INHSU 2017

Point of care and dried blood spot HCV testing

- a practical introductory workshop

8th September, 2017
Hyatt regency on the Hudson,
Jersey City / New York,
United States.

Co-chairs

Dr Tanya Applegate

The Kirby Institute,

UNSW Sydney Australia

Dr Erika Castro Bataenjer

Centre Hospitalier Universitaire Vaudois

Lausanne, Switzerland

Scope of today's workshop

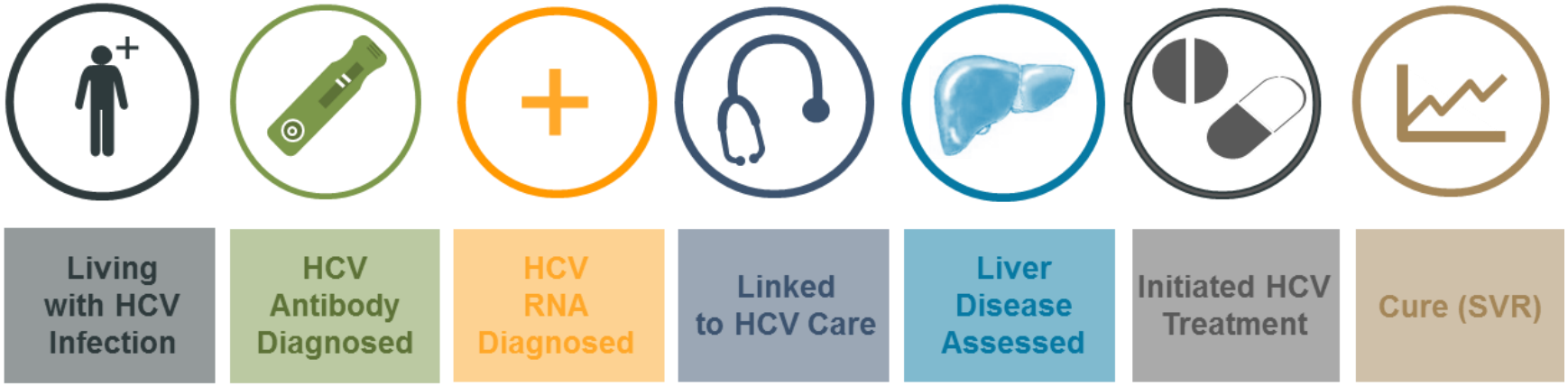
- Increase awareness of point of care testing and sample collection
- Discuss principles, advantages, limitations
- Understand what tests are here, what tests are coming
- Share our experiences, lessons learned
- Practical demonstrations
- Open access guidance documents coming soon…..

Today's workshop

1. Introduction to POC testing	**Tanya Applegate** *The Kirby Institute, UNSW Sydney, Australia*
2. Antibody testing using rapid diagnostic tests	**Jessie Schwartz** *NYC Health Department, NY, USA*
3. HCV RNA testing using GeneXpert	**Francois Lamoury** *The Kirby Institute, UNSW Sydney, Australia*
4. Dried Blood Spots	**Tanya Applegate** **Erika Castro** *Centre Hospitalier Universitaire Vaudois* *Lausanne, Switzerland*
5. Concluding remarks	**Erika Castro**

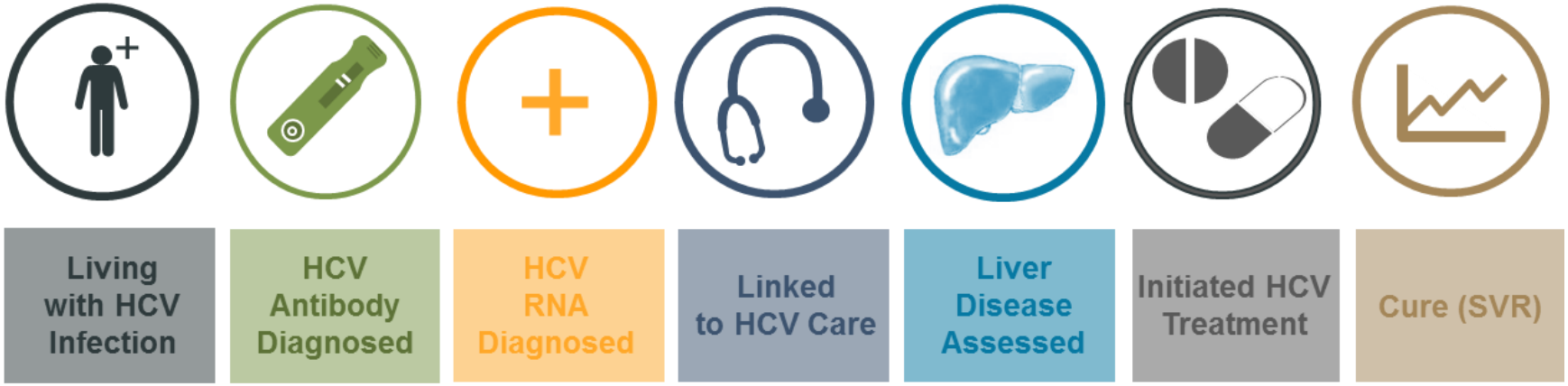
- Followed by Orasure demonstration for those interested

