X Workshop Nazionale Innovazione e Ricerca per la Pratica Clinica

TERAPIE INNOVATIVE DELLE EPATITI CRONICHE VIRALI

HCV VERSO L'ELIMINAZIONE
AGGIORNAMETO DALLA COORTE PITER

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

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Istituto Superiore di Sanità

CENTRO NAZIONALE PER LA SALUTE GLOBALE
ITALIAN CENTER FOR GLOBAL HEALTH

Firenze 14 Gennaio 2020

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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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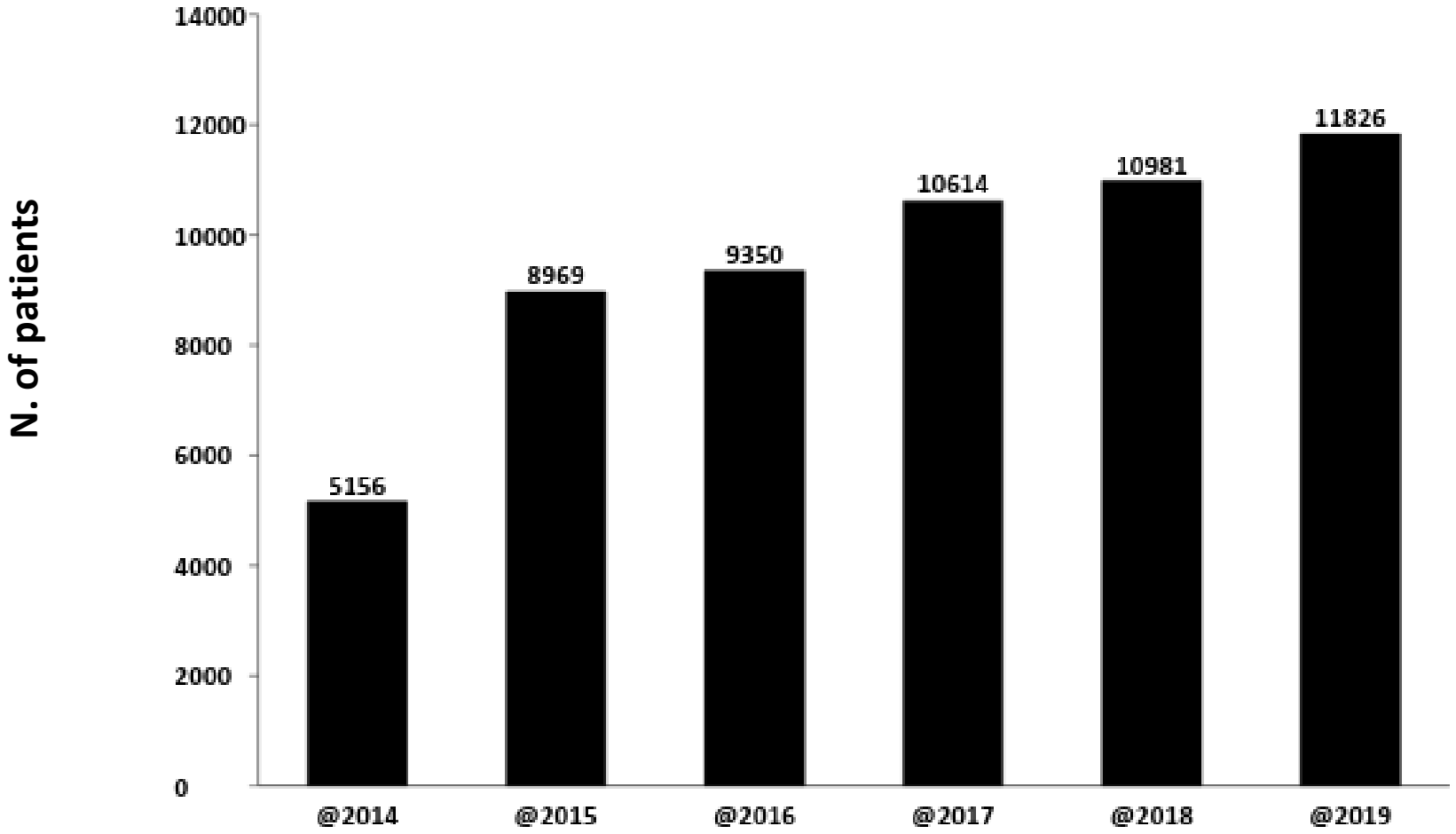
Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

Number of enrolled patients



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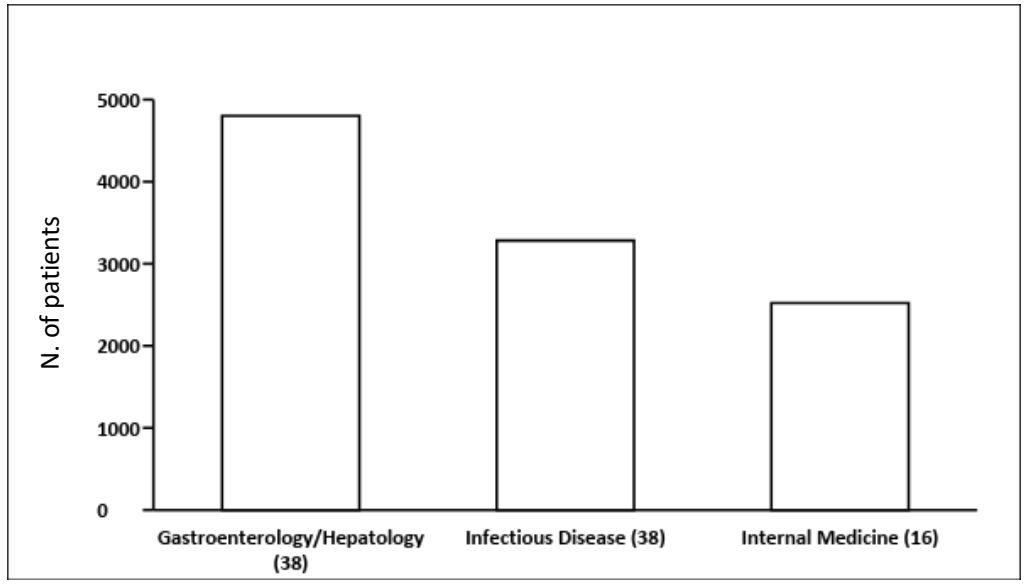
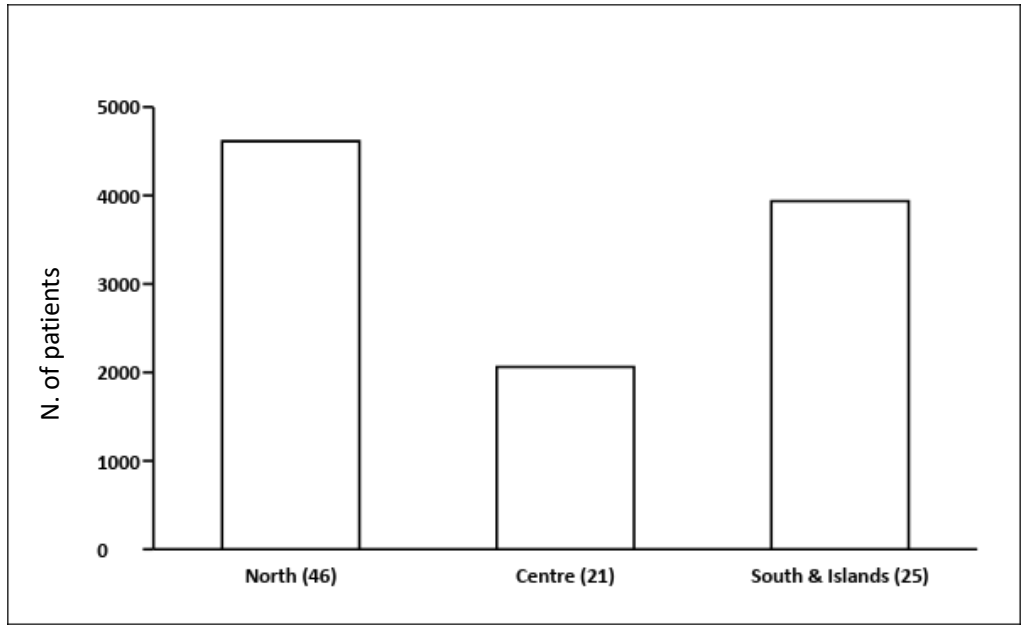
Patients' distribution according to the Clinical Centre specialty and geographical area





