
TUNISIE
HAMMAMET
du 19 au 21 nov. 2021
4e édition
AFRAMED 2021
VIH, Hépatites, Santé sexuelle
Infections émergentes
AFRAVIH
Dépistage et traitement de l'hépatite C en Méditérranée
Nabil DEBZI
Service Hépatologie
CHU Mustapha –Alger
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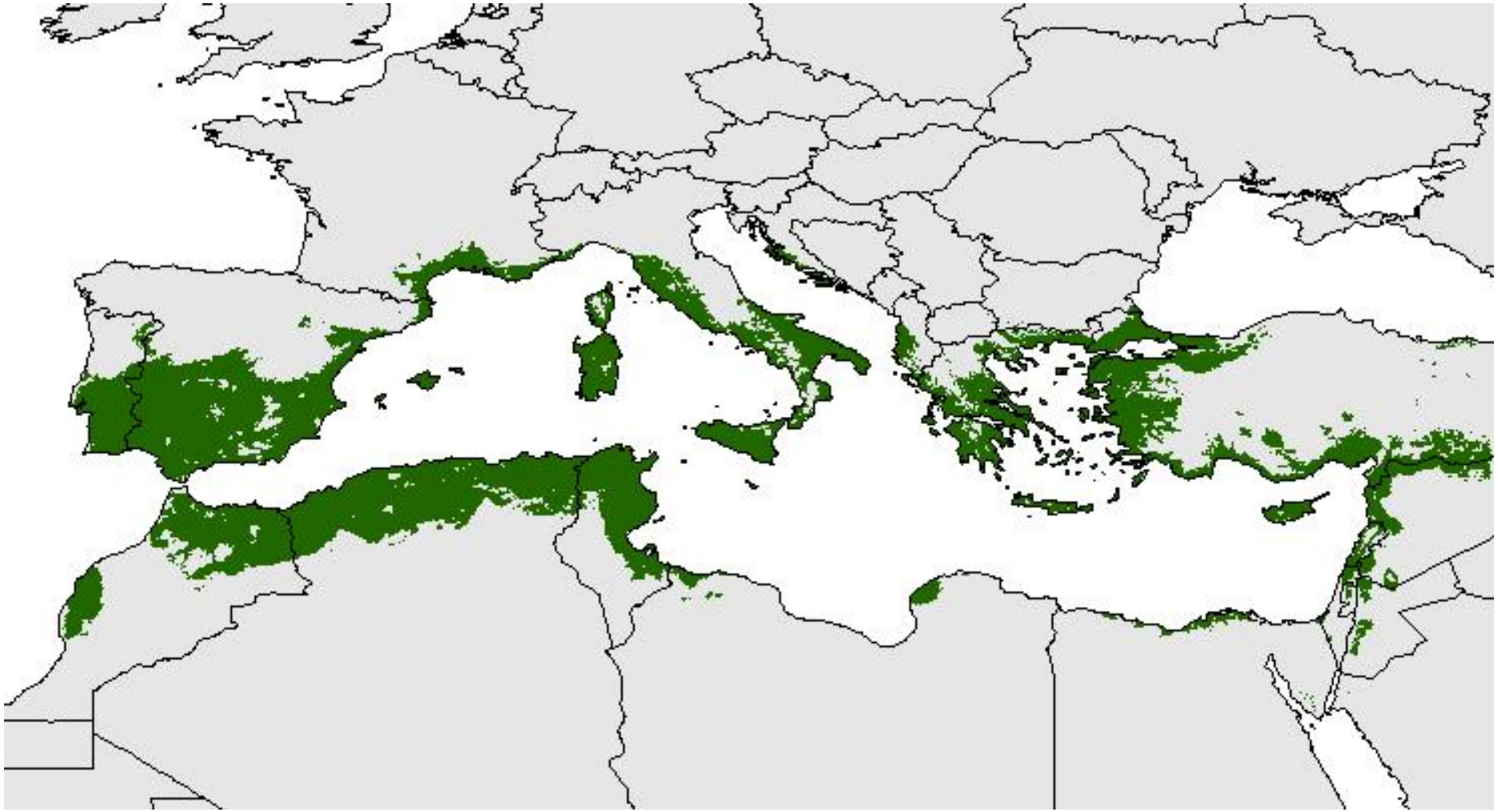
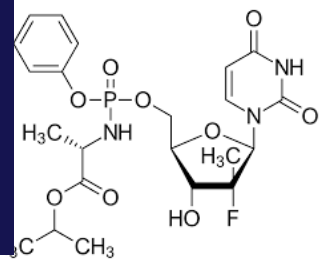
Conflits d'intérêts

