HCV Ø?
DALL'ERADICAZIONE
DEL VIRUS ALLA PRESA IN
CARICO DEL PAZIENTE

Padova, 4 dicembre 2017

STATO DELL'ARTE E NUOVI SCENARI NELL'OBIETTIVO HCV Ø

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CENTRO NAZIONALE **PER LA SALUTE GLOBALE**

ITALIAN CENTER FOR **GLOBAL HEALTH**

Research And Action To Fight Health Inequalities Worldwide

Basic and Translational Research

Clinical Epidemiology

Clinical Research

Education and Training

Health Systems Research, Innovative Models of Care

International Cooperation

Maternal, Newborn and Child Health (MNCH)

Migration Medicine

Natural Substances, Traditional Medicine, Integrated Medicine

Operational and Implementation Research

Policy and Advocacy

Work with International Organizations and the UN System

Il Centro Nazionale per la Salute Globale

*"Svolge attivita' di **ricerca**, sia nei paesi economicamente sviluppati che in quelli meno sviluppati, affrontando il "come applicare" le conoscenze della medicina e della biologia moderne alla salute di tutte persone che vivono sul territorio nazionale e nel mondo, con una filosofia generale basata sul **contrasto alle diseguaglianze di salute**, sulla lotta alle discriminazioni di genere, e **un'attenzione particolare alle popolazioni piu' fragili e marginalizzate**; lavora per contribuire, insieme ad altri attori nazionali e internazionali, a **combattere le disuguaglianze nell'accesso alla salute, in Italia e nel mondo,** attraverso attivita' di ricerca fondamentale, clinica e operativa, ricerca sui sistemi sanitari, progetti di cooperazione internazionale, attivita' di formazione, advocacy e networking"*

ISTITUTO SUPERIORE DI SANITÀ

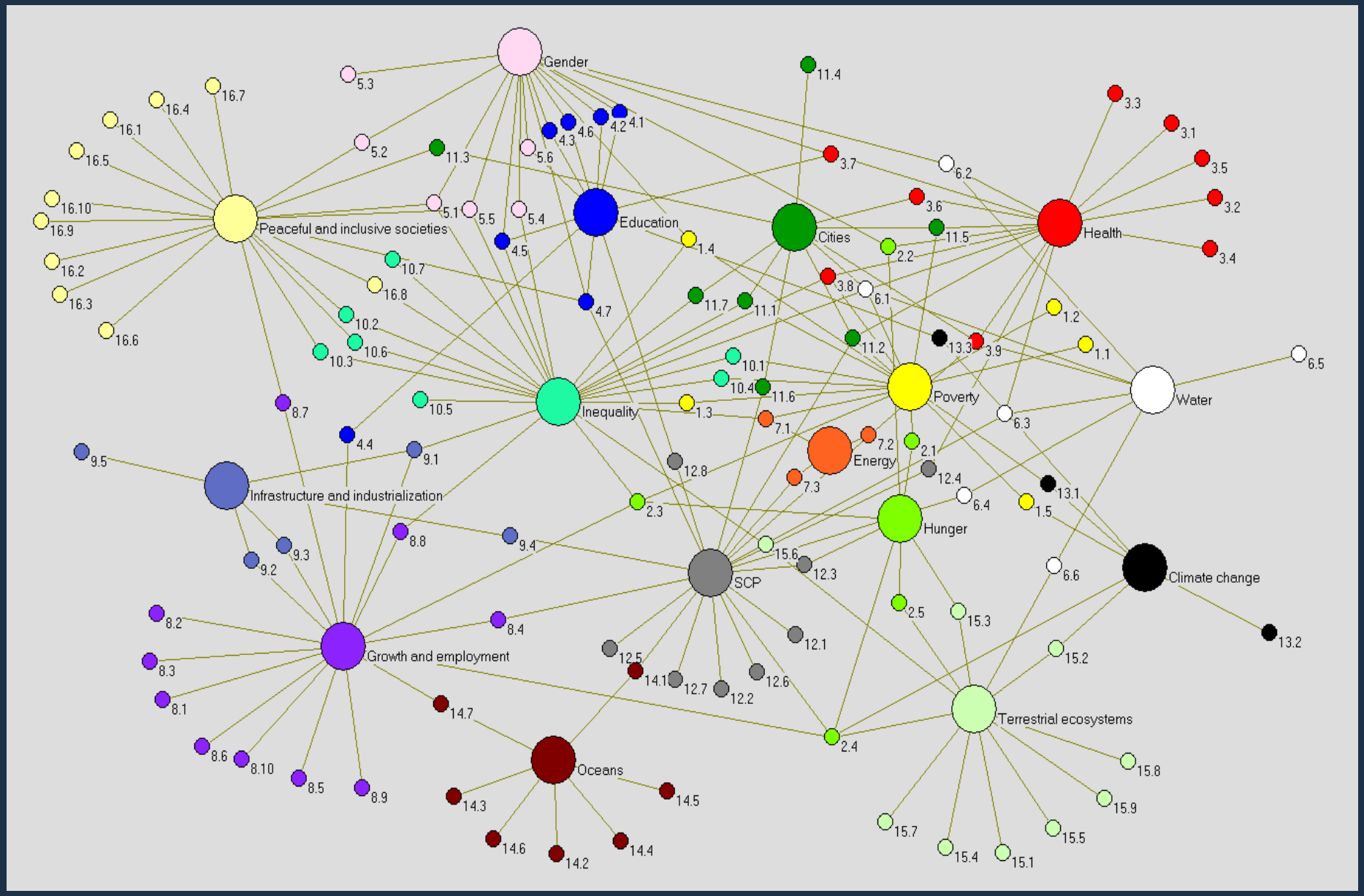
ITALIAN CENTER FOR GLOBAL HEALTH

FIGHTING HEALTH INEQUALITIES

Figure 1. The 17 Sustainable Development Goals

"Transforming our world: the 2030 Agenda for Sustainable Development", https://sustainabledevelopment.un.org/post2015/transformingourworld.

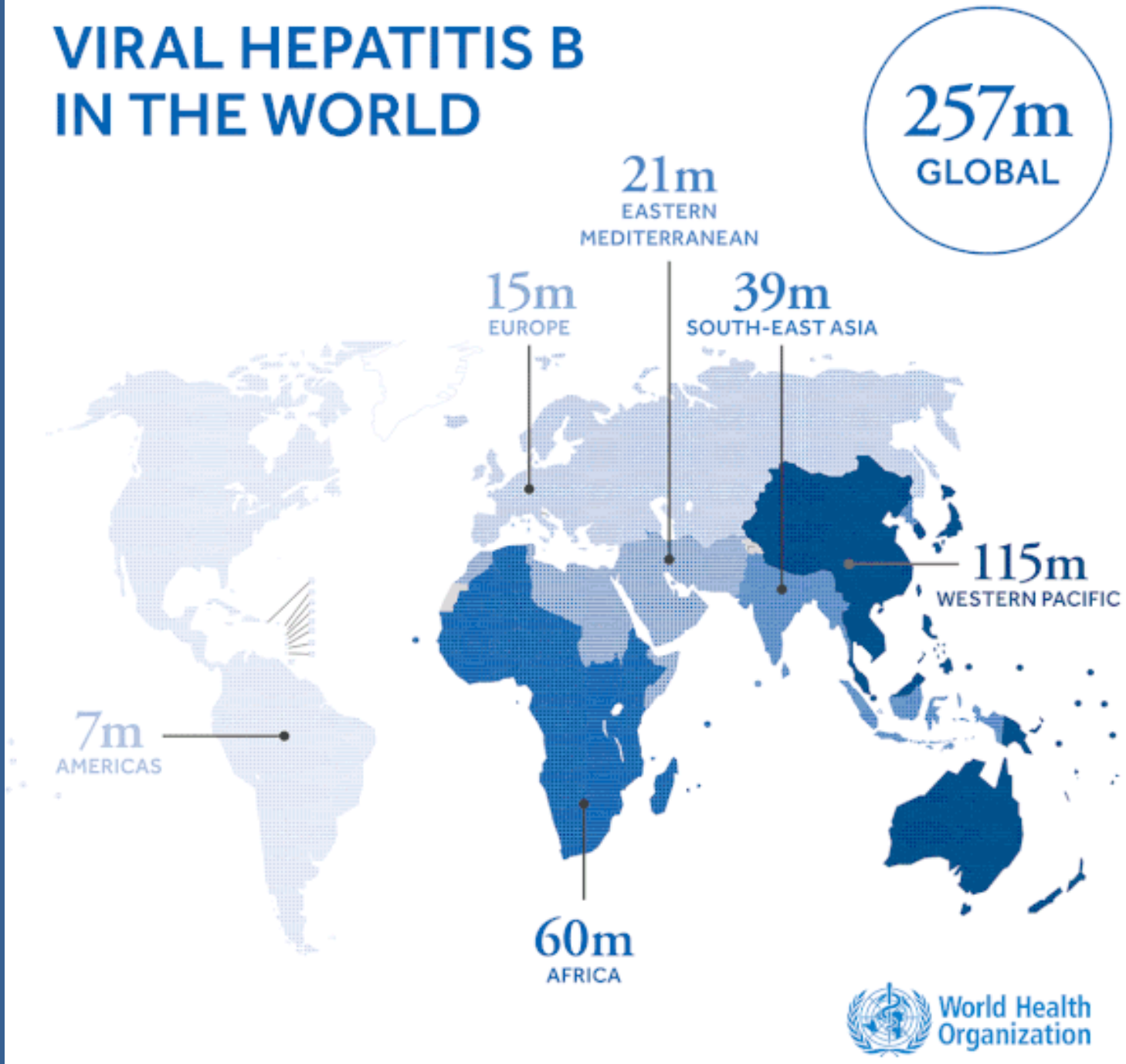
SDGs INTERLINKAGE



SDG # 3


SUSTAINABLE DEVELOPMENT GOAL 3 AND ITS TARGETS
SDG 3:
ENSURE HEALTHY LIVES AND PROMOTE WELL-BEING FOR ALL AT ALL AGES
TARGET 3.8: ACHIEVE UNIVERSAL HEALTH COVERAGE, INCLUDING FINANCIAL RISK PROTECTION, ACCESS TO QUALITY ESSENTIAL HEALTH-CARE SERVICES, MEDICINES AND VACCINES FOR ALL
MDG UNFINISHED AND EXPANDED AGENDA
3.1: Reduce maternal mortality
3.2: End preventable newborn and child deaths
3.3: End the epidemics of AIDS, TB, malaria and NTDs
and combat hepatitis, waterborne and other communicable diseases
3.7: Ensure universal access to sexual and reproductive health-care services
NEW SDG 3 TARGETS
3.4: Reduce mortality from NCDs and promote mental health
3.5: Strengthen prevention and treatment of substance abuse
3.6: Halve global deaths and injuries from road traffic accidents
3.9: Reduce deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination
SDG 3 MEANS OF IMPLEMENTATION TARGETS
3.a: Strengthen implementation of framework convention on tobacco control
3.b: Provide access to medicines and vaccines for all, support R&D of vaccines and medicines for all
3.c: Increase health financing and health workforce in developing countries
3.d: Strengthen capacity for early warning, risk reduction and management of health risks
INTERACTIONS WITH ECONOMIC, OTHER SOCIAL AND ENVIRONMENTAL SDGs AND SDG 17 ON MEANS OF IMPLEMENTATION

VIRAL HEPATITIS B IN THE WORLD



VIRAL HEPATITIS C IN THE WORLD

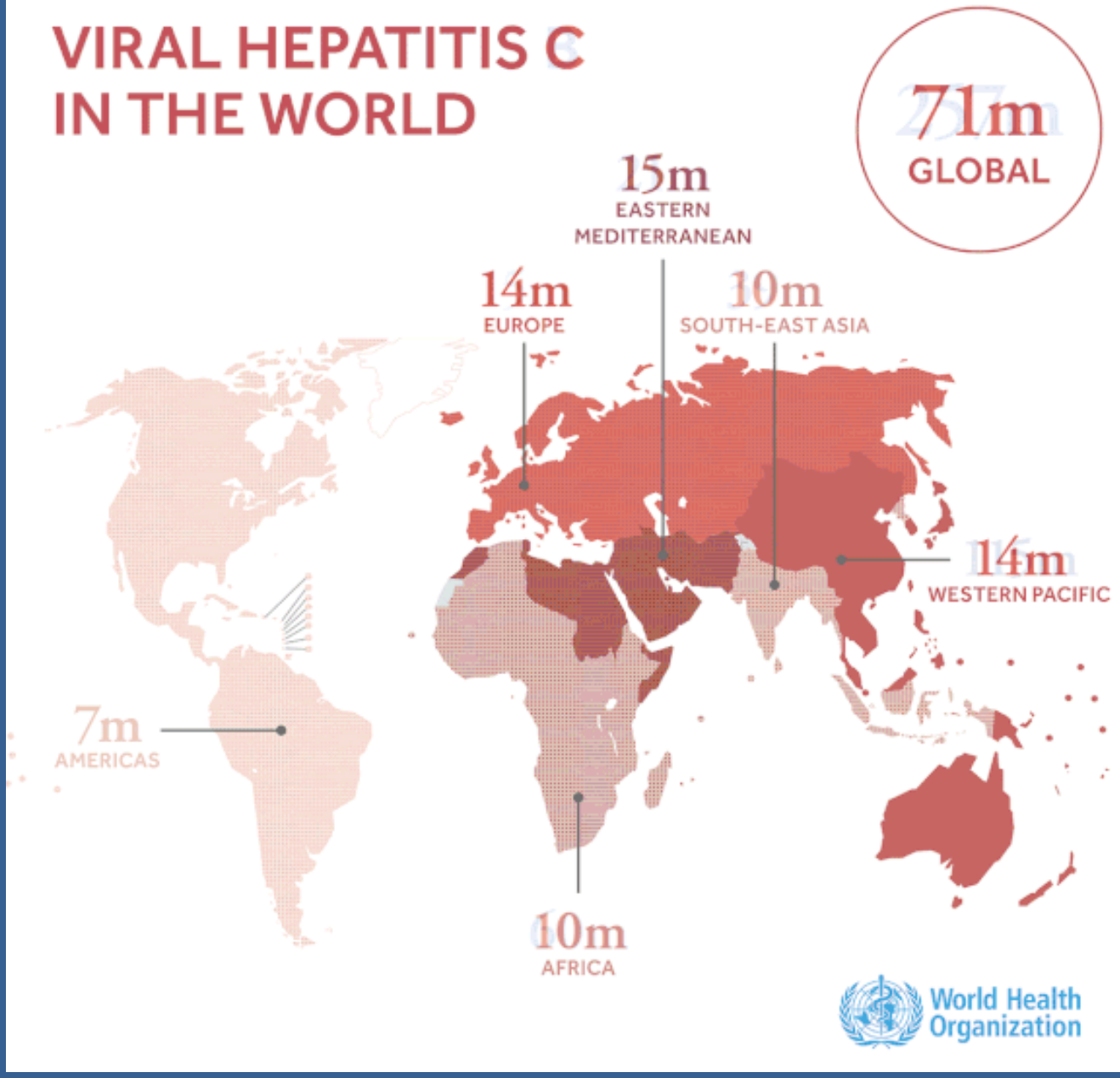
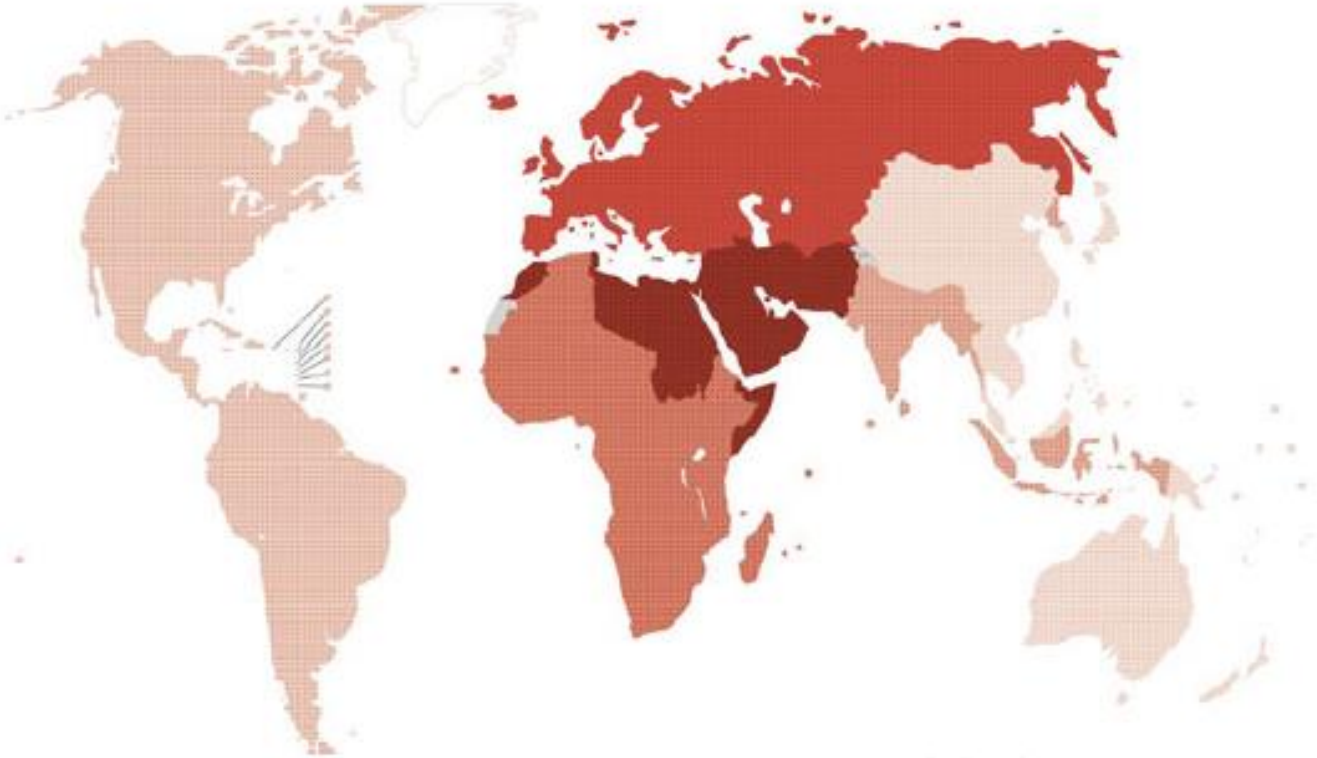


