An update on PITER The Italian National HCV cohort

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Istituto Superiore di Sanità

CENTRO NAZIONALE PER LA SALUTE GLOBALE

PITER
Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

HCV PITER cohort is a reppresentative sample of patients with chronic HCV infection in care in Italy

Geografical Distribution of PITER Network Clinical Centers

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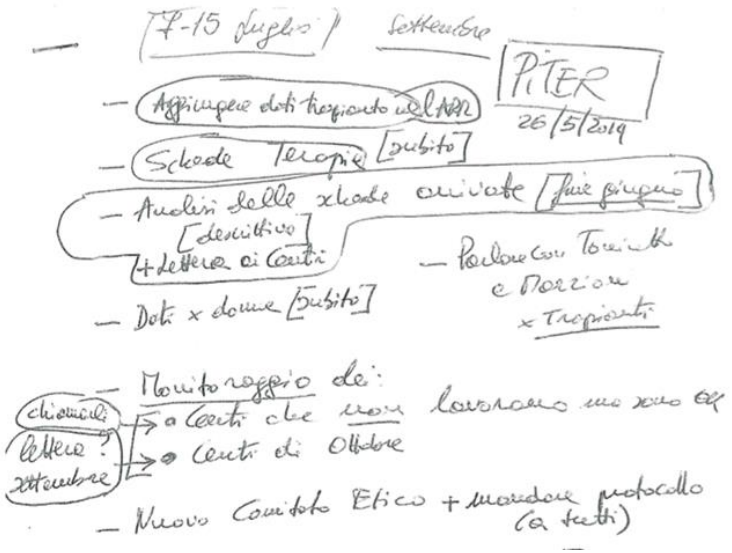
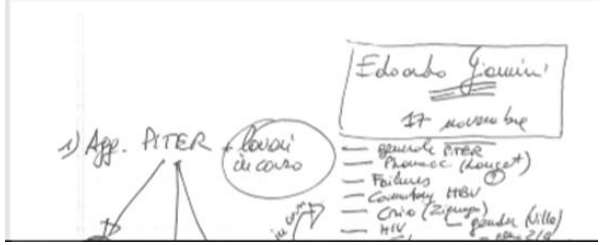
Piattaforma Italiana per lo studio delle Terapie delle Epatiti viRali
(Italian Platform for the Study of Viral Hepatitis Therapies)





Infection and Drug Resistance

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REVIEW

Conceptual framework for outcomes research studies of hepatitis C: an analytical review

This article was published in the following Dove Press journal:
Infection and Drug Resistance
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Abstract: Hepatitis C virus infection is one of the main causes of chronic liver disease worldwide. Until recently, the standard antiviral regimen for hepatitis C was a combination of an interferon derivative and ribavirin, but a plethora of new antiviral drugs is becoming available. While these new drugs have shown great efficacy in clinical trials, observational studies are needed to determine their effectiveness in clinical practice. Previous observational studies have shown that multiple factors, besides the drug regimen, affect patient outcomes in clinical practice. Here, we provide an analytical review of published outcomes studies of the management of hepatitis C virus infection. A conceptual framework defines the relationships between four categories of variables: health care system structure, patient characteristics, process-of-care, and patient outcomes. This framework can provide a starting point for outcomes studies addressing the use and effectiveness of new antiviral drug treatments.

Keywords: chronic hepatitis C, humans, treatment outcome, combination drug therapy, antiviral agents

Introduction

Discussion

Go to:

Outcomes research studies have analyzed dozens of variables in multiple categories within the domains of health care system structure, patient characteristics, and process-of-care (Table 3). The results of these studies indicated that some patient characteristics, eg, demographic (race) and behavioral (illicit drug use), were predictive of the process-of-care variable, antiviral treatment. Other patient characteristics, eg, demographic (age) and laboratory (HCV genotype), were predictive both of receiving antiviral treatment and of SVR (a patient outcome). In addition, some health care system structure variables were predictive of receiving antiviral treatment, and optimum preventative care (a process-of-care variable) was predictive of SVR.

The majority of the published outcomes research studies were conducted in the era of pegylated interferon/ribavirin as the standard for antiviral treatment, and so there are few published observational studies of the new DAAs and new DAA combinations. HCV-TARGET is an international consortium of HCV investigators who have established a common research database and are conducting a longitudinal observational study of the treatment of HCV therapy with DAAs.40 PITER is an ongoing longitudinal study of the impact of DAAs on the natural course of infection and long-term clinical outcomes.42 Clinical trials of multiple interferon-free combinations of DAAs have been completed or are ongoing.43–45 Outcomes research studies will be needed to clarify for which patient groups, and in which clinical settings, these new regimens are most effective. In the United States, the patient's health plan type may influence whether they receive the new DAAs. Most Medicaid plans currently limit access to sofosbuvir in patients with advanced cirrhosis.46 Thirty-eight percent of patients in the HCV-TARGET had cirrhosis,40 whereas much lower percentages of patients treated with interferon regimens had cirrhosis, eg, 7%–14% in Veterans Health Administration populations.41,47–52

Lo Studio PITER-HCV

Obiettivo generale

Valutare l'impatto a lungo termine dei nuovi farmaci anti-HCV ad azione antivirale diretta nella storia naturale e negli esiti dell'infezione cronica da HCV nella pratica clinica reale.

Obiettivi specifici

Ottenere dati sull'utilizzo dei nuovi farmaci DAA nella pratica clinica reale per poter guidare con evidenze scientifiche le politiche sanitarie, in modo da assicurare l'equità della cura dei pazienti affetti da infezione cronica da HCV.

Costruire una piattaforma di dati su cui formulare ipotesi sull'impatto economico e sociale della terapia dell'epatite cronica da HCV con i nuovi farmaci DAA.

Risultati attesi

Raccogliere su scala nazionale un numero adeguato di dati clinici, biologici e di gestione di pazienti con infezione da HCV.

Valutare l'impatto reale a breve e a lungo termine che i DAA avranno sugli esiti dell'infezione cronica da HCV in differenti contesti clinici e socio-economici (i cosiddetti difficili da trattare *difficult-to-treat* e *hard-to-reach/marginalized*).

Valutare la capacità dei nuovi regimi terapeutici di modificare la storia naturale della malattia e delle sue complicanze, in particolare cirrosi, HCC e trapianto di fegato, per definire l'appropriatezza d'uso dei DAA.

Contribuire all'ottimizzazione dei protocolli terapeutici e guidare le Istituzioni a prendere decisioni strategiche "informate".

Disegno dello studio

Studio di coorte longitudinale.

Partecipazione di più di 100 Centri Clinici italiani.

Popolazione target: 10.000 pazienti con infezione cronica da HCV.

Follow-up: 5-10 anni.

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Distribuzione dei Centri PITER

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Cari, cari amici:

Un'altra giornata di molto molto lavoro **SOPRATTUTTO DI MONITORAGGIO!!!.**

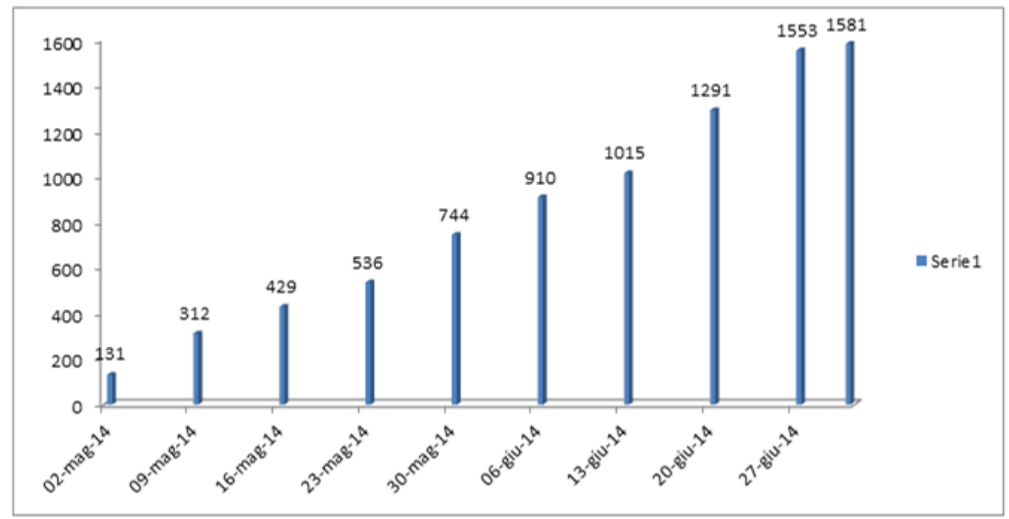
Se tutto va come organizzato oggi, domani siamo " ai primi 1600 pazienti"

Eseguiti anche oggi controlli di monitoraggio programmato:

Oggi eseguite le correzioni per " data di nascita" che, erronamente – risulta uguale e/ simile la data

OGNI MODO QUESTI CONTROLLI VERRANNO ESEGUITI DA ME OGNI LUNEDI, per poi gli altri giorni f

Un bel Istogramma in 3D per illustrare l'andamento dei pazienti arruolati:



ANCORA MONITORAGGIO CONTINUO:

Eseguito come tutti i giorni controlli di monitoraggio, questa settimana ho iniziato a chiedere " f

puliamo le diverse variabili

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I: liliana!! record 3610!! e monitoraggio, chiusura visite, risoluzione quesiti continuo continuo!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!! - Google Chrome

https://webmail.iss.it/owa/?ae=PreFormAction&a=Forward&t=IPM.Note&id=RgAAAAAt8wof7JmUSaYYnDaUXJE2BwDtSeFdliZ6TryqhIhS1DQTAAAAhatzAAB60wVlUBbESoZrToDIrT

Invia | Opzioni... | HTML

- Bozza salvata automaticamente in: 18.50

A... piter

Cc...

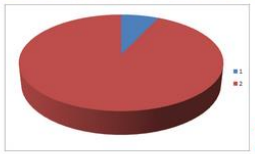
Oggetto: I: liliana!! record 3610!! e monitoraggio, chiusura visite, risoluzione quesiti continuo continuo!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!

Tahoma | 10 | B I U

Da: Weimer Liliana
Inviato: giovedì 8 gennaio 2015 17.25
A: Massella Maurizio; Mirra Marco; Quaranta Maria Giovanna; Falzano Loredana; Fucili Luca; Mallano Alessandra; Di Gregorio Massimiliano; Kondili Loreta; Tosti Maria Elena; Rosato Stefano; Lucattini Stefano
Cc: Vella Stefano
Oggetto: liliana!! record 3610!! e monitoraggio, chiusura visite, risoluzione quesiti continuo continuo!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!

Carissimi!!!!!!:

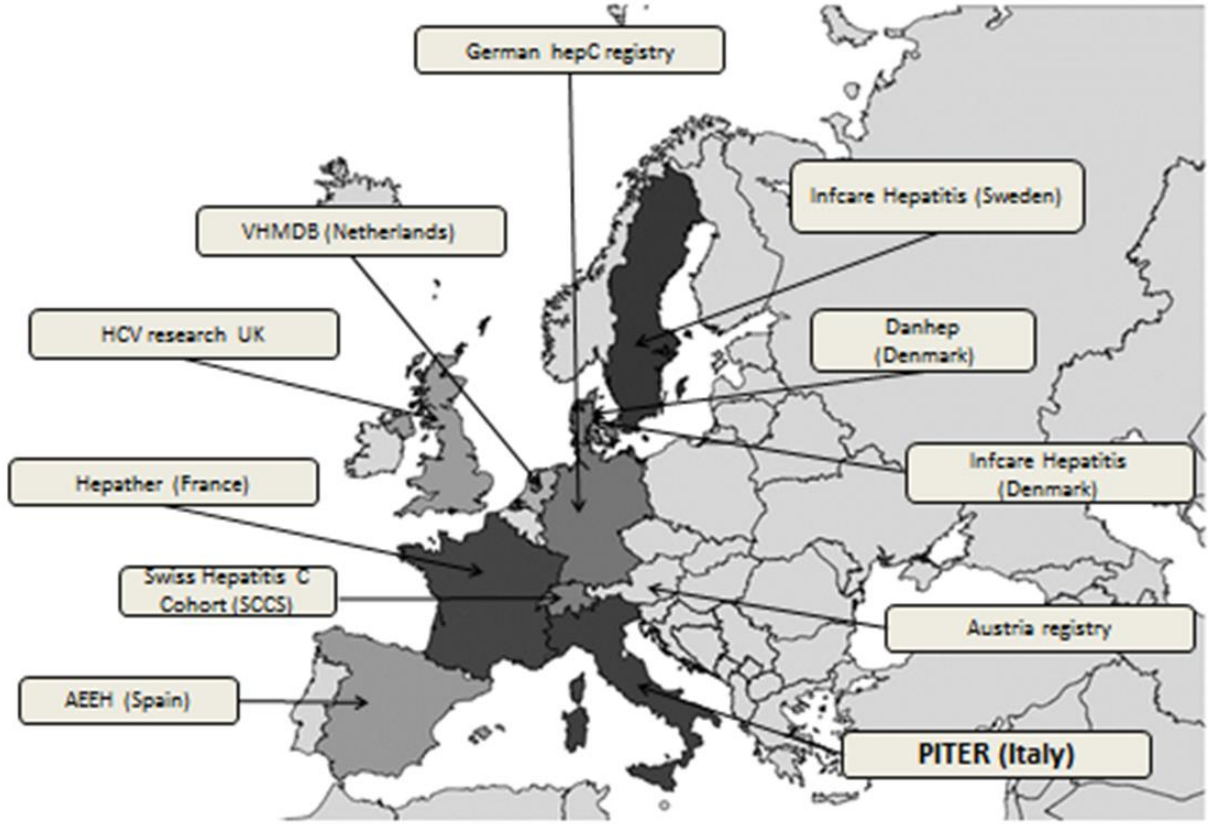
Arruolamenti Piter – mesi

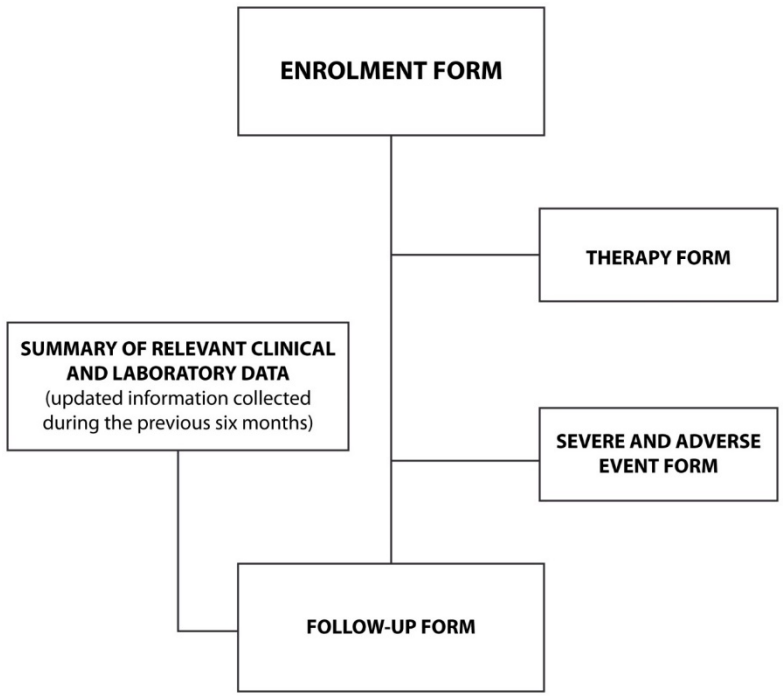


I PRIMI 3610 e 95,6% di CRF chiuse!