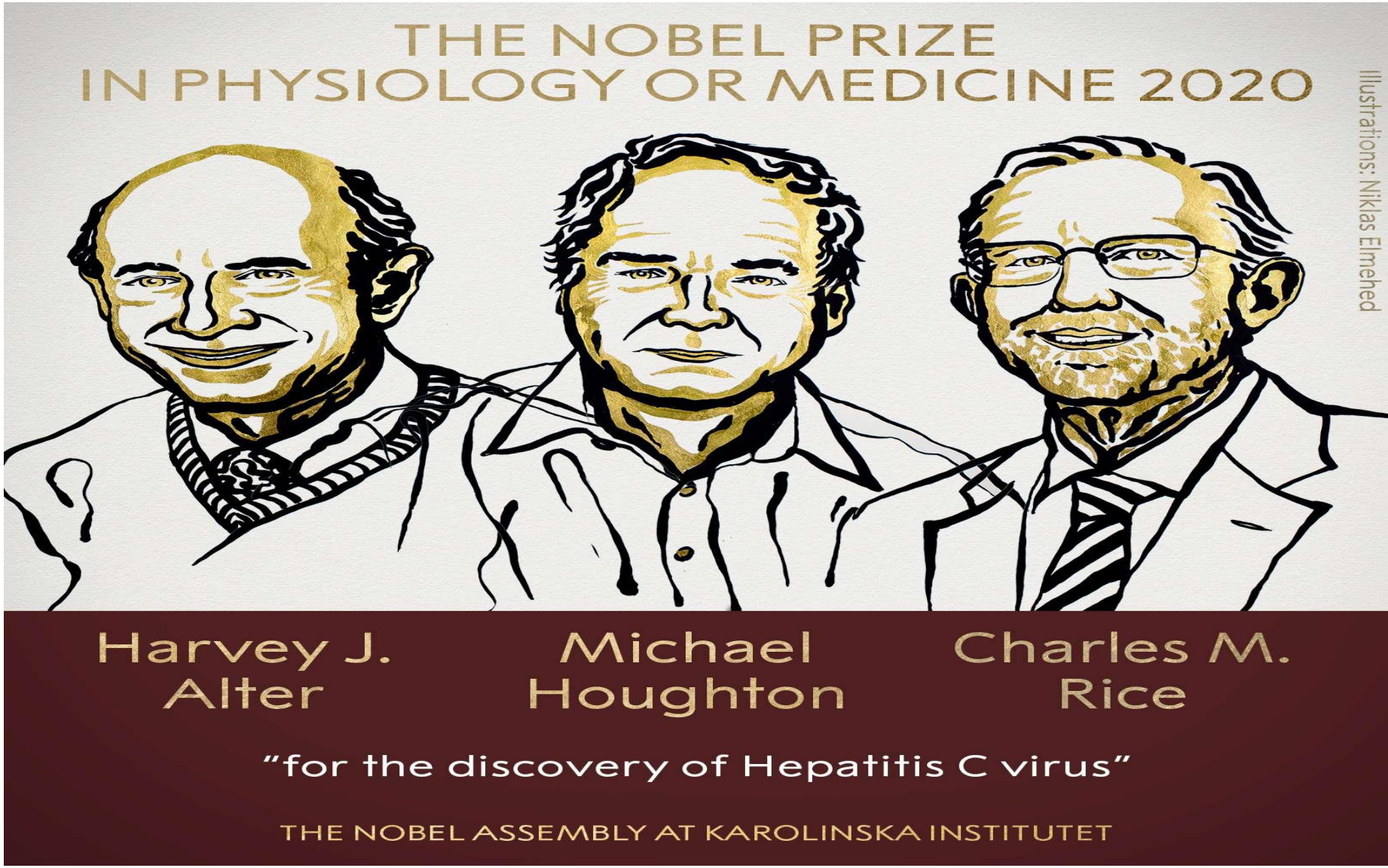
Speaker : Biotest, Gilead , Boston scientific , Roche



