Kirby Institute

Simplified HCV diagnostics - the key to success

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1st October, 2015

Today….

- What are the gaps in HCV care?
- What new diagnostic tools do we have?
- Which simplified strategies may help?
- What are the steps towards implementation?

The HCV care cascade

Grebely J et al. *Int J Drug Policy (*2015), http://dx.doi.org/10.1016/j.drugpo.2015.07.007

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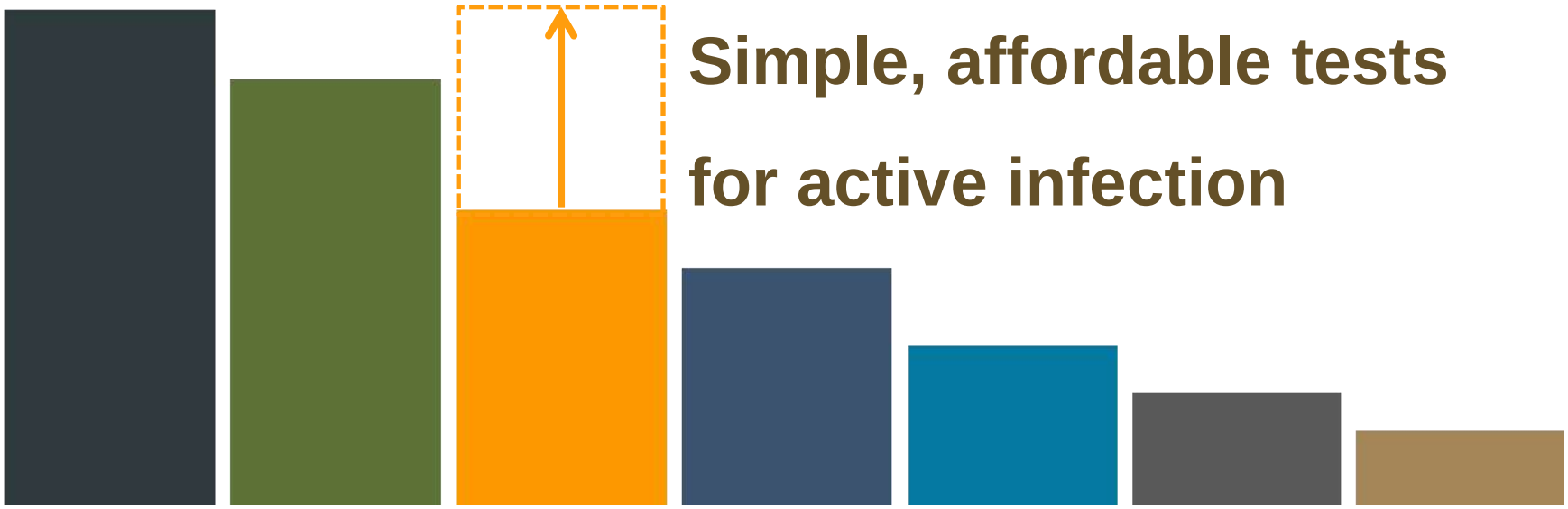
Simplified diagnostics

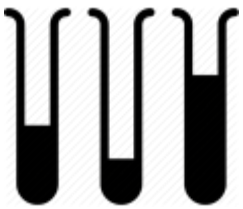


Simple, affordable tests for active infection

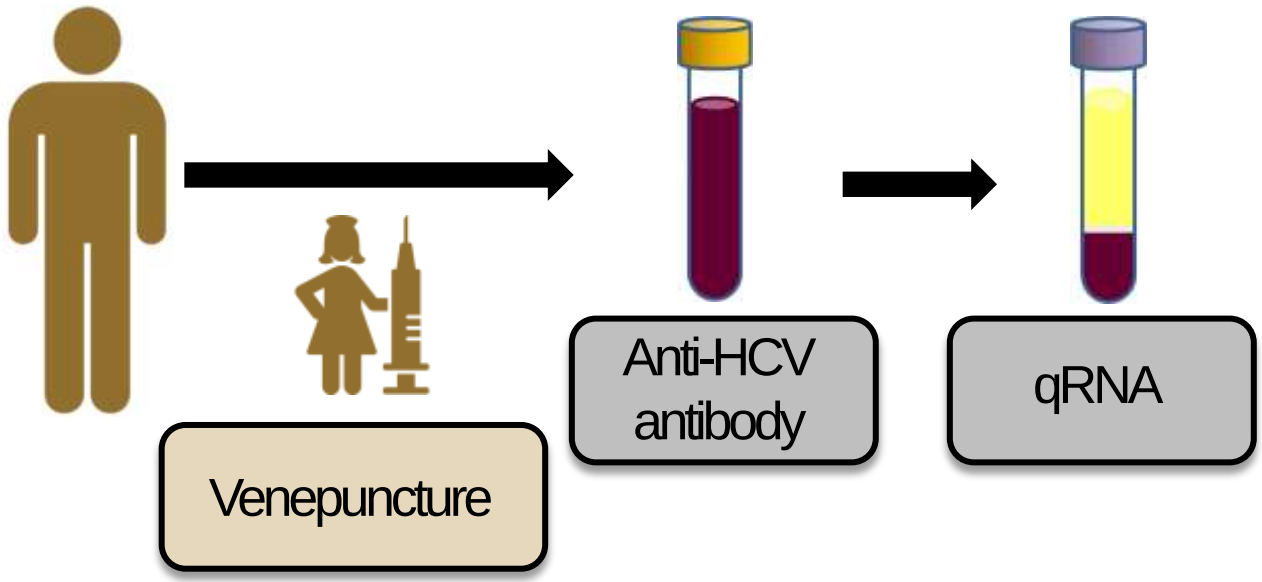
Grebely J et al. *Int J Drug Policy* (2015), http://dx.doi.org/10.1016/j.drugpo.2015.07.007

