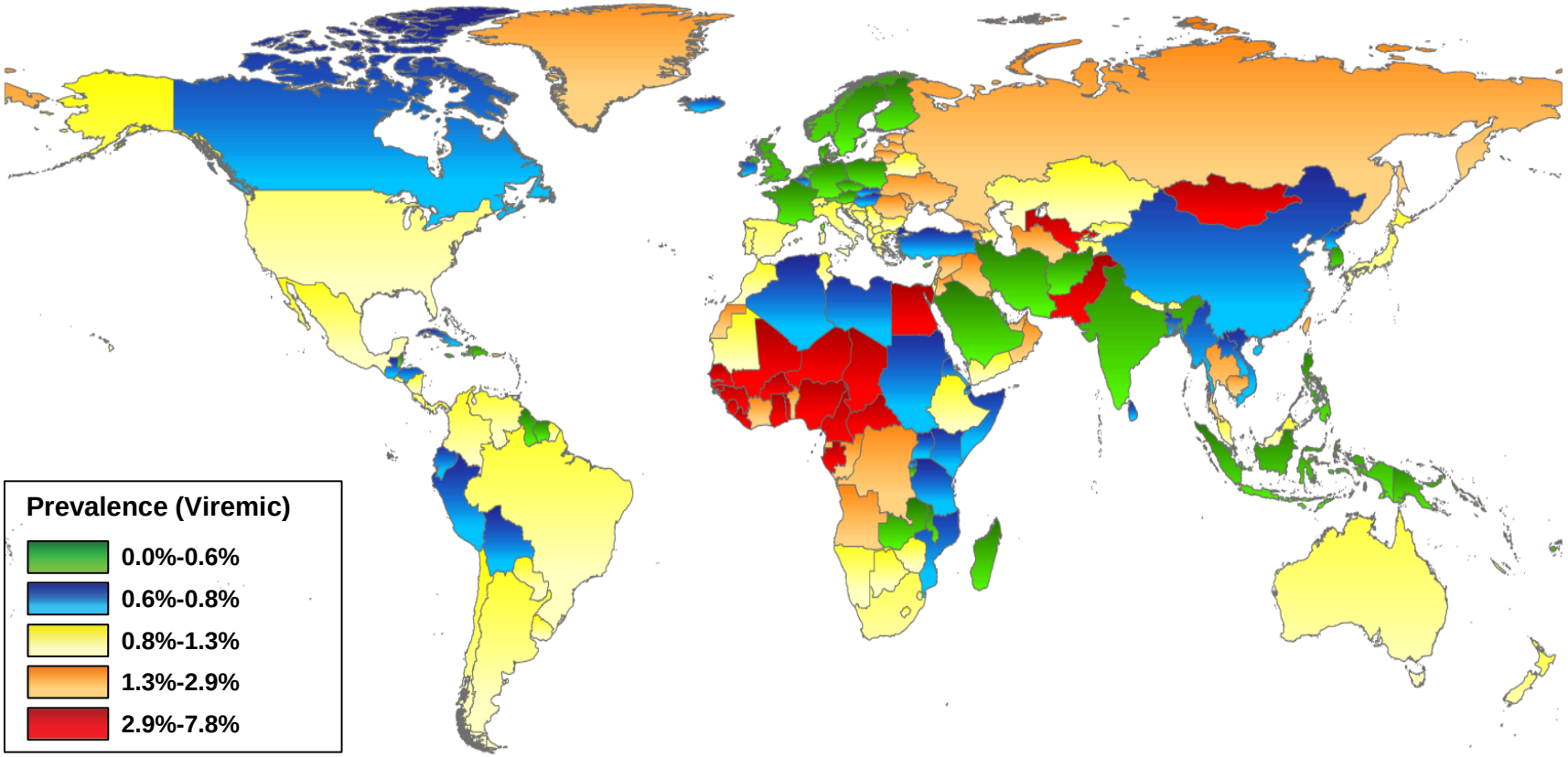
Virological Tests for Improved Access to Cure

Slim Fourati

French National Reference Center for Viral Hepatitis B, C and delta
Department of Virology & INSERM U955
Henri Mondor Hospital
University of Paris-Est
Créteil, France

Worldwide HCV RNA Prevalence



Gower et al., J Hepatol. 2014;61(1 Suppl):S45-57.

