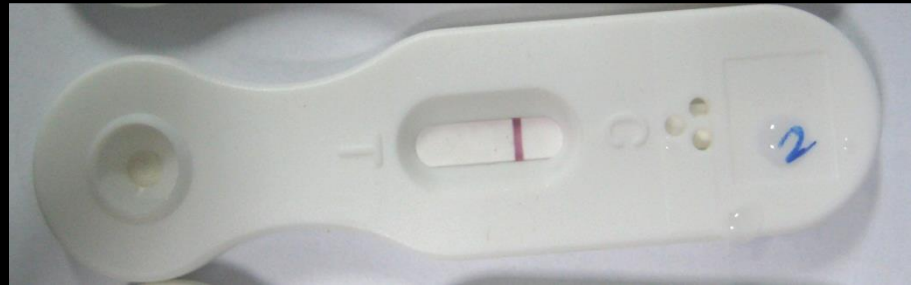


Discovery of circulating antigens



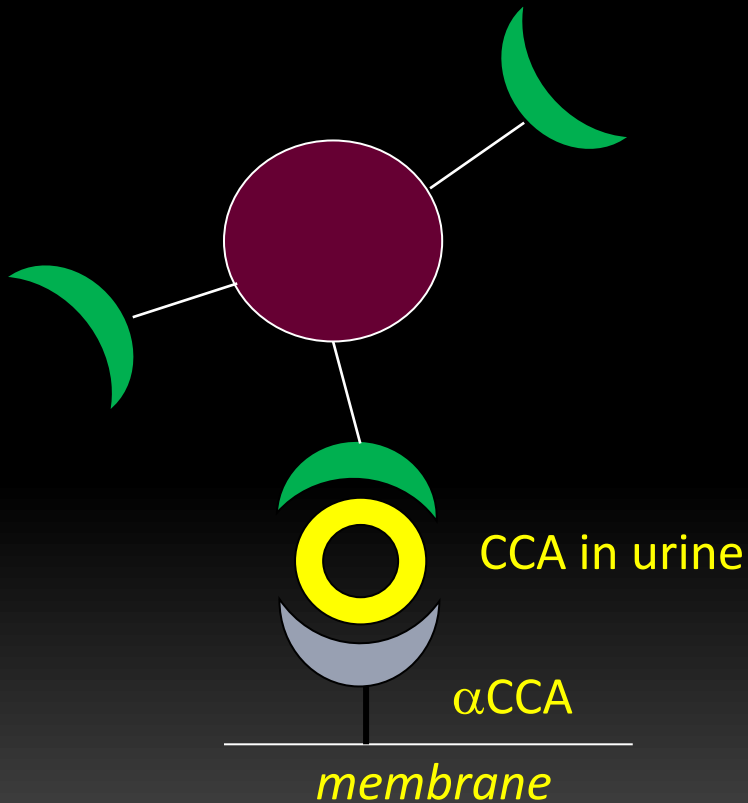
Deelder et al, Exp.
Parasitol. 1976

Urine CCA-POC test

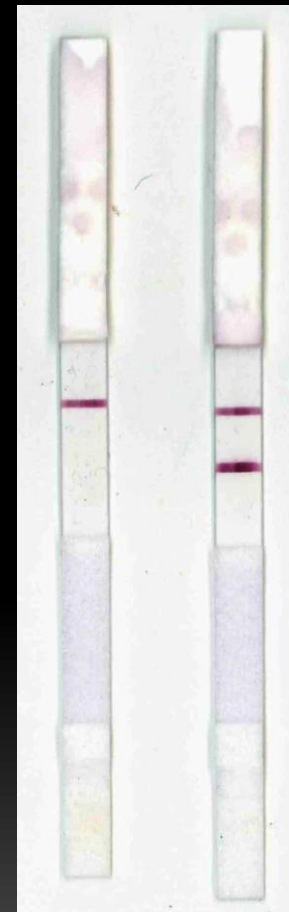


technique CCA strip

principle



strip

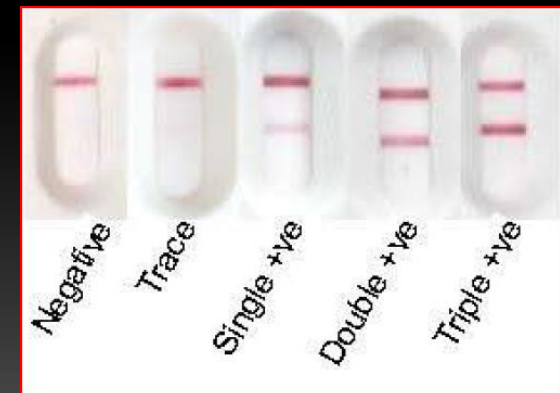
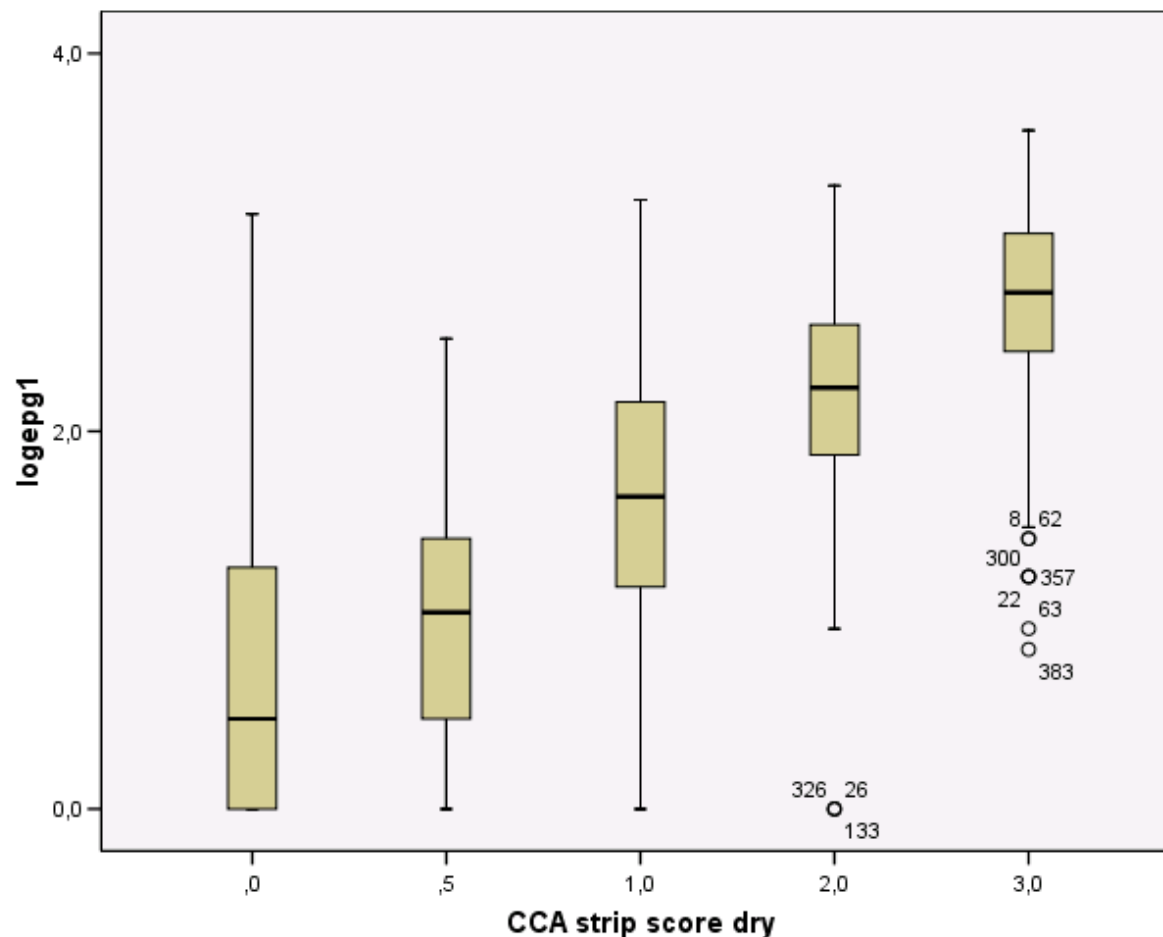