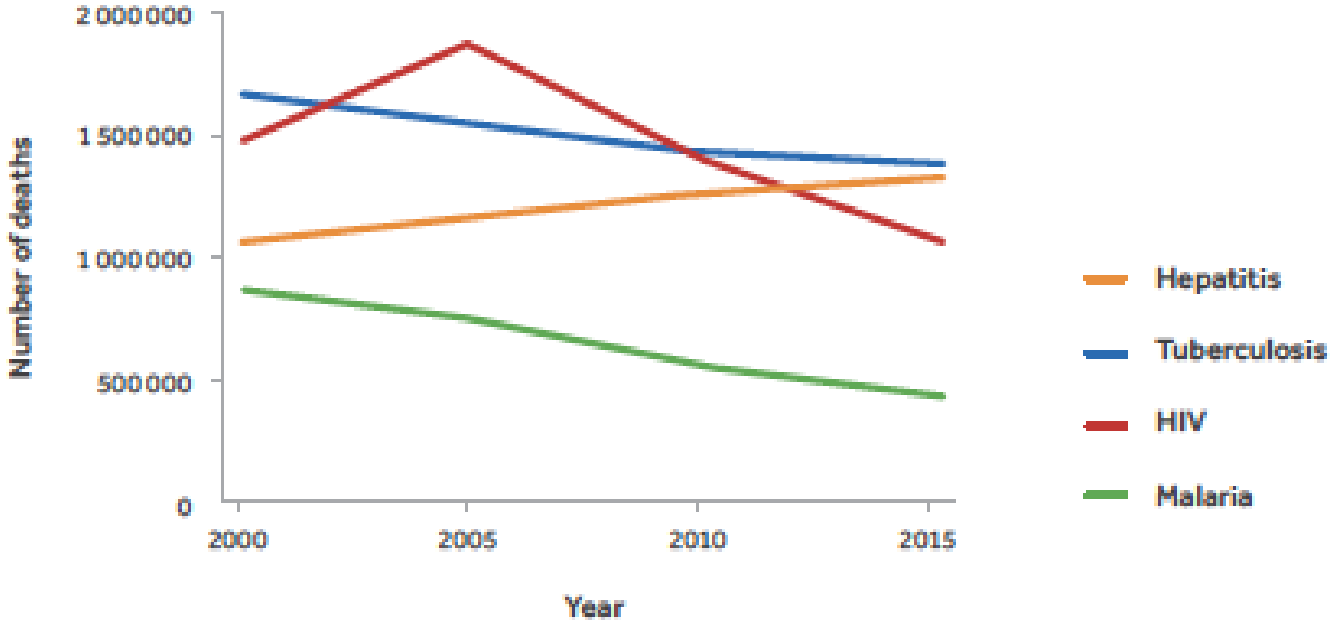
Table 3 (with map). Incidence of HCV infection in the general population, by WHO region, 2015: 1.75 million new infections in 2015



		Incidence of HCV infection			
		Incidence rate (per 100 000)		Total number (000)	
WHO region	Map key	Best estimate	Uncertainty interval	Best estimate	Uncertainty interval
African Region		31.0	22.5–54.4	309	222–544
Region of the Americas		6.4	5.9–7.0	63	59–69
Eastern Mediterranean Region		62.5	55.6–65.2	409	363–426
European Region		61.8	50.3–66.0	565	460–603
South-East Asia Region		14.8	12.5–26.9	287	243–524
Western Pacific Region		6.0	5.6–6.6	111	104–124
Global		**23.7**	**21.3–28.7**	**1 751**	**1 572–2 120**

Source: WHO, work conducted by the Center for Disease Analysis. *See* Annex 2.

Fig. 2. Global annual mortality from hepatitis, HIV, tuberculosis and malaria, 2000–2015: unlike HIV, tuberculosis and malaria, the trend in mortality from viral hepatitis is increasing

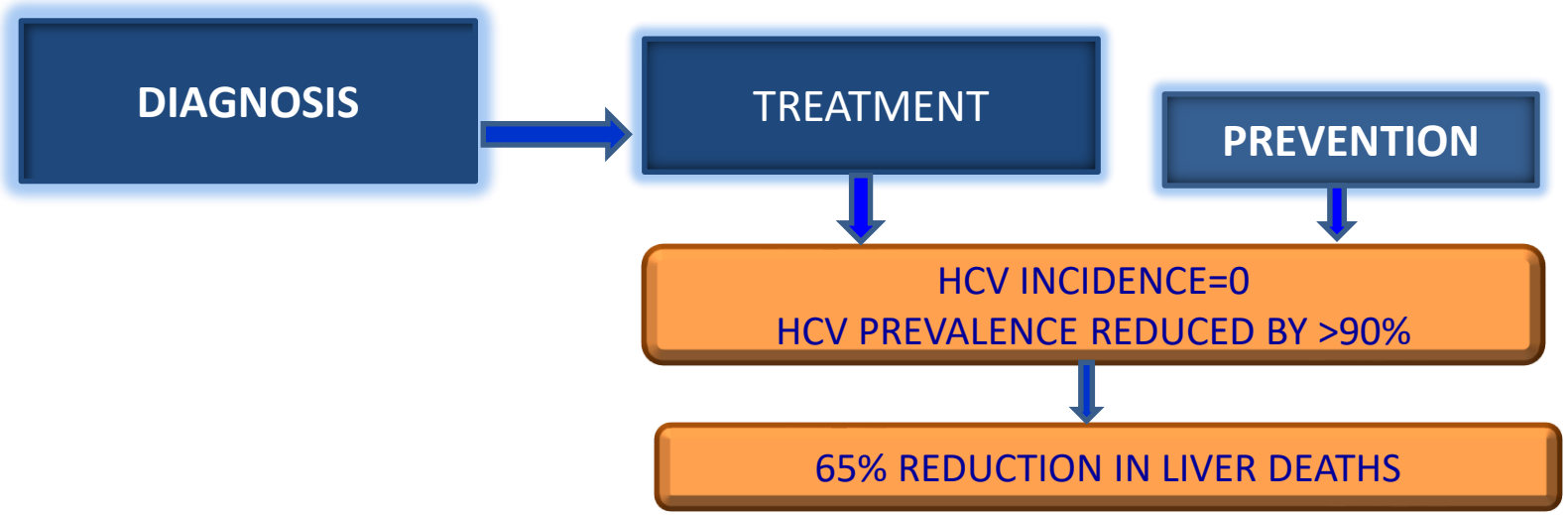


Source: WHO global health estimates (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000-2015. Geneva: World Health Organization; 2016.)

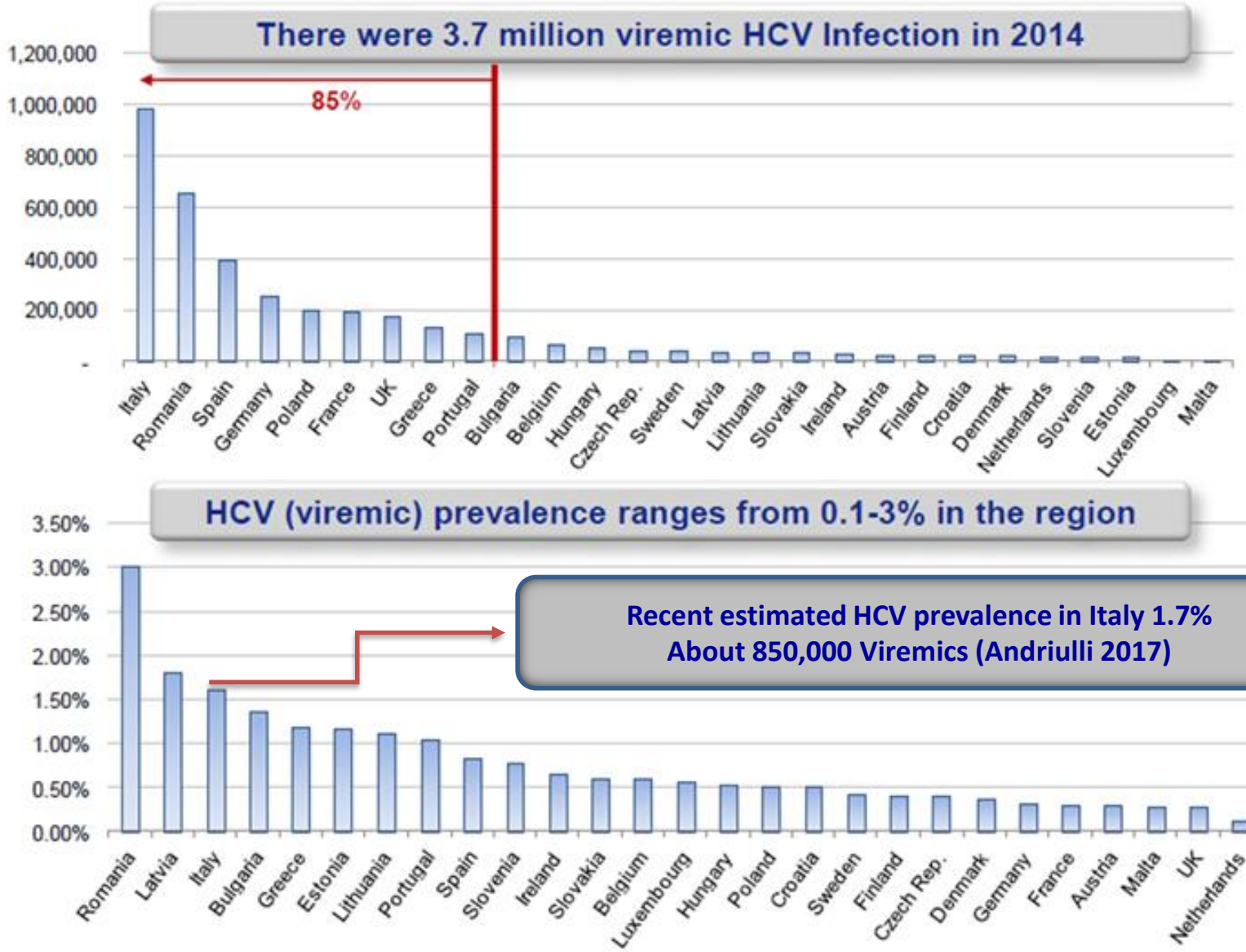
World Health Organization

Goals for HCV Elimination

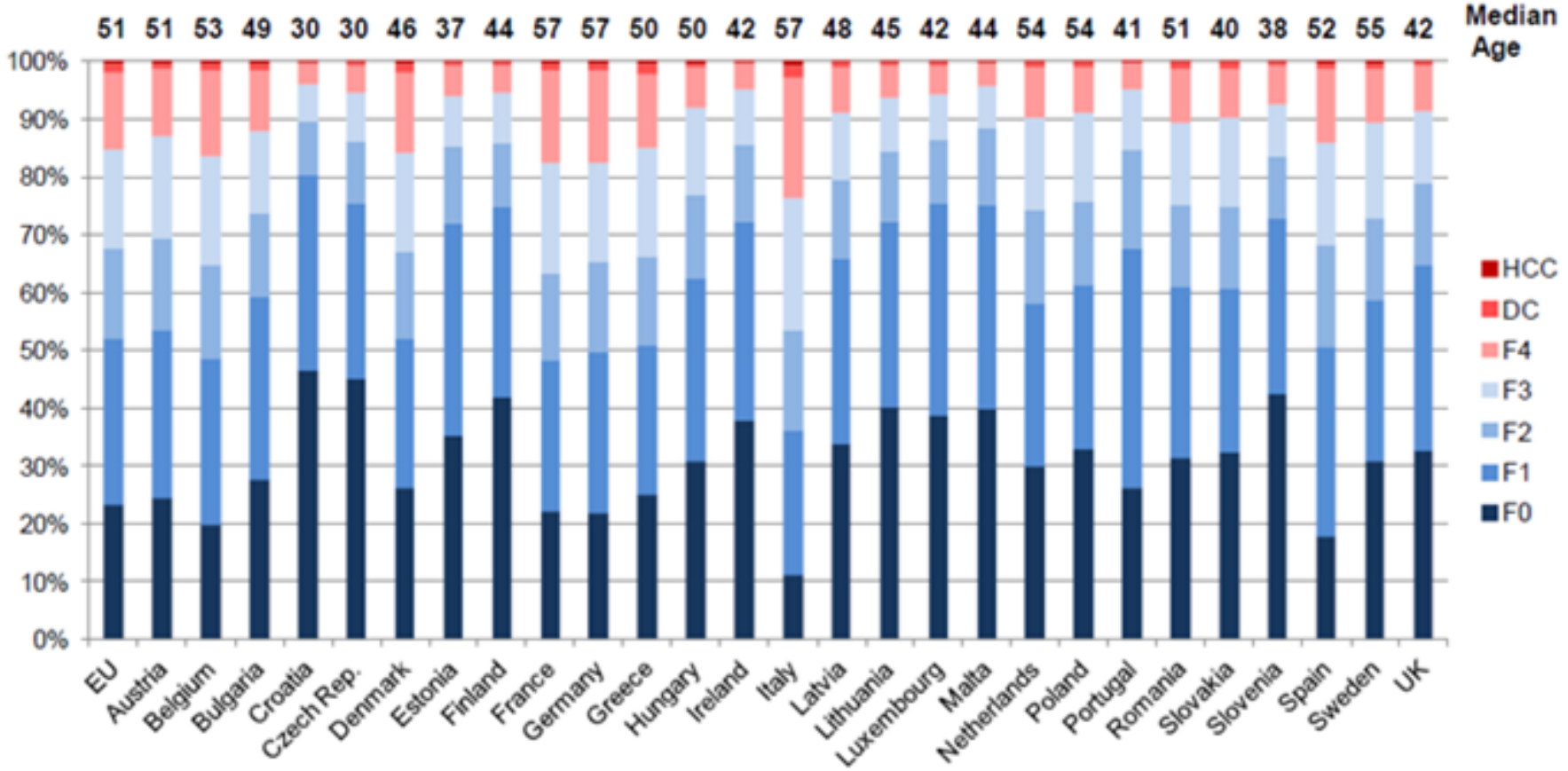
Elimination of HCV in the country treating 80% of eligible patients strengthened by prevention interventions



