E’ indicato lo screening per l’infezione da virus dell’epatite C?

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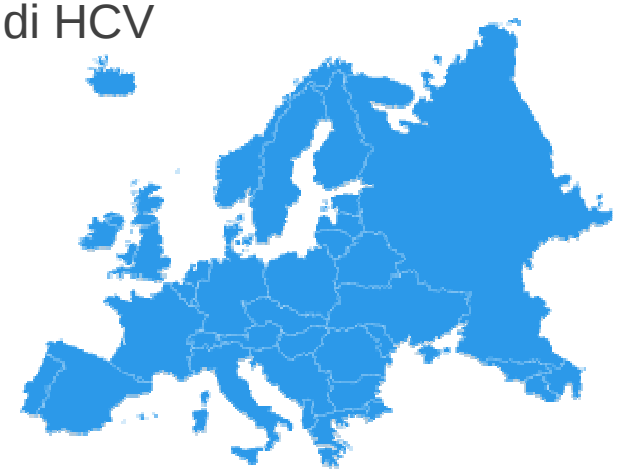
Infezione da HCV: cosa sappiamo

- 120-170 milioni malati di HCV

- 4milioni malati di HCV



- 4 milioni malati di HCV

61.142.000

- 1 milione malati di HCV

primato in Europa

- Alta percentuale di casi clinicamente manifesti
- 15-45% svilupperà cirrosi/HCC

Infezione da HCV: cosa sappiamo

- Storia clinica

LATE DIAGNOSIS

Studio osservazionale di 6000 paziente , il 17%ha una diagnosi tardiva di cirrosi e/o cirrosi scompensata

Moorman AC, 2015 May;61(5):1479-84

Infezione da HCV: cosa vorremmo sapere..?

- Casi clinicamente non manifesti
- Soggetti potenzialmente contagiosi

USA: 45-80% ignora di essere affetto da HCV

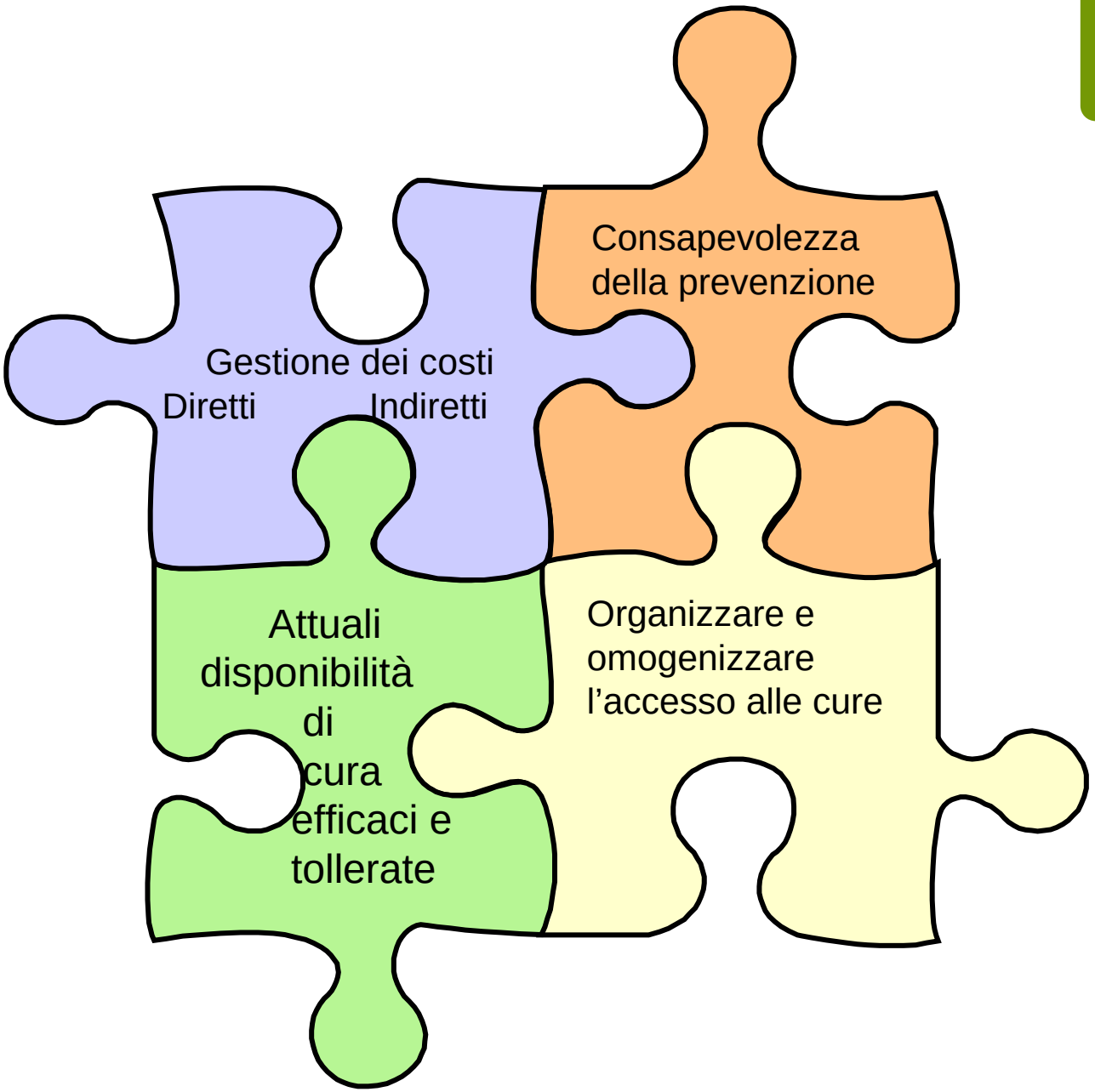
Il sommerso è l'ostacolo alla cura e al controllo dell'HCV

