Improving patient care through Gene-Drive for HCV results available in 24hrs.

BY Dr F Ntaganda

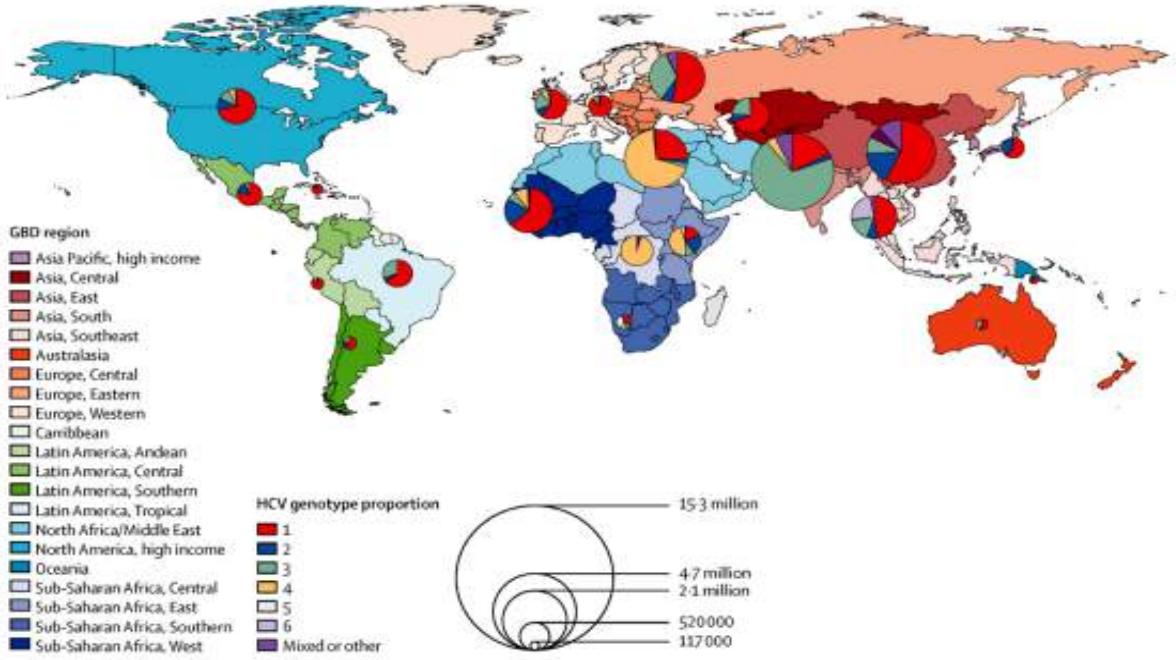
Lt Col

Dir Pathology

History and HCV burden

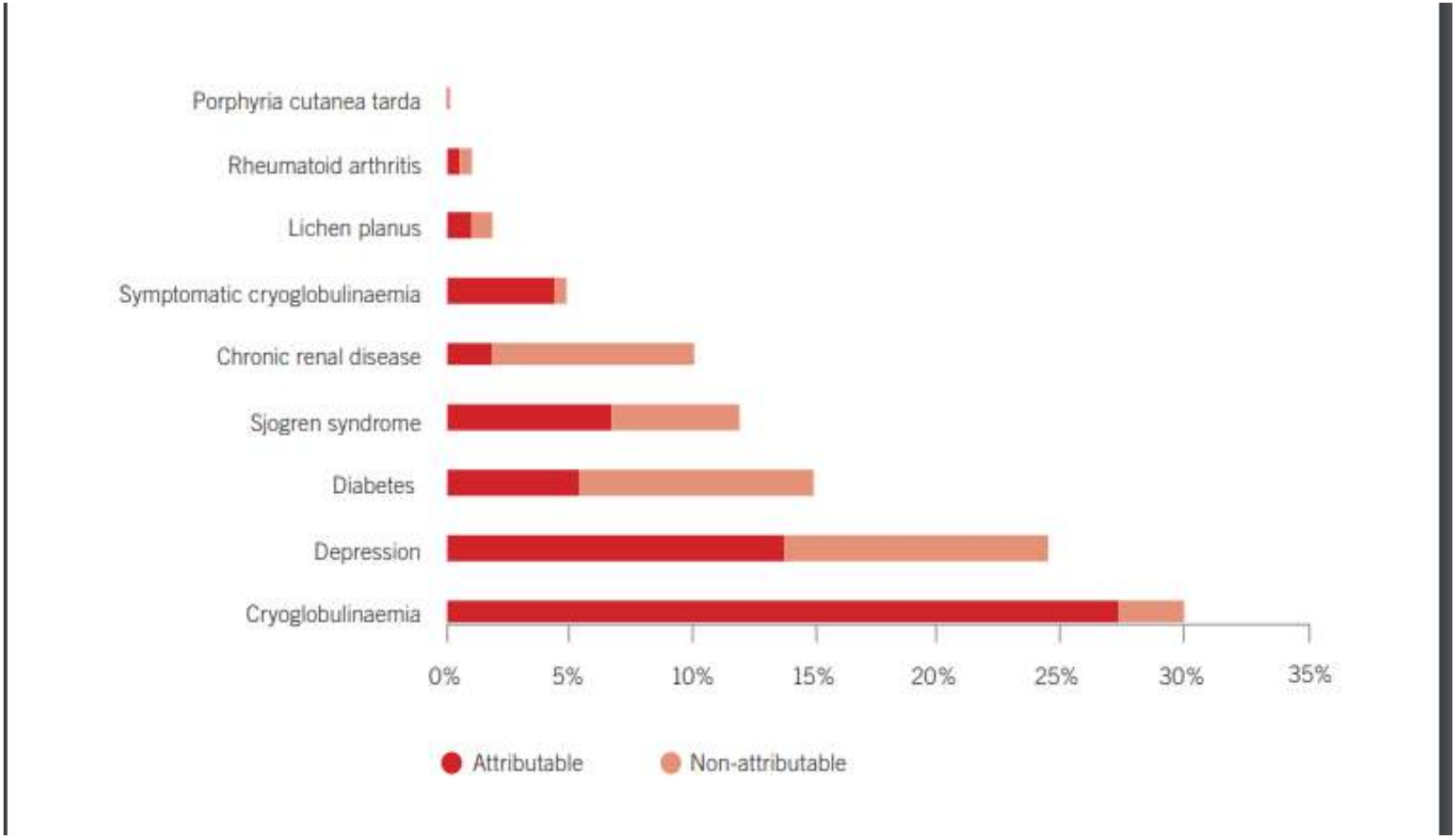
- Discovered in 1989
- The causal relationship between HCV and hepatic cancer has been proven through various case control studies.
- The risk of hepatic cancer is X 23–35
- WHO estimated
  - 2015, 71 million persons infected
  - HCV infection worldwide 1%
  - 399 000 had died from cirrhosis or hepatocellular carcinoma (HCC)
- In 2015 1.75 million new HCV infections occurred

Worldwide HCV genotype distribution



Source: The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol. 2017;2:161–76.
Disclaimer: This map is reproduced as originally published.