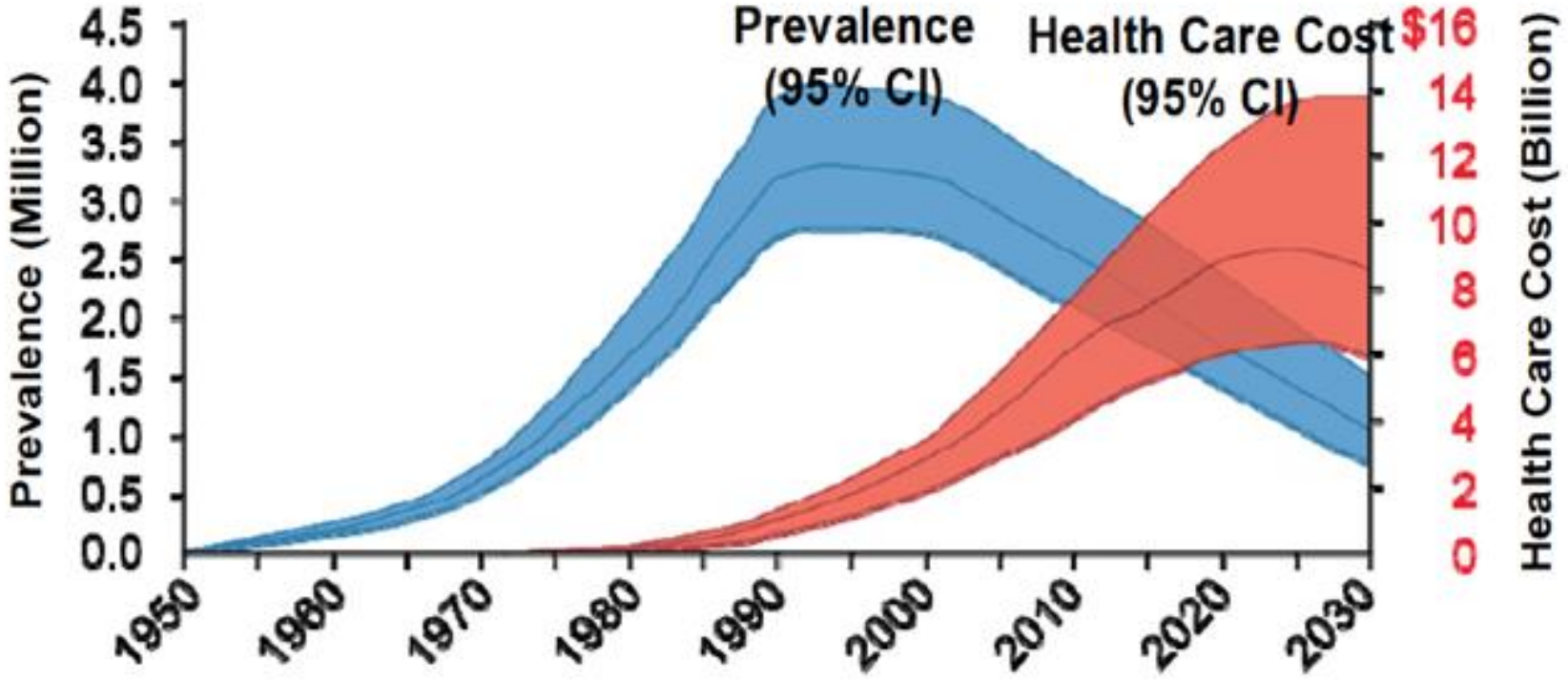
Italy, Romania, Spain, Germany, Poland , France , UK, Greece and Portugal account for 85% of total infections in EU



The fibrosis distribution in each country correlates strongly with the median age of the HCV infected population



Increasing Health Care Costs Associated With Progressive Liver Disease in the Aging HCV-Infected Population

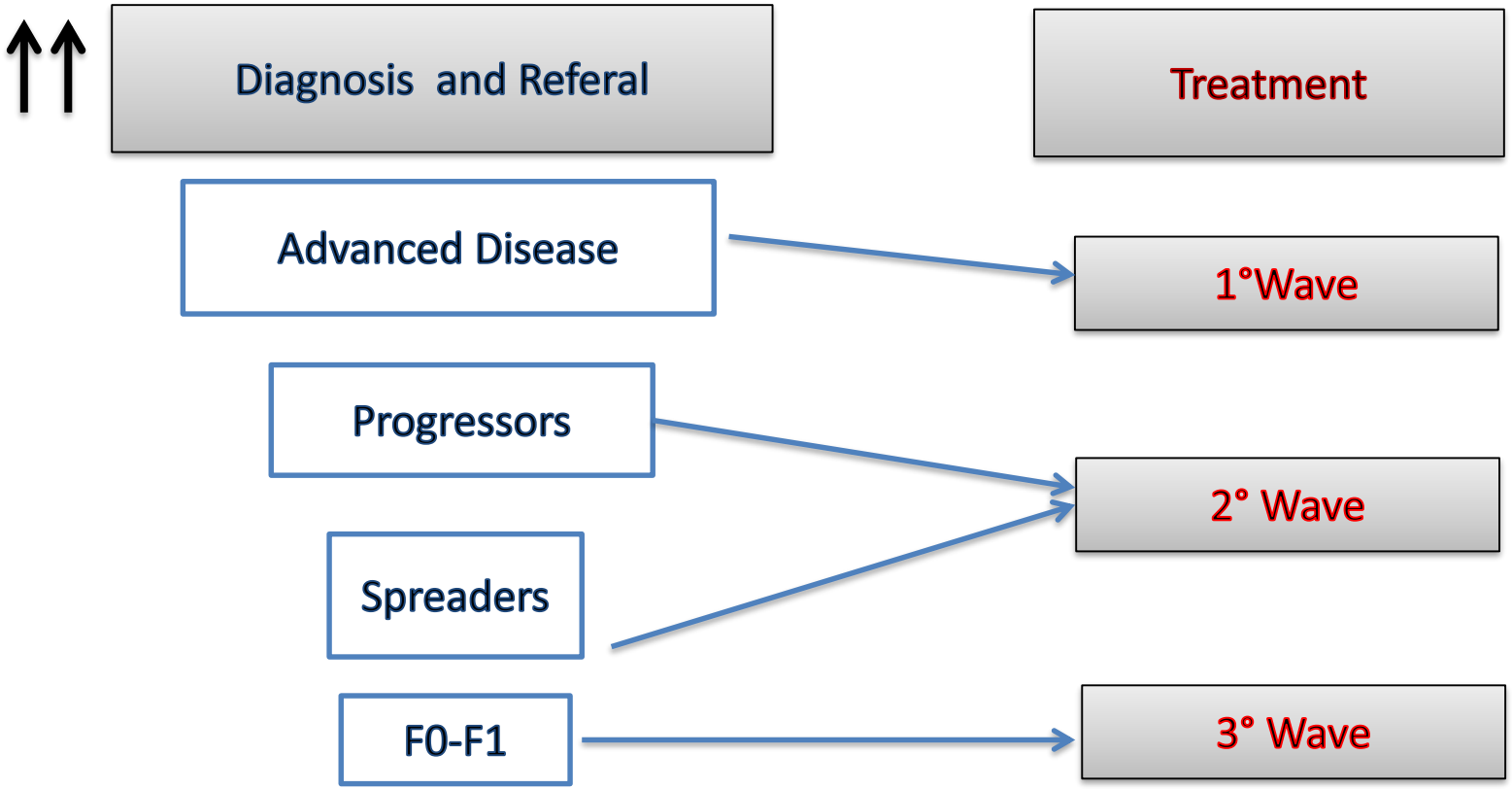


- While the prevalence of HCV infection is declining from its peak, the incidence of advanced liver disease and associated health care costs continue to rise
- Modeling does not take into account any impact of birth cohort screening

A system dynamic modeling framework was used to quantify the HCV-infected population, the disease progression, and the associated cost from 1950-2030.
CI=confidence interval.

H. Razavi, CDA

Step-wise strategy for HCV elimination



Alberti A. AISF 2017
adapted from Wedemeyer et al J. Hepatology 2016

SOME DEFINITIONS PROPEDEUTIC TO THIS TALK

Dowdle WR, WHO Bull 2006

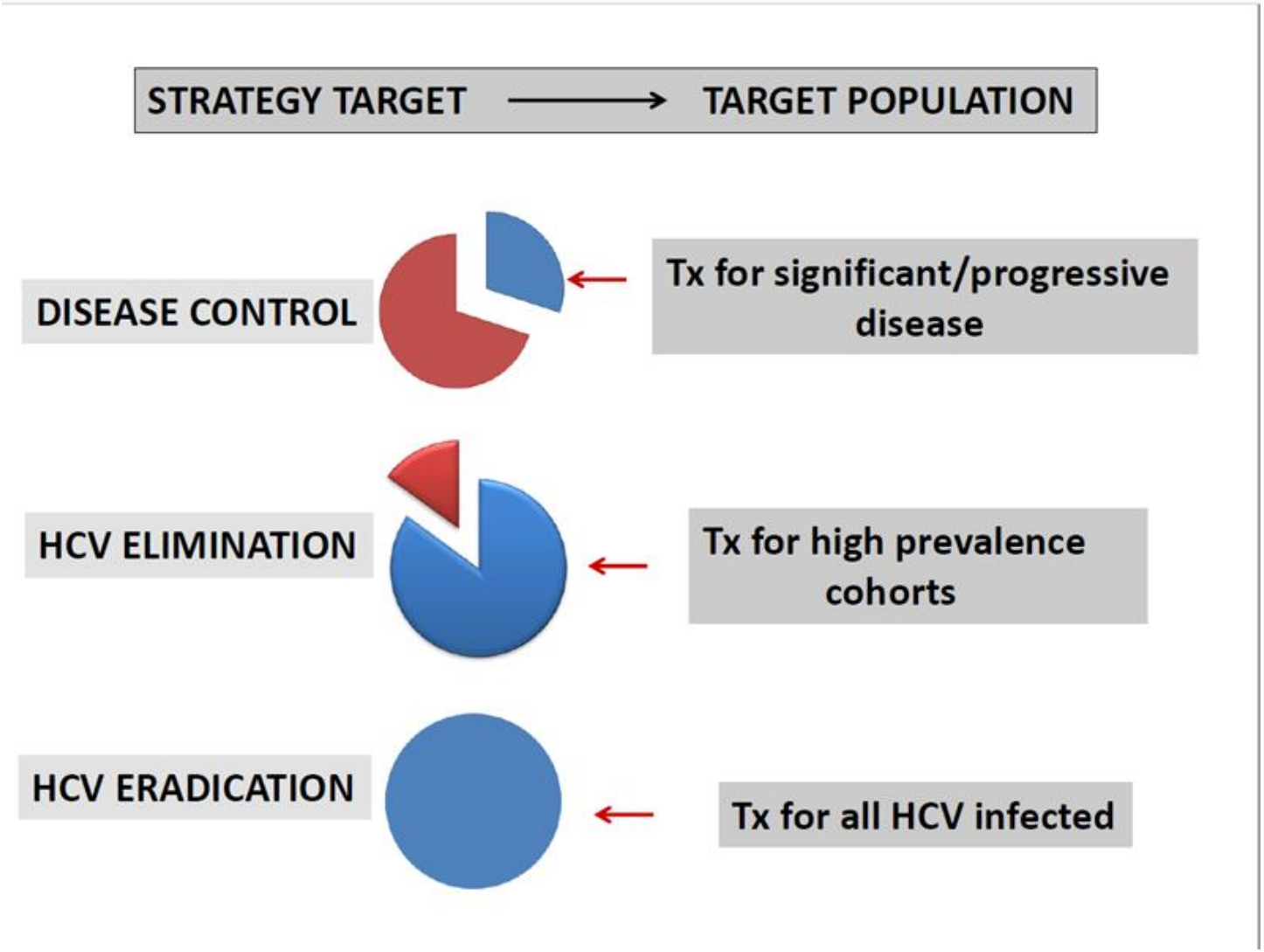
DISEASE CONTROL :
reduction in morbidity and mortality

ELIMINATION :
no transmission/zero incidence and
reduced prevalence to an «acceptable» level in a given region
Continued interventions needed
Example : POLIOMYELITIS

ERADICATION :
Global and Total absence of human cases, no reservoir in nature
Interventions can be stopped

