



Complete Summary

GUIDELINE TITLE

Management of hepatitis C. A national clinical guideline.

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Management of hepatitis C. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2006 Dec. 49 p. (SIGN publication; no. 92). [208 references]

GUIDELINE STATUS

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [July 31, 2008, Erythropoiesis Stimulating Agents \(ESAs\)](#): Amgen and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated.
- [November 8, 2007 and January 3, 2008 Update, Erythropoiesis Stimulating Agents \(ESAs\)](#): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs) stating serious adverse events, such as tumor growth and shortened survival in patients with advanced cancer and chronic kidney failure.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Hepatitis C virus (HCV) infection

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pediatrics
Surgery

INTENDED USERS

Allied Health Personnel
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide evidence based recommendations covering all stages of the patient care pathway; screening, testing, diagnosis, referral, treatment, care and follow up of persons with, or exposed to, hepatitis C virus (HCV) infection

TARGET POPULATION

Infants, children and adults with, or exposed to, hepatitis C virus (HCV) infection

INTERVENTIONS AND PRACTICES CONSIDERED

1. Testing
 - Clinical and diagnostic testing for hepatitis C virus (HCV)
2. Prevention of secondary transmission
 - Sexual and household contact
 - Injecting drug use
 - Between healthcare workers and patients
3. Referral to specialist care
4. Children and hepatitis C
 - Obstetrical management of HCV infected pregnant women
 - Hepatitis C (HCV) testing in children and infants
 - Monitoring of children with HCV infection
 - Treatment of children with hepatitis C
 - Interferon (IFN) and ribavirin (for moderate/severe liver disease)
5. Acute hepatitis C treatment
 - Pegylated or unpegylated IFN
 - Timing and duration of treatment
6. Assessment of liver disease
 - Fibrosis markers
 - Liver biopsy
7. Estimation of disease progression
8. Lifestyle modifications
 - Smoking cessation
 - Reduction/cessation of alcohol intake
9. Treatment of chronic hepatitis C
 - Antiviral therapy
 - Pegylated IFN
 - Ribavirin
 - Patient Subgroups
 - Mild chronic hepatitis
 - Cirrhosis
 - Persistently normal ALT levels
 - Human immunodeficiency virus (HIV) co-infection
 - Hepatitis B co-infection
 - Patients in drug treatment programs
 - Relapsed patients
 - Monitoring patients who are not receiving treatment
10. Treatment of advanced infection
 - Antiviral therapy (IFN and ribavirin)
 - Liver transplantation
 - Screening for hepatocellular carcinoma
11. Nutrition and supportive care
 - Nutritional screening and assessment
 - Nutritional support
 - Exercise

MAJOR OUTCOMES CONSIDERED

- Rates of secondary transmission of hepatitis C virus (HCV)
- Number of patients being offered testing
- The proportion of people diagnosed with chronic HCV who enter specialist care
- Morbidity and mortality associated with HCV infection
- Incidence of cirrhosis and hepatocellular carcinoma in HCV infected patients
- The number of people with chronic HCV who receive antiviral therapy
- The proportion of people with chronic HCV who complete their course of antiviral therapy; for those who do not complete the course, the reasons for non-completion
- Response rates
- Relapse rates
- Adverse events associated with therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence base for this guideline was synthesized in accordance with Scottish Intercollegiate Guidelines Network (SIGN) methodology. A systematic literature review was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group. Literature searches were initially conducted in Medline, Embase, Cinahl and the Cochrane Library, using the year range 2000 to 2005. Key websites on the Internet were also used, such as the National Guidelines Clearinghouse. The literature search was updated with new material during the course of the guideline development process, and was supplemented by reference lists of relevant papers and group members' own files. The Medline version of the main strategies can be found on the SIGN website.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g. case reports, case series)

4: Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The result of this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

The assessment process inevitably involves a degree of subjective judgment. The extent to which a study meets a particular criterion (e.g., an acceptable level of loss to follow up) and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of SIGN Executive staff will arbitrate to reach an agreed quality assessment.

Evidence Tables

Evidence tables are compiled by SIGN executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the [SIGN Web site](#).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Synthesising the Evidence

Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This judgment is made on the basis of an (objective) assessment of the design and quality of each study and a (perhaps more subjective) judgment on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence-based, but which is relevant to the way in which health care is delivered in Scotland and is therefore implementable.

It is important to emphasise that the grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which that data was obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved.

Considered Judgment

It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, SIGN has introduced the concept of considered judgment.

