Utility of HCV antigen core quantification for the screening of chronic hepatitis C

Karine LACOMBE - Léa Duchesne

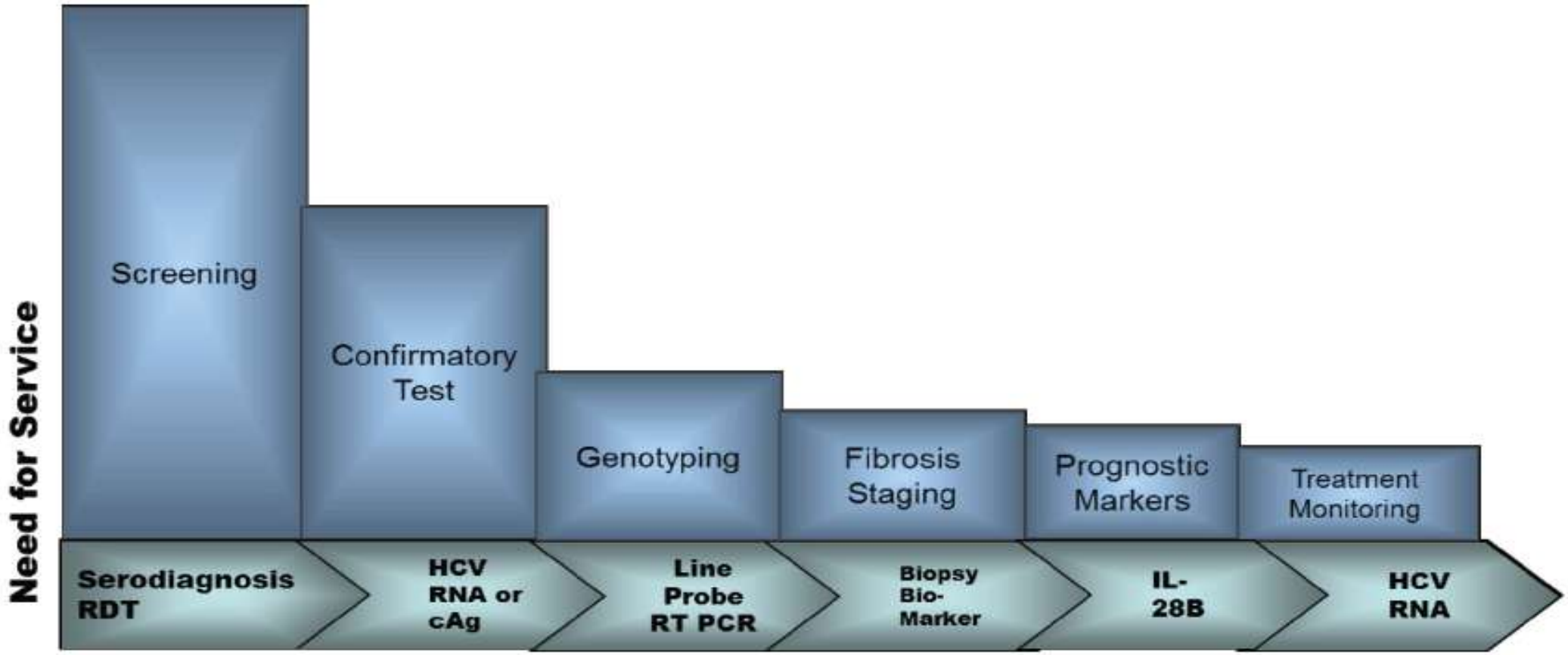
Inserm Unit UMR-S 1136, Team 2

Pierre Louis Institute of Epidemiology and Public Health

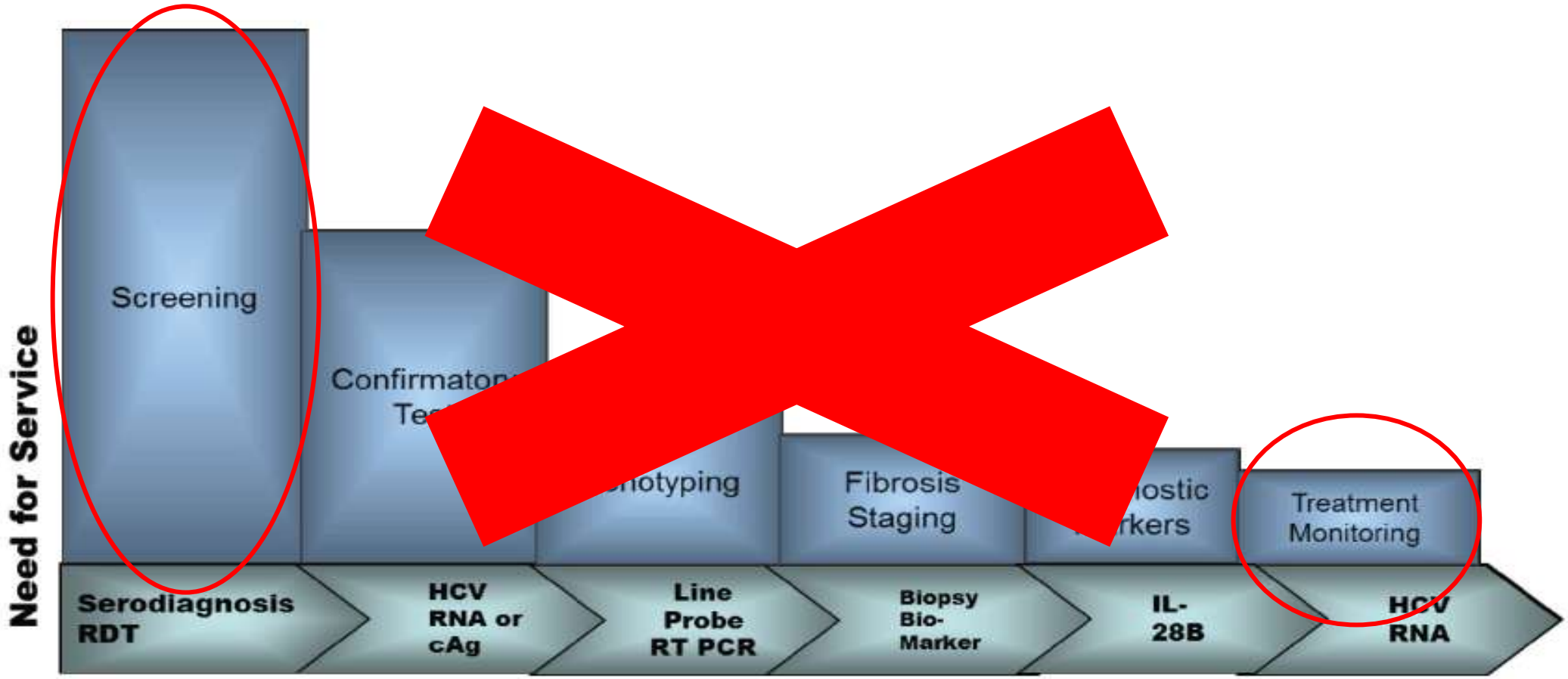
ATHS

2 octobre 2015

Continuum of biological follow-up in chronic hepatitis C



Continuum of biological follow-up in chronic hepatitis C



- Challenge: change from a multi-step procedure to a two-step procedure

Techniques in development

- **Point of care (POC) platform for HCV-RNA assays**

  HCV RNA quantitative assay

  - Alere Q *(Alere Inc.)*
  - EOSCAPE-HCV rapid RNA assay *(Wave 80 Biosciences)*
  - Truelab Uno real time Micro PCR system *(Molbio Diagnostics Pvt Ltd)*
  - GeneXpert *(Cepheid)*
  - RT CPA HCV Viral Load Test ***(****Ustar Biotechnologies****)***

  HCV RNA qualitative assays

  - Gendrive *(Epistem)*
  - PanNAT *(Micronics Inc.)*

Source: UNITAID report April 2015

Techniques in development

- **HCV antigen core (AgC) quantification**

  - To date, only one marketed test: Abbott ARCHITECT platform

  - One POC platform in development: DAKTARI

Techniques in development

DAKTARI:

POC technology which eliminates sample preparation through the use of a technology known as “microfluidic immunochromatography”, which isolates cells (or viruses) :the only user step is to apply a drop of whole blood to the cartridge.

