



# **Time to detection of hepatitis C virus infection with the Xpert HCV Viral Load Fingerstick Point-of-Care Assay: Facilitating a more rapid time to diagnosis**

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# Disclosures

- JG has received research funding and speaker fees from AbbVie, Cepheid, Gilead Sciences and Merck/MSD
  - In-kind support was provided by Cepheid for Xpert HCV Viral Load Fingerstick Point-of-Care cartridges and GeneXpert equipment related to this project
  - This presentation will include the discussion of the investigative use of medical devices (Xpert HCV Viral Load Fingerstick, Cepheid)
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# Background/rationale

- Current two-step pathway for HCV testing leads to a drop-off in diagnosis<sup>1-4</sup>
- Point-of-care HCV testing increases testing and linkage to care<sup>1</sup>
- Xpert HCV Viral Load Fingerstick assay uses real-time PCR technology for HCV RNA quantification
  - Enables same-day diagnosis of active infection in one hour with good sensitivity and specificity<sup>5-7</sup>
- Time to detection of HCV RNA varies according to the level of virus present
- Further work is needed to reduce the time from sample collection to diagnosis of active infection

# Study Aim

- To evaluate the time to HCV RNA detection using the Xpert HCV Viral Load Fingerstick assay among participants attending drug treatment and needle and syringe program services in Australia

