Global Hepatitis Programme

Guideline development for Hepatitis C virus Screening, Care and Treatment in low- and middle- income countries

PICO QUESTIONS for the WHO Hepatitis C Treatment Guidelines Evidence Reviews

PICO 1: Testing

**PICO question 1:** Who should be tested for HCV?

**Population:** People with a history of behaviours or exposures that place them at increased risk of hepatitis C infection.

**Intervention:** Targeted HCV antibody testing. “Targeted” means testing of individuals based either on their being part of a defined risk group (e.g. injecting drug user, person with HIV) or through questions to elicit a history of HCV-risk behaviours (see CDC document [need to get reference]).

**Comparison:** Symptomatic HCV antibody testing. “Symptomatic” means antibody testing based on the presence of liver-related signs or symptoms.

**Outcomes:** Number of referrals to care/treatment for HCV, number of cases of HCV transmission, HCV disease progression (liver cirrhosis, HCC, DCC), SVR, quality of life, all-cause mortality

**Study type/limits:** Experimental or observational studies published between 1994 and the present.

PICO 2: Testing

**PICO question 2:** When should RNA testing be carried out?

**Population:** People who are HCV antibody positive

**Intervention:** HCV RNA testing at the time of receipt of a positive HCV antibody result

**Comparison:** HCV RNA test in the context of HCV care as part of assessment for HCV therapy

**Outcomes:** Number of cases of HCV transmission, number achieving sustained virological response to HCV treatment (SVR), number of cases of decompensated liver disease/hepatocellular carcinoma/liver-related deaths/all-cause mortality, quality of life

**Study type/limits:** Experimental or observational studies published between 1994 and the present.
PICO 3: Care PICO question 1: Should a behavioural intervention for alcohol reduction be carried out?

**Population:** Individuals with chronic HCV infection  
**Intervention:** Behavioural alcohol-reduction interventions  
**Comparison:** No behavioural alcohol-reduction intervention  
**Outcomes:** Reduction or cessation of alcohol intake, SVR, liver fibrosis, decompensated liver cirrhosis, hepatocellular carcinoma, quality of life, All-cause mortality – since LR mortality isn’t always accurately identified.  
**Study type/limits:** Experimental studies (human) published between 1994 and the present.

PICO 4: Care PICO question 2: How should staging be carried out?

**Population:** People living with chronic HCV infection being assessed for HCV therapy  
**Intervention:** Fibrosis stage determined by: liver biopsy, Fibroscan, FIB4, or Fibrotest.  
**Comparison:** Fibrosis stage determined by: APRI score.  
**Outcomes:**  
1. Sensitivity/Specificity to detect F0-1 vs. F2-3-4 and F0-1-2-3 vs. F4  
2. Cost/Cost-effectiveness  

**Study type/limits:** Diagnostic test accuracy studies published between 1994 and the present. The preferred comparisons would be studies that compared these tests head-to-head, but it is likely that there will be more articles comparing the different tests to histology.

PICO 5-7: Treatment PICO questions: 1. Is treatment better than no treatment? 2. Is pegylated interferon and ribavirin superior to standard interferon and ribavirin? 3. Are direct-acting antivirals efficacious?

**Population:** Adults and children with chronic HCV infection  
**Intervention 1:** any HCV anti-viral therapy  
**Comparison 1:** no HCV anti-viral therapy  
**Intervention 2:** pegylated interferon and ribavirin therapy  
**Comparison 2:** standard interferon and ribavirin therapy  
**Intervention 3:** direct-acting anti-viral therapy in addition to pegylated interferon and ribavirin therapy  
**Comparison 3:** pegylated interferon and ribavirin therapy only  
**Outcomes:** Rates of SVR, decompensated liver disease, hepatocellular carcinoma, all-cause mortality, and treatment-related adverse events leading to discontinuation of therapy. Quality of life, resource use\(^1\).  
**Study type/limits:** Systematic reviews and meta-analyses published from 1994 to the present.

\(^1\) will require economic modelling which will be conducted separately with another institution
**Method:** For this systematic review, results will be stratified by:

- Population: adults and children
- Genotype: types 1 and 4 separately and 2 and 3 combined
- Fibrosis stage: F0, F1, F2, F3, F4
- Active injecting drug user vs. non-active injecting drug user
- HIV-infected vs. not infected

**Outcomes:** Number achieving SVR; number of cases of decompensated liver disease/hepatocellular carcinoma; treatment-related serious adverse events; number of deaths, quality of life, transmission?, adherence?

**Study type/limits:** 1) Observational studies that compare outcomes in these groups within the same study. 2) In studies that did not include both population groups, do separate meta-analyses of treatment effectiveness in the different populations.