neg pos



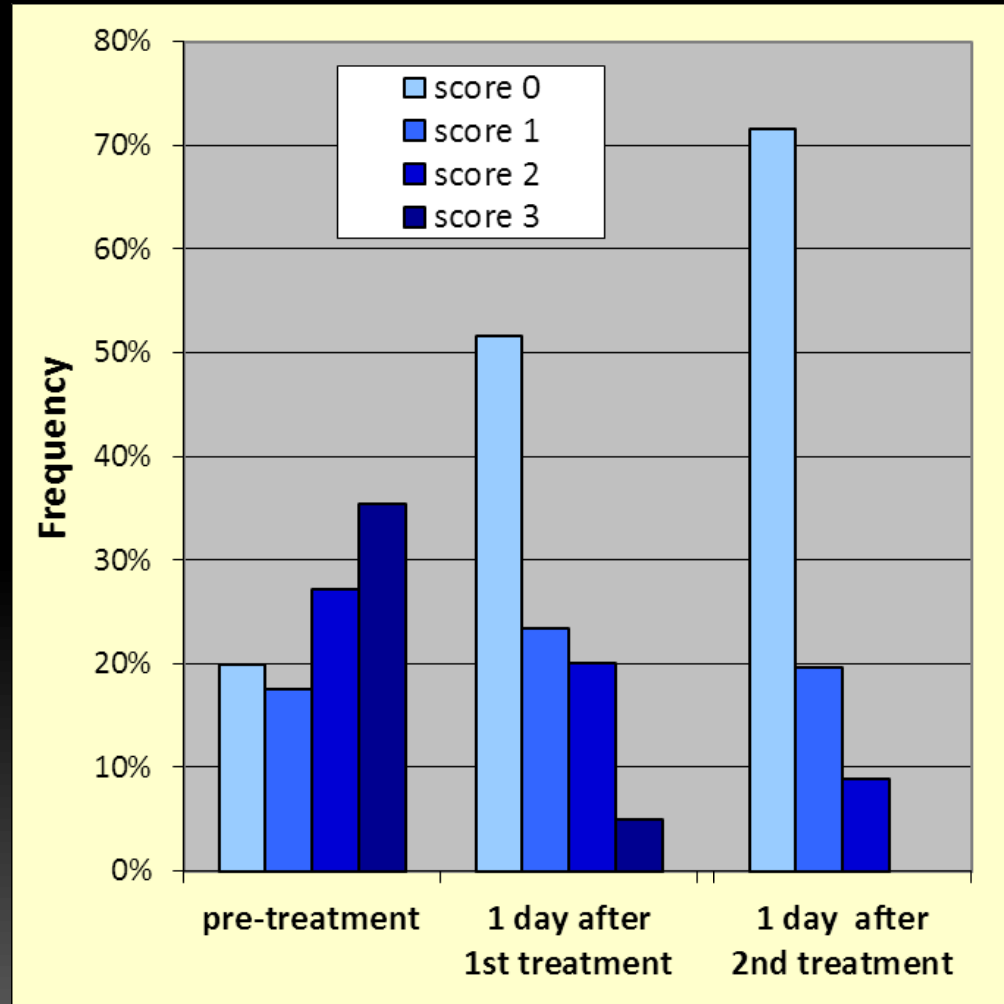
Evaluation of CCA urine strip Uganda EU

Correlation of egg counts and CCA strip



Distribution of CCA strip intensities

Effect of treatment after 1 day



Linking control and diagnostics

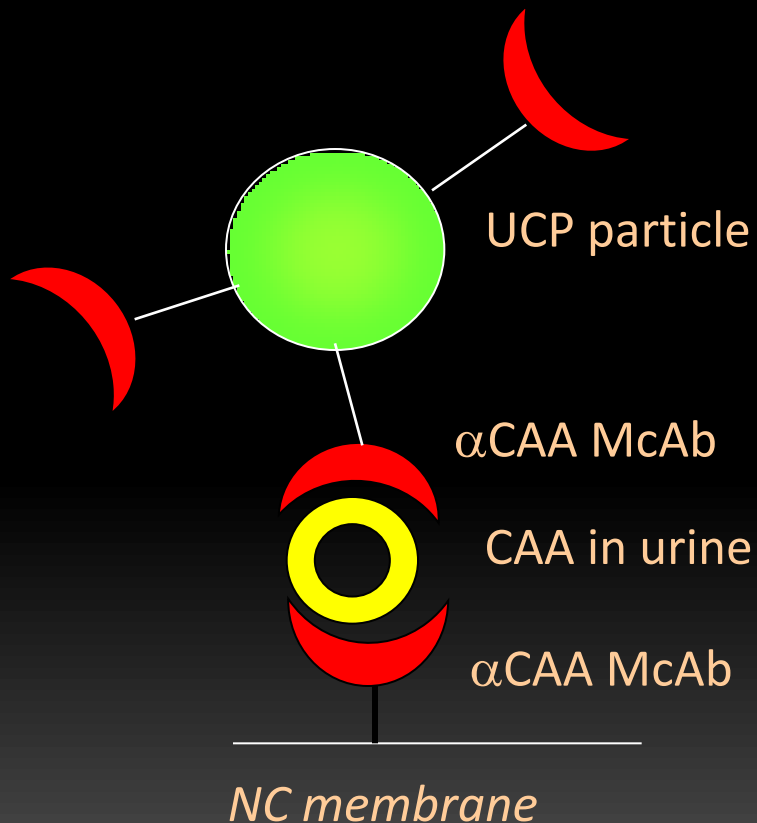


Accuracy of test

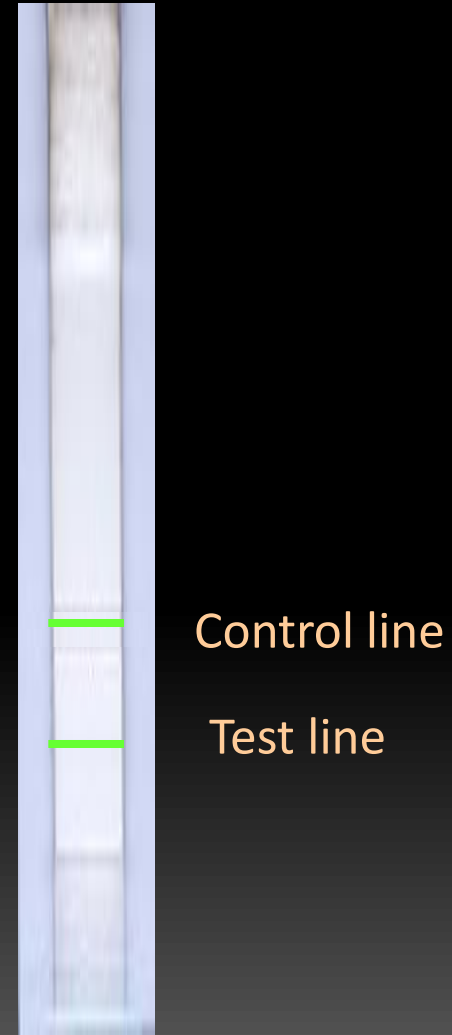


Technique CAA strip

principle

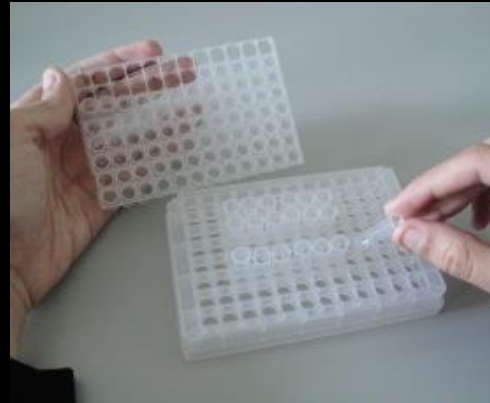


strip



UCP-LF CAA assay

Dry reagents



Sample pre-treatment

Mix 50 μ L serum with
50 μ L 4% (w/v) TCA

Add 20 μ L clear supernatant
to 100 μ L assay-buffer

incubate 1 h at 37 $^{\circ}$ C, shaking

Spin

Mix

incubate



add LF strips, run for 1 h



read strips, quantitate



Outline

Ultrasensitive urine/serum CAA assay

Evaluations in low endemic settings

- 1. Zanzibar (ZEST), tests done in-country