Ward JD, 2013; 17:1-11

Infezione da HCV: Perché tanto attuale..?

- Impatto sociale dell'infezione
- Impatto psicologico sulla vita di relazione del paziente
- Peso economico della malattia
    - costi diretti: trattamento della malattia
    - costi indiretti: ridotta produttività, morte prematura

Infezione da HCV: Perché tanto attuale..?



Infezione da HCV: Prevenzione

SCREENING

- Rappresenta il passo fondamentale nel raggiungimento degli obiettivi di prevenzione e cura per fini di sanità pubblica.
- Garantisce la rilevazione dei soggetti infetti e il trattamento precoce.
- Strategie di screening sono raccomandate da diverse organizzazioni per la salute pubblica in tutto il mondo.

Infezione da HCV: Prevenzione

SCREENING

La 63° Assemblea Mondiale della sanità approva il WHA63.18 per perseguire l'impegno di un approccio integrato di controllo e prevenzione della malattia

AASLD e IDSA iniziano a collaborare per produrre linee guida sulla gestione e il trattamento di soggetti HCV http://www.hcvguidelines.org

In Italia il Ministero della Salute si attiva con un gruppo di esperti nel settore per implementare programmi di prevenzione

2010 **2011** **2013** **2014** **2015**

Negli USA il dipartimento della salute servizi umani (HHS) convoca un Interagency Working Group per sviluppare un piano d'azione e raggiungere obiettivi di prevenzione

La 67° Assemblea Mondiale della sanità rinnova l'invito a sviluppare piani concreti per ridurre l'impatto dell'HCV nel mondo

Infezione da HCV: a chi è rivolto lo screening

Soggetti a rischio asintomatici

- ***Esposti ad almeno un fattore di rischio individuale:***
  - Adulti nati tra il 1945 e il 1965 (Baby Boomers)

Prevalenza 4.3%
6 volte> che in altre coorti di nascita

Mote VA, screening for hepatitis C virus infection in adults: U.S. preventive services task force recommendation statement, Ann Int Med 20013, sept. 159(5):349-357

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES
AASLD

IDSA
Infectious Diseases Society of America

EASL
European Association for the Study of the Liver

U.S. Preventive Services TASK FORCE

NIH National Institutes of Health
Turning Discovery Into Health

Infezione da HCV: a chi è rivolto lo screening

Soggetti a rischio asintomatici

- ***Esposti ad almeno un fattore di rischio individuale:***
  - Adulti nati tra il 1945 e il 1965 (Baby Boomers)
  - Politrasfusi prima della diffusione dei test sierologici
  - Dializzati

Prevalenza 10-30%

Mote VA, screening for hepatitis C virus infection in adults: U.S. preventive services task force recommendation statement, Ann Int Med 20013, sept. 159(5):349-357

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Infezione da HCV: a chi è rivolto lo screening