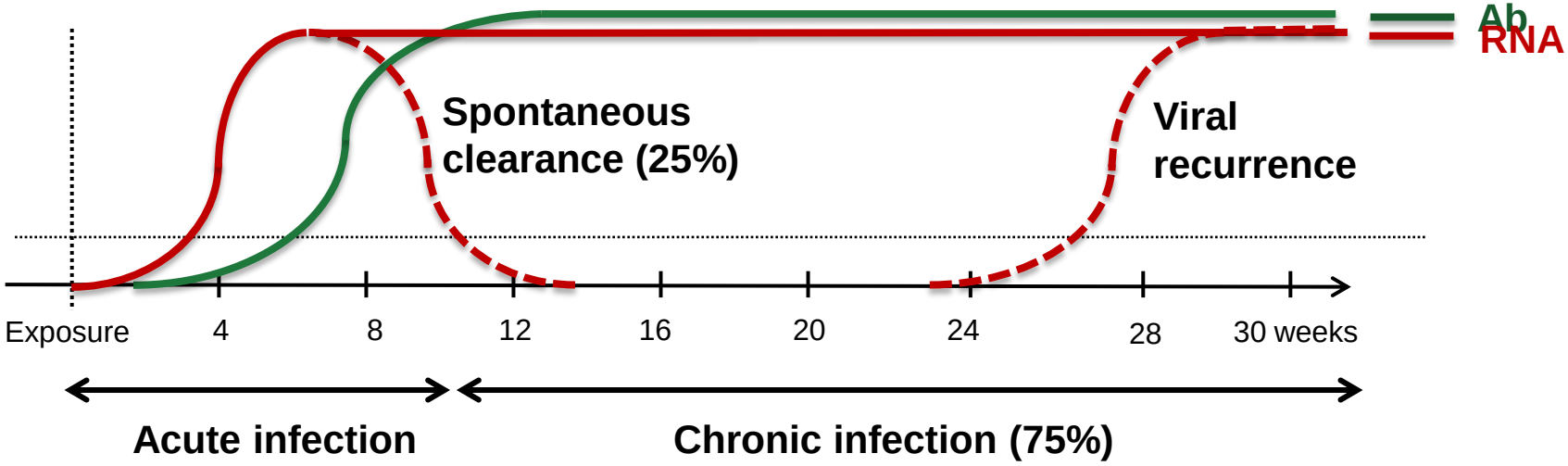
What tools do we have?

