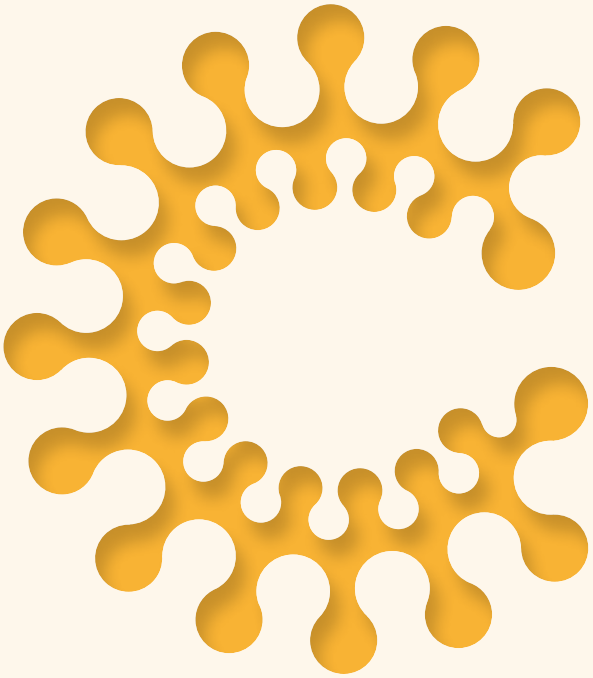
NHS

The Association of Greater Manchester Primary Care Trusts



Guidelines for Laboratory Testing of Patients with hepatitis C in Greater Manchester

Author: PE Klapper on behalf of the Laboratory Consultative Group

Hepatitis C

Greater Manchester Hepatitis C Strategy

These Guidelines should be read in conjunction with the *'Treatment Guidance for Patients with hepatitis C in Greater Manchester'* issued 5th August 2009. The Guidance refers to virological testing of patients and does not detail biochemical, haematological or histopathological testing of patients with hepatitis C.

Definitions of responses to treatment

Sustained viral response (SVR)
Undetectable levels of hepatitis C RNA* (PCR) on blood testing 6 months after completion of antiviral therapy. This is the ultimate aim of therapy as it is associated with long term remission from active infection and marked reduction in the frequency of complications of liver failure and hepatocellular carcinoma.

End-of treatment response (ETR)
Undetectable levels of hepatitis C RNA on blood testing at the end of planned treatment.

Primary non-responder
A patient who fails to achieve an end of treatment response, or in whom treatment is stopped early because to early blood tests show failure of viral suppression below pre-determined values that predict failure of response.

Responder-relapser
A patient who achieves an end-of treatment response but has recurrence of detectable virus six-months after treatment cessation.

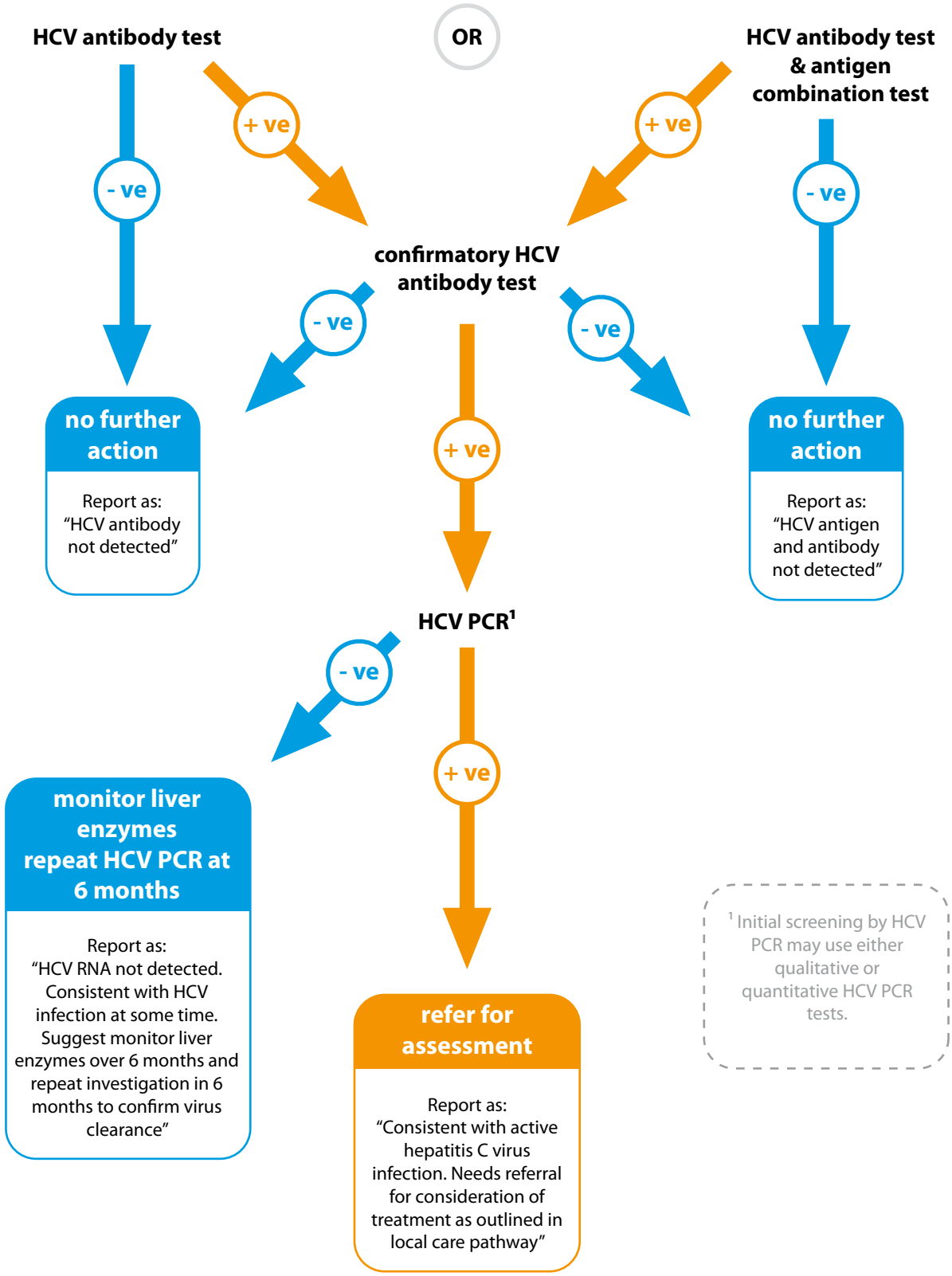
Early viral response (EVR)
A 2-log or greater reduction in viral levels 12 weeks after starting treatment. EVRs may be classed as complete (negative PCR at week 12 – cEVR) or incomplete (positive PCR but viral load shows greater than 2 log reduction from pre-treatment levels – iEVR).