# Study Design and Participants - ETHOS Engage Cohort



ETHOS ENGAGE

**Study design:** Observational cohort study

**Study setting:** Drug treatment clinics and needle and syringe programs

**Study recruitment period:** May 2018-May 2019

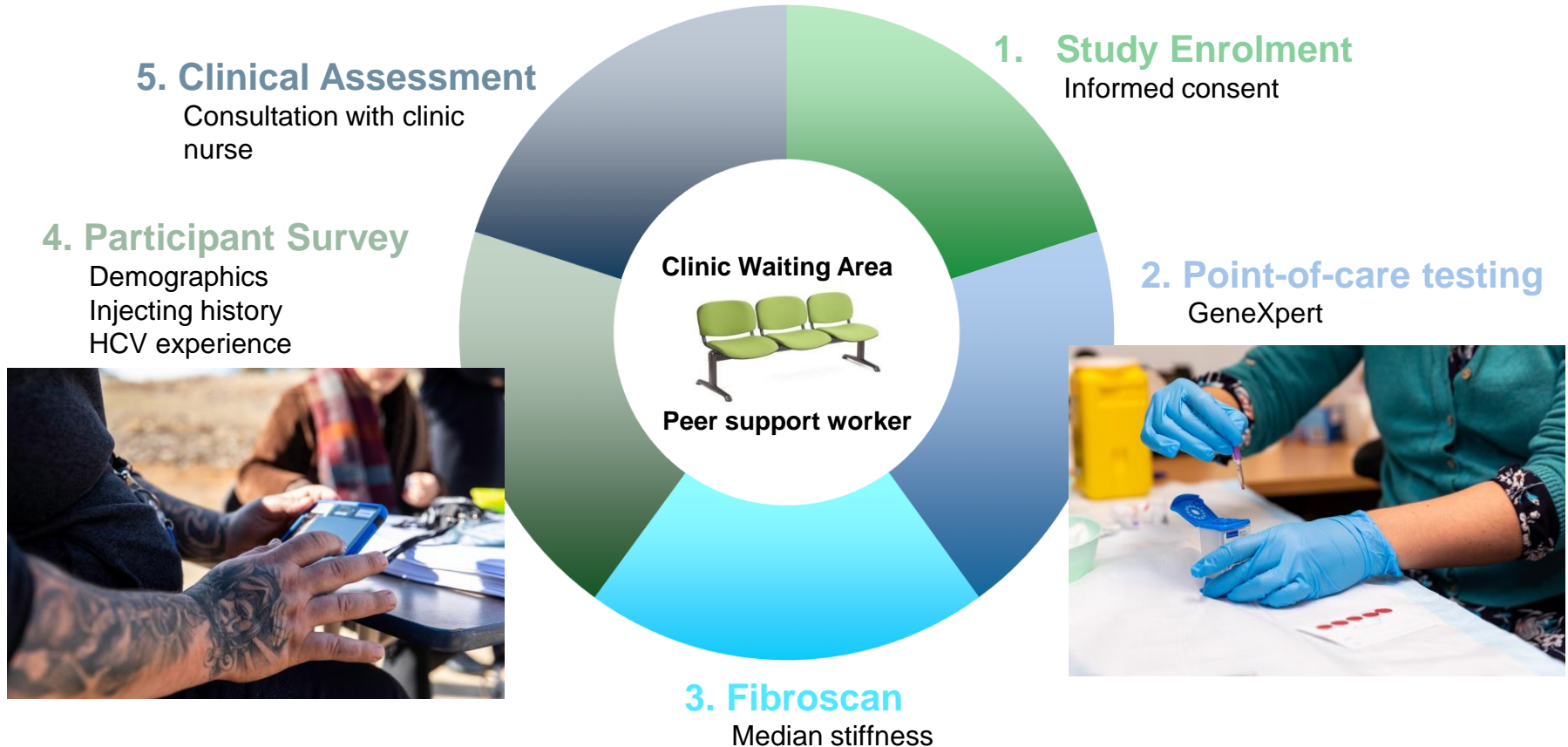
***Inclusion criteria:***

- 18 years of age or older;
- Written informed consent;
- History of injecting drug use;
- Recent injecting drug use (previous 6 months) OR currently receiving OST.

***Exclusion criteria:***

- Women who are pregnant

# ETHOS Engage campaign recruitment days



# Xpert HCV Viral Load Fingerstick testing



**Puncture the fingertip  
with a lancet**



**Collect 100µL capillary  
blood by fingerstick into a  
Minivette**



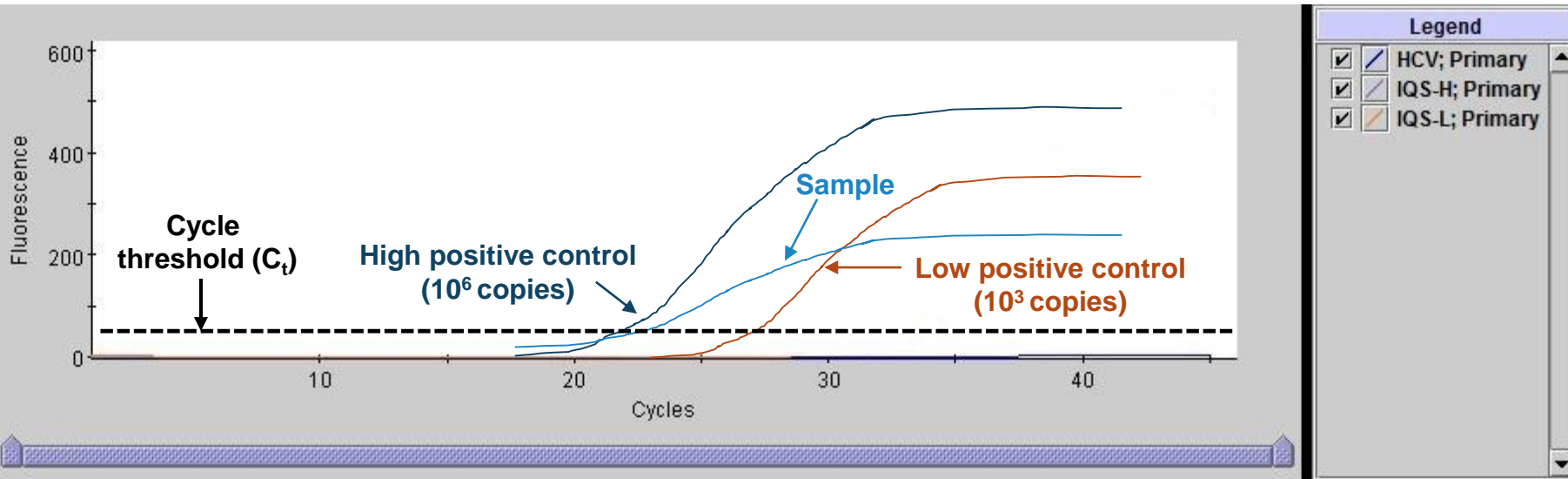
**Load blood directly into  
Xpert HCV Viral Load  
Fingerstick cartridge**



**Place Xpert HCV Viral  
Load Fingerstick cartridge  
into GeneXpert machine**

# Xpert HCV Viral Load Fingerstick

- Xpert HCV Viral Load Assay Fingerstick testing was performed on a GeneXpert R2 6-colour, 4 module machine (GXIV-4-L System, 900-0513, GeneXpert Dx software v4.6a)



- Problem: While the assay is running, it is not possible to see what the cycle threshold is or at what point the sample crosses the cycle threshold (detectable HCV RNA)