(vs. urine eggs, microhaematuria)
- 2. Burundi, tests done in Leiden
(vs. Kato-Katz, POC-CCA)
- 3. China, tests done in-country
(vs. Kato-Katz, serology, serum CAA)
- 4. Brazil, tests done in Leiden
(vs. Kato-Katz, serology, POC-CCA, PCR)

Evaluation in LUMC

Evaluation in experimental infection, Kenya

1. Zanzibar – ZEST project

Zanzibar Elimination of Schistosomiasis Transmission



RESEARCH ARTICLE

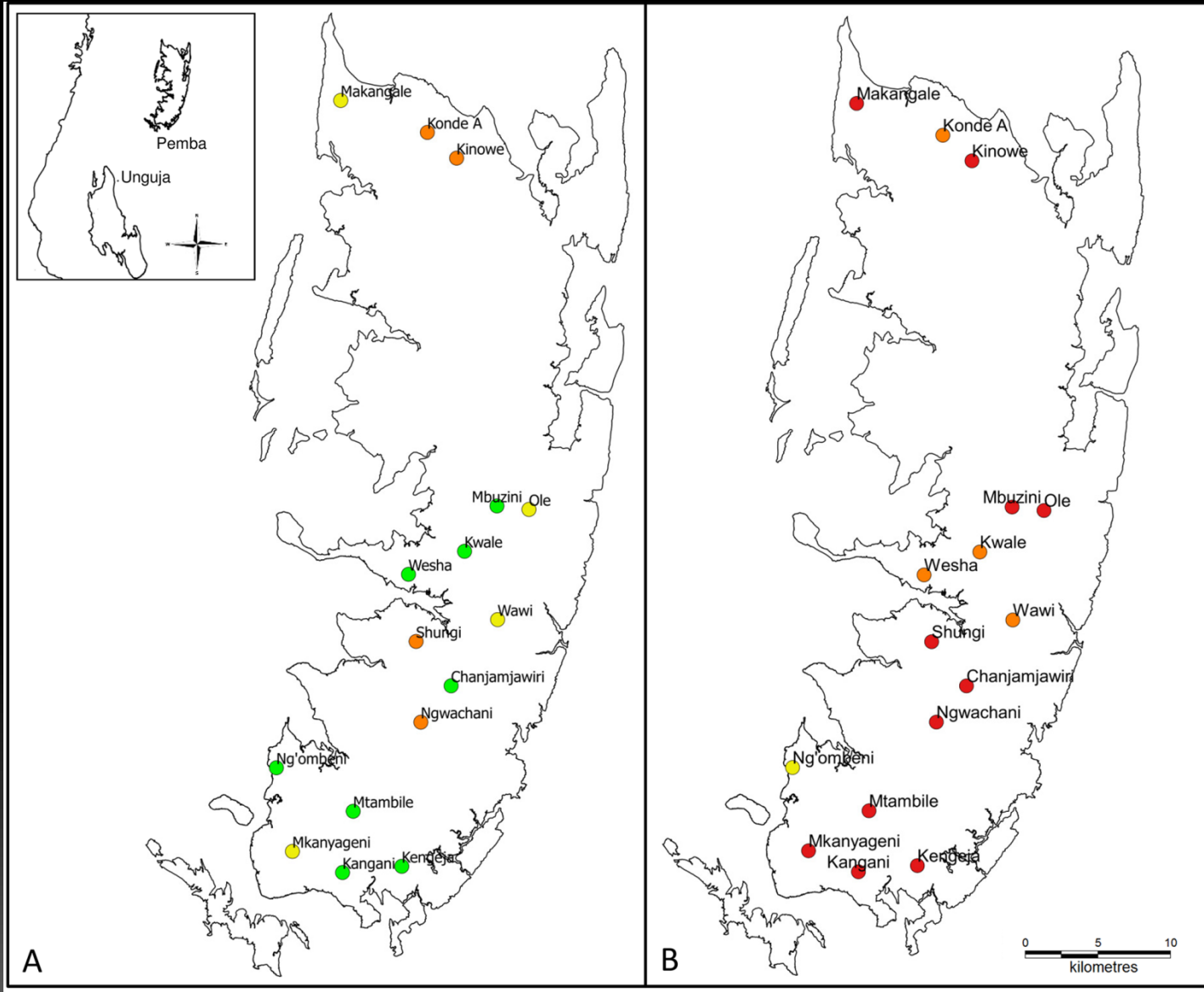
Sensitivity and Specificity of a Urine Circulating Anodic Antigen Test for the Diagnosis of *Schistosoma haematobium* in Low Endemic Settings

Stefanie Knopp^{1,2,3*}, Paul L. A. M. Corstjens⁴, Artemis Koukounari⁵, Colin I. Cercamondi⁶, Shaali M. Ame⁷, Said M. Ali⁷, Claudia J. de Dood⁴, Khalfan A. Mohammed⁸, Jürg Utzinger^{2,3}, David Rollinson¹, Govert J. van Dam⁹