Rapid viral response (RVR)
Undetectable levels of hepatitis C RNA 4 weeks after starting treatment.

Sample dilutution
Undetectable levels of HCV RNA are reported as HCV RNA NOT detected (<30 iu/ml: log iu/ml = <1.48). The HCV RNA test requires a minimum volume of 1.5ml serum or plasma if this volume is not available to test a 1/10 dilution of the sample is made in HCV RNA negative plasma before the test is performed. This reduces the test sensitivity slightly. Positive samples will be reported after the quantity of HCV RNA has been corrected for the dilution factor negative samples will be reported as: HCV RNA NOT detected (<300 iu/ml: log iu/ml = <2.48).

Diagnosis of Hepatitis C

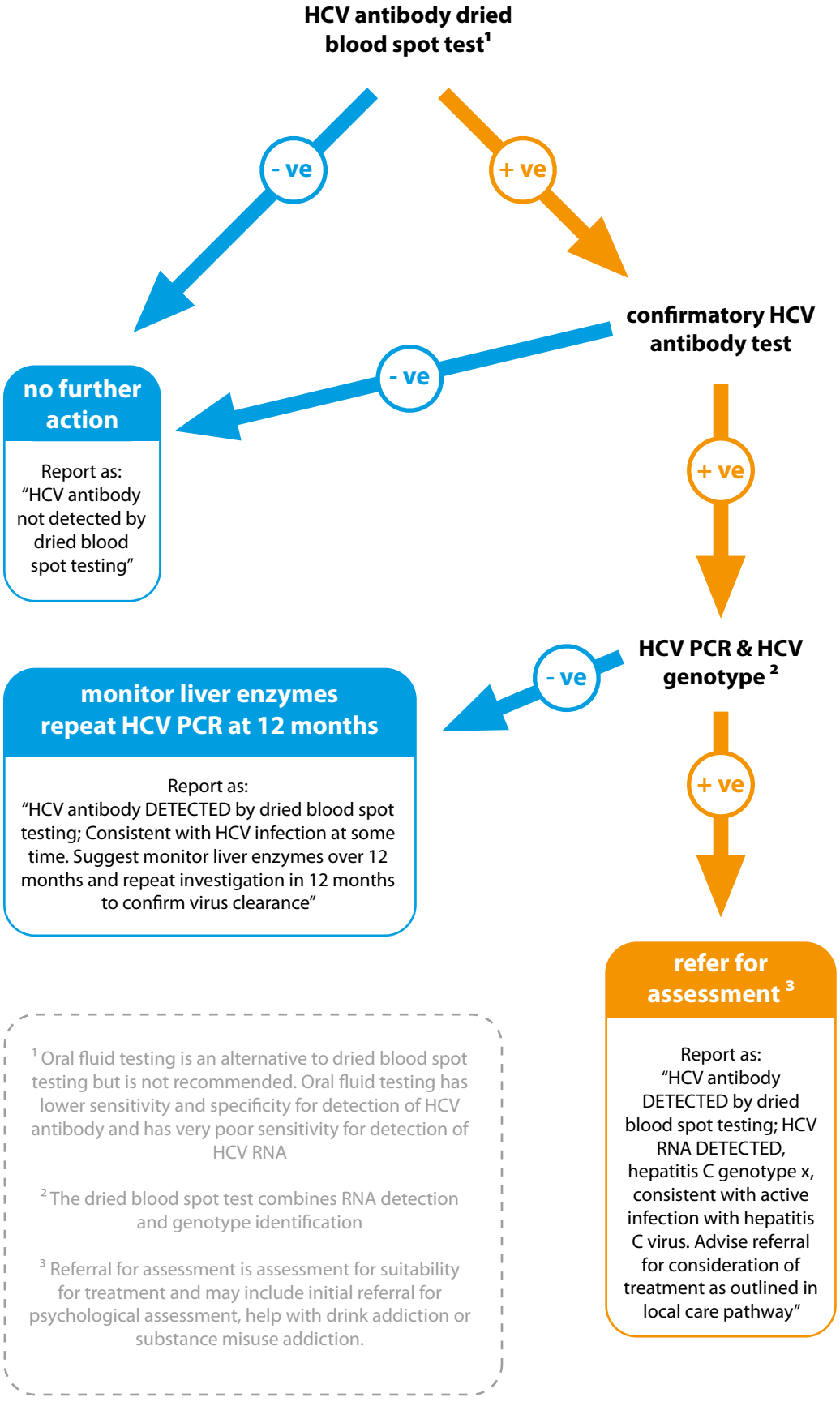
Screening in primary care



HCV PCR may be performed on either serum samples or plasma samples.

Diagnosis of Hepatitis C

Non-healthcare settings on people with poor venal access



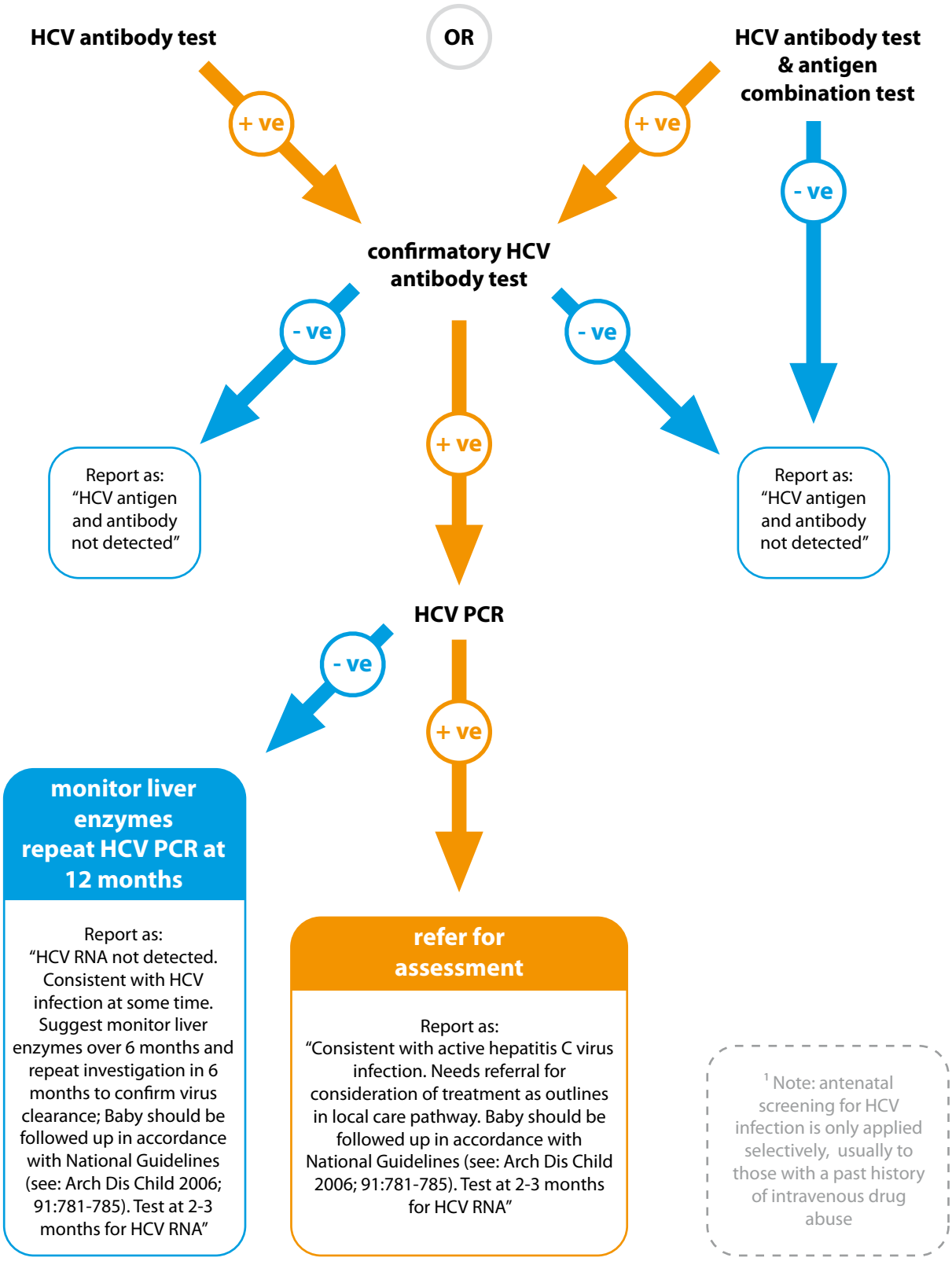
[1] Oral fluid testing is an alternative to dried blood spot testing but is not recommended. Oral fluid testing has lower sensitivity and specificity for detection of HCV antibody and has very poor sensitivity for detection of HCV RNA