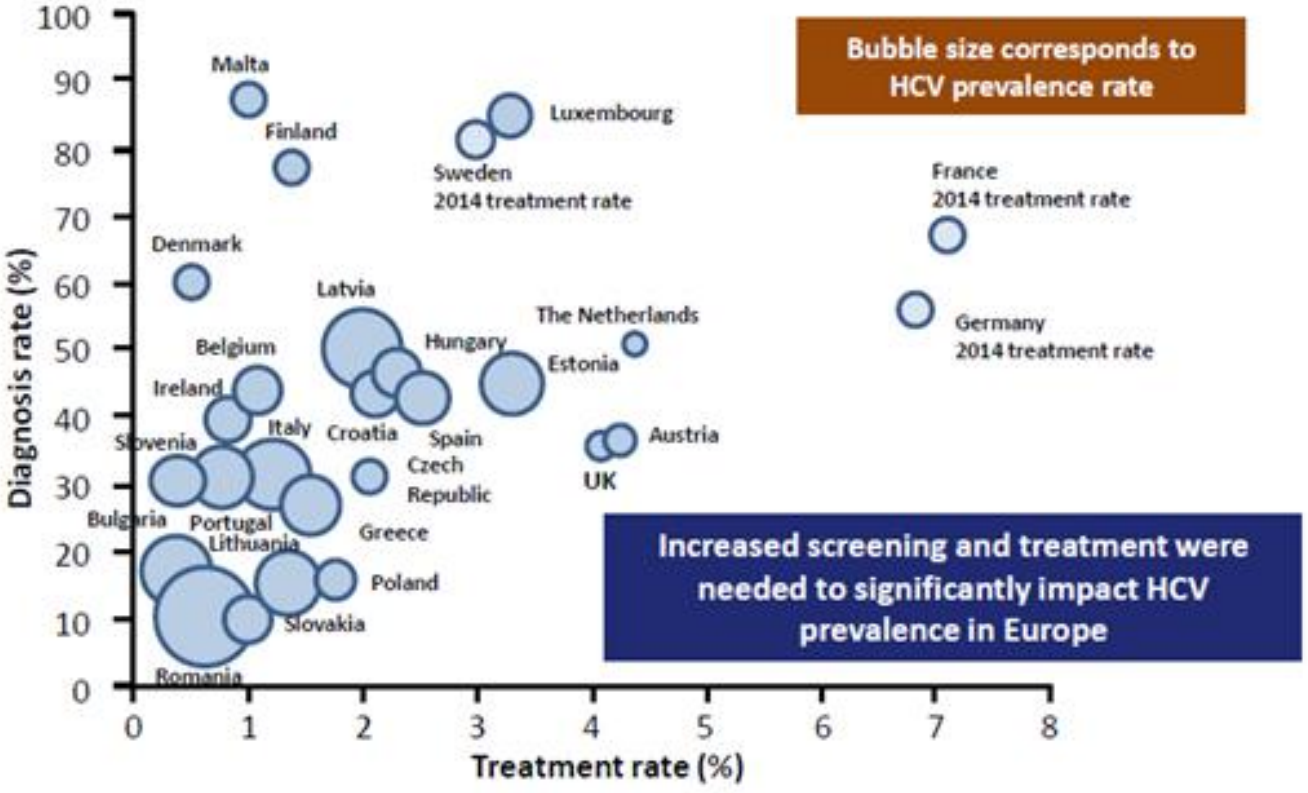
Example : SMALLPOX

Adapted by Alberti AISF 2017



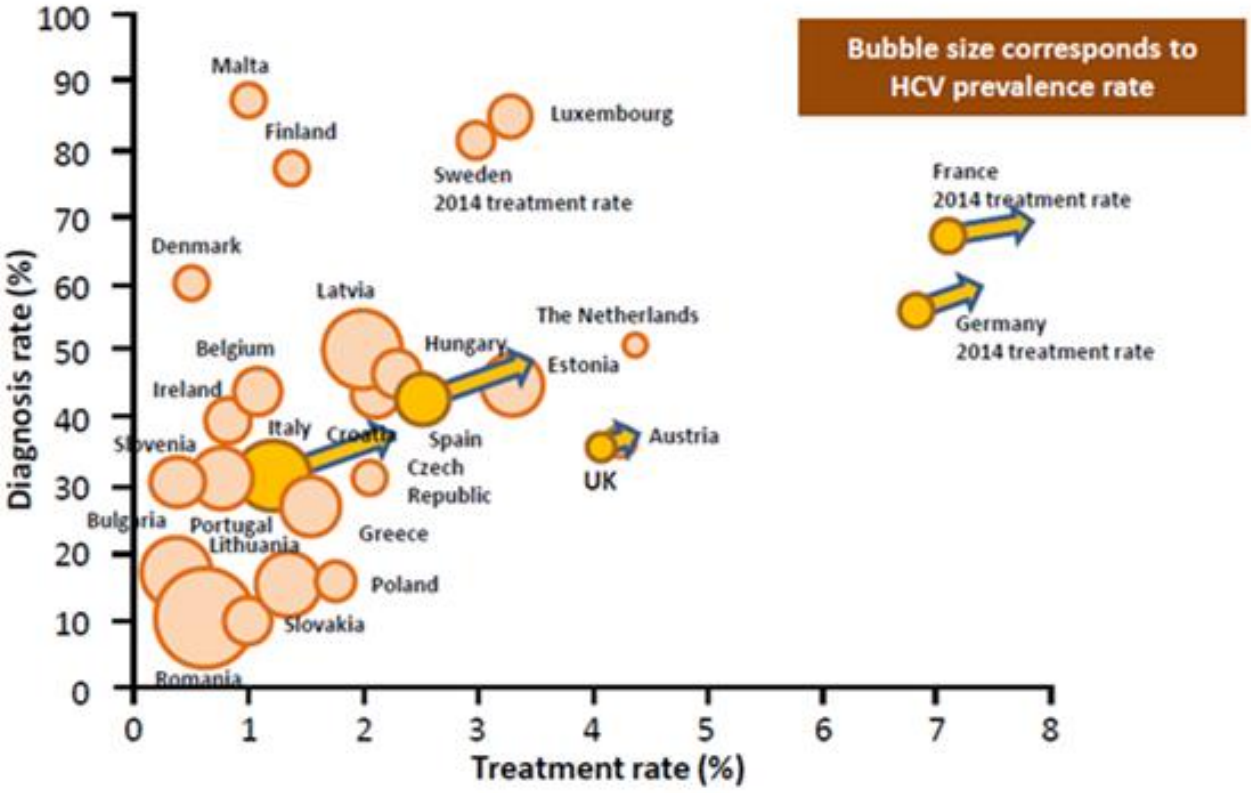
Alberti AISF 2017

In 2013, treatment rates across most of Europe were very low



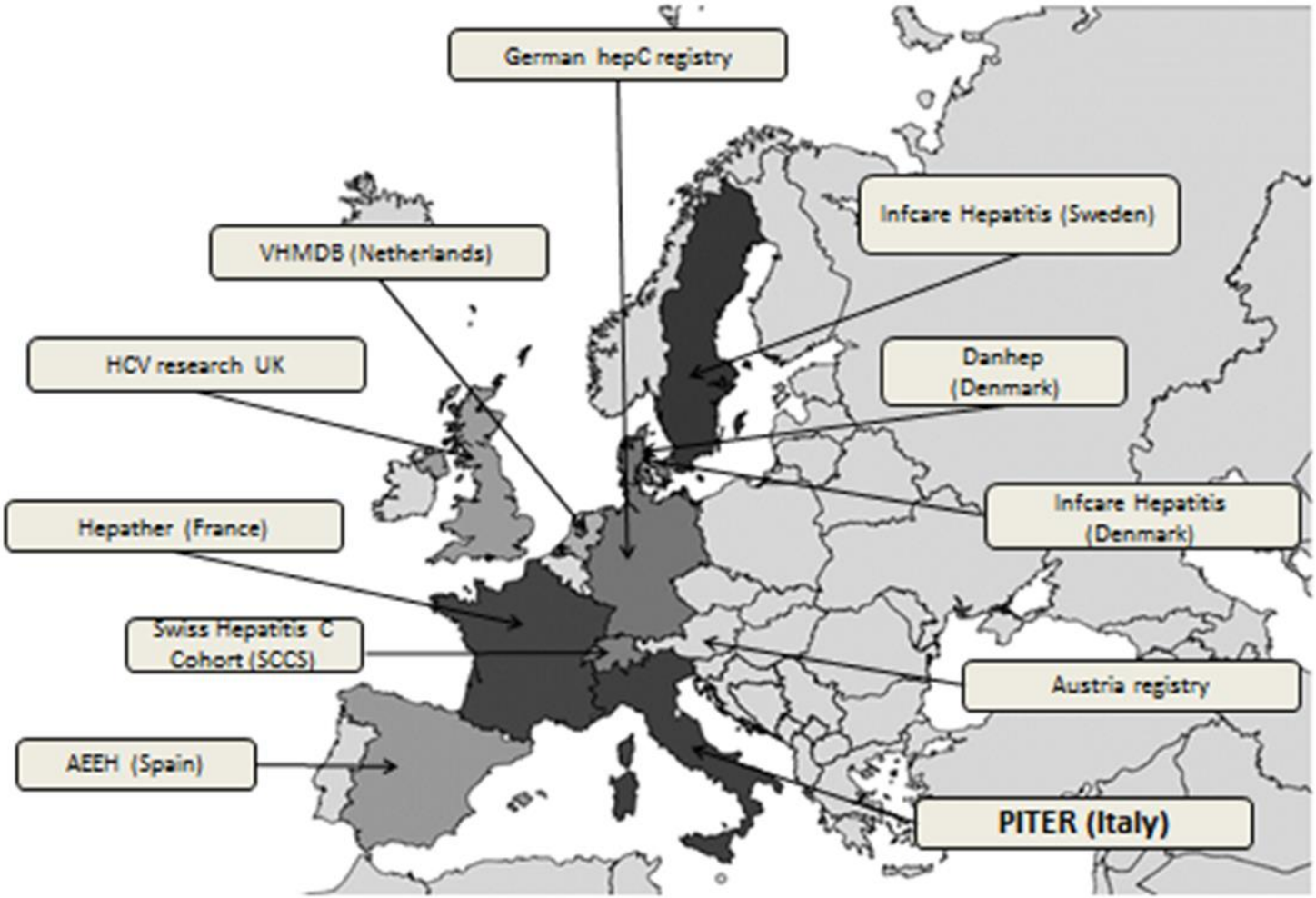
Razavi H. Current Epidemiology Data on HCV/HBV in Europe.
Available at: http://regist2.virology-education.com/2015/1euhep/03_Razavi.pdf (accessed April 2016)

In 2016, rates are increasing



Updated from Razavi H. Current Epidemiology Data on HCV/HBV in Europe. Available at: http://regist2.virology-education.com/2015/1euhep/03_Razavi.pdf; Center for Disease Analysis: Polaris Observatory. Available at: http://centerforcda.com/polaris/ (both accessed April 2016).

Coorti HCV in EUROPA
STRUMENTI PER LA CREAZIONE DI EVIDENZE

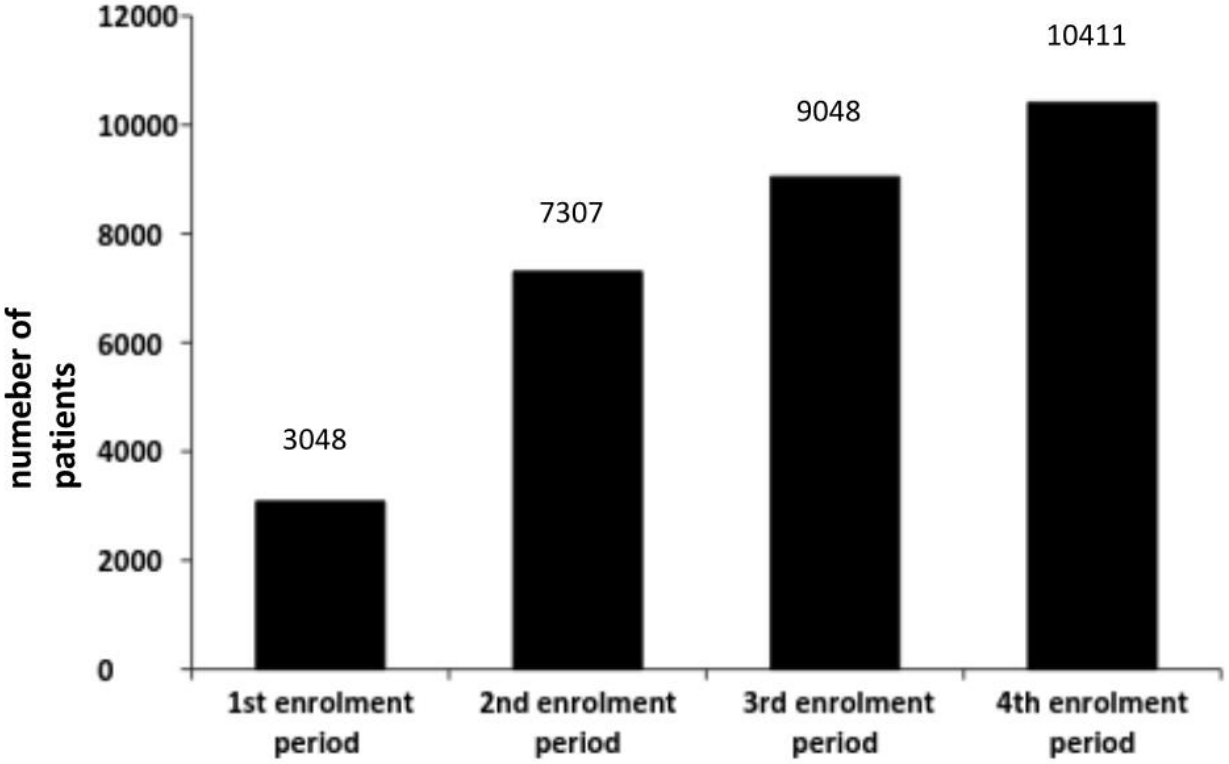


PITER è il primo Studio Nazionale su HCV

La Coorte PITER dei pazienti HCV è rappresentativa dei pazienti con infezione cronica da HCV *in cura* in Italia

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

Number of enrolled patients



Pubblicazioni

- Modelling cost-effectiveness and health gains of a “universal” vs. “prioritized” HCV treatment policy in a real-life cohort. Hepatology 2017
- Premature ovarian senescence and high miscarriage rate impair fertility in women with hepatitis C virus infection. Journal of Hepatology 2017.
- 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. PLoS One 2017
- Mixed cryoglobulinemia: an important but frequently unrecognized and underestimated HCV-related condition in the real life practice. Liver International 2017
- 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. PLoS One 2017
- PITER-HCV cohort study as part of the Italian platform for the study of viral hepatitis therapies. Rapporti ISTISAN. 2015
- PITER: An ongoing nationwide study on the real-life impact of direct acting antiviral based treatment for chronic hepatitis C in Italy. Digestive and Liver Disease 2015
- La Piattaforma Italiana per lo Studio della Terapia delle Epatiti Virali (PITER): il primo grande studio nazionale sull'infezione cronica da virus dell'epatite C. Notiziario Istituto Superiore di Sanità 2015

HEPATOLOGY

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Viral Hepatitis

Modelling cost-effectiveness and health gains of a "universal" vs. "prioritized" HCV treatment policy in a real-life cohort

Loreta A. Kondili, Federica Romano, Francesca Romana Rolli, Matteo Ruggeri, Stefano Rosato, Maurizia Rossana Brunetto, Anna Linda Zignego, Alessia Ciancio, Alfredo Di Leo, Giovanni Raimondo, Carlo Ferrari, Gloria Taliani, Guglielmo Borgia, Teresa Antonia Santantonio, Pierluigi Blanc, Giovanni Battista Gaeta, Antonio Gasbarrini, Luchino Chessa, Elke Maria Erne, Erica Villa, Donatella Ieluzzi, Francesco Paolo Russo, Pietro Andreone, Maria Vinci, Carmine Coppola, Liliana Chemello, Salvatore Madonia, Gabriella Verucchi, Marcello Persico, Massimo Zuin, Massimo Puoti, Alfredo Alberti, Gerardo Nardone, Marco Massari, Giuseppe Montalto, Giuseppe Foti, Maria Grazia Rumi, Maria Giovanna Quaranta, Americo Cicchetti, Antonio Craxì, Stefano Vella, on behalf of PITER Collaborating Group

Accepted manuscript online: 24 July 2017 Full publication history

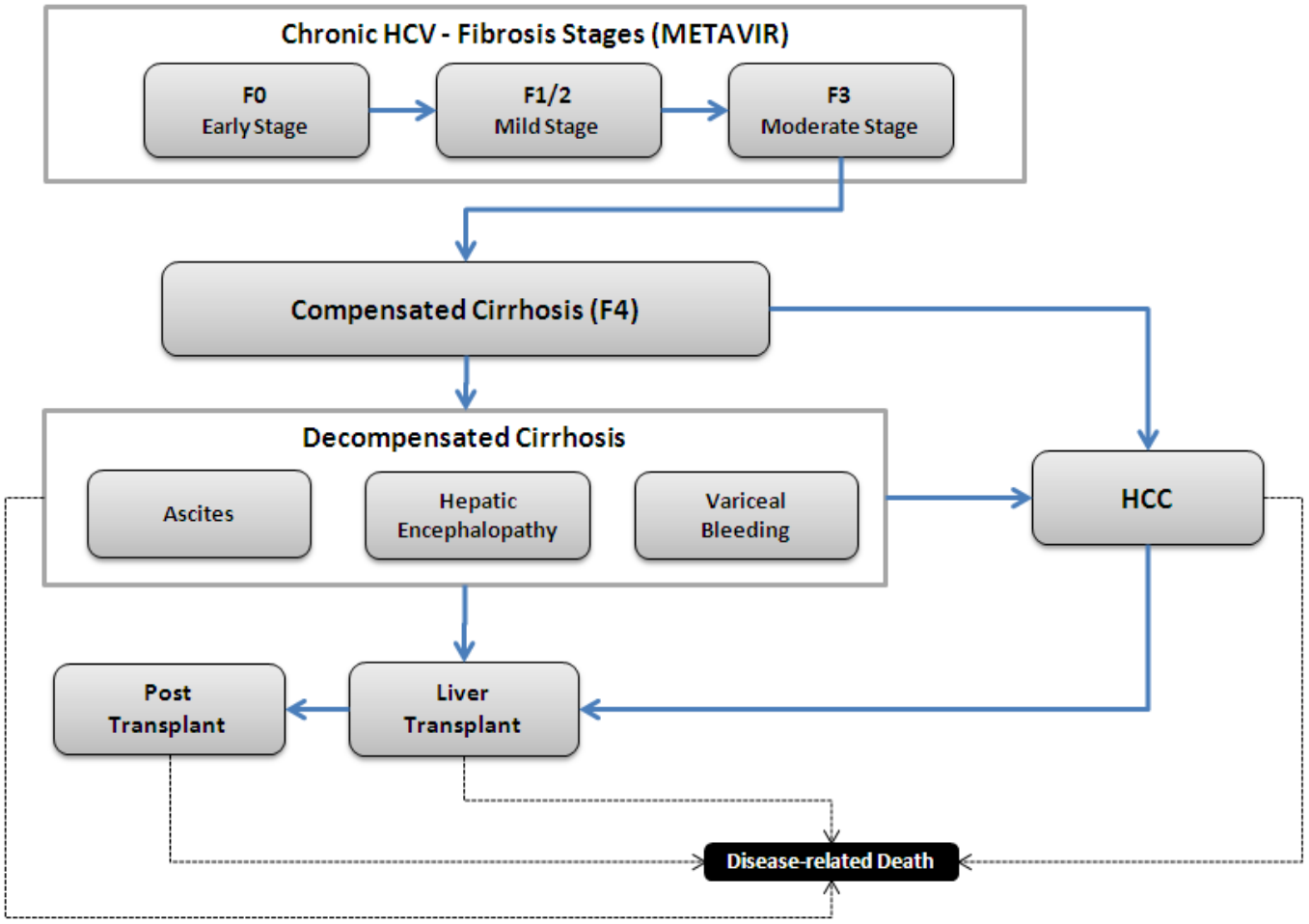
Cost-Effectivness Analysis

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.

Markov model for liver disease progression



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	

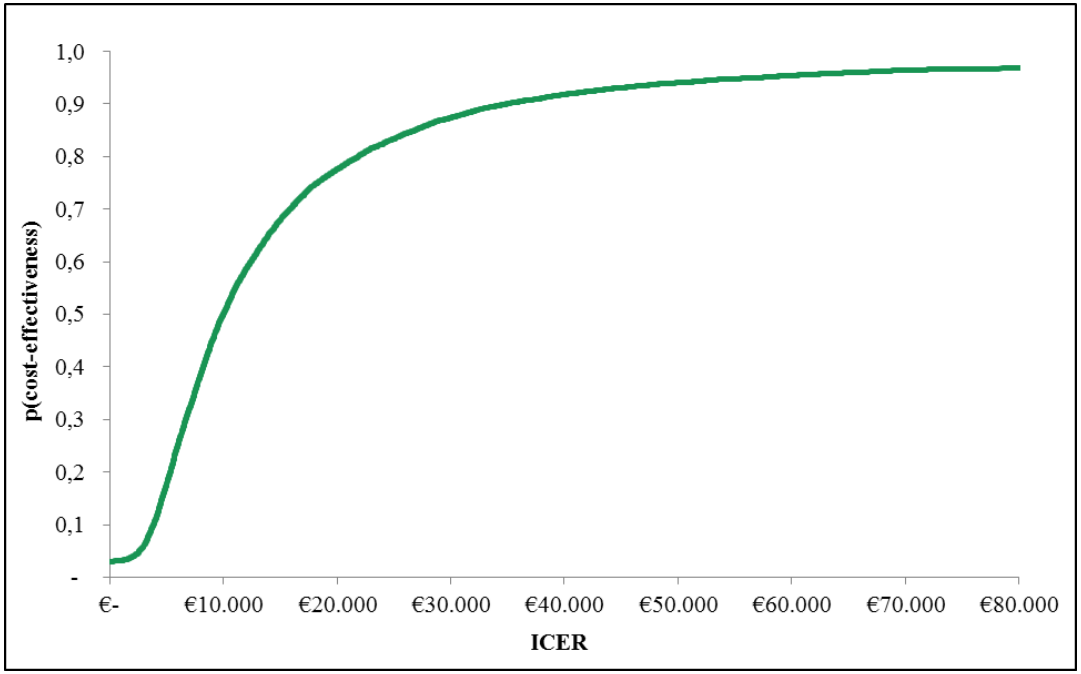
European scenario

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.

