British HIV Association
BHIVA
20th Annual Conference

BASHH
12th Annual Conference

Third Joint Conference

of the
British HIV Association (BHIVA)
with the
British Association for Sexual Health and HIV (BASHH)

1–4 April 2014

Arena and Convention Centre · Liverpool

Mr Robert Carney

Royal Free London NHS Foundation Trust

A hepatitis C virus core antigen assay is a cost-effective, sensitive and specific test in the detection of acute hepatitis C in HIV infection

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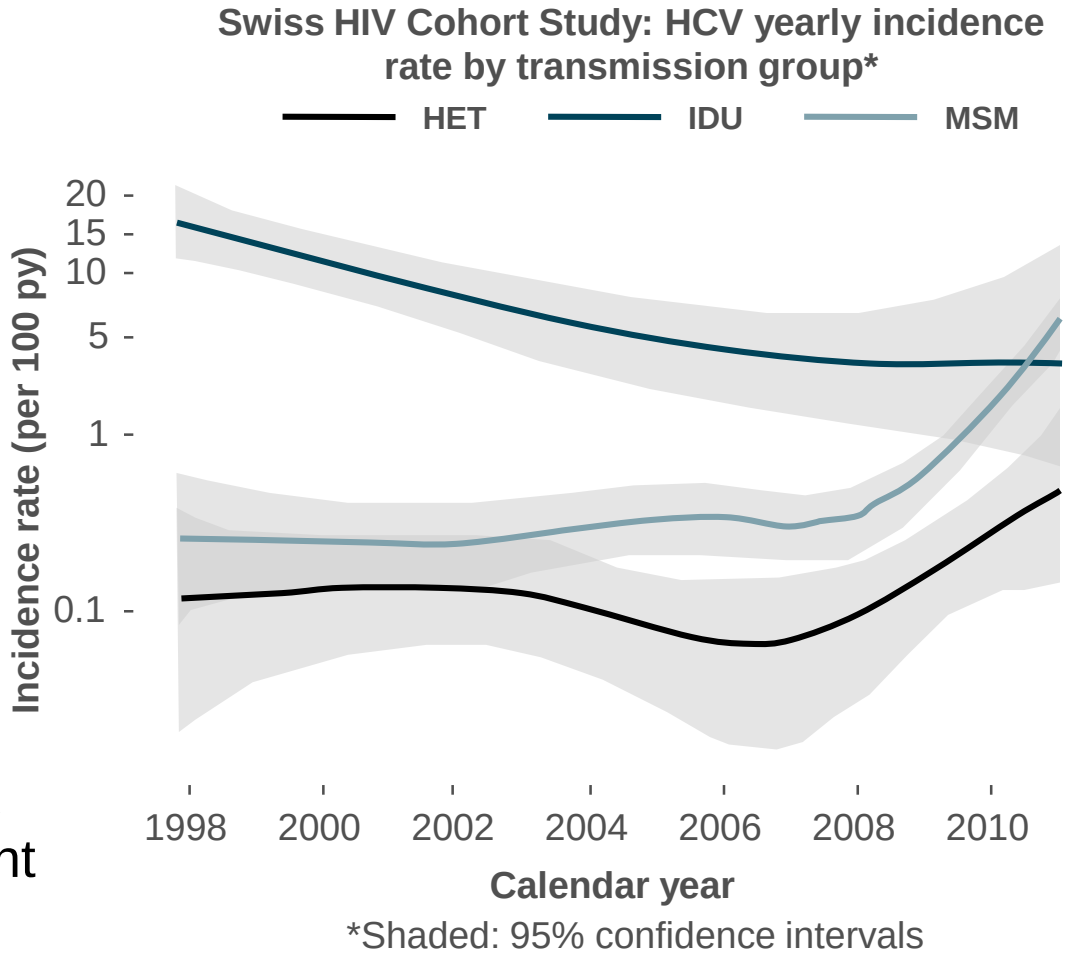
Work carried out at Royal Free Hospital, London