The HCV cascade of care

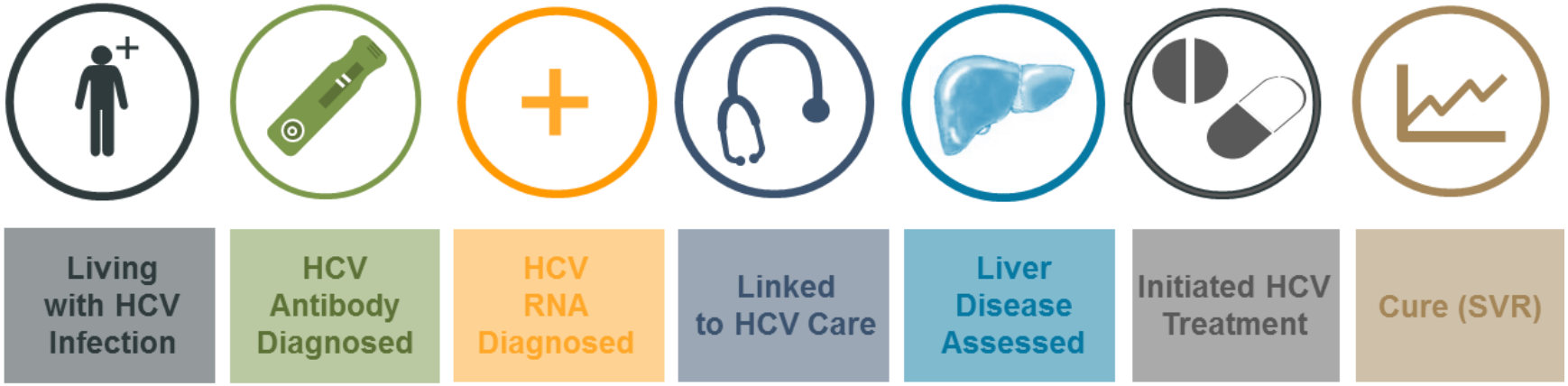


Grebely J et al. *Int J Drug Policy* (2015

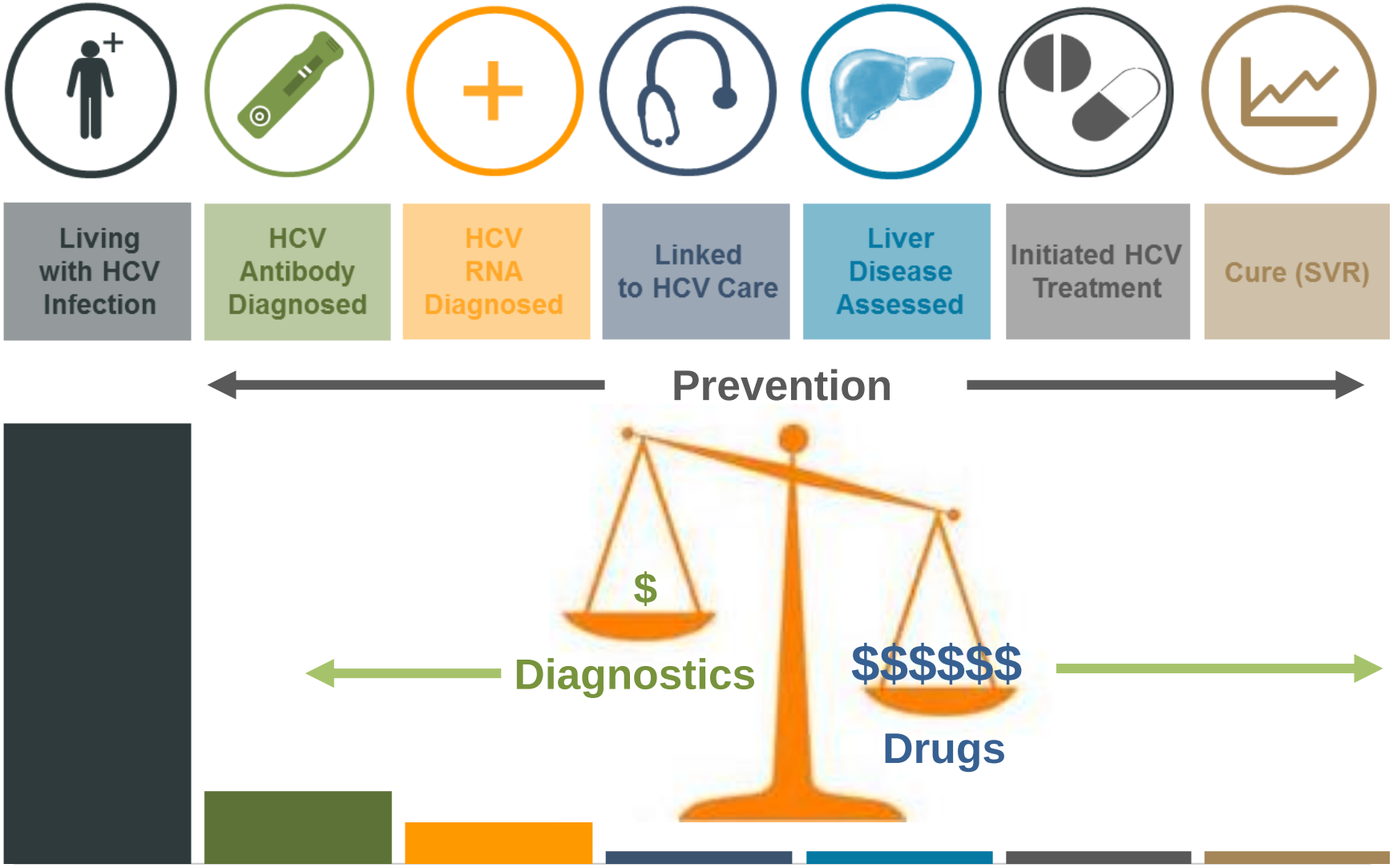
The HCV cascade of care



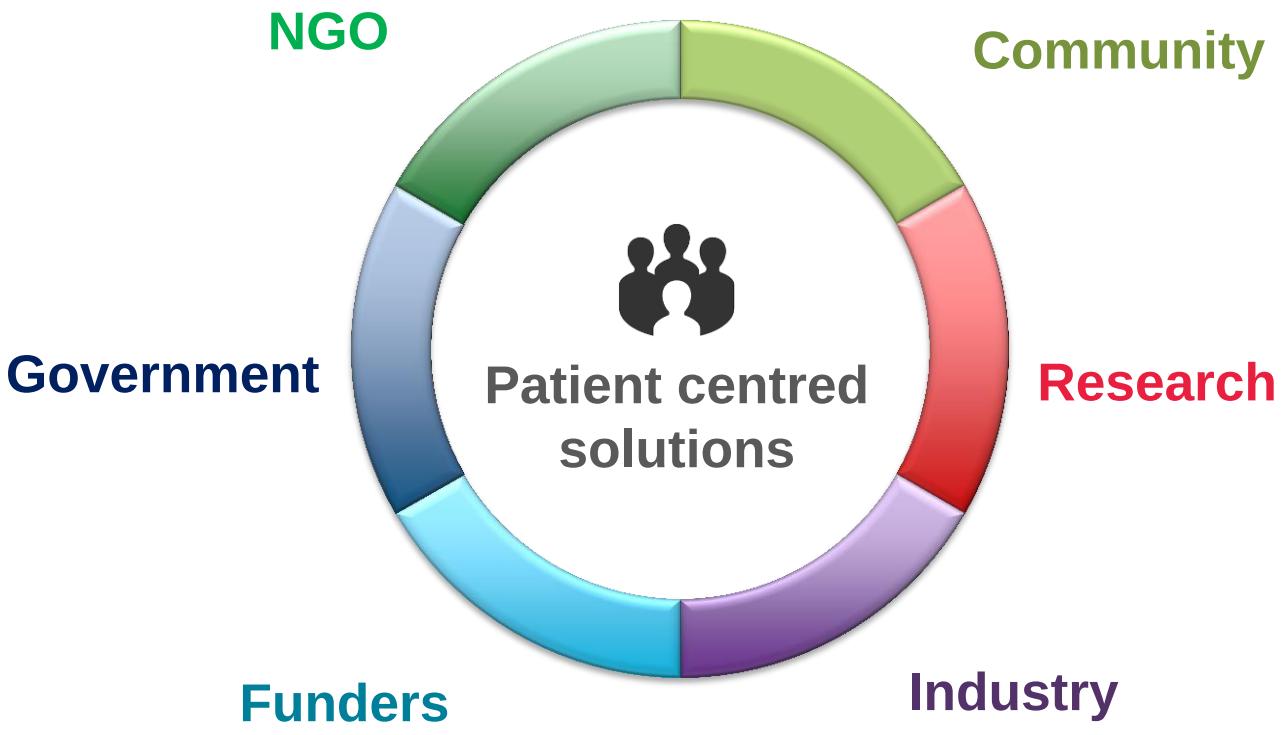
WHO 2030 HCV elimination goals



Increased access to diagnostics – our next challenge



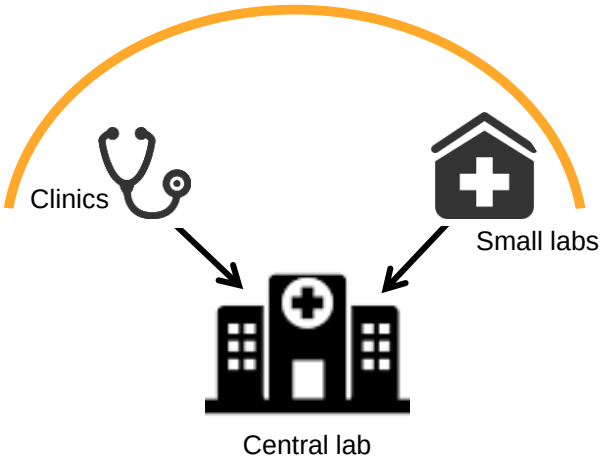
Increased access to diagnostics – how?



Collaborative partnerships – <u>everyone</u> has a role

1. A quick introduction – point of care testing

How is testing for HCV done now?



Centralized testing

Visit #1
HCV antibody
(Physician)

Visit #2
Phlebotomy
(Phlebotomist)

Central Lab
Antibody test
1-2 weeks

Visit #3
Receive diagnosis
(Physician)

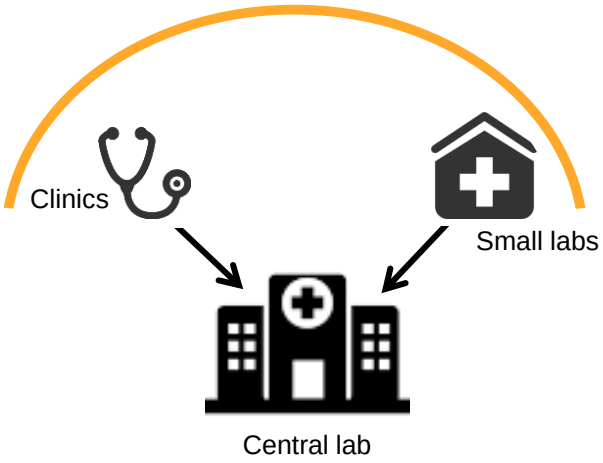
Visit #4
Phlebotomy
(Phlebotomist)

Central Lab
RNA test
1-2 weeks

Visit #5
Diagnosis
(Physician)

Increased time, visits and loss of follow up

How is testing for HCV done now?



Centralized testing

Visit #1

HCV antibody
(Physician)

Visit #2

Phlebotomy
(Phlebotomist)

Central Lab

Antibody test
1-2 weeks

Visit #3

Receive diagnosis
(Physician)

Reflex RNA

Visit #4

Phlebotomy
(Phlebotomist)

Central Lab

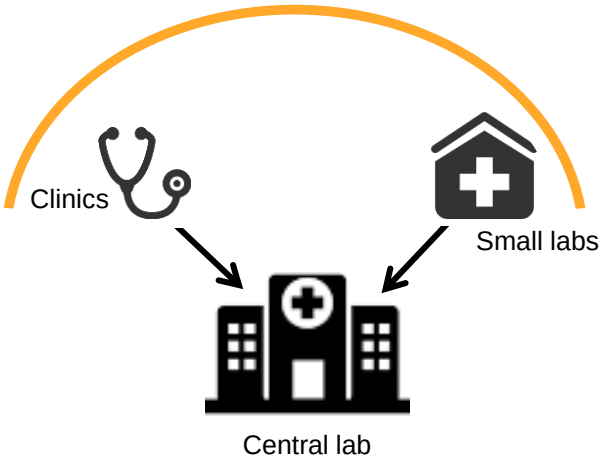
RNA test
1-2 weeks

Visit #5

Diagnosis
(Physician)

Increased time, visits and loss of follow up

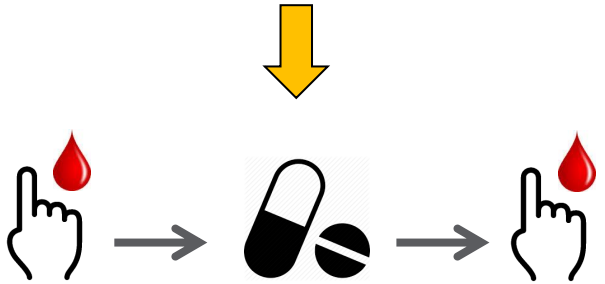
How can this be improved?



