

# PROGRAMMA



## CONOSCERE L'EPATITE C: SCREENING, DIAGNOSI E CLINICA

BRESCIA, 18 MAGGIO 2019

SALA CONFERENZE  
ORDINE DEI MEDICI CHIRURGHI  
E DEGLI ODONTOIATRI  
DELLA PROVINCIA DI BRESCIA

Via Alessandro Lamarmora, 167

Promotore



FONDAZIONE  
MALATTIE INFETTIVE E  
SALUTE INTERNAZIONALE

Con il Patrocinio di



ORDINE  
MEDICI CHIRURGHI  
E ODONTOIATRI  
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DI BRESCIA



Centro di Documentazione  
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FONDAZIONE  
MALATTIE INFETTIVE E  
SALUTE INTERNAZIONALE  
MISI

## Epatite C una malattia da non sottovalutare: Differenze di genere nella la progressione della malattia epatica

**Dr. Paola Nasta**  
UO Malattie infettive Spedali Civili di Brescia  
Fondazione MISI

# Malattia virale di fegato: perché parlare di genere



- Cambio dell'epidemiologia
- Trasmissione verticale: screening in età fertile
- Evoluzione della malattia epatica peculiare
- Terapia vecchia e nuova : diverso genere diversa tollerabilità
- La malattia dopo la cura : Follow up gender based



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- La malattia dopo la cura : Follo up gender based



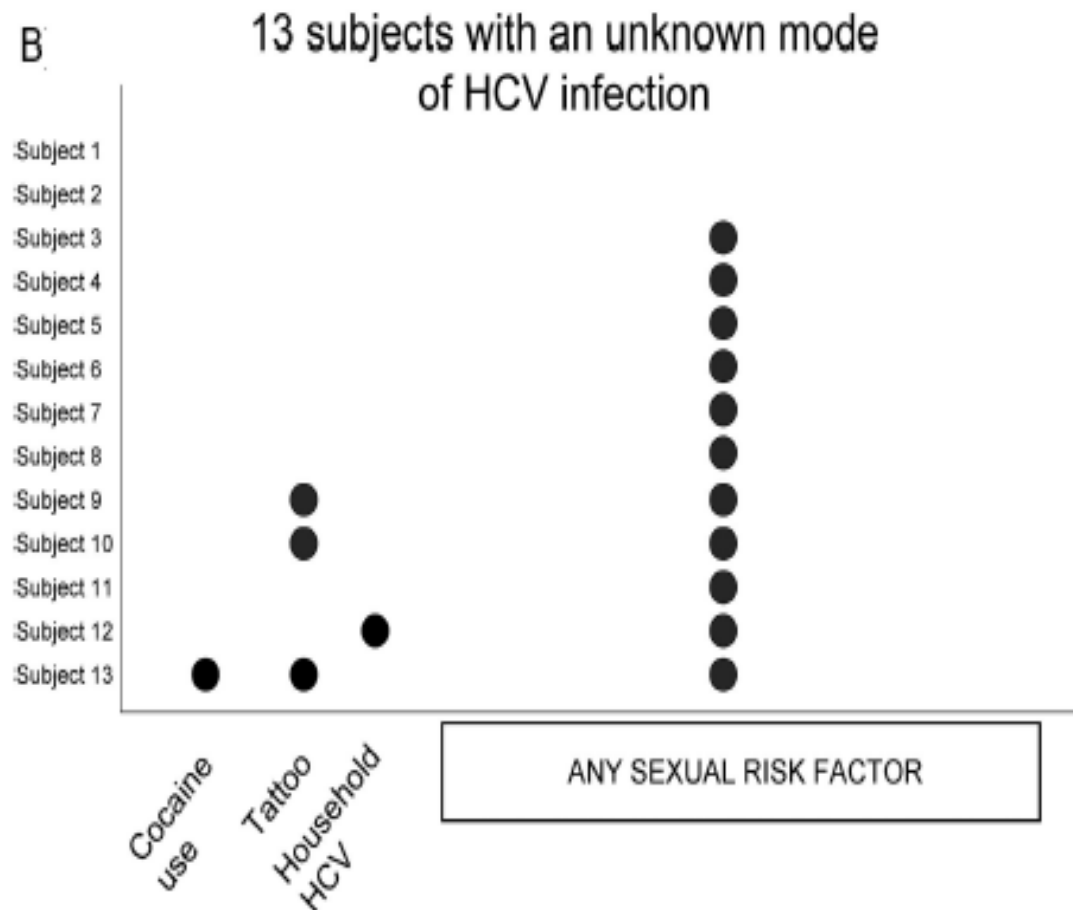
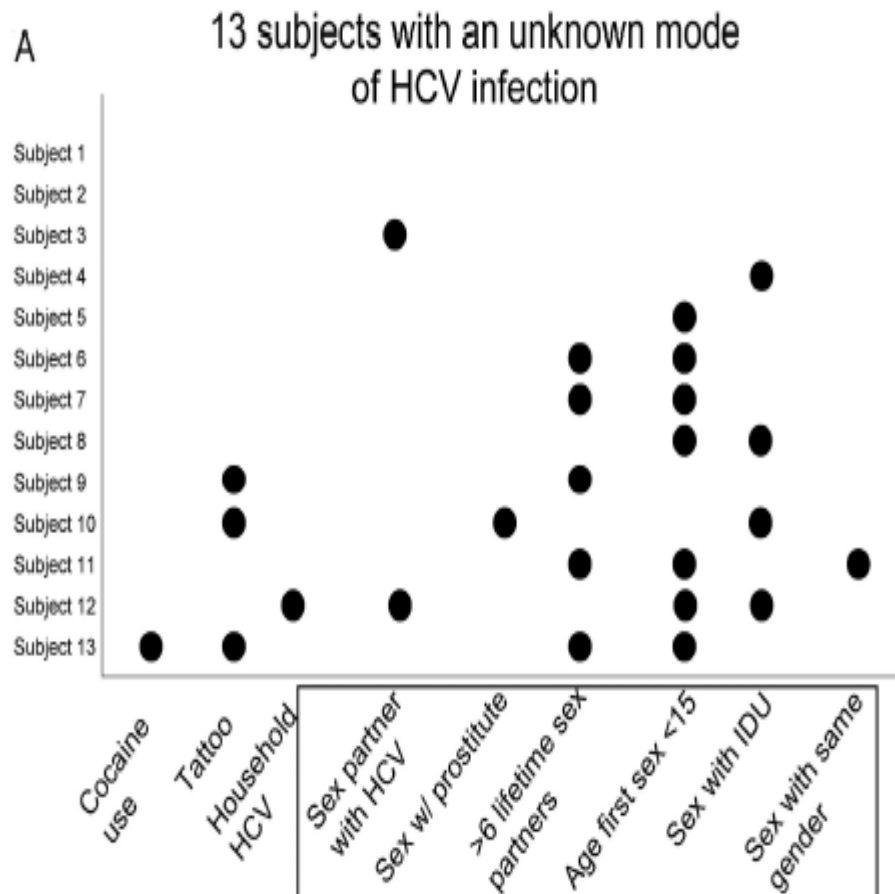
# The new generation of HCV infection trends toward increased prevalence among teenager, young adult and women