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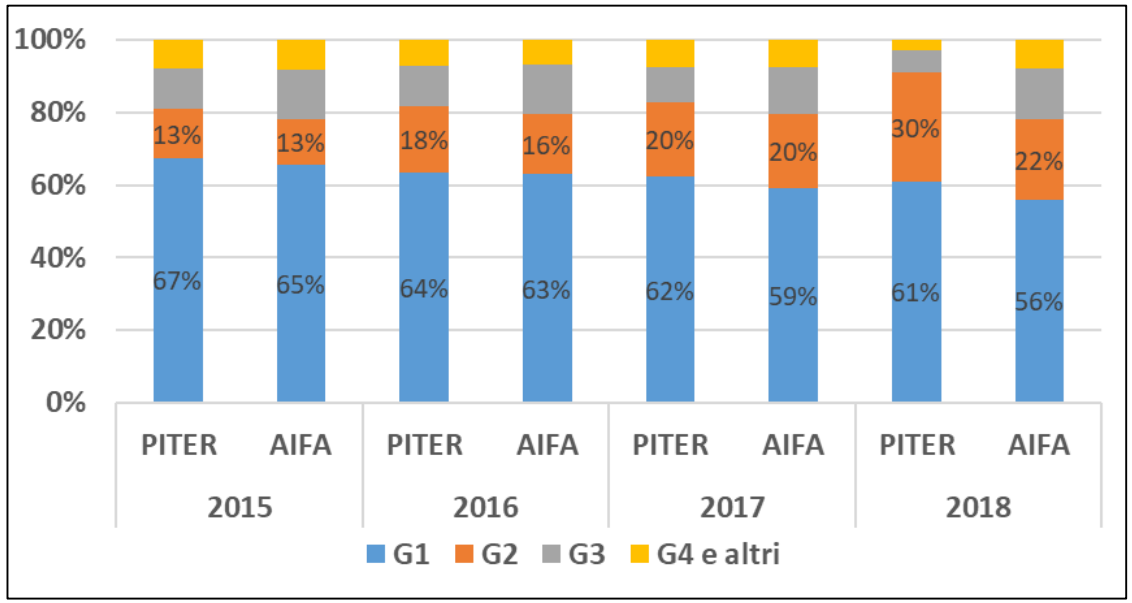
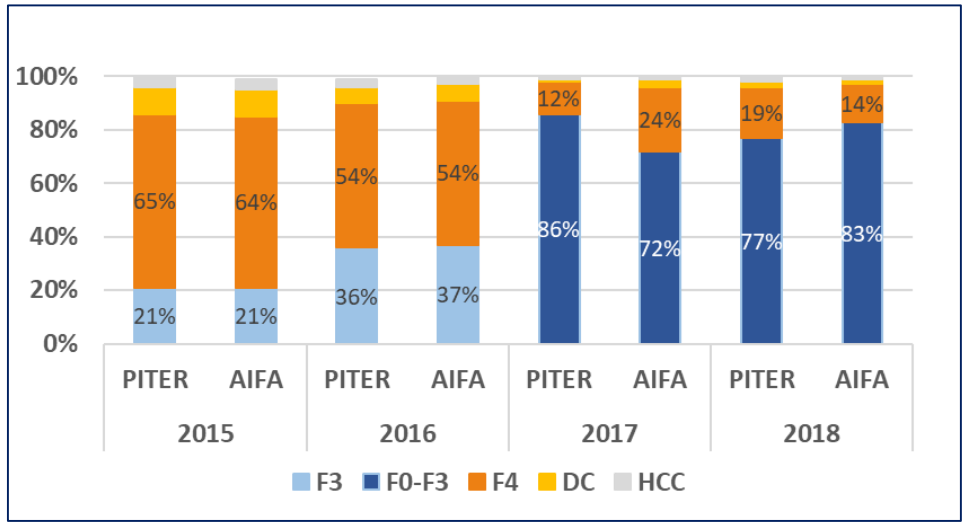
Agenzia Italiana del Farmaco
AIFA