Centralized testing

Take the test to the patient

Decentralized services

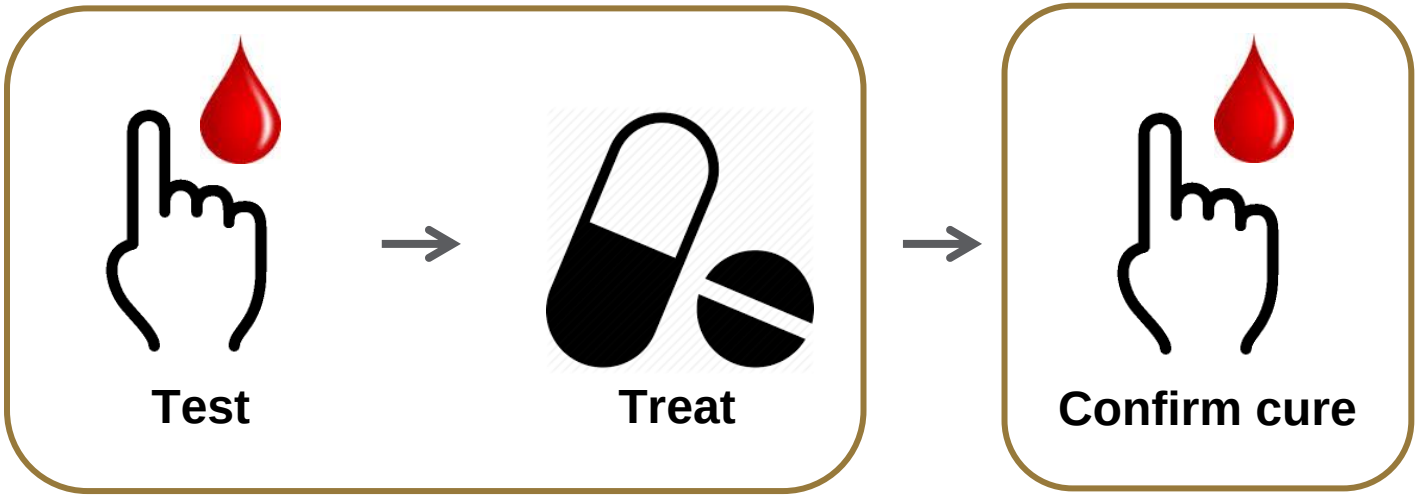


Test **Treat** **Confirm cure**

Point of care testing

What are “point of care tests” (POCT) ?

A test performed near the patient that changes patient care



Benefits?

- Rapid, simple collection method (finger-prick, oral)
- Enables screening or diagnosis
- Facilitates single visit diagnosis and treatment
- Integration into a range of services
- Improves access for people using these services

The World Health Organization

ASSURED guidelines for POCTs[1]

1. Affordable (for populations at risk)
2. Sensitive
3. Specific
4. User-friendly (simple to perform in a few steps with minimal training)
5. Rapid & Robust (results available in less than 30 minutes)
6. Equipment-free
7. Deliverable to those who need them

[1] *Peeling RW, et al. Rapid test for sexually transmitted infections (STIs): the way forward. Sex Transm Infect. 2006.*

Remind me again…what is “sensitivity and specificity”?

Sensitivity = true positive result +++++

Ability to correctly identify those with the disease

Specificity = true negative result +++++

Ability to correctly identify those without the disease

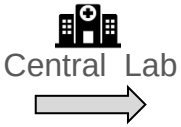
What tools might make it easier to get tested?

Visit #1

Rapid anti-HCV antibody test
(Health care worker)

#2

Phlebotomy
(Phlebotomist)



#3

Receive diagnosis
(Physician)

Jessie Schwartz

What tools might make it easier to get tested?

Visit #1

Rapid anti-HCV antibody test
(Health care worker)

#2

Phlebotomy
(Phlebotomist)

Central Lab

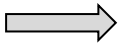
Antibody test
1-2 weeks

#3

Receive diagnosis
(Physician)

Dried blood spot sample
(Health care worker)

Central Lab



Ab / reflex
RNA test
1-2 weeks

Receive diagnosis
(Physician)

Tanya and Erika

What tools might make it easier to get tested?

Visit #1

Rapid anti-HCV antibody test
(Health care worker)

#2

Phlebotomy
(Phlebotomist)

Central Lab

Antibody test
1-2 weeks

#3

Receive diagnosis
(Physician)

Dried blood spot sample
(Health care worker)

Central Lab

Ab / reflex
RNA test
1-2 weeks

Receive diagnosis
(Physician)

POC HCV RNA and diagnosis
(Health care worker)

Francois Lamoury

Accessing quality tests – approvals and registration

WHO pre-qualification

FDA - registration

CE - marking

Local approval

- **Sample type** (eg. plasma, serum, whole blood, capillary, saliva, DBS)
- **Intended use** (screening, diagnosis, monitoring**)**

⟹ **In country procurement, price negotiations and access**

2. Antibody Testing Using Rapid Hepatitis C Diagnostic Tests in NYC: Tips for Local Implementation

Jessie Schwartz, RN, MPH

Clinical Coordinator, Viral Hepatitis Program
New York City Health Department

HCV antibody testing using “Rapid Diagnostic Tests”

- Test kit detect antibodies to HCV (anti-HCV) produced by the body’s immune system – the majority of persons will develop antibodies within 8 weeks of exposure

- Kits can use blood or oral (not in the U.S.) specimens for diagnosis

- Hepatitis C viral testing to confirm infection is crucial; in NYC as many as 50% with a positive anti-HCV test do not have active infection
  - Natural clearance of virus (15-25%)
  - Successful treatment
  - False positives

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Many Rapid anti-HCV antibody Diagnostic Tests

Test name	Manufacturer	Country	Certification
SD Bioline HCV	Standard Diagnostics, Inc	South Korea	WHO; CE
OraQuick HCV Rapid Antibody Test	OraSure Technologies, Inc	USA	WHO, FDA; CE
HCV Card	Axiom Diagnostics	Germany	CE
ImmunoFlow HCV	Core Diagnostics	UK	CE
Hepa-Scan HCV card test	Bhat Biotech	India	CE
Toyo anti-HCV test	Türklab A.S.	Turkey	CE
Signal HCV	SPAN Diagnostics Ltd	India	CE
HCVTOP	BioSynex S.A.	France	CE
OneStep HCV Rapid Test	Span Biotech Ltd	China	CE
HCV Rapid Test	UAB Euro Genomas	Lithuania	CE
Hepatitis C Antibody Test	Artron Laboratories	Canada	CE
Diaquick HCV Cassette	Dialab GmbH	Austria	CE
MultiSure HCV	MP Biomedicals,	Singapore	
First Response HCV Card Test	Premier Medical Corporation Ltd	India	
VEDA.LAB HCV	VEDA.LAB, Alençon	France	
…….	…….	…….	Note – list is incomplete!

Two Rapid Diagnostic Tests are WHO prequalified

OraQuick HCV Rapid Antibody Test (OraSure Technologies, Inc)

- **WHO sample type**: oral fluid, fingerstick whole blood, venipuncture whole blood, plasma specimens (EDTA, sodium heparin, lithium heparin, and sodium citrate), and serum (serum separator tube (SST).
- **CE-marked:** as above.
- **FDA-approved:** All samples except oral in US

SD Bioline (Standard Diagnostics, Inc)

- **WHO sample type:** human serum, plasma (heparin, EDTA and sodium citrate) or venous whole blood. (not fingerstick)
- **CE-marked and FDA-approved** – all samples (not fingerstick)