Zanzibar – different villages

urine eggs

urine CAA assay



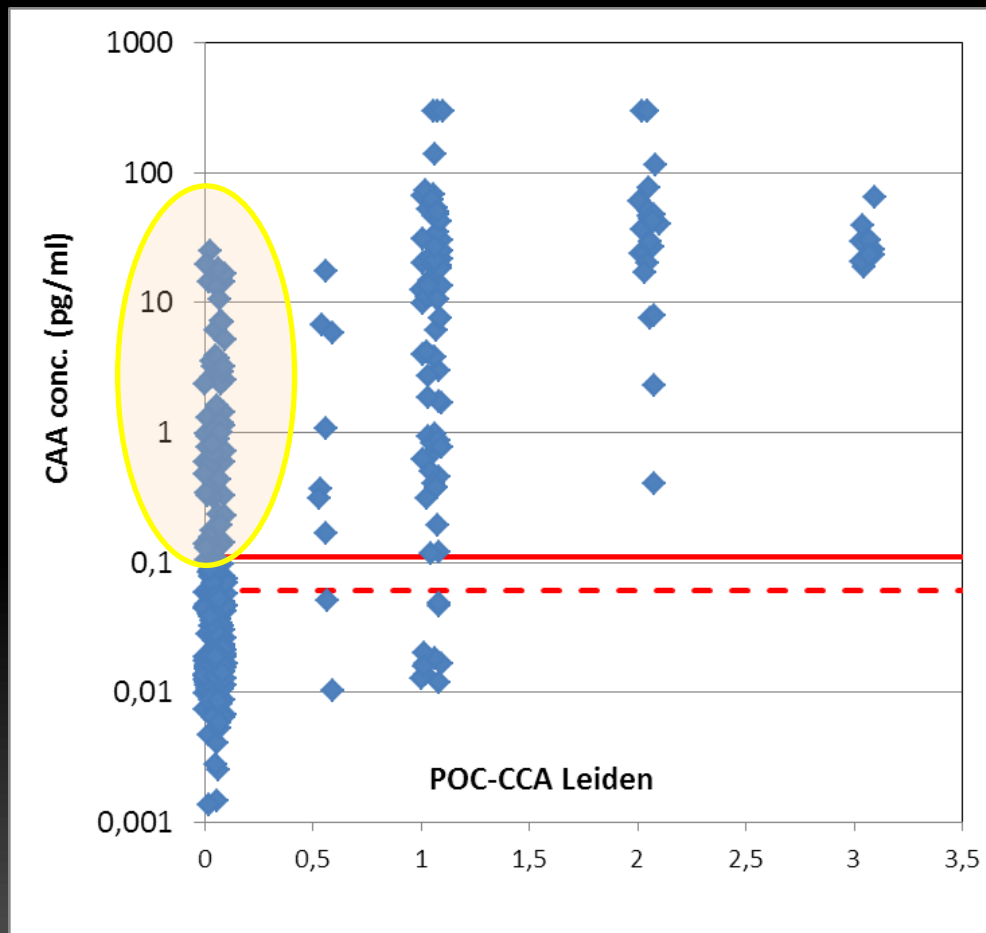
2. Burundi – POC-CCA mapping

Prevalences determined by various diagnostic tests on samples from schoolchildren of Burundi (n=399)

Diagnostic Test	Prevalence (%)
Kato-Katz (in-country)	7%
POC-CCA (Leiden)	31%
UCAA2000 (Leiden)	47%

Burundi – POC-CCA mapping

Correlation of urine CAA concentrations
vs. POC-CCA tests



Spearman's rho = 0,59 / 0,65, with $p < 0,0001$

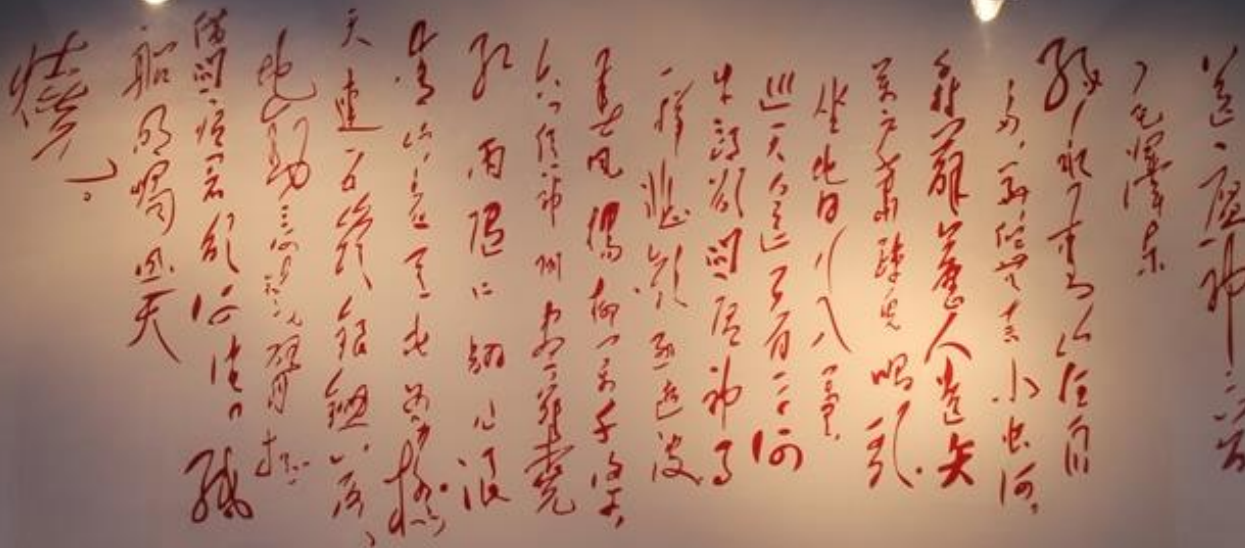
3.

China – very low endemic area

Dongting lake, Hunan province

Aiming for transmission interruption

Mao Zedong - Farewell to the god of plague - July 1, 1958



送瘟神二首
毛泽东
绿水青山枉自多，
华佗无术奈春何。
千村万落生瘟疫，
无药可医愁万般。
也知造物无言好，
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National Institute of Parasitic Diseases, Chinese Center for Diseases Control and Prevention
Shanghai, People's Republic of China

China – very low endemic area

Dongting lake, Hunan province

March 2014, 371 urine and 178 serum samples



China – very low endemic area

Dongting lake, Hunan province

**Prevalence (n=371) increased from
1.6% by Kato-Katz to
10% by UCAA**

fishing village:	from 6% up to 19%
agricultural village:	from 0% up to 6%

An ultra-sensitive assay targeting the circulating anodic antigen for the diagnosis of *Schistosoma japonicum* in a low-endemic area, People's Republic of China.