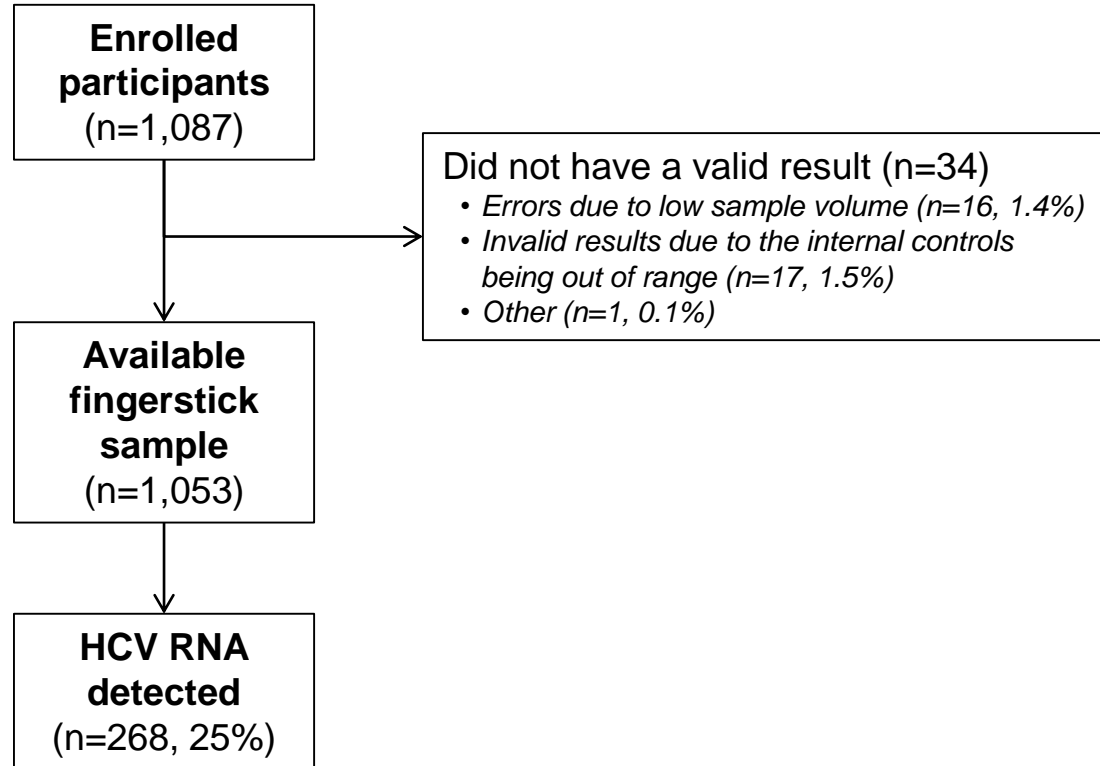
# Statistical Analyses

- Assessed the time to detectable result with the Xpert HCV Viral Load Fingerstick
  - evaluated by multiplying the cycle threshold (cycle at which the HCV RNA crosses the threshold and is considered detectable) by the cycle time (~80 seconds)
- Analyses were performed to assess the time to HCV RNA detection in relation to the high and low internal controls, given that the positive controls always need to be positive (and reflects the minimum time to detection which is possible)
- Assessed the number and proportion of tests in this population sample that could be detected at an earlier time