How to use a Rapid anti-HCV antibody Diagnostic Test

Collect blood or…

…oral sample

Insert device into or add buffer solution

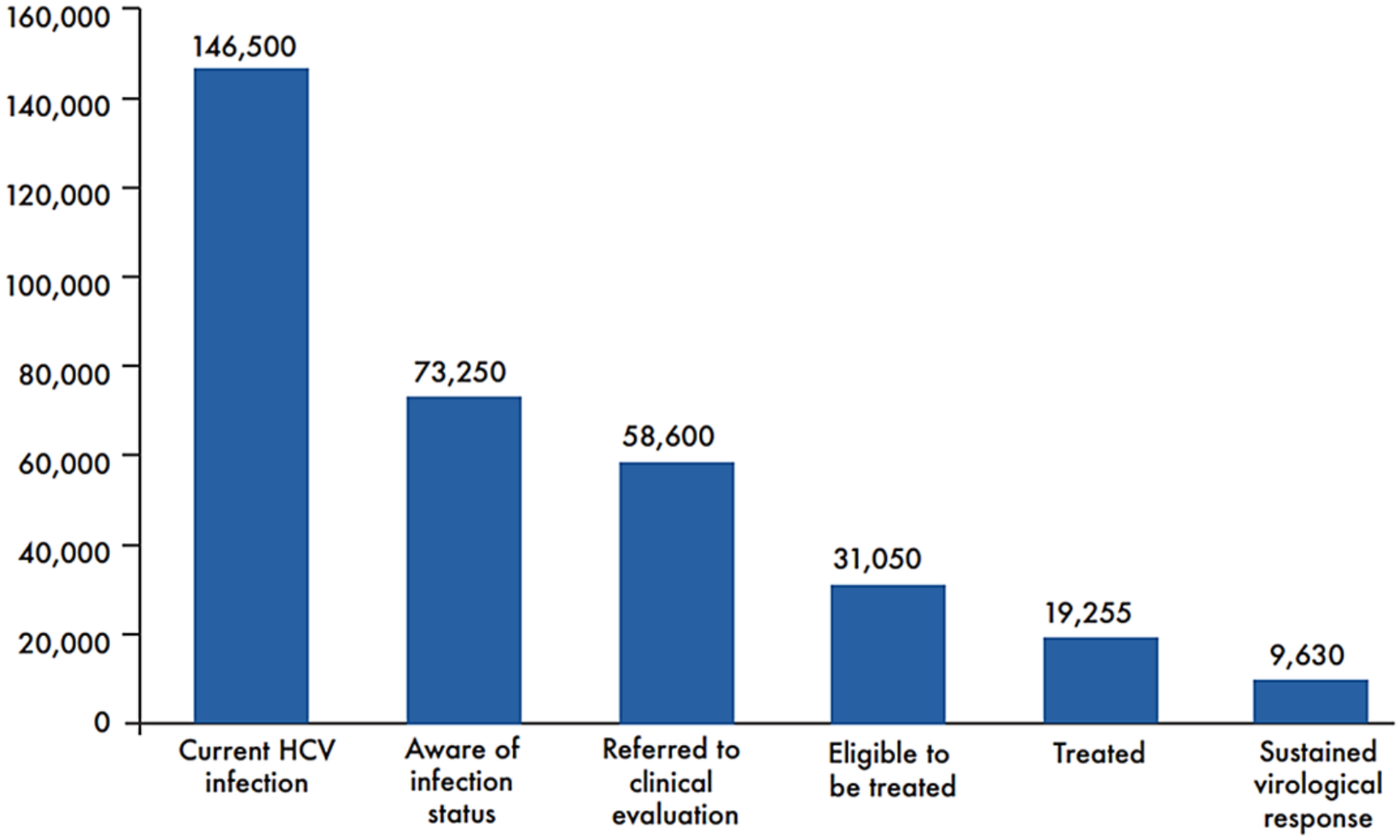
Read results in 20-40 minutes

Hepatitis C in New York City

- Largest city in the United States
- Estimated that around 146,500 are living with chronic hepatitis C infection[3]
- Up to 50% not aware of their status[4]
- Highest rates in very high poverty neighborhoods[5]
- Prevalence 71% in persons who inject drugs[6]
- 1.2% increase in rates of newly reported HCV infection in adults aged 20-29 between 2005 - 2015[5]

3 Balter S, et al. Estimating the prevalence of hepatitis C infection in New York City using surveillance data. Epidmiol Infect, 2014.
4 Holemberg SD, et al. Hepatitis C in the United States. NEJM, 2013.
5 New York City Department of Health and Mental Hygiene. Hepatitis B and C Annual Report, 2015. Published October, 2016.
6 Des Jarlais DC, et al. Can intranasal drug use reduce HCV infection among injection drug users? Drug Alcohol Depend, 2011.

New York City Hepatitis C Care Cascade (2013)



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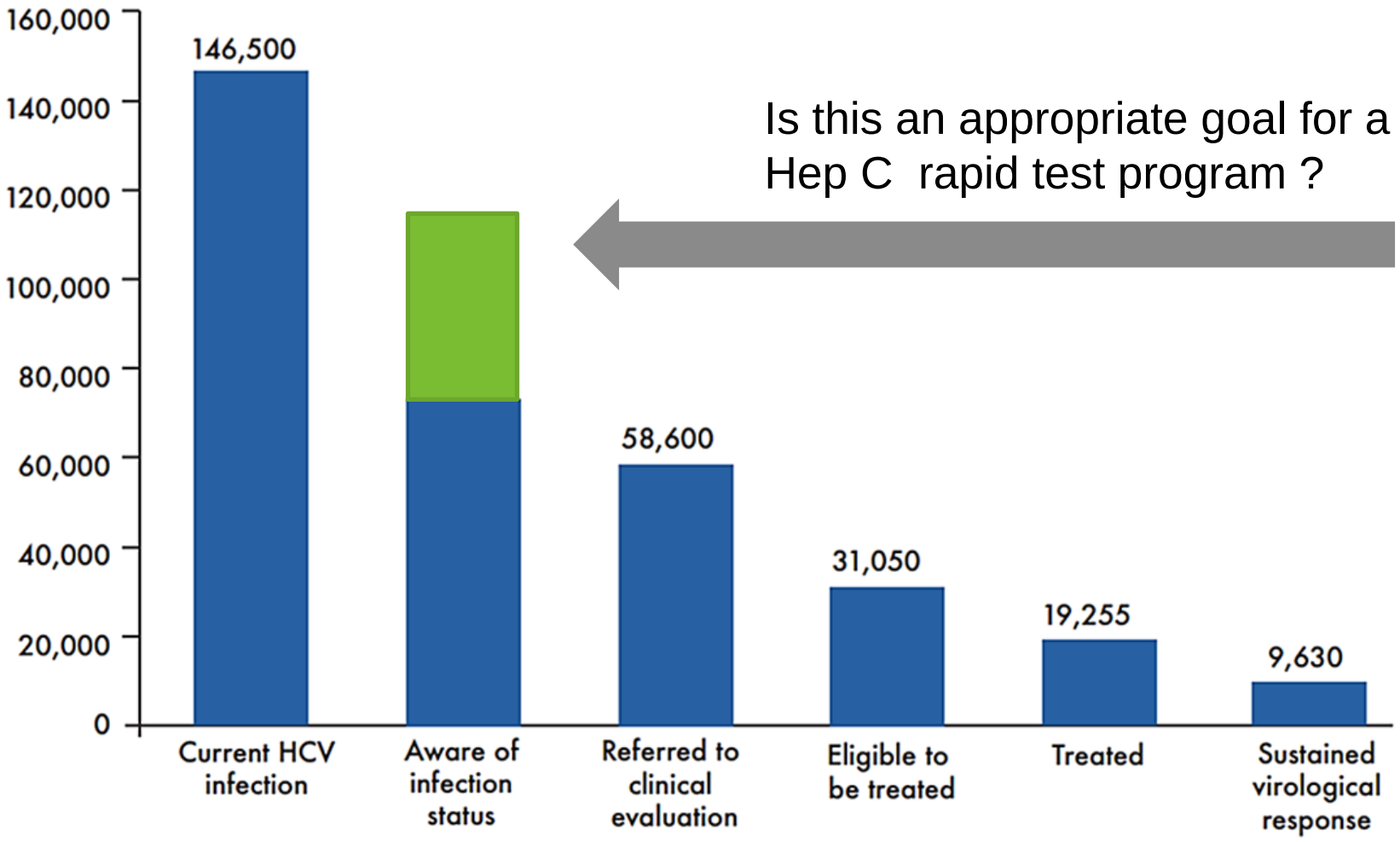