Soggetti a rischio asintomatici

- ***Esposti ad almeno un fattore di rischio individuale:***
  - Adulti nati tra il 1945 e il 1965 (Baby Boomers)
  - Politrasfusi prima della diffusione dei test sierologici
  - Dializzati
  - Soggetti esposti a cure mediche/odontoiatriche (<6%)
- ***Appartenenti a gruppi demografici ad elevata prevalenza di infezione:***
  - HIV
  - Tossico dipendenti (60%)
  - Carcerati (16-35 % HCV+)
  - Operatori sanitari (1-2%)
  - Partner monogami (rischio1%)
- ***Soggetti con evidenza di malattia epatica:***
  - Alto livello sierico di ALT (8.2% HCV+)

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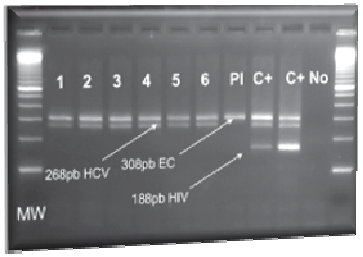
Infezione da HCV: TEST di screening

Ricerca sierologica di Ab anti HCV con tecnica ELISA di 3^ generazione



Il NAT test acido nucleico HCV-RNA conferma l'infezione cronica (il test deve essere sensibile nel rilevare <25 UI/ml di RNA)

Prima scelta nei soggetti immunodepressi o con contatto recente

U.S Food and Drug Administration

La FDA Americana ha approvato un kit di autosomministrazione domestica per la ricerca di Ab nel sangue. E' ancora in fase di valutazione il kit per la ricerca di Ab nella saliva.

Infezione da HCV: TEST di screening

- In soggetti <u>senza fattori rischio in corso</u> è sufficiente eseguire il test una sola volta.
- In soggetti <u>con fattori rischio in corso</u> (t.d. attivi, HIV siero positivi con attività sessuale promiscua) è appropriato ripetere il test almeno una volta all'anno (raccomandazione IIa-C).

Practice Guidance, 2015 Sept;62(3): 932-49

Piano Nazionale per la prevenzione delle Epatiti Virali

1. Epidemiologia
2. Prevenzione
3. Sensibilizzazione, informazione e formazione
4. Cura, trattamento e accesso
5. Impatto sociale

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5. Impatto sociale

- Conoscere la prevalenza delle infezioni croniche (studi epidemiologici obsoleti e disomogenei che non possono fornire la prevalenza reale) ➔ 18 mesi
- Realizzare progetti pilota regionali di screening su HCV su soggetti a rischio di infezione ➔ 24 mesi + 3 analisi dati
  - Costo/efficacia della diagnosi precoce
  - La malattia epatica avanzata ha costi più elevati rispetto a una infezione guarita (studio COME)
- Implementare la qualità dei dati (notifica e sorveglianza) interfacciare i database (nazionali e regionali) per delineare la prevalenza

Piano Nazionale per la prevenzione delle Epatiti Virali

1. Epidemiologia
2. Prevenzione ➔ 12 mesi
3. Sensibilizzazione, informazione e formazione
4. Cura, trattamento e accesso
5. Impatto sociale

- Ridurre la trasmissione su tutto il territorio
    - Intervenendo su popolazioni a rischio (es: TD)
    - Prevenendo le esposizioni nosocomiali e trattamenti estetici (anche tramite interventi normativi)
    - Disegnare modelli di comunicazione e counseling di soggetti target
    - Elaborare materiale per la formazione di personale sanitario che avrà contatti con popolazioni a rischio

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1. Epidemiologia
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5. Impatto sociale

- Aumentare il grado di consapevolezza sul problema:
    - Valutare il grado di conoscenza e consapevolezza (rischio percepito) sulle epatiti virali ➔ 12 mesi
    - Effettuare campagne informative, educative e di prevenzione nella popolazione ➔ 24 mesi
    - Realizzare attività di formazione per il personale sanitario ➔ 12 mesi

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5. Impatto sociale

- Uniformare sul territorio Italiano i sistemi di accesso alle cure:
    - Rete Nazionale di centri specializzati per garantire percorsi standard (equità di accesso qualificato alle cure) ➔ 18 mesi
        - Definizione dei requisiti minimi dei centri specializzati (aggiornamento periodico)

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    - Rete Nazionale di centri specializzati per garantire percorsi standard (equità di accesso qualificato alle cure)
    - Aggiornare e armonizzare le linee guida nazionali e creare un unico PDTA nazionale

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    - Aggiornare e armonizzare le linee guida nazionali e creare un unico PDTA nazionale
    - Realizzare un registro nazionale cure ed esiti dei trattamenti ➔ 18 mesi
        - Promuovere studio di costo efficacia dei diversi trattamenti e l'impatto complessivo sulla spesa sanitaria a breve e lungo termine