Other comoerbidities associated with HCV



Pathology in the current era

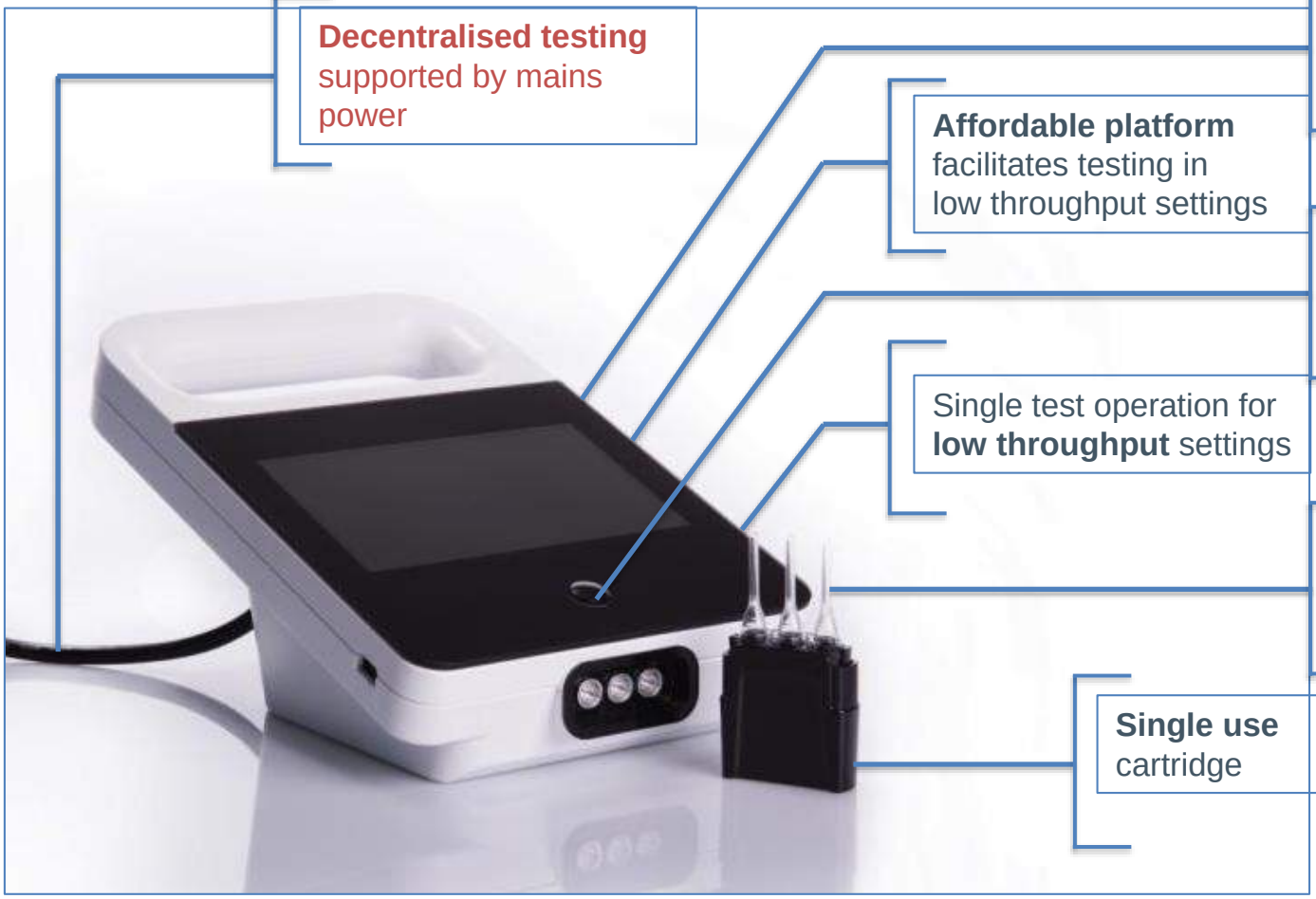
- Evolving department
- Testing a big number of people in short period of time
- At a low cost
- With a high precision
- The delay have many implications
  - Disease progression
  - Poor clinical decision
  - Resistance to treatment
  - Cost implication

What do we know so far

- Recent direct-acting antiviral therapies have provided transformative therapeutic options for chronic hepatitis C virus (HCV) infection, yet the challenge remains to identify the 1% of the world's population that is chronically infected with HCV.
- Current WHO guidelines highlight the lack of quick-based platforms for HCV RNA testing.
- The Cepheid Xpert HCV Viral Load assay (Cepheid) is currently the only In Vitro Diagnostic (IVD)-certified assay for decentralised HCV viral load determination, yet according to the WHO, it presents many limitations.

Gene drive

Genedrive Description



Decentralised testing supported by mains power

Rapid results from a **plasma sample**

Affordable platform facilitates testing in low throughput settings

Easy to use single button operation

Single test operation for **low throughput** settings

Triplicate testing and calling logic for superior performance

Single use cartridge

Specifications

Parameter	Minimal Spec'	Genedrive HCV
Target Users	Health care workers	✔
Setting Implementation	District Hospitals (II)	✔
Analytical sensitivity	1000 – 3000 IU/ml	✔
Diagnostic sensitivity	>98%	✔ (TBD)
Quantitation	Qualitative	✔
Specimen Type	Venous blood/plasma	✔
Steps	2	~4
Time to result	<60 mins	90 mins
Instrument cost	< 20,000 USD	✔
Assay Cost (price?)	<15 USD	

Specifications

Technology	Detection of viral RNA by post PCR melt analysis
Time to result	90 minutes
Hands on time	<5 minutes
Sample type	Fresh human whole blood derived plasma in K2 or K3 EDTA anticoagulant
Sample stability	EDTA Whole blood: 6 hours at room temperature (21.5°C – 25.4°C) or 72 hours at 4°C. EDTA plasma : 24 hours at room temperature (25°C) or 4 days at 4°C
Genotypes	Pan-genotypic - 1a, 1b, 2, 3, 4, 5 and 6
Product code	ID-HCV-03
Pack size	10 tests

Results

- The results are interpreted automatically by the Genedrive instrument based on the measurement of discrete fluorescent signals produced by each probe.