**Table 1** Differing characteristics of individuals with hepatitis C

Previous cohort	New cohort
Baby Boomers	Young adults
Blood transfusion	Injectable drug use
Mostly men	Men and women similarly represented
HCV screening recommended	No concentrated screening effort
Engaged in healthcare system	Not engaged in healthcare system

**The increased incidence of new cases and prevalence of existing disease among individuals from 20 to 29 years of age has primarily been associated with widespread injection drug use**

# Acute Hepatitis C in a Contemporary US Cohort: Modes of Acquisition and Factors Influencing Viral Clearance



# Cambiamenti Epidemiologici dell'infezione da HCV aumenta la prevalenza nelle donne

**Data from the National Health and Nutrition Examination Survey (NHANES) in 2010 suggested that the male to female prevalence was approximately 1.56% and 0.75%, respectively, at the national level**

**Among the new generation of patients with HCV, there is increasing prevalence among females, with trend toward equalized risk among men and women.**

*Hall EW, . BMC Infect Dis. 2018;18:224.*

**From 2006 to 2012 demonstrated that among 1202 newly reported HCV + young patients, 52% were female**

*Suryaprasad AG, Clin Infect Dis. 2014;59:1411–1419*

**National Notifiable Diseases Surveillance System, and estimates that up to 29,000 HCV-infected women gave birth annually from 2011 to 2014**

*Jhaveri R, . Clin Infect Dis. 2018;67:1493–1497 24. Ly KN, Ann Intern Med. 2017;166:775–782*

**Of these births, was calculated the presence of HCV infection in up to 3.4 cases per 1000 live births by 2014**

*Patrick SW MMWR Morb Mortal Wkly Rep 2017; 66:470.73*

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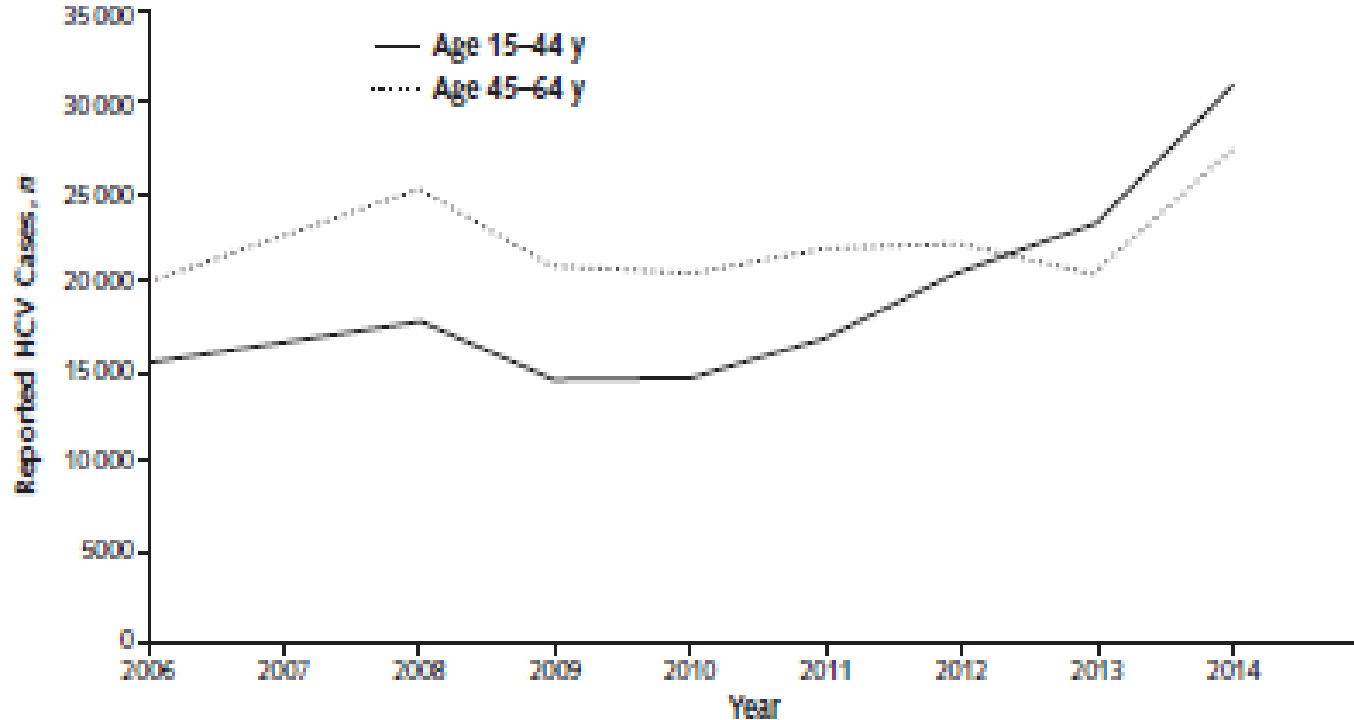


# Hepatitis C Virus Infection Among Reproductive-Aged Women and Children in the United States, 2006 to 2014

Kathleen N. Ly, MPH; Ruth B. Jiles, PhD, MPH; Eyasu H. Teshale, MD; Monique A. Foster, MD, MPH; Rick L. Pesano, MD, PhD; and Scott D. Holmberg, MD, MPH



Figure. Number of reported cases of HCV infection among women aged 15–44 years and 45–64 years in the United States, 2006–2014.



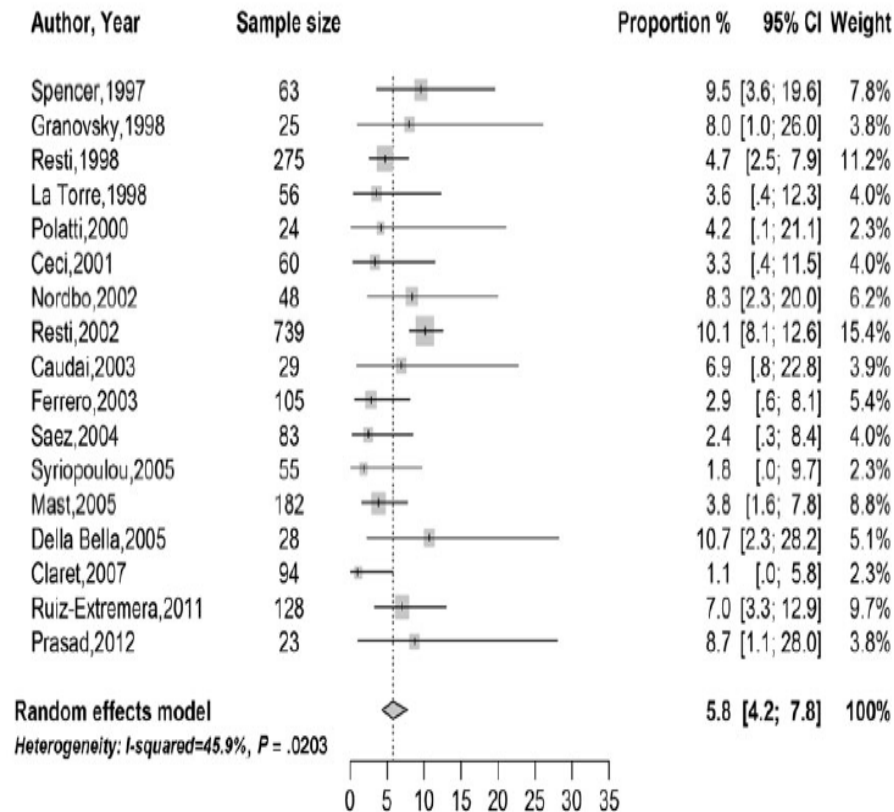
Data source: Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System. HCV = hepatitis C virus.