ANRS 12336 Study: Assessment of the performance of the HCV core antigen as a diagnostic tool for chronic hepatitis C in Africa

Léa Duchesne, Karine Lacombe

Inserm Unit UMR-S 1136, Team 2

Pierre Louis Institute of Epidemiology and Public Health

Richard Njouom

Centre Pasteur of Yaoundé

TAC (Treatment Africa hepatitis C) trial
ANRS 12311 study

- Objective: to assess the efficacy of an antiviral treatment combining sofosbuvir and ribavirin for the treatment of genotype 1, 2 and 4 hepatitis C virus-infected patients in Sub-Saharan Africa
- Therapeutic trial, phase IIb
- N= 120 patients
- Treatment: 3 to 6 months + 6 month-course of follow-up
- Duration: October 2015- November 2016
- Ancillary studies: medico-economic, diagnosis and screening

Objectives

Principal objective: Assessment of the performance of HCV core antigen quantification as a diagnostic tool for chronic hepatitis C in Africa

Secondary objectives:

- To assess the impact of the following covariables on the AgC diagnostic performance:
  - Demographic variables (age, gender)
  - HCV genotype
  - HIV infection
  - HBV infection

Methods

- AgC quantification: Abbott ARCHITECT HCV Ag Assay
  - < 3 fmol/L : negative
  - ≥ 10 fmol/L: positive
  - 3 ≤ [AgC] < 10 fmol/L: « grey zone » ⇨ retested twice
- HCV RNA quantification by quantitative rt-PCR : gold standard
- Anti-HCV Ab
- Anti-HHs Ab
- Ag HBs

} ELISA serologies

Population

1037 serum samples from the Pasteur Center of Cameroon in Yaounde

Inclusion criteria

- HCV+:
  - HCV antibody (HCV Ab) positive serology
  - Quantifiable HCV RNA
- HCV-:
  - HCV Ab negative serology
  - OR undetectable HCV RNA
- HIV status known
- HBV status known

Exclusion criteria

- 11 Tri-infection (HCV/HIV/HBV)
- 7 Infection status unknown
- 10 Retest unavailable

Included samples: n=1009

- 475 VHC-
- 545 VHC+

Table 1: Socio-demographic and virologic caracteristics of the sera

	Uninfected (n=335)	HCV-monoinfected (n=489)	HIV-infected (n=78)	HBV-infected (n=107)
HCV+ (n, %)	na	na	27 (34.6)	28 (59.6)
Gender, woman (n, %)	194 (57.9)	251 (51. 3)	42 (53.9)	55 (51.40)
Age (mean, sd)	40.8 (17.5)	59.8 (11.2)	46.4 (13.7)	40.6 (15.1)
VHC+	na	na	57.3 (8.8)	54.9 (11.9)
VHC-	na	na	40.6 (12.2)	35.5 (12.7)
Genotype (n, %)				
1	na	45	2	2
2	na	39	1	1
4	na	37	2	3
Virology (mean, sd)				
ARN VHC (IU/mL)	na	1 864 908 (2 339 039)	3 357 046 (4 613 890)	1 337 306 (1 676 788)
Indetectable HCV viral load	na	126	13	19
AgC VHC (fmol/L)	13.927 (251.28)	2063.24 (3073.74)		
VHC+	na	na	4637.09 (7780.75)	1602.69 (2742.27)
VHC-	na	na	2.336 (6.820)	5.477 (41.17)

Results: correlation between AgC and HCV RNA, by infection group

Figure 1a: correlation between AgC quantification and HCV RNA in HCV mono-infected