[2] The dried blood spot test combines RNA detection and genotype identification

[3] Referral for assessment is assessment for suitability for treatment and may include initial referral for psychological assessment, help with drink addiction or substance misuse addiction.

Diagnosis of Hepatitis C

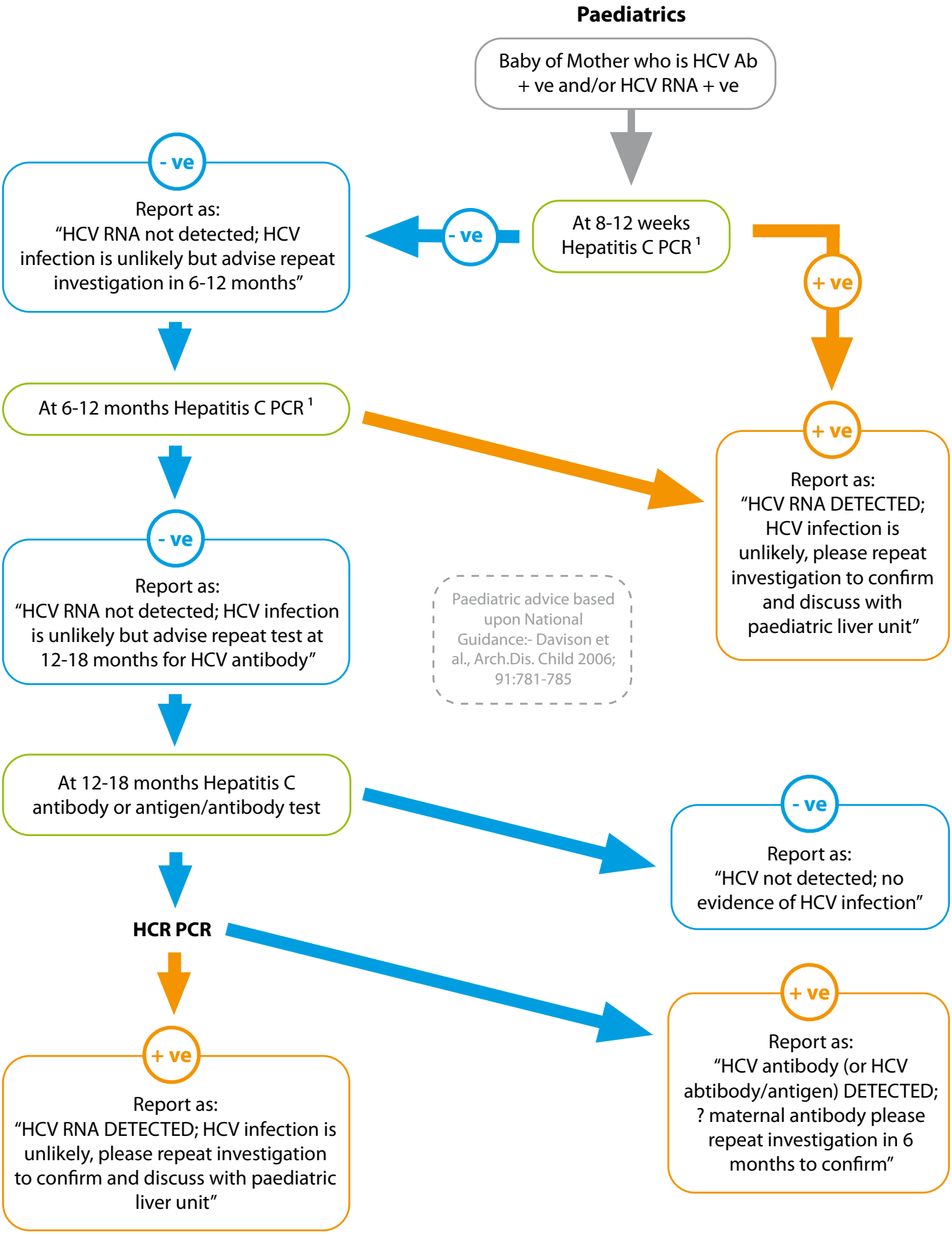
Antenatal screening[1]



[1] Note: antenatal screening for HCV infection is only applied selectively, usually to those with a past history of intravenous drug abuse