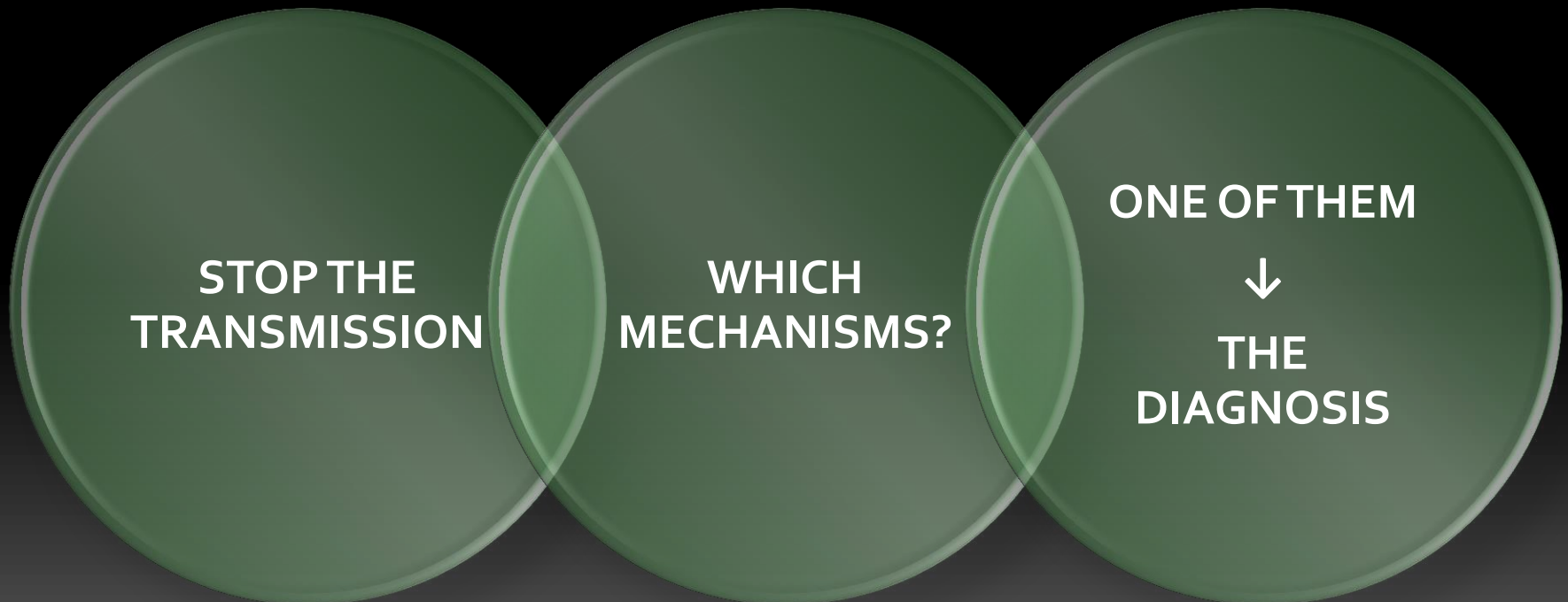
van Dam GJ, Xu J, Bergquist R, de Dood CJ, Utzinger J, Qin ZQ, Guan W, Feng T, Yu XL, Zhou J, Zheng M, Zhou XN, Corstjens PL. Acta Trop. 2015

4.

SCHISTOSOMIASIS CONTROL IN LOW ENDEMIC AREAS IN BRAZIL: ACCURACY ISSUES IN DIAGNOSTICS.