-

HCV Cohorts in EUROPE
INSTRUMENTS TO CREATE EVIDENCES





Inclusion criteria

- All HCV-infected patients
  (any clinical and histopathologic stage of HCV infection, infection by any HCV genotype, HBV, HDV,or HIV coinfected patients)

and

- At least 18 years of age who will consecutively visit the outpatient clinics of the participating clinical centres in a given time span (approximately 3- 6 months),

and

- Not on therapy **at the time of enrolment**

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Phases of the Project	Period	Stage
First Enrolment	May-November 2014	Closed
Second Enrolment	December 2014-May 2015	Closed
Third Enrolment	November 15- Jannuary 2016	Closed
Fourth Enrolment	April 2017- October 2017	Closed
Fifth Enrolment	September 2018-February 2018	Closed
Follow-up/ Antiviral Therapies	February 2015	Ongoing
Quality Data Control	Continous Monitoring	Ongoing
Subsequent short enrolment periods	Spring /Fall (each year)	Subsequent short enrolment periods

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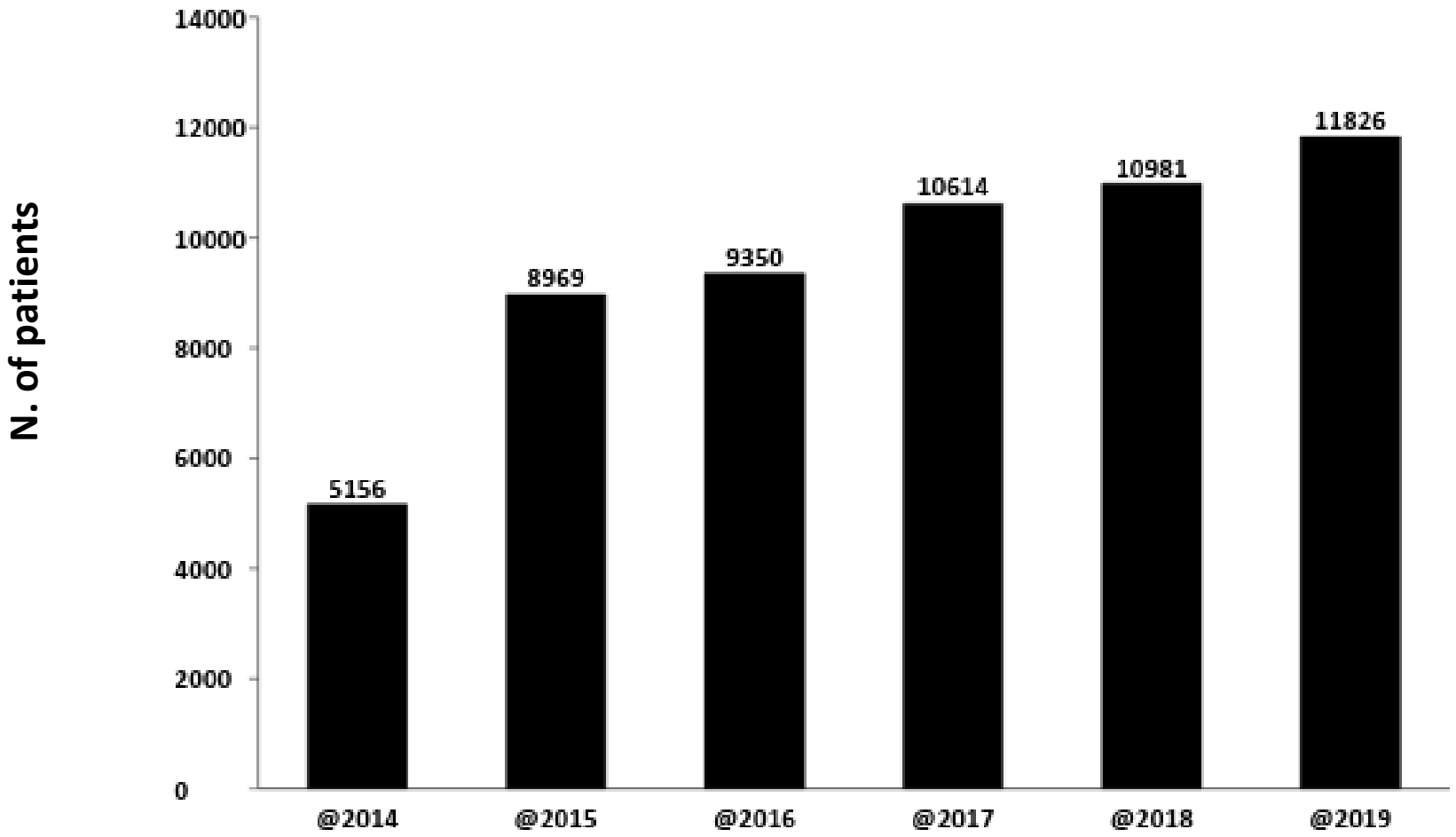
Number of enrolled patients



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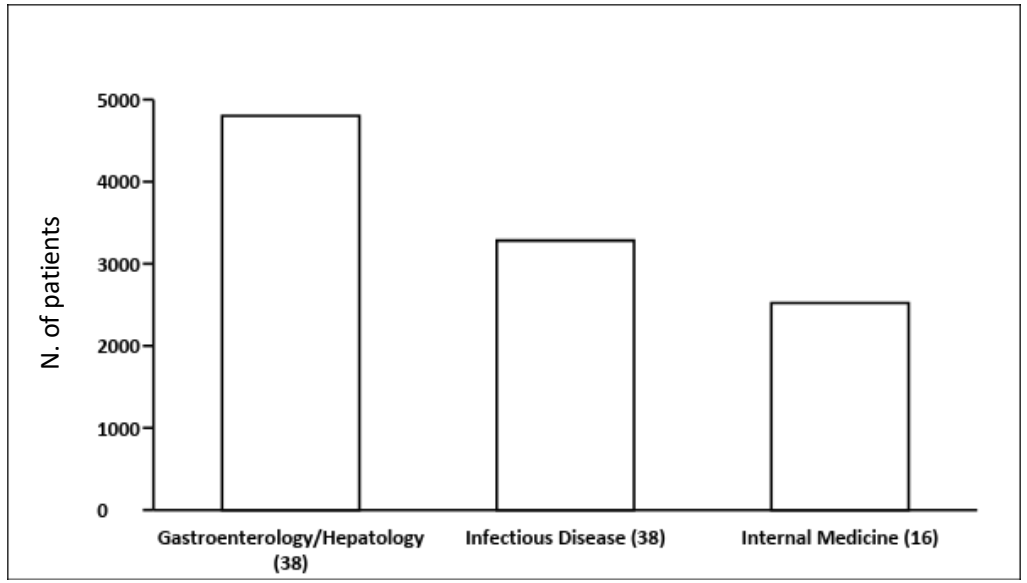
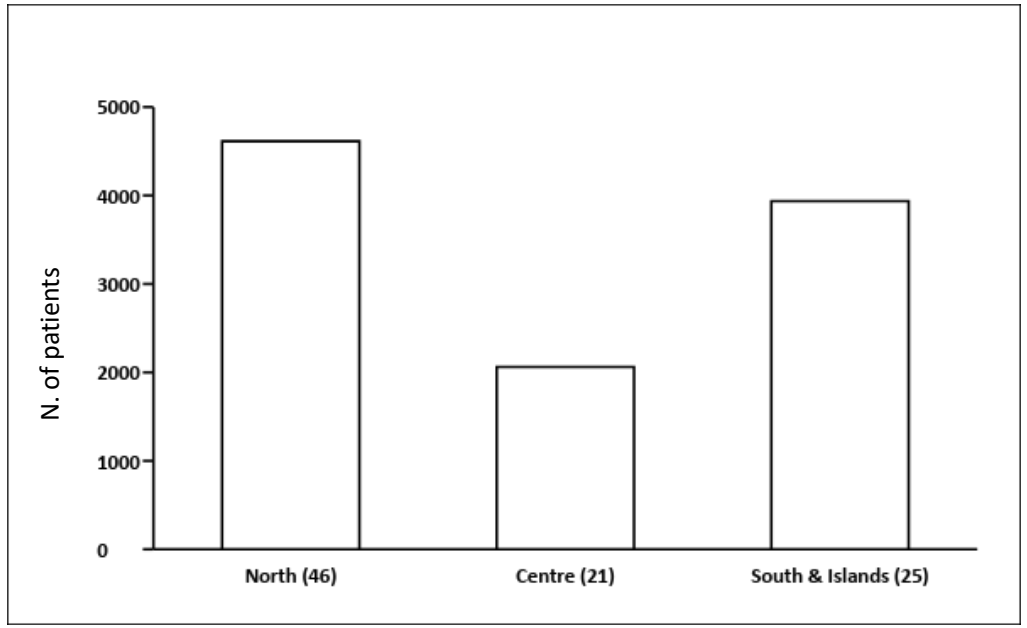
Patients' distribution according to the Clinical Centre specialty and geographical area





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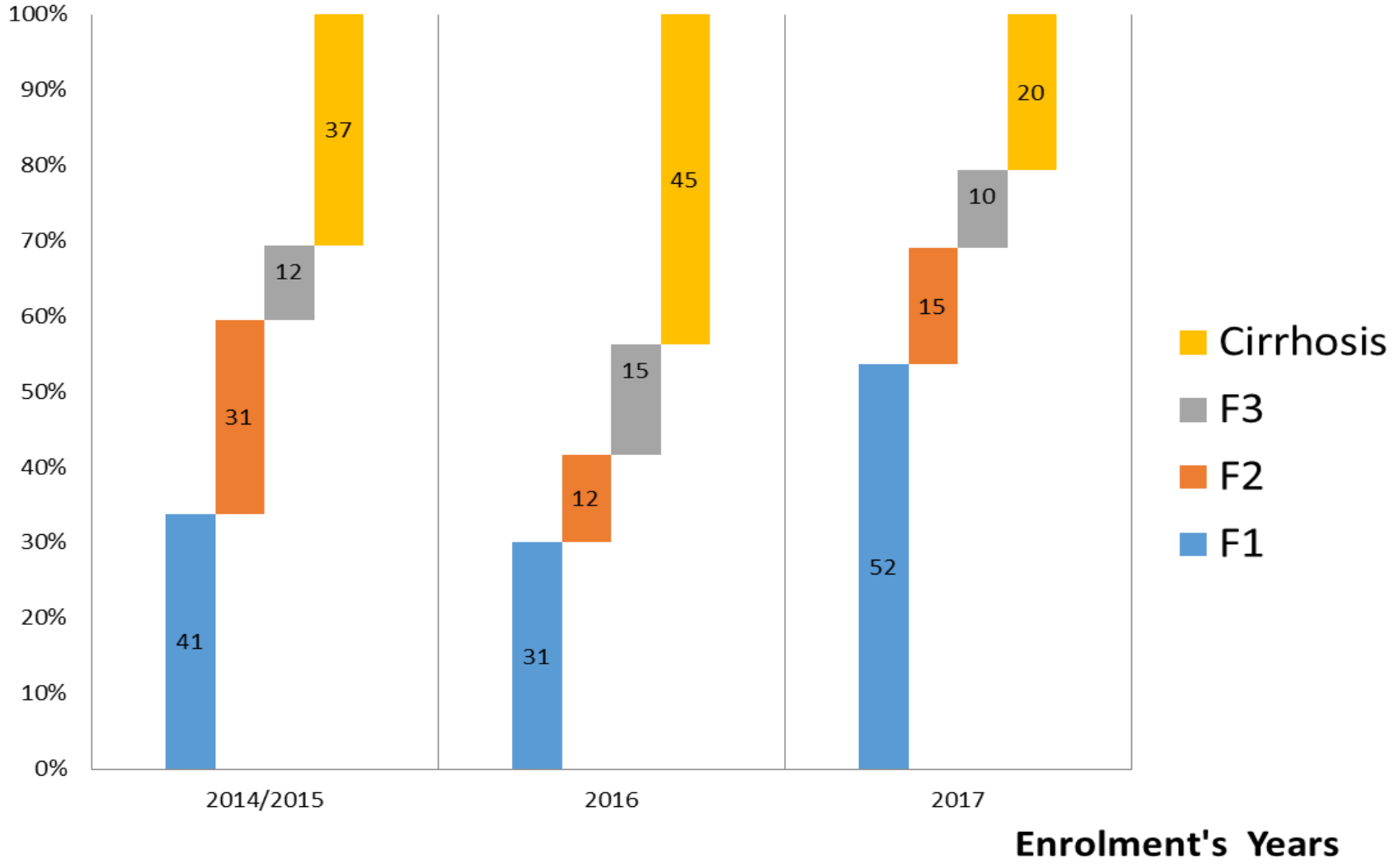
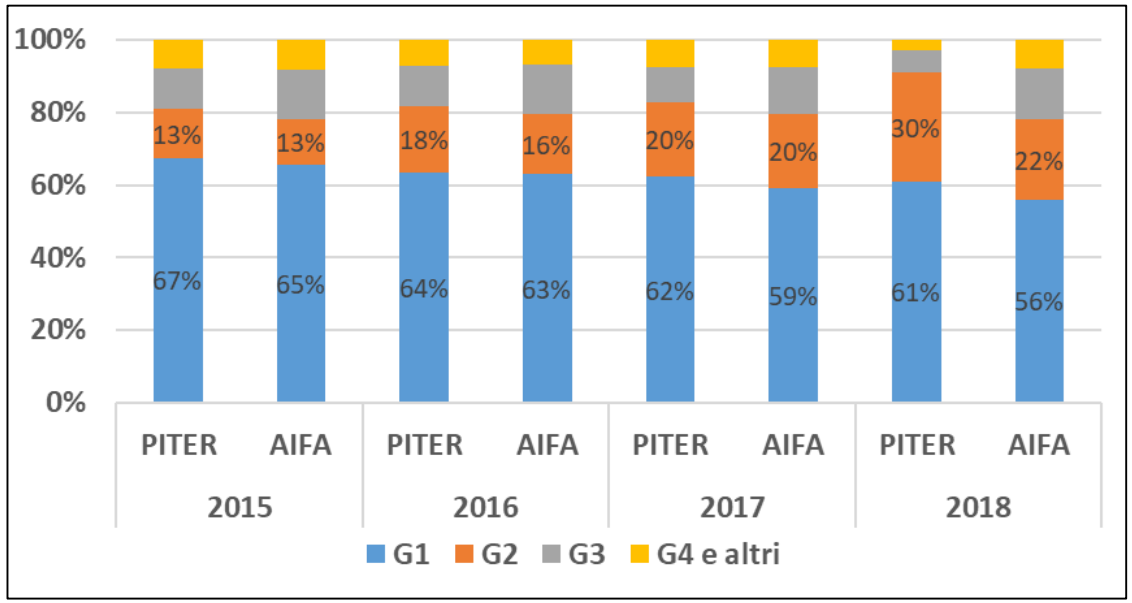
Changes of Fibrosis Stage by Enrolment's periods

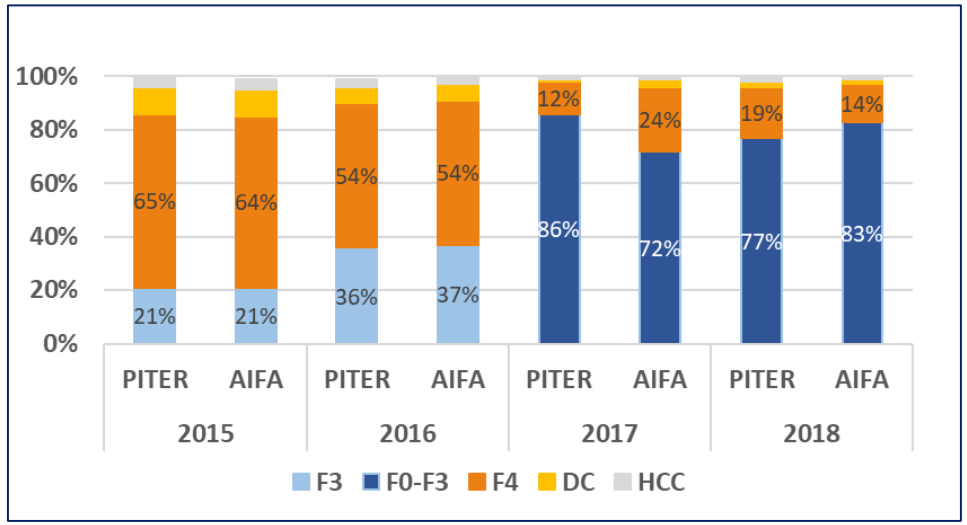


PITER IS A RAPRESENTATTIVE SAMPLE OF PATIENTS TREATED WITH DAA

Genotype Distribution PITER vs Overall Treated patients



Distribution of patients according to the Fibrosis Stage*



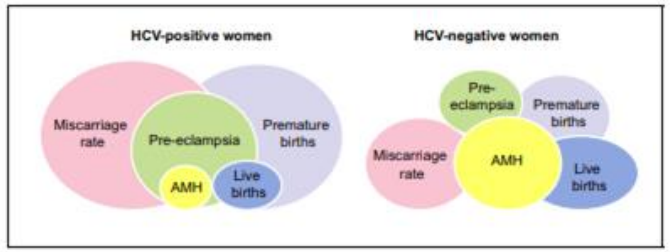
* 2015-2016: same distribution of PITER and overall treated patients (AIFA data)
2017-2018: small differences for AIFA criteria of ellegibility that do not consider fibrosis stage; in PITER all patients are classified by fibrosis stage
2018: data in evaluation

Research Article
Viral Hepatitis

JOURNAL
OF HEPATOLOGY

Premature ovarian senescence and a high miscarriage rate impair fertility in women with HCV

Graphical abstract



Highlights

- Women of child-bearing age who are HCV positive undergo premature ovarian senescence.
- Such women have fewer live births, and higher rates of miscarriage and gestational diabetes.
- Total fertility rate in women who are HCV positive *vs.* the general population is 0.7 *vs.* 1.37.
- Miscarriage rate is significantly reduced by successful HCV treatment.
- Antivirals should be tested for their effects on other adverse pregnancy outcomes.

Authors

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(E. Villa)

Lay summary

Most new cases of HCV infection are among people who inject drugs, many of whom are young women in their child-bearing years. Women of reproductive age who are HCV+ display markers of ovarian senescence. This is associated with an increased burden in terms of infertility and adverse pregnancy outcomes, including stillbirth, miscarriage, fewer live births, and gestational diabetes. Early viral suppression with therapy is likely to mitigate these risks.

Karampatou A, Han X Kondili L, Taliani G, Cianci A, Morisco F, Critelli RM, Baraldi E, Bernabucci V, Troshina G, Guarino M, Tagliavini S, D'Ambrosio F, Bristot L, Turco L, Rosato S, Vella S, Trenti T, Neri I La Marca A, Manthena S, Goldstein AS, Brubo S, Bao Y, Gonzales Y S, Villa E.
&
PITER framework Investigators
Journal of Hepatology 2017

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Data from PITER HCV cohort

- Among 650 women who were HCV positive and miscarriage data were available 42% had a history of miscarriage of whom 44.6% had history of multiple miscarriages (2-8 miscarriages).