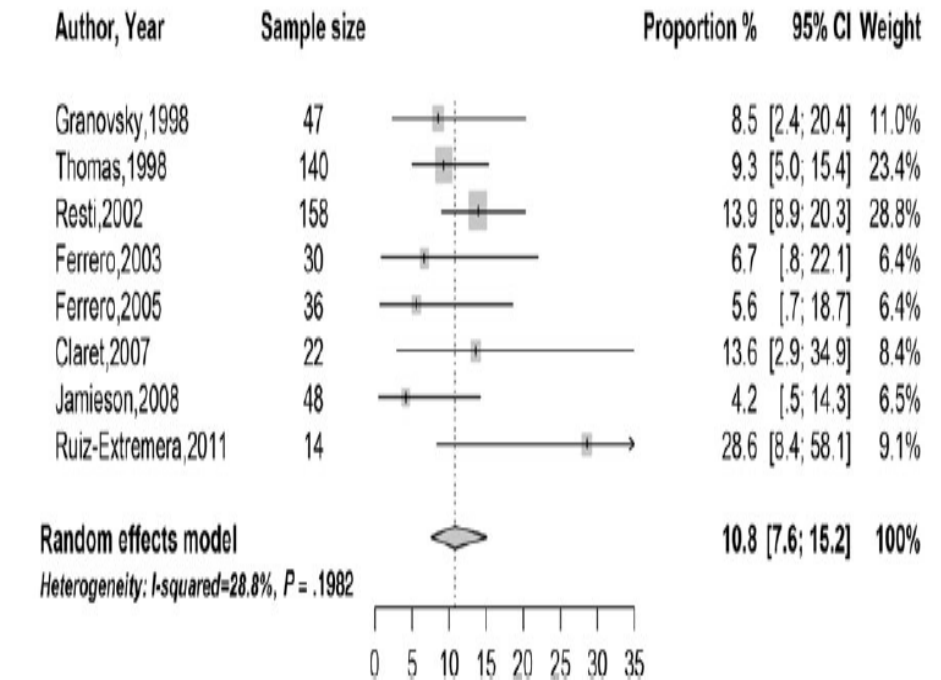
# Vertical Transmission of Hepatitis C Virus: Systematic Review and Meta-analysis

Lenka Benova,<sup>1,2</sup> Yousra A. Mohamoud,<sup>1</sup> Clara Calvert,<sup>2</sup> and Laith J. Abu-Raddad<sup>1,3,4</sup>

## HIV-negative women



## HIV-positive women



**The risk of HCV vertical transmission from HCV antibody-positive and RNA-positive women approximates at 5.8% (95% CI 4.2%–7.8%) and increases to 10.8% (95% CI 7.6%–15.2%) among mothers coinfecting with HIV**

# Nuovi paradigmi per lo screening della popolazione femminile

**La gravidanza potrebbe essere l'unico momento nel quale una donna viene a contatto con una struttura sanitaria**

**Le linee guida attuali suggeriscono di screenare per epatite C solo le donne gravide ritenute a rischio**  
*(AASLS/IDSA HCV guidance: recommendations for testing, managing, and treating hepatitis C)*

**Il cambio epidemiologico in atto suggerisce che vengano screenate per HCV tutte le donne gravide**

**Non vi sono farmaci per la cura di HCV approvati in gravidanza**

**Lo screening dovrebbe quindi essere suggerito durante l'età fertile(?)**

**Screening universale per le donne dai 14-50 anni?**

**Considerare che il 5-8% delle donne HCVAb+ risultano co-infette con HIV**

# Malattia virale di fegato: perché parlare di genere

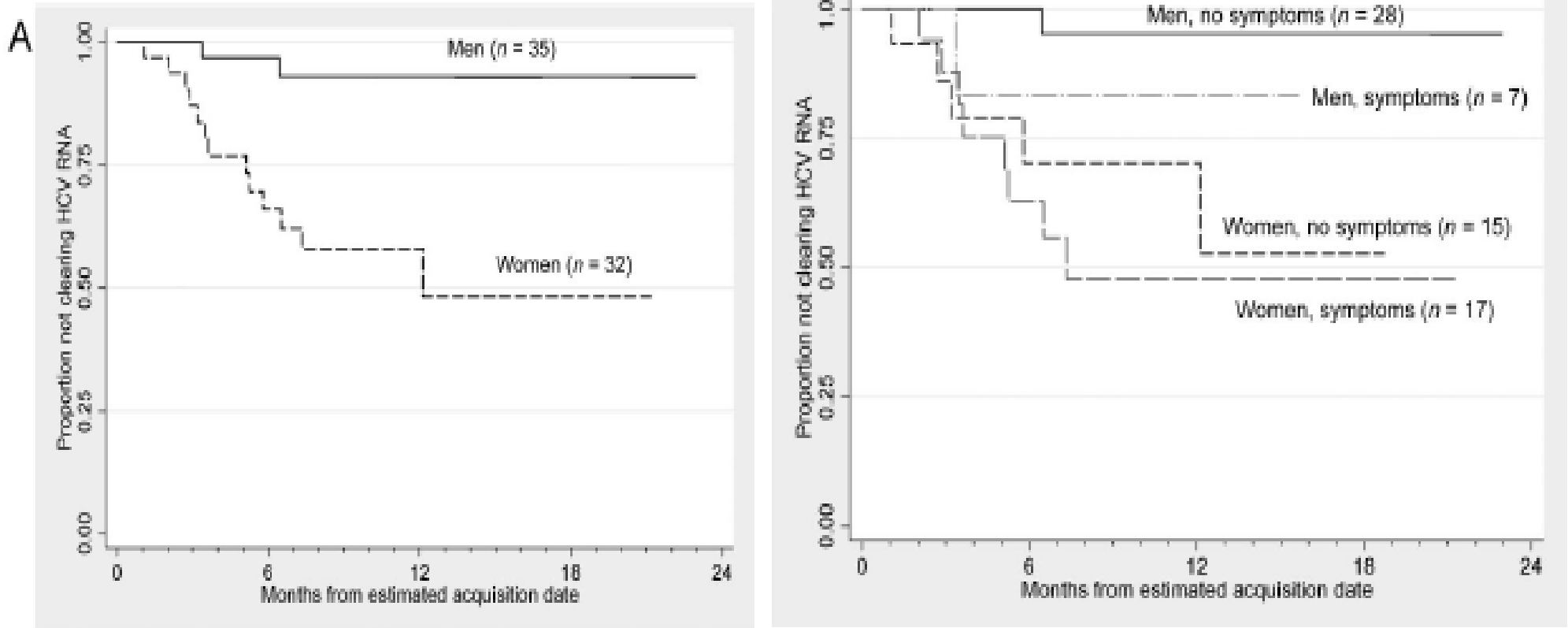


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# Female is an independent predictor of Clearance in acute HCV infection among different models of transmission

Wang CC, Krantz E, Klarquist J, et al.. *J Infect Dis.* 2007;196:1474–1482.