Under the heading of considered judgment, guideline development groups summarise their view of the total body of evidence covered by each evidence table. This summary view is expected to cover the following aspects:

- Quantity, quality, and consistency of evidence
- Generalisability of study findings
- Directness of application to the target population for the guideline
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them)
- Implementability (i.e., how practical it would be for the NHS in Scotland to implement the recommendation)

Guideline development groups are provided with a pro forma in which to record the main points from their considered judgment. Once they have considered these issues, the group is asked to summarise their view of the evidence and assign a level of evidence to it, before going on to derive a graded recommendation.

Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 6 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the [SIGN Web site](#)).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

COST ANALYSIS

Clinical and Cost-Effective Testing for Hepatitis C Virus (HCV)

Controlled trials or cohort studies to gauge the cost effectiveness of offering an HCV test to different population groups have not been undertaken. Limited evidence from economic modeling work, indicates that offering an HCV test to former injecting drug users (IDU) in drug treatment and perhaps other settings would convey cost-effective clinical benefits. Former IDU are more likely to have a higher prevalence of HCV and comply with therapy than current IDU. Models of best practice for the identification and testing of former IDU have not been developed and evaluated. Expert opinion suggests that general practices, particularly those that serve areas with a high prevalence of drug use, may constitute environments where focused, well supported testing initiatives might be successful. Prisons may also offer similar opportunities. Targeted and generalised HCV awareness/testing campaigns have been conducted but no evaluations of their success in encouraging people (including former IDU) at high risk of HCV to engage with services have been reported.

In populations where the prevalence of HCV is low (e.g., genitourinary medicine clinic attendees), economic modelling indicates that universal testing does not convey cost-effective clinical benefit.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development. The national open meeting for this guideline was held on 3 November 2005 and was attended by 215 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

Peer Review

All SIGN guidelines are reviewed in draft form by independent expert referees, who are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. A number of general practitioners (GPs) and other primary care practitioners also provide comments on the guideline from the primary care perspective, concentrating particularly on the clarity of the recommendations and their assessment of the usefulness of the guideline as a working tool for the primary care team. The draft is also sent to a lay reviewer in order to obtain

comments from the patient's perspective. The comments received from peer reviewers and others are carefully tabulated and discussed with the chairman and with the guideline development group. Each point must be addressed and any changes to the guideline as a result noted or, if no change is made, the reasons for this recorded.

As a final quality control check prior to publication, the guideline and the summary of peer reviewers' comments are reviewed by the SIGN Editorial Group for that guideline to ensure that each point has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. Each member of the guideline development group is then asked formally to approve the final guideline for publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): *In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the full-text guideline document.*

The grades of recommendations (A–D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Testing

Clinical and Cost-Effective Testing for Hepatitis C Virus (HCV)

D - The following groups should be tested for HCV:

- Blood/tissue donors
- Patients on haemodialysis
- Healthcare workers who intend to pursue a specialty that requires them to perform exposure prone procedures

D - The following groups should be offered an HCV test:

- Patients with an otherwise unexplained persistently elevated alanine aminotransferase
- People with a history of injecting drug use
- People who are human immunodeficiency virus (HIV) positive
- Recipients of blood clotting factor concentrates prior to 1987
- Recipients of blood and blood components before September 1991 and organ/tissue transplants in the UK before 1992
- Children whose mother is known to be infected with HCV
- Healthcare workers following percutaneous or mucous membrane exposure to blood which is, or is suspected to be, infected with HCV
- People who have received medical or dental treatment in countries where HCV is common and infection control may be poor

- People who have had tattoos or body piercing in circumstances where infection control procedure is, or is suspected to be, suboptimal
- People who have had a sexual partner/household contact who is HCV infected.

HCV Diagnostic Testing

B - Diagnostic testing for HCV should be performed on serum or plasma where possible.

D - HCV genotyping should be undertaken if antiviral therapy is being considered.

D - Following an isolated acute percutaneous exposure to blood infected, or strongly suspected of being infected, with HCV, healthcare workers should be offered HCV RNA testing at six, 12 and 24 weeks and anti-HCV testing at 12 and 24 weeks.

Prevention of Secondary Transmission

Transmission Through Sexual and Household Contact

D - Individuals co-infected with HIV/HCV should be advised always to practise safe sex and use condoms.

D - Individuals infected with HCV should be advised to avoid activities which could result in percutaneous or mucous membrane exposure to their infected blood, such as the sharing of razors and toothbrushes.