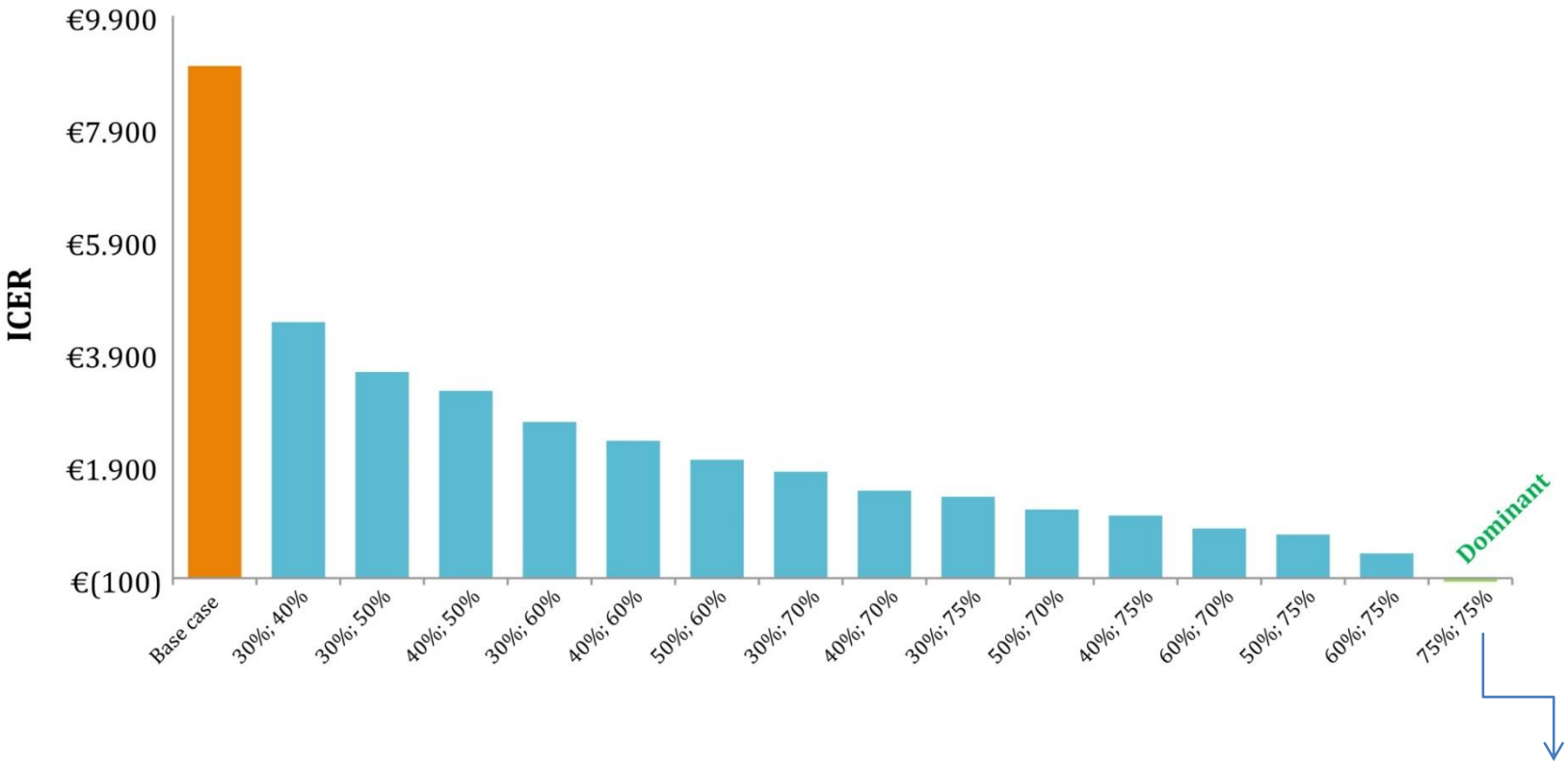
PITER
Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

Cost- Effectiveness Acceptability Curve Italy (PITER) Scenario



When treating all stages of liver disease, ICERs remained below €30,000/QALY gained in 94% of the simulations assumed

Decreasing DAA price scenario analysis



DAA costs= € 3750

Universal Policy = Cost Saving

Periodo: 2015-Aprile 2017

Processo di modulazione di accesso alle nuove terapie che prevede in via prioritaria il trattamento dei pazienti in base ad un criterio di urgenza clinica, come definito dalla Commissione Tecnico Scientifica dell'AIFA.

Eleggibili al DAA
le prime 3 categorie

Categoria I	TERAPIA DEL PAZIENTE CON CIRROSI IN CLASSE DI CHILD-PUGH A e B e/o CON HCC CON RISPOSTA COMPLETA A TERAPIE RESETTIVE CHIRURGICHE O LOCO-REGIONALI, NON CANDIDABILI A TRAPIANTO EPATICO, NEI QUALI LA MALATTIA EPATICA SIA DETERMINANTE PER LA PROGNOSI
Categoria II	TERAPIA DEL PAZIENTE CON RECIDIVA DI EPATITE DOPO TRAPIANTO DI FEGATO CON FIBROSI METAVIR ≥2 (O S3 ISHAK) O CON VARIANTE FIBROSANTE COLESTATICA
Categoria III	TERAPIA DEL PAZIENTE CON EPATITE CRONICA CON GRAVI MANIFESTAZIONI EXTRA-EPATICHE HCV-CORRELATE (SINDROME CRIOGLOBULINEMICA CON DANNO D'ORGANO, SINDROMI LINFOPROLIFERATIVE A CELLULE B)
Categoria IV	TERAPIA DEL PAZIENTE CON EPATITE CRONICA CON FIBROSI METAVIR F3 (O CORRISPONDENTE ISHAK)
Categoria V	TERAPIA DEL PAZIENTE IN LISTA PER TRAPIANTO EPATICO CON CIRROSI MELD <25 e/o CON HCC ALL'INTERNO DEI CRITERI DI MILANO CON LA POSSIBILITA' DI ATTESA IN LISTA DI ALMENO 2 MESI
Categoria VI	TERAPIA DEL PAZIENTE CON EPATITE CRONICA DOPO TRAPIANTO DI ORGANO SOLIDO (NON FEGATO) O DI MIDOLLO CON FIBROSI METAVIR ≥2 (O CORRISPONDENTE ISHAK)
Categoria VII	TERAPIA DEL PAZIENTE CON EPATITE CRONICA CON FIBROSI METAVIR F0-F2 (O CORRISPONDENTE ISHAK)

Revisione ed aggiornamento delle stime epidemiologiche

Prevalenza di soggetti anti-HCV positivi* [5, 6]	
	1.0% – 2.24%
Prevalenza di soggetti anti-HCV positivi in Italia**[4]	↓
	506,994 – 1,135,667
Soggetti per i quali l'infezione è nota: 79.5% [6]	↓
	403,060 – 902,855
Soggetti positivi per HCV RNA : 74.1% [6]	↓
	298,667 – 669,015
Frazionamento per gravità di malattia epatica [3]:	↓
- F0-F1 (39%)	**116,480 – 260,915**
- F2 (15%)	**44,800 – 100,352**
- F3 (12%)	**35,840 – 80,281**
- F4 (34%)	**101,546 – 227,465**

* Dati Rete HCV Sicilia e studio epidemiologico italiano [5, 6]

** Popolazione residente >18 anni: 50,699,447 [4]

3 Kondili, Quaranta MG, Studio Piter
4 ISTAT
5 Andriulli et al, submitted
6 Di Marco V, Cartabellotta F. – Dati Rete Sicilia

Agenzia Italiana del Farmaco
AIFA

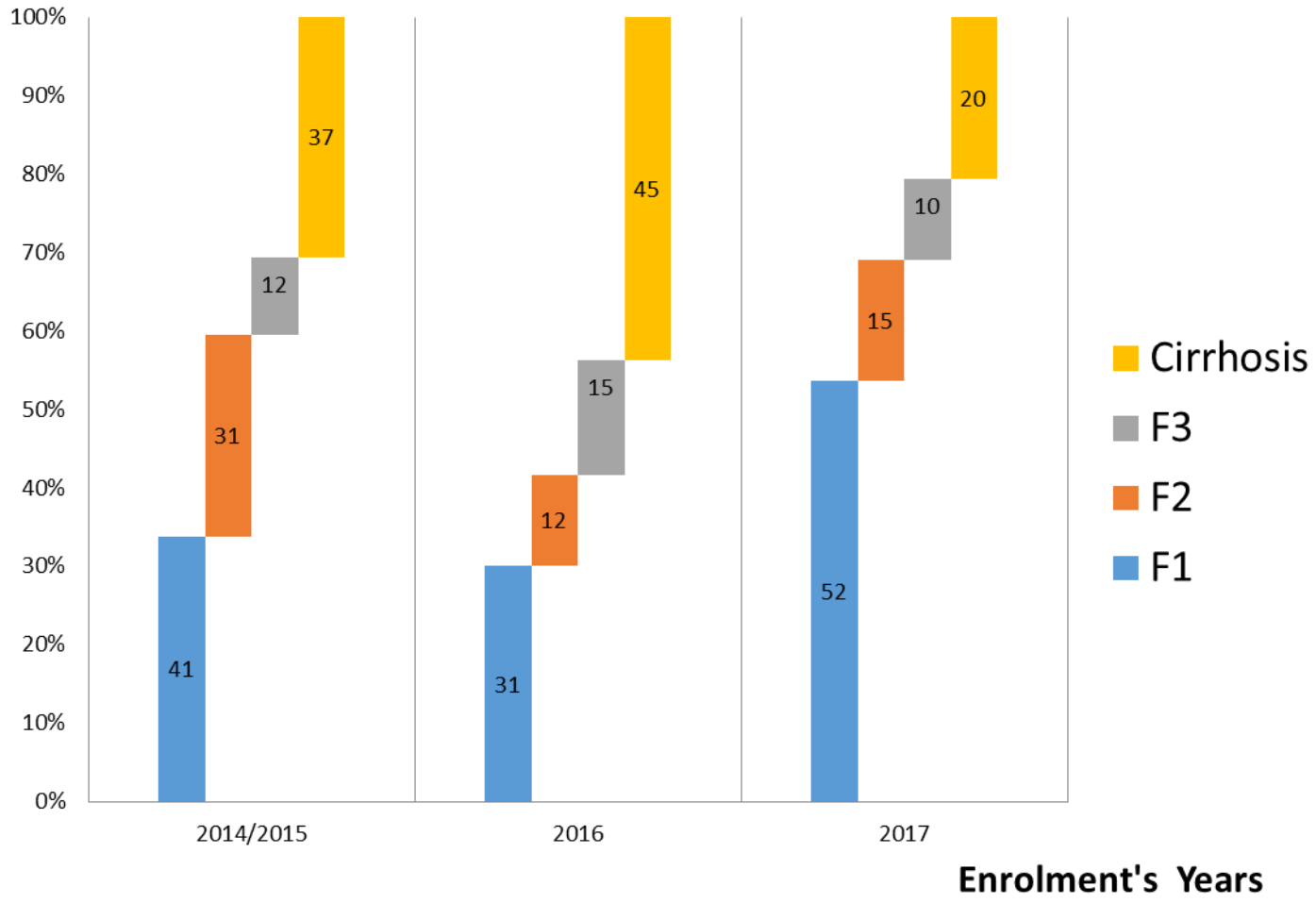
Melazzini M. AISF 2017

Il nuovo Algoritmo per la terapia dell'Epatite C cronica

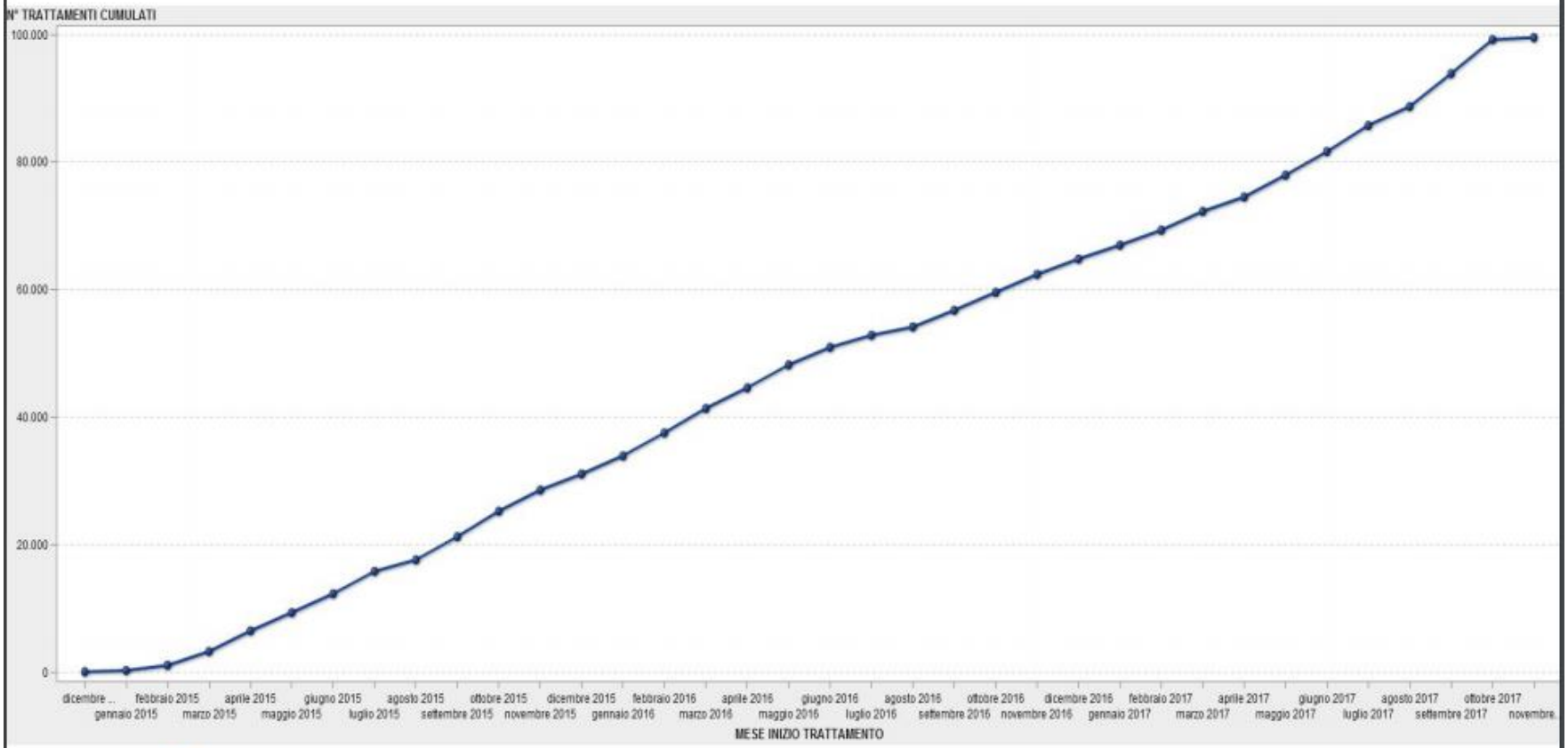
Determina AIFA n. 500/2017 pubblicata nella G.U. n. 75 del 30/03/2017

- **Criterio 1:** Pazienti con cirrosi in classe di Child A o B e/o con HCC con risposta completa a terapie resettive chirurgiche o loco-regionali non candidabili a trapianto epatico nei quali la malattia epatica sia determinante per la prognosi.
- **Criterio 2:** Epatite ricorrente HCV-RNA positiva del fegato trapiantato in paziente stabile clinicamente e con livelli ottimali di immunosoppressione.
- **Criterio 3:** Epatite cronica con gravi manifestazioni extra-epatiche HCV-correlate (sindrome crioglobulinemica con danno d'organo, sindromi linfoproliferative a cellule B, insufficienza renale).
- **Criterio 4:** Epatite cronica con fibrosi METAVIR F3 (o corrispondente Ishak).
- **Criterio 5:** In lista per trapianto di fegato con cirrosi MELD <25 e/o con HCC all'interno dei criteri di Milano con la possibilità di una attesa in lista di almeno 2 mesi.
- **Criterio 6:** Epatite cronica dopo trapianto di organo solido (non fegato) o di midollo in paziente stabile clinicamente e con livelli ottimali di immunosoppressione.
- **Criterio 7**: Epatite cronica con fibrosi METAVIR F2 (o corrispondente Ishak) e/o comorbilità a rischio di progressione del danno epatico [coinfezione HBV, coinfezione HIV, malattie croniche di fegato non virali, diabete mellito in trattamento farmacologico, obesità (body mass index ≥30 kg/m^2), emoglobinopatie e coagulopatie congenite].
- **Criterio 8:** Epatite cronica con fibrosi METAVIR F0-F1 (o corrispondente Ishak) e/o comorbilità a rischio di progressione del danno epatico [coinfezione HBV, coinfezione HIV, malattie croniche di fegato non virali, diabete mellito in trattamento farmacologico, obesità (body mass index ≥30 kg/m^2), emoglobinopatie e coagulopatie congenite].
- **Criterio 9:** Operatori sanitari infetti.
- **Criterio 10:** Epatite cronica o cirrosi epatica in paziente con insufficienza renale cronica in trattamento emodialitico.
- **Criterio 11:** Epatite cronica nel paziente in lista d'attesa per trapianto di organo solido (non fegato) o di midollo.