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    - Rete Nazionale di centri specializzati per garantire percorsi standard (equità di accesso qualificato alle cure)
    - Aggiornare e armonizzare le linee guida nazionali e creare un unico PDTA nazionale
    - Realizzare un registro nazionale cure ed esiti dei trattamenti
    - Promuovere studi dei meccanismi di trasmissione verticale per ridurre l'infezione del feto (0-36%) ➔ 36 mesi
        - Sconosciuto il meccanismo biologico alla base
        - Cellule trofoblastiche non infettate dal virus
        - HCV RNA mai identificato nel liquido amniotico
        - Contagio parto?
        - No ruolo protettivo cesareo

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    - Aggiornare e armonizzare le linee guida nazionali e creare un unico PDTA nazionale
    - Realizzare un registro nazionale cure ed esiti dei trattamenti
    - Promuovere studi dei meccanismi di trasmissione verticale per ridurre l'infezione del feto (0-36%).
    - Stabilire il follow-up dei pazienti guariti ➔ 12 mesi

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3. Sensibilizzazione, informazione e formazione
4. Cura, trattamento e accesso
5. Impatto sociale

- Migliorare la qualità della vita dei pazienti e delle loro famiglie attraverso counselling
- Migliorare l'aderenza terapeutica ➔ 24 mesi
- Sperimentare modelli di assistenza domiciliare epatologica in cazienti con cirrosi avanzata ➔ 18 mesi

The Hepatitis C Trust Testing Van

Ente no profit che si impegna con i suoi volontari a distribuire informazioni affidabili e basati sull'evidenza rivolgendosi alle popolazioni più esposte al rischio soprattutto in zone in cui i test diagnostici sono meno accessibili

Da novembre 2011 al novembre 2014 hanno promosso eventi, coinvolgendo oltre 4.000 persone di cui 2.000 sono stati testati per HCV sul loro “VAN”. Coerentemente con quanto atteso per le popolazioni a rischio il 10% dei test fino ad oggi eseguiti hanno individuato anticorpi dell'epatite C

E’ indicato lo screening per l’infezione da virus dell’epatite C?

Vantaggi dello screening

Van der MeerAJ, Veldt Bj, et al. “Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis”. JAMA. 2012 Dec 26;308(24):2584-93. doi: 10.1001/jama.2012.144878.

La SVR è associata a un miglioramento della sopravvivenza in pazienti con infezione cronica da HCV e cirrosi

Morgan RL, Baack B, et al “Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies”. Ann Intern Med. 2013 Mar 5;158(5 Pt 1):329-37. doi: 10.7326/0003-4819-158-5-201303050-00005.

La SVR in pazienti con qualunque stato di fibrosi è associata a una riduzione dell’incidenza di HCC

Vantaggi dello screening

RESEARCH ARTICLE Open Access

Achieving sustained virologic response in hepatitis C: a systematic review of the clinical, economic and quality of life benefits

Jayne Smith-Palmer[1*], Karin Cerri[2] and William Valentine[1]