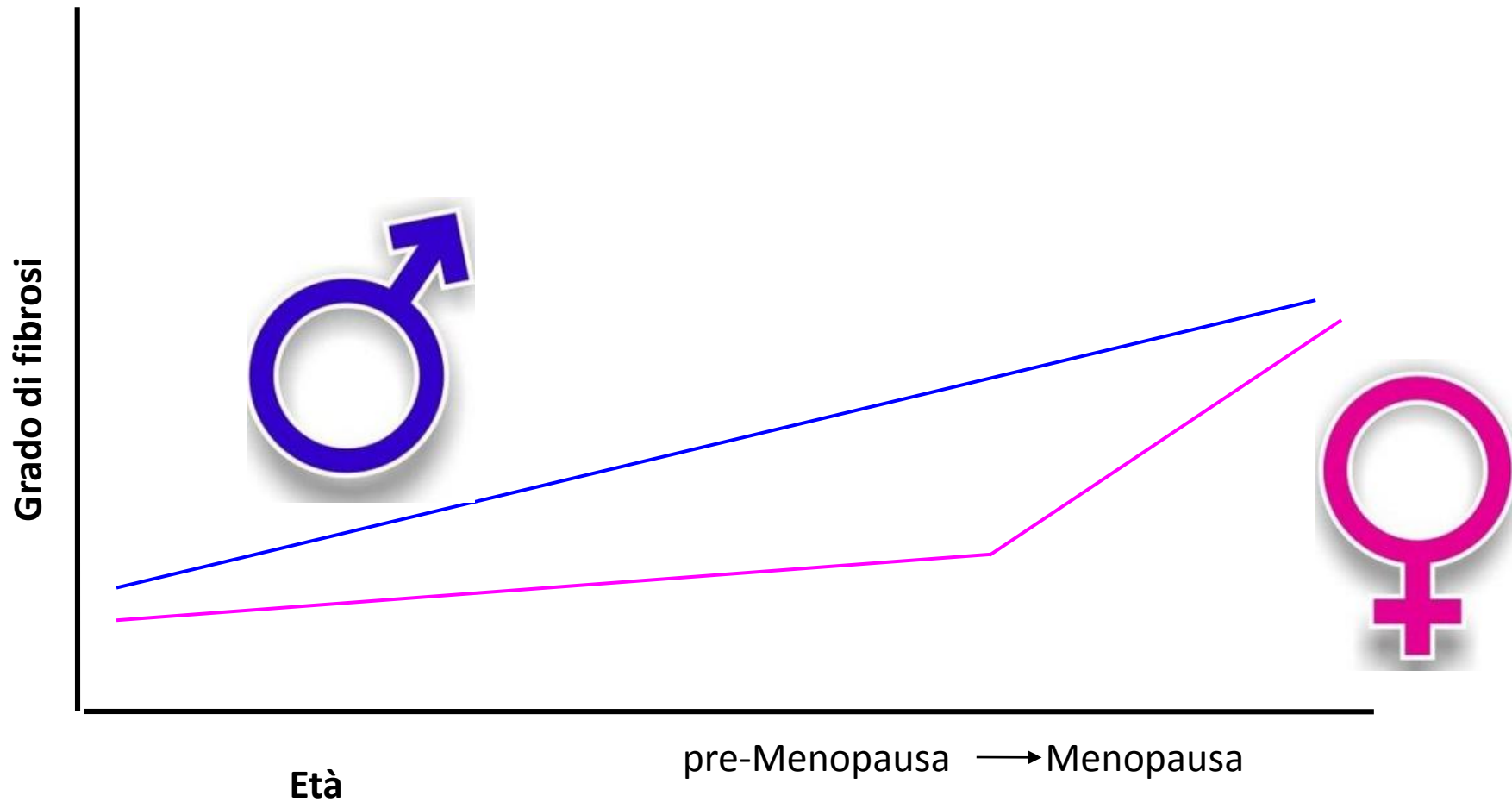


**The spontaneous viral clearance rate after 6 months of infection was 18% (95% confidence interval, 11%–31%).**

**The rate of viral clearance varies significantly by sex (34% vs. 3% for women vs. men; P .001).**

**Additional effect: clearance with IL28b and HCV genotype 1 was stronger in women compared to men**

# Progressione della fibrosi epatica in base al genere



# Progression of Liver Fibrosis in Women Infected With Hepatitis C: Long-Term Benefit of Estrogen Exposure

Vincent Di Martino,<sup>1</sup> Pascal Lebray,<sup>1</sup> Robert P. Myers,<sup>1</sup> Emmanuelle Pannier,<sup>2</sup> Valérie Paradis,<sup>3</sup> Frédéric Charlotte,<sup>4</sup> Joseph Moussalli,<sup>1</sup> Dominique Thabut,<sup>1</sup> Catherine Buffet,<sup>5</sup> and Thierry Poynard<sup>1</sup>



Four hundred seventy-two HCV-infected women received a survey regarding prior pregnancies, menopause, and the use of oral contraceptives and HRT