Fibrosis Stage by Enrolment's periods

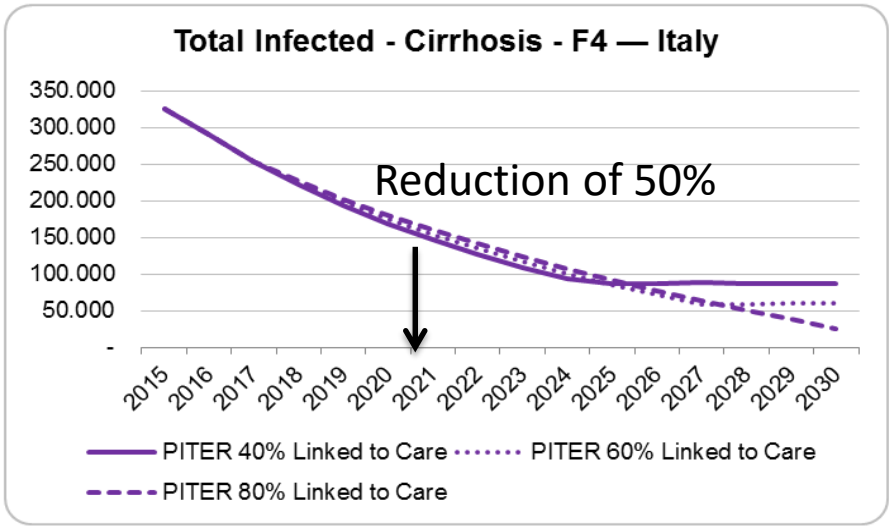


Trend cumulativo dei trattamenti avviati



Agenzia Italiana del Farmaco
AIFA

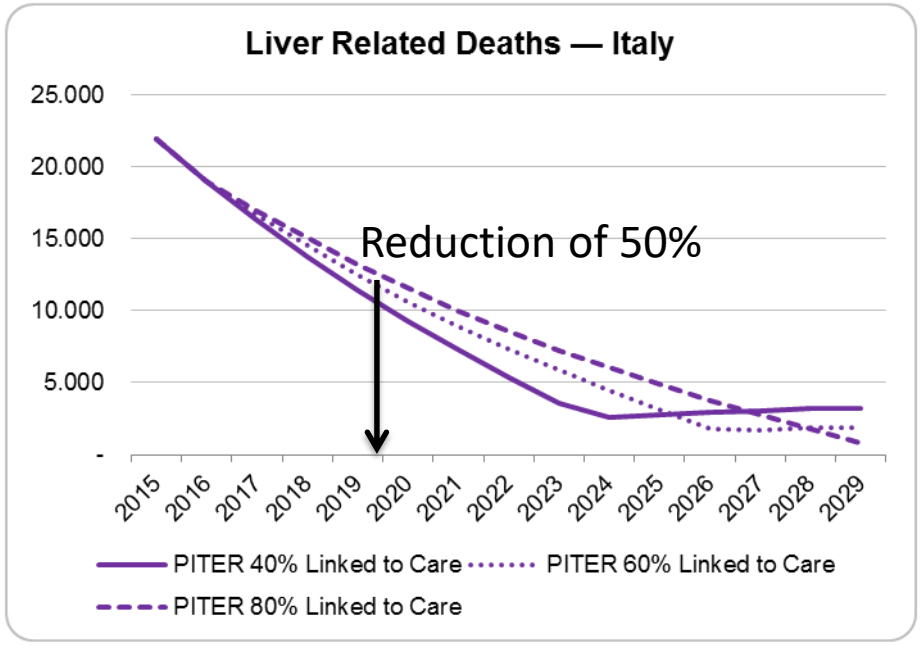
99.502 «avviati» sono i trattamenti (solo pazienti eleggibili) con almeno una scheda di Dispensazione farmaco



How to achieve the WHO elimination Goals by 2030?

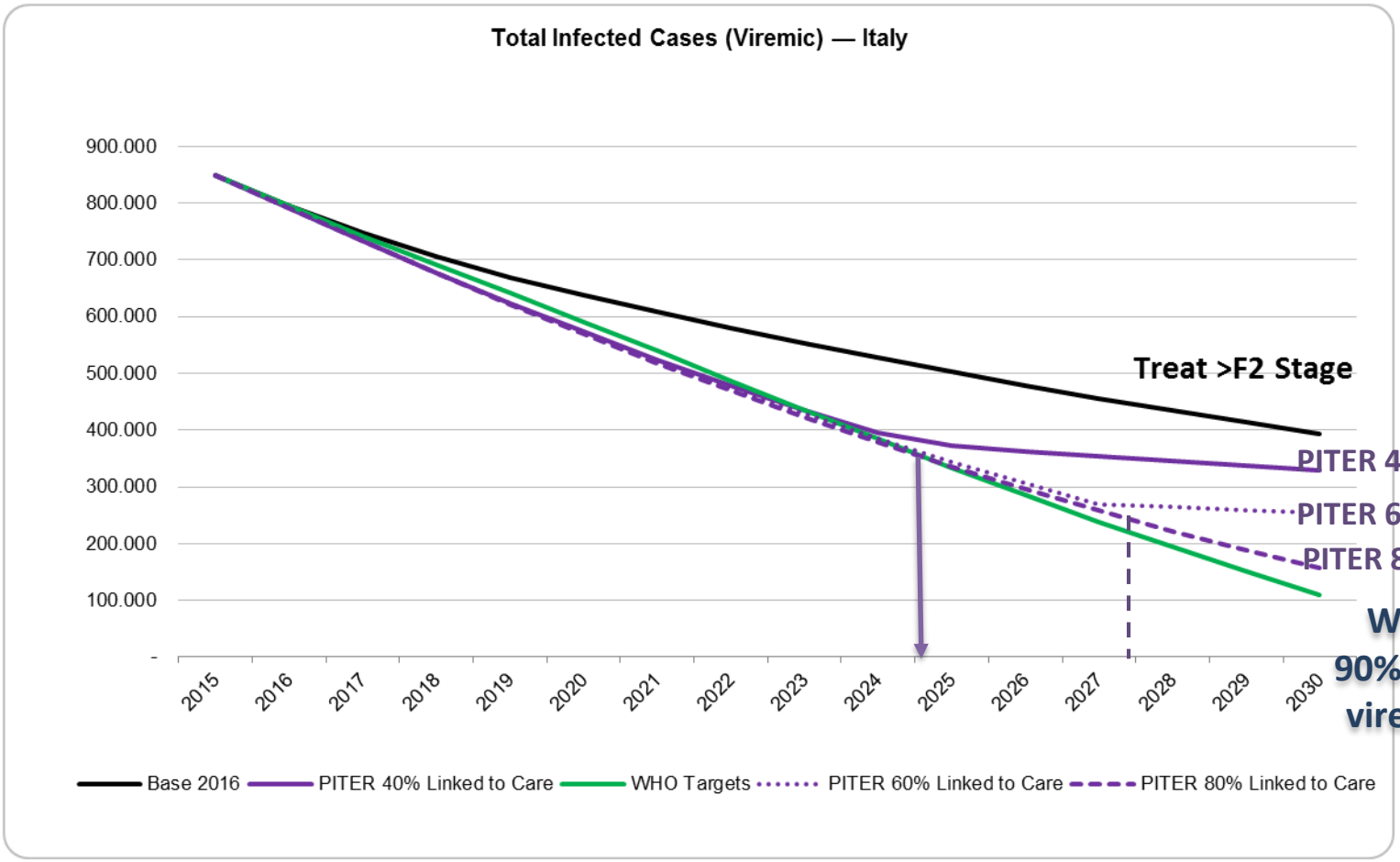
A disease burden model was grounded in Italy-specific cohort data (PITER) and Italy general population data (Polaris Observatory)

Estimated Prevalence 850.000 viremics (Andriulli 2017)



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

Potential target screening strategies according to the distribution of fibrotic stage patients by birth year in the PITER and Polaris models

Years of Birth	Fibrotic Cases by PITER Specific Polaris Observatory Model	Fibrotic Cases in the General Population by Polaris Observatory
1938-1948	28%	24%
1948-1958	35%	30%
1958-1968	41%	32%
1968-1978	23%	28%
1978-1988	10%	17%
>1988	3%	5%

If the number of treated patients <= 35 000/year until the year 2025

A screening strategy in 2020-2025 in individuals born in the years 1948-1978 *could aliment the pool of diagnosed and treated patients by finding approximately 80% of fibrotic cases*

If the number of treated patients => 35 000/year until the year 2028 a more than 80% linked to care scenario could be possible

No screening/or specific age groups screening *could possibly make achievable the WHO goal of 90% reduction of viremics by 2030*

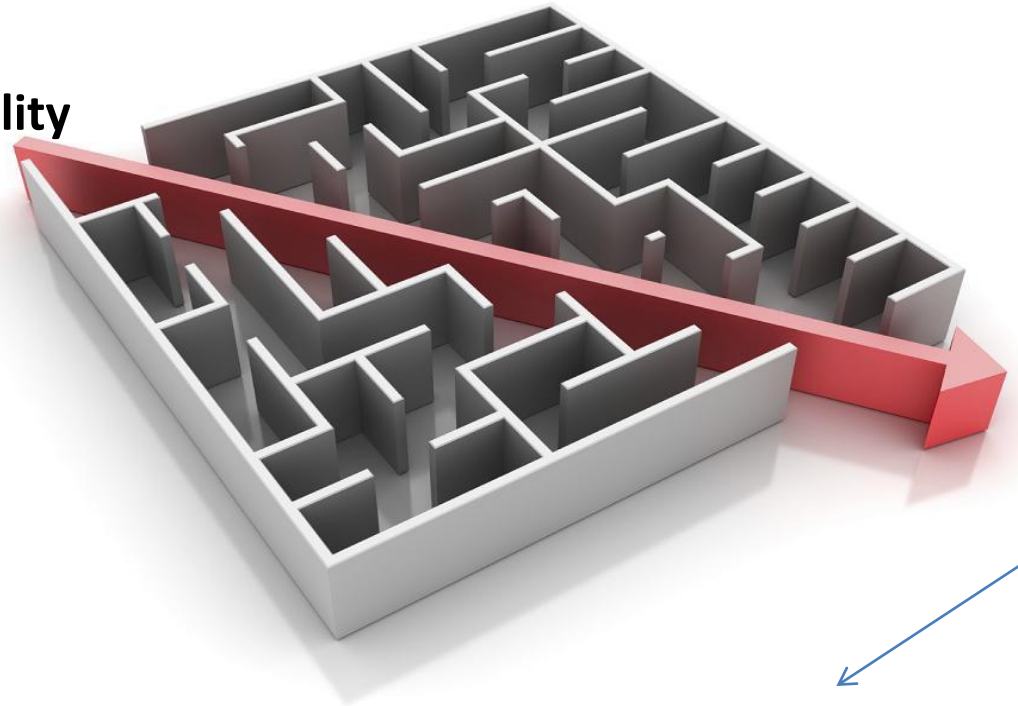
How to achieve the WHO elimination Goals by 2030?

- **This analysis highlights care and increased access to DAAs, Italy is on track to meeting the WHO target of 65% reduction in liver-related mortality by 2030.**
- **However the eligible pool of patients to treat will run out between 2025-2031, leaving a proportion of infected individuals undiagnosed and without access to care.**
- **Based on the number of treated patients /year, intensive case finding and potential targeted screening strategies, aimed in finding the *underwater portion of the iceberg*, are needed for achieving the WHO goals.**

Access to DAA Therapy

Main Barriers

Costs and Sustainability

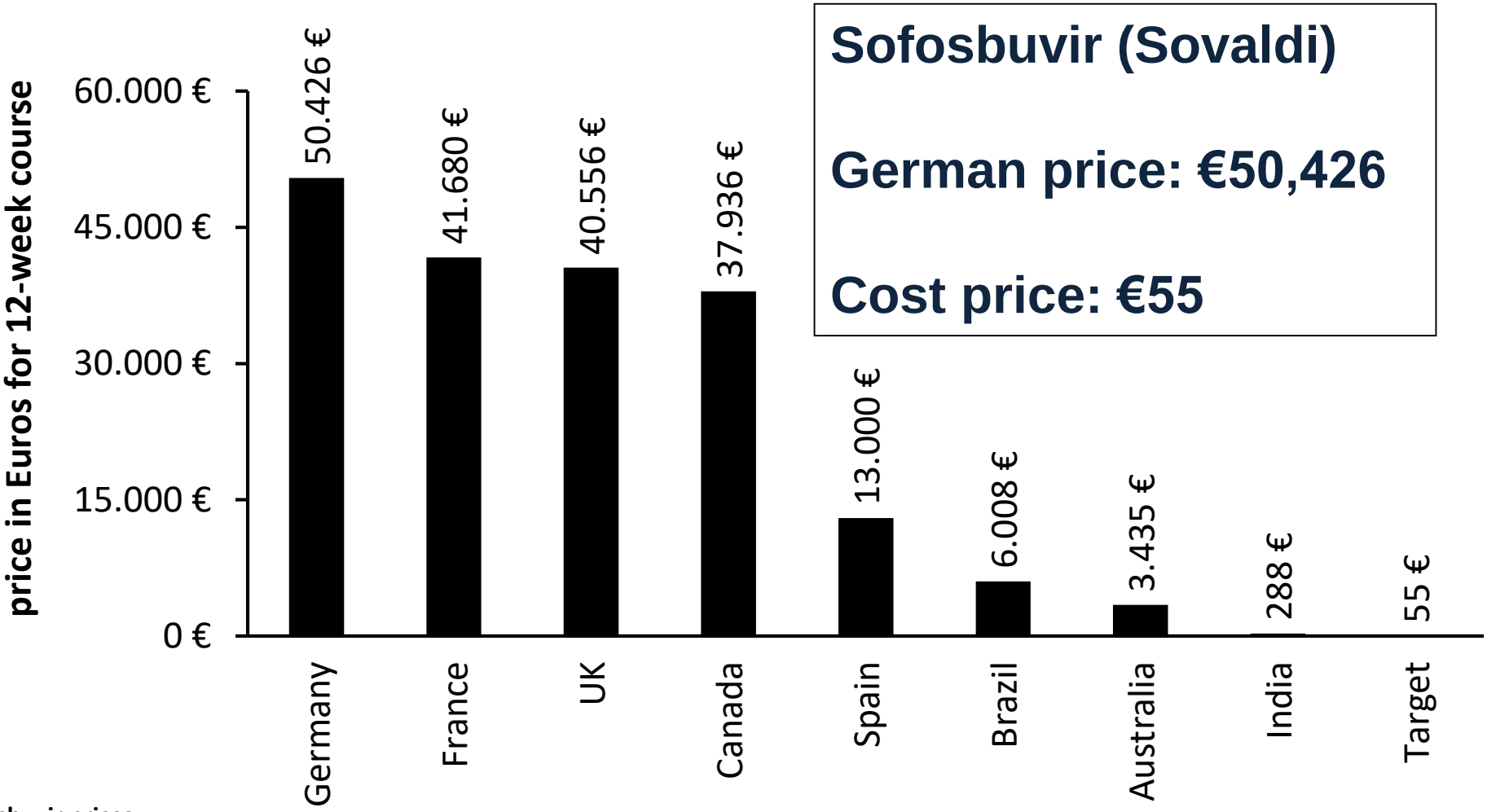


NEGOTIATION
COMPETITION
GENERICS

Voluntary Licensing

Compulsory Licensing

Price of sofosbuvir by country (12 weeks)