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

PITER

Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

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

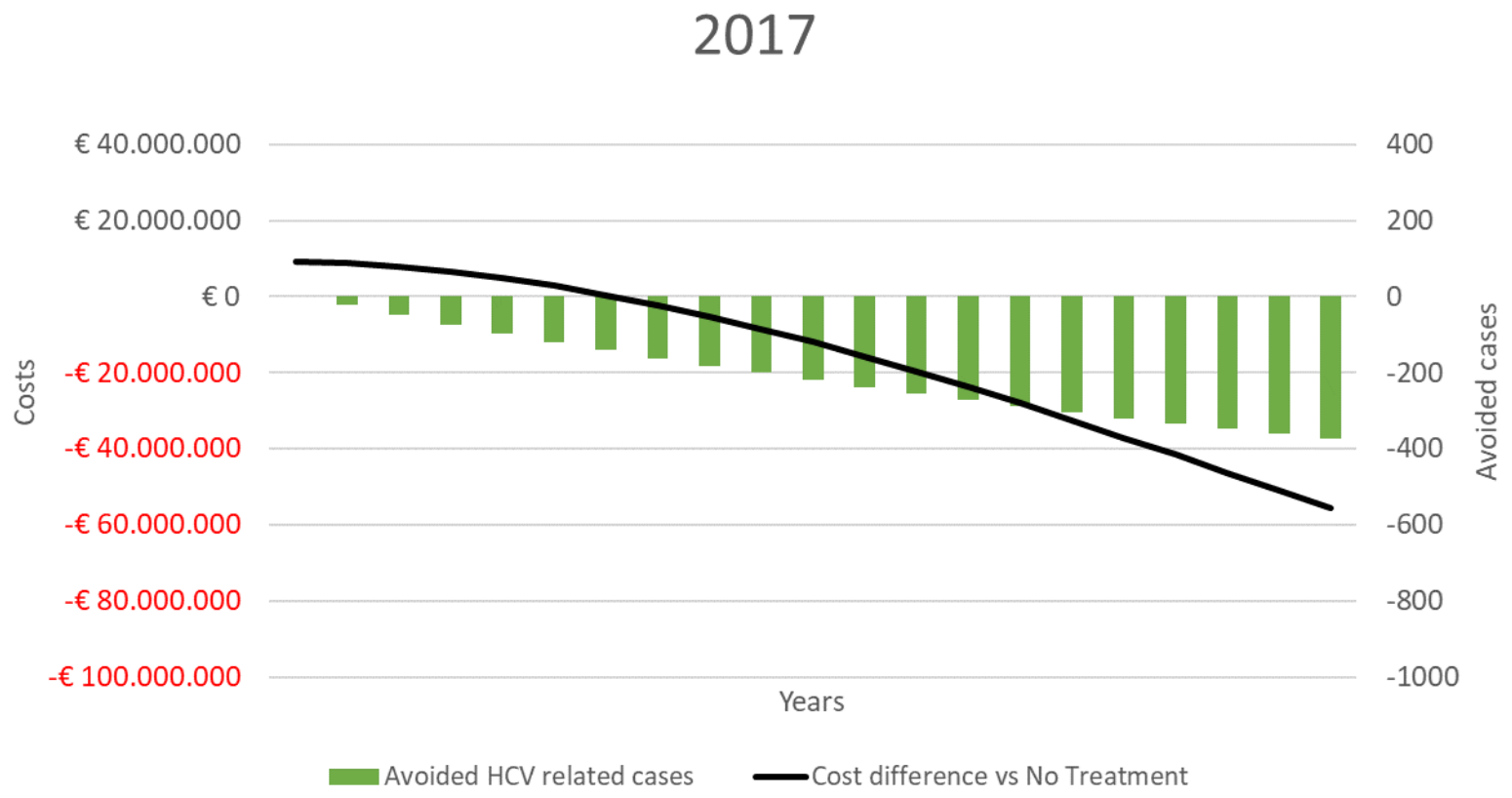
Andrea Marcellusi[1,2] · Raffaella Viti[1] · Loreta A. Kondili[3] · Stefano Rosato[3] · Stefano Vella[3] · Francesco Saverio Mennini[1,2] on behalf of PITER Collaborating group available at www.progettopiter.it