Transmission Through Injecting Drug Use

D - Injecting drug users known to be infected with HCV should be given advice on how they can prevent transmission of infection to other injecting drug users.

Transmission Between Healthcare Workers and Patients

Risk of Healthcare Worker Infection

D - Healthcare workers who are aware they are HCV RNA positive should not undertake exposure prone procedures.

Referral

D - Individuals, including injecting drug users, diagnosed with chronic HCV should be offered integrated multidisciplinary care as it can maximise their uptake of, and retention in, services.

A - Patients with acute HCV infection should be referred to specialist care immediately.

Children and Hepatitis C

Mother to Child Transmission

B - In pregnant women knowledge of HCV RNA positive status should not influence obstetric management or standard advice regarding breast feeding.

HCV in Children and Infants

B - Infants born to women who are HCV antibody positive and HCV RNA negative do not need to be tested.

B - In children born to women infected with HCV, an HCV antibody test should be performed at 12 months of age or thereafter to identify the majority of children who are not infected.

B - In children whose mothers are co-infected with HIV, and in infants found to be HCV antibody positive after 12 months, an HCV RNA test should be performed, and if positive, confirmed on a second sample.

B - If information regarding the risk of HCV infection in an individual child is required before 12 months of age, an HCV RNA test and retest can be performed after two months of age. Further testing is still required to make a definitive diagnosis.

Natural History of HCV Infection in Children

D - Children infected with HCV should be monitored to identify the minority who are at risk of progressive fibrosis during childhood, and who may be candidates for treatment.

Treatment of Children with Hepatitis C

D - Children with evidence of moderate or severe liver disease should be considered for treatment with pegylated IFN and ribavirin.

D - In children who are asymptomatic with mild or no liver disease, benefits of treatment need to be weighed against the risk of side effects.

Acute Hepatitis C

Natural History

D - Patients with acute hepatitis C virus infection require clinical and laboratory monitoring (*looking for spontaneous viral clearance*) for the initial three months following diagnosis as they will often have a self limiting illness.

Treatment of Patients with Acute Hepatitis C

Timing of Treatment

D - Treatment should start between three and six months after diagnosis of acute hepatitis C, if the infection has not resolved spontaneously.

Choice and Duration of Treatment

A - Patients with acute HCV infection should be treated with interferon (IFN) therapy if the infection does not resolve spontaneously.

D - Patients can be treated with either pegylated IFN or non-pegylated IFN.

D - Patients with acute HCV infection should be treated with IFN therapy for 24 weeks irrespective of genotype.

Assessment of Liver Disease

Fibrosis Markers

B - Biochemical markers should not be used as an alternative to liver biopsy for staging of intermediate grades of fibrosis.

B - Biochemical tests may be used as an alternative to liver biopsy to diagnose cirrhosis or to direct screening for complications of fibrosis.

Liver Biopsy

When to Biopsy

D - Liver biopsy should be performed if there is concern about additional causes of liver disease.

D - Repeat liver biopsies should be considered in patients with mild disease who remain untreated, if progression of liver fibrosis would influence the decision to opt for antiviral therapy.

Biopsy and Genotype

D - Liver biopsy should not be considered an essential test prior to using antiviral therapy, especially in patients with genotype 2 and 3 disease.

Progression of Untreated Disease

Age, Gender and Ethnicity

D - When estimating the likely rate of progression of liver disease age at infection, gender and ethnicity should be considered.

Tobacco Smoking

D - Patients with chronic hepatitis C (CHC) should be advised that smoking tobacco can accelerate progression of liver disease.

Alcohol

B - Patients with CHC should be advised that drinking alcohol (*even in moderation*) can accelerate progression of liver disease.

Alanine Aminotransferase

D - When defining persistently normal serum alanine aminotransferase (PNALT) serum transaminases (ALT) measurement should be undertaken every two to three months to ensure that flares in ALT are not missed.

HIV Co-Infection

B - The increased rate of progression to decompensated liver disease in patients with HCV and HIV co-infection should prompt early consideration of antiviral therapy.

Co-Infection with Hepatitis A or B Viruses

D - Vaccination against hepatitis A and B should be considered for patients infected with hepatitis C.

D - When estimating the likely rate of progression of liver disease as a result of hepatitis C infection, active or previous hepatitis B virus (HBV) infection should be considered.

Iron Status

D - Modest iron loading does not justify specific intervention prior to antiviral therapy as it is unlikely to be of clinical importance.

D - Patients with significant iron retention require further investigation for additional conditions known to result in iron overload.