Diagnosis of Hepatitis C

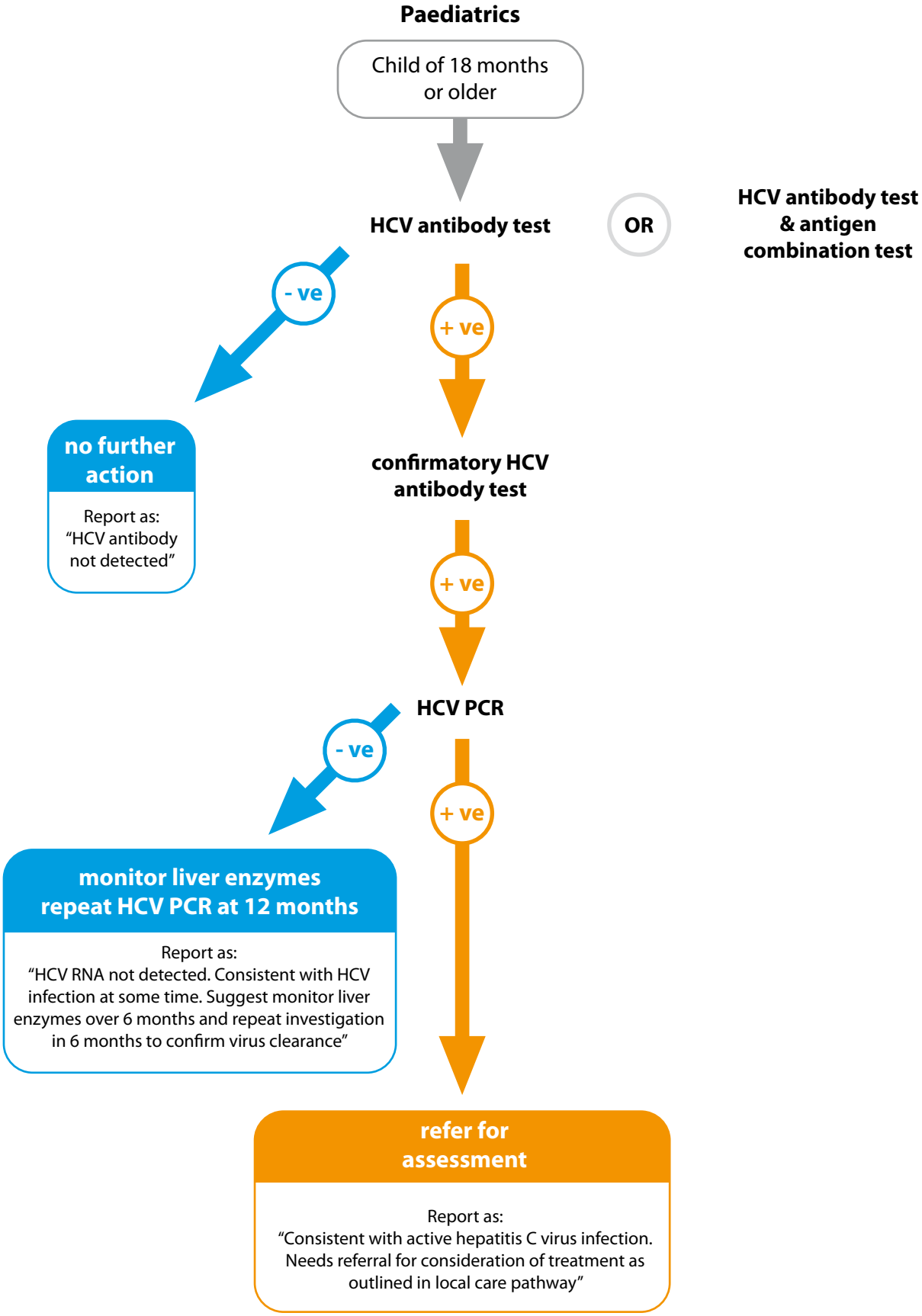
Screening of babies Under 12 months born to HCV infected mothers



Paediatric advice based upon National Guidance:- Davison et al., Arch.Dis. Child 2006; 91:781-785