**Aim:** The impact of these variables on liver fibrosis and its progression

201 women completed the survey (43% response rate),

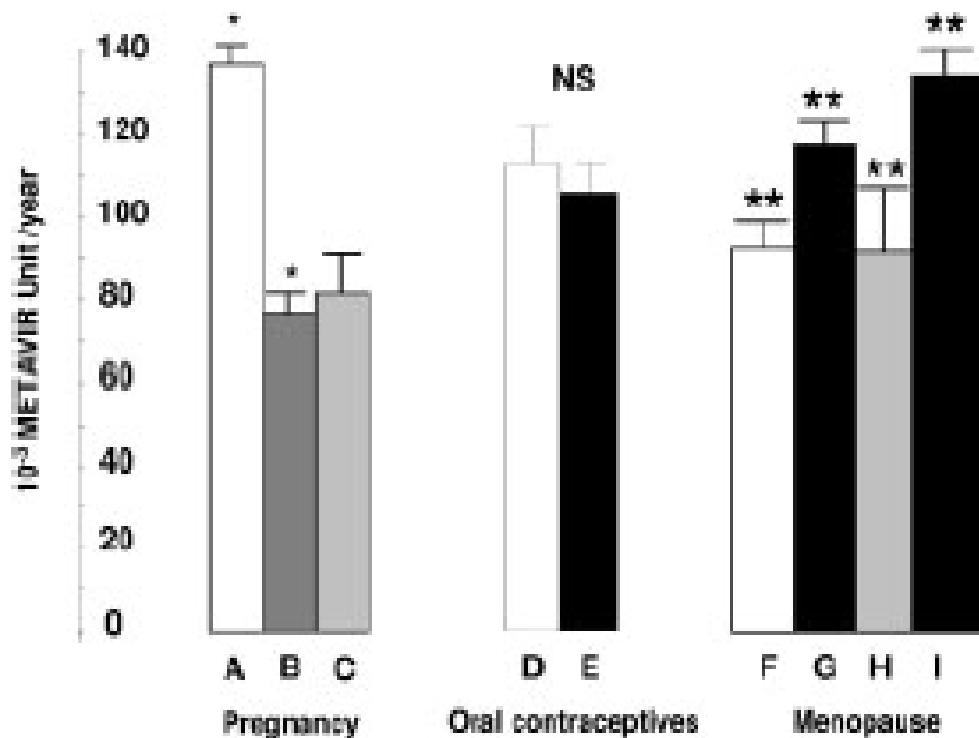
96 postmenopausal women,

96 women with previous pregnancies,

105 women with past use of oral contraceptives

L

# Comparison of fibrosis progression rate (FPR) in HCV-infected women according to past history of pregnancies, oral contraceptives, menopause, and HRT.



\*P.001;

\*\*P.02.

NS, not significant.

(A) Nulliparous women.

(B) Women with one or more past pregnancies.

(C) Women with one or more children.

(D) Women not taking oral contraceptives.

(E) Women with past or present use of oral contraceptives.

(F) Nonmenopausal women.

(G) Menopausal women (total).

(H) Menopausal women receiving HRT.

(I) Menopausal women not receiving HRT.

The significant results are as follows: (1) FPR was significantly higher in nulliparous women, suggesting a long protective effect of pregnancies against liver fibrosis progression.

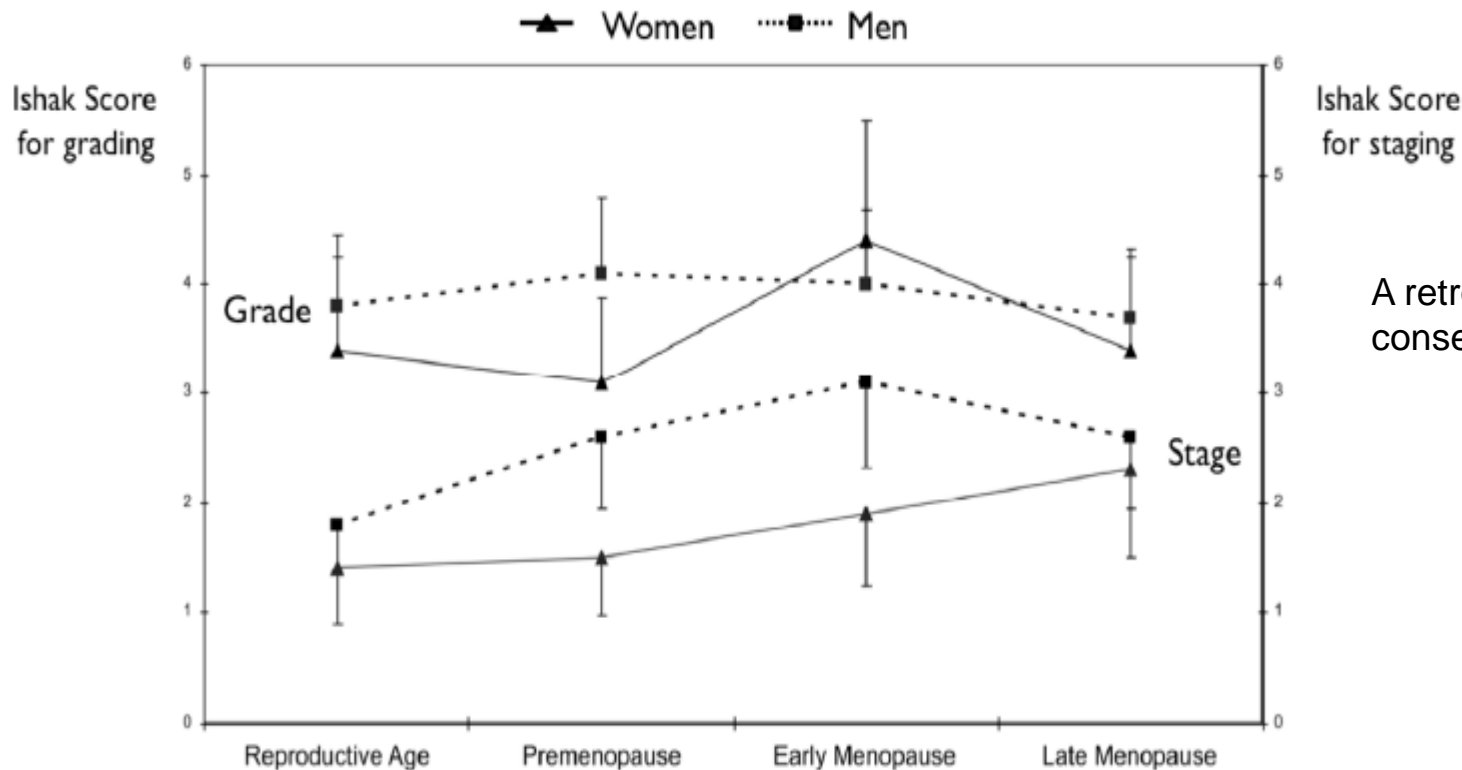
(2) Postmenopausal women had a higher FPR compared with premenopausal women.

Among postmenopausal women, the mean FPR was lower in users than nonusers of HRT, and similar to that of premenopausal women.

These results suggest a deleterious effect of menopause on liver fibrosis progression that may be prevented by HRT.

# Reproductive Status Is Associated with the Severity of Fibrosis in Women with Hepatitis C

Erica Villa<sup>1\*</sup>, Ranka Vukotic<sup>1†</sup>, Calogero Cammà<sup>2</sup>, Salvatore Petta<sup>2</sup>, Alfredo Di Leo<sup>3</sup>, Stefano Gitto<sup>1</sup>, Elena Turola<sup>1†</sup>, Aimilia Karampatou<sup>1†</sup>, Luisa Losi<sup>4†</sup>, Veronica Bernabucci<sup>1†</sup>, Annamaria Cenci<sup>5</sup>, Simonetta Tagliavini<sup>5</sup>, Enrica Baraldi<sup>5</sup>, Nicola De Maria<sup>1</sup>, Roberta Gelmini<sup>6</sup>, Elena Bertolini<sup>1†</sup>, Maria Rendina<sup>3†</sup>, Antonio Francavilla<sup>7</sup>



A retrospective study of 710 consecutive patients with biopsy-

**Liver fibrosis was more advanced in the early menopausal than in the fully reproductive (P,0.0001) or premenopausal (P = 0.042) group.**