- Carries of genotype 1 had lower risk of miscarriages (OR 0.62; 95% CI 0.4-0.9)

- Combination of GT1 and GT2 had lower rate of miscarriages vs GT3 and GT 4

(OR =.4; 95% CI 0.2-0,8).

- History of miscarriages was not associate with: fibrosis stage (F3-4 vs F0-F2); BMI (<25 kg/m^2 vs >25 kg/m^2); presence of cirrhosis, hypertension, diabetes, (presence/vs absent) drug addiction (past/present vs absent) or emloyment status .($p>0.05$)

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Liver INTERNATIONAL

LETTER TO THE EDITOR | Full Access

Mixed cryoglobulinaemia: An important but frequently unrecognized and underestimated HCV-related condition in the real life practice

Loreta A. Kondili, Stefano Vella, Anna Linda Zignego, On behalf of PITER collaborating Group

First published: 09 June 2017 | https://doi.org/10.1111/liv.13490 | Cited by: 3

Dear Editor:

We read with interest the paper "Effectiveness and cost of hepatitis C virus cryoglobulinaemia vasculitis treatment: from interferon-based to direct acting antivirals era",1 and we feel that the combination of effectiveness with a cost analysis is original and increases the awareness about patients with Mixed Cryoglobulinaemia (MC).

A dedicated approach, focusing on the diagnosis and on the impact of treatment of MC, have been included within the Italian Platform for the Study of Viral Hepatitis Therapies (PITER).2 Of the 8005 HCV+ patients enrolled in PITER, only 1678 (21%) have been evaluated for the presence of MC, that was shown in 771 (46%) patients, 266 (35%) of whom were symptomatic (cryoglobulinaemic vasculitis -CryoVas- or MC syndrome –MCS-). Among the centres that considered MC, 64% evaluated cryoglobulinaemia only if MC was clinically suspected. Cryocrit was determined at admission based on Complement/Rheumatoid Factor (RF) levels or only in case of RF positivity (58% and 42% of the centres respectively). Cryo testing was not adequate in 39% of the centres. These results, showed the real-life variability in the diagnostic approach to MC, suggesting, on the one hand, that MC prevalence in HCV+ individuals is generally underestimated, and, on the other hand, that the percentage of MC patients with CryoVas was probably overestimated in centres where MC is not routinely assessed.

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RESEARCH ARTICLE

Real-life data on potential drug-drug interactions in patients with chronic hepatitis C viral infection undergoing antiviral therapy with interferon-free DAAs in the PITER Cohort Study

Loreta A. Kondili, Giovanni Battista Gaeta, Donatella Ieluzzi, Anna Linda Zignego, Monica Monti, Andrea Gori, Alessandro Soria, Giovanni Raimondo, Roberto Filomia, Alfredo Di Leo, Andrea Iannone, Marco Massari, Romina Corsini, [...], Massimo Puoti [view all]

Published: February 28, 2017 • https://doi.org/10.1371/journal.pone.0172159

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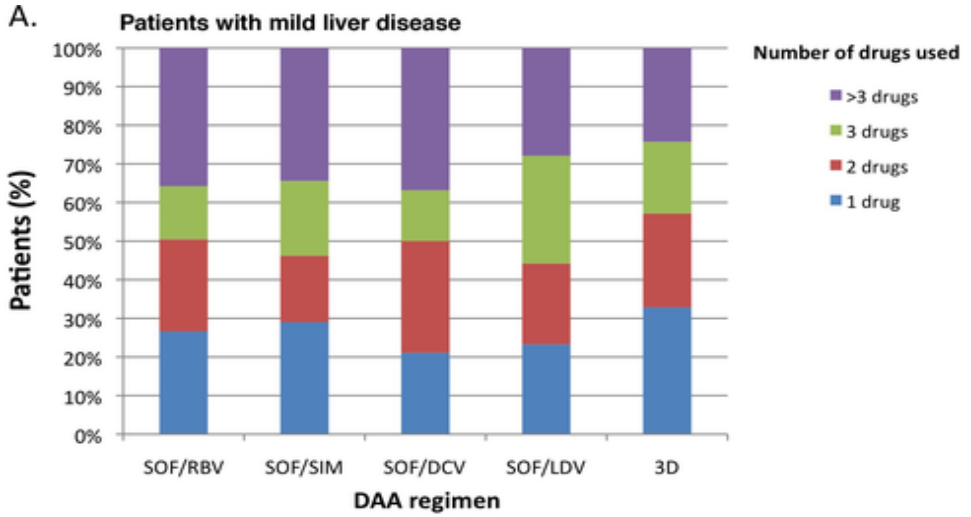
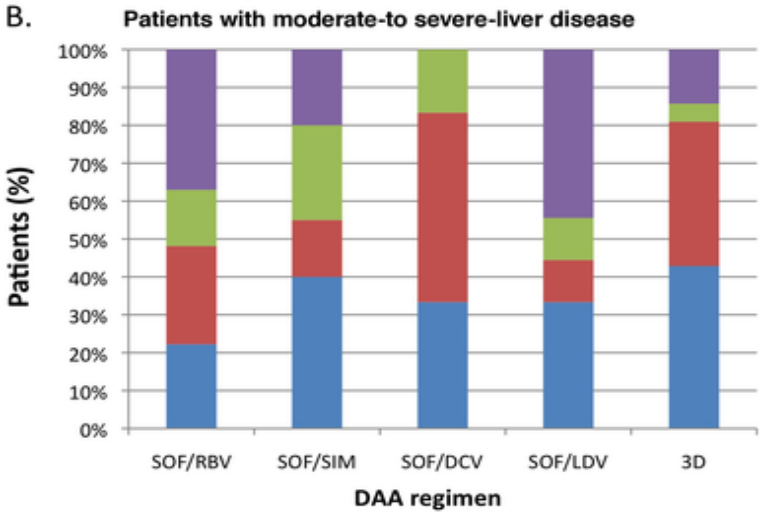
Number of co-medications used and percentage of patients, by DAA regimen, among HCV-infected patients





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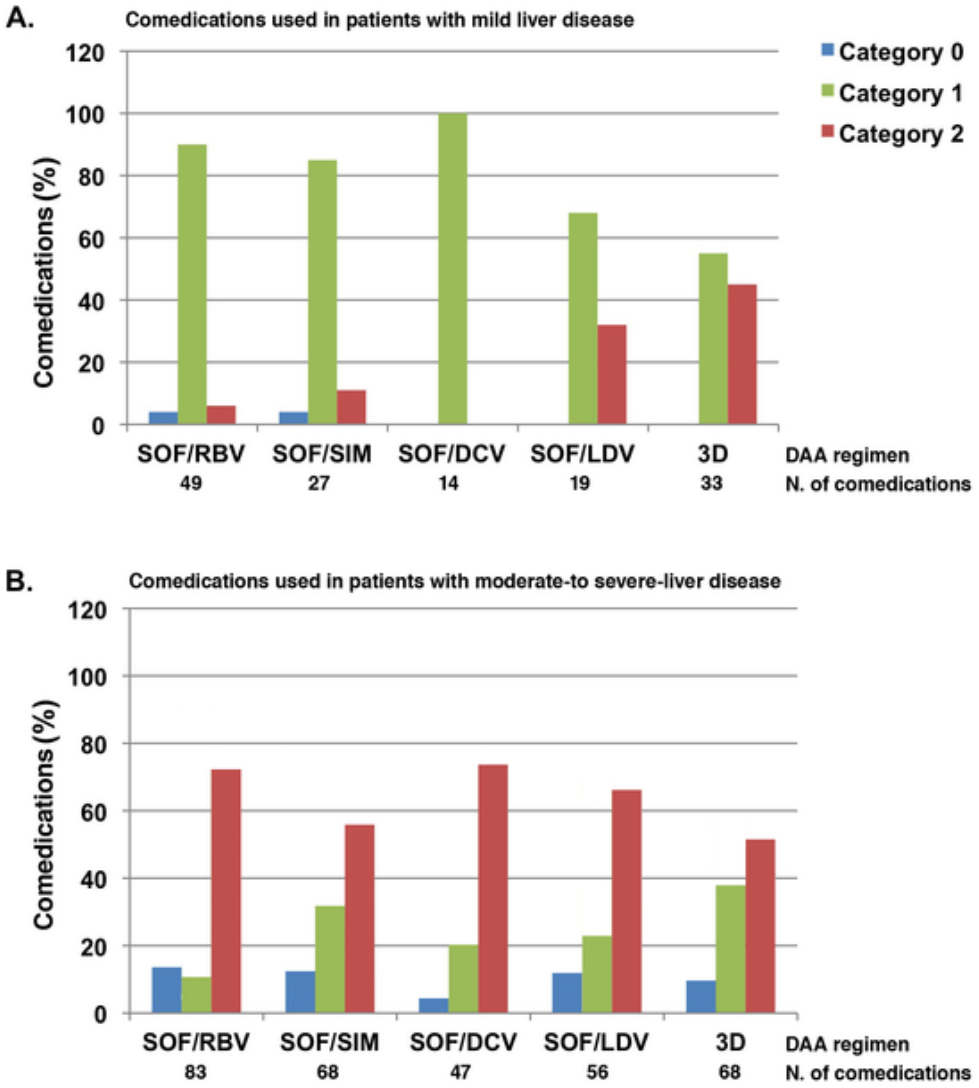
Category of potential DDIs, by DAA regimen and severity of liver disease, among HCV-infected patients



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RESEARCH ARTICLE

Incidence of DAA failure and the clinical impact of retreatment in real-life patients treated in the advanced stage of liver disease: Interim evaluations from the PITER network

Loreta A. Kondili, Giovanni Battista Gaeta, Maurizia Rossana Brunetto, Alfredo Di Leo, Andrea Iannone, Teresa Antonia Santantonio, Adele Giammario, Giovanni Raimondo, Roberto Filomia, Carmine Coppola, Daniela Caterina Amoruso, Pierluigi Blanc, Barbara Del Pin, [...], Edoardo Giovanni Giannini [view all]

Published: October 4, 2017 • https://doi.org/10.1371/journal.pone.0185728

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Failure rates following the first DAA regimen, by HCV genotype and treatment regimen in patients who completed the 12 weeks post treatment evaluation (n = 3,830 patients)

	Overall	HCV genotype N. of failures/N. of treated patients (%)					
DAA regimen	N. of failures/N. of treated patients (%)	1a	1b	2	3	4	5
	139/3830 (3.6)						
SOF+RBV	68/710 (9.6)	5/15 (33.3)	20/56 (35.7)	8/499 (1.6)	32/132 (24.2)	3/8 (37.5)	-
SOF+SIM±RBV	38/683 (5.6)	8/99 (8)	24/520 (4.6)	1/2 (50)	1/1 (100)	3/60 (5)	1/1 (100)
SOF+LDV±RBV	16/1002 (1.6)	3/200 (1.5)	10/752 (1.3)	-	0/1 (0)	3/44 (6.8)	0/5 (0)
3D±RBV	9/894 (1)	3/86 (3.5)	6/806 (0.7)	-	-	0/2 0	-
2D+RBV	2/64 (3.1)	-	-	-	-	2/59 3.4%	0/5 (0)
SOF+DCV±RBV	6/471 (1.3)	0/47 0	1/115 (0.9)	0/55 (0)	5/244 (2)	0/10 (0)	
SIM+DCV	0/6 (0)	-	0/6 (0)	-	-	-	-

https://doi.org/10.1371/journal.pone.0185728.t003

Failure Rate: 140/3.926 (3.6%)

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Univariate and logistic regression analysis linking failure with independent variables

Variables	Crude OR 95% CI	Adjusted OR 95% CI
Age	0.97 (0.95–0.99)	0.97 (0.94–0.98)
Female	0	
Male	1.7 (0.9–2.6)	1.3 (0.8–2.2)
IFN experienced	0	
Naive	1 (0.68–1.46)	1.5 (0.9–2.2)
Genotypes 1	0	
Genotype 2		
Genotype 4/5		
Genotype 3	3.4 (2.2–5.4)	1.9 (1.1–3.5)
F3 Fibrosis stage	0	
F4/Cirrhosis	1.79 (0.9–3.4)	1.25 (0.6–2.5)
Bilirubin levels ≤1.5	0	
Bilirubin levels >1.5	2.08 (1.4–3.06)	1.8 (1.1–3.4)
Platelets count >120,000	0	
Platelets count ≤120,000	1.68 (1.2–2.4)	1.9 (1.1–3.4)
2DAA±RBV treatment	0	
SOF/RBV treatment	2.5 (1.8–3.6)	2.6 (1.6–4.3)

https://doi.org/10.1371/journal.pone.0185728.t002

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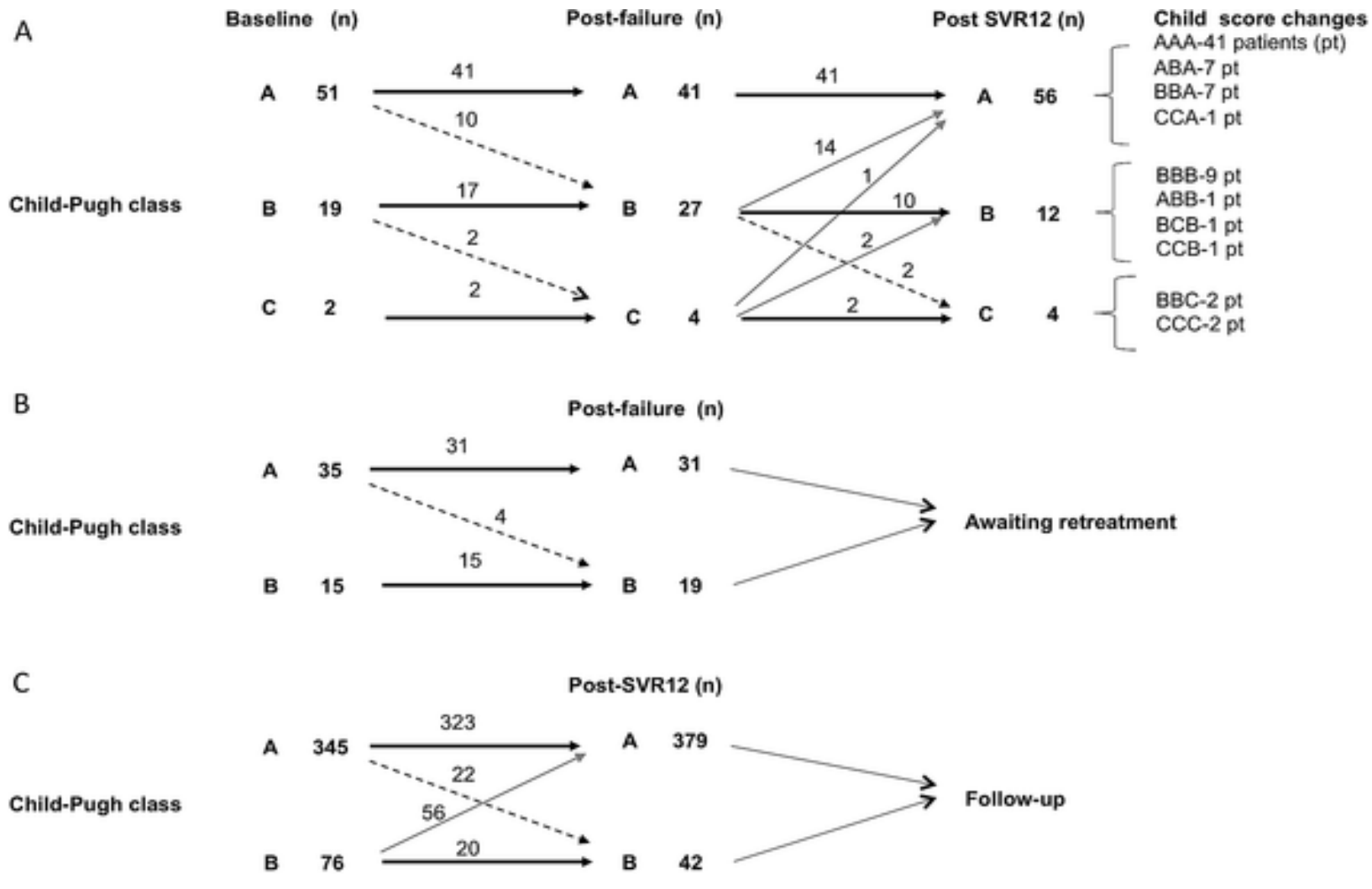
Modifications of liver disease stage following DAA treatment in patients with cirrhosis.



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Clinical Events following the first DAA treatment failure

Overall Median Time:196 days (Range: 38-579 days: 6.42 months).

- Five patients with liver cirrhosis underwent OLT, 3 for liver failure and 2 for development of HCC in patients with child B cirrhosis.

- HCC overall occurrence rate of 16.4% (23/121 cirrhotic patients);
  - diagnosed either during or after treatment in 13%
  - recurrence of a previously cured HCC in 6% (all Child-Pugh class A).