The Global Burden of HCV Infection

- **HCV is responsible for >350,000 deaths a year worldwide (195 000 HCC)**
- **Up to 50% of HCV-infected patients are unaware of their infection**
- **Less than 10% of the HCV-infected population has received treatment in the US**

GBD 2013 Mortality and Causes of Death Collaborator., Lancet 2015;385(9963):117-71; Parkin DM., Int J Cancer 2006;118(12):3030-44; Thomas DL., Nat Med 2013;19(7):850-8; Denniston et al., Hepatology 2012;55(6):1652-61; Meffre et al., J Med Virol 2010;82(4):546-55.

Global control of HCV infection is now a realistic objective

Chronic HCV infection is curable by DAAs

large-scale screening of HCV infection is now needed to identify infected patients and provide them with efficacious therapies.

Alternative Tests

- **Point-of-care tests (POCT)**
  - Rapid diagnostic tests
  - Molecular tests

OraQuick®

Daktari™

Alere™ q

- **Dried blood spot (DBS)**

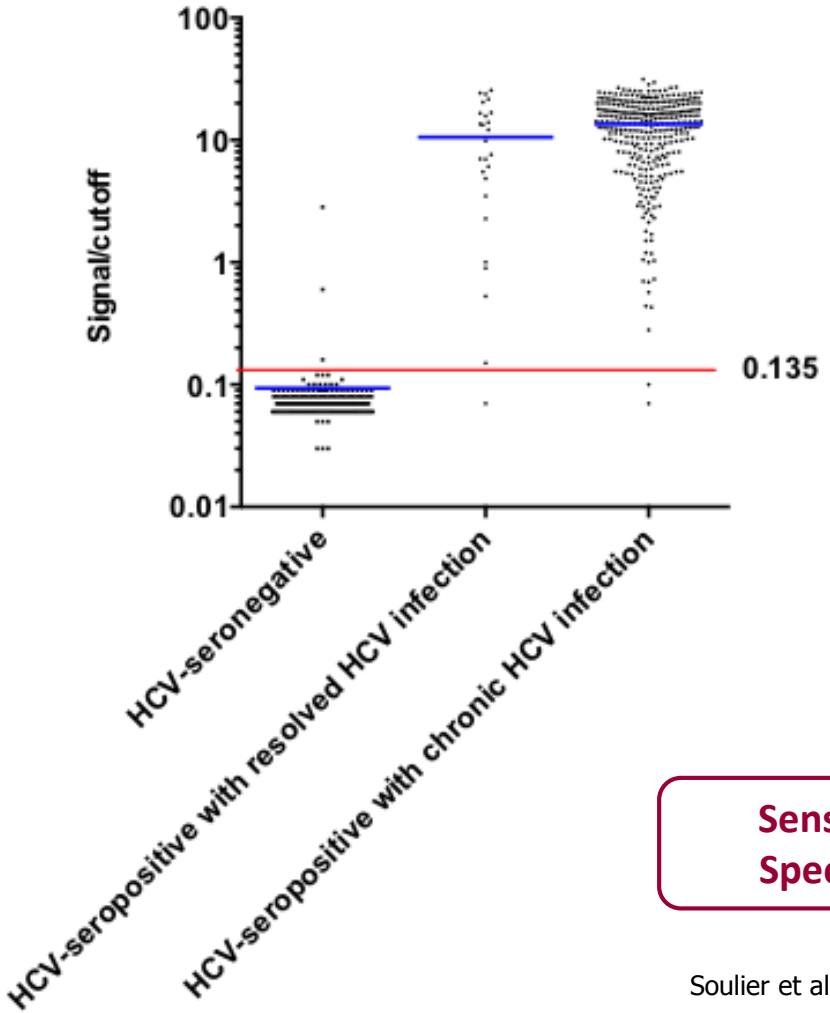
Fingerstick WB

Advantages and Disadvantages of DBS

- **Advantages**
  - Low volume required (50-70 µL)
  - Good stability of the biological matrix
  - Easy to collect and mail at room temperature
  - Serological, molecular and pharmacological analysis can be performed