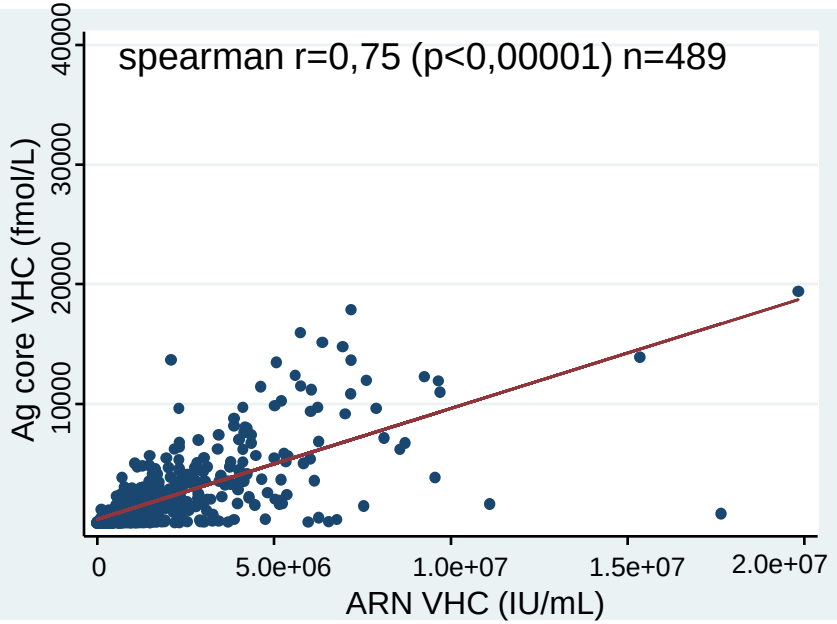


Figure 1b: correlation between AgC quantification and HCV RNA in HIV-HCV co-infected sera