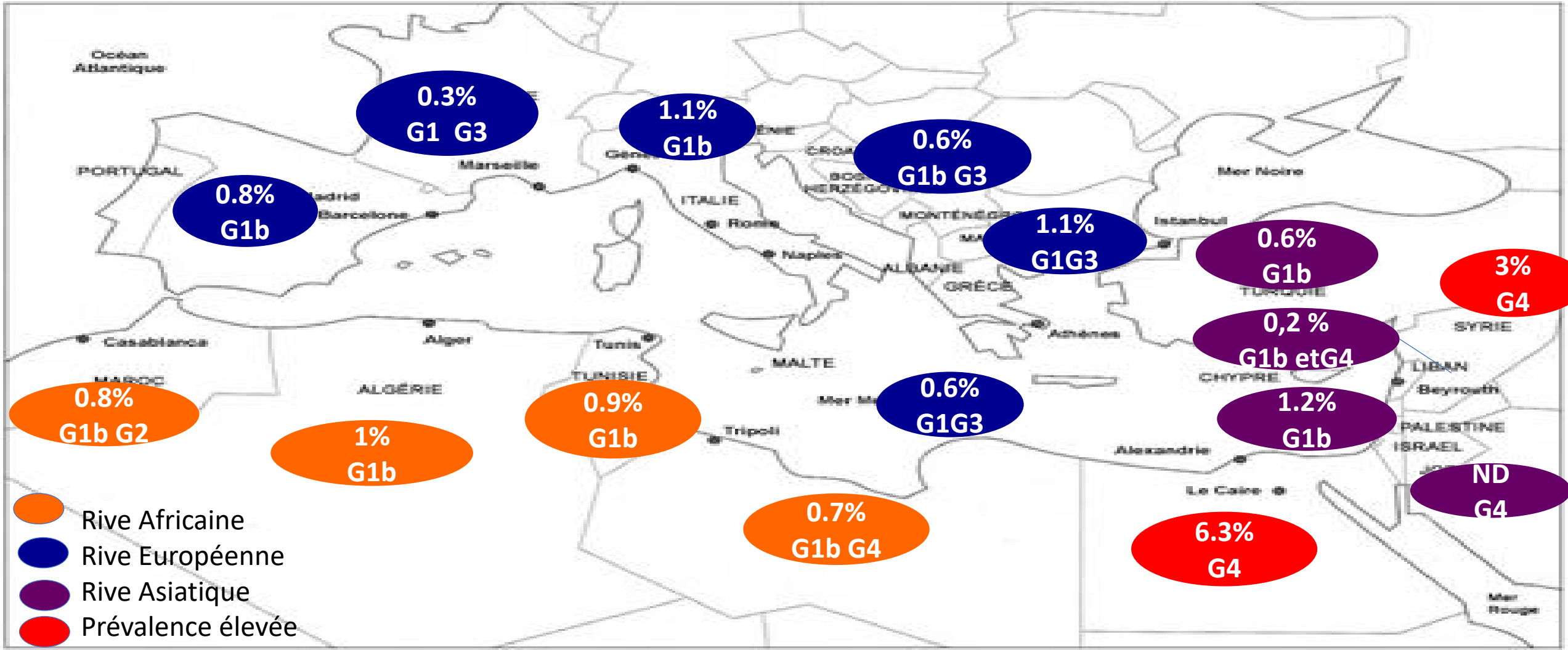
Oteros Jose (2014) Modelización del ciclo fenológico reproductor del olivo (Tesis Doctoral). Universidad de Córdoba, Córdoba,



Michaël Sofia



Prévalence des patients virémiques et génotypage



*The Polaris Observatory HCV Collaborators** ***Lancet Gastroenterol Hepatol* 2017; 2: 161–76**

Stratégies de Dépistage

- Dépistage institutionnel
- Micro-élimination
- Dépistage universel = Macro-Élimination

WHO Vision: Eliminate Viral Hepatitis as a Major Health Threat by 2030

World Health Organization

"A world where viral hepatitis transmission is halted and everyone living with hepatitis has access to safe, affordable and effective care and treatment services"