- **Disadvantages**
  - Lower analytical sensitivity than classical biological matrices (serum or plasma)
  - No standardized procedures
  - Storage at -20° C required for long-term conservation

Detection of anti-HCV Ab in Whole Blood from DBS by 3rd-generation EIA (Vitros)



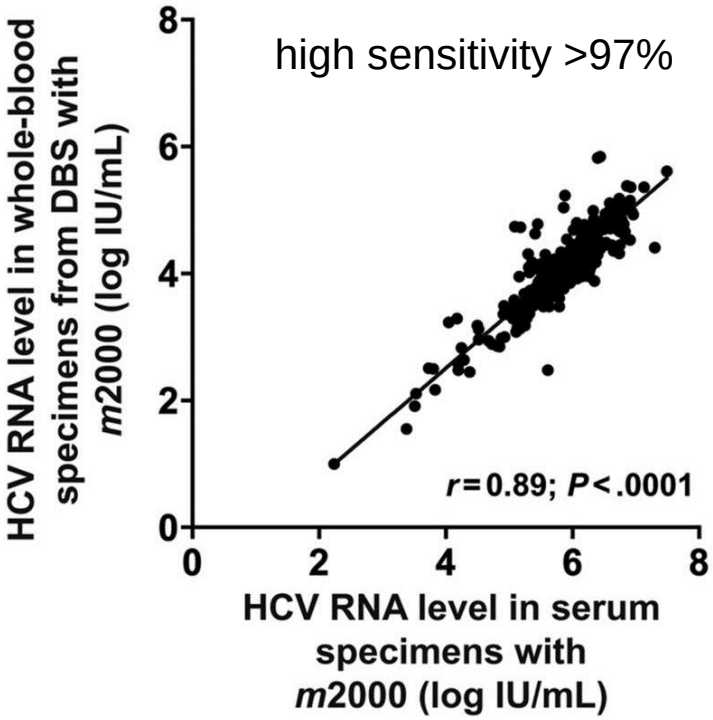
ROC curve analysis

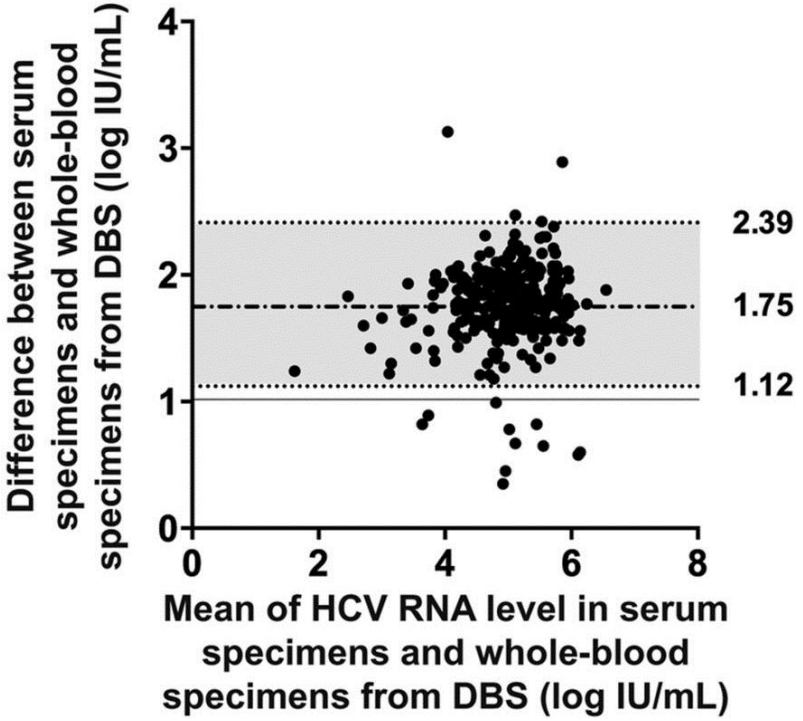
Samples from DBS can be confidently used for anti-HCV antibody detection by means of standardized, commercially available methods