- With inbuilt IPC control:

Results

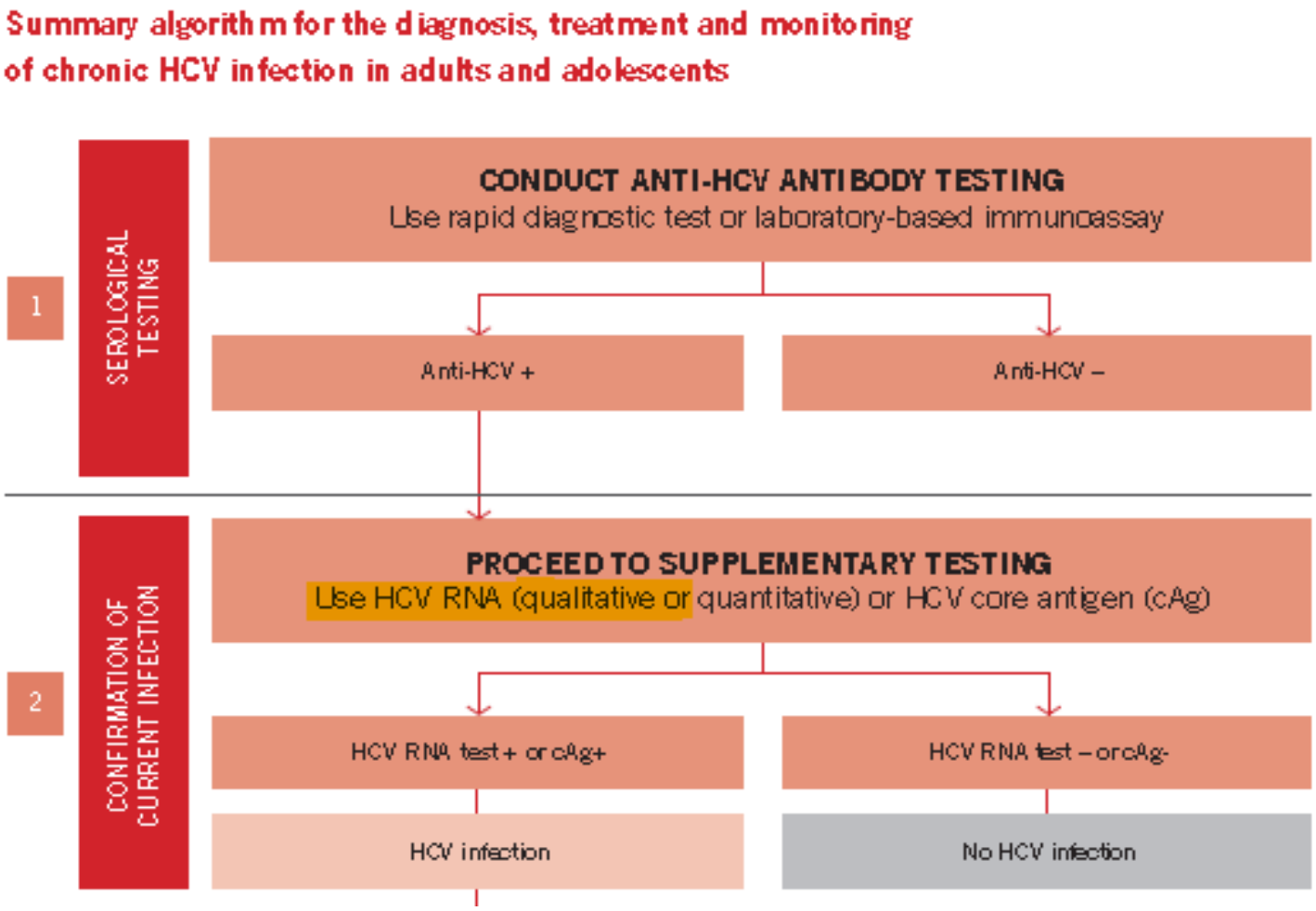
Result	Significance
Detected, Positive 	Hepatitis C virus has been detected.