FIND → TEST → TREAT

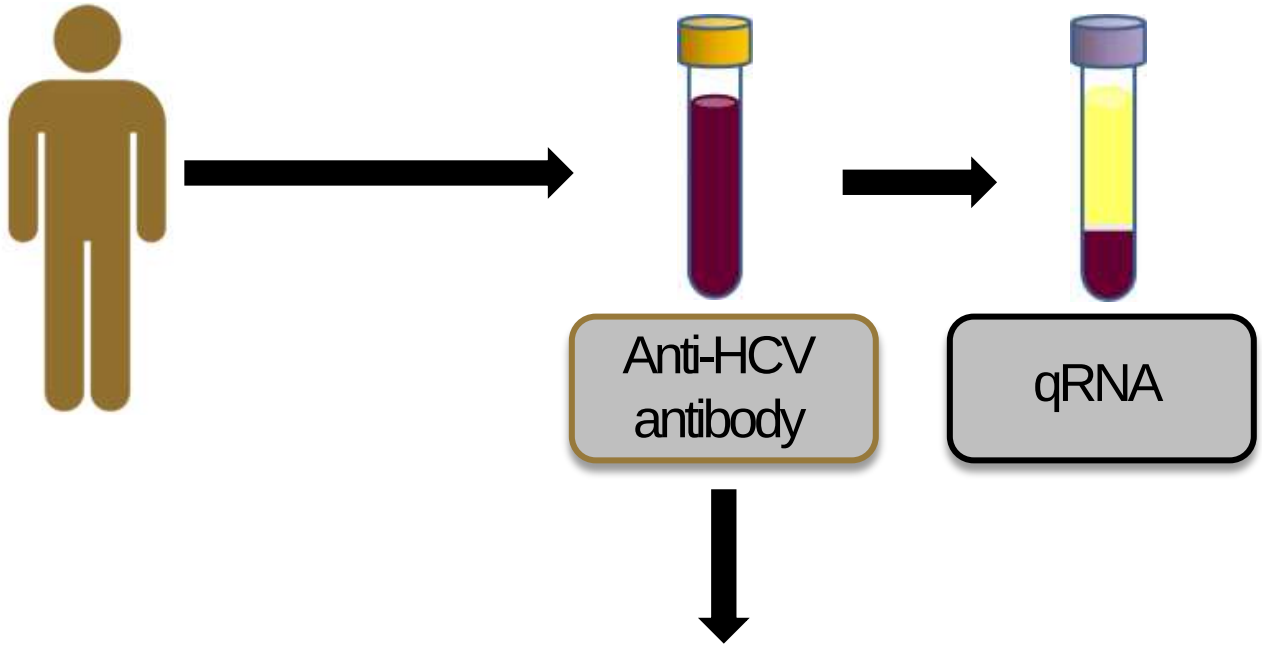


Current HCV diagnosis





Anti-HCV antibody

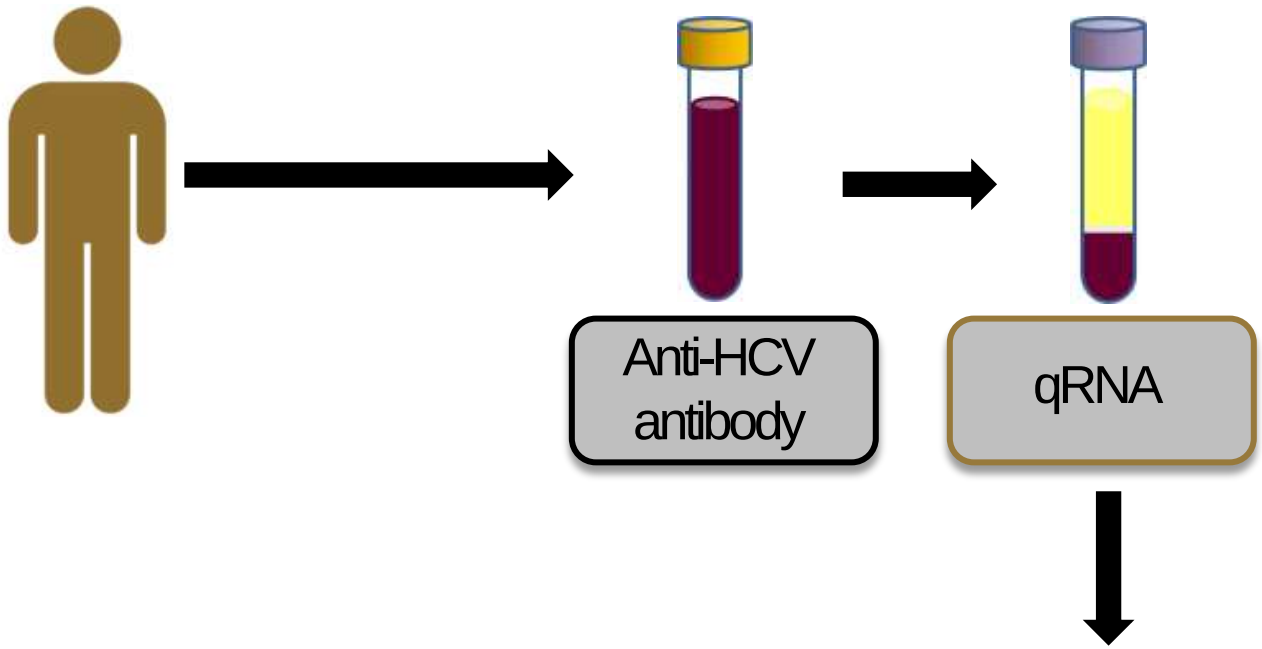


Limitations

- Unable to distinguish active / resolved infection
- Unreliable in detection of acute infection
- Impaired in HIV-positive individuals

(Dokubo et al. 2014. J Clinical Virology; Vanhommerig et al. 2014. Clinical Infectious Diseases; Cresswell et al. 2015. CID

RNA testing



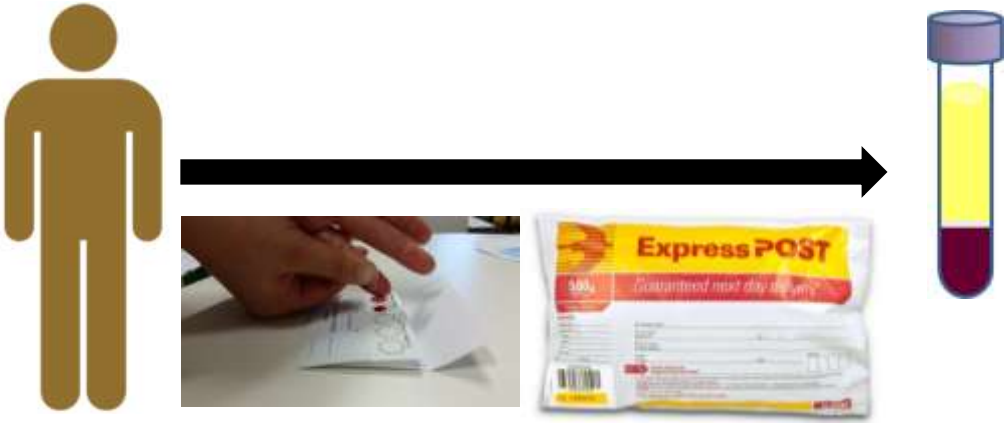
Limitations

- Expensive
- Requires careful sample handling
- Complex equipment and training
- Prone to contamination

Florea et al. 2014. J Gastrointestinal and Liver Disease ; Long et al. 2014. BMC Infectious Diseases ; Seme et al. 2005. J Clinical Virology

What new diagnostic tools exist?

Dried blood spots



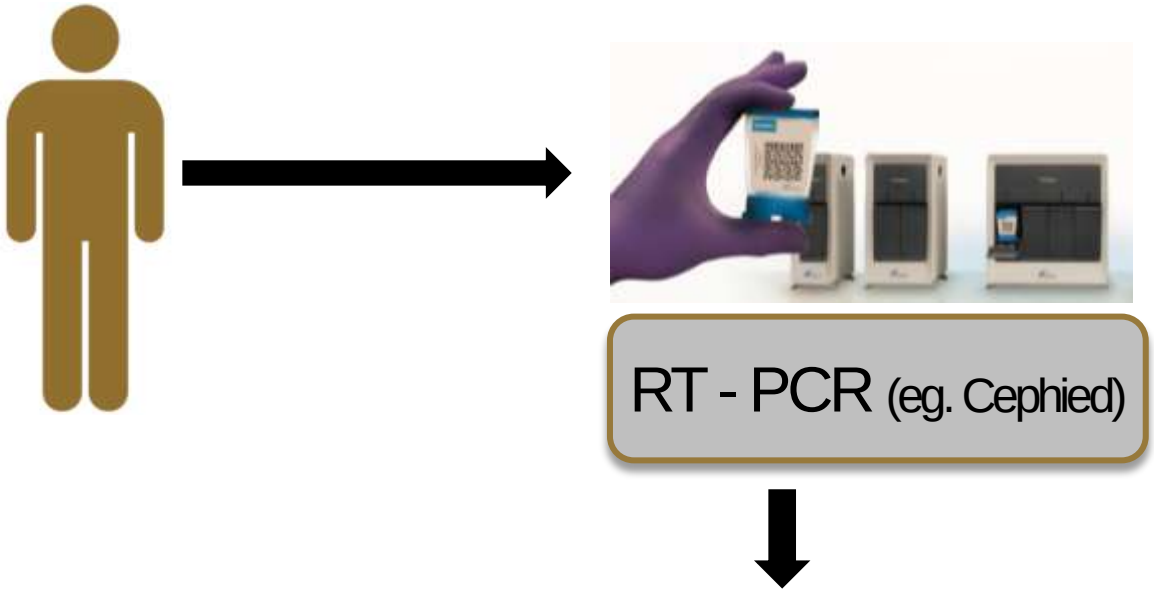
Capillary dried blood spot

Advantages

- Painless / non-invasive
- Less medical training
- Simplified transport
- Helps access to high risk populations

Dokubo et al. 2014. J Clinical Virology 59 (4):223-7; (Johannessen, 2015. J Viral Hepatitis, 22:362-65;
Snijdewind et al 2012 Antiviral Res, 93: 309-21; Tuaillon Hepatology 2010 51(3): 752-8.