90% reduction in new chronic HCV infections

Treatment of 80% of eligible persons with chronic HCV infection

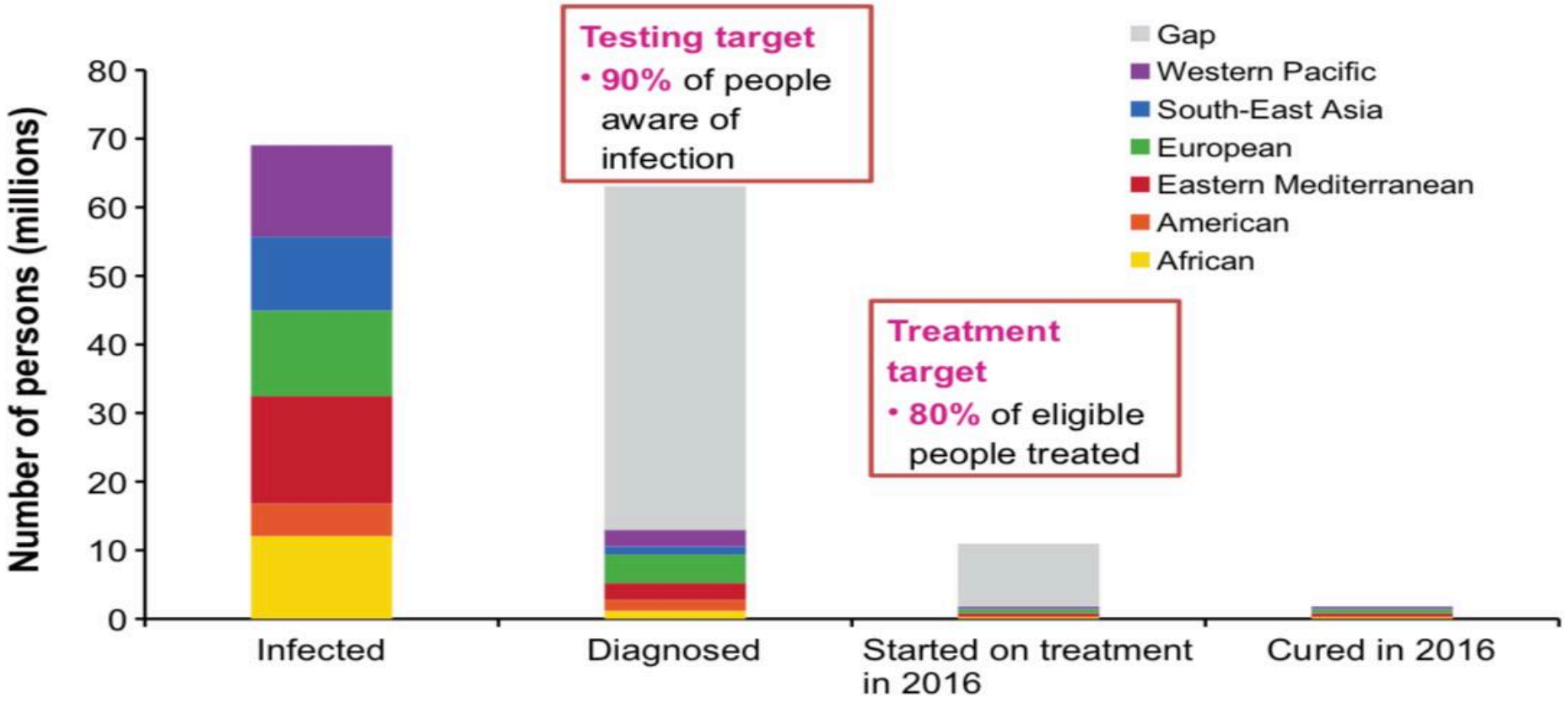
65% reduction in mortality rates

WHO. https://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/. Accessed November 17, 2020.