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

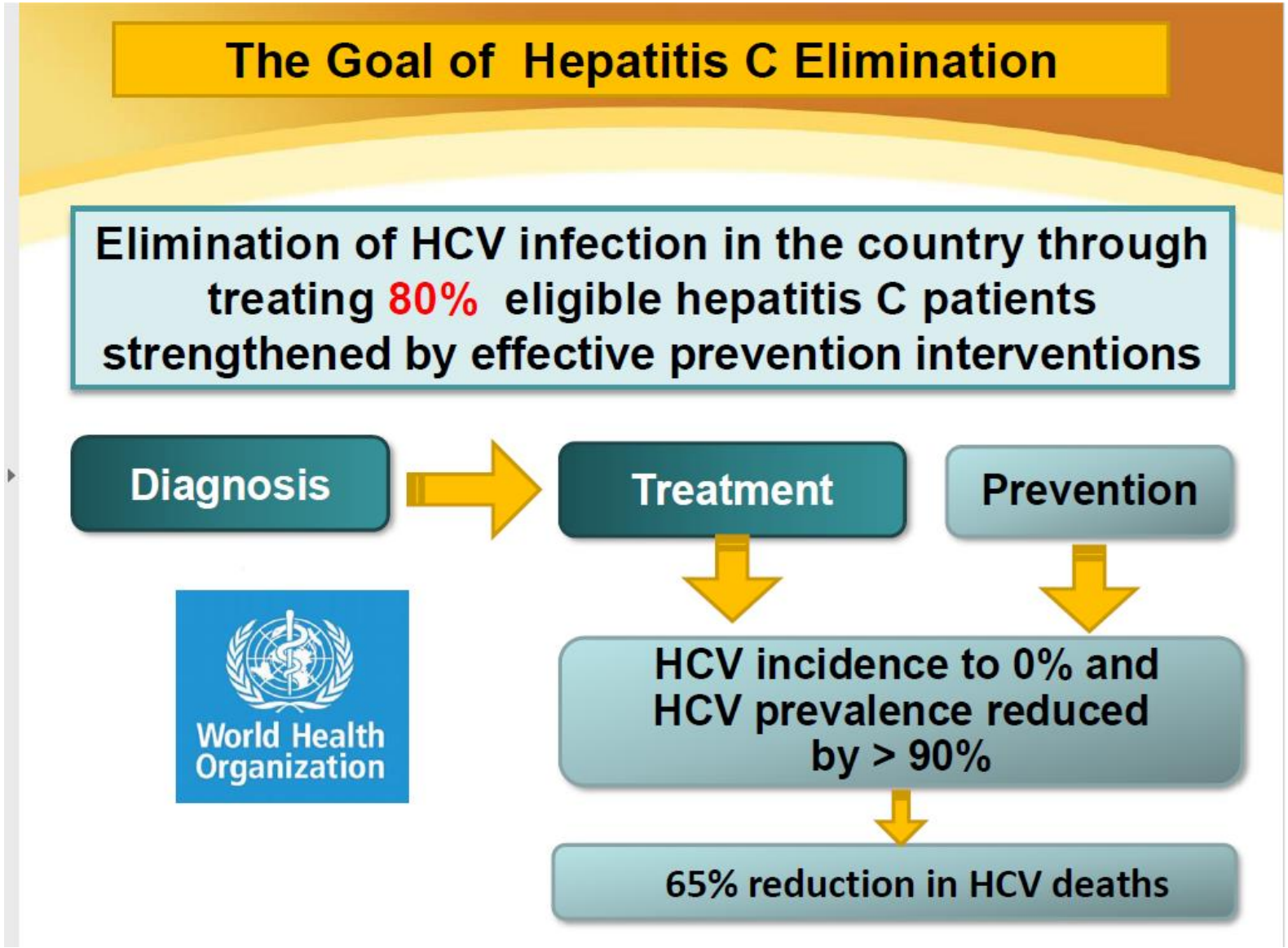
Final results : Ongoing evaluation

Results

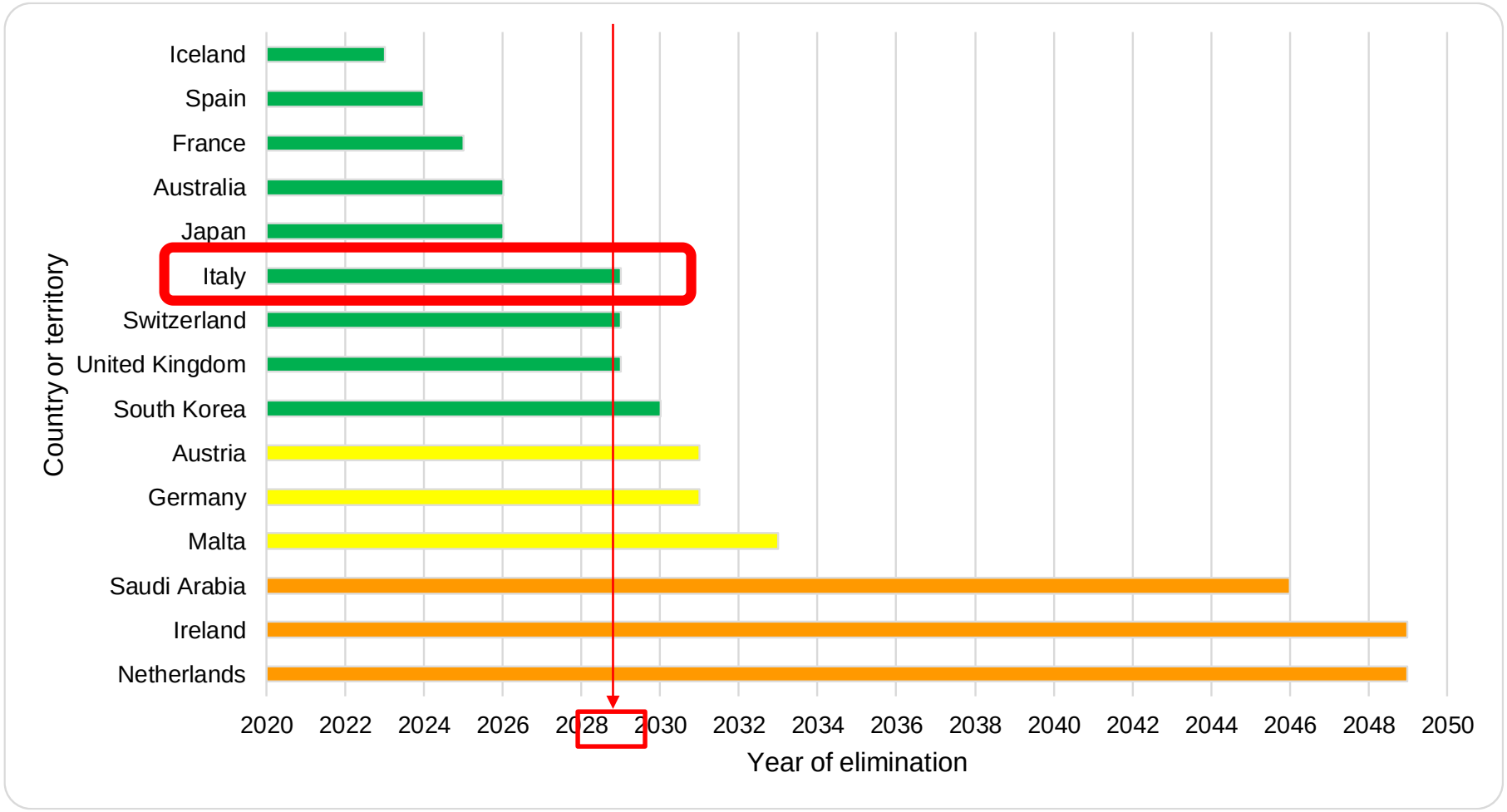
- Standardized for 1.000 treated patients



- **OMS: Target di eliminazione HCV**



Only 20% of 45 high income countries are forecasted to reach the WHO elimination targets by 2030 and only 33% by 2050



Razavi H, Sanchez Y, Pangerl A, Cornberg M, Global timing of hepatitis C virus elimination: estimating the year countries will achieve theWorld Health Organization elimination targets, EASL poster SAT-290, 2019

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*

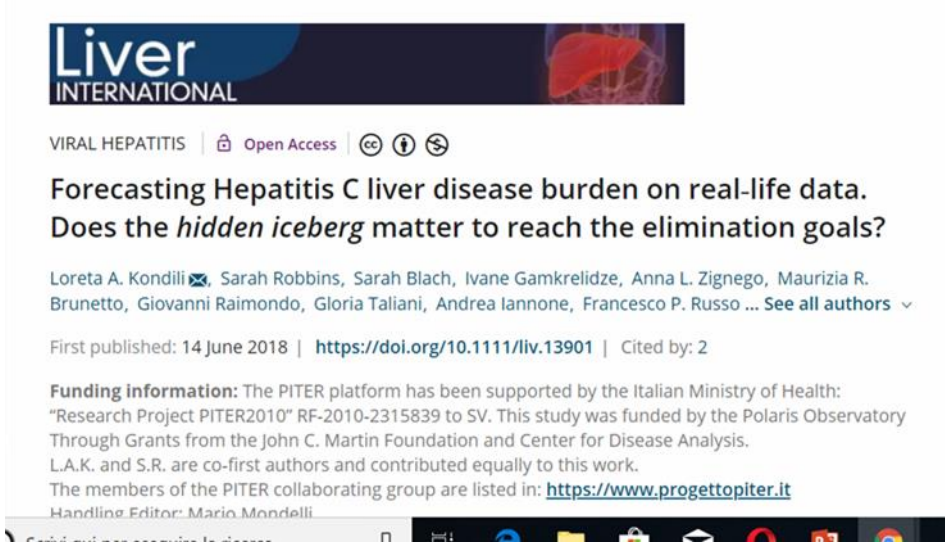
New data on the world's hepatitis C epidemic, presented at this week's Global Hepatitis Summit in Toronto, Canada (14-17 June) shows that only 12 countries in the world are on track to meet the WHO elimination targets that 194 countries globally signed up to in 2016. The data is presented by Dr Homie 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**.