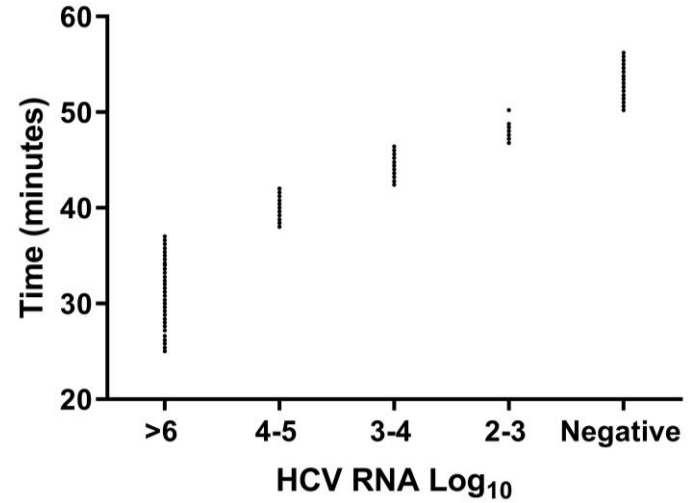
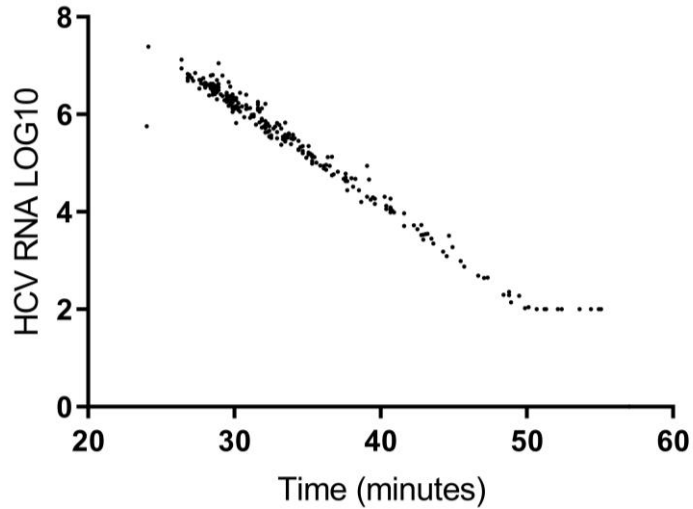
# Participant characteristics

Characteristic	n=1,087
Age, median (25%, 75%)	43 (37-50)
Gender	
Male	698 (64%)
Female	383 (35%)
History of injecting drug use	1,087 (100%)
Injecting drug use in the last month	
No	380 (35%)
Yes	704 (65%)
Unknown	3 (0.3%)
Frequency of drug use in the last month	
Less than weekly	187 (27%)
More than weekly, but not daily	187 (27%)
Daily or more	330 (47%)
Unknown	3 (0.4%)

# Participant disposition



# HCV RNA level versus time

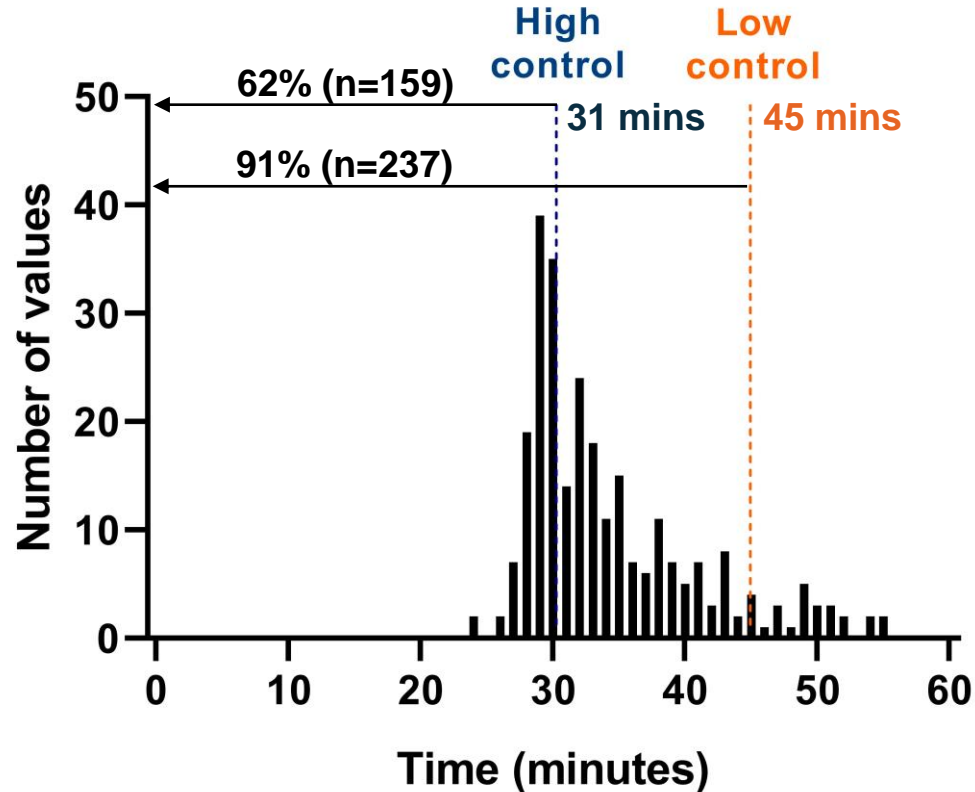


# Time to HCV RNA detection

		Time (minutes) n=1,053
<b>HCV status</b>		
Undetectable (n=785)		57 minutes
Detectable (n=268)		34 minutes
<b>HCV RNA level</b>		
$\geq 10,000,000$ IU/mL (n=3)		26 minutes
1,000,000-9,999,999 IU/mL (n=113)		29 minutes
100,000-999,999 IU/mL (n=72)		33 minutes
10,000-99,999 IU/mL (n=38)		38 minutes
1,000-9,999 IU/mL (n=19)		43 minutes
Quantifiable – <1,000 IU/mL (n=23)		50 minutes