Slide credit: clinicaloptions.com

We still have a long way to go to achieve the WHO HCV elimination targets

World Health Organization



WHO. Progress report on access to hepatitis C treatment. Available at: http://www.who.int/hepatitis/publications/hep-c-access-report-2018/en/ (accessed Sepetember 2018)

Table 3 Comparative HBV and HCV screening policies in the non-EU Mediterranean countries

	Algeria	Egypt	Israel	Jordan	Lebanon	Libya	Morocco	Tunisia
Antenatal screening					HBV	HBV		HBV
Blood and organ donors	Both	Both	Both	Both	Both	Both	Both	Both
Blood transfusion or products prior to 1992 in EU, or any transfusion outside EU			Both	Both				
Clinical signs or laboratory signs (including cirrhosis and HCC)	Both	Both	HCV	Both	Both	Both		Both
Candidates for chemotherapy or immunosuppressive treatment			HBV		HBV	HBV		Both
Haemophiliacs who received concentration factors prior to 1987			Both		Both			
Haemodialysis	Both	Both	Both	Both	Both	Both	HBV	Both
History of shared injecting equipment	Both	Both	Both	Both	Both	Both		
History of long-term imprisonment	Both							
Hospital surgery patients						Both		
Household contacts	Both		Both	Both		Both		
HIV	Both				Both			
IVF candidates			Both			Both		
Men who have sex with men								
Migrants from high prevalence countries			Both					
Military recruits	Both	Both		Both	Both			Both
Organ or tissue transplants prior to 1992 in EU or outside EU			Both		Both			
Pre-employment		Both	HCV, health care	Both				
Pregnant women and newborns			Selective risk groups: HBV	HBV	HBV	HBV		HBV
Prenuptial	Both				HBV			HBV
STI clinic patients			Both	HBV	Both	HCV		
Traditional medicine exposure	HBV							
Unvaccinated healthcare workers	Both		HBV	Both				HBV
Occupational exposure and/or carrying out exposure-prone procedures	Both	Both	Both	Both	Both	HBV		HBV

A Hatzakis et al. Journal of Viral Hepatitis, 2013, 20 (Suppl. 2), 1–20

Table 4 HCV screening recommendations included in the HCV Hellenic National Plan

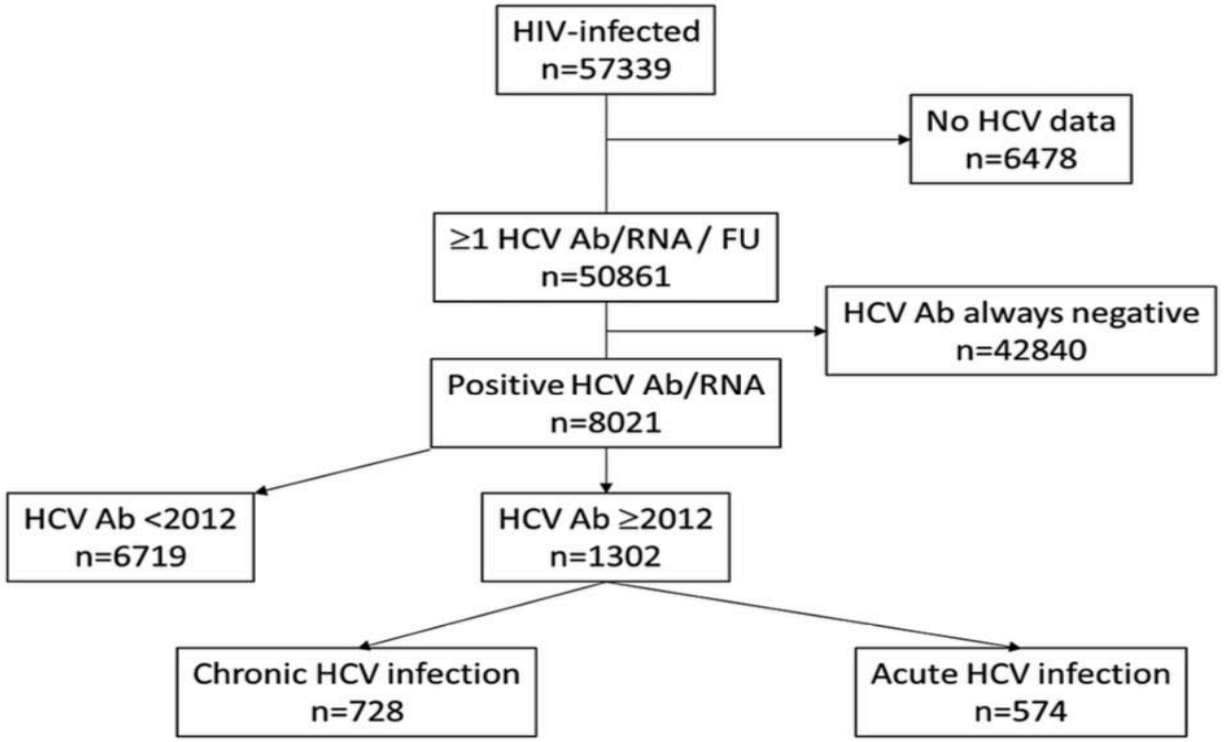
Target population	HCV screening recommendations
General	Birth cohort screening: Adults born from 1945 to 1980
High-risk groups	• Persons with elevated transaminases • People who inject drugs (current and former IV drug users) • Recipients of a transfusion of blood, blood components, or an organ transplant before 1992 • Persons who are receiving or have received hemodialysis • Persons who have been parenterally exposed to potentially HCV infected medical instruments or paramedical procedures • Long-term steady sex partners of HCV-positive persons • Persons with a history of multiple sex partners • Children born to HCV-positive women • Persons with HIV infection • Persons with HBV infection • Incarcerated persons • Immigrants from high HCV prevalence countries