Sensitivity = 99.1%
Specificity = 98.2%

Soulier et al., J Infect Dis 2015

HCV RNA Quantification by the RealTi*me* HCV Assay in Whole Blood from DBS





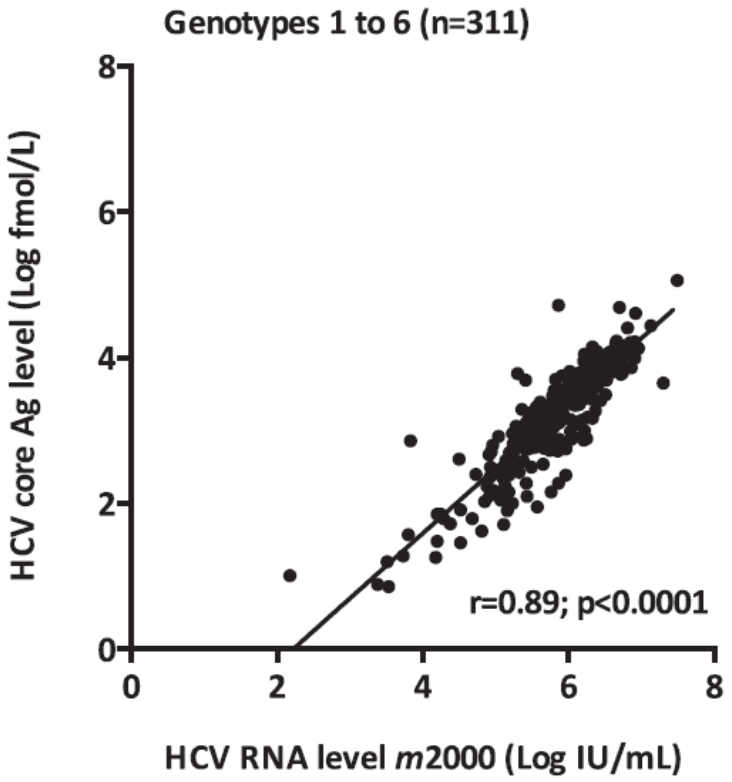
Absolute amount of HCV RNA should not be considered when quantification is performed on DBS. The HCV RNA levels are usually high in patients who do not eradicate infection. The DBS result, if negative, can be trusted as indicative of a sustained virological response.

Soulier et al., J Infect Dis 2015

HCV Core Ag Quantification

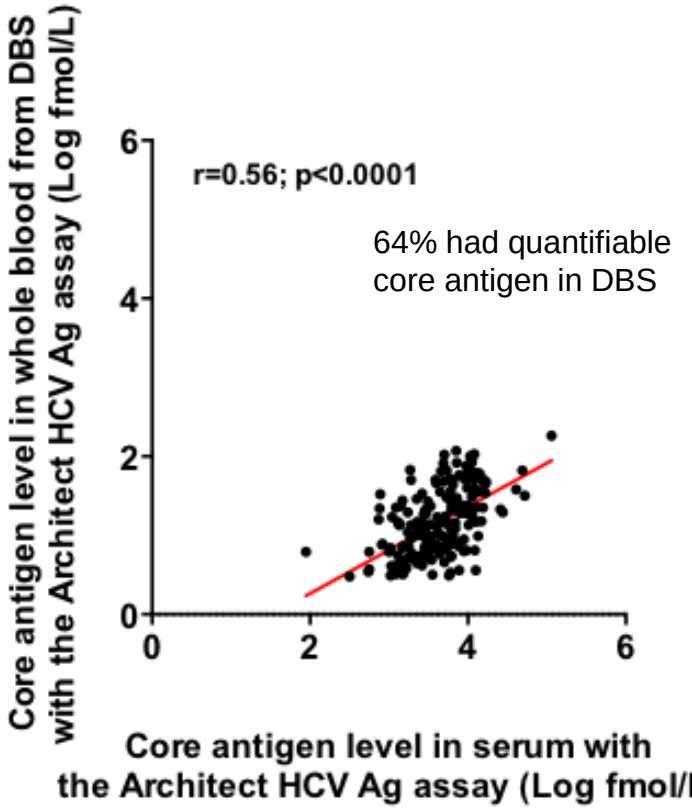
- **Attractive alternative to molecular methods**
- **Advantages over molecular methods**
  - Cheap (50% to 70% less expensive)
  - Stability of the marker at RT for 96 hours
  - Easy to perform through automated EIA
- **New HCV treatment monitoring tool, well suited to IFN-free regimens**