- Child-Pugh class changed from A to B in 12 (10.3%) patients and from B to C in 1 (0.8%) patient.

- Ascites appeared in 15 of 121 patients with cirrhosis (12.3%); in 3 (20.%) of these 15 patients, it constituted the first decompensation.

- Hepatic encephalopathy happened in 9 (7.4%) patients, in 3 (30%) of whom it appeared for the first time following treatment failure.

Predictive Factors for Liver Disease Progression Following the Direct Acting Antivirals Induced Sustained Virological Response: Data from the Italian Platform for the Study of Viral Hepatitis Therapies (PITER) Cohort

LA Kondili[1], MG Quaranta[1], S Rosato[1], LE Weimer[1], F D'Angelo[1], C Coppola[1], AL Zignego[1], MR Brunetto[1], G Raimondo[1], TA Santantonio[1], A Iannone[1], G Taliani[1], M Zuin[1], L Chessa[1], A Craxi[1], G Borgia[1], P Andreone[1], FP Russo[1], P Blanc[1], F Morisco[1], G Parruti[1], F Barbaro[1], S Madonia[1], F Capra[1], M Vinci[1], M Persico[1], L Chemello[1], A Gori[1], M Massari[1], M Puoti[1], A Licata[1], E Villa[1] and PITER Collaborating Group (available at www.progettopiter.it)

[1]Istituto Superiore di Sanità, Rome, [2]Gragnano Hospital, Naples, [3]University of Florence, [4]University Hospital of Pisa, [5]University Hospital of Messina, [6]Ospedali Riuniti, Foggia, [7]University Hospital of Bari, [8]Umberto I Hospital-Sapienza University, Rome, [9]ASST Santi Paolo e Carlo, Milan, [10]University of Cagliari, [11]University of Palermo, [12]Federico II University, Naples, [13]University of Bologna, [14]University of Padua, [15]S.M. Annunziata Hospital, Florence, [16]Spirito Santo General Hospital, Pescara, [17]University Hospital of Padua, [18]Villa Sofia-Cervello Hospital, Palermo, [19]University Hospital of Verona, [20]Niguarda Hospital, Milan, [21]University of Salerno, [22]San Gerardo Hospital, Monza, [23]Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, [24]University Hospital P. Giaccone, Palermo, [25] University of Modena and Reggio Emilia

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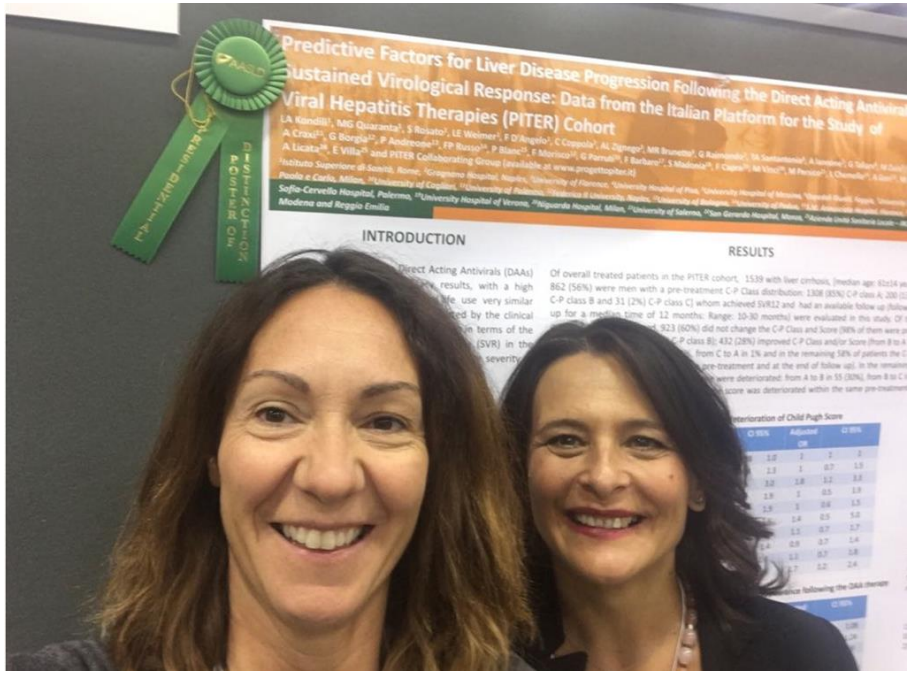

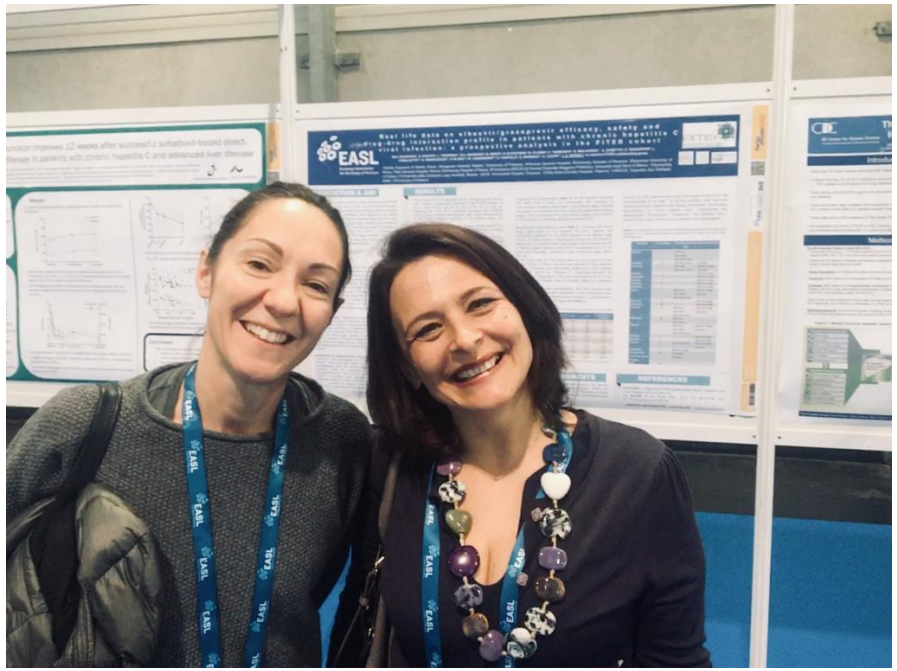

Real life data on elbasvir/grazoprevir efficacy, safety and drug-drug interaction profile in patients with chronic hepatitis C viral infection: a prospective analysis in the PITER cohort

M.G. QUARANTA[1], S. ROSATO[1], L. FERRIGNO[1], D.C. AMORUSO[2], M. MONTI[3], P. DI STEFANO[4], R. FILOMIA[5], F. TAMBURINI[6], G. MIGLIORINO[7], A. ZANETTO[8], E. DEGASPERI[9], L. CAVALLETTO[10], G. BRANCACCIO[11], P. BLANC[12], M. CANNIZZARO[13], E. CASTELLI[9], G. MORSICA[14], A. LICATA[15], L.A. KONDILI[1] on behalf of PITER collaborating group

1Istituto Superiore di Sanità, Rome; 2Gragnano Hospital, Naples; 3University of Florence; 4Pescara General Hospital; 5University Hospital of Messina; 6Sapienza University of Rome; 7San Gerardo Hospital, Monza; 8University Hospital of Padua; 9Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano; 10University of Padua; 11Università della Campania Luigi Vanvitelli, Naples; 12S.M. Annunziata Hospital, Florence; 13Villa Sofia-Cervello Hospital, Palermo; 14IRCCS, Ospedale San Raffaele, Milan; 15University of Palermo

EASL European Association for the Study of the Liver

PITER Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

Expected Outcomes

- 1) Production of a continuously updated picture of the epidemiology of HCV chronic infection at the national level;
- 2) Evaluation of the real-life long-term impact of new DAA therapies on the outcomes of chronic HCV infection in terms of morbidity and mortality in patients at different stages of disease;
- 3) Monitoring of the use of the different options for DAA therapy and the long-term safety of DAAs and DAA combinations in a real-life setting, as well as access to DAAs by geographic area and gender;
- 4) Development of appropriate algorithms for care and therapy for special, difficult-to-treat and difficult to reach populations;

Evaluation of the economic impact of the progressive introduction of DAAs and their cost-effectiveness in patients at different stages of liver disease

Treatment indipendently by the fibrosis stage brings significant improvements in the health status and is sustainable

HEPATOLOGY

HEPATOLOGY, VOL. 66, NO. 6, 2017

Modeling Cost-Effectiveness and Health Gains of a "Universal" Versus "Prioritized" Hepatitis C Virus Treatment Policy in a Real-Life Cohort

Loreta A. Kondili,[1] Federica Romano,[2] Francesca Romana Rolli,[2] Matteo Ruggeri,[2] Stefano Rosato,[1] Maurizia Rossana Brunetto,[3] Anna Linda Zignego,[4] Alessia Ciancio,[5] Alfredo Di Leo,[6] Giovanni Raimondo,[7] Carlo Ferrari,[8] Gloria Taliani,[9] Guglielmo Borgia,[10] Teresa Antonia Santantonio,[11] Pierluigi Blanc,[12] Giovanni Battista Gaeta,[13] Antonio Gasbarrini,[2] Luchino Chessa,[14] Elke Maria Erne,[15] Erica Villa,[16] Donatella Ieluzzi,[17] Francesco Paolo Russo,[15] Pietro Andreone,[18] Maria Vinci,[19] Carmine Coppola,[20] Liliana Chemello,[15] Salvatore Madonia,[21] Gabriella Verucchi,[18] Marcello Persico,[22] Massimo Zuin,[23] Massimo Puoti,[19] Alfredo Alberti,[15] Gerardo Nardone,[13] Marco Massari,[24] Giuseppe Montalto,[25] Giuseppe Foti,[26] Maria Grazia Rumi,[23] Maria Giovanna Quaranta,[1] Americo Cicchetti,[2] Antonio Craxì,[25] and Stefano Vella,[1] on behalf of the PITER Collaborating Group*

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Cost-Effectiveness Analysis

Scenarios of treatment policy

Two scenarios of policies for DAA IFN-free regimens were simulated and compared:

- Policy 1: “universal”: Treat all patients, independently of the fibrosis stage;
- Policy 2: Treat only “prioritized” patients and delay treatment of the remaining patients until reaching fibrosis stage F3.

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Results of the base case analysis
Italy Scenario

	Costs	QALYs	Incremental Costs	Incremental QALYs
Strategy 1	€ 271.366.854	90.926	€ 31.083.475	3.495
Strategy 2	€ 240.283.379	87.430		
ICER			€ 8.893/QALY	

European scenario

Medium European costs of liver disease stages was used

DAA prices were varied : € 15,000-45,000 (Mean cost= € 30,000)

ICER obtained using Policy1 was € 19,541.75/QALY

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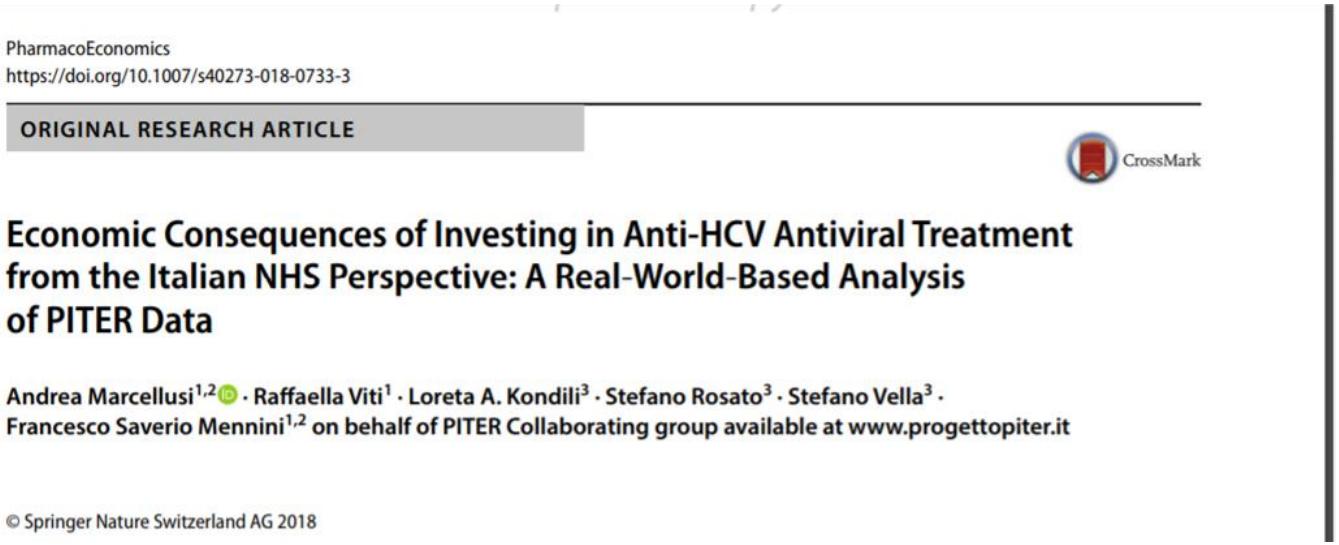
CEIS TOR VERGATA

Economic Evaluation and HTA



PharmacoEconomics
https://doi.org/10.1007/s40273-018-0733-3

ORIGINAL RESEARCH ARTICLE

CrossMark

Economic Consequences of Investing in Anti-HCV Antiviral Treatment from the Italian NHS Perspective: A Real-World-Based Analysis of PITER Data

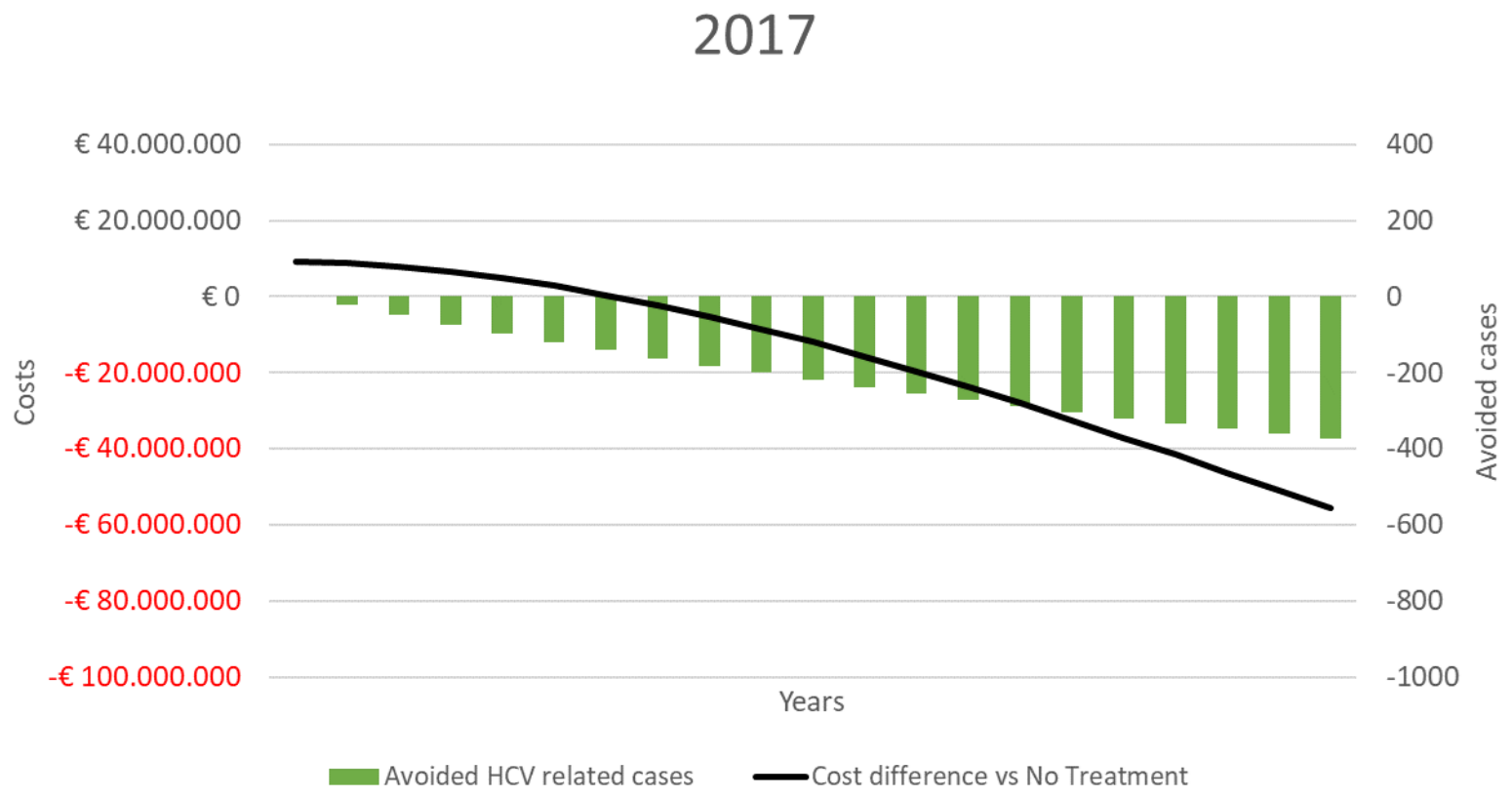
Andrea Marcellusi[1,2] · Raffaella Viti[1] · Loreta A. Kondili[3] · Stefano Rosato[3] · Stefano Vella[3] · Francesco Saverio Mennini[1,2] on behalf of PITER Collaborating group available at www.progettopiter.it