Diagnosis of Hepatitis C

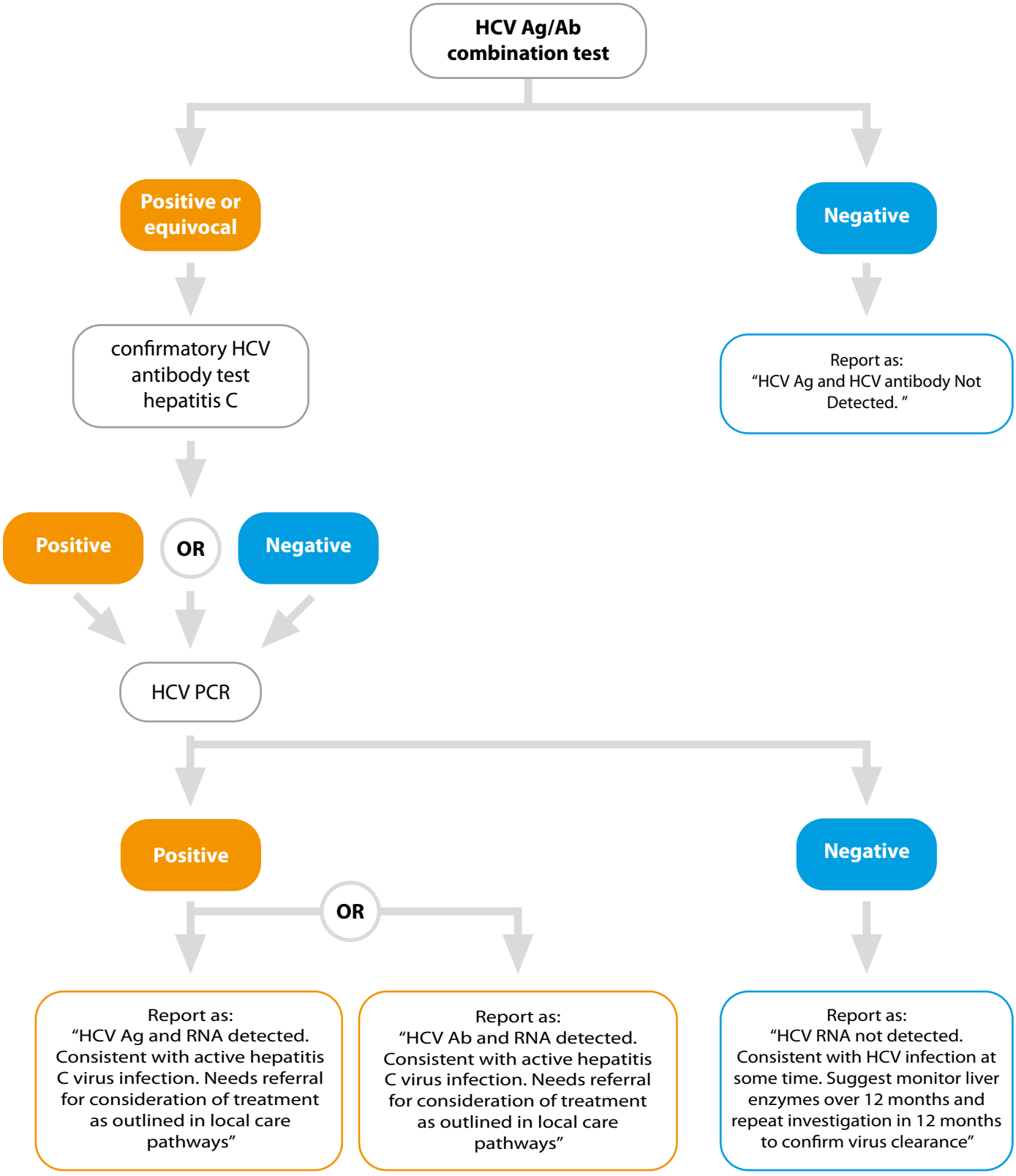
Screening of babies/children over 12 months born to HCV infected mothers



Child guidance based upon: Corristine et al., "Guidelines for the testing of looked after children who are at risk of a blood-borne infection. A joint Children's Services and Health Document. Greater Mancheter 2008.

Diagnosis of Hepatitis C

Screening for hepatitis C infection in renal dialysis patients



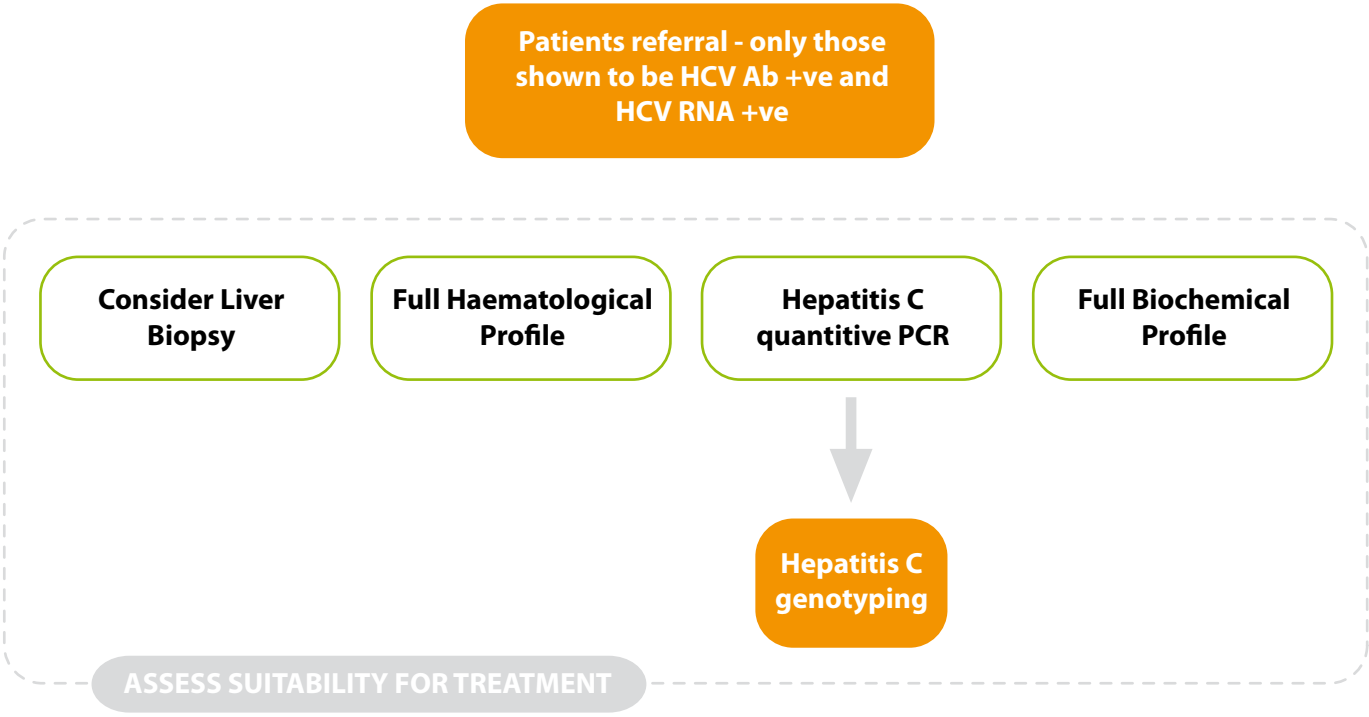
See also: *"Good practice guidelines for renal dialysis/transplantation units: prevention and control of blood-borne virus infection"* (Department of Health 2002) and the renal association guidelines: http://www.renal.org/pages/media/download_gallery/BBVinfectionFINAL14July09.pdf