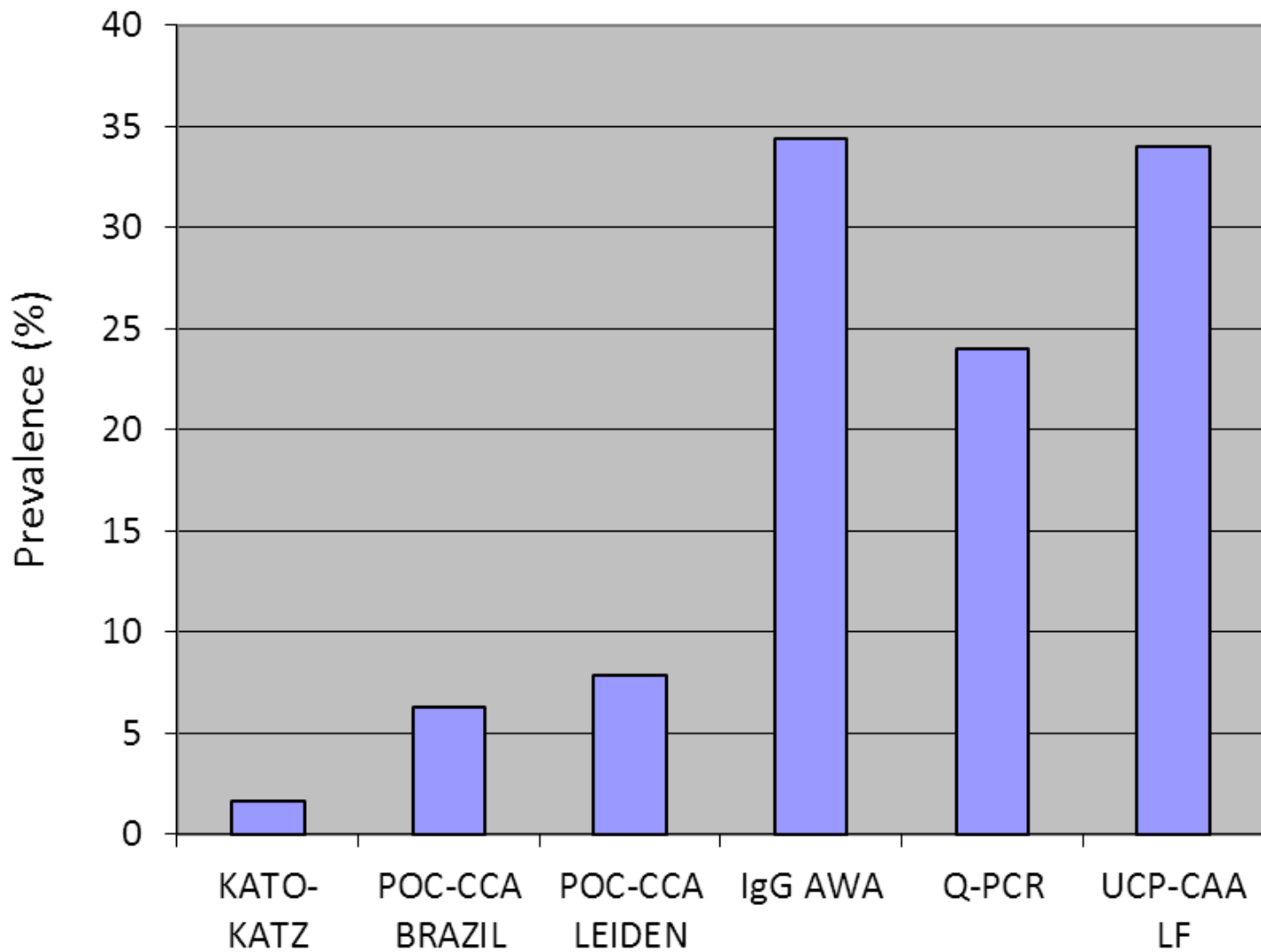


**WHICH IS OUR BIG CHALLENGE
ESPECIALLY AT LOW ENDEMICITY AREA ?**



PROF. DR. FERNANDO SCHEMELZER MORAES BEZERRA

Baseline prevalence by various tests

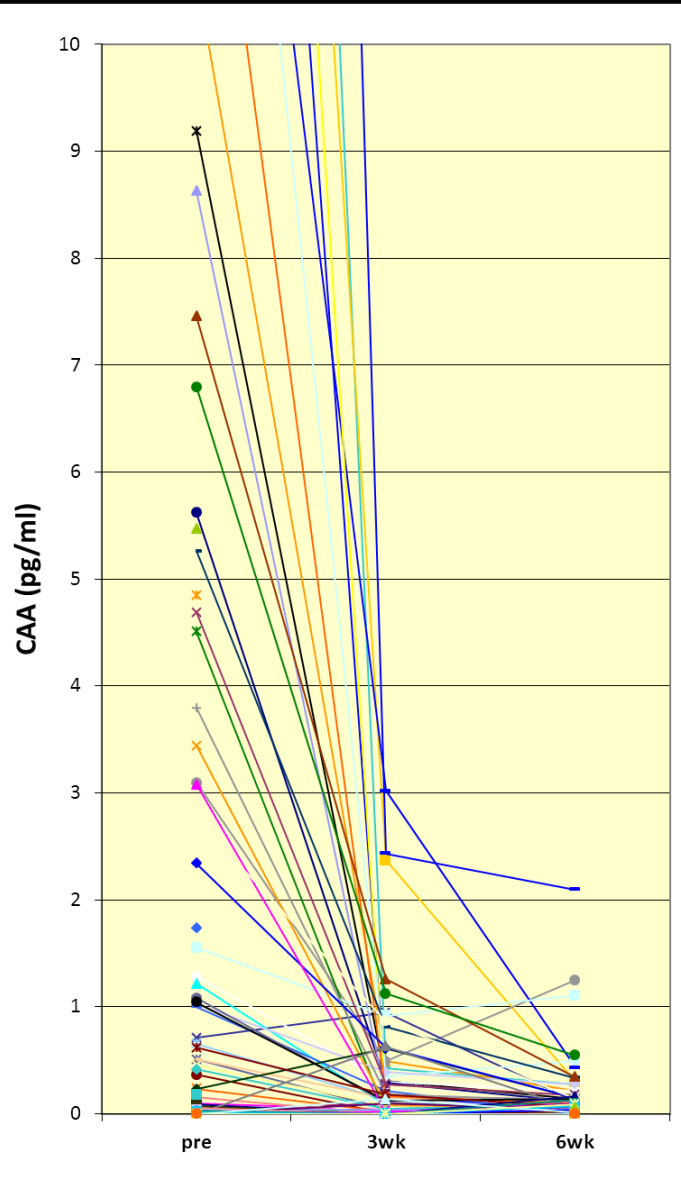


Sensitivities and Specificities

**Se and Sp vs. combined Gold Standard:
KK / Q-PCR / UCAA**

	Kato-Katz	Q-PCR	UCAA2000
	n=258	n=50	n=132
Sensitivity	7%	60%	92%
	IgG-AWA	POC-CCA	
	n=258	n=258	
Sensitivity	47%	29%	
Specificity	61%	98%	

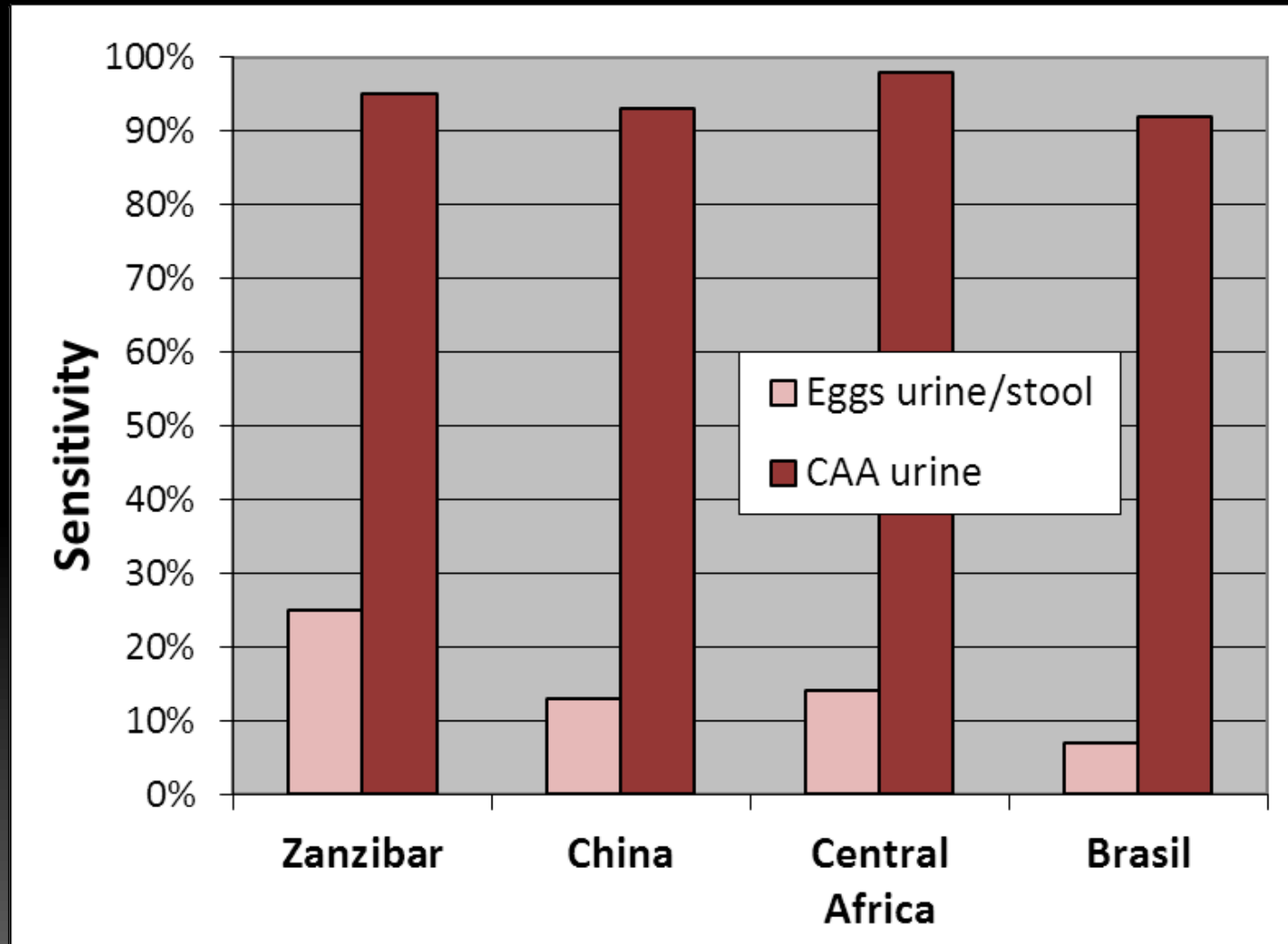
Urine CAA levels before and after treatment UCAA2000