Treatment of Chronic Hepatitis C

Antiviral Therapy

A - A combination of pegylated IFN and ribavirin is the treatment of choice for patients with hepatitis C.

Sustained Viral Response

B - Sustained viral response should be used as a marker for viral clearance.

Genotype and Duration of Treatment

B - The duration of treatment with a combination of pegylated IFN with ribavirin, should be 12-24 weeks for patients with genotype 2 or 3 and 48 weeks for patients with genotype 1 or 4.

A - Patients with genotype 1 infection should be tested for an early viral response at 12 weeks.

A - Patients with genotype 1 infection who fail to achieve an early viral response (EVR) at 12 weeks should be considered for cessation of treatment.

A - Patients with genotype 1 infection with an EVR at 12 weeks should continue treatment for 48 weeks. Those who are still HCV RNA positive at 24 weeks should be considered for cessation of treatment.

B - Patients with genotype 2 or 3 infection should have an HCV RNA test performed four weeks after starting antiviral therapy, and if this is negative, may be considered for a reduced duration of therapy of 12 or 16 weeks.

Patient Subgroups

Patients With Mild Chronic Hepatitis

B - Patients with mild CHC should be considered for treatment with a combination of pegylated IFN with ribavirin.

Patients With Persistently Normal ALT Levels

A - Patients with chronic hepatitis C and normal ALT should be considered for treatment with pegylated IFN and ribavirin.

Patients With HIV Co-Infection

A - Patients with CHC and HIV should be considered for treatment with a combination of pegylated IFN and ribavirin for 48 weeks irrespective of genotype.

A - For patients with HCV genotype 1 infection and HIV, the lack of an early viral response at week 12 predicts those who are unlikely to obtain an sustained viral response (SVR), and treatment can be stopped.

Patients With Hepatitis B Co-Infection

C - Patients with chronic hepatitis B and C co-infection should be considered for combination treatment with pegylated IFN and ribavirin.

Patients in Drug Treatment Programmes

C - Patients with CHC who are on a drug treatment programme can be considered for treatment with a combination of pegylated IFN and ribavirin.

Factors Influencing Effectiveness

Age, Gender and Ethnicity

A - Patients should be advised that older age at the time of treatment leads to a lower sustained viral response.

B - Patients should be advised about the likelihood of sustained viral response according to their ethnic origin.

Contraindications

Patients with Renal Failure

D - Patients with CHC and renal failure may be treated with IFN monotherapy, with careful monitoring required.

Patients with Mental Health Problems

B - Patients with stable mental health problems should not be excluded from treatment for CHC.

B - Patients with mental health problems should have their psychiatric symptoms monitored prior to and throughout IFN treatment.

Management of Adverse Effects

Flu-Like Symptoms

D - Patients experiencing flu-like side effects from pegylated IFN and ribavirin can be advised to use paracetamol within manufacturers' guidelines.

D - Patients should be advised to maintain an adequate fluid intake throughout treatment with pegylated IFN and ribavirin.

D - Patients should be advised to coordinate their injections of pegylated IFN and ribavirin with periods of reduced activity, such as weekends and holidays.

Anaemia and Neutropenia

B - Erythropoietin should be considered in CHC patients receiving pegylated IFN and ribavirin therapy who develop anaemia, to prevent curtailment or dose reduction of ribavirin.

D - Granulocyte-colony stimulating factor (G-CSF) should be considered on a case-by-case basis for patients who develop significant neutropenia while receiving treatment with pegylated IFN and ribavirin for CHC infection, to prevent curtailment or dose reduction of pegylated IFN.

Depression

B - All patients receiving pegylated IFN and ribavirin should be monitored for signs of depression before, during and immediately post-treatment.

B - Patients treated with pegylated IFN and ribavirin who experience depression should be considered for treatment with antidepressants and for referral to a specialist, if necessary.

Skin Reactions

D - All patients on pegylated IFN and ribavirin should be advised to ensure appropriate skin hygiene and hydration.

D - Patients should be advised to avoid overexposure to sun.

D - Patients should be advised to rotate injection sites.

D - The use of emollients and topical corticosteroids can be considered for non-specific rashes.

Thyroid Dysfunction

D - Thyroid function should be monitored at baseline before IFN therapy, at week 12 of treatment and at any time where there is a suspicion of thyroid dysfunction.

Dyspnoea

D - Patients treated with pegylated IFN or ribavirin who report dyspnoea that is not related to anaemia should be urgently assessed medically for cardiopulmonary problems.