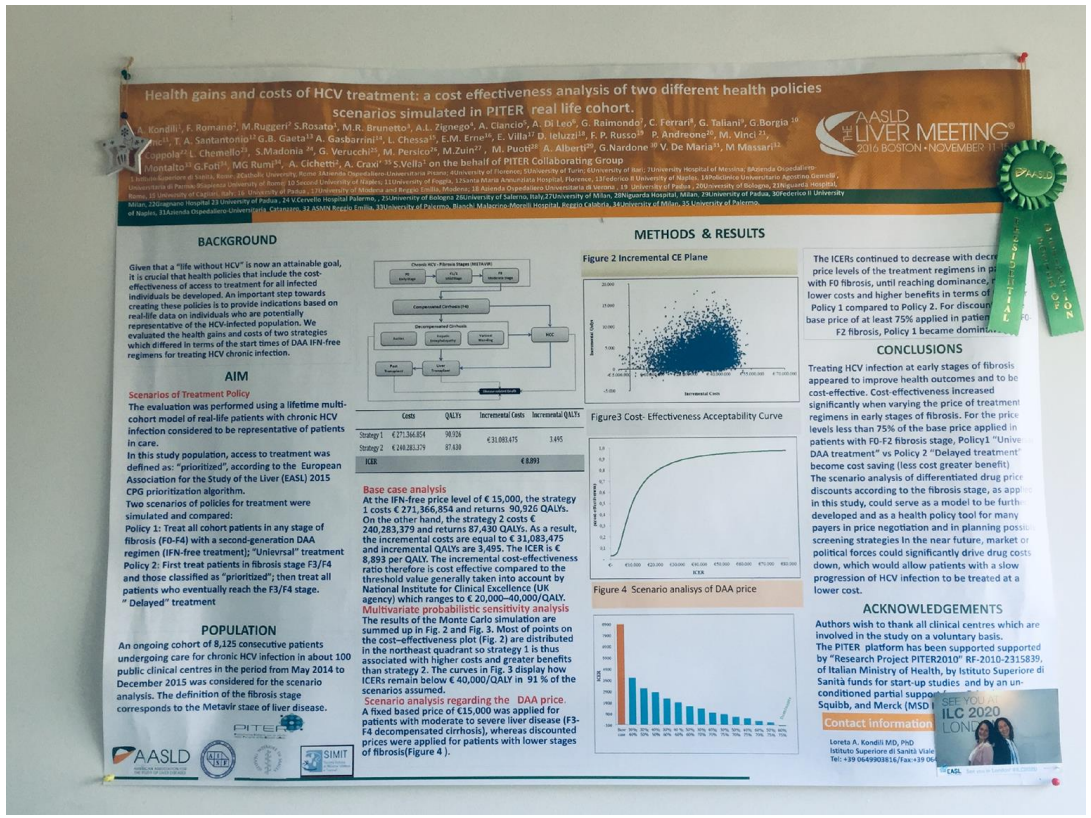
Interim Evaluation confirmed for Overall treated patients in Italy, Romania, Spain England

Final results : Ongoing evaluation

Results

- Standardized for 1.000 treated patients





Health gains and costs of HCV treatment: a cost effectiveness analysis of two different health policies scenarios simulated in PITER real life cohort.

A. Kondili[1], F. Romano[2], M.Ruggeri[3] S.Rosato[4], M.R. Brunetto[5], A.L. Zignego[6], A. Clancio[7], A. Di Leo[8], G. Raimondo[9], C. Ferrari[8], G. Taliani[3], G.Borgia[10] [11], T. A. Santantonio[12] G.B. Gaeta[13] A. Gasbarrini[14], L. Chessa[15], E.M. Erne[16], E. Villa[17] D. Ieluzzi[18], F. P. Russo[19] P. Andreone[20], M. Vinci[21], Coppola[22] L. Chemello[23], S.Madonia[24], G. Verucchi[25], M. Persico[26], M.Zuin[27], M. Puoti[28] A. Alberti[29], G.Nardone[30] V. De Maria[31], M Massari[32] Montalto[33] G.Foti[34], MG Rumi[35], A. Cichetti[1], A. Craxi'[13] S.Vella[1] on the behalf of PITER Collaborating Group

1 Istituto Superiore di Sanità, Rome , 2Cattolic University, Rome 3Azienda Ospedaliero-Universitaria Pisana, 4University of Florence; 5University of Turin; 6University of Bari; 7University Hospital of Messina; 8Azienda Ospedaliero Universitaria di Parma, 9Sapienza University of Rome; 10 Second University of Naples; 11University of Foggia, 12Santa Maria Annunziata Hospital, Florence, 13Federico II University of Naples, 14Policlinico Universitario Agostino Gemelli , Rome; 15 University of Cagliari, Italy; 16 University of Padua , 17University of Modena and Reggio Emilia, Modena; 18 Azienda Ospedaliero Universitaria di Verona , 19 University of Padua, 20University of Bologna, 21Niguarda Hospital, Milan, 22Grugnano Hospital 23 University of Padua , 24 V.Cervello Hospital Palermo, , 25University of Bologna 26University of Salerno, Italy,27University of Milan, 28Niguarda Hospital, Milan, 29University of Padua, 30Federico II University of Naples, 31Azienda Ospedaliero-Universitaria Catanzaro, 32 ASMN Reggio Emilia, 33University of Palermo, Biagio Maltagirone Morelli Hospital, Reggio Calabria, 34University of Milan, 35 University of Palermo

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BACKGROUND

Given that a "life without HCV" is now an attainable goal, it is crucial that health policies that include the cost-effectiveness of access to treatment for all infected individuals be developed. An important step towards creating these policies is to provide indications based on real-life data on individuals who are potentially representative of the HCV-infected population. We evaluated the health gains and costs of two strategies which differed in terms of the start times of DAA IFN-free regimens for treating HCV chronic infection.

AIM

Scenarios of Treatment Policy

The evaluation was performed using a lifetime multi-cohort model of real-life patients with chronic HCV infection considered to be representative of patients in care.

In this study population, access to treatment was defined as: "prioritized", according to the European Association for the Study of the Liver (EASL) 2015 CPG prioritization algorithm.

Two scenarios of policies for treatment were simulated and compared:

Policy 1: Treat all cohort patients in any stage of fibrosis (F0-F4) with a second-generation DAA regimen (IFN-free treatment); "Univrsal" treatment

Policy 2: First treat patients in fibrosis stage F3/F4 and those classified as "prioritized"; then treat all patients who eventually reach the F3/F4 stage.

" Delayed" treatment

POPULATION

An ongoing cohort of 8,125 consecutive patients undergoing care for chronic HCV infection in about 100 public clinical centres in the period from May 2014 to December 2015 was considered for the scenario analysis. The definition of the fibrosis stage corresponds to the Metavir staee of liver disease.

METHODS & RESULTS

	Costs	QALYs	Incremental Costs	Incremental QALYs
Strategy 1	€ 271,366,854	90,926	€ 31,083,475	3,495
Strategy 2	€ 240,283,379	87,430		
ICER			€ 8,893	

Figure 2 Incremental CE Plane

Figure3 Cost- Effectiveness Acceptability Curve

Figure 4 Scenario analisys of DAA price

Base case analysis

At the IFN-free price level of € 15,000, the strategy 1 costs € 271,366,854 and returns 90,926 QALYs. On the other hand, the strategy 2 costs € 240,283,379 and returns 87,430 QALYs. As a result, the incremental costs are equal to € 31,083,475 and incremental QALYs are 3,495. The ICER is € 8,893 per QALY. The incremental cost-effectiveness ratio therefore is cost effective compared to the threshold value generally taken into account by National Institute for Clinical Excellence (UK agency) which ranges to € 20,000–40,000/QALY.

Multivariate probabilistic sensitivity analysis

The results of the Monte Carlo simulation are summed up in Fig. 2 and Fig. 3. Most of points on the cost–effectiveness plot (Fig. 2) are distributed in the northeast quadrant so strategy 1 is thus associated with higher costs and greater benefits than strategy 2. The curves in Fig. 3 display how ICERs remain below € 40,000/QALY in 91 % of the scenarios assumed.

Scenario analysis regarding the DAA price.

A fixed based price of €15,000 was applied for patients with moderate to severe liver disease (F3-F4 decompensated cirrhosis), whereas discounted prices were applied for patients with lower stages of fibrosis(Figure 4).

The ICERs continued to decrease with decr… price levels of the treatment regimens in p… with F0 fibrosis, until reaching dominance, … lower costs and higher benefits in terms of … Policy 1 compared to Policy 2. For discoun… base price of at least 75% applied in patien… F2 fibrosis, Policy 1 became domin…

CONCLUSIONS

Treating HCV infection at early stages of fibrosis appeared to improve health outcomes and to be cost-effective. Cost-effectiveness increased significantly when varying the price of treatment regimens in early stages of fibrosis. For the price levels less than 75% of the base price applied in patients with F0-F2 fibrosis stage, Policy1 "Unive… DAA treatment" vs Policy 2 "Delayed treatment" become cost saving (less cost greater benefit)

The scenario analysis of differentiated drug price discounts according to the fibrosis stage, as appl… in this study, could serve as a model to be furth… developed and as a health policy tool for many payers in price negotiation and in planning possi… screening strategies In the near future, market or political forces could significantly drive drug costs down, which would allow patients with a slow progression of HCV infection to be treated at a lower cost.

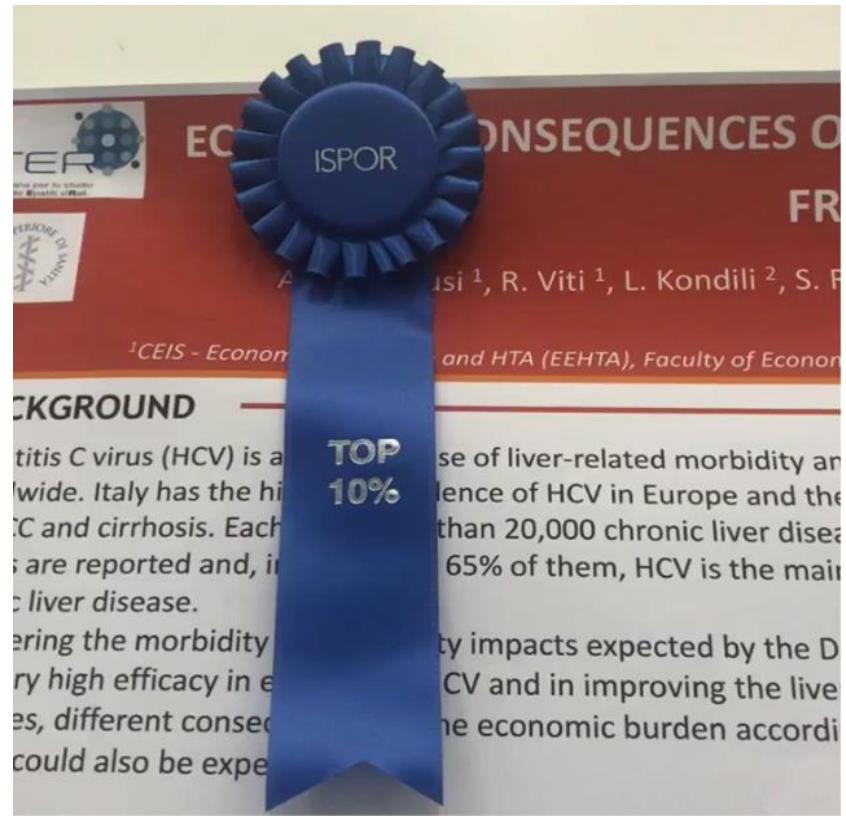
ACKNOWLEDGEMENTS

Authors wish to thank all clinical centres which are involved in the study on a voluntary basis.

The PITER platform has been supported supported by "Research Project PITER2010" RF-2010-2315839, of Italian Ministry of Health, by Istituto Superiore di Sanità funds for start-up studies and by an un-conditioned partial suppo… Squibb, and Merck (MSD …

Contact information

Loreta A. Kondili MD, PhD
Istituto Superiore di Sanità Viale …
Tel: +39 0649903816/Fax:+39 06…



Tutto Non letti Più recente ↓

ALFREDO ALBERTI
Re: Congratulazioni a Tutti 24/07/2017
Molti, molti complimenti per

Kondili Loreta
I: Congratulazioni a Tutti 23/07/2017
Questo era il piu' bello e

Gasbarrini Antonio
Re: Congratulazioni a Tutti 23/07/2017
Complimenti Loreta e

Luchino Chessa
Re: Congratulazioni a Tutti 23/07/2017
Carissima Loreta, tantissimi

Maria Vinci
Re: Congratulazioni a Tutti 23/07/2017
Grazie Loreta mi unisco a

Massari Marco
RE: Congratulazioni a Tutti 23/07/2017
Cara Loreta, grazie a te per

Americo Cicchetti
Re: Congratulazioni a Tutti 23/07/2017
Cara Loreta grazie per

Kondili Loreta
Re: Congratulazioni a Tutti 23/07/2017
Invece io ti voglio piu' bene

Massimo Puoti
Re: Congratulazioni a Tutti 23/07/2017
Cara Loreta, Complimenti

Pietro Andreone
Re: Congratulazioni a Tutti 23/07/2017
Grande Loreta. Ti voglio più

Prof. Guglielmo Borg...
Re: Congratulazioni a Tutti 23/07/2017
Cara Loreta, Grazie e

Prof Gerardo Nardone
R: Congratulazioni a Tutti 23/07/2017

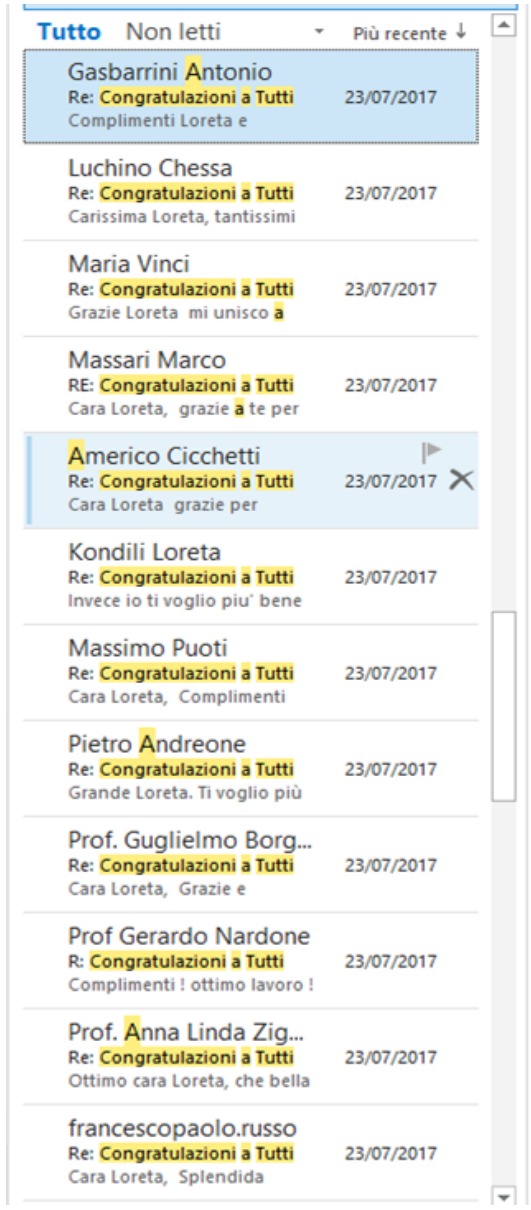
ALFREDO ALBERTI <alfredo.alberti@gmail.com> Kondili Loreta 24/07/2017

Re: Congratulazioni a Tutti

L'utente ha risposto al messaggio in data 22/10/2017 22:14.
Le interruzioni di riga in eccesso sono state rimosse dal messaggio.

Molti, molti complimenti per un importante contributo in un settore scientificamente "delicato" e grazie A Alberti

Il 22 luglio 2017 22:40, Kondili Loreta <loreta.kondili@iss.it> ha scritto:
> Carissimi Professori e colleghi,
>
>
> avete gia' ricevuto la notizia dell'accettazione del nostro lavoro
>
> Modelling cost-effectiveness and health gains of a universal vs.
> prioritized HCV treatment policy in a real-life cohort per la
> publicazione in Hepatology.
>
> A nome del gruppo collaborattivo di PITER e di Stefano ringrazio
> tanttissimo voi, i vostri collaboratori e tutto il PITER
> Collaboratting Group per aver fatto di PITER un enorme potenzialita'.
> Abbiamo circa 9700 pazienti arruolati, circa 6000 dati di follow up e
> piu' di 3000 dati di terapia tutto in aggiornamento continuo!
>
> Vi volevo anche comunicare che l'ufficcio stampa dell'ISS ha chiesto
> di publicare la notizia e preparera' un comunicato stampa che aparira'
> nonappena la comparsa del lavoro. (Il lavoro e' ancora sotto embargo
> di publicazione da Hepatology).
>
> Inoltre il Notiziario dell'ISS pubblichera' una sintesi del lavoro che
> riconoscera' come authorship il contributo di tutto PITER
> Collaborating Group. (anche qui non prima della comparsa del lavoro
> in Hepatology)
>
> Altri lavori sia di modellistica che di outcome clinici sono in corso
> e come sempre l'authorship includera' TUTTI voi che credete e avete
> tanto contribuito in PITER.
>



Gasbarrini Antonio <Antonio.Gasbarrini@unicatt.it> Luchino Chessa; Kondili Loreta; + 41 23/07/2

Re: Congratulazioni a Tutti

Messaggio inoltrato in data 23/07/2017 23:42.
Fare clic qui per scaricare le immagini. Per motivi di privacy, il download automatico di alcune immagini del messaggio non è stato eseguito.