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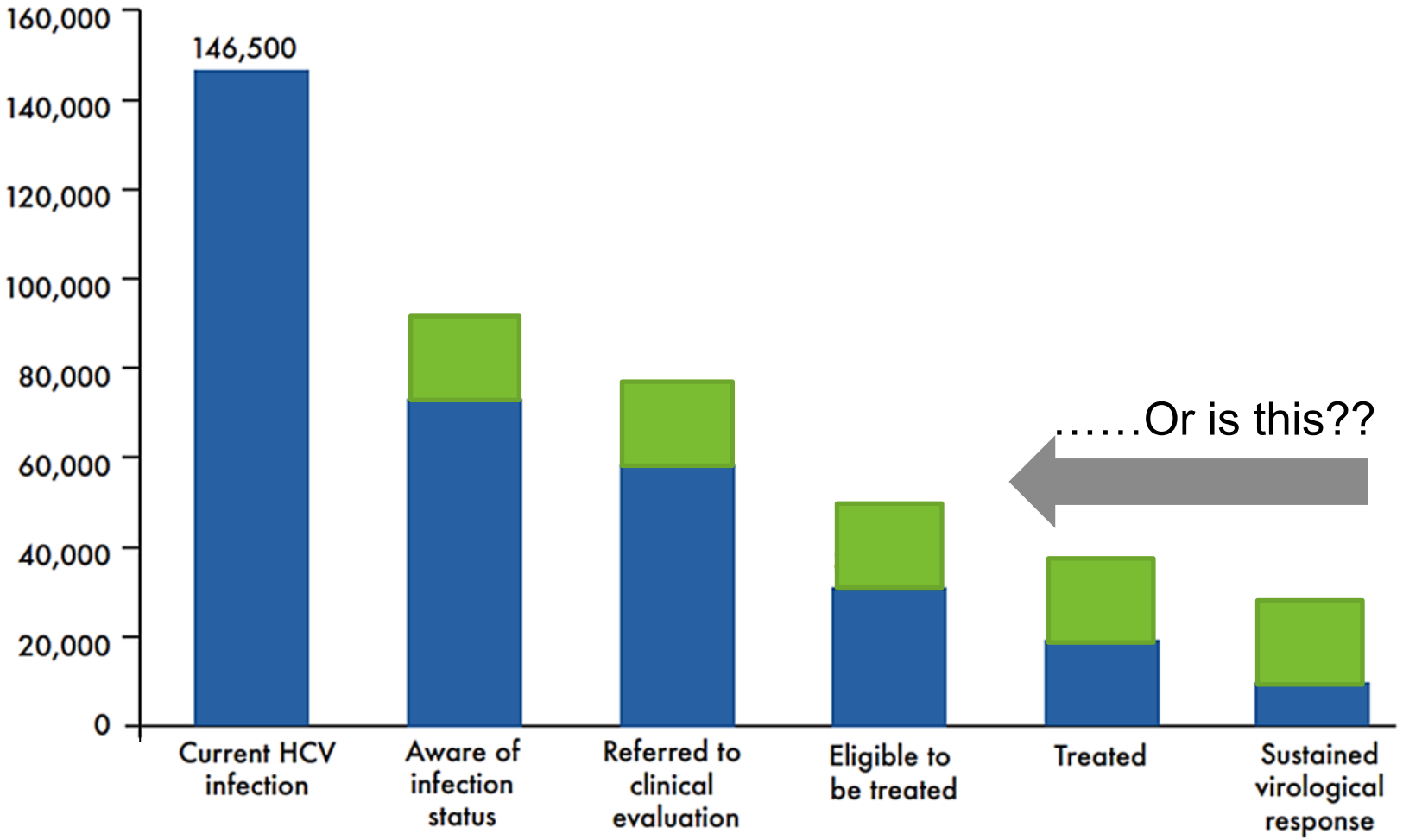


NYC Hep C Peer Navigation

at Syringe Exchange Programs

- Part time peer navigators support people at risk or living with Hep C to complete Hep C testing, link or return to medical care, and prevent infection or re-infection

- Implemented at 15 NYC syringe exchange and harm reduction programs affiliated with Injection Drug User Health Alliance (IDUHA)

Demographics

Gender:

- 65% male
- 26% female
- 7% transgender

Race & ethnicity:

- 40% Latinx
- 33% Non-Hispanic Black

Age:

- 51% 30 – 50 years old
- 32% 51 – 71 years old
- 16% 29 years or younger

Psychosocial factors*:

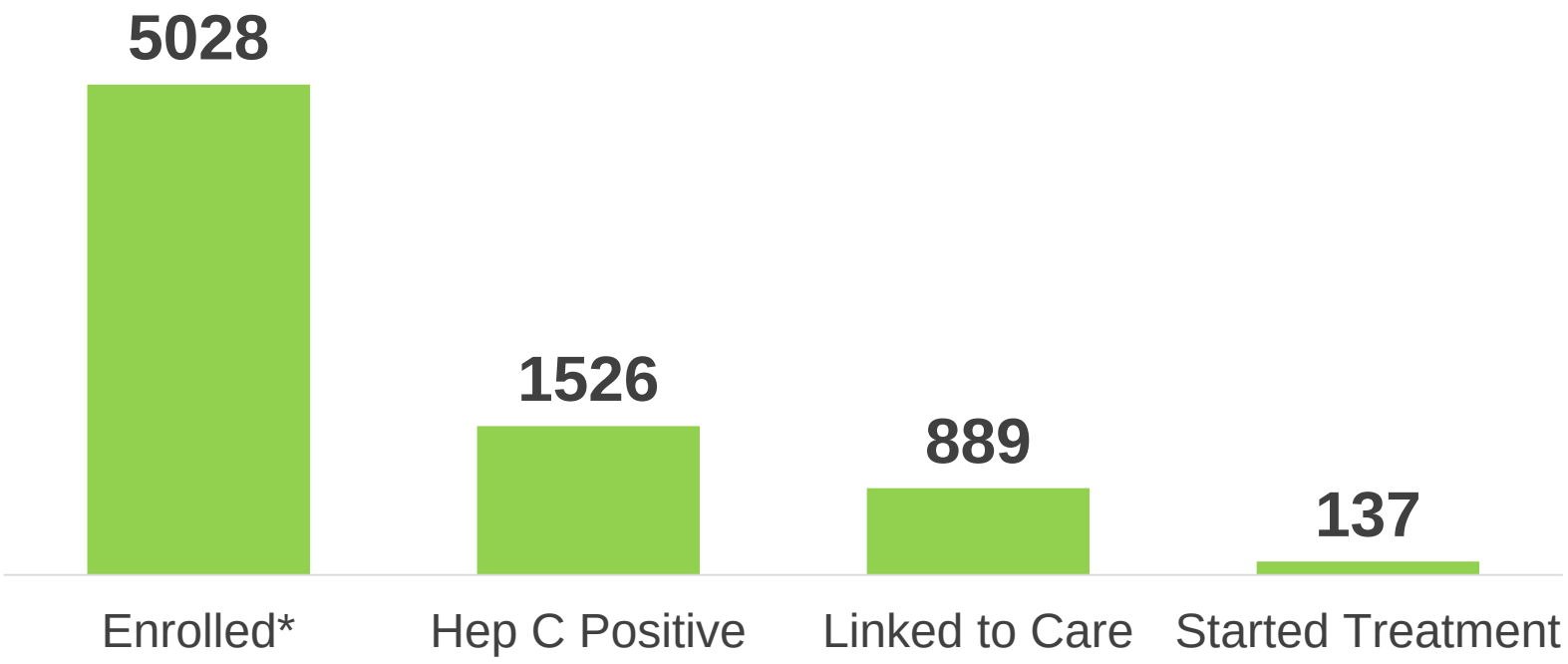
- 74% mental health issue
- 65% homeless or unstably housed
- 61% have injected drugs

42% not aware of Hep C status at intake

*Source: IDUHA Citywide Evaluation Study, 2015 Report

NYC Hep C Peer Navigation Program

Implemented at 15 NYC syringe-exchange and harm reduction programs (all with rapid test programs)



Overall Program Outcomes: December 2014 – March 2017

* Hepatitis C education and prevention services provided

Tips - local implementation of Rapid HCV test programs

1. Set clear & measurable programmatic goals
2. Create a registry of hepatitis C patients & track health outcomes
3. Identify appropriate referral sites & providers for your client population
4. Provide active referrals (i.e. make appointments for clients) - do not expect clients to do this independently
5. Use a team-based approach – avoid isolating your hepatitis C testing programs
6. Coordinated mental health, substance use, and hepatitis treatment services can increase hepatitis C treatment uptake, adherence, and cure[6]

[6] *Zhou K, et al. Interventions to optimize the care continuum for chronic viral hepatitis: aa systematic review and meta-analysis. Lancet, 2016.*

Questions?

Contact:
Jessie Schwartz, RN, MPH
jschwartz2@health.nyc.gov
347-396-2627
Hepfree.nyc

3. HCV RNA testing on the GeneXpert

François Lamoury

Research Officer
Viral Hepatitis and Clinical Research Program
The Kirby Institute, UNSW Sydney

Xpert® HCV Viral Load assay

- ✓ Automated, self-contained, single use, random access
- ✓ European CE-IVD, WHO pre-qualified (plasma only)
- ✓ Single platform for integration (HIV, HPV, TB)
- ✓ Minimal training, fast (108min)
- ✓ Multiple configurations

- ? Not available in all countries
- Cost - pricing per test and platform access.