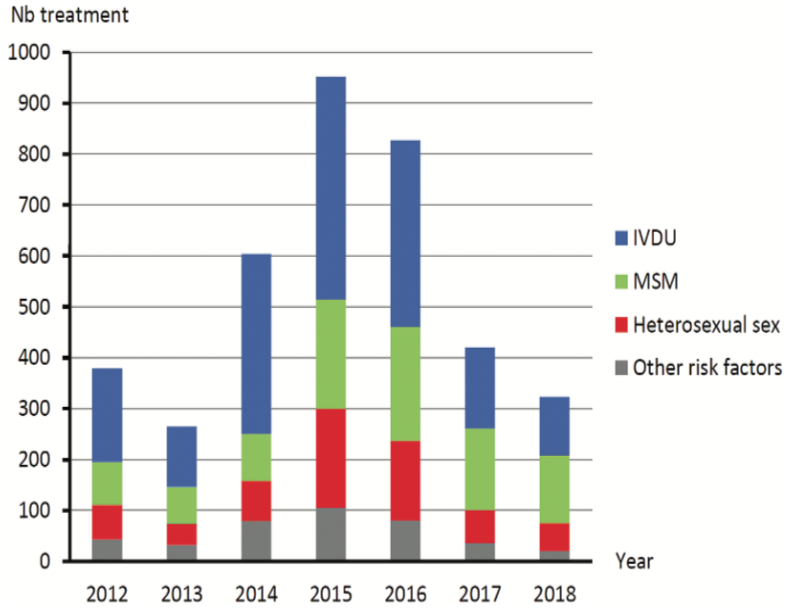
HBV, hepatitis B virus; HCV, hepatitis C virus

G. V. Papatheodoridis *et al* .Aiming towards hepatitis C virus elimination in Greece .
Annals of Gastroenterology (2019) **32,** 321-329

Patients with advanced liver disease
Haemophilia patients
Prisoners
Children
Patients engaged with drug treatment units
Migrant communities from high prevalence regions
People who inject drugs in networks
Men who have sex with men
Generational cohorts of high prevalence
Geographically defined areas

Lazarus JV, Wiktor S, Colombo M, Thursz M. Microelimination – apath to global elimination of hepatitis C. *J Hepatol*. 2017;67:665-666.





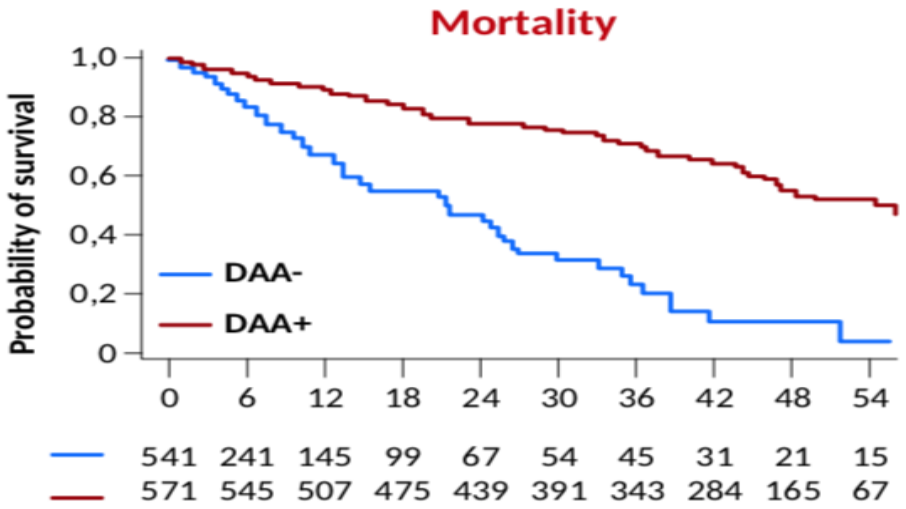
Prévalence VHC : 15.4 → 13.2%
Nouveaux cas : MSM 1.9 → 3.9%
Indication DAA : 11.4 → 61.5%
2018 41.2% MSM
Who Target : OUI sauf Nouvelles infections