DOI 10.1186/s12879-015-0748-8

Table 2 Summary of clinical studies reporting the impact of SVR on HCC

Study	Setting	Sample size	Mean follow up	Study details	Key findings
Coverdale *et al.* 2004 [47]	Australia	455	9 years[a]	Retrospective cohort study including 384 treated with IFN alone, (n = 71 untreated) including patients with cirrhosis	Overall 9-year incidence of HCC was 10% for untreated, 11% for non-response and 2% for SVR
Van der Meer *et al.* 2013 [20]	Europe and Canada	248	8.3 years[a]	Cohort of consecutive genotype 1 patients with advanced fibrosis, 24% with SVR	HR (95% CI) for HCC for SVR versus non-SVR was 0.20 (0.06–0.69) (p = 0.011)
Van der Meer *et al.* 2012 [38]	Europe and Canada	530	8.4 years[a]	Retrospective cohort study in patients with advanced fibrosis/cirrhosis treated with IFN, IFN plus ribavirin or pegIFN plus ribavirin, median follow up 8.4 years, 68% genotype 1	Rate (per 100 patient years) for HCC were 0.55 (0.14–0.96) for SVR vs. 2.63 (1.83–3.82) without SVR (p < 0.001)
Braks *et al.* 2007 [43]	France	113	8.2 (3.1) years	Retrospective cohort study in patients with compensated cirrhosis treated with IFN or pegIFN-based treatment	Proportion of patients with HCC was 2.7% for SVR versus 31.6% for non-SVR
Cardoso *et al.* 2010 [42]	France	307	3.5 years[a]	Retrospective analysis in patients with bridging fibrosis or cirrhosis treated with IFN, pegIFN or pegIFN plus ribavirin	Adjusted HR (95% CI) for non-SVR versus SVR was 3.06 (1.12–8.39) (p = 0.029) for HCC
Bruno *et al.* 2007 [44]	Italy	883	96.1 months	Retrospective database analysis in patients treated with IFN monotherapy with no cirrhosis or decompensation, 73.5% genotype 1	Adjusted HR (95% CI) for non-SVR versus SVR was 2.59 (1.13–5.97) (p = 0.025) for HCC
Calvaruso *et al.* 2013 [23]	Italy	444	69 months[a] (range 24–130 months)	Prospective cohort study in PR-treated patients with compensated cirrhosis, 83% genotype 1, 24% with SVR	HR (95% CI) for HCC for non SVR versus SVR = 4.44 (1.30–15.11) (p = 0.017)
Pellicelli *et al.* 2013 [27]	Italy	172	5 years[a]	Retrospective-prospective study in patients with HCV genotype 1 treated with pegIFN plus ribavirin, 34% with cirrhosis	Multivariate OR (95% CI) for development of HCC for no SVR versus SVR = 3.58 (0.9–14.3) (p = 0.06)
Hara *et al.* 2014 [24]	Japan	1,125	Not stated	Retrospective cohort study in PR-treated (SVR and non SVR) and untreated patients	HR (95% CI) for HCC for SVR versus non-SVR and untreated = 0.12 (0.03–0.48) (p = 0.003)
Ikeda *et al.* 2006 [35]	Japan	2,166	15 years	Retrospective cohort study in patients with HCV patients (n = 512 untreated, n = 1,654 treated with IFN-based therapy)	Crude rate of HCC at 15 years was 13.9% for all treated patients, 23.9% for untreated and 7.5% for SVR
Imai *et al.* 2010 [28]	Japan	568	11 years	Retrospective cohort study in consecutive HCV patients treated with IFN monotherapy	HR (95% CI) for HCC for SVR versus non-treated patients was 0.20 (0.08–0.50) (p < 0.001) for patients <60 years and 0.23 (0.08–0.64) (p = 0.005) for patients >60 years
Imazeki *et al.* 2005 [46]	Japan	459	8.9 (3.2) years	Retrospective cohort study in patients, inc patients with cirrhosis, treated with IFN alone (n = 355) or untreated (n = 104), n = 116 patients achieved SVR	In the total population, annual incidence of HCC was 0.5% for SVR versus 2.6% for non-responders; corresponding figures for patients with cirrhosis were 9% and 34%, respectively
Kobayashi *et al.* 2007 [29]	Japan	1,124	66 months[a] (range 12–197 months)	Retrospective cohort study in HCV patients treated with IFN or IFN plus ribavirin (373 with SVR, 751 without SVR)	HCC developed in 3.5% SVR patients versus 8.1% non-SVR patients. SVR HCC patients had a significantly more advanced stage of fibrosis (p < 0.001)
Maruoka *et al.* 2012 [40]	Japan	721	9.9 (5.3) years	Retrospective cohort study in patients treated with monotherapy (n = 577, of which n = 221 (38.3%) achieved SVR and n = 144 untreated patients	Annual rate of HCC development was 2.71% for untreated patients, 2.31% for non-SVR and 0.24% for SVR (p < 0.0001)