Result	Significance
Undetected, Negative 	Hepatitis C virus has NOT been detected. The internal positive control has been detected.

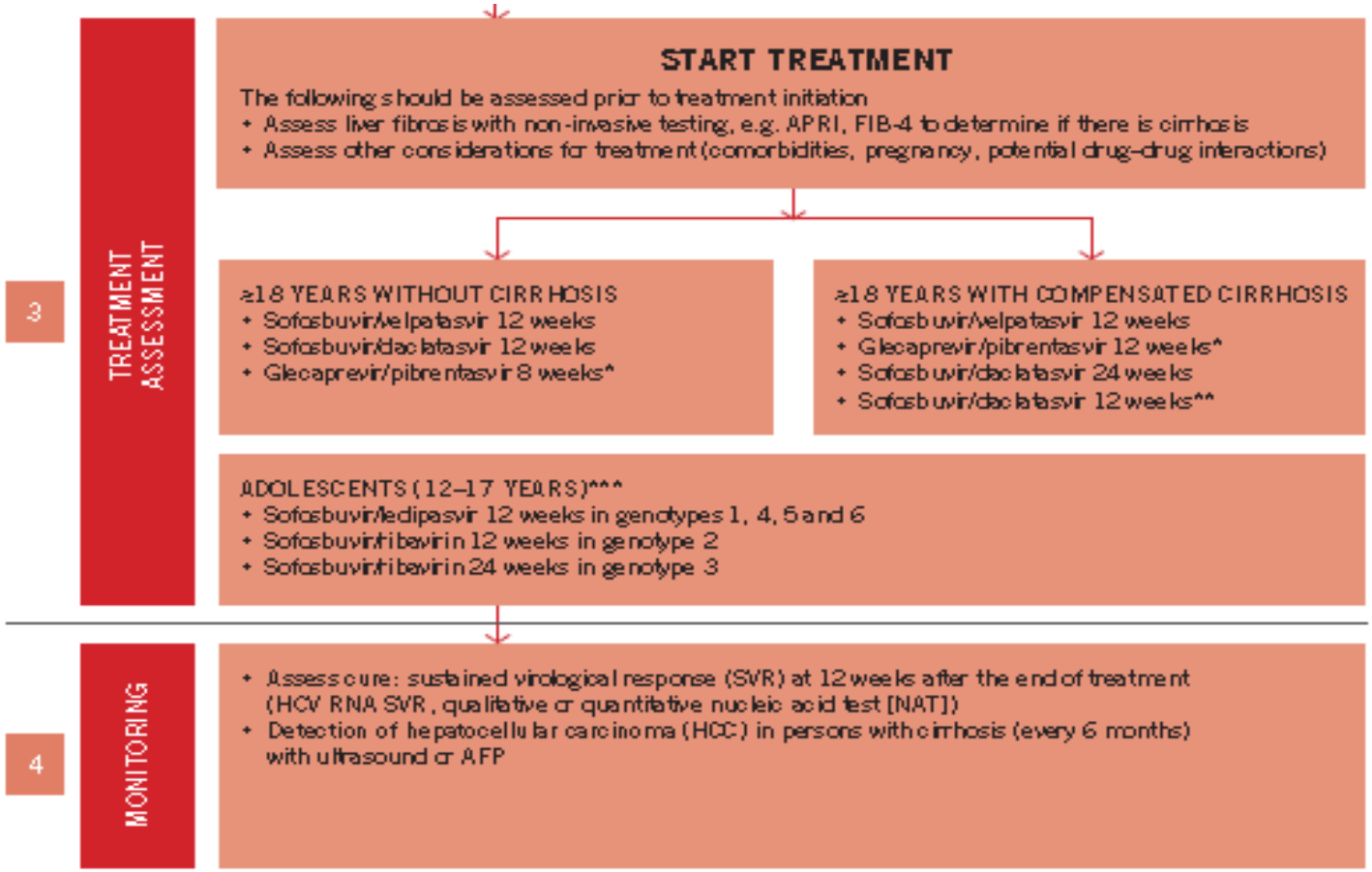
Result	Significance
Indeterminate, Retest 	Hepatitis C virus has been detected in one of the channels, however for confirmation a retest is required.