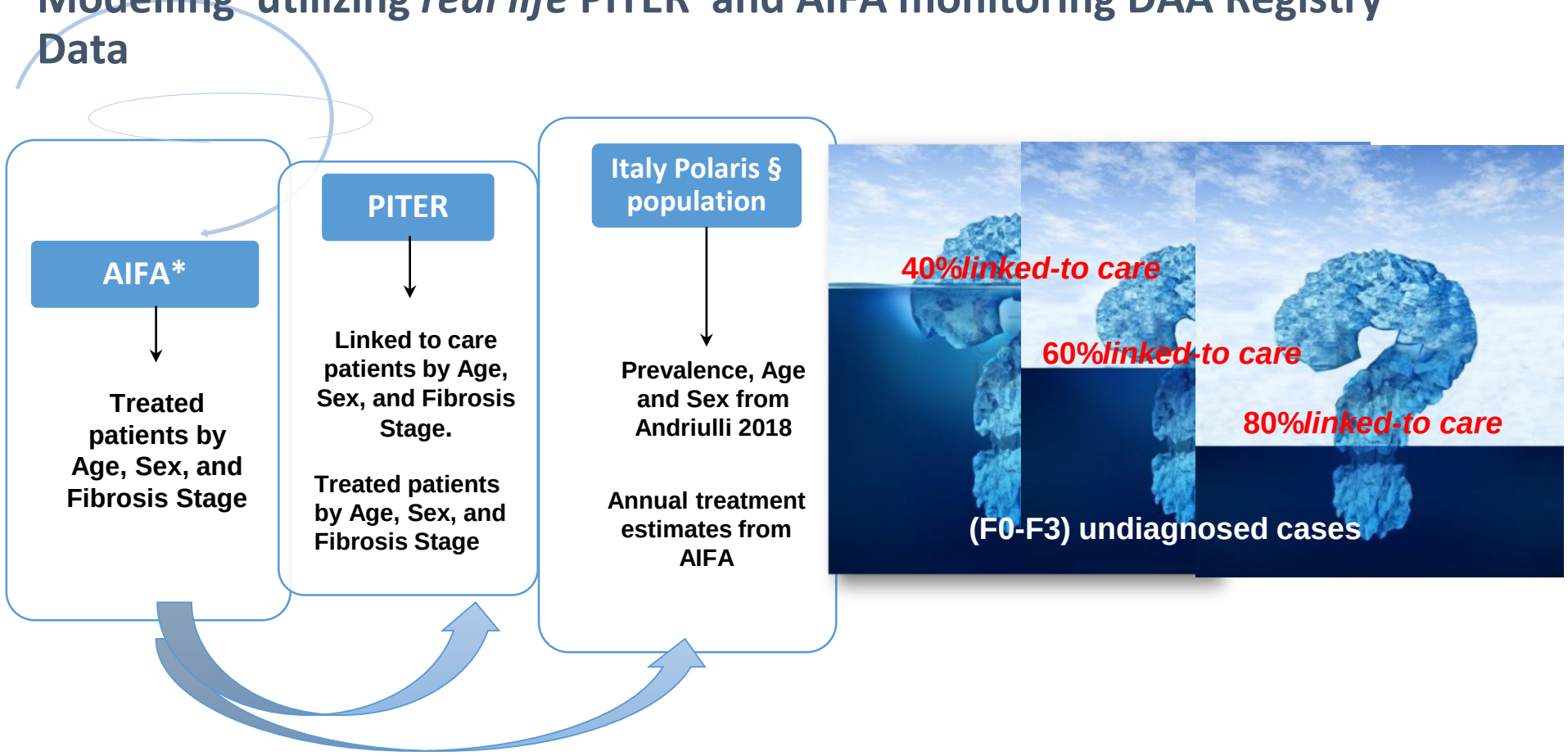
ISTITUTO SUPERIORE DI SANITÀ

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

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

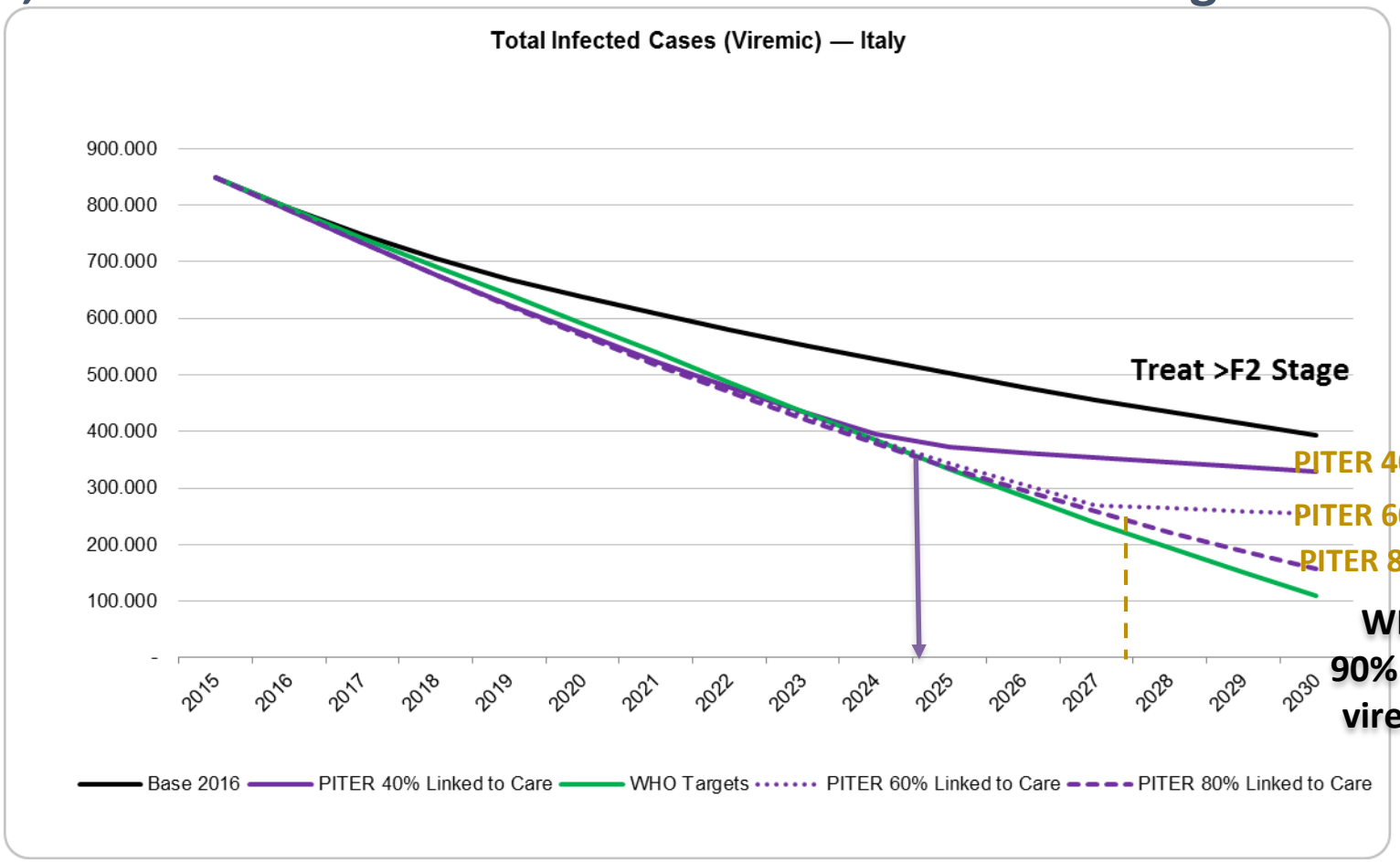


Linkage to Care Scenarios

*Registro per il Monitoraggio dei DAA AIFA

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

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

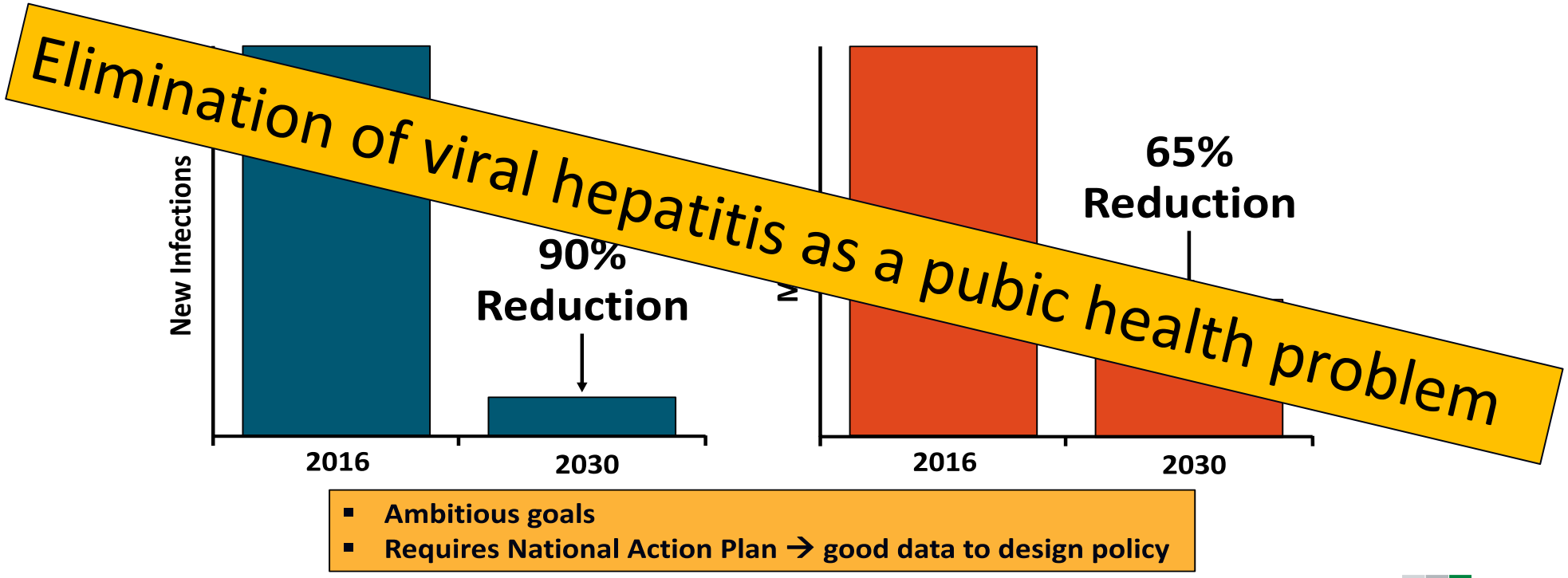
Distribution of F0-F3 cases by birth years in both models in 2020

Birth Year	Proportion of F0-F3 infected cases in PITER Model (%)	Proportion of F0-F3 infected cases in Italy Polaris Model (%)
1938-1948	28	32
1948-1958	35	42
1958-1968	41	26
1968-1978	23	17
1978-1988	10	10
1988+	5	8

40% linkage to care
Treatment sustained up to 2025

Rational of HCV screening

WHO HCV Elimination Targets



- Ambitious goals
- Requires National Action Plan → good data to design policy

WHO. Draft WHO Global Hepatitis Strategy, 2016-2021.

Slide credit: clinicaloptions.com

Scenari di eliminazione:
4 strategie di screening vs status quo

- Screening Universale
- Screening nelle coorti di nascità 1948–77
- Screening nelle coorti di nascità 1958–77
- Screening Graduato per coorti di nascita

- iniziare lo screening nelle coorti 1968–87 in 2020 –identifica anche le popolazioni giovanni più a rischio di trasmissione HCV
- **Successivamente**
- espandere lo screening alle coorti di nascita 1948–67 in 2023 - identifica le popolazioni più anziane

Costi diretti di screening e l'effetto sulla salute (QALY= anni di vita guadagnati in salute)

	Parameter	Base (Range)	Distribution Type	Reference