Rapid point of care (PoC) tests

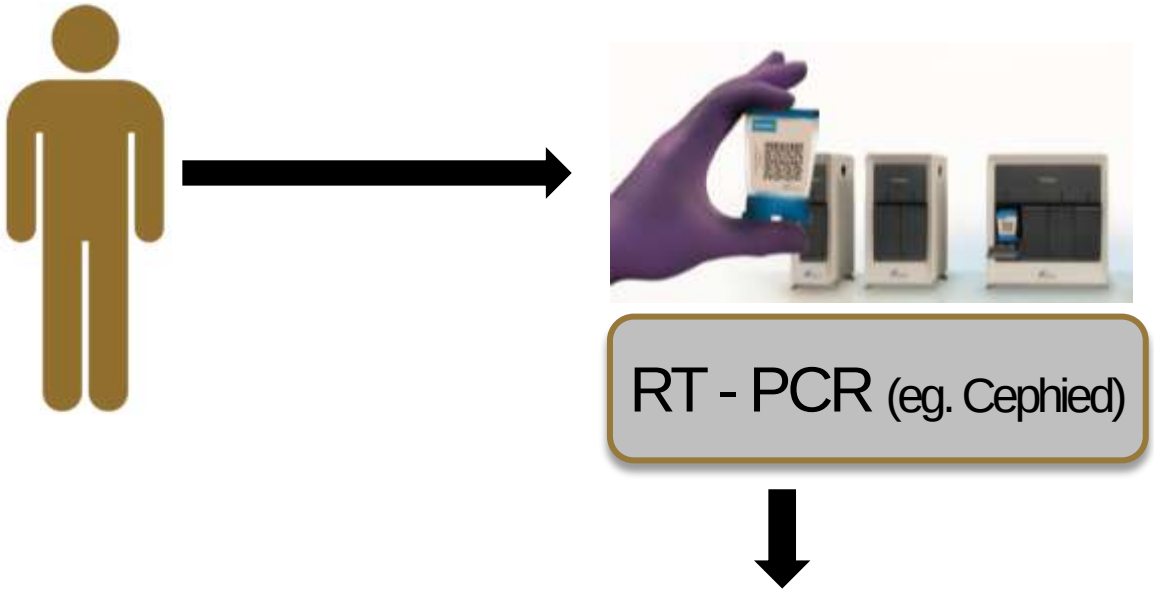


Advantages

- Increased cost-effectiveness
- Suitable for primary care
- Portable, remote settings
- Test-and-treat cycle in one visit
- Improved linkage to care / satisfaction

Huddy BMJ Open 5:e007840.doi:10.1136/bmjopen-2015 007840; Cepheid product information

Rapid point of care (PoC) tests



Disadvantages

- Higher costs per test
- Quality assurance / regulatory issues
- Data management and connectivity
- Sensitivity and device performance
- User / provider perceptions

Quinn 2015 Crit Rev Cli Lab Sci Aug 18: 1-12; Drain Lancet ID 2014: 14(3): 239-49, Pai PLOS Medicine 2012 9 (9): e1001306

HCV core antigen (Ag) assay

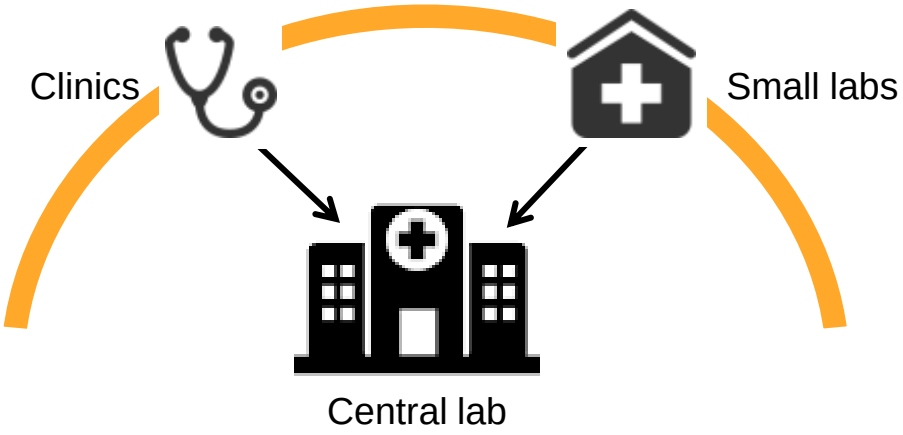
Advantages

- Detects active infection
- Easy to perform
- Less expensive
- More stable

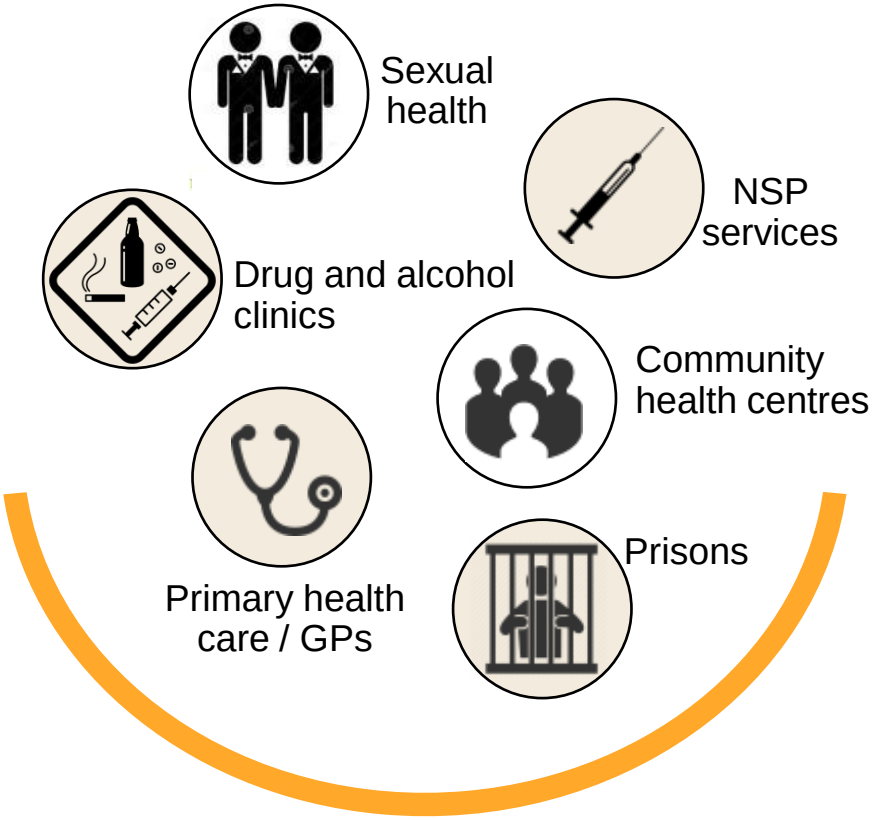
Tillman 2014 WJG 20(22): 6701-676; Dawson AVT 17 1431-5; (Kuo et al. 2012. J Clinical Microbiology 50 (6); 1989-1993.