Result	Significance
Control Failed, Retest 	Hepatitis C virus and the internal positive control have not been detected. This may be due to the sample containing PCR inhibitors.

WHO 2018 Algorithm



WHO 2018 Algorithm



Performance Institut Pasteur and Queen's Medical Centre

Compared to the Abbott RealTi*me* HCV Viral Load Assay the performance of Genedrive HCV ID Kit is presented in the table

Sensitivity – 98.6%

Specificity – 100%

Efficiency – 97.2% (899/925)

n	925
True positive	412
False negative	6
False positive	0
True negative	497
Sensitivity (%)	98.6
Specificity (%)	100
PPV (%)	100
NPV (%)	98.8
Sensitivity CI (%)	96.9% to 99.5%
Specificity CI (%)	99.3% to 100%
PPV CI (%)	N/A
NPV CI (%)	97.4% to 99.5%

Performance
Lancet Laboratories - Johannesburg

Compared to the Abbott RealTi*me* HCV Viral Load Assay the performance of Genedrive HCV ID Kit is presented in the table

Sensitivity – 100%

Specificity – 100%

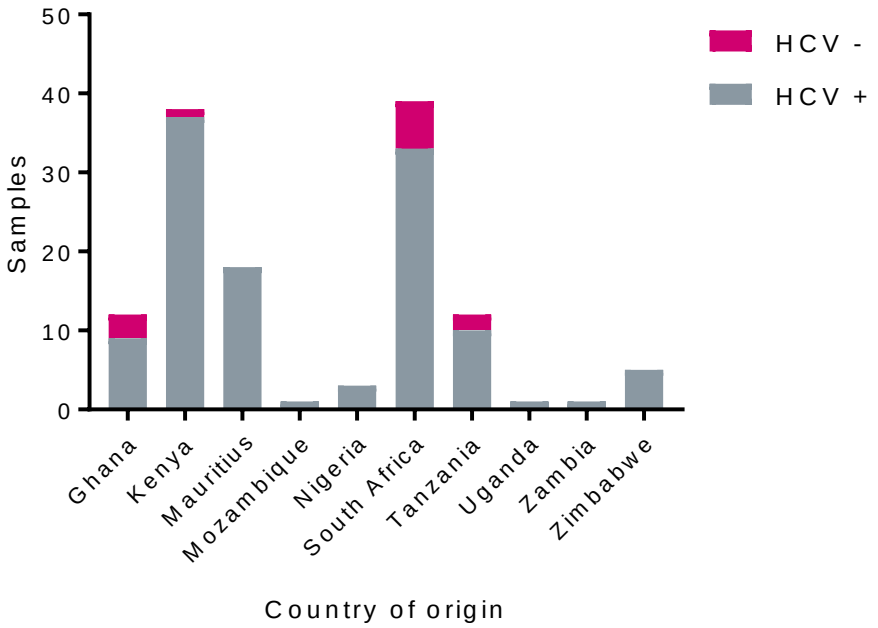
Efficiency – 94.3%

n	126
True positive	114
False negative	0
False positive	0
True negative	12
Sensitivity (%)	100
Specificity (%)	100
PPV (%)	100
NPV (%)	100
Sensitivity CI (%)	96.8 to 100.0
Specificity CI (%)	73.5 to 100.0
PPV CI (%)	N/A
NPV CI (%)	N/A

Origin of specimens

Lancet Laboratories - Johannesburg

Country	HCV +	HCV -	Total	%
Ghana	9	3	12	9.2
Kenya	37	1	38	29.2
Mauritius	18	0	18	13.8
Mozambique	1	0	1	0.8
Nigeria	3	0	3	2.3
South Africa	33	6	39	30
Tanzania	10	2	12	9.2
Uganda	1	0	1	0.8
Zambia	1	0	1	0.8
Zimbabwe	5	0	5	3.8
Grand total	118	12	130	



Conclusion

Roche	Gene drive
Cost 75,000 frw	Cost 12,000 frw
Time 2 weeks	Time : 1 day
User : easy	User : multiple step
Application : local	Application: remote

Future direction

- Similar study at RMH
  - Compare findings
  - Cheaper, affordable
  - Quick
  - Reliable