Sofosbuvir (Sovaldi)

German price: €50,426

Cost price: €55

Sofosbuvir prices:

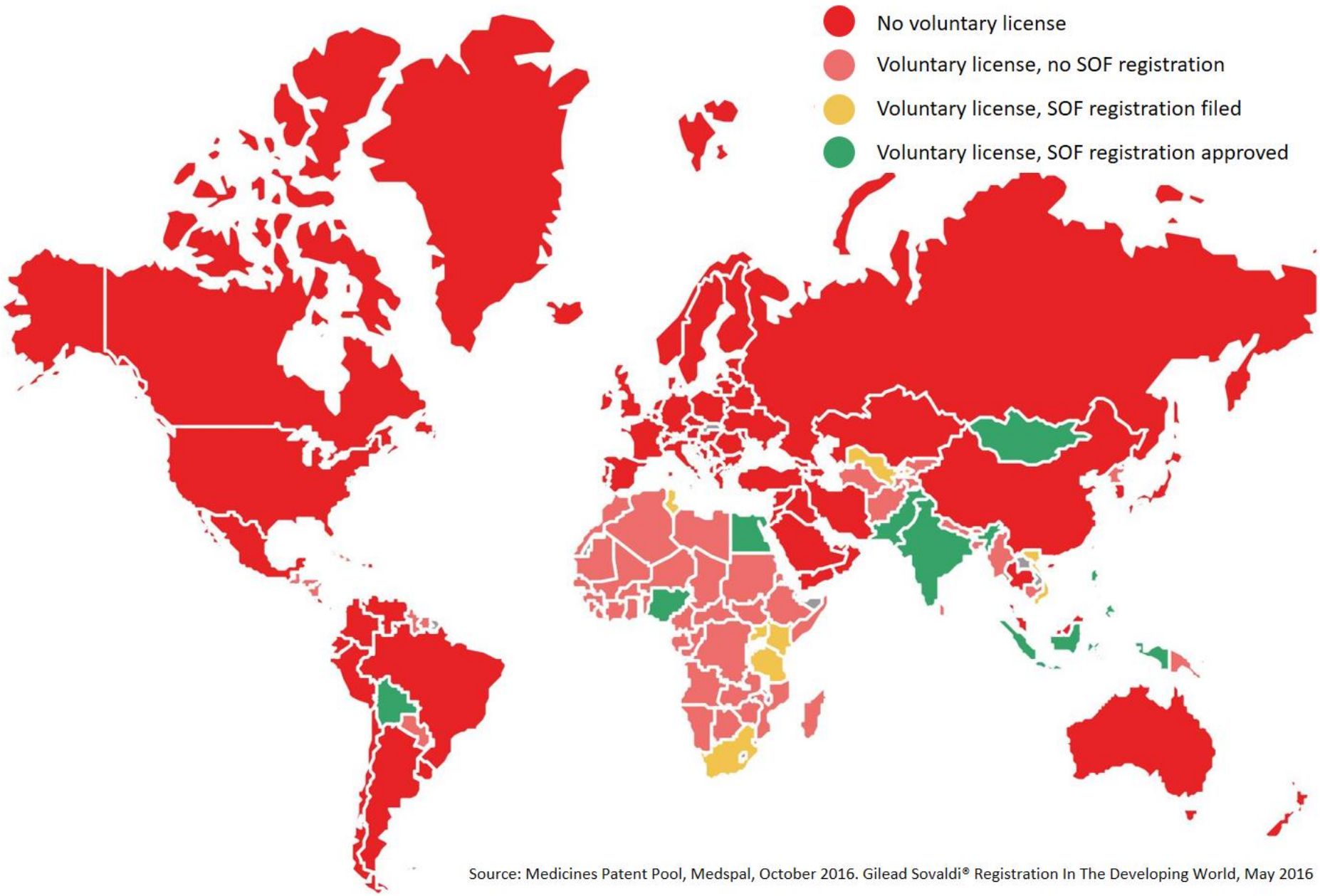
1. Canada (Quebec): http://www.ramq.gouv.qc.ca/SiteCollectionDocuments/liste_med/liste_med_2016_10_03_fr.pdf
2. France: http://www.medecinsdumonde.org/actualites/presse/2016/09/29/mdm-soppose-au-brevet-sur-le-sovaldir-decision-le-5-octobre-2016
3. Germany: medizinfuchs.de
4. Spain: http://politica.elpais.com/politica/2016/04/05/actualidad/1459873421_480033.html?id_externo_rsoc=TW_CC
6. UK: British National Formulary 2016
7. Brazil: http://www.portaltransparencia.gov.br/despesasdiarias/empenho?documento=250005000012015NE801493
8. Australia: Based on total annual government expenditure (AU$200 million) and 40,000 treated in 2016
9. India: http://hepcasia.com/wp-content/uploads/2016/03/31-Jan-2016-Indian-generic-sofosbuvir.pdf

Hepatitis C medicines, prices and estimated minimum cost of production

Medicine	Price range per bottle in high-income countries *[56]*	Lowest recorded price per bottle in Egypt and India *[56]*	Global sales, 2014 (US$ millions)	Estimated minimum cost of production for a 12-week course of treatment *[57]*
sofosbuvir	US$ 14 000–20 590	US$ 161 (India)	US$ 10 283m *[58]*	US$ 68–136
simeprevir	US$ 9166–14 865	US$ 241 (Egypt)	US$ 2302m *[59]*	US$ 130–270
daclatasvir	US$ 1128–14 899	US$ 175 (Egypt)	US$ 201m *[60]*	US$ 10–30
ledipasvir	Sold as an FDC*			US$ 93
ombitasvir	Sold as an FDC*			
ledipasvir + sofosbuvir	US$ 12 604–$4890	US$400 (Egypt)	US$ 2127m *[58]*	US$ 193
ombitasvir + paritaprevir + ritonavir	US$ 15 344–20 215	US$400 (Egypt)	US$ 48m *[61]*	

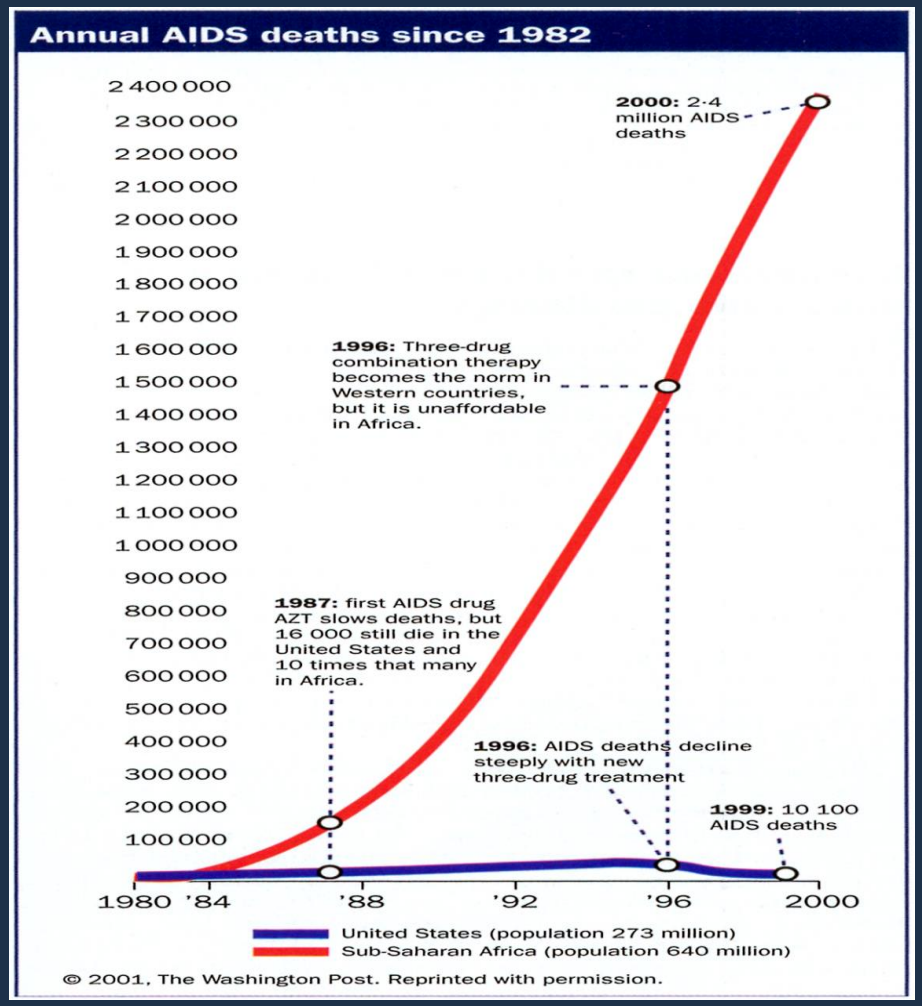
*FDC = fixed-dose combination.

Sofosbuvir voluntary license coverage

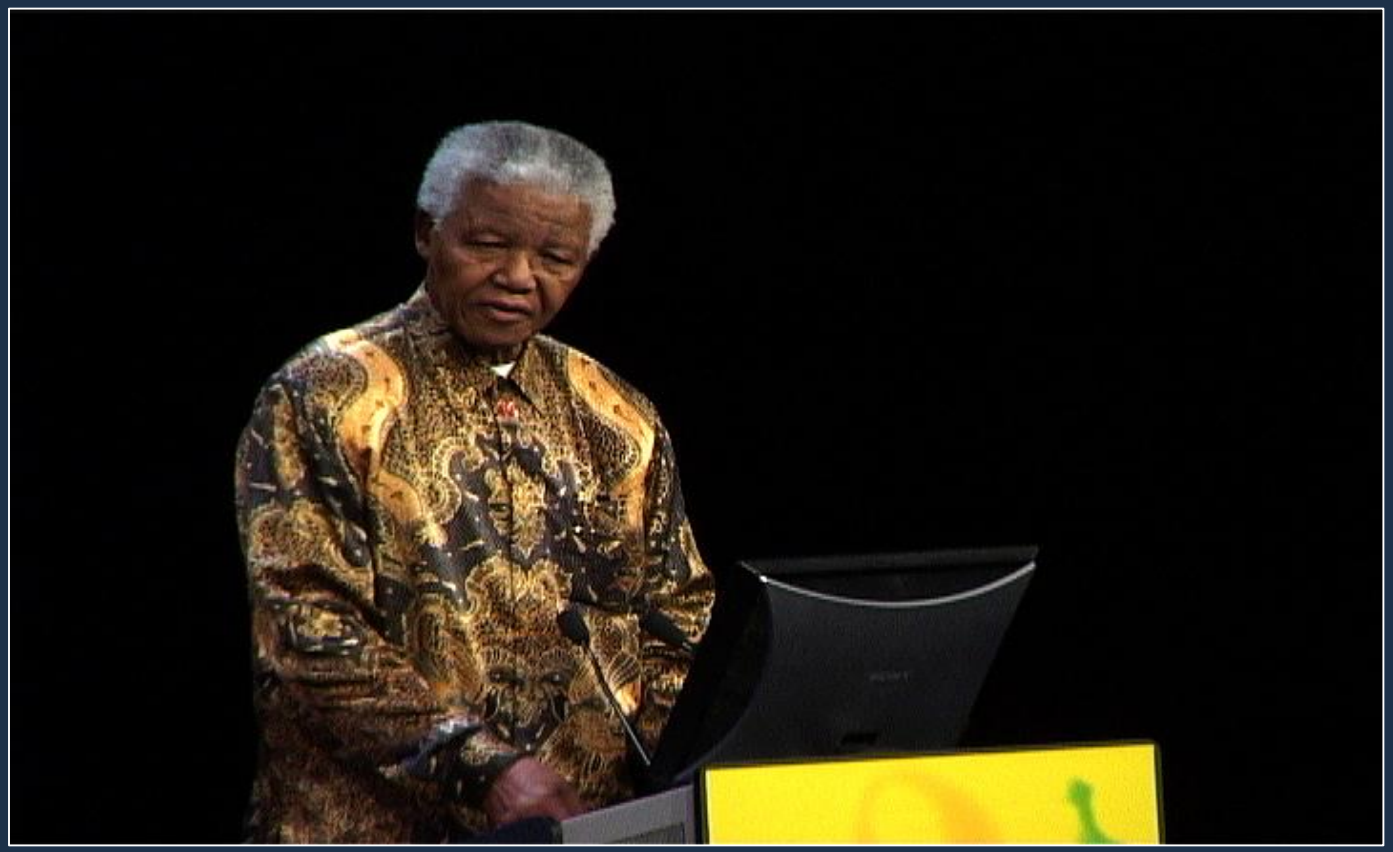


Source: Medicines Patent Pool, Medspal, October 2016. Gilead Sovaldi® Registration In The Developing World, May 2016

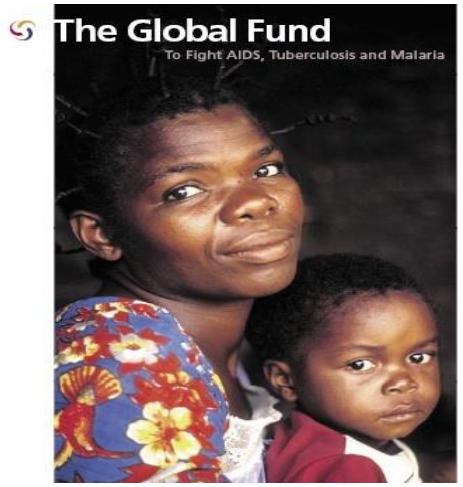
YEAR 2000: difference in mortality between the rich and the poor



World AIDS Conference
DURBAN, *2000*



20 milioni di persone con HIV in trattamento nel 2016



(Milioni)

30
25
20
15
10
5
0

2020 target

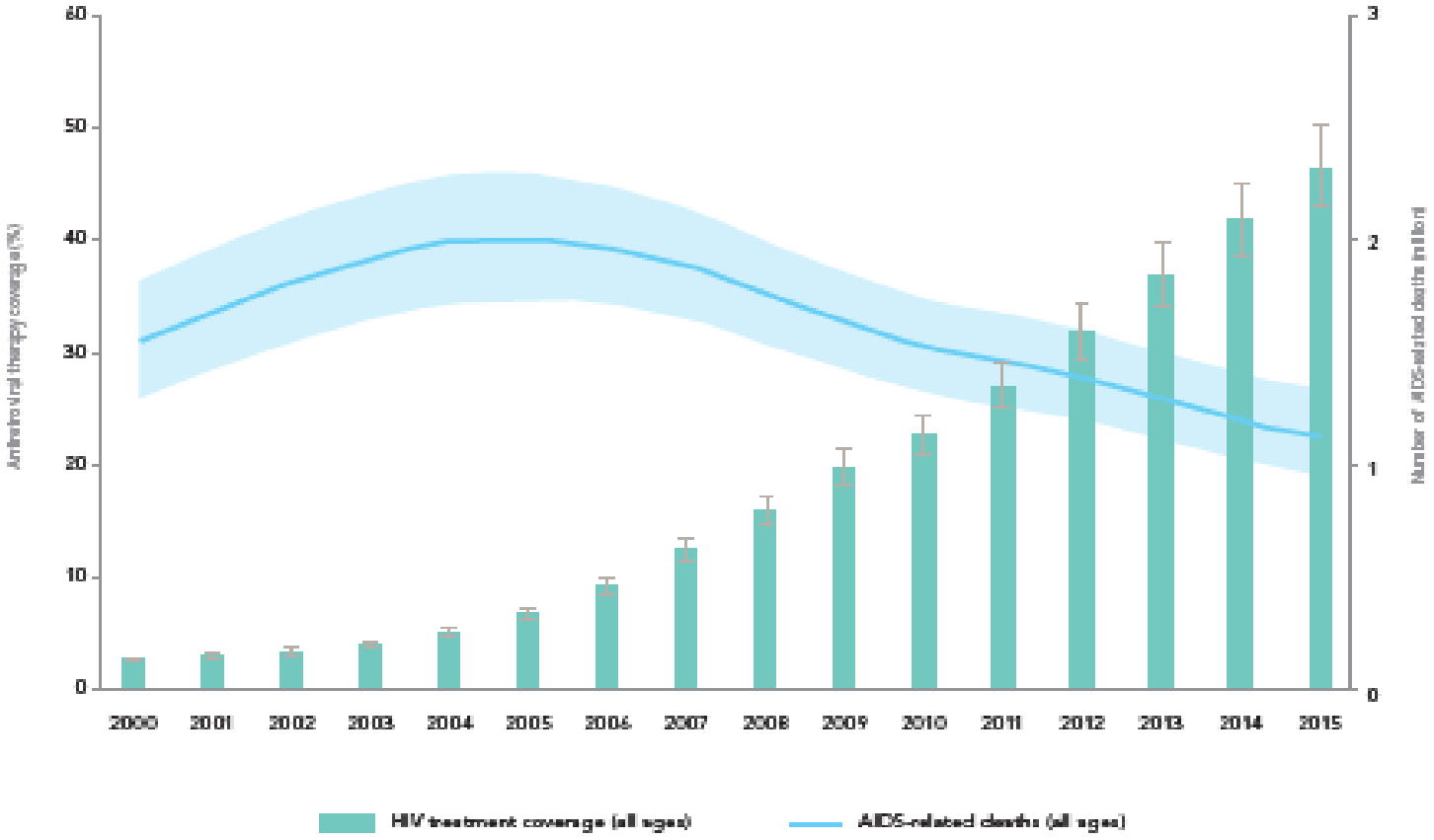
2010 2011 2012 2013 2014 2015 mid-2016 2016 2017 2018 2019 2020

Source: UNAIDS/WHO estimates.