Patients who are HCV infected may have fluctuating levels of HCV antibody there is evidence that those who are chronically infected are better monitored by application of HCV antigen or HCV combined antigen antibody tests.

Treatment of Hepatitis C

Referral to treatment

Initial assessment at treatment centre



Two forms of treatment are envisaged, treatment within the community for non-cirrhotic and non-co-infected individuals, and treatment of more complex cases within tertiary referral centres. In either case ONLY patients who are known to be hepatitis C RNA positive should be referred for treatment.

For treatment centre testing hepatitis C RNA should be quantified. HCV RNA is measured at intervals through the treatment pathway to allow treatment decisions and to monitor the outcome of treatment .

Quantitative PCR and HCV genotyping are repeated at the treatment centre to confirm the results of testing in the referring centre and to identify those who have spontaneously cleared HCV RNA between the time of diagnosis and their arrival at the treatment centre.

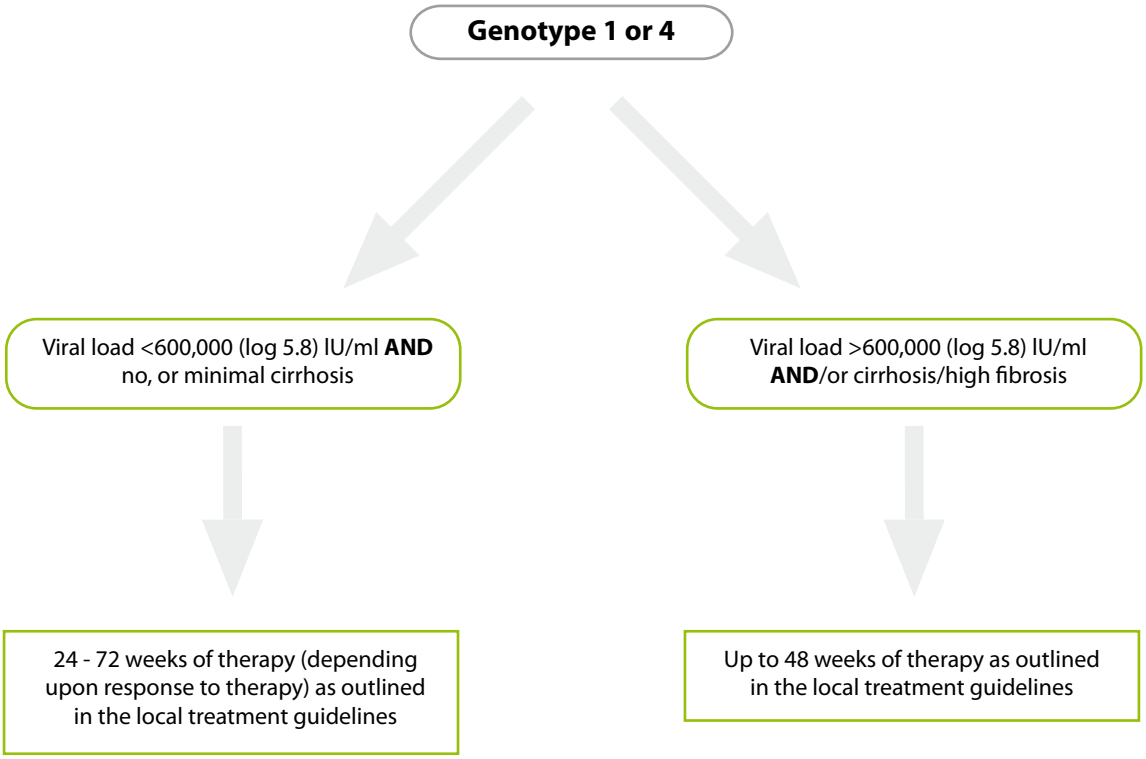
Quantitative PCR has a limit of detection of 30 IU/ml. Samples containing 30 IU/ml or more are reported as HCV RNA detected HCV RNA DETECTED (x iu/ml: log iu/ml = y) [where x and y are the actual values determined].
Samples containing no detectable HCV RNA are reported as: HCV RNA NOT detected (<30 iu/ml: log iu/ml = <1.48)