91%  
>1,000 IU/mL

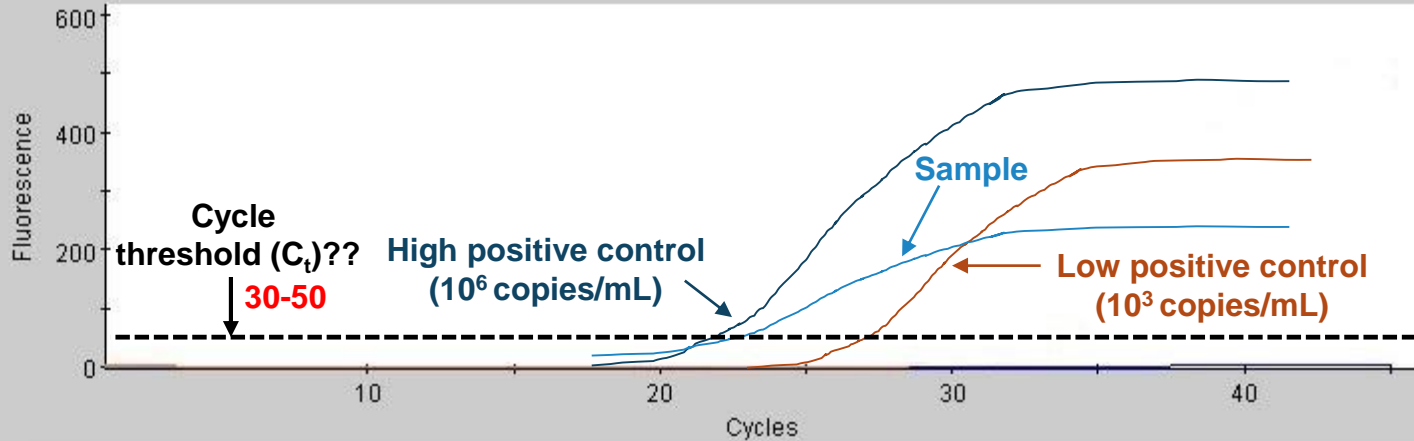
# Time to HCV RNA detection in HCV RNA+ (n=260)






# High and low controls

	High internal control n=260	Low internal control n=260
Minimum (minutes)	29	43
Median (minutes)	31	45
Maximum (minutes)	34	49

# Xpert HCV Viral Load Fingerstick



## Legend

-  HCV; Primary
-  IQS-H; Primary
-  IQS-L; Primary



# Practical utility

- Wait for the high internal control to amplify first (e.g. you could use 30-50 fluorescence units as the cut-off with an expected cycle threshold (Ct) range)
  - This is a first step quality control check
- With negative samples, there should be no/limited fluorescence for the HCV target
- With positive samples, you could use the same 30-50 fluorescence unit cut-off for the expected cycle threshold (Ct) range
- With suspected HCV RNA detection, could begin discussions about treatment
- Wait until the assay has completed to ensure validity

# Conclusions

- The time to HCV detection was lower in people with detectable HCV RNA (34 minutes) compared to people with undetectable HCV RNA (57 minutes)
- Faster time to HCV RNA detection with higher HCV RNA levels
- These findings suggest that a more rapid time to an HCV diagnosis could be achieved by monitoring the time at which HCV RNA is first detected with the Xpert HCV VL FS test, rather than waiting until assay completion
- These findings could lead to reduced wait times for an HCV diagnosis and improve linkage to treatment

# Implications

- Assay was originally developed as a quantitative assay and requires both the high and low internal controls to be completed for a valid test result
  - CE-IVD registration of a new assay would require substantial work including verification and validation studies
  - Need to consider potential modifications that would enable the user to easily determine once an HCV RNA level is above the detectable threshold (e.g. software notification or alarm when detectable threshold is reached)
    - Consideration of the high and low internal controls is required
  - Are there other potential solutions (e.g. “middleware” software)?
-

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