Method: Plasma versus finger-stick samples

Venous whole blood

Xpert® HCV Viral Load

1 Collect venous whole blood by venepuncture

2 Centrifuge

3 Load **1.2mL plasma** into Xpert ® HCV Viral load cartridge

4 **Result in 108min (“fast”)**

WHO pre-qualified

CE - IVD marked

Not yet available in the US

Finger-stick capillary blood

Xpert ® Fingerstick HCV Viral Load

1 Collect 100µL capillary blood by finger-stick into a Minivette

2 Load 100µL capillary blood into Xpert ® Fingerstick HCV Viral load cartridge

3 **Result in 58min (“rapid”)**

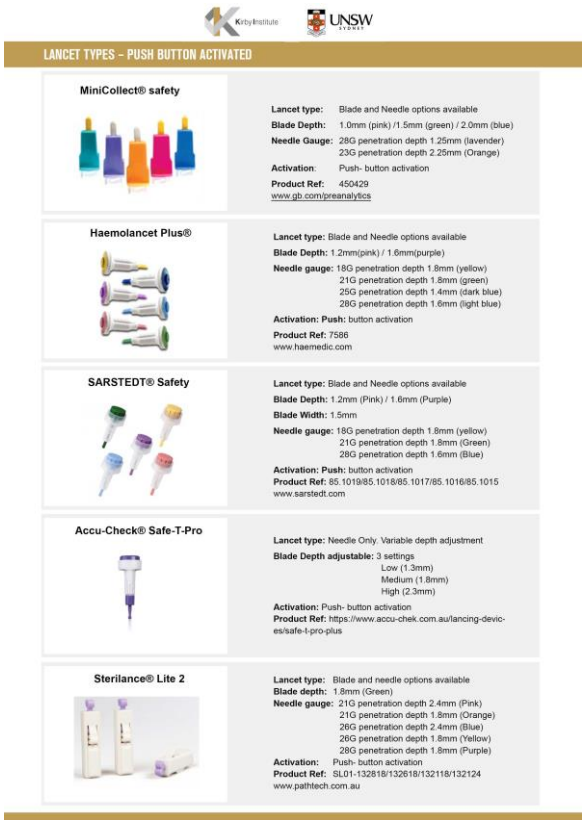
Research Use only

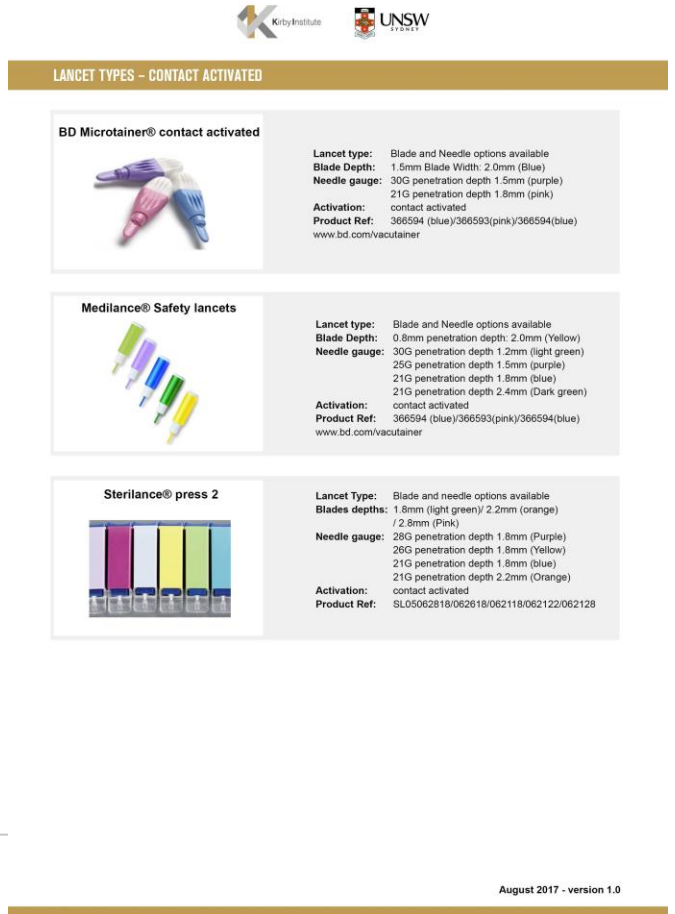
Not registered

Targeted availability 2018

Open access resources / videos – available soon…

Examples





Xpert® Fingerstick HCV Viral Load assay

(Not available for diagnostic use)

Consumables

Lab Bench coat

SARSTEDT® Safety Lancet Super

MULTIGATE® sterile Cotton Balls

Curity™ Sheer Adhesive Bandage

Minivette® POCT 100µl K3E

BRIEMARPAK® Skin Cleansing Swabs

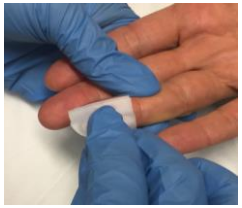
Examination Gloves

Choice

Fingerstick capillary blood collection and sample loading

1

2



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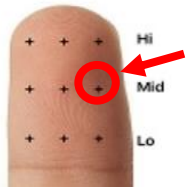

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Demonstration of capillary blood by fingerstick and minivette collection for the GeneXpert

4. Dried Blood Spot sampling and testing

Tanya Applegate

Senior Lecturer

The Kirby Institute,

UNSW Sydney Australia

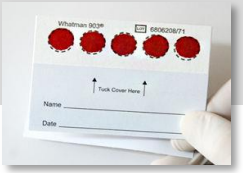
Erika Castro

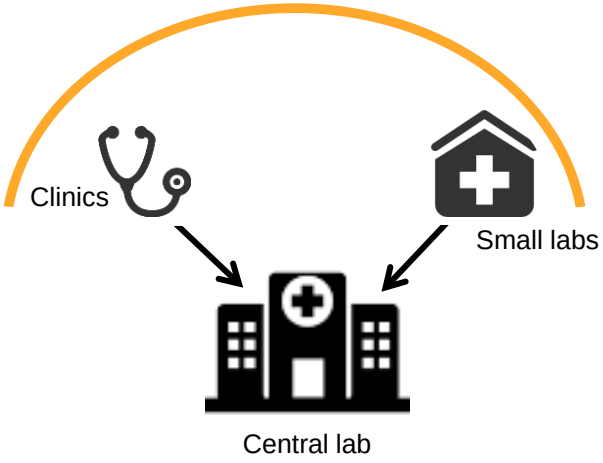
Head of Internal Medicine in Addiction clinic

Centre Hospitalier Universitaire Vaudois

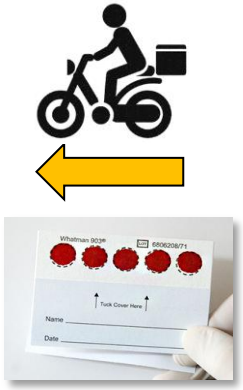
Lausanne, Switzerland

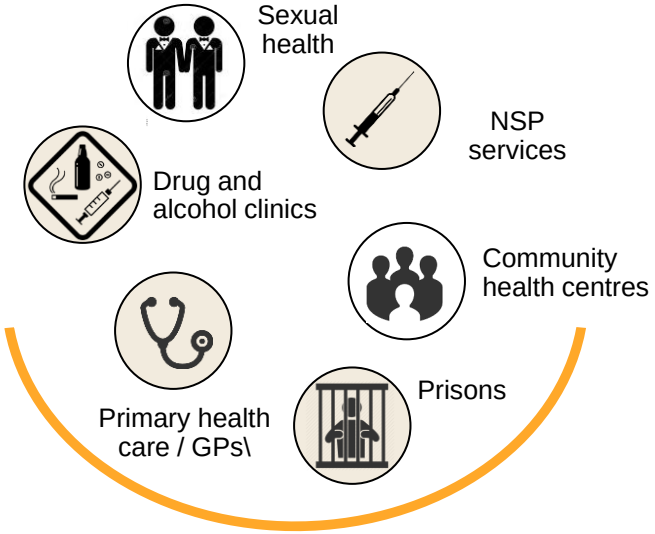
What are Dried blood Spots (DBS)?





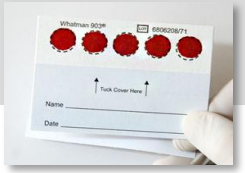
Centralized testing





Decentralized services

What are the pros and cons of DBS?



Pros

- ✓ Linkage to care
- ✓ Easy and inexpensive to collect
- ✓ No medical training required
- ✓ Facilitate access
- ✓ Self-collection possible at home
- ✓ Reflex testing (no second test)
- ✓ RNA, Ab (including RDT), core antigen

Cons

- ✗ Low sample volume
- ✗ Reduced sensitivity
- ✗ Analyte degradation can occur
- ✗ Centralised testing in specialized lab
- ✗ Processing, storage
- ✗ Cost (?? country dependent)
- ✗ **No registered tests for clinical use**

How are dried blood spots collected?

Consumables

Bench coat

Safety Lancet

Sterile Cotton Balls

Adhesive Bandage

Alcohol Cleansing Swabs

Gloves

+

Whatman® 903 protein saver card

Humidity Indicator card

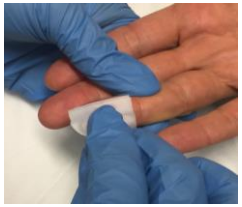
Absorbent packets

Whatman® Foil barrier bags

Fingerstick capillary dried blood spot collection

1

2



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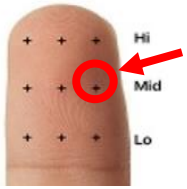

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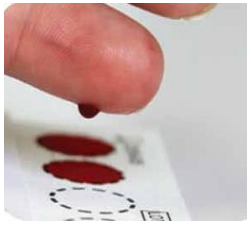

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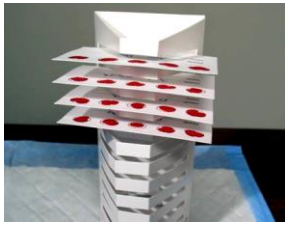

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Open access resources / videos – available soon

Kirby Institute UNSW SYDNEY

HCV DRIED BLOOD SPOT (DBS) COLLECTION GUIDE

1 ASSEMBLE DBS CONSUMABLES


Whatman® 903 protein saver card


Whatman® Foil barrier reusable bags


SARSTEDT® Safety-Lancet Super


BRIEMARPAK® Skin Cleansing Swabs


Clariant Humidity Indicator card


MiniPax® absorbent packets


MULTIGATE® sterile Cotton Balls


Curity™ Sheer Adhesive Bandage


Examination Gloves


Lab Bench Coat

2 PATIENT ASSESSMENT AND PREPARATION


Ask patient to warm hands by rubbing together

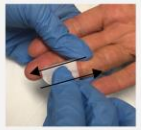

Increase circulation by doing fist clenches


Massage to further help blood flow


Best practice is to use the middle ring finger of the non-dominant hand


Assess suitable fingers

3 SITE CLEANING AND DISINFECTION


Use 1st swab Clean the finger well moving in both directions

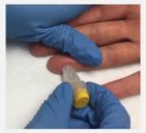

Use 2nd swab to disinfect in a single stroke

4 PERFORMING FINGERSTICK AND DBS COLLECTION

Do not touch the spots with bare fingers to avoid contamination

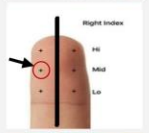

Open pre-labelled protein saver card. Do not touch the spots with bare fingers to avoid contamination


Show and explain to the patient that the lancet is unused then break seal


Hold lancet firmly against finger on the side closest to the little finger and press the button.