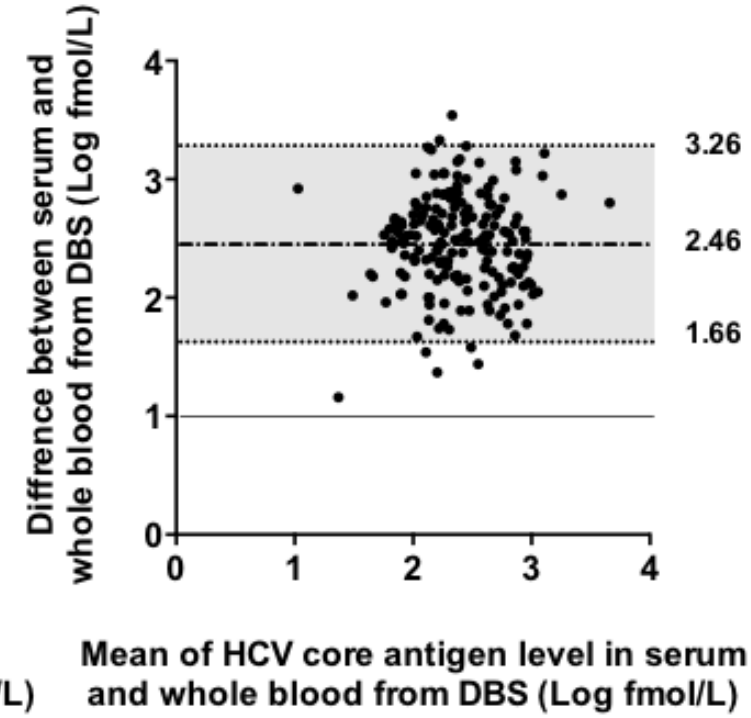
Relationship between HCV Core Ag and HCV RNA Levels



Chevaliez et al., J Clin Virol 2014;61(1):145-8.

HCV Core Ag Quantification by the Architect HCV Assay in Whole Blood from DBS





When whole-blood specimens from DBS are used, HCV RNA testing should be preferred to HCV core Ag testing

Soulier et al., J Infect Dis 2015

POCT: Benefits to Patients

Reduced waiting times

Fewer or no follow-up visits

Immediate discussion of results

Improved healthcare accessibility

Rapid Diagnostic Test (RDTs)

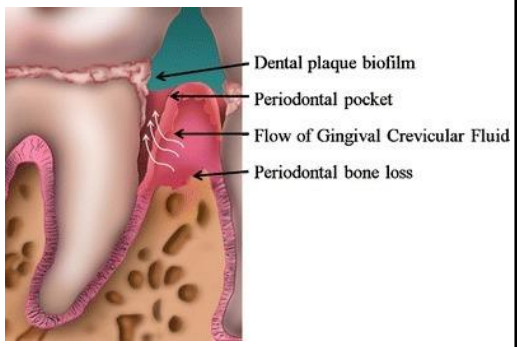
- **Can be used at the site of patient care**
  - Physician' office
  - Emergency room, ICU
  - Outpatient clinics, rural areas
- **Can use original specimen matrices in addition to serum or plasma**
  - Oral fluid
  - Fingerstick whole blood

Interest of Oral fluid as an Alternative Matrix

- Simple, safe, painless, cheap to collect
- Contains lower amount of immunoglobulins (and viral markers) than whole blood