Moriyama *et al.* 2005 [31]	Japan	269	>6 years	Retrospective study in patients with cirrhosis treated with IFN-based treatment	Mean annual incidence of HCC was 0.78% for SVR versus 0.17% for non-responders with ALT <80 IU and 4.68% for ALT >80 IU
Ogawa *et al.* 2013 [25]	Japan	1,013	3.6 years[a]	Prospective multicenter study in patients treated with pegIFN plus ribavirin, 70.1% had HCV genotype 1 and 14.8% had cirrhosis at baseline	HR (95% CI) for HCC relative to SVR = 1.50 (0.65–3.44) (p = 0.34) for relapse and breakthrough and 3.72 (1.69–8.18) (p = 0.001) for non-response
Ogawa *et al.* 2012 [37]	Japan	1,015	3.8 years (2–6 years)	Prospective multicenter study in patients treated with pegIFN plus ribavirin (n = 712 genotype 1, n = 303 genotype 2)	6-year cumulative incidence of HCC was 3.4% for SVR versus 21.2% for non-response group (p < 0.0001) and 6.4% for transient response (ns)
Sasaki *et al.* 2014 [22]	Japan	916	Not stated	Retrospective study of IFN-treated patients	Incidence of HCC was 3.6% in patients who achieved SVR vs. 21.2% in non-SVR patients
Sasaki *et al.* 2011 [34]	Japan	236	50 months[a]	N = 236 patients with IFN-based treatment, median follow up 50 months	No significant difference in incidence of HCC for SVR versus non-SVR
Watanabe *et al.* 2011 [32]	Japan	1,865	4.25 years[a]	Retrospective cohort study in patients treated with pegIFN plus ribavirin, n = 999 (54%) with SVR	5 year cumulative incidence of HCC was 1.1% in patients with SVR and 7.1% in non-SVR patients (p < 0.001)
Yoshida *et al.* 2004 [36]	Japan	2,787	>6.5 years[a]	Retrospective database analysis in HCV patients (n = 395 untreated, n = 836 SVR, and n = 1,556 non-SVR)	HR (95% CI) for HCC for non-SVR versus no treatment was 0.835 (0.625–1.125) (p = ns). Annual incidence of HCC in SVR was 0.05–0.40% for F0–F1 and 0.15–3.20% for F4. For non-SVR annual incidence was 0.05–1.03% for F0–F1 and 0.29–12.5% for F4 (depending on age and gender)
Velosa *et al.* 2011 [39]	Portugal	130	6.4 (4.0) years	Retrospective cohort study in patients with cirrhosis treated with IFN, IFN plus ribavirin or pegIFN plus ribavirin	HR (95% CI) for HCC for SVR versus non-SVR was 0.09 (0.01–0.77) (p = 0.024)
Aleman *et al.* 2013 [26]	Sweden	351	5.3 years	Prospective multicenter study in patients with HCV-related cirrhosis treated with pegIFN plus ribavirin, 50% genotype 1	HR (95% CI) for HCC for SVR versus non-SVR = 0.38 (0.14–0.88) (p = 0.04)
Hung *et al.* 2006 [30]	Taiwan	132	37 months[a] (12–63 months)	Retrospective cohort study in HCV patients with cirrhosis , inc. patients with HBV or HIV coinfection, 56% genotype 1b, treated with pegIFN plus ribavirin	4 year cumulative incidence of HCC was 28% in non-SVR versus 8% in SVR group (p = 0.0178)
Shih *et al.* 2012 [48]	Taiwan	3,988	34.6 months[a]	Retrospective analysis of patients with HCV monoinfection, (n = 344 patients treated with IFN-based treatment, n = 216 with SVR)	Adjusted HR (95%CI) for SVR versus untreated was 0.23 (0.06–0.94) (p = 0.041) for HCC
Wang *et al.* 2011 [33]	Taiwan	164	8 years	Retrospective cohort study in patients treated with pegIFN plus ribavirin	Incidence of HCC was 8.8% for patients with an SVR versus 14.3% for untreated patients (p = 0.352)
Yu *et al.* 2006 [45]	Taiwan	1,619	5.2 years	Prospective study in patients with or without cirrhosis (n = 562 untreated and n = 1,057 treated with IFN or IFN plus ribavirin)	RR (95% CI) for HCC versus untreated was 0.245 (0.13–0.46) (p < 0.0001) for SVR and 0.990 (0.635–1.541) (p = 0.963) for non-SVR
Morgan *et al.* 2010 [41]	United States	140	78.6 (15.9) months	Prospective analysis from the HALT-C trial in patients with advanced fibrosis treated with pegIFN plus ribavirin and achieving SVR	HR (95% CI) for SVR versus non response was 0.19 (0.04–0.80) for HCC
Wang *et al.* 2013 [21]	Not stated	138	8 years	Patients (mean age 56 years) treated with PR, 80% achieved SVR	8-year incidence of HCC was 13.5% for SVR patients, 23.5% for relapsers and 20% for non-responders (p = 0.518)