✓ **Which diagnostic strategies hold promise?**

Diagnostic models of care

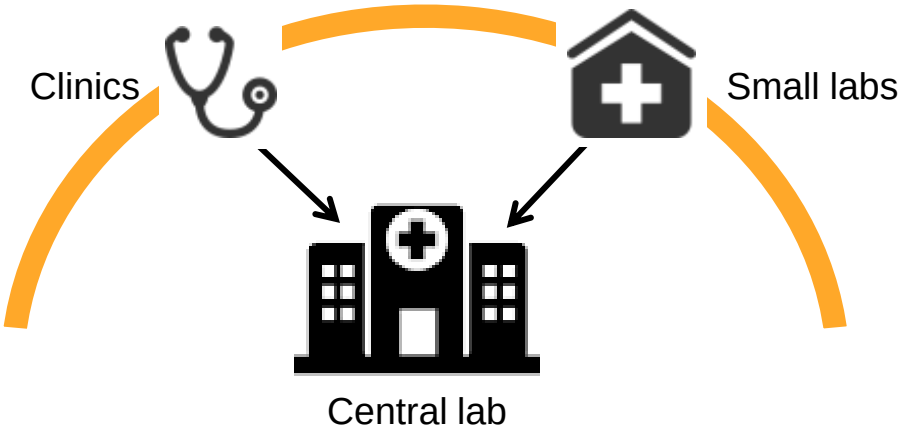


Centralised



Decentralised

Diagnostic models of care



Centralised

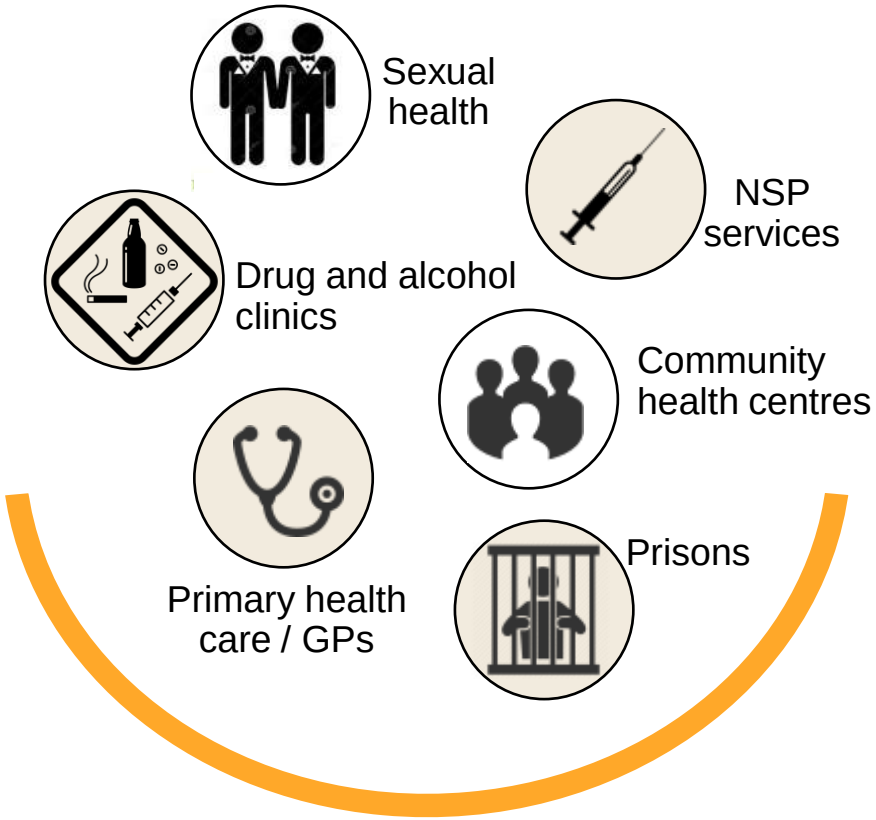
Advantages

- Developed countries
- Automation, batch testing
- Reduced operator time
- Quality assurance
- Integrated with electronic records

Disadvantages

- Highly trained staff
- Specialized facilities and equipment
- Sample transport, processing
- Time to result
- Reduced linkage to care

Diagnostic models of care



Decentralised

Advantages

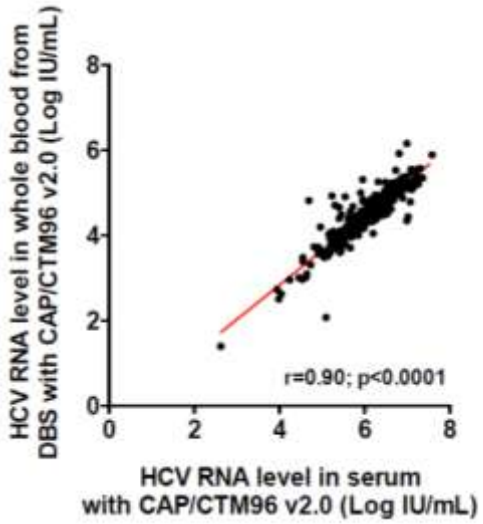
- Decreased time to result
- Increased linkage to care
- Remote, or resource limited settings
- Engage key affected communities

Disadvantages

- Regulatory approval
- Quality assurance programs
- Technical support

HCV RNA DBS testing

DBS RNA detection, quantification and genotyping (9 studies)



- Strong correlation with plasma
- Limit of detection = 150-250 IU/ml
- Most untreated HCV > 1000 IU/ml

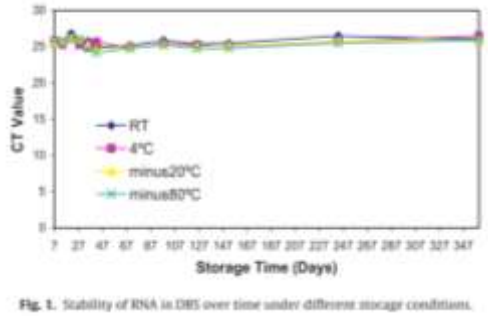


Fig. 1. Stability of RNA in DBS over time under different storage conditions.