Complimenti Loreta e Stefano, grande lavoro di squadra.
La Vostra dedizione e caparbieta' sono state peraltro straordinarie.
Antonio

Inviato da iPad

Il giorno 23 lug 2017, alle ore 22:01, Luchino Chessa <lchessa@medicina.unica.it> ha scritto:

> Carissima Loreta, tantissimi complimenti a te per il tuo continuo lavoro e la tua dedizione!!! E' un grande risultato, ma non solo scientifico; è infatti la dimostrazione che fare comunità, lavorare tutti insieme, è la chiave del successo.
> Un abbraccio e buona estate a te, a Stefano e a tutti.
> Luchino
>
> Luchino Chessa, MD
> Medicina Interna e Malattie del Fegato,
> Ambulatori di Epatologia
> Policlinico Universitario Duilio Casula, AOU di Cagliari
> S.S. 554 09042 Monserrato (CA)
>
> Professore Aggregato
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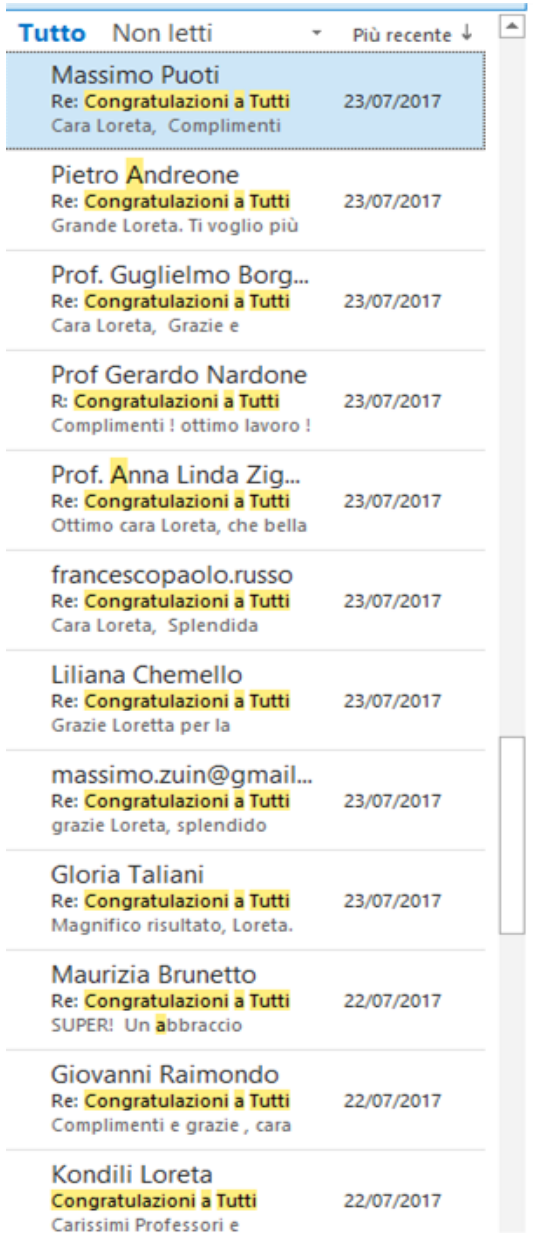
> Cittadella Universitaria
> S.S. 554 09042 Monserrato (CA)
>
> Recapiti telefonici:
> Studio:Tel/Fax 0706754304
> Ambulatorio di Epatologia: 07051096099
> Mobile: 3287298942



Massimo Puoti <massimo.puoti@fastwebnet.it> federica.romano@unicatt.it; + 42 23/07/20

Re: Congratulazioni a Tutti

Messaggio inoltrato in data 05/05/2019 14:19.

Cara Loreta,
Complimenti sopratutto a te ed a tutti. E' un lavoro estremamente rilevante che partendo dai dati di vita reale forniti da tutti noi definisce le coordinate farmaco economiche dei progetti di trattamento di HCV. Credo sia stato estremamente utile per la politica del farmaco italiana e sarà molto utile per tanti altri paesi. Un lavoro di "comunita'" di cui la nostra comunità epatologia deve andare orgogliosa. Brava Loreta è bravo Stefano
Massimo

Inviato da iPhone

Il giorno 22 lug 2017, alle ore 16:40, Kondili Loreta <loreta.kondili@iss.it> ha scritto:

> Carissimi Professori e colleghi,
>
> avete gia' ricevuto la notizia dell'accettazione del nostro lavoro
>
> Modelling cost-effectiveness and health gains of a universal vs. prioritized HCV treatment policy in a real-life cohort per la publicazione in Hepatology.
>
> A nome del gruppo collaborattivo di PITER e di Stefano ringrazio tanttissimo voi, i vostri collaborattori e tutto il *PITER Collaboratting Group* per aver fatto di PITER un enorme potenzialita'. Abbiamo circa 9700 pazienti arruolati, circa 6000 dati di follow up e piu' di 3000 dati di terapia tutto in aggiornamento continuo!
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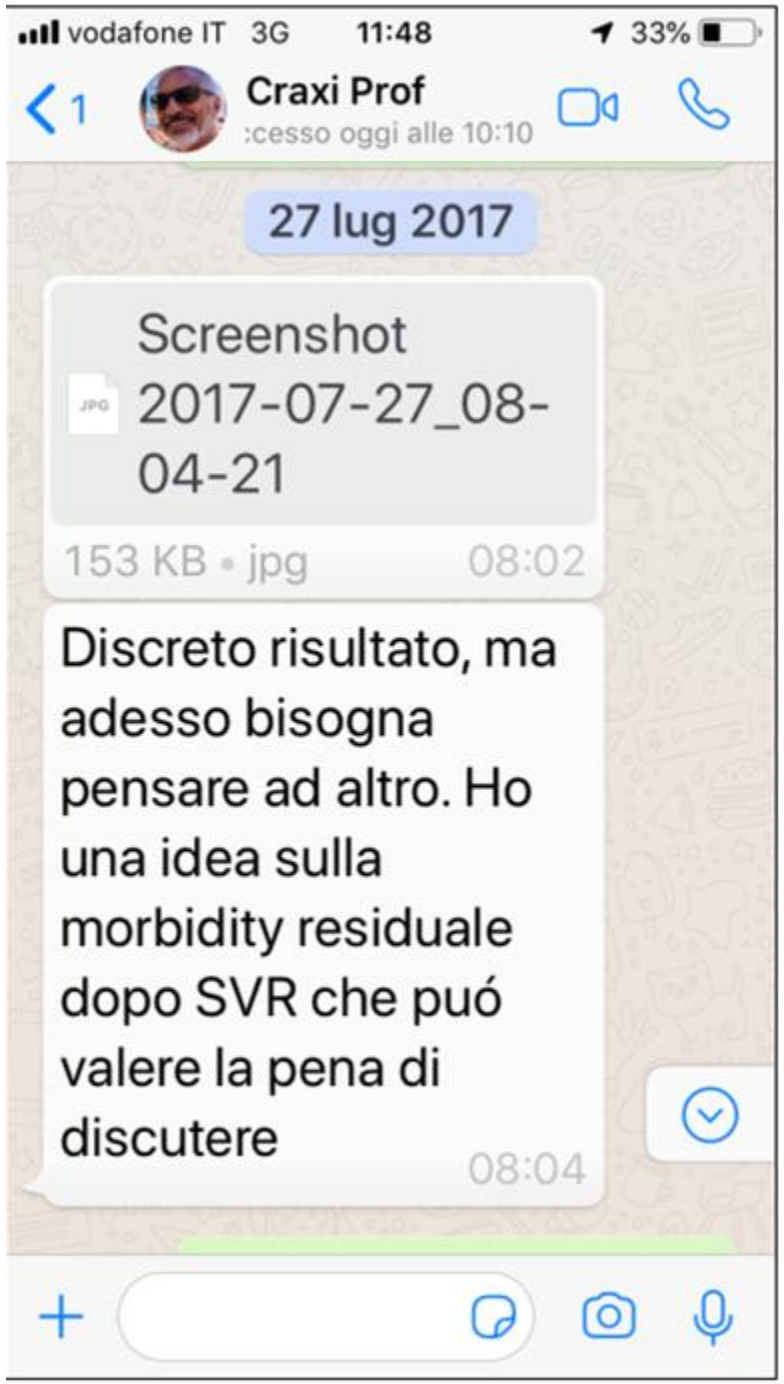
> Vi volevo anche comunicare che l'ufficcio stampa dell'ISS ha chiesto di publicare la notizia e preparera' un comunicato stampa che aparira' nonappena la comparsa del lavoro. (Il lavoro e' ancora sotto embargo di publicazione da Hepatology).
>
> Inoltre il Notiziario dell'ISS pubblichera' una sintesi del lavoro che riconoscera' come authorship il contributo di tutto *PITER Collaborating Group*. (anche qui non prima della comparsa del lavoro in Hepatology)


vodafone IT 3G 11:48 33%
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Craxi Prof
:cesso oggi alle 10:10
27 lug 2017
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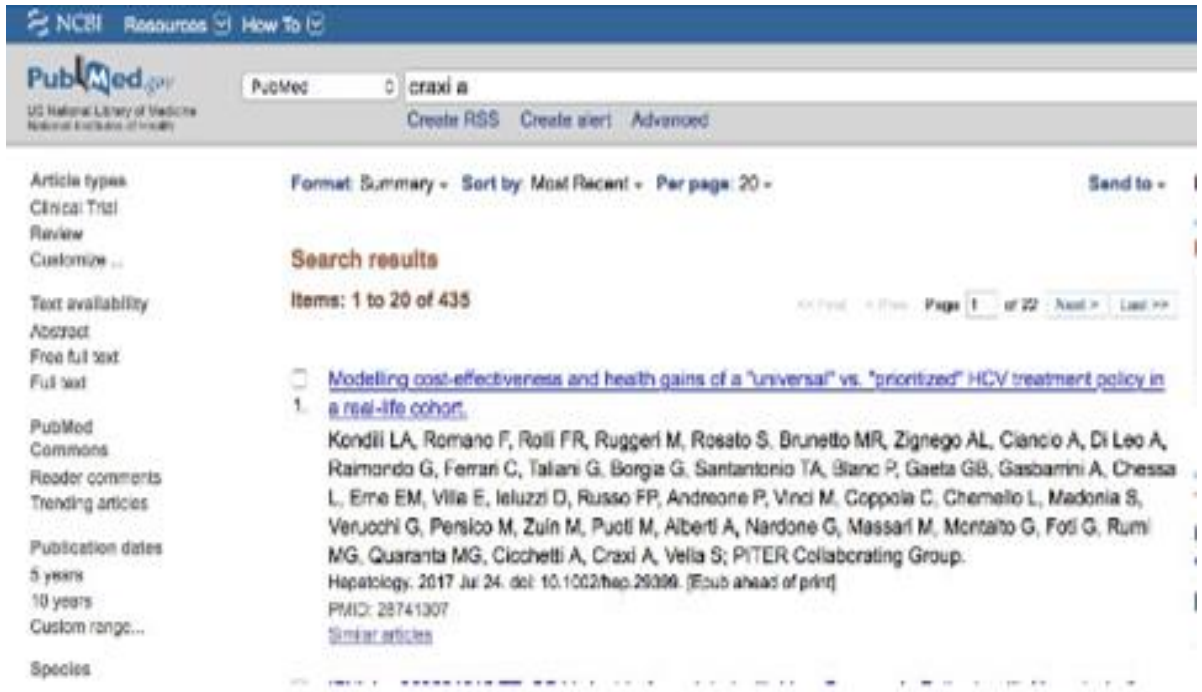
153 KB • jpg 08:02
Discreto risultato, ma adesso bisogna pensare ad altro. Ho una idea sulla morbidity residuale dopo SVR che puó valere la pena di discutere
08:04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Kondili LA, Romano F, Rolli FR, Ruggeri M, Rosato S, Brunetto MR, Zignego AL, Ciancio A, Di Leo A, Raimondo G, Ferrari C, Taliani G, Borgia G, Santantonio TA, Blanc P, Gaeta GB, Gasbarrini A, Chessa L, Erne EM, Villa E, Ieluzzi D, Russo FP, Andreone P, Vinci M, Coppola C, Chemello L, Madonia S, Veruocchi G, Persico M, Zuin M, Puoti M, Alberti A, Nardone G, Massari M, Montalto G, Foti G, Rumi MG, Quaranta MG, Cicchetti A, Craxi A, Vella S; PITER Collaborating Group.
Hepatology. 2017 Jul 24. doi: 10.1002/hep.29399. [Epub ahead of print]
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HCC Incidence
HCV
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Loreta Kondili


Loreta Kondili

Multifactor risk evaluation in patients who have eradicated HCV infection. An interim analysis in the PITER cohort

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INTRODUCTION

High SVR rates are reported in patients treated with DAAs in the real life. However, other than HCV, several factors as NAFLD/NASH, HBV and HIV infection, alcohol use, present in patients with chronic HCV infection are also involved in the progression of liver damage. Potential liver disease progression in patients who present other than HCV risk factor following HCV eradication need to be better evaluated (1-4).

AIM

We aimed to evaluate the prevalence of cofactors involved in liver disease progression in HCV-treated patients who achieved the SVR12 following a DAA therapy in the PITER cohort (5).

METHOD

Data of HCV infected patients, consecutively enrolled in PITER (from January 2015 to September 2017), who were treated and achieved the SVR12, were evaluated. In patients for whom at least 6 months follow-up post-SVR12 was available, the Liver Function Tests and Child Pugh score changes according to the presence of alcohol use, non-virus- non-alcohol fatty liver, diabetes, hypertension, cardiovascular disease, Body Mass Index higher than 25, HBs Ag positivity, HIV positivity, were evaluated.

RESULTS

Of 3485 patients who achieved the SVR12, mean age 61 (SD 11 years), 1985 (54%) were men and 1965 (56%) had liver cirrhosis.

Factors independently associated with liver cirrhosis by Logistic Regression Analysis in patients who achieved the SVR12 in PITER cohort are reported in Table 1.

Parameters	Adjusted OR	95% Confidence Limits	
Age	1.03	1.02	1.04
Male sex	1.19	1.09	1.29
BMI>25	1.29	1.02	1.63
Actual alcohol use	1.21	1.10	1.33
HCV Genotype 3	1.22	1.07	1.39
HIV positivity	1.08	0.91	1.29
HBV positivity	1.02	0.81	1.70
Previous IFN Therapy	1.22	1.13	1.31
Diabetes	1.53	1.37	1.71

Table 1

Age, male sex, BMI>25, actual alcohol use, HCV genotype 3, previous IFN treatment and diabetes were independent factors associated to cirrhosis by logistic regression analysis.

Of the overall patients evaluated (3485) following the SVR12:

- 1164 (33%) reported actual alcohol use
- 693 (20%) had non-virus-non-alcohol-related fatty liver
- 567 (16%) were diabetics
- 1781 (51%) had BMI>25 of whom 60% had hypertension and 30% had BMI≥30,
- 1060 patients had hypertension of whom 80% were on anti-hypertensive therapy
- 212 patients had ongoing cardiovascular disease (reported as chronic coronary artery disease)
- 43 (1%) were HBsAg positive
- 185 (5%) were HIV infected

Prevalence of none, 1 or more than 1 of the potential risk factors for liver disease progression (or progression from NAFLD to NASH) are reported in Figure 1.

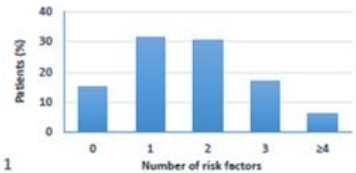

Figure 1

The prevalence of cofactors of liver disease progression in patients with liver cirrhosis according to the Child Pugh Class are reported in Table 2.

	CHILD				
	A		B or C		Total
	N. patients	%	N. patients	%	
Total	1680	85	285	15	1965
Steatosis	379	22.5	37	13.0	416
Actual alcohol use	565	33.6	105	36.8	670
HBsAg+	25	1.5	3	1.1	28
HIV+	52	3.1	39	13.7	91
Diabetes	355	21.1	67	23.5	422
Hypertension	577	34.3	79	27.7	656
BMI > 25	931	55.4	161	56.5	1092
Cardiovascular	108	6.4	13	4.6	121
NAFLD (Steatosis+Diabetes+Hypertension+BMI>25)	50	3.0	8	2.8	337
Number of risk factors					
0	208	12.4	33	11.6	241
1	537	32.0	90	31.6	627
2	531	31.6	97	34.0	628
3	313	18.6	48	16.8	361
4	73	4.3	16	5.6	89
5	18	1.1	1	0.4	19

Table 2

Diabetes, non-alcoholic liver steatosis and BMI>25 were present in 2% of patients with Fibrosis F0-F3 and in 3% of patients with cirrhosis.