**Late menopausal women had higher liver fibrosis compared with the other groups (fullyreproductive, P,0.0001; premenopausal, P =,0.0001; early menopausal, P = 0.052).**



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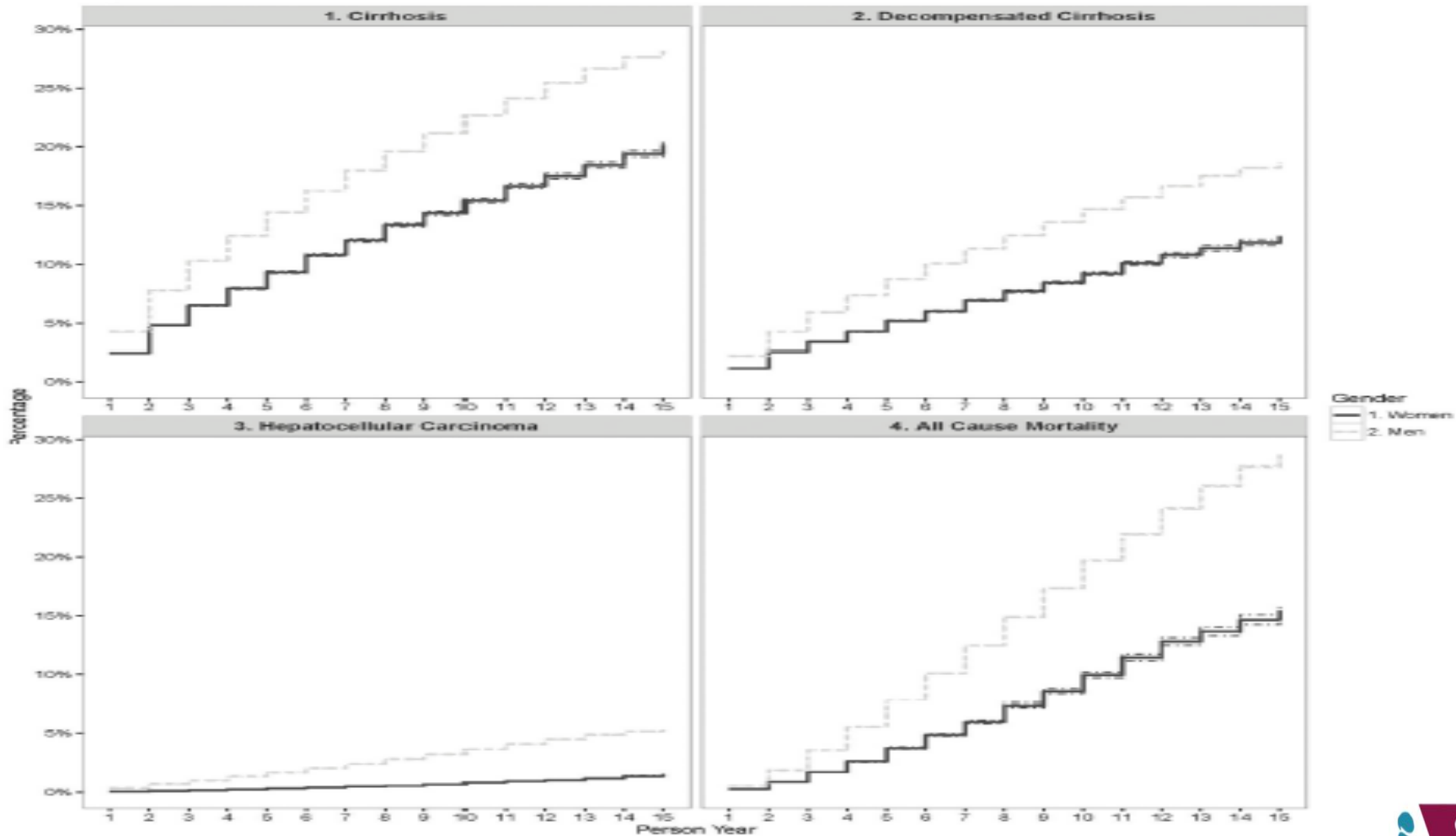
Experimental data suggest that estrogens may have an antifibrotic effect.

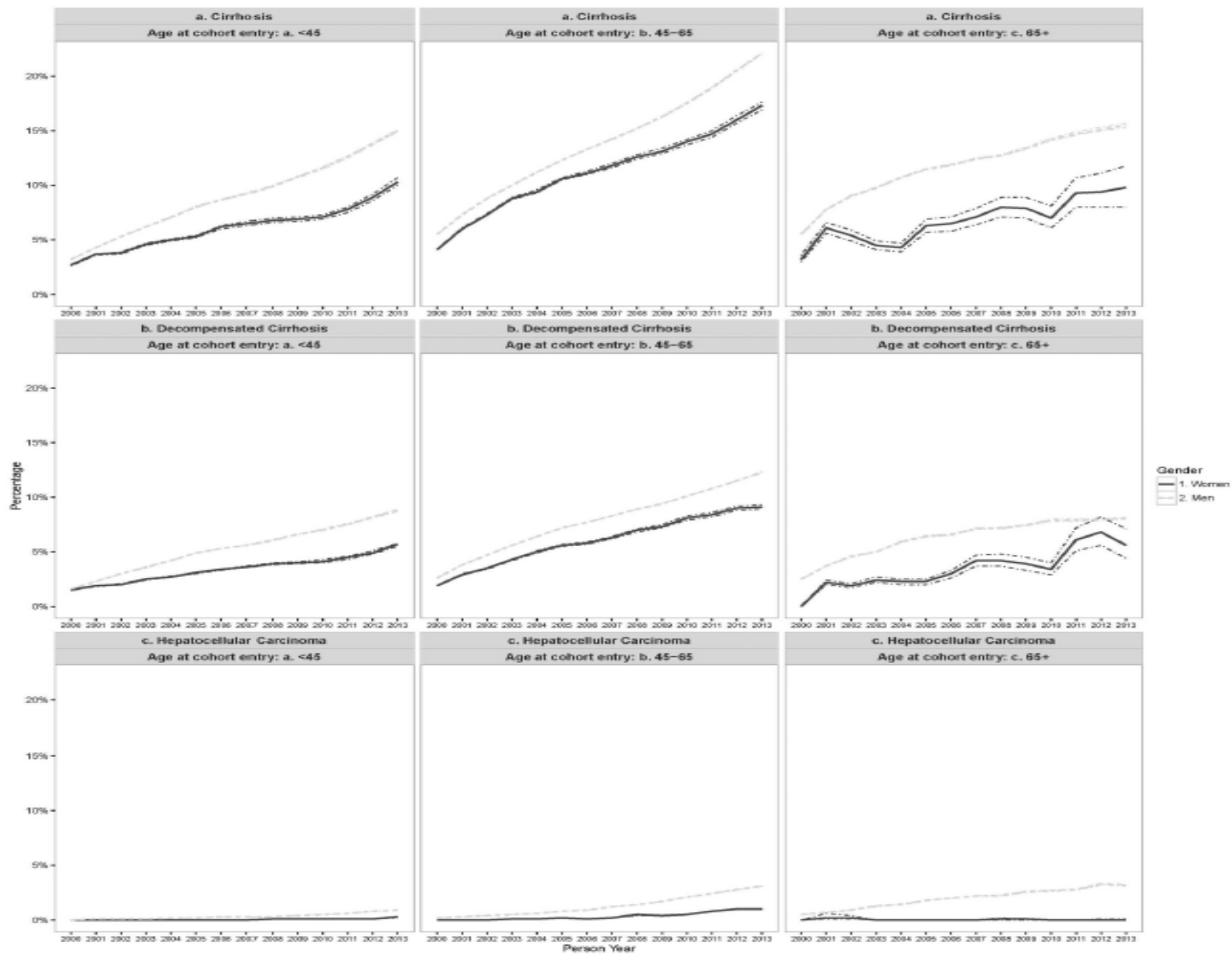
These results suggest a deleterious effect of menopause on liver fibrosis progression that may be prevented by HRT.