	pre	3wks	6 wks
Prevalence	35%	27%	27%
Cure rate		27%	39%
CAA decrease		93%	100%

Summary very low prevalence settings

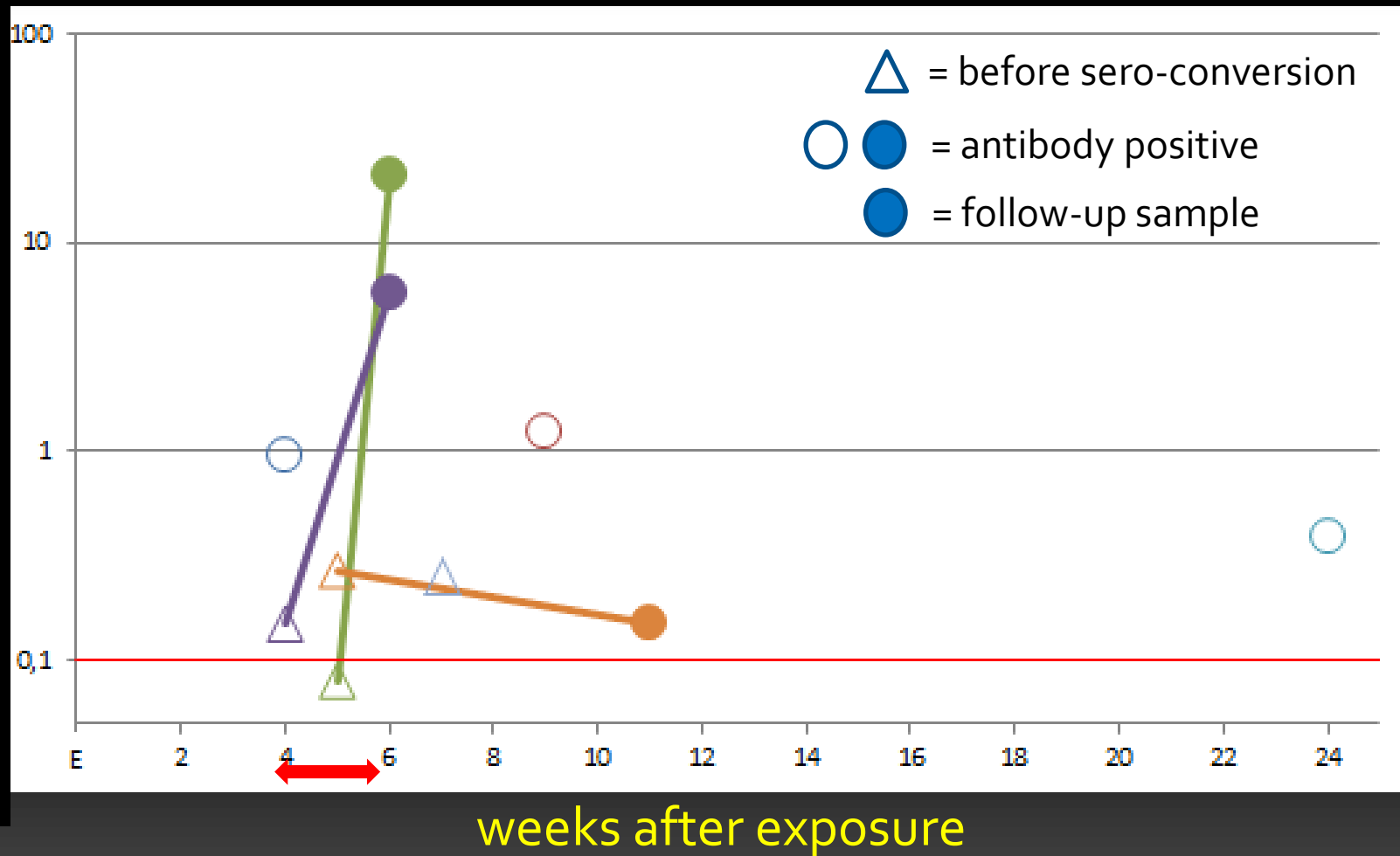
Zanzibar, China, Burundi and Brasil
S. haematobium, S. japonicum, S. mansoni



Evaluation in LUMC

CAA-concentration after exposure

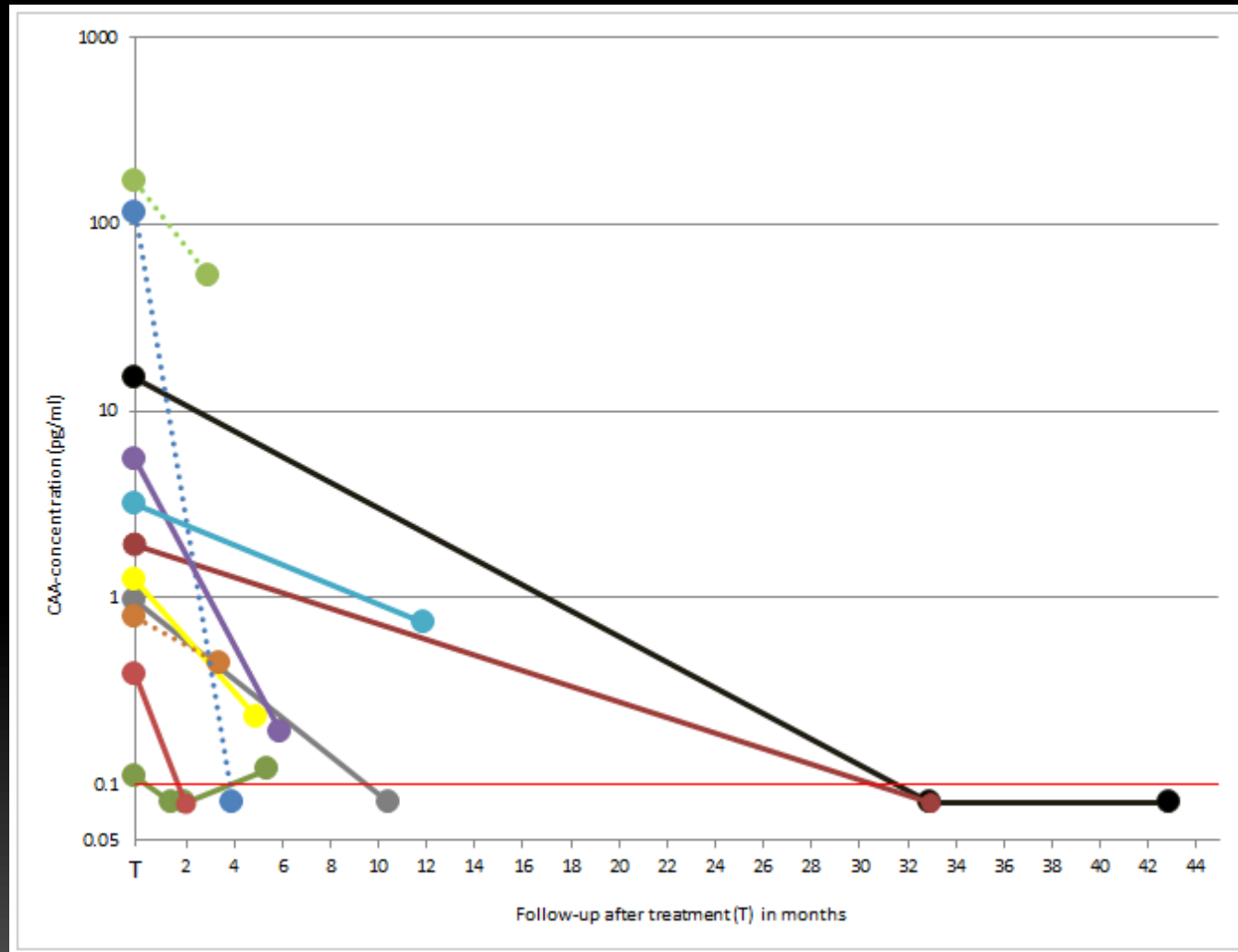
CAA concentration pg/ml



Recent infection: 15/27 CAA pos. Chronic infection: 33/42 CAA pos.