Of 1450 patients (942 patients with cirrhosis) for whom follow-up were available at least 6 months following the SVR12, no differences regarding liver function tests were observed according to the comorbidity pattern.

During a median follow-up of 10 months, improvement in Child Pugh score were observed in 72% of 324 patients with Child Pugh score higher than A6, in 25% of whom more than 2 points of Child Pugh score, without differences (p>0.5) according to the comorbidity pattern of concurrent risk factors for liver disease progression.

CONCLUSIONS

Concurrent risk factors for liver disease progression are present in a significant proportion of patients who successfully eradicated HCV infection. Although no further liver disease progression was associated to the presence of such cofactors in a short term evaluation, their role in the overall morbidity and mortality is a health issue that need to be addressed. In the lack of longer prospective studies, a modelling of liver disease progression after HCV eradication, using these real life data, is ongoing (6).

ACKNOWLEDGEMENTS

Authors wish to thank the PITER collaborating group (available at www.progettopiter.it) and CDA Foundation's Polaris Observatory which are collaborating in this project on a voluntary basis.

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CONTACT INFORMATION

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Modeling NAFLD-Related Disease Progression among the PITER SVR12 Cohort

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INTRODUCTION

- Nonalcoholic fatty liver disease (NAFLD) is frequent among patients with chronic hepatitis C virus (HCV) infection (1)
  - The cured HCV population may be susceptible to worsening of NAFLD and development of nonalcoholic steatohepatitis (NASH), due to advancing age (2) combined with high levels of obesity and metabolic risk factors (3)
- The prevalence of NAFLD is increasing across Europe (4) and relatively high rates of fibrosis have been observed in the general adult population of Italy, after excluding cases of viral hepatitis and excessive alcohol consumption (5)
- Liver disease among the Italian population is often multifactorial, with historically high levels of HCV infection, co-existing with metabolic disorder (3, 6)
- Prevalence of NAFLD and NASH in Italy is recognized as a cause of advanced liver disease (7), including hepatocellular carcinoma (HCC), and liver mortality (7, 8)
- An urgent need exists to understand risk factors for ongoing disease progression among patients cured of HCV infection
- Modeling can help assess how continued liver disease progression would alter the outcome of HCV cure

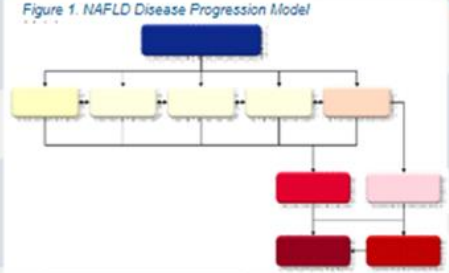
AIM

- Use NAFLD modelling to simulate morbidity and mortality among a representative cohort of HCV cured patients

METHOD

- A model of NAFLD-related disease burden was applied to participants in the PITER cohort (9) who achieved sustained viral response at 12 weeks (SVR12) to quantify potential continued disease progression
- Estimated prevalence of NAFLD in the cohort was based on previous estimates (10), and adjusted for the increased age of the cohort as compared to the general Italian population
- Estimated prevalent NAFLD cases entered the model based on PITER cohort data for sex, age group, disease stage and year at the time of SVR12 achieved after DAA therapy, and were followed over time through 2030
- Cases were tracked by fibrosis stage (Figure 1) with mortality tracked at every stage classified as background, excess cardiovascular and liver-related
  - Model fibrosis transition rates varied by sex, age group, and BMI class of PITER cohort participants
  - Background mortality rates were adjusted to account for incremental increased mortality related to cardiovascular disease (11, 12)
  - NASH cases were estimated based on the modeled distribution of NAFLD cases, with most F0 cases assumed to be simple steatosis, and the likelihood of NASH increasing with advancing fibrosis stage
  - Continued fibrosis progression was followed, and subsequent morbidity and mortality were estimated
    - Cumulative incident cases of decompensated cirrhosis, HCC, and liver-related deaths were calculated for the cohort

Figure 1. NAFLD Disease Progression Model



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RESULTS

- 2394 patients achieved SVR12 during 2014-2018 in the PITER cohort dataset, after excluding cases with excessive alcohol consumption
- An estimated 870 patients were classified as NAFLD based on modeled prevalence for Italy during 2014-2018 (30% of cohort)
  - 46% were male due to higher rates of exclusion among males due to alcohol consumption
- Over 80% of the cohort entered the model at fibrosis stage ≥F2 and 65% were classified as F4
- Modeled NAFLD cases peaked at 640 cases in 2017, declining 40% to 380 cases by 2030
- Median age was estimated at 68 years in 2018, increasing to 74 years by 2030
- The proportion of model cases classified as NASH peaked in 2015 at 97% as large numbers of advanced cases entered the model, declining to 84% in 2030 due to mortality among advanced fibrosis cases
- F0-F1 cases comprised 14% of the modeled cases in 2018, increasing to 22% by 2030, due to lower rates of disease progression and related mortality among this population (Figure 2)
  - In 2018, 86% of cases were classified as ≥F2 (530 cases), 77% as ≥F3 (480 cases) and 64% as F4 (400 cases), reflecting the high burden of disease attributable to previous viral infection
  - By 2030, the proportion of cases classified as ≥F2 declined to 78% (300 cases) of total prevalent NAFLD, due to lower mortality among participants with no/mild fibrosis. Likewise, the proportion of cases estimated as ≥F3 declined to 70% and F4 cases declined to 56% of the total
- There were an estimated 140 incident decompensated cirrhosis and 15 incident HCC cases from 2014-2030 (Figure 3)
  - Incident decompensated cirrhosis decreased 48% from 12 cases in 2018 to 7 cases in 2030
  - Incident HCC decreased 48% from 1.3 cases in 2018 to 0.7 cases in 2030
- There were an estimated 320 total deaths among the model cohort by 2030
  - 160 deaths were classified as background mortality (including excess cardiovascular mortality)
    - 13% of background deaths were classified as excess cardiovascular mortality
  - 160 deaths were classified as liver-related mortality, largely due to the advanced stage at which patients entered the NAFLD model
  - Liver deaths peaked at 24 deaths in 2019, declining 34% to 8 deaths in 2030

Figure 2. Prevalent NAFLD Cases by Fibrosis Stage – SVR 12 PITER Cohort, 2014-2030

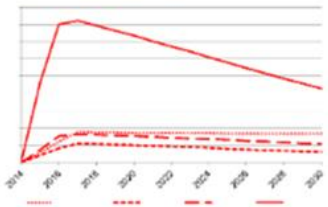
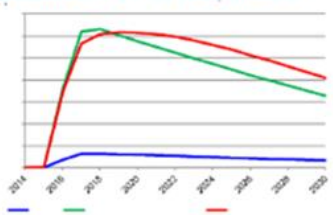


Figure 3. Incident HCC, Decompensated Cirrhosis, and Liver Deaths – SVR 12 PITER Cohort, 2014-2030



CONCLUSIONS

- In the presence of NAFLD, liver disease progression may continue among a portion of the cured HCV population
- Achieving SVR results in better health outcomes, but more research is needed to identify patients at risk for continued liver disease progression (13, 14)
- Liver disease progression was evaluated according to the specific fibrosis stage of each patient at the time of SVR
  - A limitation of this modeling is the uncertainty around the likelihood of continued fibrosis progression among cured cases with advanced fibrosis and metabolic risk factors
  - Improved diagnostic technologies are needed to quantify the probability of NASH and related disease among post-SVR cases
- Results support increased screening and prevention efforts for HCV patients who achieve SVR but in whom other risk factors for liver disease progression could not be excluded
- NAFLD modeling strongly supports the impact of HCV treatment among early stage (F0-F2) cases on preventing potential progression to advanced disease, which are associated with high rates of mortality and economic costs (15, 16)

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CDAF SPONSORED PROJECTS

Projects Funded by CDA Foundation

Mozambique – HBV and HCV Disease Burden and Economic Impact

CDAF is working with the Mozambique MoH to update HBV and HCV disease burden and economic analyses and develop elimination strategies in support of the national Plan of Action and Guidelines. [+]

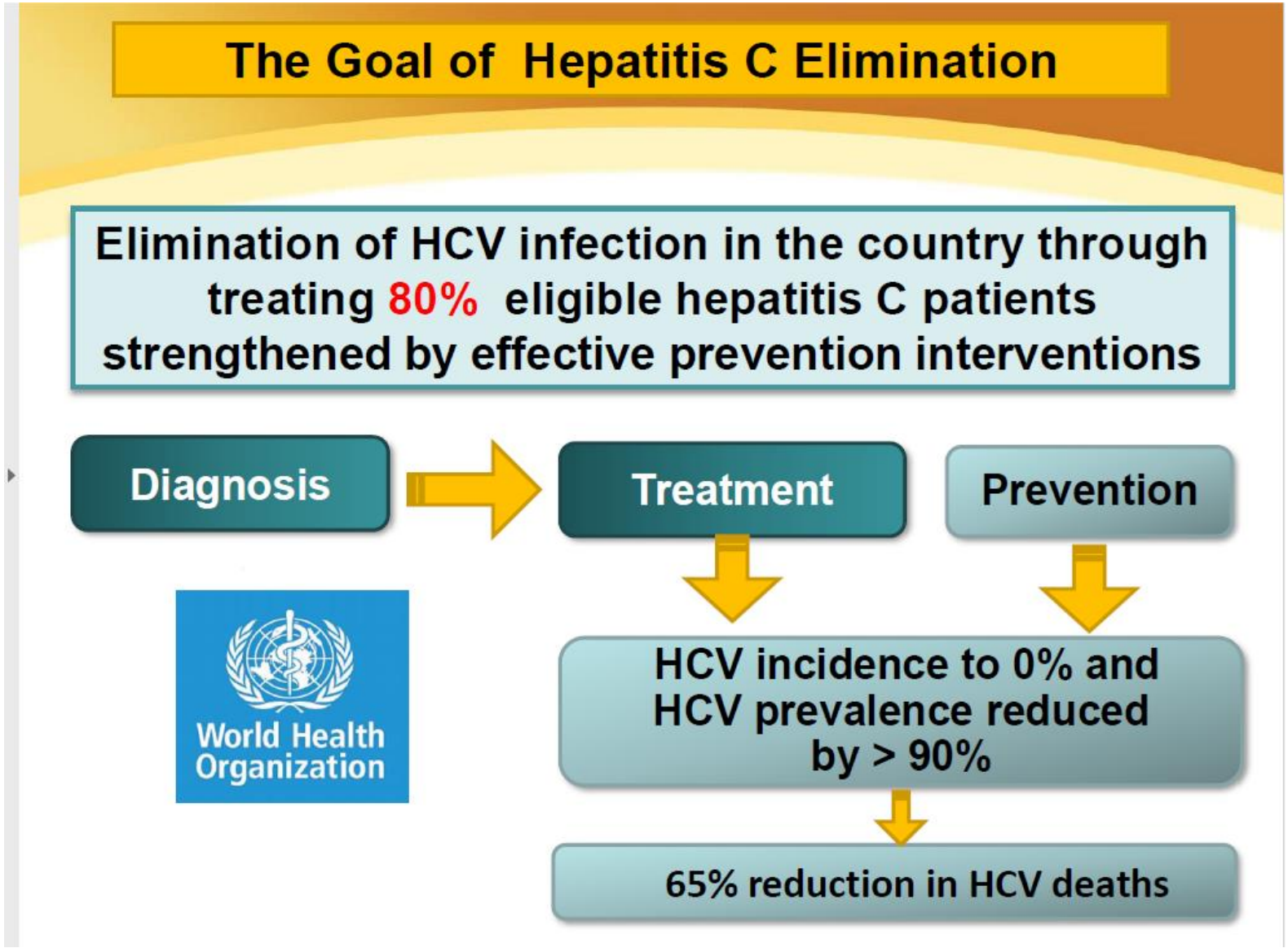
Italy – NAFLD/NASH Disease Progression Modeling

The CDA Foundation is working with Dr. Loreta Kondili and Dr. Stefano Vella of the Istituto Superiore di Sanità (ISS) of Italy to model liver disease progression among patients at risk for NAFLD/NASH, following an HCV cure. [+]

Tibet – HBV Disease Burden

CDA Foundation (CDAF), in collaboration with the Central Tibetan Authority (CTA), aimed to determine the current and future prevalence of chronic hepatitis B infection and identify the future public health impact of the disease. [+]

- **OMS: Target di eliminazione HCV**



Italia- verso il traguardo di eliminazione dell'HCV

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JUST 12 COUNTRIES WORLDWIDE ON TRACK TO ELIMINATE HEPATITIS C INFECTION BY 2030, WITH UNITED KINGDOM, ITALY AND SPAIN AMONG THOSE JOINING THE LIST

June 16, 2018 *by Kimberly Murphy*

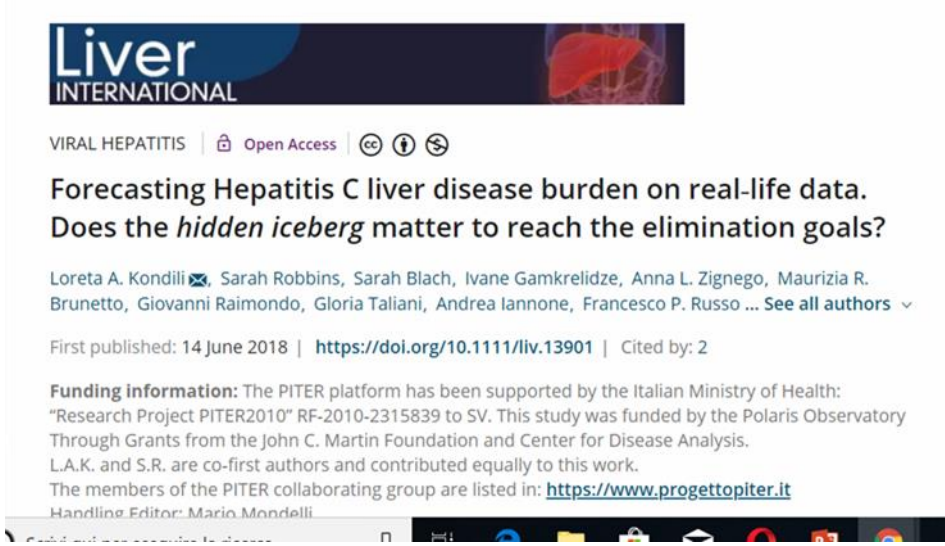
New data on the world's hepatitis C epidemic, presented at this week's Global Hepatitis Summit in Toronto, Canada (14-17 June) shows that only 12 countries in the world are on track to meet the WHO elimination targets that 194 countries globally signed up to in 2016. The data is presented by Dr Homie Razavi and his team from the Polaris Observatory, Center for Disease Analysis Foundation (CDAF), Lafayette, CO, USA.

Since the last global update in 2017, Italy, Spain, Switzerland, the UK and Mongolia have all been added to the list, thanks to the number of patients they treated in 2017, plus the lifting of treatment restrictions to include all patients with hepatitis C regardless of their degree of liver damage. These

L'Italia nel 2018 si colloca tra I 12 paesi incamminati positivamente verso l'eliminazione dell'HCV .
Ma per farlo dobbiamo scovare I "sommersi" e curarli

P.I.T.E.R.
Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali

Forecasting Hepatitis C disease burden based on real life data. Does the *hidden iceberg* matter to reach the eradication goals?



Kondili LA, Robbins S, Blach S, Gamkrelidze I, Zignego AL, Brunetto MR, Raimondo G, Taliani G, Iannone A, Russo FP, Santantonio T, Zuin M, Chessa L, Blanc PL, Puoti M, Vinci M, Erne EM, Strazzabosco M, Massari M, Lampertico P, Rumi MG, Federico A, Ferrari C, Ciancio A, Borgia G, Andreone P, Caporaso N, Persico M, Ieluzzi D, Gori A, Gasbarrini A, Coppola C, Brancaccio G, Andriulli A, Montilla S,

Razavi H, Melazzini M, Vella S, Craxi A **on behalf of PITER collaborating group**.