Gaps in the literature

- Long term storage data
- Humid / hot environments

Soulier 2015 JID In press; Bennett JCV 2012 54: 106-109;; Greenman JVM 2015 doi: 10.111/jvh.12345..

Clinical impact of DBS testing

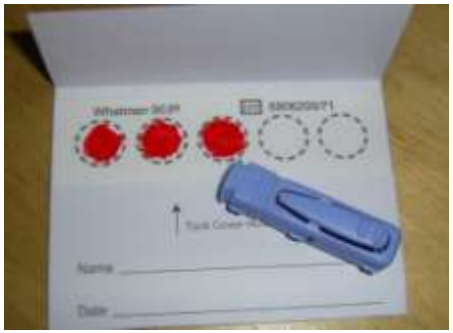
Few studies have assessed DBS as an intervention and quantitative impact on uptake of HCV testing / diagnosis

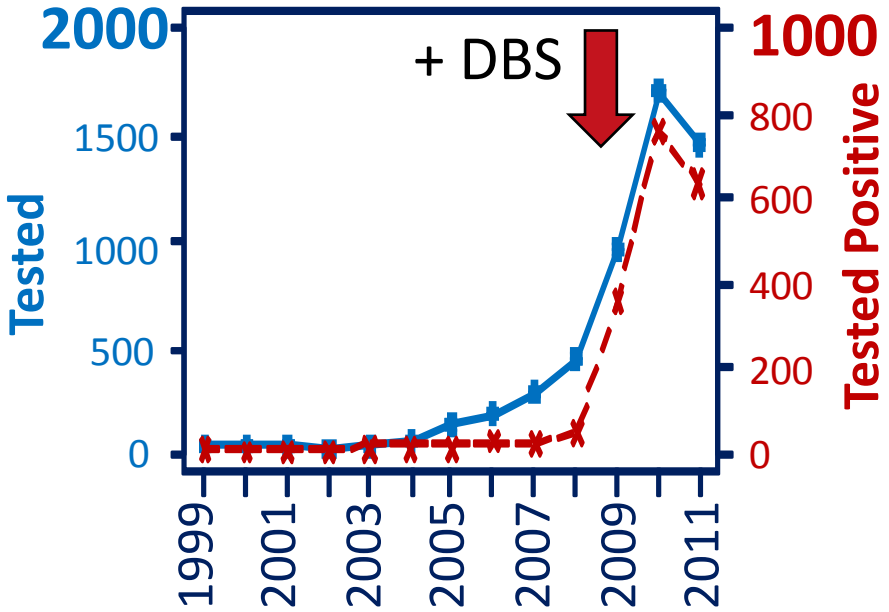
Study	Type	Population	Effect on testing
Craine et al. (2014).	Step-wedged cluster-randomised control trial	Prison	No effect
Hickman et al. (2008)	Cluster-randomised controls trial	D&A	Increased
Tait et al. (2013)	Prospective cohort study	NSP	Increased
Abou-Saleh et al. (2013)	Prospective cohort study		Increased
McLeod et al. (2014)	Ecological study	Scottish action plan	Increased
Carine et al. (2009)	Clinical audit		Increased

Coats J.T., & Dillon, J.F (2015) Int J Drug pol. http;//dx/doi.org/10.1016/j.drugpo.2015.05.001

DBS: specialist drug services

Scotland: Increased testing, diagnosis and treatment

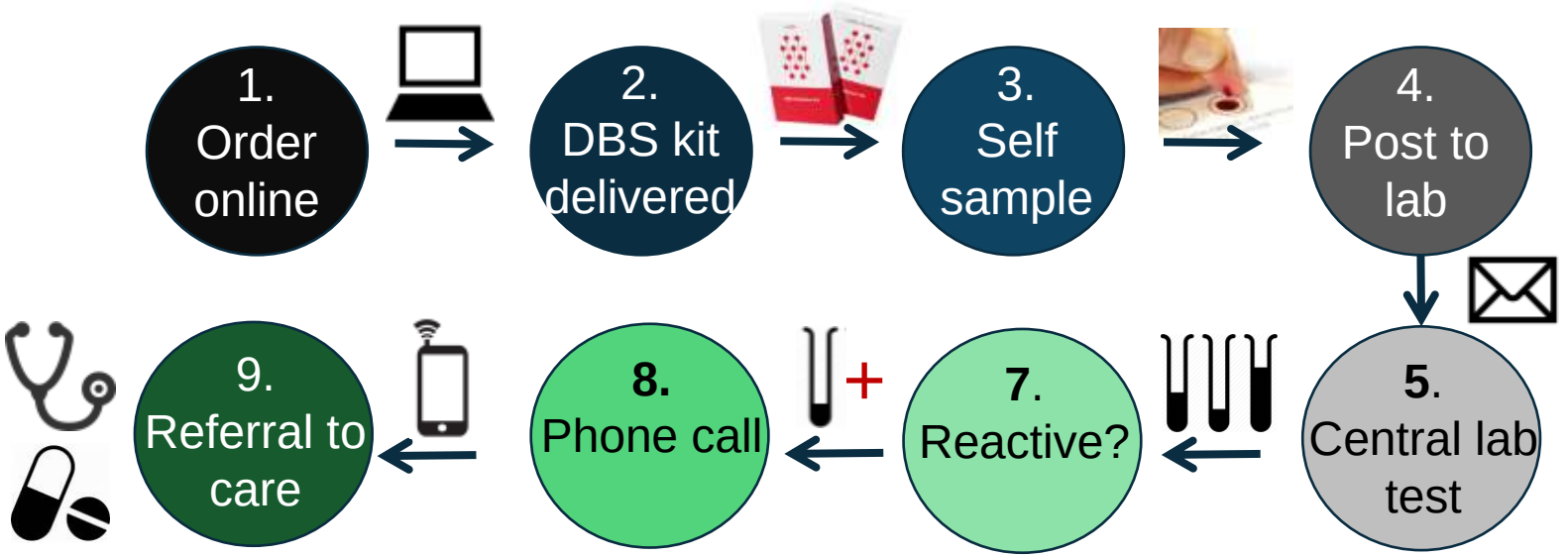




Annual number of people tested for HCV in specialist drug services across Scotland

McLeod JECH Sug 28, 2014 10.1136/jech-2014-204451; Hutchinson Int J Drug Pol 2015 in press);; McAllister JCV 61:359-364.