Retinopathy

D - Patients with CHC and hypertension or diabetes should have an ophthalmic examination prior to commencing treatment, paying particular attention to cotton wool spots and retinal haemorrhage.

D - Any patient reporting visual disturbance during treatment should be examined further by an ophthalmologist.

D - IFN should be discontinued in any patient with visual disturbance until it has resolved or an ophthalmologist has confirmed there is no retinal injury.

Alopecia

D - Patients should be advised that treatment related hair loss is reversible on cessation of treatment.

Relapse or Failed Treatment

IFN and Ribavirin

D - Patients with CHC who have had unsuccessful treatment with non-pegylated IFN and ribavirin should be considered for pegylated IFN and ribavirin retreatment.

Other Therapies

C - The following therapies are not recommended for the treatment of patients infected with CHC, whether they are being treated for the first time, previously relapsed, or have never responded to treatment:

- Amantadine in addition to pegylated IFN alone or in combination with ribavirin
- Ribavirin monotherapy
- Interleukin 12

Treatment of Advanced Infection

Antiviral Therapy

Patients with Cirrhosis

A - Patients with compensated cirrhosis should be considered for therapy with pegylated IFN and ribavirin, unless contraindicated.

A - Patients with compensated HCV cirrhosis may benefit from IFN treatment to reduce the risk of development of HCC. The duration of therapy required to achieve this is not clear.

Patients Referred for Liver Transplant

D - Patients in whom transplant is planned should not receive antiviral therapy in the pretransplant or peri-transplant stages, except as part of clinical trials.

D - Patients should be considered for antiviral therapy post liver transplant to achieve HCV clearance in cases of recurrence of HCV related liver disease.

Liver Transplantation

C - Patients with hepatitis C virus and concurrent operable hepatocellular carcinoma should be offered liver transplantation.

C - Patients with HCV associated chronic liver failure should be offered liver transplantation.

Screening for Hepatocellular Carcinoma

A - The measurement of alpha fetoprotein should not be used in isolation for screening or surveillance of the development of HCC in patients with hepatitis C.

D - Surveillance using ultrasound should take place at six monthly intervals.

C - Surveillance should be confined to patients with cirrhosis.

Nutrition, Supportive Care and Complementary Therapies

Nutritional Interventions

Dietary Interventions

D - Nutritional care for people infected with hepatitis C should involve promotion of optimal nutrition and prevention or treatment of malnutrition or deficiencies of specific nutrients.

D - Patients should have a nutritional screen and if needed a nutritional assessment and appropriate advice by a dietitian.

D - Patients with advanced liver disease should be given nutritional support to minimize malnutrition.

Overweight

C - Patients who are overweight should be advised to lose weight, within a realistic weight loss target, as this may have a beneficial effect on the degree of liver damage associated with hepatitis C infection.

Exercise

D - Patients with hepatitis C should be encouraged to take mild to moderate exercise. Those on antiviral therapy should be advised that they may find their capacity for exercise reduced.

Definitions:

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g. case reports, case series)

4: Expert opinion

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for "Initial laboratory diagnosis of hepatitis C infection (except infants)"

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of patients with or exposed to hepatitis C virus (HCV)

POTENTIAL HARMS

Adverse effects of interferon and ribavirin therapy include:

- Flu-like symptoms
- Anaemia and neutropenia
- Depression
- Skin reactions
- Thyroid dysfunction
- Weight loss
- Dyspnoea
- Retinopathy
- Alopecia
- Other side effects (insomnia, poor concentration, oral disease, nausea, fatigue and post-treatment withdrawal symptoms)

CONTRAINDICATIONS

CONTRAINDICATIONS

Pegylated interferon and ribavirin must not be prescribed to women who are pregnant.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is, however, advised that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.
- The remit encompasses prevention of secondary transmission of the virus but specifically excludes primary prevention of hepatitis C virus (HCV) infection.

Primary prevention of hepatitis C infection is an important public health concern but is a difficult topic for an evidence based guideline to cover. The principles and evidence for the prevention of all blood borne viruses are generic and reviewing all of this evidence would have been beyond the capacity of any guideline development group, whilst reviewing the HCV evidence alone would have produced a distorted view.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Board and is an essential part of clinical governance. It is acknowledged that every Board cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

Key points for audit are identified in the original guideline document.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Management of hepatitis C. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2006 Dec. 49 p. (SIGN publication; no. 92). [208 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Dec