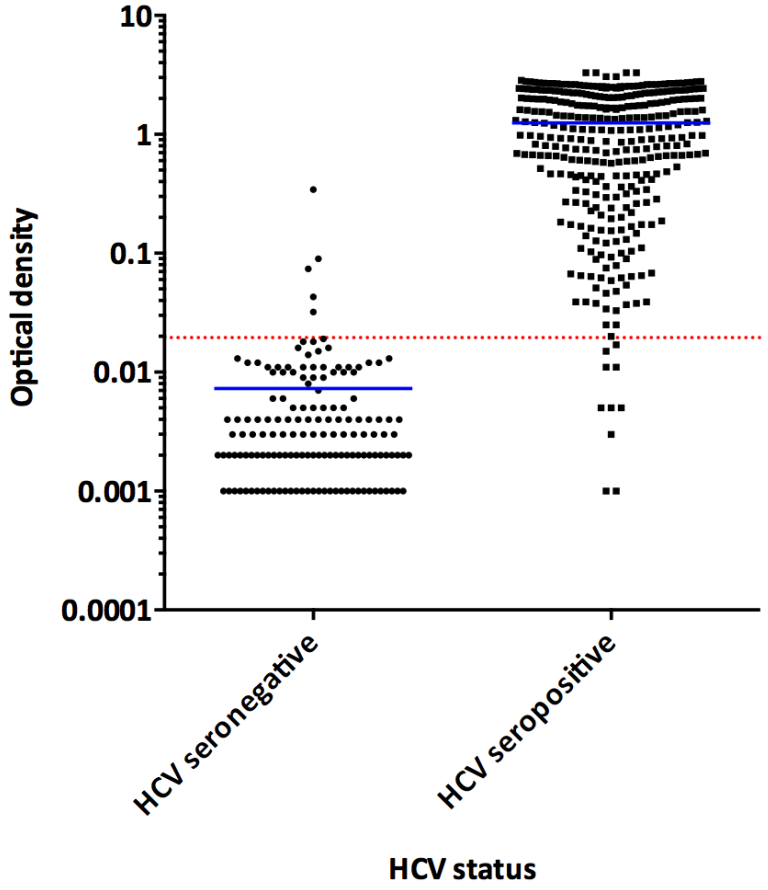
Specimen	IgG (mg/L)	IgM (mg/L)	IgA (mg/L)
Plasma	14730	1280	2860
Whole saliva	14.4	2.1	19.4
Parotid saliva	0.36	0.43	39.5
Crevicular fluid	**3500**	**250**	**1110**

Transudate from the capillary bed



McKie et al., Lancet Infect Dis 2002;2(1):18-24.

Performance of a RDT to detect anti-HCV Ab in Oral Fluid



ROC curve analysis

Sensitivity = 97,1% (94.7%-98.6%)
Specificity = 97,1% (93.3%-99.0%)

Chevaliez et al.,. Clin Microbiol Infect 2016 Jan S1198-743X(16)00025-2

Performance of RDTs: Meta-Analysis

- **More than 13,000 individuals included in 18 studies between 1994 and 2011**
  - Stratification according to matrix specimens
    - Whole blood (venous and capillary): 4,259 specimens
    - Saliva: 3,994 specimens

Specimen	Specificity	Sensitivity
Whole blood	**99.5%**	**98.9%**
Saliva	**98.2%**	**97.1%**