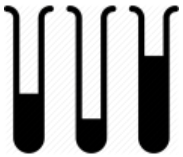
On-line, self collected DBS



HIV testing in comparison with STI clinics (UK)

- Equal recruitment, return results, and reactivity
- DBS covered broader geographic area
- Diagnosed higher number of African American heterosexual men

Terrence Higgins Trust. Public Health England. 56 Dean St.



Point of care HCV testing

Gap in the literature: Studies introducing HCV PoC testing of active HCV infection to determine its effect on frequency of testing or new diagnoses

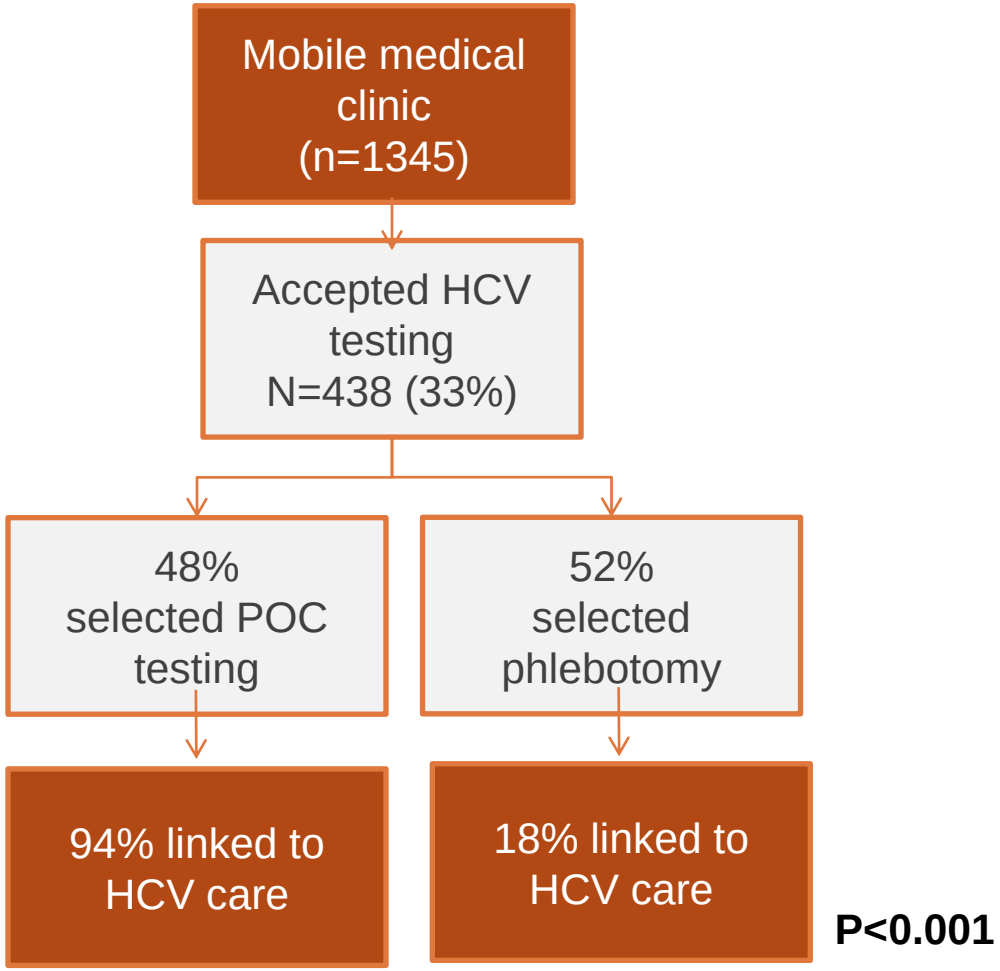
Evaluations of HCV POC tests required

- Include accuracy at the clinical point-of-care
- Impact on relevant patient-centred outcomes

  (eg. rate of diagnosis, time to treat, retention in care and mortality)
- Assessment of differences in cost and cost-effectiveness.

Huddy BMJ Open 5:e007840.doi:10.1136/bmjopen-2015 007840;
Coats J.T., & Dillon, J.F (2015) Int J Drug pol. http;//dx/doi.org/10.1016/j.drugpo.2015.05.001

PoC in mobile medical clinics



Morano J, *J Comm Health* 2014; 39(5):922-34.

PoC in mobile medical clinics

Free testing

1neThing.com

http://www.1nething.com/

Free IFN-free DAA treatment

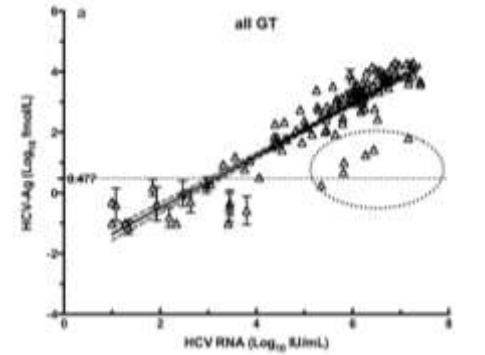
International HIV / AIDS alliance in Ukraine