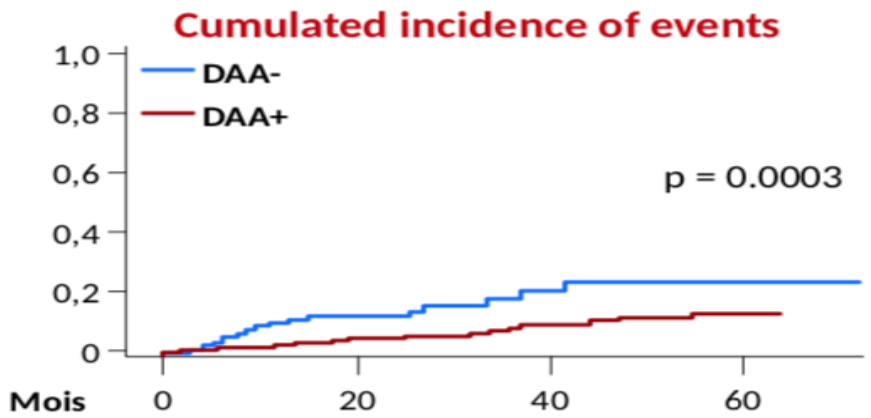
Cotte L, Hocqueloux L, Lefebvre M, Pradat P, Bani-Sadr F, Huleux T, Poizot-Martin I, Pugliese P, Rey D, Cabié A; Dat'AIDS Study Group .Microelimination or Not? The Changing Epidemiology of Human Immunodeficiency Virus-Hepatitis C Virus Coinfection in France 2012-2018.Clin Infect Dis. 2021 Nov 2;73(9):e3266-e3274. doi: 10.1093/cid/ciaa1940.

ANRS France Recherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm
CO22
HEPATHER

HCV Micro-elimination in easy-to-screen population: decompensated cirrhosis

- HEPATHER : prospective cohort including 699 patients prior decompensation of HCV cirrhosis with a median follow-up of 37 months
- SVR : 86 % (84 % in patients with CP-C and/or MELD > 20)