World Health Organization

L’impatto della battaglia per l’accesso ai farmaci anti-HIV

Antiretroviral therapy coverage and number of AIDS-related deaths, global, 2000–2015



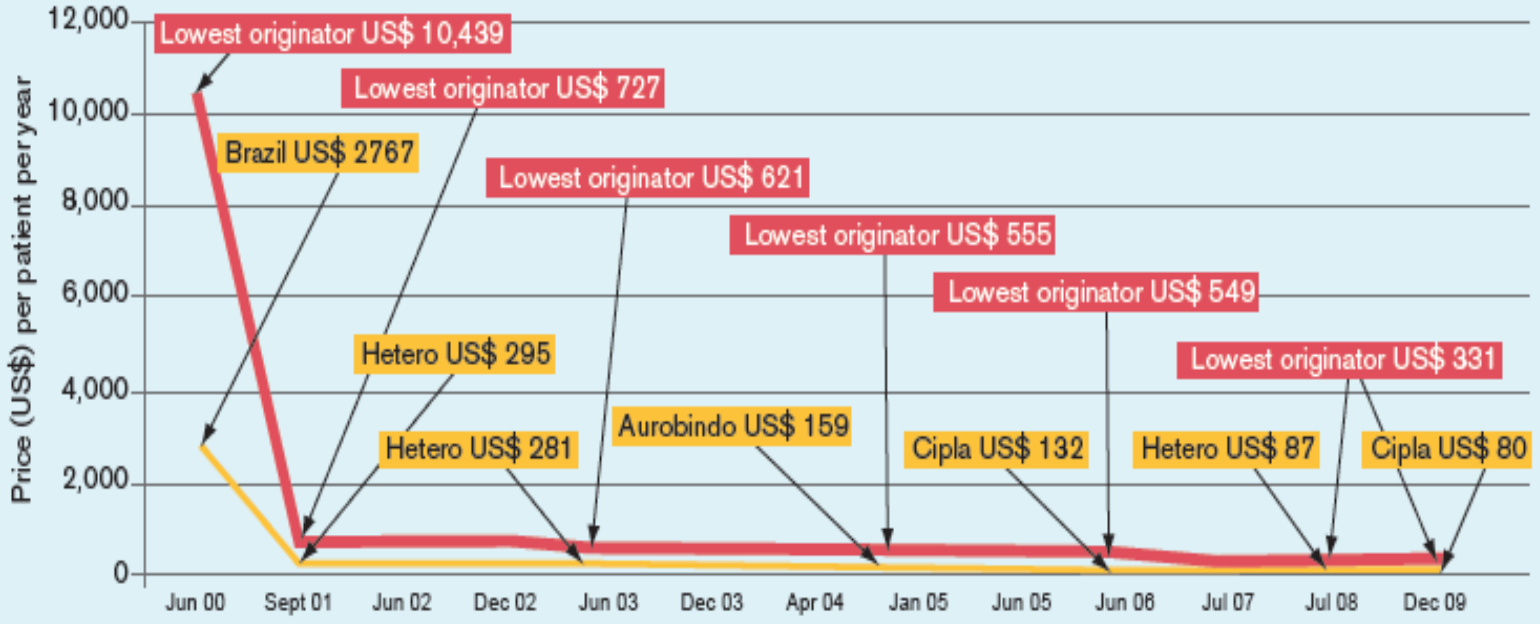
Sources: GARPR 2016; UNAIDS 2016 estimates.

Health
zation

Box 4: Access to medicines and the Doha Declaration on TRIPS and Public Health

Measuring access to medicines is a complex task, but price is one key factor among others. The Doha Declaration on TRIPS and Public Health recognized concerns about effects on prices while noting the need for innovation. Since the Declaration was adopted in 2001, prices for many treatments have fallen significantly, in part due to generic competition and tiered pricing schemes (see graph below). Surveys also show a marked increase in the use of TRIPS flexibilities to promote access to medicines.

Falling prices of first-line combinations of some first-line anti-retroviral therapies for HIV-AIDS since 2000



Source: Extract from MSF, *Untangling the Web of Price Reductions*, January 2010 at http://www.msfaccess.org.

WORLD TRADE ORGANIZATION

WT/MIN(01)/DEC/1
20 November 2001

(01-5859)

MINISTERIAL CONFERENCE
Fourth Session
Doha, 9 - 14 November 2001

MINISTERIAL DECLARATION

Adopted on 14 November 2001

- **"Each member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted" and**
- **"to determine what constitutes a national emergency or other circumstances of extreme urgency".**

- **Public health crises include "those relating to HIV/AIDS, tuberculosis, malaria and other epidemics" and "other circumstances of extreme urgency".**

SUSTAINABLE DEVELOPMENT GOAL 3 AND ITS TARGETS

SDG 3: ENSURE HEALTHY LIVES AND PROMOTE WELL-BEING FOR ALL AT ALL AGES

TARGET 3.8: ACHIEVE UNIVERSAL HEALTH COVERAGE, INCLUDING FINANCIAL RISK PROTECTION, ACCESS TO QUALITY ESSENTIAL HEALTH-CARE SERVICES, MEDICINES AND VACCINES FOR ALL

MDG UNFINISHED AND EXPANDED AGENDA

3.1: Reduce maternal mortality

3.2: End preventable newborn and child deaths

3.3: End the epidemics of AIDS, TB, malaria and NTDs

and combat hepatitis, waterborne and other communicable diseases

3.7: Ensure universal access to sexual and reproductive health-care services

NEW SDG 3 TARGETS

3.4: Reduce mortality from NCDs and promote mental health

3.5: Strengthen prevention and treatment of substance abuse

3.6: Halve global deaths and injuries from road traffic accidents

3.9: Reduce deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination

SDG 3 MEANS OF IMPLEMENTATION TARGETS

3.a: Strengthen implementation of framework convention on tobacco control

3.b: Provide access to medicines and vaccines for all, support R&D of vaccines and medicines for all

3.c: Increase health financing and health workforce in developing countries

3.d: Strengthen capacity for early warning, risk reduction and management of health risks

INTERACTIONS WITH ECONOMIC, OTHER SOCIAL AND ENVIRONMENTAL SDGs AND SDG 17 ON MEANS OF IMPLEMENTATION

Essential medicines for universal health coverage

Veronika J Wirtz, Hans V Hogerzeil, Andrew L Gray, Maryam Bigdeli, Cornelis P de Joncheere, Margaret A Ewen, Martha Gyansa-Lutterodt, Sun Jing, Vera L Luiza, Regina M Mbindyo, Helene Möller, Corrina Moucheraud, Bernard Pécoul, Lembit Rägo, Arash Rashidian, Dennis Ross-Degnan, Peter N Stephens, Yot Teerawattananon, Ellen F M 't Hoen, Anita K Wagner, Prashant Yadav, Michael R Reich

Executive summary

Essential medicines satisfy the priority health-care needs of the population. Essential medicines policies are crucial to promoting health and achieving sustainable development. Sustainable Development Goal 3.8 specifically mentions the importance of "access to safe, effective, quality and affordable essential medicines and vaccines for all" as a central component of Universal Health Coverage (UHC), and Sustainable Development Goal 3.b emphasises the need to develop medicines to address persistent treatment gaps.

The recognition of the importance of essential medicines is not new. At the 1985 Nairobi Conference on the Rational Use of Drugs, government representatives and other stakeholders proposed a comprehensive set of essential medicines policies. 30 years later, The Lancet's Commission on Essential Medicines Policies convened to explore these questions: what progress has been achieved? What challenges remain to be addressed? Which lessons have been learned to inform future approaches? And how can essential medicines policies be harnessed to promote UHC and contribute to the global sustainable development agenda? This report addresses these questions, with the intent to reposition essential medicines policies on the global development agenda.

The Commission identified five areas that are crucial to essential medicines policies: paying for a basket of essential medicines, making essential medicines affordable, assuring the quality and safety of medicines, promoting quality use of medicines, and developing missing essential medicines. The Commission located essential medicines policies within the context of current global debates about balancing trade and intellectual property policies with human rights, assuring health security, strengthening people-centred health systems, and advancing access to essential technologies. In all policy areas, particular attention was paid to furthering equity in access, strengthening relevant institutions, and creating accountability. For each policy area, the Commission made actionable recommendations, thereby reaffirming essential medicines policies as a central pillar of the global health and development agenda.

Paying for a basket of essential medicines to promote sustainable access for all

Globally, a quarter of all health expenditure is on medicines. In many countries, the main source of financing for medicines is direct payment by the individual and households—this source is both highly inequitable and inefficient, and its reduction is a key target for UHC. Furthermore, the Commission found that the available data on pharmaceutical expenditure in many countries lack sufficient detail on the types of medicines procured or sold, public and private sector spending, and the degree of access by key population subgroups.

For this report, the Commission developed a new model-based global estimate of the total financing that would be needed to achieve universal access to a basic package of essential medicines in low-income and middle-income countries (LMICs). A costing model was developed on the basis of disease prevalence, current or projected consumption of medicines, and international reference prices. Using two consumption scenarios, the Commission estimated that between US$77·4 and $151·9 billion (or $13 to $25 per capita) is required to finance a basic package of 201 essential medicines (576 dosage forms) in all LMICs. Yet in 2010, the majority of low-income countries (LICs) and 11 out of 47 middle-income countries, spent less than $13 per capita on pharmaceuticals. Thus, the Commission confirmed that many people worldwide do not have access to even a limited basket of essential medicines. Countries should adapt the Commission's model to their national context to create a locally relevant estimate as a benchmark for measuring performance on essential medicines. The Commission's recommendations on financing of essential medicines are:

- Governments and national health systems must provide adequate financing to ensure inclusion of essential medicines in the benefit packages provided by the public sector and all health insurance schemes.
- Governments and national health systems must implement policies that reduce the amount of out-of-pocket spending on medicines.
- The international community must fulfil its human rights obligations to support governments of LICs in financing a basic package of essential medicines for all, if they are unable to do so domestically.
- Governments and national health systems must invest in the capacity to accurately track expenditure on medicines, especially essential medicines, in both the public and private sectors, disaggregated between prepaid and out-of-pocket expenditure, and among important key populations.

Making essential medicines affordable is necessary to achieve equity in access

The affordability of essential medicines is a core challenge for any health system working to achieve UHC,

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See Online/Comment http://dx.doi.org/10.1016/S0140-6736(16)32039-0, http://dx.doi.org/10.1016/S0140-6736(16)31928-1, http://dx.doi.org/10.1016/S0140-6736(16)31894-4, http://dx.doi.org/10.1016/S0140-6736(16)31831-2, and http://dx.doi.org/10.1016/S0140-6736(16)31862-2

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Towards access 2030

The Lancet Commission on Essential Medicines Policies[1] identifies five areas as crucial to ensure access to medicines for 2030: "paying for a basket of essential medicines, making essential medicines affordable, assuring the quality and safety of medicines, promoting quality use of medicines, and developing missing essential medicines". These are issues that WHO has promoted for some time. The question, however, is whether the Commission's recommendations—mostly aimed at governments—are sufficient to ensure progress towards universal health coverage and the Sustainable Development Goals.

The Commission estimates that between US$77·4 and $151·9 billion per year (or $13 to $25 per capita) is needed to provide a basic package of 201 essential medicines for all low-income and middle-income countries.[1] Affordability and pricing of quality medicines is perhaps the major challenge on the path to access and this concern is what we focus on here.

Everyone relies on the pharmaceutical industry to manufacture and deliver essential medicines. Yet we have at present a problem with two facets. The pharmaceutical industry is demanding higher prices for most new products that are being developed, so that medicines such as the direct-acting antivirals for hepatitis C are unaffordable even in high-income and middle-income countries.[2] At the same time, some key essential medicines, such as benzathine penicillin[3] or methotrexate for cancer,[4] are disappearing from the market globally, due in part, we think, to prices that have become so low that it seems no longer commercially viable for manufacturers to supply them.

What the Lancet Commission[1] proposes for addressing this problem is a combination of policies that are clearly important. These include information systems for routine monitoring of affordability, price, and availability; implementation of a comprehensive set of existing pricing policies, including Trade-related Aspects of Intellectual Property Rights (TRIPS) flexibilities, to achieve affordable prices; use of health technology assessment to define benefits packages and determine value; and increased transparency.

Our concern, however, is whether these recommendations, which have featured in many WHO publications over the past years,[5] take us far enough. Will monitoring national prices in relation to international reference prices and using external reference pricing in combination with other pricing policies for setting prices, be sufficient? Or will the push for low prices for generic products in particular be a real pathway to affordability? It is unlikely in our view, and some countries are already struggling with access to essential medicines as a result of inadequate pricing policies based only on lowering prices and external price referencing. At the WHO European Regional Committee in September, 2016, countries discussed the impact of pricing regulations on access to medicines, especially in small countries with limited markets.

We believe that it is time to develop new approaches for setting prices of pharmaceuticals. To do that much more information is needed about what drives price-setting strategies for new medicines, as well as what the market needs to do to retain disappearing essential medicines at prices that ensure quality products and a viable commercial model. Discussion to date, including in the report of the UN High-Level Panel on Access to Medicines,[6] has focused on the effect of research and development costs on prices and, therefore, the need to delink these two issues. But there is insufficient published information about the effect of investment strategies and hedge funds on price setting of new medicines, even though financial markets and shareholder expectations are driving drug prices up, especially for products with limited markets.[7] None of the current policies used for price setting

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See Online/Comment http://dx.doi.org/10.1016/S0140-6736(16)32039-0, http://dx.doi.org/10.1016/S0140-6736(16)31928-1, http://dx.doi.org/10.1016/S0140-6736(16)31831-2, and http://dx.doi.org/10.1016/S0140-6736(16)31862-2

Access to medicines: lessons from the HIV response

Just two decades ago, HIV/AIDS treatments were prohibitively expensive and accessible in only a few affluent countries. But remarkable reductions in costs have enabled treatment expansion that has reduced mortality and transmission. Today, first-line HIV drugs cost less than US$100 per person per year, a 99% reduction from more than $10 000 in 2000. The number of people receiving HIV treatment doubled in just 5 years, from 9 million in 2011 to more than 18 million today.[1]

In a world facing growing inequalities, the HIV response has lessons for low and middle-income countries (LMIC)—but also for high-income countries—on access to care and treatment for communicable diseases and for non-communicable chronic diseases, a global pandemic that dwarfs the HIV epidemic in scale.[2]

The transformative power of the HIV response was underpinned by moral rather than technical arguments. A unique coalition of activists, scientists, celebrities, and religious and community leaders from all over the world argued that no one should be denied life-saving treatment because of area of residence or income. The moral imperative was operationalised by activism for more urgent drug discovery, regulatory approval, and voluntary and compulsory licensing, followed by shifts towards large-scale generic production. Economies of scale underpinned a drive towards more efficient, cheaper production, and drove prices down. Major donors such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the US President's Emergency Plan for AIDS Relief bought generic drugs. The Clinton Health Access Initiative negotiated price-volume discounts

Vella S, Wilson D. Access to medicines: lessons from the HIV response.
Lancet HIV. 2017 Apr;4(4):e147-e149. doi: 10.1016/S2352-3018(17)30052-8.

The concept of “public goods”

non exclusive: anyone can use them

non competitve: their use do not limit others to use them

Progress of medicine and essential drugs shall be considered as global public goods and be accessible to all human beings living on our planet

GRAZIE

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