The HCV RNA test requires a minimum volume of 1.5ml serum or plasma. If this volume is not available to test a 1/10 dilution of the sample is made in HCV RNA negative plasma before the test is performed. This reduces the test sensitivity slightly. Positive samples will be reported after the quantity of HCV RNA has been corrected for the dilution factor negative samples will be reported as: HCV RNA NOT detected (<300 iu/ml: log iu/ml = <2.48)

Assessment for suitability for treatment may include initial referral for psychological assessment, help with drink addiction or substance misuse addiction.

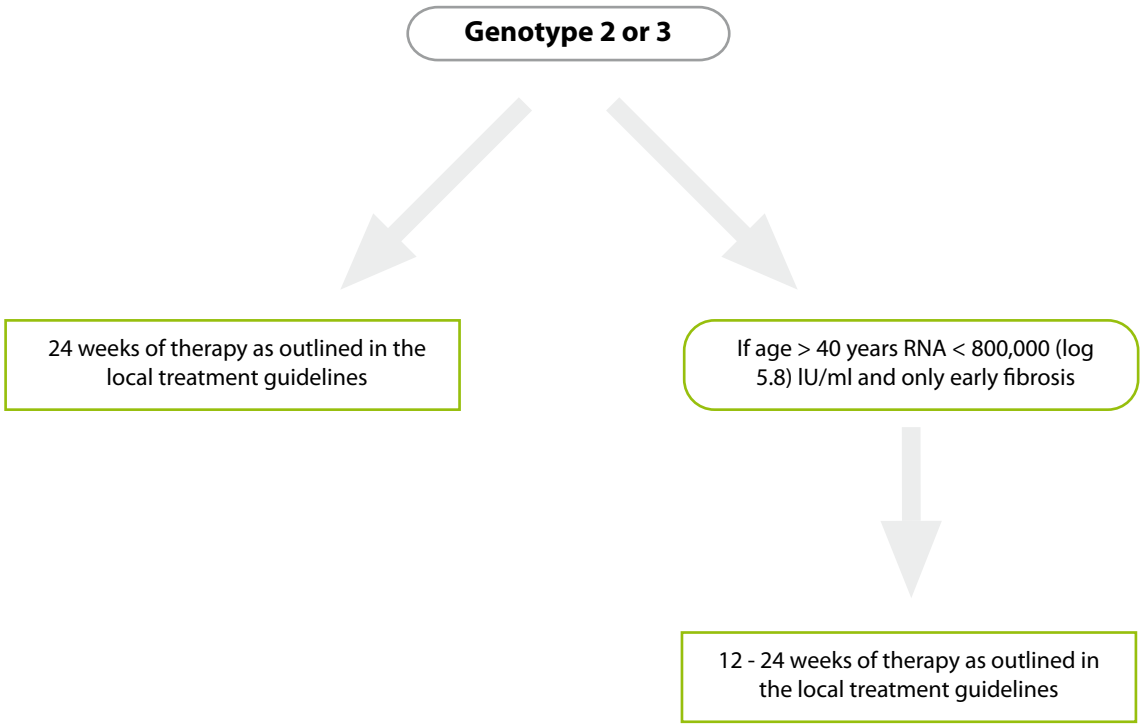
Treatment of Hepatitis C

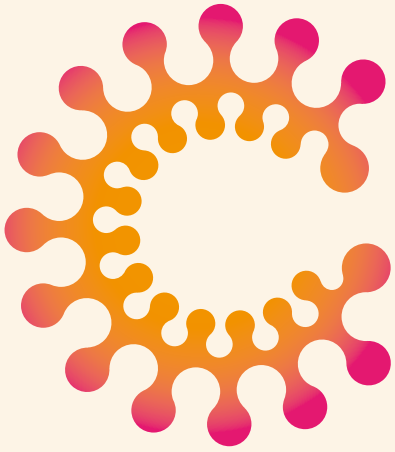
Genotype 1/4 hepatitis C without HIV co-infection



Treatment of Hepatitis C

Genotype 2/3 hepatitis C without HIV co-infection





Hepatitis C

Greater Manchester Hepatitis C Strategy

For further information please contact
Siobhan Fahey, Programme Manager,
The Greater Manchester Hepatitis C Strategy
siobhan.fahey@hmrpct.nhs.uk

Approved by Laboratory Consultative Group November 2009.
For Review November 2010.