Evaluation in LUMC

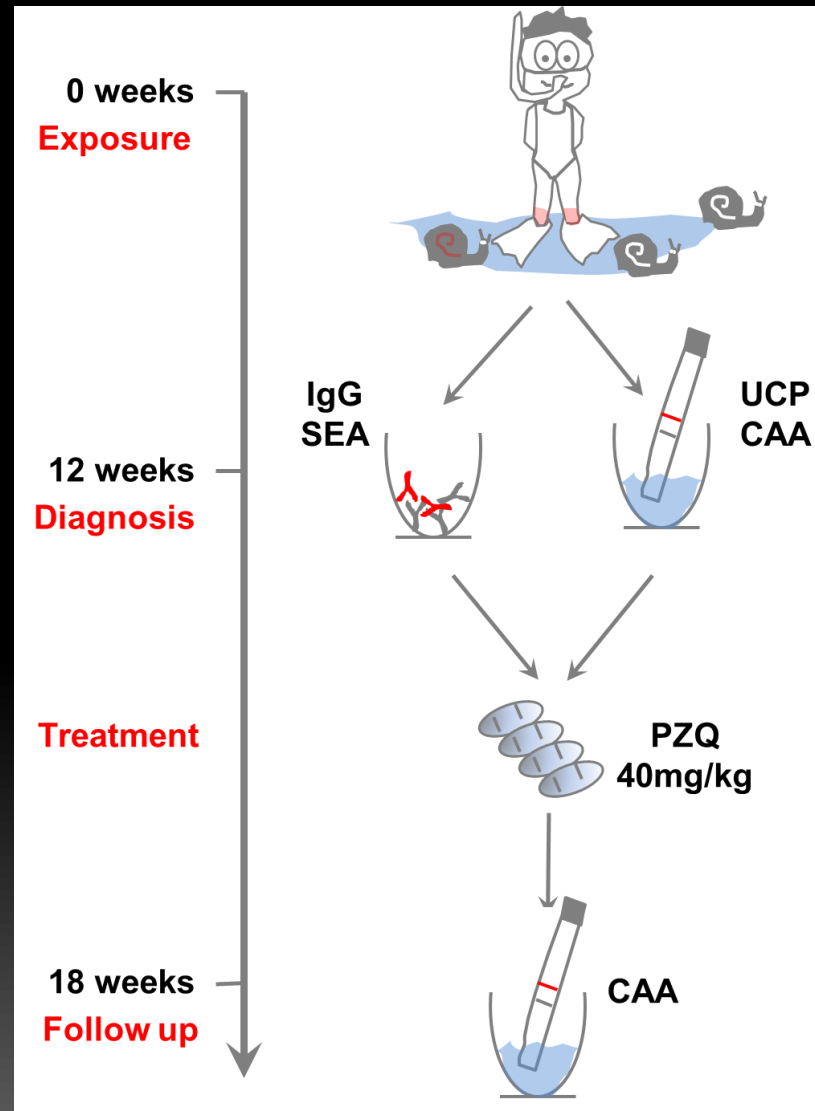
CAA-concentration after treatment



Evaluation in LUMC

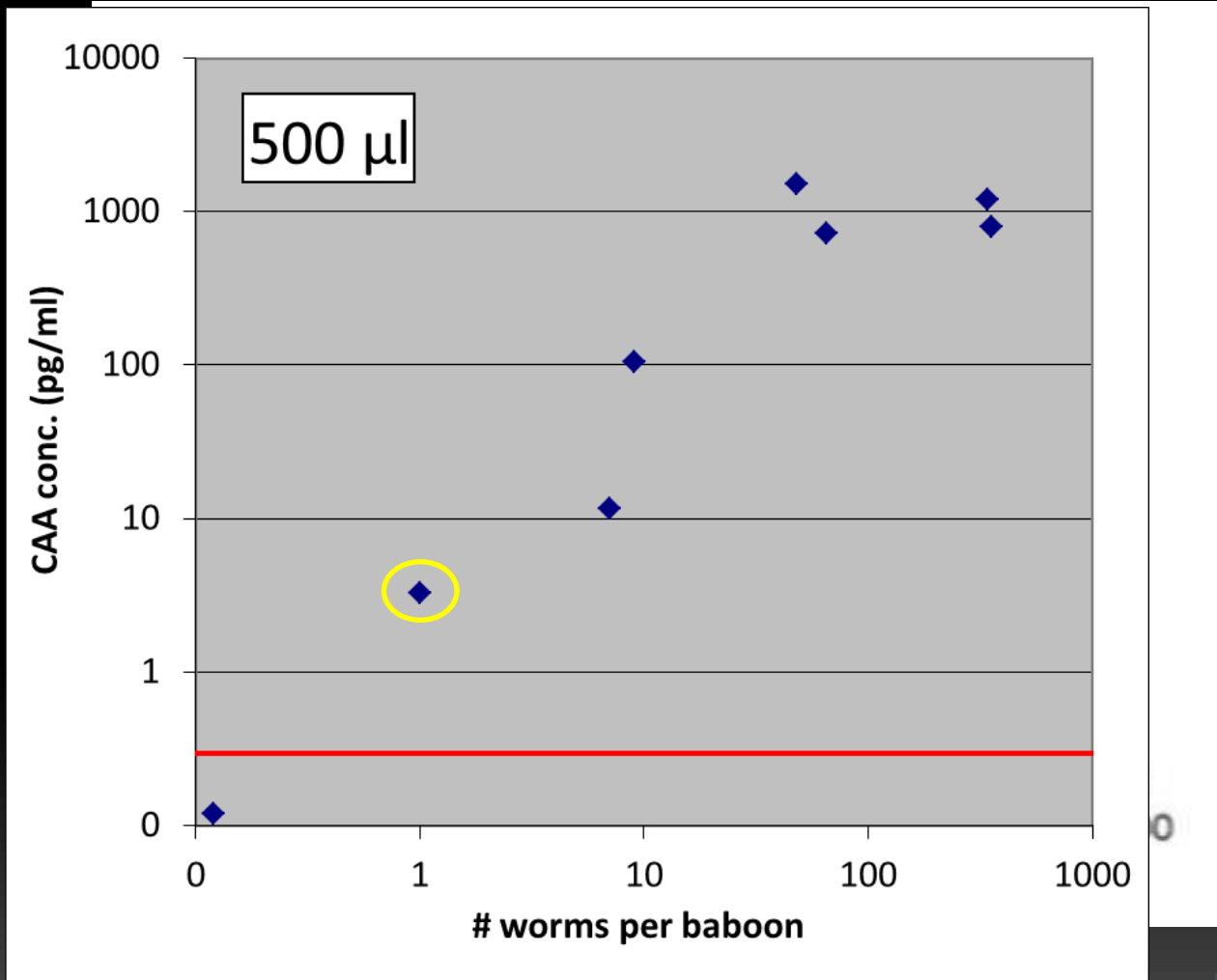
SNAIL study – CAA in travellers

Meta
Roestenberg



Evaluation in experimental infection, Kenya

Correlation of CAA levels in serum to worm numbers



Tools for diagnosis, monitoring and screening of *Schistosoma* infections utilizing lateral-flow based assays and phosphor labels. Corstjens PL, De Dood CJ, Kornelis D, Fat EM, Wilson RA, Kariuki TM, Nyakundi RK, Loverde I Tanke HJ, Van Lieshout L, Deelder AM, Van Dam GJ. Parasitology. 2014

Unpublished

Conclusions

In low endemic settings, egg microscopy is not able to find up to 90% of active schistosome infections, urging the need for an alternative test.

The urine CAA lateral flow strip is a good candidate to measure schistosomiasis transmission decline or even interruption.

Promising tool in the diagnosis of schistosomiasis:

- Quantification of worm burden**
- Useful in evaluating treatment**
- Differentiate past exposure from active infection**



Thank you!



Funding is much appreciated, but real value lies in colleagues and friends