3 April 2014; The Third Joint Conference of BHIVA & BASHH

Due to shared routes of transmission HCV-HIV co-infection is common

- Liver disease is a leading cause of death in HIV-infected individuals
- Incidence among IDUs has decreased whereas in MSM cases have risen **18-fold since 1998**
- Reduced rates of HCV spontaneous clearance and poorer response to treatment

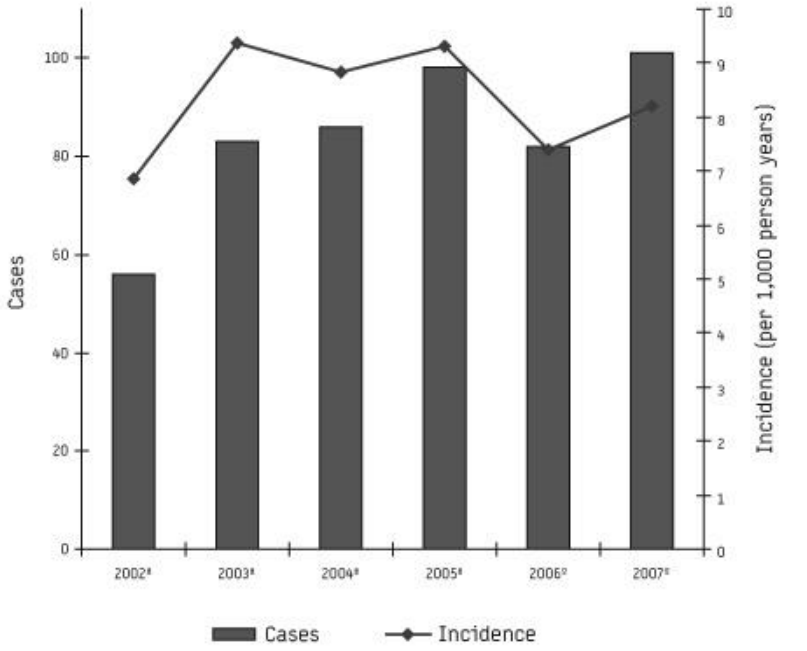


Since 2000 there has been an ongoing epidemic of acute HCV infection among MSM

- HCV infection is more likely in those with existing HIV infection, past syphilis and inconsistent condom use
- Mucosal trauma during **high-risk sexual practices** most likely route of transmission
- UK and German case–control studies identified higher levels of **nasally administered drug use** in cases

FIGURE

Numbers of cases and estimated incidence of newly acquired HCV in diagnosed HIV-infected MSM reported by HIV clinics in London and Brighton, 2002-2007

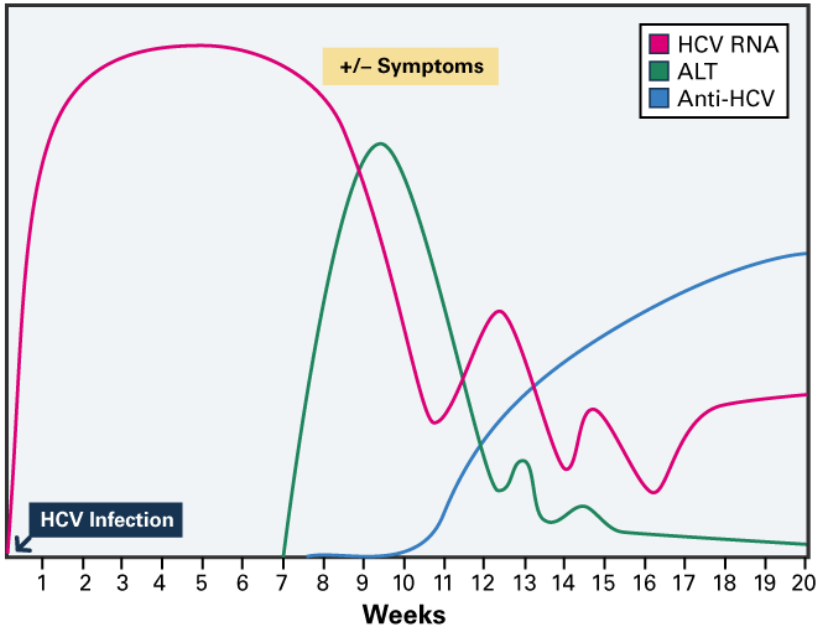


[a] Reported in reference [6].
[b] Report from one clinic outstanding
HCV: hepatitis C virus; HIV: human immunodeficiency virus; MSM: men who have sex with men.