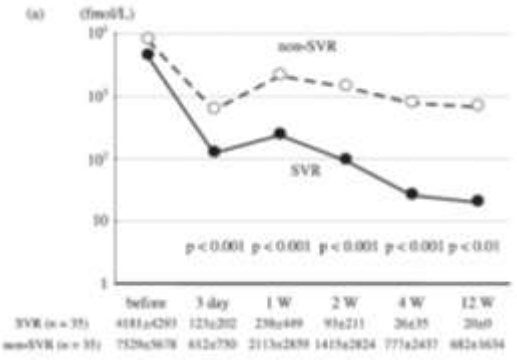
Альянс
International HIV/AIDS Alliance in Ukraine

http://www.aidsalliance.org

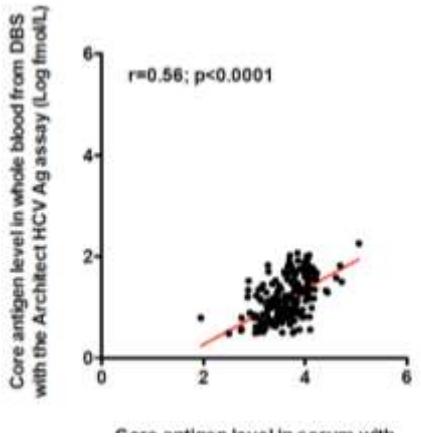
Core antigen testing in HCV

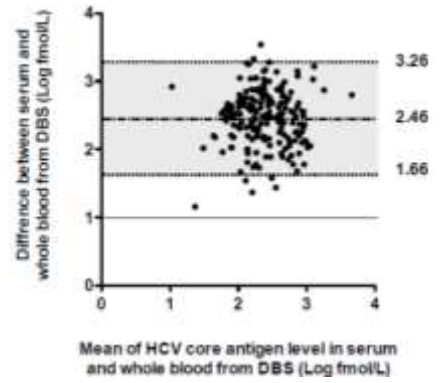
Plasma





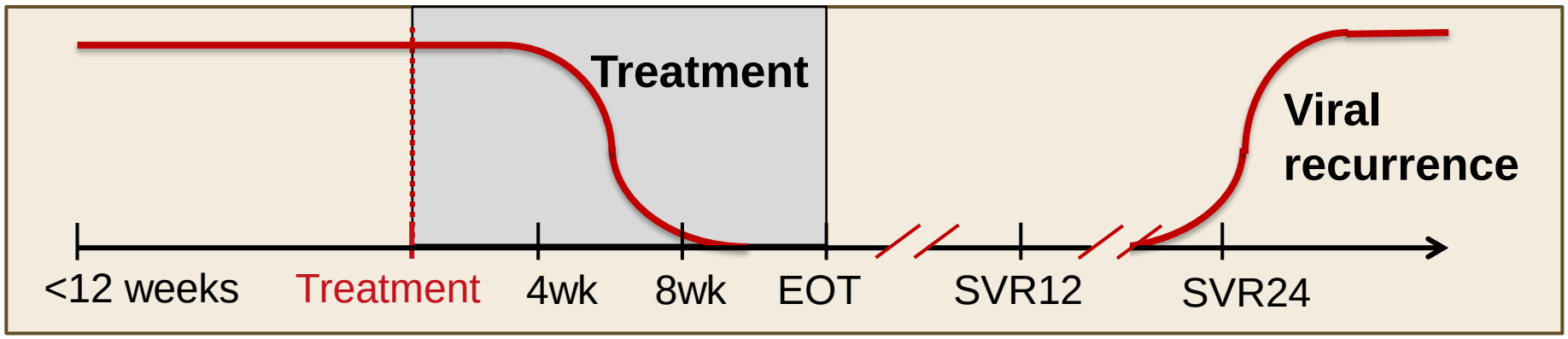
DBS



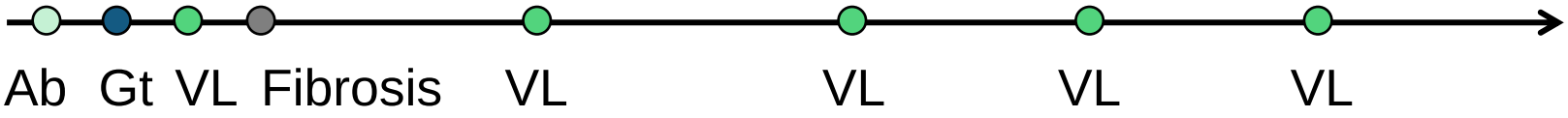


Chevaliez JCV 2014; 61: 145-148.; Ottiger JCV 2013: 58: 535-540; Garbuglia JCV 2015 69: 68-73. Fugin J Dog Dis 2009. Soliman 2015 ERMP S 19:2240-2245; Vanhemmmerig J Virol method 2015 213:147-50.; Soulier 2015 JID In press;

Simplified monitoring



Current HCV diagnostics



Simplified diagnostics

Self collected DBS kit

Cohn et al. 2015. Curr Opinio. Simplified diagnostic monitoring for hepatitis C in the new era of directly acting antivirals.

Steps towards implementation

1. Studies

- Diagnostic design, validation
- Clinical studies
  (diagnostic accuracy, clinical impact, costs).

2. Data

- Data analysis
- Cost effectiveness modelling
- Business case
- WHO prequalification

3. Approval

- Submission and regulatory approval for claim
  (FDA, CE, TGA , eg. sample type / aid in diagnosis)

4. Funds

- Government price negotiations
- Reimbursement
- Implementation and roll out

Summary: Simplified HCV diagnostics

- Likely to help close gaps in HCV care
- Promising strategies include
  - *Centralised dried blood spot RNA testing*
  - *Centralised core Ag testing in plasma*
  - *Portable point of care devices*
  - *Self-collected DBS for diagnosis and treatment*
- Implementation requires strong collaboration between affected communities, public, private and NGO research and funding bodies for success.

Acknowledgments

Viral Hepatitis and Clinical Laboratory Program

Gregory Dore
Pip Marks
Jason Grebely
Gail Matthews
Amie Lucas
Danica Martinez
Francois Lamoury
Brendan Jacka
Sofia Bartlett
Angelica Soker

Immunovirology and Pathogenesis Program

Tony Kelleher and team

St Vincent's Applied Medical Research, Sydney

Philip Cunningham and team
Beth Catlett

Funding:

National Health and Medical Research Council (Program grant).
Department of Health and Aging, Australian Government.

Thank you….