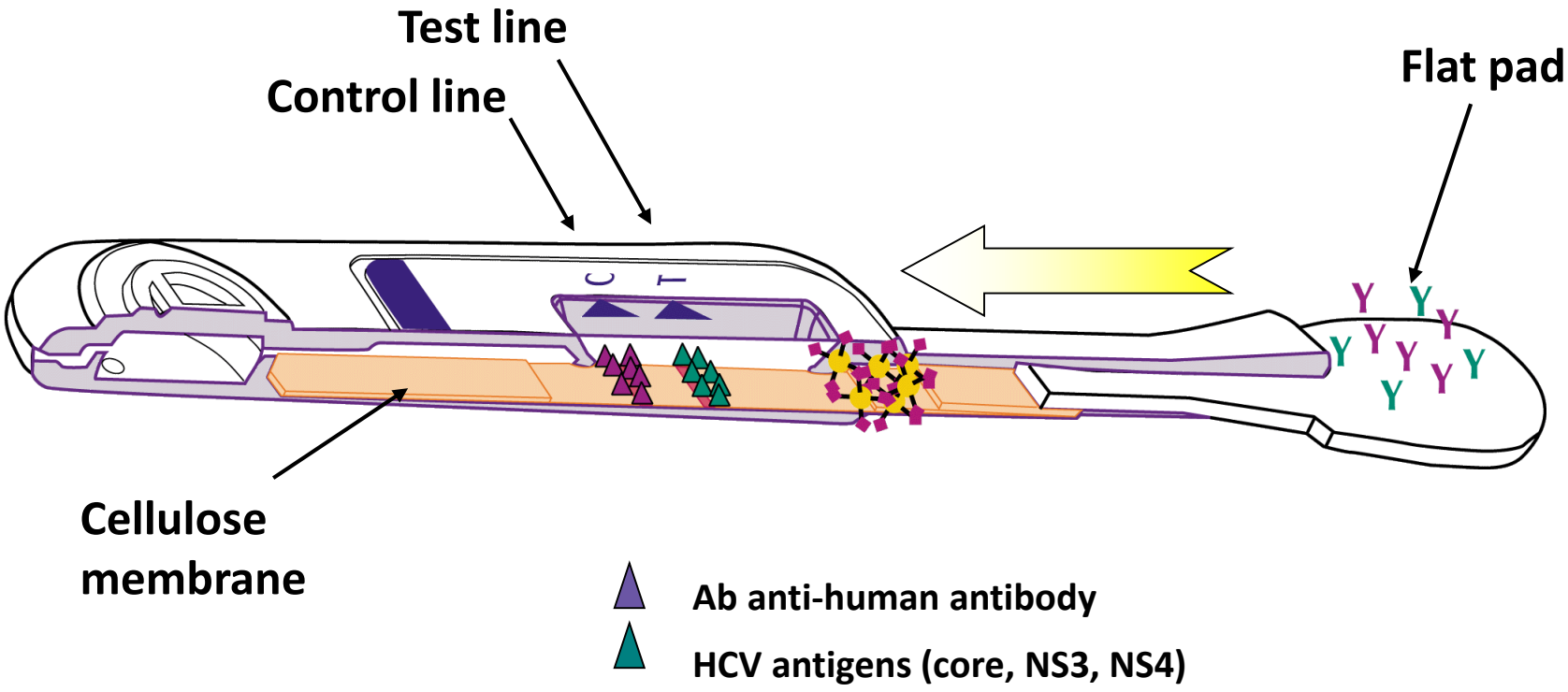
Shivkumar et al., Ann Intern Med 2012;157(8):558-66.

Available RDTs for anti-HCV Detection (CE-marked)

	Oraquick® HCV	**Toyo® HCV**	**Labmen® HCV**	**Multisure HCV**	**Assure® HCV**	**First Response HCV**
Manufacturer	Orasure	Turklab	Turklab	MP Diagnostics	MP Diagnostics	Premier Medical Corporation Ltd
Specimen type	**oral fluid**, **whole blood**, serum, plasma	**whole blood**, serum, plasma	**whole blood**, serum, plasma	**whole blood**, serum, plasma	**whole blood**, serum, plasma	**whole blood** serum, plasma
Volume required (µL)	40 (oral fluid) 20	30	10	25	50	35
Time to read (min)	20	15	15	15	15	20

Principle of an RDT

Example of OraQuick®



Performance of RDTs for anti-HCV Ab Detection from Fingerstick Whole Blood

- **318 patients with chronic HCV infection, 25 patients with resolved HCV infection and 170 HCV-seronegative subjects (N=513)**

Tests	Specificity	Sensitivity
OraQuick® HCV Rapid Ab Test	100%	99.4%
TOYO® anti-HCV test	98.8%	95.8%
Labmen® HCV test	100%	63.1%

Chevaliez et al.,. Clin Microbiol Infect 2016 Jan S1198-743X(16)00025-2

Performance of RDTs for anti-HCV Ab Detection from Oral Fluid

- **318 patients with chronic HCV infection, 25 patients with resolved HCV infection and 170 HCV-seronegative subjects (N=513)**