[a]Median follow up.

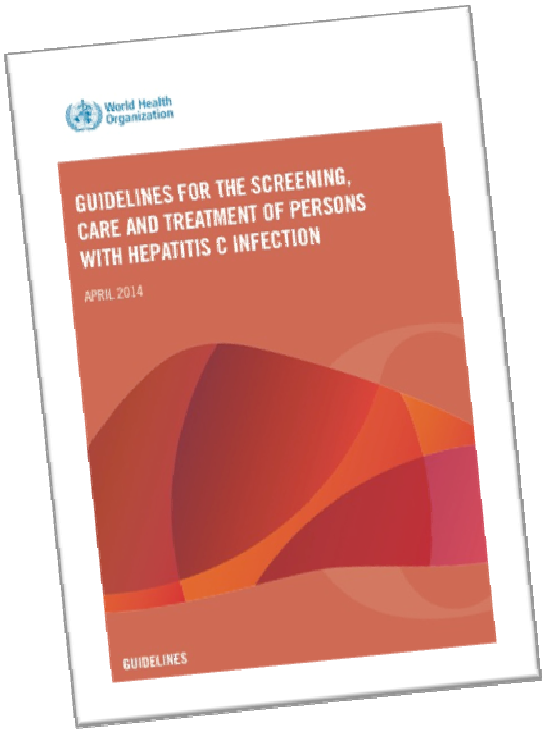
ALT, alanine aminotransferase; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; IFN, interferon; ns, not significant; SVR, sustained virologic response.

- Jezequel C, et al. Survival of patients infected by chronic hepatitis C and F0F1 fibrosis at baseline after a 15 year follow-up. Abstract PO709.
- Øvrehus ALH, et al. Impact of prioritizing treatment in a high resource setting-minimizing the burden of HCV related disease in 15 years. Abstract PO714.
- McC0mbs JS, et al. Can hepatitis C treatment be safely delayed? Evidence from the Veterans Administration Healthcare System. Abstract 0003

Proceedings of the 50th Annual Meeting of the European Association for the Study of the Liver (EASL). April 22-26, 2015; Vienna, Austria.

Si ha un maggior beneficio sulla mortalità se il trattamento è effettuato in fase precoce (<F3)

5. RECOMMENDATIONS ON SCREENING



5.1 Screening to identify persons with HCV infection

It is recommended that HCV serology testing be offered to individuals who are part of a population with high HCV seroprevalence or who have a history of HCV risk exposure/ behaviour.

Strong recommendation, moderate quality of evidence

Notes: The WHO list of prequalified serological diagnostic tests for hepatitis C infection are available at. http://www.who.int/diagnostics_laboratory/evaluations/en/hcv_rep1.pdf and http://www.who.int/diagnostics_laboratory/evaluations/en/hcv_rep2.pdf

This list will be updated in 2014.

Background

In many countries, people have very limited access to HCV testing and thus remain undiagnosed until they present at a health centre with symptoms of cirrhosis or liver cancer.[107] Testing at this time is referred to as "symptomatic testing". At this point, HCV-induced liver damage is often advanced and therapy may be contraindicated. Therefore, it is critical to identify approaches that will lead to a diagnosis of chronic HCV infection earlier in the course of disease. The Guidelines Development Group considered the value of a risk group-based and prevalence-based approach. These approaches, where testing is based on whether a person belongs to a group that practises behaviours that place them at risk of HCV infection or belongs to a population of known high HCV prevalence, are recommended in many high-income countries.[108,109] The difficulty in considering these approaches is that the relative importance of risk factors and history of behaviours linked to HCV infection vary substantially, depending on the geographical setting and population studied (Table 5.1).

TABLE 5.1 Populations with high HCV prevalence or who have a history of HCV risk exposure/ behaviour

- Persons who have received medical or dental interventions in health-care settings where infection control practices are substandard
- Persons who have received blood transfusions prior to the time when serological testing of blood donors for HCV was initiated or in countries where serological testing of blood donations for HCV is not routinely performed
- Persons who inject drugs (PWID)
- Persons who have had tattoos, body piercing or scarification procedures done where infection control practices are substandard
- Children born to mothers infected with HCV
- Persons with HIV infection
- Persons who have used intranasal drugs
- Prisoners and previously incarcerated persons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COMMENTS FROM THE EDITORS

The New Hepatitis C Virus Bottleneck: Can Delaying Therapy Be Justified?