## HCV-related complications are increasing in women veterans: A national cohort study

Jennifer R. Kramer<sup>1,3</sup>, Hashem El-Serag<sup>1,2,3</sup>, Thomas J. Taylor<sup>4</sup>, Donna White<sup>1,2,3</sup>, Steven Asch<sup>5</sup>, Susan Frayne<sup>5</sup>, Yumei Cao<sup>1</sup>, Donna Smith<sup>1</sup>, and Fasiha Kanwal<sup>1,2,3</sup>

There were statistically significant increases over time in the incidence rates of cirrhosis, decompensated cirrhosis, and HCC for both men and women





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# Autoantibodies in chronic hepatitis C virus infection: impact on clinical outcomes and extrahepatic manifestations

Andrew J Gilman,<sup>1</sup> An K Le,<sup>2</sup> Changqing Zhao,<sup>3</sup> Joseph Hoang,<sup>2</sup> Lee A Yasukawa,<sup>4</sup> Susan C Weber,<sup>4</sup> John M Vierling,<sup>5</sup> Mindie H Nguyen<sup>2</sup>

**Table 3** Baseline characteristics

	Autoantibody testing positive (n=388)	Autoantibody testing negative (n=1168)	P value
Sex (column % (row %))			
Male	43.8% (20.9%)	55.1% (79.1%)	<0.001
Female	56.2% (29.3%)	45.0% (70.7%)	
SVR achieved (n=149/452)	37.2%	47.1%	0.031
IFN-based therapy	29.0%	42.7%	0.012
DAA therapy	67.6%	71.4%	0.65

Auto-ab positivity played no role in the progression of liver disease in patients with chronic HCV, including development of cirrhosis, hepatic decompensations, hepatocellular carcinoma (HCC) nor mortality.

However, auto-ab positivity was associated with a decreased achievement of sustained virological response with PegIFN (SVR).  
Gilman AJ, et al. *BMJ Open Gastro* 2018;5:



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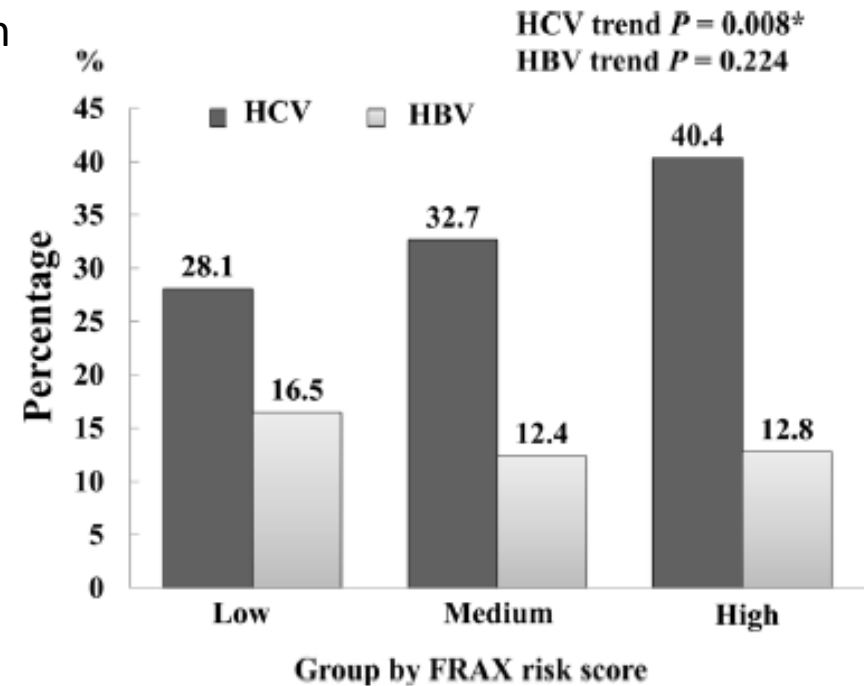
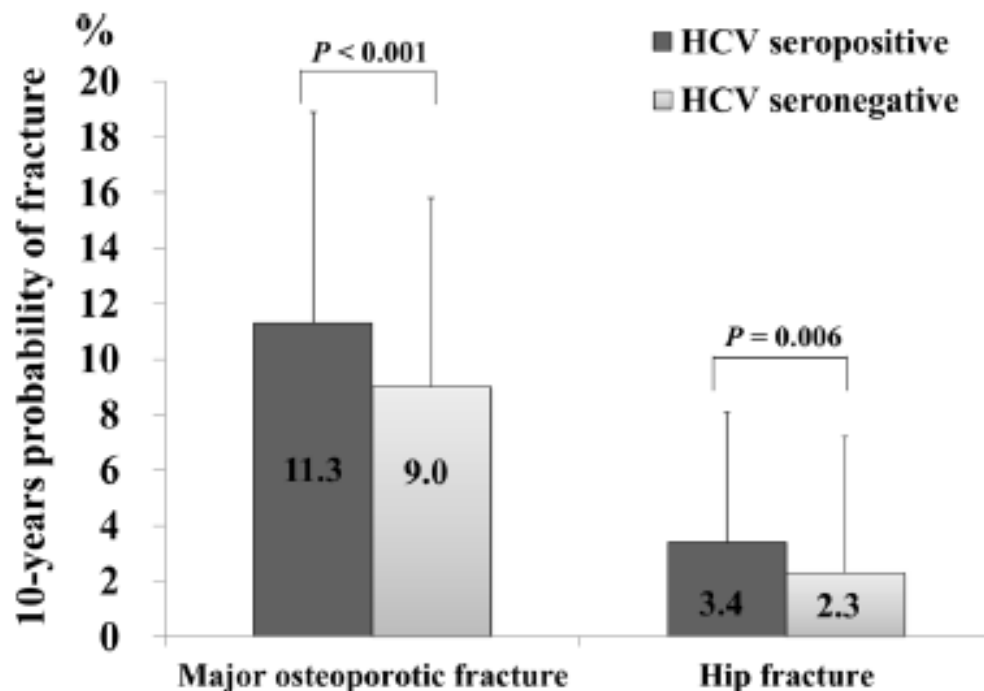