	Anti-HCV, test only	5 (1–9)		Assumption and (Ruggeri 2013)
Diagnostic	Screening costs, low-risk groups	10.00 +5 fee for organization = 15		Assumption– per screen costs to implement
and	Screening costs, high-risk groups	50.00 + 5 fee for organization = 55		Assumption– per screen costs to implement
Treatment	RNA Test/PCR	63.01		Ministero della Salute 2013 (code 91.19.3)
Costs (€)	Genotyping	77.47		Ministero della Salute 2013 (code 91.20.2)
	Fibroscan	50.00		Marcellusi 2018, Marcellusi 2016
	Lab costs	50.00		Marcellusi 2018, Marcellusi 2016
	Antiviral Treatment	4000		Marcellusi 2018, Marcellusi 2016
Healthcare	Fibrotic (F0–F3)	277 (176-292)	Beta-PERT	Marcellusi 2018, Marcellusi 2016
Costs (€)	Comp. Cirrhosis	876 (397-1354)	Beta-PERT	Marcellusi 2018, Marcellusi 2016
	DCC	6,626 (4385-8868)	Beta-PERT	Marcellusi 2018, Marcellusi 2016
	HCC	12,896 (5792-20,000)	Beta-PERT	Marcellusi 2018, Marcellusi 2016
	LTx, first year	73,774 (62,648-84,900)	Beta-PERT	Marcellusi 2018, Marcellusi 2016
	LTx, subs years	2,365 (0-4729)	Beta-PERT	Marcellusi 2018
	Death	–		Marcellusi 2016
	Post SVR Monitoring for cirrhotic patients	50.00		Cost of 1 ultrasound
	Fibrotic (F0–F3)	0.88 (0.06)	Normal	Kondili2017
QALY	Comp. Cirrhosis	0.83 (0.077)	Normal	Kondili2017
Utility	DCC	0.73 (0.113)	Normal	Kondili2017
Weights	HCC	0.53 (0.395)	Normal	Kondili2017
Pre-SVR	LTx, first year	0.73 (0.183)	Normal	Kondili2017
	LTx, subs years	0.73 (0.183)	Normal	Kondili2017
	Healthy	1		Kondili2017
	Fibrotic (F0–F3)	1		Kondili2017
QALY	Comp. Cirrhosis	0.83 (0.077)	Normal	Kondili2017
Utility	DCC	0.73 (0.113)	Normal	Kondili2017