Apply gentle pressure and allow a drop of blood to form and fall onto the card. Continue until five spots are collected. DO NOT DAB FINGER ONTO THE CARD.


Position the hand flat on the surface

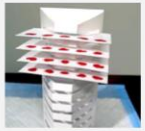


Determine the best site for taking the sample which is either side of the midline of the finger


Wipe away the first blood drop


Stop blood flow by applying pressure for 5 minutes and place spot band on finger

5 DRYING AND PACKING OF DBS FOR TRANSPORT


Dry cards horizontally in a DBS drying rack for minimum 4 hrs or overnight


Close flap on DBS card insert into a sealable foil bag then add humidity indicator card + two absorbent packs. Apply pressure to ensure air is expelled from foil bag prior to sealing

6 STORAGE OF DBS CARDS


Sealed foil bags can be stored at room temperature away from sunlight and moisture in a cool, dry environment for up to 14 days before sending in standard postal envelope to a central reference laboratory

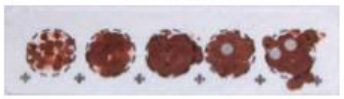
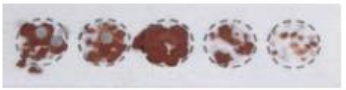
References:
1. World Health Organization. Blood collection and Handling – Dried Blood Spots (DBS). | http://cdrwww.who.int/diagnostics_laboratory/ documents/guidance/pm_module14.pdf
2. WHO manual for HIV drug resistance testing using dried blood spot specimens march 2010 (updated July 2012). http://apps.who.int/iris/bitstream/10665/75829/1/WHO_HIV_2012.30_eng.pdf?ua=1

What makes a good DBS?

Scoring DBS – valid / invalid

Quantity

DBS quantity encompasses both the number of DBS collected (i.e., number of DBS collected out of maximum of 5) and the amount of blood collected on the filter paper (i.e., whether the area was fully covered with blood, half, spotted etc.). This information must be recorded on the DBS receipt log and if necessary must be described on the 'DBS quantity comment' section.

DBS Quantity	Image	Comment
		Sufficient
		Insufficient
		Insufficient
	Front view  Back view 	Not soaked through

Quality

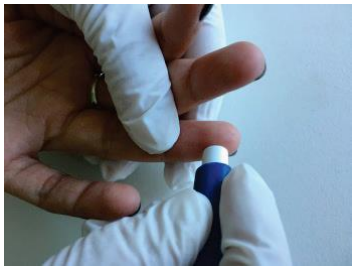
DBS quality determines whether a DBS specimen is valid or invalid. The laboratory receiving the DBS specimen must classify whether a sample is considered valid or invalid. In the case that a specimen is classified as invalid, it is important that the reason for such classification is indicated. Please refer to the images below when recording the DBS specimen quality score. Use the scoring code indicated in this guide in filling out the DBS receipt log.

DBS Quality score	Image	Comment
1		Insufficient quantity for testing
2		Specimen is scratched or abraded
3		Specimen was not dry before mailing
4		Specimen is supersaturated
5		Specimen appears diluted, discoloured or contaminated
6		Specimen exhibit serum separating from cells may also appear as serum rings
7		Specimen appears to be clotted or layered
8		Specimen obtained with incorrect filter paper
9		No blood spot was added

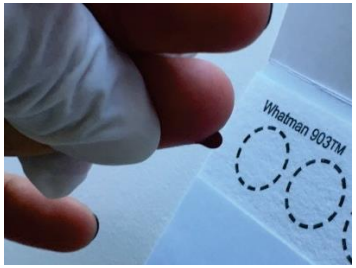
Tips to improve DBS collection

- The best place middle or 4th finger
  - Non-dominant hand

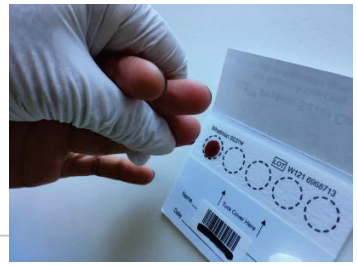
- Prick the finger on the side (not on the pad).
  - Nearest the little finger (to help the next steps)



- Let the blood accumulate until a drop forms.
  - You can encourage blood flow
  - “To milk or not to milk?”



- Let the blood drop where possible



DBS collection demonstration

How are DBS stored and tested?

Storage

1 *Intact card (Research)*

Foil bag

Drawers

2 *Punch / elute (Service provider)*

Eluate stored

Racks

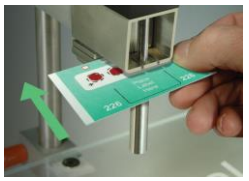
-70 freezer

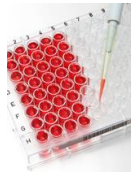
Testing

1 *Punch*

Elute

2





HCV RNA assays (research use only)

1

Panther system (Hologic)

2

m2000sp/rt (Abbott)

3

AmpliPrep / COBAS Taqman (Roche)

HCV RNA quantification on DBS

A concept of proof in Swiss settings

Disclosure

This study was co-sponsored with an unrestricted grant of Gilead.

HCV RNA quantification on DBS – A Swiss study

Nested projects
2018

- Expand virologic applications
- Run monitoring surveys

Multicenter Validation
2017

- Compare external HCV RNA plasma standards to local DBS lab standard

Local DBS lab standard
2016

- Integrate DBS HCV RNA analysis to local lab standards as a routine test

A Swiss case study – why?

Why HCV screening with DBS in tertiary referral hospital?

A Swiss case study - background

The need of optional blood collection strategies for people who inject drugs with difficult venous

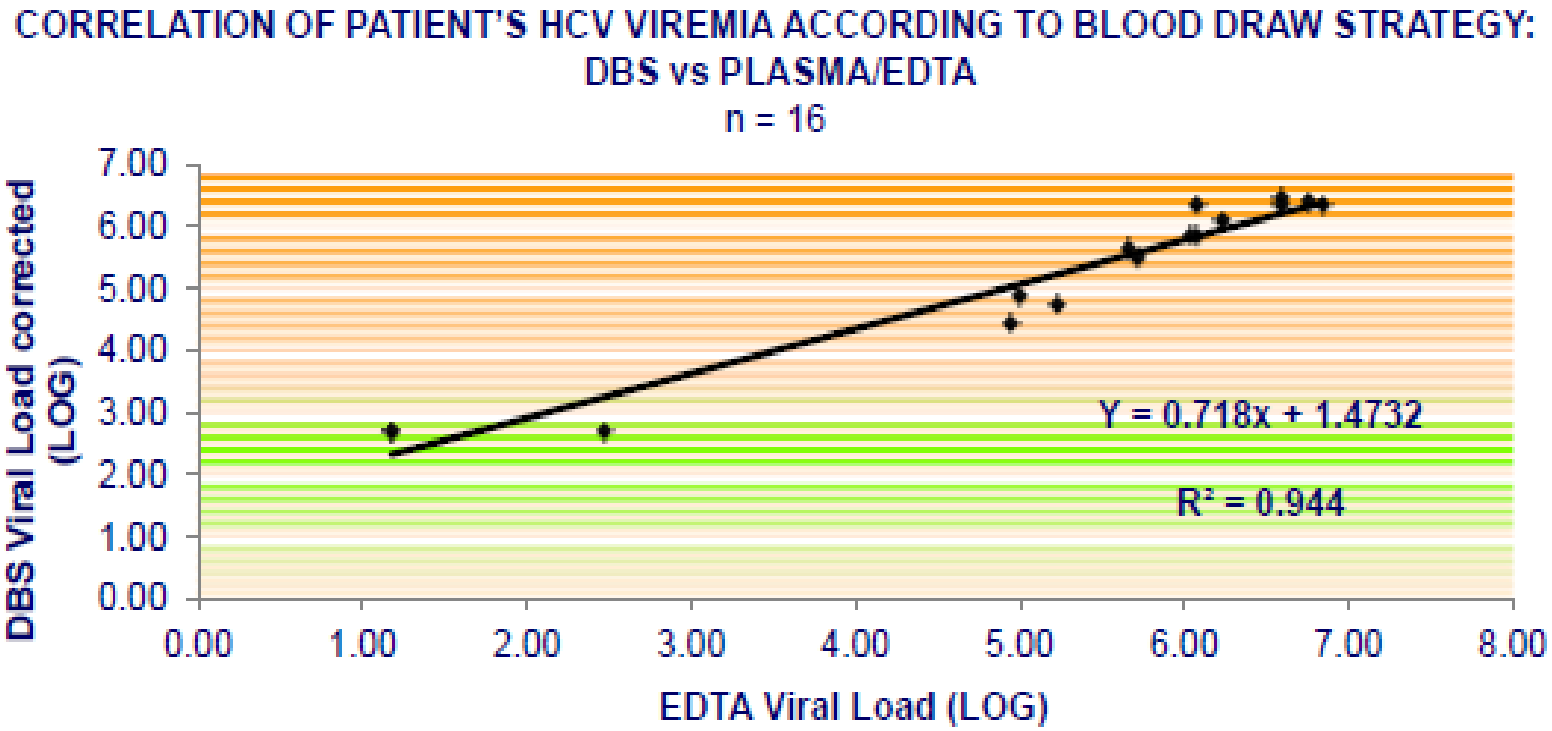
- Poor vascular health consecutive to years of intravenous drug injection is a common constraint.