# BMJ Open Association between hepatitis C virus infection and osteoporotic fracture risk among postmenopausal women: a cross-sectional investigation in Taiwan



Ming-Shyan Lin,<sup>1,2</sup> Po-Han Chen,<sup>3</sup> Po-Chang Wang,<sup>1,2</sup> Huang-Shen Lin,<sup>4</sup> Tung-Jung Huang,<sup>5,6</sup> Shih-Tai Chang,<sup>1,2</sup> Wen-Nan Chiu,<sup>7</sup> Mei-Yen Chen<sup>1,8,9</sup>

Between October 2015 and July 2016, 1070 women living in a coastal Yunlin County (Taiwan) annual health check, including a dual-energy X-ray absorptiometry (DXA) BMD analysis. We enrolled 636 menopausal women,



**Table 3** Association of HCV with risk of osteopenia and osteoporosis in various adjustment models

Model	Osteoporosis			Osteopenia or Osteoporosis		
	OR	95% CI of OR	P value	OR	95% CI of OR	P value
Model 1: unadjusted model	1.65	1.12 to 2.44	0.012*	1.83	1.25 to 2.68	0.002*
Model 2: adjusted for substance use	1.64	1.11 to 2.43	0.013*	1.83	1.25 to 2.68	0.002*
Model 3: further adjusted for BMI, waist and SBP	1.62	1.08 to 2.43	0.019*	1.69	1.14 to 2.51	0.009*
Model 4: further adjusted for inflammatory index	1.77	1.16 to 2.70	0.008*	1.92	1.26 to 2.93	0.002*
Model 5: further adjusted for lipid profiles	1.76	1.13 to 2.72	0.012*	1.99	1.30 to 3.06	0.002*
Model 6: further adjusted for HBV	1.78	1.15 to 2.76	0.010*	1.99	1.30 to 3.06	0.002*
Model 7: further adjusted for age	1.52	0.97 to 2.39	0.068	1.80	1.16 to 2.81	0.009*

\*P<0.05.

strong association between HCV, seropositivity and lower BMD in postmenopausal women. These results suggest that HCV infection might be a risk factor for osteopenia and potential osteoporotic fractures according to FRAX score.

A future, larger cohort could provide more evidence of osteoporosis prevention in both sexes.



# Conclusioni



**1) Gli Uomini hanno un rischio superiore di infettarsi con HCV (rischio > 1,7 volte rispetto alle donne )**

*Uhanova J, et al. J Hepatol. 2012; 57:736–742. [PubMed: 22668641]*

**2) I nuovi trend epidemiologici dimostrano, tuttavia , un incremento delle giovani donne infette**  
*(Tiffany Wu1 et al Digestive Diseases and Science <https://doi.org>)*

**3) Gli uomini hanno una progressione più rapida di malattia epatica e sviluppano cirrosi ed End liver disease più spesso delle donne**

*(Deuffic S, et al. Hepatology. 1999; 29:1596–1601;. Evans JL, et al J Urban Health. 2003; 80:137–146. Poynard T, et al.. Lancet. 1997; 349:825–832.)*

**4) Gli estrogeni potrebbero avere un ruolo protettivo nei confronti dei processi fibrogenetici con inibizione dell'attivazione delle cellule stellate.**

**Questo vantaggio è ridotto dalla menopausa precoce**

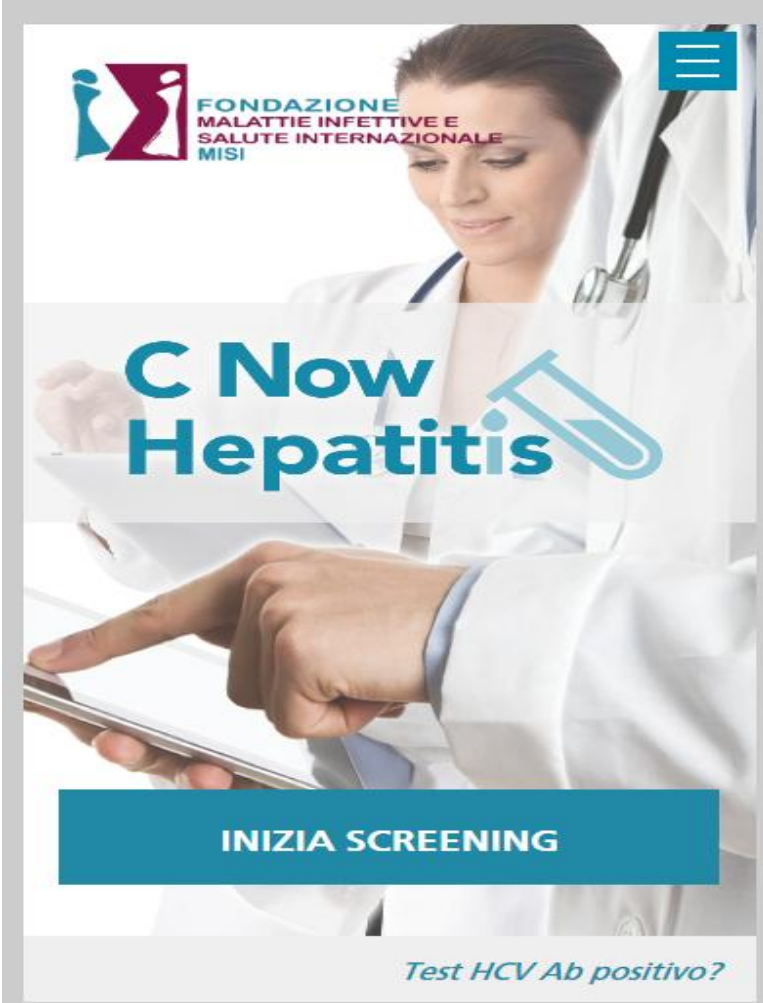
**In post menopausa si assisterebbe ad una accelerazione dei processi fibrogenetici anche superiori rispetto al sesso maschile** *(Di MV, Lebray et Al. Hepatology. 2004; 40:1426–1433; Codes L, et al. Gut. 2007; 56:390–395.)*

**5) Rivalutare lo screening universale in gravidanza e possibilmente in età fertile**

*(Benova L, Clin Infect Dis. 2014;59:765–773)*



**2**Disponibilità del  
fondo speciale per i  
DAA fino a Aprile  
2020: necessario  
elaborare strategie  
Utili a fare emergere i  
casi di infezione  
sommersi



FONDAZIONE  
MALATTIE INFETTIVE E  
SALUTE INTERNAZIONALE  
MISI

**C Now  
Hepatitis**

**INIZIA SCREENING**

*Test HCV Ab positivo?*

The advertisement features a female doctor in a white lab coat with a stethoscope, looking at a tablet. The background is a light blue and white gradient. The MISI logo is in the top left, and a menu icon is in the top right. The text 'C Now Hepatitis' is prominently displayed in the center, with a test tube icon. A blue button at the bottom says 'INIZIA SCREENING'. At the very bottom, there is a question: 'Test HCV Ab positivo?'.

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