Parametri per gli scenari di screening

Status quo	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2025+**
Trattamenti	45,000	56,400	44,600	33,700	23,200	15,100	15,100
Nuove diagnosi/ linked to care	30,400	30,400	20,000	20,000	20,000	20,000	20,000
Restrizione per la Fibrosi	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0
Nuove infeztioni diagnosticate	8,200	7,500	6,700	6,100	5,600	5,200	5,200
Età	15+	15+	15+	15+	15+	15+	15+
SVR	95%	95%	98%	98%	98%	98%	98%
OMS GHSS targets per l'eliminazione	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2025+**
Treated	45,000	56,400	44,600	35,700	35,700	36,700	38,000
"Incremental" nuove diagnosi	–	–	10,400	13,400	13,400	15,400	16,400
Restrizioni per la Fibrosi	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0
Nuove infezioni diagnosticate	8,200	7,500	6,700	5,500	5,000	4,100	2,600
Età	15+	15+	15+	15+	15+	15+	15+
SVR	95%	95%	98%	98%	98%	98%	98%

SVR — sustained virologic response; GHSS — Global Health Sector Strategy

Parametri utilizzati per gli scenari di screening

GHSS elimination	<2020	2020-2022	2023-2025	% PWID*	Screening Cost (per person, €)
Screening 1948–1977	Risk	1948–1977	1948–1977	8.2%	18
Screening 1958–1977	Risk	1958–1977	1958–1977	12.1%	20
Screening Graduato	Risk	1968-1977	1948-1967	9.7%	19
Screening Universale	Risk	Tutta la popolazione	Tutta la popolazione	6.2%	17

GHSS — Global Health Sector Strategy; PWID — Persons who inject drugs; Risk — risk-based screening assumes that those offered a test are approximately 5 times more likely to be infected than the general population PWID prevalence –United Nations Office on Drugs and Crime

Direct costs and health effects, by scenario, 2018–2031

Scenario		Cost (€Millions), 2018–2031	QALYs Gained, 2018–2031	ICER Relative to Status Quo (€/QALY)	ICER relative to previous least costly scenario (€/QALY)
Status quo		5,463	–	–	
GHSS Targets	**Graduated screening 1**	**5,974**	**144,000**	**3,552**	**3,552**
	Graduated screening 2	6,028	125,000	4,532	*
	Screening 1948–1977	6,081	142,000	4,349	*
	Screening 1958–1977	6,083	128,000	4,831	*
	Universal screening	6,441	145,000	6,758	562,855

Values have been rounded, so ICERs may not be reproducible using table values

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)*

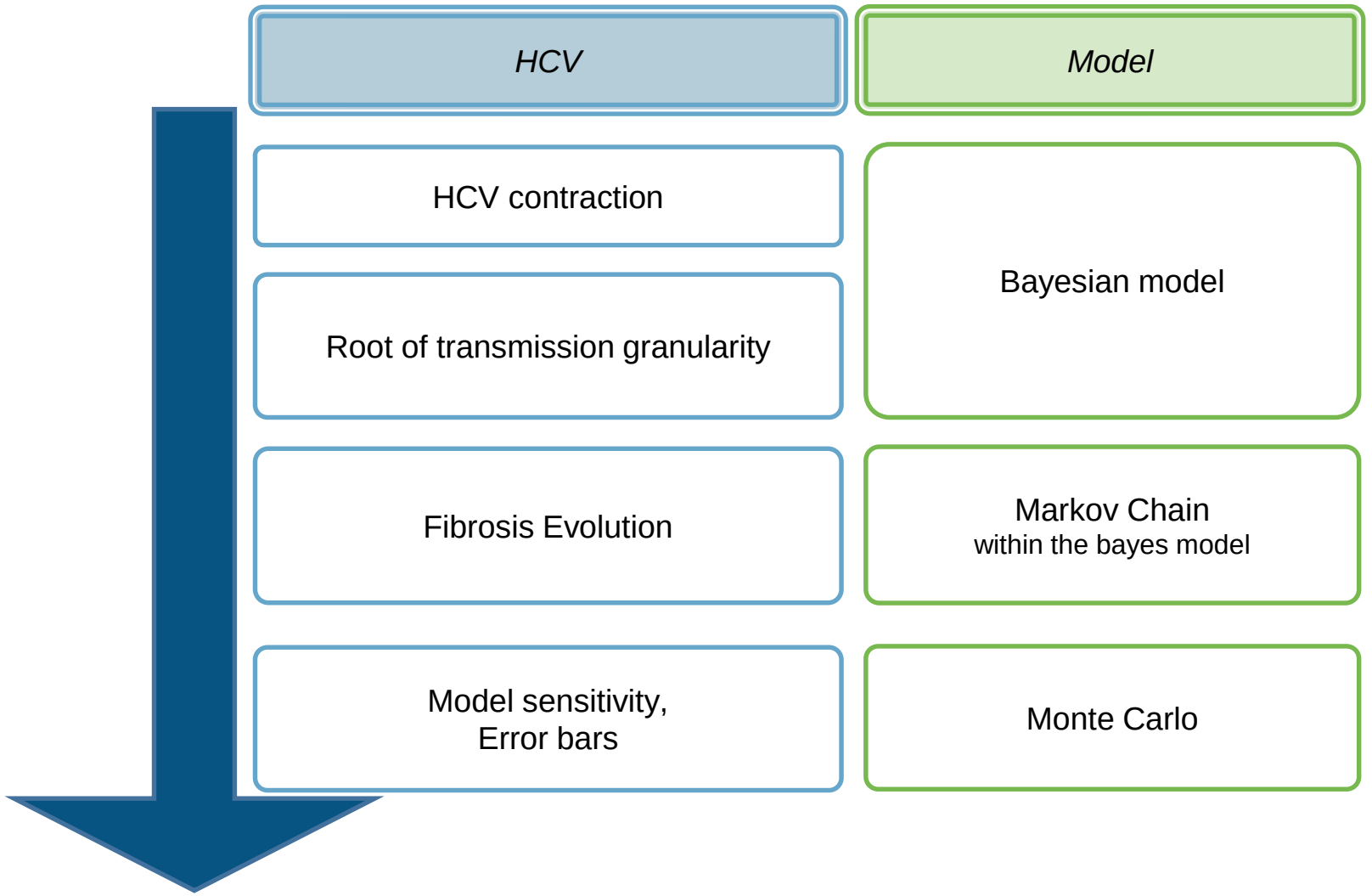
- **Graduated Screening 1**:iniziare lo screening nelle coorti 1968–87 in 2020 –identifica le popolazioni giovanni più a rischio di trasmissione HCV **successivamente** espandere lo screening alle coorti di nascita 1948–67 in 2023 - identifica le popolazioni più anziane.
- Graduated Screening 2:iniziare lo screening nelle coorti 1948–67 in 2020 –identifica le popolazioni più anziane **successivamente** espandere lo screening alle coorti di nascita 1968–87 in 2023 - identifica le popolazioni giovanni.