- Routine limb vein puncture can become a barrier for screening and treatment of HCV infection.

Hepatitis C Virus RNA quantitation using DBS

Erika Castro, Rachel Mamin, Cyril Andre, Lorenza Oprandi

P12
INHSU
2016



HCV RNA quantification:

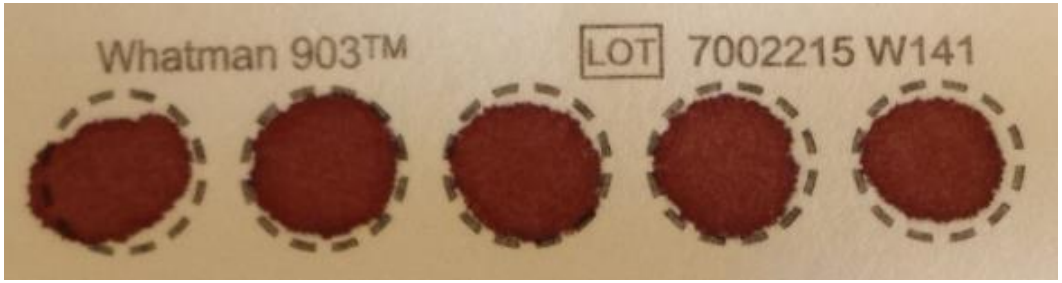
COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Test v2.0).

Conclusions

- We found a positive and strong correlation of patient's DBS and plasma/EDTA HCV viremia values.

- In this dataset EDTA plasma RNA average was 5.16 log (range: 1.17 6.85) with a limit detection value of 1.17 log (≤15 IU/mL).

- DBS RNA detection limit was 2.69 log (480 IU/mL).



HCV RNA quantification on DBS:

A proof of concept in Swiss settings

Small dataset..to argue for quantitative use.

HCV RNA quantification on DBS:

A proof of concept in Swiss settings

Nested projects

2018

- Expand virologic applications
- Run monitoring surveys

Multicenter Validation

2017

- Compare external HCV RNA plasma standards to novel DBS lab standard

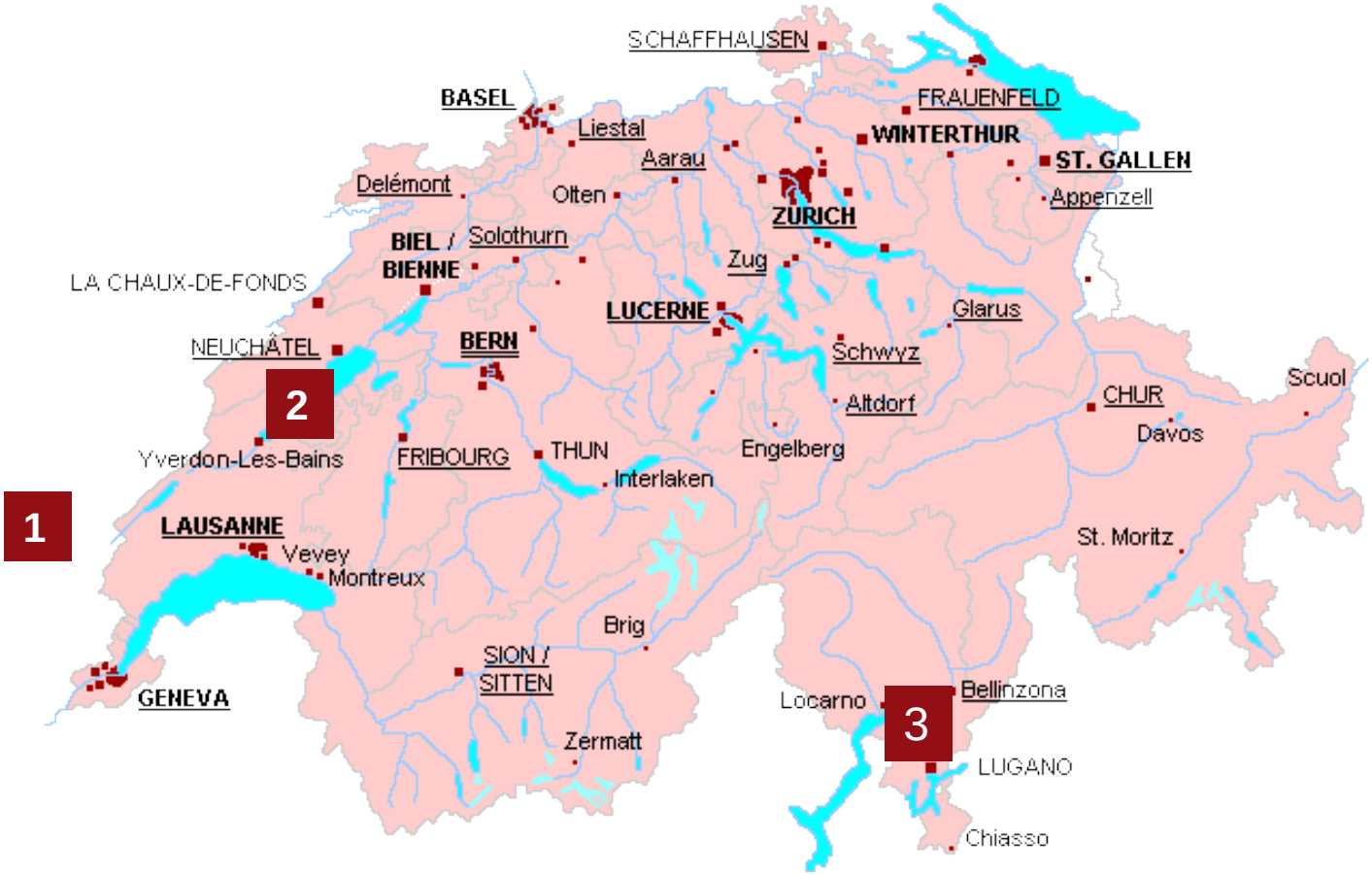
Local DBS lab standard

2016

- Integrate DBS HCV RNA testing to local lab standards as a routine test

HCV RNA quantification on DBS:

A proof of concept in Swiss settings



1. CHUV: DBS central lab + Addiction medicine clinic
2. Unité de traitement des addictions, Dr Laurianne Mer.
3. Fondazione Epatocentro Ticino, Dr Alberto Moriggia.

INHSU 2017

CHUV

Poster 24

A Cost-Effectiveness Analysis of Increasing Hepatitis C Virus Screening in People Who Inject Drugs in Switzerland Using Rapid Antibody Saliva and Dried Blood Spot Testing

François Girardin[1], Natalie Hearmon[2], Francesco Negro[3], Lucy Eddowes[2], Philip Bruggmann[4], Erika Castro[5*]

[1]Medical Direction and Division of Clinical Pharmacology and Toxicology, Geneva University Hospitals (HUG), University of Geneva, Geneva, Switzerland; [2]Costello Medical Consulting Ltd, Cambridge, UK; [3]Divisions of Gastroenterology and Hepatology, and of Clinical Pathology, HUG, Geneva, Switzerland; [4]ARUD, Centres for Addiction Medicine, Zurich, Switzerland; [5]Center for Addiction Medicine, Service of Community Psychiatry, Department of Psychiatry, University of Lausanne (CHUV), Lausanne, Switzerland; *Erika.Castro-Bataenjer@chuv.ch.

- Cost-effective due to the increased screening uptake via rapid saliva and DBS testing instead of venipuncture.
- The proposed test package is less expensive than venipuncture.
- Would likely increase the number of diagnoses and result in a greater number of PWID initiating treatment.

6. Closing remarks

Point of care testing strategies can globally:

- **Scale-up HCV screening/monitoring in LMIC and HIC**
- **Improve linkage to care**
- **Be adapted to settings' needs**
- **Enhance collaborative partnerships**

7. Acknowledgments

Study participants, coordinators, nurses, investigators

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Sharon Hutchinson

Orasure for providing training today

Thanks in advance……Abbott, Hologic and Roche for pushing DBS registration!

Orasure demonstration – for those who are keen.