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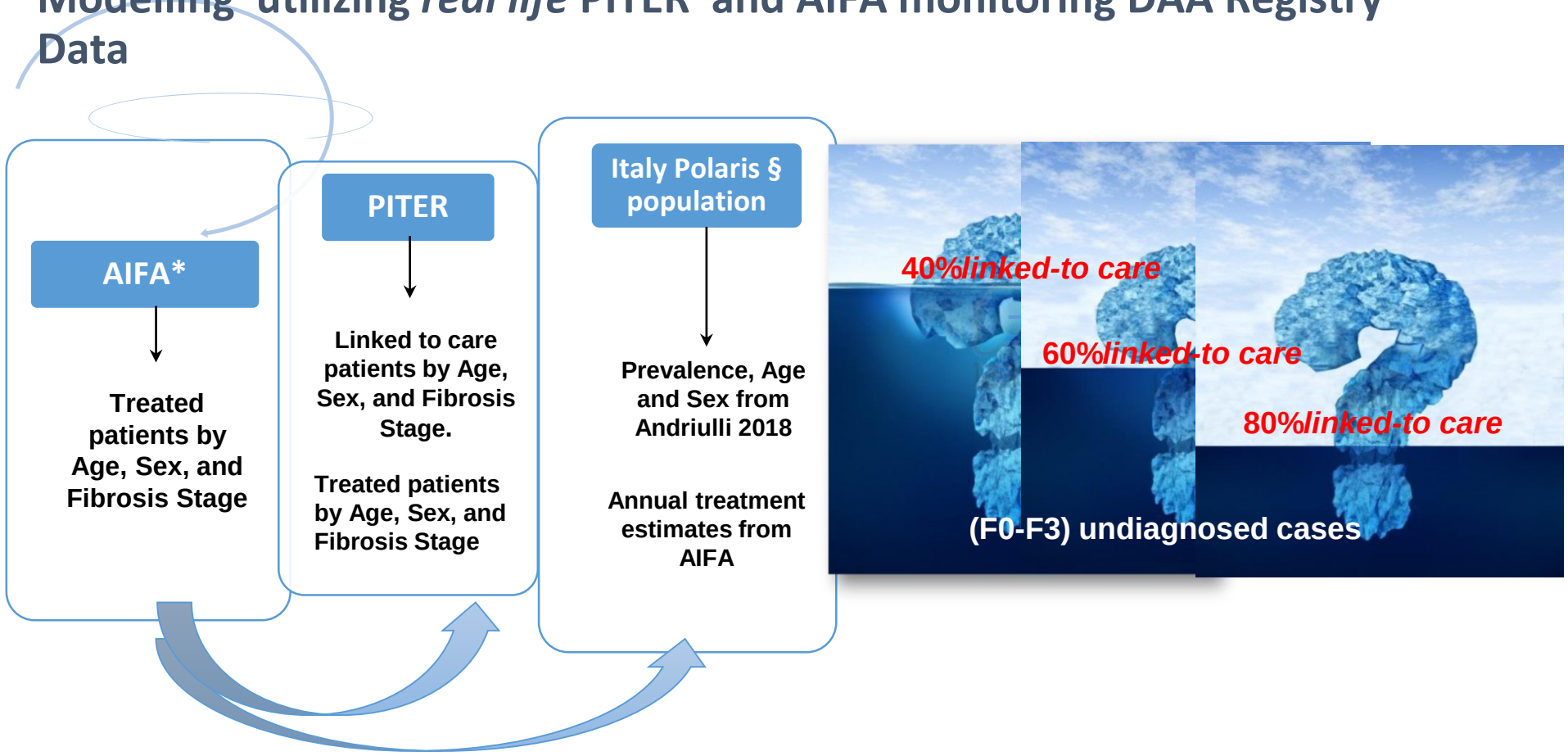
ASSOCIAZIONE ITALIANA PER LO STUDIO DEL FEGATO · A I S F · 1970 ·

SIMIT Società Italiana di Malattie Infettive e Tropicali

Evaluation of possible strategies to achieve WHO targets of elimination

Modelling utilizing *real life* PITER and AIFA monitoring DAA Registry Data

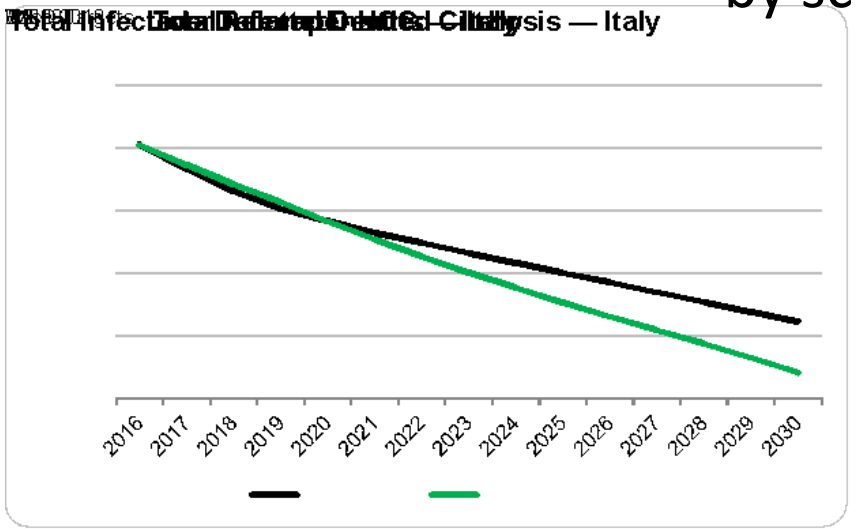


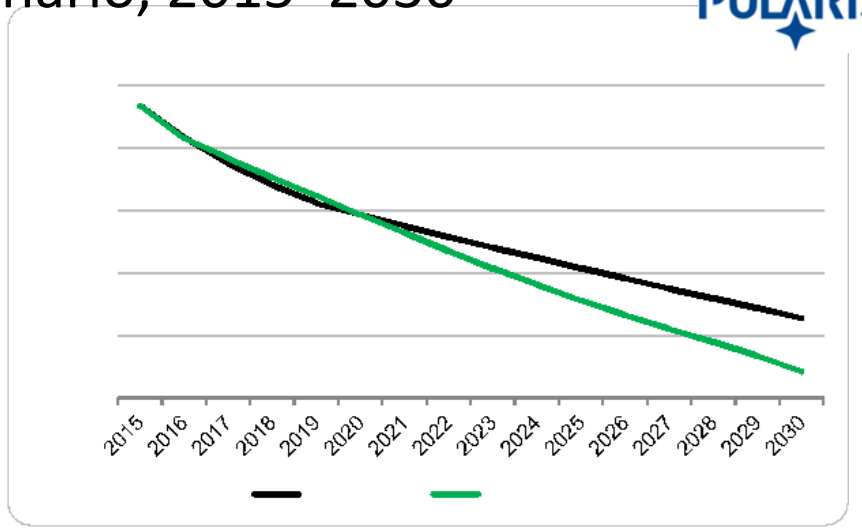
Linkage to Care Scenarios

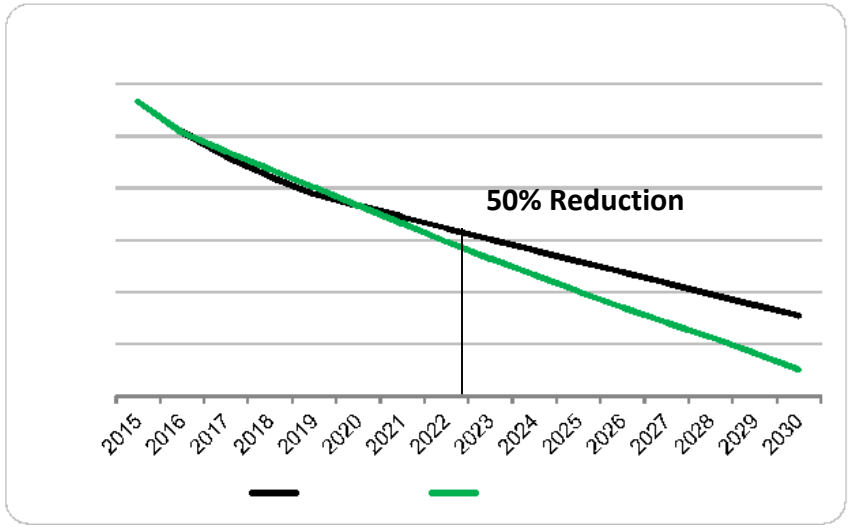
*Registro per il Monitoraggio dei DAA AIFA

§ Andriulli et al 2018 (*in press*) European J . Intern. Med

Liver-related morbidity and mortality by scenario, 2015–2030

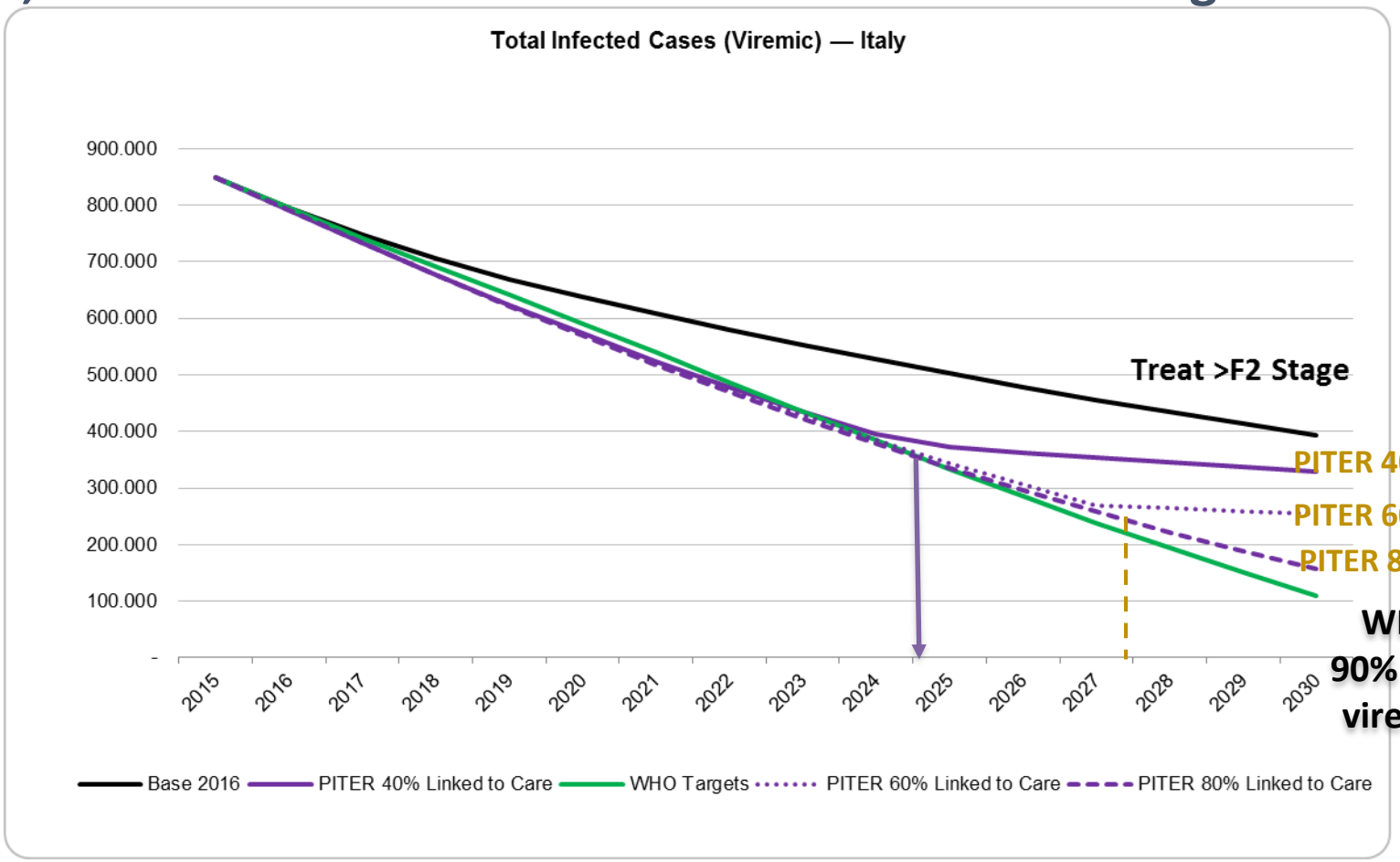






Italy is closed to meeting the WHO target of a 65% reduction in liver related mortality by 2030, without requiring further interventions

However, the number of total infections would remain high..



With an annual rate of treatment =>35.000 patients

40% linked to care: Depletion of cases to be treated in 2025
60% linked to care: Depletion of cases to be treated in 2028
80% linked to care: Depletion of cased to be treated in 2031

Screening strategies for hepatitis C virus elimination in Italy

I. Gamkrelidze[1], L. Kondili[2], A. Marcellusi[3], S. Robbins[1], S. Blach[1], A. Craxi[4], M. Puoti[5], H. Razavi[1], F.S. Mennini[3]

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Presented at The International Liver Congress • 10–14 April 2019 • Vienna, Austria

THU-397

INTRODUCTION

Hepatitis C virus (HCV) elimination could be achieved in Italy by newly linking 36,400 patients to care and treating 38,000 patients annually by 2025. However, cost-effective screening strategies are needed to make the elimination a reality.

AIM

HCV is more prevalent in the older Italian population, so our objective was to determine if birth cohort-based screening would be cost-effective in Italy.

METHOD

A Markov model was populated with Italian data[1–5] to quantify the annual HCV-infected population by stage of liver disease, sex, and age. An economic impact module was added to quantify medical costs and health effects, denominated in quality-adjusted life years (QALYs), associated with HCV infection. The incremental cost-effectiveness ratio (ICER) was defined as the incremental cost of a scenario divided by its incremental benefit, relative to the status quo. A cost-effectiveness threshold of €25,000, commonly accepted in Italian guidelines, was applied. Prevalence of asymptomatic HCV infections not yet linked to care was used to calculate the number of HCV antibody screens needed.

Modeled outcomes over 2018–31 were assessed under the status quo and as well as a scenario that met the World Health Organization's (WHO) Global Health Sector Strategy (GHSS) targets for eliminating HCV by 2030:[6–7]

- 80% reduction in incidence of chronic HCV infections over 2015–30
- 65% reduction in chronic HCV infection-related deaths over 2015–30
- 90% diagnosis coverage of the HCV-infected population in 2015
- 80% treatment coverage of the eligible HCV-infected population in 2015

The elimination scenario was assessed under four screening strategies:

- Universal screening
- Screening the 1948–77 birth cohort
- Screening the 1958–77 birth cohort
- Graduated birth cohort screening (screening the birth cohort 1968–87 beginning in 2020 to identify young populations at risk for transmitting HCV, and expanding to the birth cohort 1948–67 beginning in 2023 to identify older populations before their disease advances)

RESULTS

The graduated screening scenario was the least costly, with €6.0 billion in total medical costs by 2031. This was €107.4 million less than screening in the 1948–77 birth cohort, €109.1 million less than screening in the 1958–77 birth cohort, and €467.1 million less than universal screening. Relative to the status quo, graduated screening would gain 143,929 QALYs by 2031, compared to 142,244, 128,384, and 144,759 QALYs for the 1948–77 birth cohort, the 1958–77 birth cohort, and universal screening, respectively. Graduated screening would see a reduction of 89.3% in prevalent HCV-infected cases over 2018–31, compared to 89.0%, 89.7%, and 88.7% for the 1948–77 birth cohort, the 1958–77 birth cohort, and universal screening, respectively. Relative to the status quo, graduated screening yielded the lowest ICER of €3,552 per QALY. Screens necessary to realize each scenario, screening costs, total medical costs (including those of screening), and QALYs gained are presented in Figures 1–4.

Finally, excluding the two scenarios that were costlier and less effective than graduated screening (screening the 1948–77 birth cohort and screening the 1958–77 birth cohort), universal screening yielded an ICER of €562,855 per QALY relative to graduated screening.

Table 1. Total medical costs, health effects, and ICER, by scenario

Scenario		Cost (€ millions), 2018–31	QALYs gained relative to status quo, 2018–31	ICER relative to status quo (€/QALY)	ICER relative to previous least costly scenario (€/QALY)
Status quo		5,463	–	–	
GHSS targets	Graduated screening	5,974	143,929	3,552	3,552
	Screening 1948–77 birth cohort	6,081	142,244	4,349	*
	Screening 1958–77 birth cohort	6,083	128,384	4,831	*
	Universal screening	6,441	144,759	6,758	562,855

ICER — incremental cost-effectiveness ratio; QALY — quality-adjusted life year; GHSS — Global Health Sector Strategy
* Strongly dominated scenario (costlier and less effective than another scenario)

Figure 1. Cumulative HCV antibody screens, 2018–31

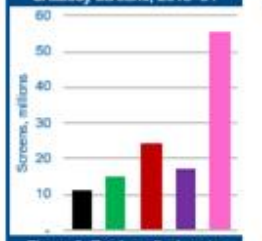

Figure 2. Screening costs, annual

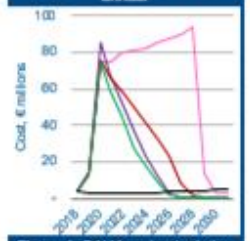

Figure 3. Total medical costs, annual

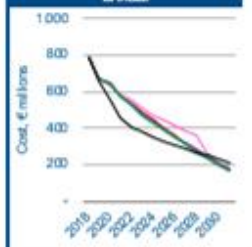

Figure 4. QALYs gained relative to status quo, annual

HCV — hepatitis C virus; QALY — quality-adjusted life year; GHSS — Global Health Sector Strategy

CONCLUSIONS

Universal screening, although cost-effective relative to the status quo, had an ICER higher than the willingness to pay for the Italian National Health System relative to graduated screening. On the contrary, implementing graduated screening in Italy — beginning with the 1968–87 birth cohort in 2020, followed by the screening of the 1948–67 birth cohort from 2023 — was the most cost-effective option, and showed the second largest reduction in overall disease burden by 2031. This strategy should be considered to sustain Italy's momentum towards achieving HCV elimination goals.

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