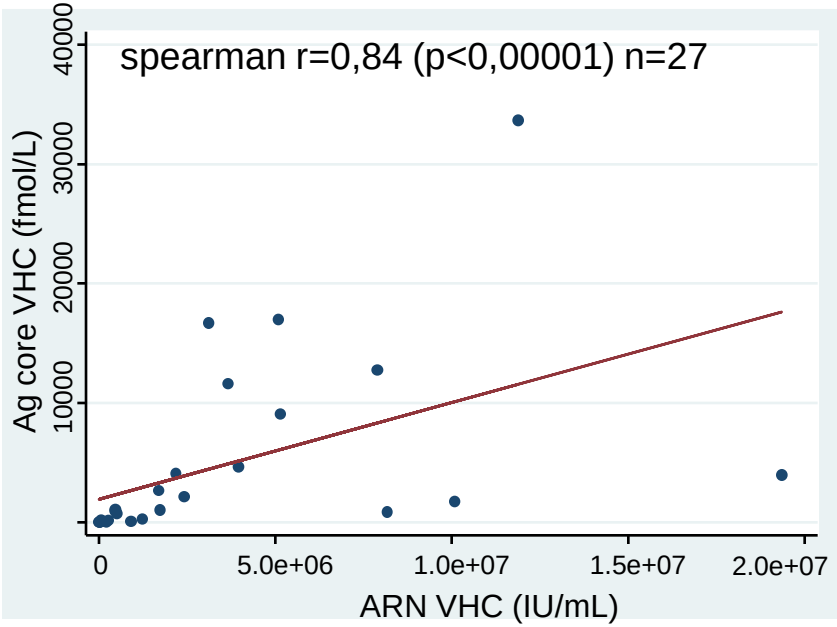
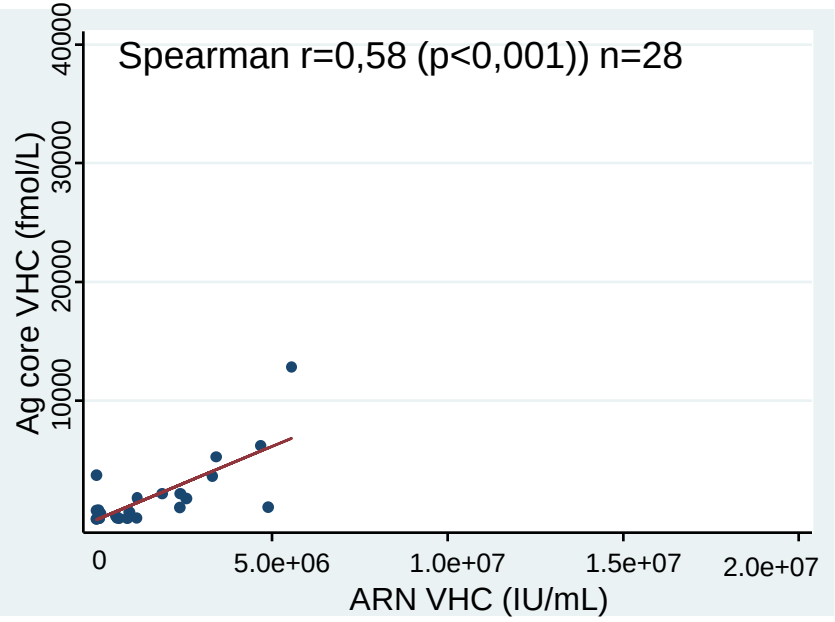
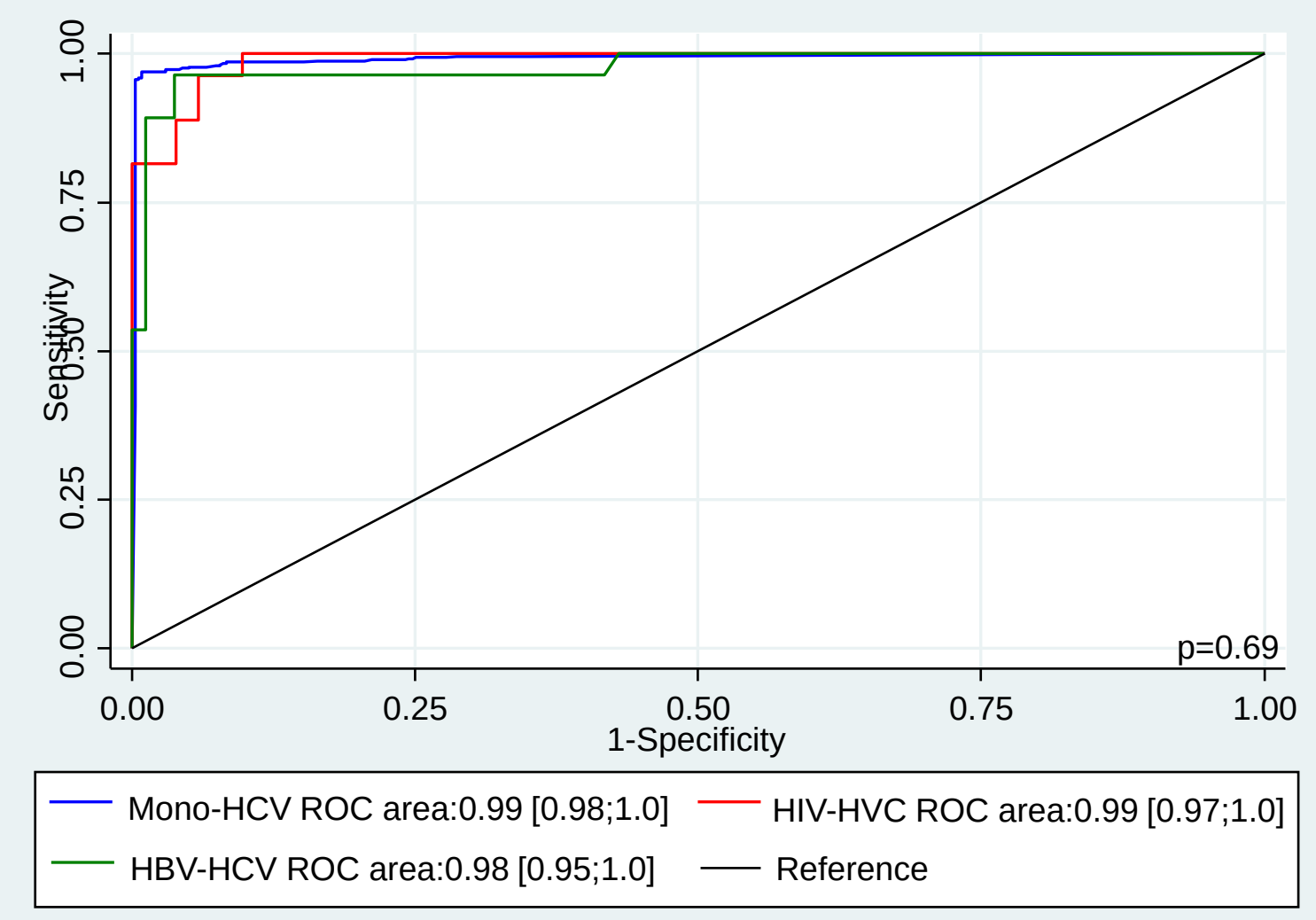