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Chronic hepatitis C (CHC) infection is one of the most common causes of chronic liver disease worldwide and the leading indication for liver transplantation.[1] In the United States, CHC afflicts more than 3.2 million people, resulting in cirrhosis, hepatic decompensation, hepatocellular carcinoma, and death.[1] Although the incidence of hepatitis C viral (HCV) infection is declining in the United States, the incidence of cirrhosis is rising; and the number of deaths related to CHC is not projected to peak until 2030.[2] Successful eradication of HCV remains a priority and is associated with clear reductions in all-cause and liver-related outcomes, as well as alleviation of symptoms, improved quality of life, and the prevention of person-to-person transmission.[3]

The regulatory approval of second-generation direct-acting antiviral medications marked an extraordinary turning point in HCV therapeutics. The once-daily oral nucleotide polymerase inhibitor sofosbuvir and the once-daily protease inhibitor simeprevir were each heralded as medical breakthroughs. They were soon followed by other agents, including all-oral combination regimens comprised of sofosbuvir and ledipasvir and paritaprevir/ritonavir/ombitasvir/dasabuvir with or without ribavirin. With these regimens, it became possible to offer patients safe and effective (sustained virological response rates exceeding 90% in most populations) alternatives to interferon and ribavirin–based therapy. These regimens have an excellent safety profile and proven effectiveness across many genotypes, regardless of prior treatment failure or degree of underlying fibrosis. With their release comes the hope that we might one day witness the worldwide eradication of HCV.

Enthusiasm for these medications, however, has been dampened by the reality of their high costs, a major obstacle to their delivery. Twelve weeks of treatment costs $84,000 for sofosbuvir, $66,360 for simeprevir, $94,500 for sofosbuvir and ledipasvir, and $83,320 for paritaprevir/ritonavir/ombitasvir/dasabuvir.[4] Recent studies have collectively indicated that for genotype 1 these direct-acting antiviral agent–based regimens are cost-effective,[5,6] and recent discounting efforts promise to make them even more cost-effective. However, cost effectiveness and cost are not the same thing. As a result of these treatments now being applied to so many persons over so brief a period, there has been a significant short-term budgetary strain. It was recently reported that Medicare Part D spending on HCV regimens exceeded $4.5 billion in 2014, more than 15 times the $286 million spent in 2013.[7] Overall, 2014 saw a 13.1% rise in prescription drug spending, and it has been estimated that total health care expenditures related to HCV therapy could soon reach $27 billion per year.[8]

Saddled by skyrocketing prescription costs, many state-funded Medicaid programs and private insurance payers have responded by restricting access to direct-acting antiviral agent–based regimens to those with advanced (Metavir F3 or F4) fibrosis or severe extra-hepatic manifestations.[9] Others have gone further; in Texas, Medicaid has elected not to cover sofosbuvir at all.

Are these restrictions justified? It is possible, if there exists an equally effective alternative therapy for a particular condition, at a less expensive price. However, this is not the case for HCV, particularly for those patients who are intolerant of or not candidates for interferon and ribavirin–based treatment. Furthermore, restricting allocation implies that certain patients would derive greater benefit from treatment than others and that the choice to delay therapy will not place a patient at undue risk of harm. While persons with advanced fibrosis are clearly at highest risk for short-term complications, it is not clear that persons with lesser degrees of fibrosis are not at risk for harm.

The true cost of delaying HCV treatment is not well understood. It has been shown that disease progression in CHC is nonlinear,[10] and recent analysis of the Department of Veterans Affairs database has demonstrated that rates of fibrosis progression may be far more accelerated than previously thought.[11] Thus, any decision to defer or delay treatment runs the risk of allowing a subset of patients to progress to cirrhosis and thereby

Abbreviations: CHC, chronic hepatitis C; HCV, hepatitis C virus.

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- I fattori di rischio specifici per la progressione della malattia in soggetti con fibrosi minima non sono ancora definiti. Il preciso vantaggio della terapia precoce è ancora poco conosciuto.
- Il rapporto costo/beneficio deve tener conto anche delle frequenti complicanze extraepatiche (diabete, patologie cardiovascolari, insufficienza renale, disordini psichiatrici e problematiche reumatologiche)

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PRACTICE GUIDANCE

Hepatitis C Guidance: AASLD-IDSA Recommendations for Testing, Managing, and Treating Adults Infected With Hepatitis C Virus

AASLD/IDSA HCV Guidance Panel*

Identificare l'infezione attiva è il primo passo verso il miglioramento dei risultati di salute, prevenzione e trasmissione

Considerare come prioritari per il trattamento coloro che hanno un maggior rischio di trasmissione dell'infezione

Table 4. Persons With Risk of HCV Transmission* or in Whom Treatment May Reduce Transmission

- Men who have sex with men with high-risk sexual practices
- Active injection-drug users
- Incarcerated persons
- Persons on long-term hemodialysis
- HCV-infected women of childbearing potential wishing to get pregnant
- Infected health care workers who perform exposure-prone procedures

Rating: Class IIa, Level C

*Patients at substantial risk of transmitting HCV should be counseled on ways to decrease transmission and minimize the risk of reinfection.