GUIDELINE DEVELOPER(S)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

Scottish Executive Health Department

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Guideline Development Group: Dr John Dillon (Chair) Consultant Hepatologist, Ninewells Hospital, Dundee; Dr Philip Newsome (Secretary) Specialist Registrar in Hepatology, Royal Infirmary of Edinburgh; Professor Jeremy Bagg Professor of Clinical Microbiology, Glasgow University Dental School; Dr Peter Bramley Consultant Gastroenterologist, Stirling Royal Infirmary; Dr Sandy Elder Consultant Occupational Health Physician, SALUS, Coatbridge; Dr Andrew Fraser Consultant Gastroenterologist, Aberdeen Royal Infirmary; Mr Jeff Frew Patient Representative, Edinburgh; Professor David Goldberg Consultant Epidemiologist, Scottish Centre for Infection and Environmental Health, Glasgow; Ms Ysobel Gourlay Senior Pharmacist, Gartnavel General Hospital, Glasgow; Dr Rosie Hague Consultant in Paediatric Infectious Diseases and Immunology, Royal Hospital for Sick Children, Glasgow; Dr Janina Harvey Consultant in Genitourinary Medicine, Falkirk and District Royal Infirmary; Dr Mary Hepburn Honorary Consultant Obstetrician and Gynaecologist, Princess Royal Maternity Hospital, Glasgow; Dr Nick Kennedy Consultant in Infectious Diseases, Monklands Hospital, Airdrie; Dr Clifford Leen Consultant in Infectious Diseases, Western General Hospital, Edinburgh; Mr Krishnakumar Madhavan Transplant Surgeon, Royal Infirmary of Edinburgh; Ms May McCreaddie Research Associate, Department of Nursing Studies, University of Edinburgh; Dr Elizabeth McCrudden Senior Lecturer and Honorary Consultant in Virology, Institute of Virology, Glasgow; Ms Margot Miller Clinical Nurse Practitioner (Gastrointestinal/Liver), Royal Infirmary of Edinburgh; Dr Peter Mills Consultant Gastroenterologist, Gartnavel General Hospital, Glasgow; Mrs Margaret Neilson Clinical Nurse Specialist (Liver Disease), Glasgow Royal

Infirmary; Dr J J Kennedy Roberts General Practitioner and Lead Specialist Senior Medical Officer, Glasgow Addiction Service; Mrs Kay Roberts Pharmacy Consultant, Glasgow; Mr Ian Robertson Social Worker, Fife Positive Support, Rosyth; Dr Nicola Rowan Director of Blood Borne Viruses, UK Hepatitis C Resource Centre, Glasgow; Ms Ailsa Stein Information Officer/Programme Manager, SIGN; Dr Lorna Thompson Programme Manager, SIGN; Dr Henry Watson Consultant Haematologist, Aberdeen Royal Infirmary; Ms Tracy Wilson Senior Dietitian, Western General Hospital, Edinburgh; Dr Steven Yule Consultant Radiologist, Aberdeen Royal Infirmary

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Declarations of interests were made by all members of the guideline development group. Further details are available from the Scottish Intercollegiate Guidelines Network (SIGN) Executive.

GUIDELINE STATUS

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Quick reference guide: Management of hepatitis C. Scottish Intercollegiate Guidelines Network, 2006. 2 p. Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).
- SIGN 50: A guideline developer's handbook. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network. (SIGN publication; no. 50). Available from the [SIGN Web site](#).
- Appraising the quality of clinical guidelines. The SIGN guide to the AGREE (Appraisal of Guidelines Research & Evaluation) guideline appraisal instrument. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2001. Available from the [SIGN Web site](#).

PATIENT RESOURCES

The following is available:

- Information about hepatitis C for patients and carers. Scottish Intercollegiate Guidelines Network, 2006. 3 p.

Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on March 7, 2007. This summary was updated by ECRI Institute on July 9, 2007, following the FDA advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on March 21, 2008 following the FDA advisory on Erythropoiesis Stimulating Agents. This summary was updated by ECRI Institute on August 15, 2008 following the U.S. Food and Drug Administration advisory on Erythropoiesis Stimulating Agents (ESAs).

COPYRIGHT STATEMENT

Scottish Intercollegiate Guidelines Network (SIGN) guidelines are subject to copyright; however, SIGN encourages the downloading and use of its guidelines for the purposes of implementation, education, and audit.

Users wishing to use, reproduce, or republish SIGN material for commercial purposes must seek prior approval for reproduction in any medium. To do this, please contact sara.twaddle@nhs.net.

Additional copyright information is available on the [SIGN Web site](#).

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC

Inclusion Criteria which may be found at
<http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 10/6/2008