Tests	Specificity	Sensitivity
OraQuick® HCV Rapid Ab Test	100%	97.6%

Chevaliez et al.,. Clin Microbiol Infect 2016 Jan S1198-743X(16)00025-2

Performance of RDTs for anti-HCV Ab Detection from Whole Blood Collected on DBS

- **129 patients with chronic HCV infection, 10 patients with resolved HCV infection and 68 HCV-seronegative subjects (N=207)**

Tests	Specificity	Sensitivity
OraQuick® HCV Rapid Ab Test	100%	100%
First Response® HCV Card test	100%	99.3%
Assure HCV Rapid Test	100%	98.6%
MultiSure HCV	100%	98.6%

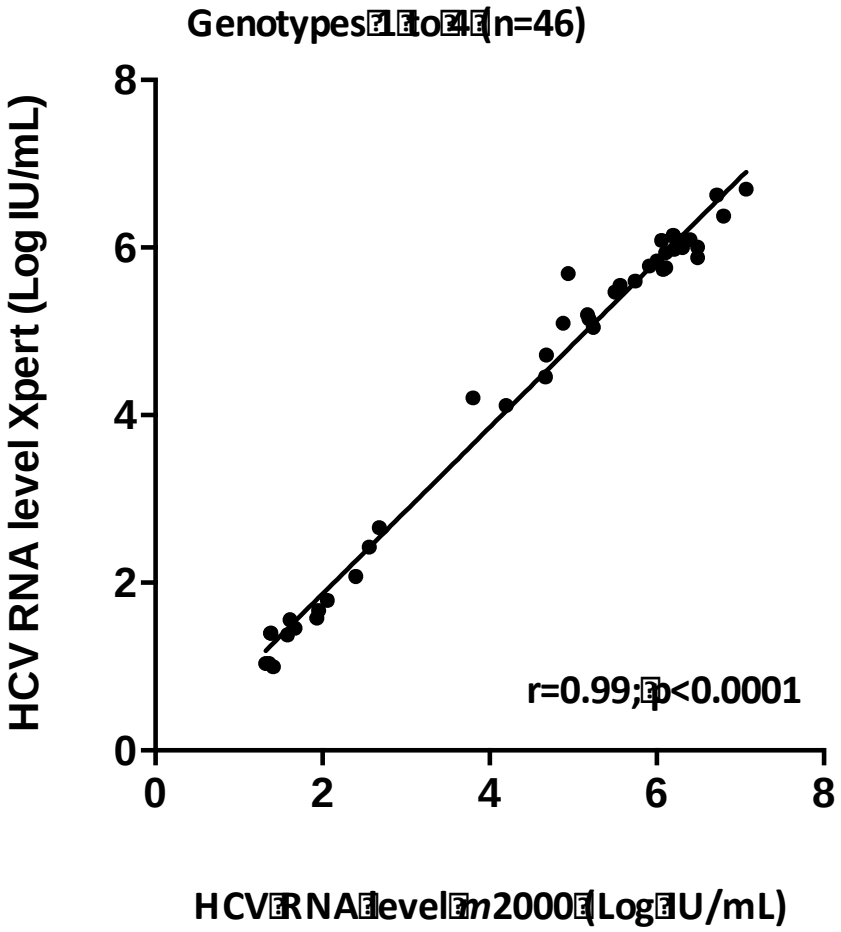
Poiteau et al.,. J Viral Hepat 2016 Feb

Molecular POCT

Alere™ q

GeneXpert® I

HCV RNA Quantification by means of GenXpert



Unpublished data.

Summary

- RDTs and DBS are reliable tools for the screening and diagnosis of HCV infection
- Treatment monitoring can be simplified by the use of DBS, ideally as qualitative tests due to their altered ability to accurately quantify HCV RNA or core antigen
- HCV core Antigen quantification may be an attractive alternative tool to monitor patients receiving IFN-free regimens

Conclusions

- The advent of new, highly effective therapies, makes it possible to control HCV infection globally
- Such control will be possible only if infected patients are diagnosed and provided access to affordable therapies in an organized healthcare system
- Alternative virological tools exist, including RDTs, molecular POCTs, core antigen detection and DBS, that will help improve global access to care and control of HCV infection worldwide

Thank you for your attention