Sources: Price, H et al.(2013), Hepatitis C in men who have sex with men in London – a community survey. HIV Medicine, 14: 578–580
Bradshaw, D et al.(2013). Sexually transmitted hepatitis C infection: the new epidemic in MSM? Current Opinion in ID. 26(1):66-72

The diagnosis and monitoring of HCV relies on the detection of anti-HCV and RNA

- HCV antibody test following HIV antibody positive
  - HCV PCR and genotype if positive
- Doubling the number of patients on HCV therapy could **avert 6000 deaths** over next 30 years
- Number of HCV sufferers will increase to **370,000** in 2035
- Healthcare costs will rise to **£115 million** in 2035



Sources: BHIVA Hepatitis Guidelines 2013
PHE, Hepatitis C in the UK: 2013
RAND, Hepatitis C: A projection of the healthcare and economic burden in the UK, January 2013

Aims: Validation and assessment of a HCV core antigen assay

- PCR is **costly, labour-intensive** and requires **advanced technical skills** and specialist equipment
- Larger diagnostic centres have the capability to utilise the antigen assay
- In the haemodialysis population the core antigen assays have been shown to have a **high sensitivity and specificity**
- The use of HCV core antigen testing for both screening and monitoring are currently not recommended – could the assay be used in HIV positive MSM populations?

Source: Li Cavoli G et al., Hepatitis C virus core antigen test in monitoring of dialysis patients. Hepatitis research and treatment, 2012

STUDY DESIGN
Part 1 - Validation

- ***Sensitivity***: HCV seroconversion panels **(n=45,** genotypes 1a, 1b, 2b, 3a)
- ***Specificity:*** Known HCV RNA negative stored sera **(n=28)**
- ***Cross-reactivity:***
  - HCV RNA negative AND antibody positive (**n=5**)
  - HIV-1 antibody positive (**n=4**)
  - HBsAg positive (**n=4**)
- **Threshold of detection:** A dilution series of WHO standards
  - HCV viral load of 10000, 5000, 2500, 1250, 625 and 312.5 IU/mL were tested in triplicate

Part 2 - Assessment in HCV-HIV MSM

- RFH HIV clinic database was searched for HIV patients presenting with acute HCV infection between 1st January 2008 and 31st August 2013 **(n=30; HCV RNA positive)**

Results – Key Points

- HCV core antigen detected in all HCV RNA positive samples
  - Including those in the HCV-HIV MSM group
- HCV RNA levels of 1250 IU/mL were reliably detected by the HCV antigen assay
- HCV RNA levels of 625 IU/mL were not reliably detected
- No cross-reactivity was observed with HIV-1 or HBsAg positive samples
- 1 false positive result
- Good correlation between HCV viral load and HCV core antigen
  - **$r^2 = 0.99$**
- **<u>Overall test characteristics:</u>**
  - **Sensitivity 100%**
  - **Specificity 97.7%**
  - **Positive predictive value 100%**
  - **Negative predictive value 100%**

Potential limitations of the HCV Ag assay

- Presence of a positive grey-zone result at low level HCV viraemia
- Unsuitable for monitoring treatment response?
- Replacing PCR with the Ag assay may mean less information on seroprevalence
- No detection of cleared infection
- Calibration/daily maintenance/ARCHITECT software problems
- Carry-over of antigen/antibody from different test-kits giving low level false-positive results

Advantages of the HCV Ag assay

- Highly sensitive and specific in the diagnosis of acute HCV in co-infected individuals
- Test considerably shortens the diagnostic window
- Utility in diagnosing the majority of HCV genotypes
- No evidence of cross-reaction
- Fast, cheaper, less labour intensive
- Useful in resource-limited settings without PCR
- Potentially useful in screening high-risk groups

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Questions and Discussion

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