Estimated prevalence of undiagnosed hepatitis C virus infected individuals in Italy: a mathematical model to accurately measure HCV prevalence by route of transmission with a route of transmission granularity

Presented AASLD Boston 2019

L.Kondili, M.Andreoni, A. Alberti, S. Lobello, S. Babudieri, A.S. Roscini, R. Merolla, W. Marrocco, A. Craxì

Parameters used in the Bayesian Approach modelling



Results – Prevalence

I pazienti trattati sia con terapie a base di Interferone che con antivirali secondo i dati del registro AIFA sono stati esclusi dal modello

		Absolute number	
	Reference	Lower 95% CI	Upper 95% CI
Total	**410775**	388627	425800
Total F0-F3	**281809**	209531	364910
Total F4	**128966**	44471	198119
High risk groups			
PWID			
F0-F3	**146652**	106911	187821
F4	**58001**	17356	95199
Tattoo/body piercing			
F0-F3	**81153**	64865	91101
F4	**11928**	2791	27734
Sexual transmission			
F0-F3	**33871**	26922	38691
F4	**2615**	404	7750
GS + transfusion			
F0-F3	**18038**	6867	50081
F4	**54567**	22598	65670
Vertical transmission			
F0-F3	**2095**	1058	3331
F4	**1854**	589	2634

Transmission routes relative prevalence

The asymptomatic population (F0-F3) is composed:

1) PWID: 52.1% (95% CI: 49.4%-53.8%)

2) TATTOO: 28.8% (95% CI:24.4%-31.4%)

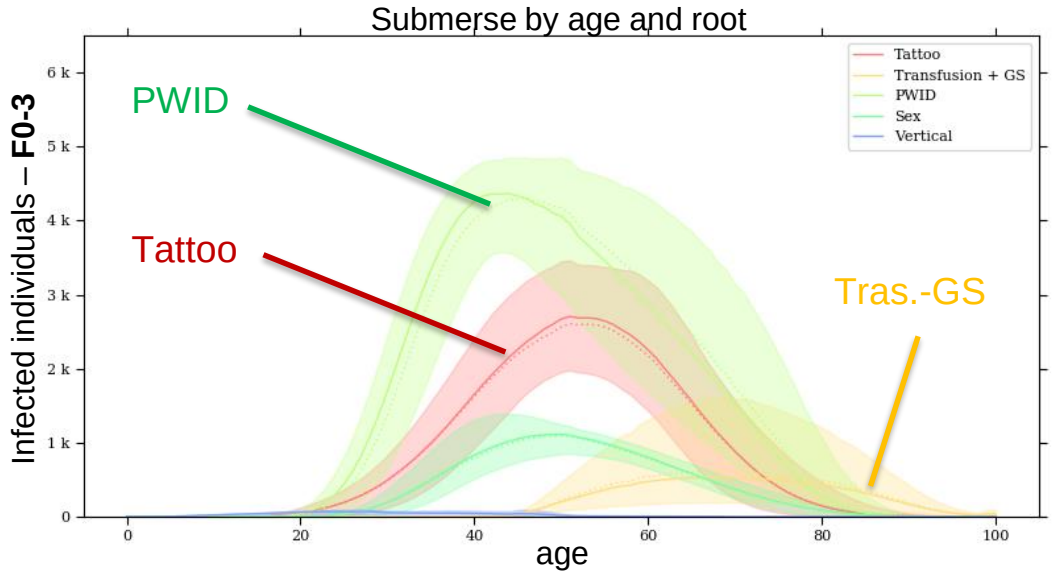
3) SEX: 12.0% (95% CI:9.5%-14.9%)

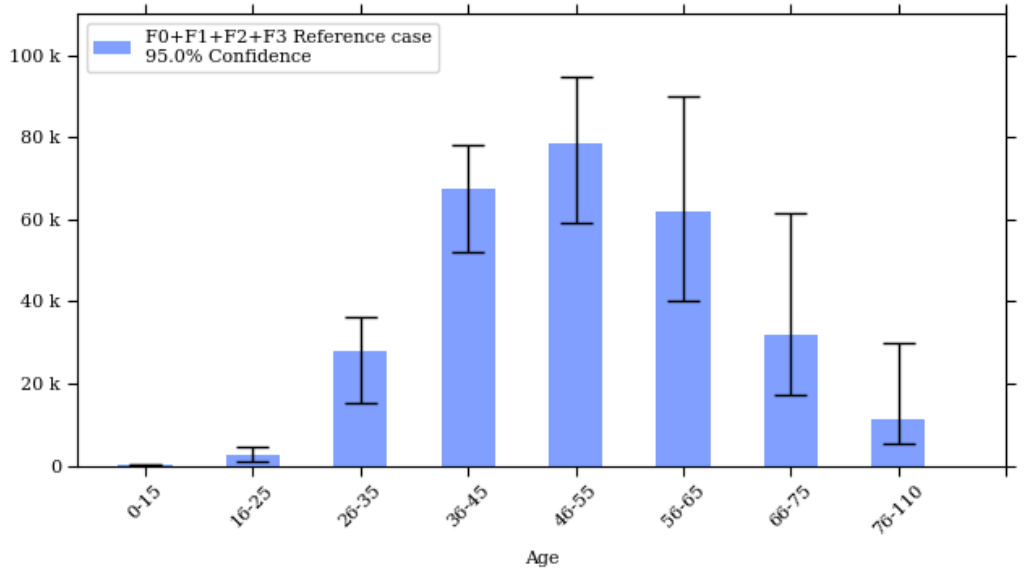
4) GLASS SYRINGE + TRANSFUSION: 6.4% (95% CI: 3.3%-13.9%)

5) VERTICAL: 0.7% (95% CI:0.5%-1.0%)

Where is the submerse (F0–F3, asymptomatic and undiagnosed/unlinked to care)

- The most abundant routes are: PWID and Tattoo
- Nosocomial infection (glass syringe and transfusion) is only found in aged population
- Sex and Vertical are marginal roots of transmissions
- **HCV peaks at 50 years of age**
- 2/3 of the population >46 years old





Conclusioni

- In Italia, l'implementazione di uno screenimg graduato, cominciando dalle coorti di nascita 1968–87, a seguire successivamente con lo screening delle coorti di nascita più anziane 1948–67 è la stretegia più costo efficace nel raggiungere gli obbiettivi dell'eliminazione.

- L'implementazione di uno screening graduato a partire dalle coorti piu' anziane è costo efficace rispetto allo status quo e allo screening Universale e puo' essere preso in considerazione in alcune regioni Italiane secondo le prevalenze dell'infezione per età.

Acknowledgments

- **PITER Collaborating Group**

available in www.progettopiter.it

- **Monitoring DAA AIFA Registry**

- ***Center Disease Analysis & Polaris Observatory Team***

(Laffayette Colorado USA)

- **Facolta di Economia Università di Tor Vergata**

(Roma)