

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 use¹.

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.