Figure 1c: correlation between AgC quantification and HCV RNA in HBV-HCV co-infected sera



Results: AgC overall performance

Figure 2: ROC curves of the performance of AgC quantification for the diagnostic of chronic hepatitis C in HCV mono-infected and HCV uninfected, HIV-infected and HBV-infected patients



Results: AgC's overall performance

Table 2: Performance of the AgC quantification by infection group

	n	Se [IC97.5%]	Spe [IC97.5%]	VPP*	VPN*	AUC [IC95%]	LR+	LR-
Mono	824	95.7 [93.2 ; 97.5]	99.7 [98.1 ; 100]	98.1	99.3	0.99 [0.98-1.0]	319	0.043
HIV	78	100 [85.0 ; 100]	88.2 [74.3 ; 96.2]	57.6	100	0.99 [0.97-1.0]	847	0
HBV	107	96.4 [79.2 ; 99.9]	96.2 [88.1 ; 99.4]	80.2	99.4	0.98 [0.95-1.0]	25	0.037

Table 3: Performance of the AgC quantification by genotype among the mono-infected and not infected sera group

	n	Se [IC 97.5%]	Spe [IC 97.5%]	VPP*	VPN*	AUC [IC95%]	LR+	LR-
Genotype 1	488	97.7 [86.4-99.9]	98.9 [97.2-99.7]	93.4	99.6	0.99 [0.99-1.0]	88.8	0.023
Genotype 2	482	94.9 [80.7-99.6]	98.9 [97.1-99.7]	93.2	99.2	0.99 [0.97-1.0]	86.3	0.052
Genotype 4	480	100 [88.8-100]	98.9 [97.1-99.7]	93.4	100	0.99 [0.99-1.0]	90.9	0

*Estimated HCV prevalence in Cameroon: 13,8%

Results: false results

- 32 wrong results (3.2%) : 22 false negative (FN) and 10 false positive (FP)

- FN compared to TP
  - HCV viral load significantly lower:
    => $\bar{m}$ =32 851 UI/mL vs $\bar{m}$ =1 992 335 UI/mL (p<0.00001)
  - Percentage of women significantly lower:
    => 22.7% vs 52.2% (p=0.007)

- FP compared to TN
  - Percentage of HIV-infected sera significantly higher:
    => 60% vs 11.8% (p<0.0001)

Conclusion

- High performance
- No influence of genotype
- No influence of HBV and HIV infection on the overall performance
- Lower specificity in HIV-infected patients
- Reliable diagnostic tool

- Limits: not a study in real world setting => feasibility?

- Perspective: assessment of the performance of AgC quantification as a monitoring tool of HCV antiviral therapy

Perspective: Which role for AgC in hepatitis C diagnosis and screening?

- Unique diagnosis test or confirmatory test?
- Test available only on a specific Abbott platform
- Need for a POC test
- Alternative solution: use of DBS technique + laboratory test
  => BUT lower AgC quantification performance[1]
- Need for screening strategy evaluation

[1] Chevaliez, J Infect Dis., 2015

Thank you for your attention