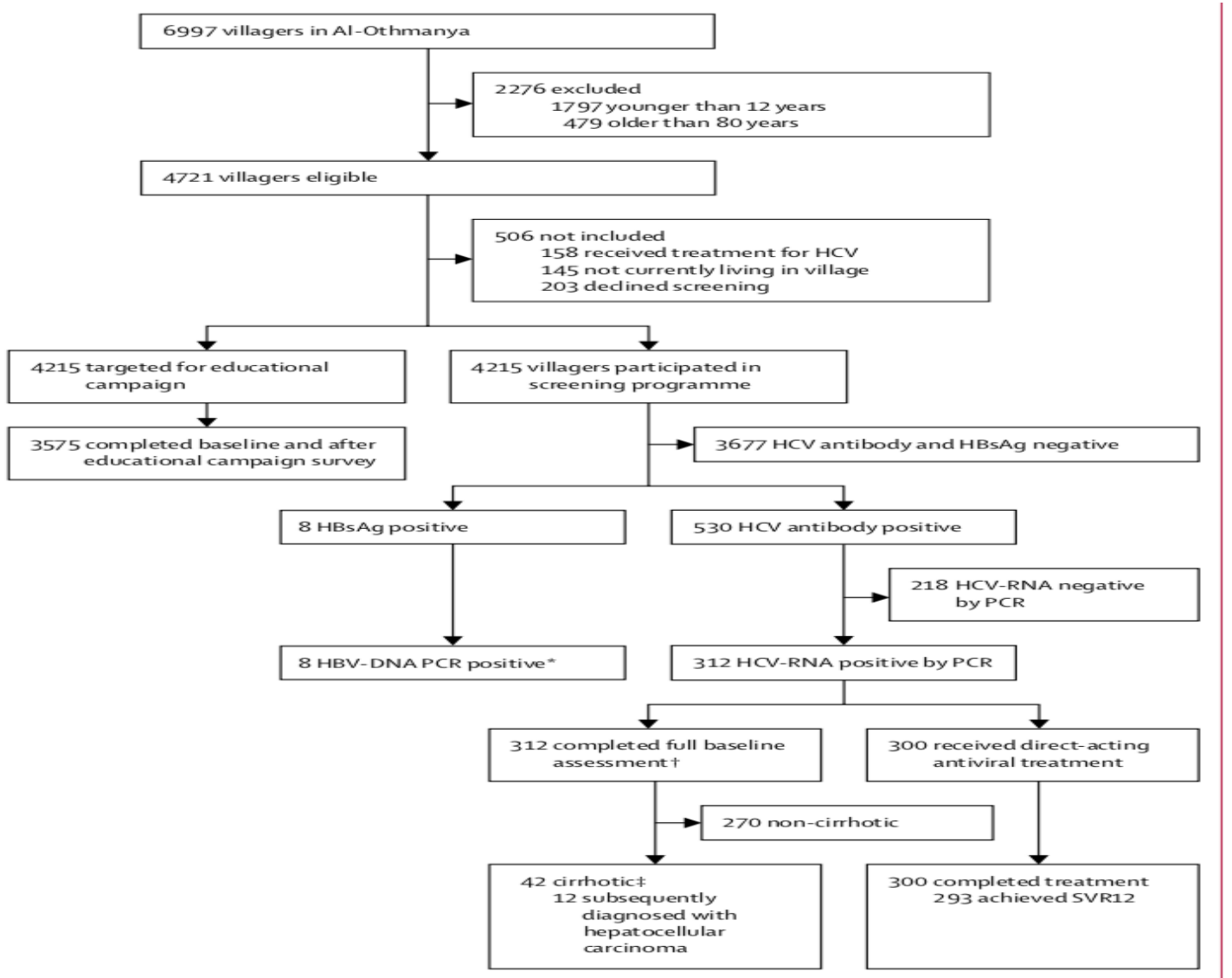
Mortality: adjusted HR 0.44, 95% CI 0.26-0.74 p=0.002

- **571 DAA+ and 128 (18.3%) untreated patients (DAA-)**

Pageaux GP et al. AASLD 2019; A1524

	Mode	Key topics or content
Booklets	Four booklets in Arabic to raise awareness distributed in public places in the village—eg, mosques, schools, and health-care units	Entitled: *How to protect yourself from catching hepatitis*, *How to live with hepatitis*, *How to support a patient with hepatitis*, and *Infection control measures for paramedical workers*
Animated cartoon films	Nine episodes of an Arabic 3D animated cartoon film titled *Abo Eloraif* (meaning "*Father of Knowledge*") each 2–3 min long; and regular broadcasting of *Abo Eloraif* through local channels	Episodes covered modes of transmission, risk behaviours for transmission, and recommended behaviours to reduce transmission and social stigma
Song	"How a patient with viral hepatitis can protect his family and neighbours?"; taught to school children and circulated by use of public health broadcasts on local satellite channel	Emphasis was put on the following points for the general public: how personal items (eg, sponge, towel, shaving tools, and nail cutter or scissors) should be personal to them, while at home, travelling, or at the barber shop or hairdressers; cups and needles for hijama (cupping) or acupuncture should be personal; and for health workers: any wound should be disinfected and covered; they should be committed to complying with infection control standards and use of non-reusable syringes; the importance of using sterile instruments for dental procedures, and doing renal dialysis and surgical procedures in a clean sterilised environment
Posters	Five posters in community and health-care facilities	Key messages included prevalence of hepatitis worldwide and in Egypt; practices that do and do not transmit infection; people at higher risk and how to protect yourself from acquiring hepatitis C infection

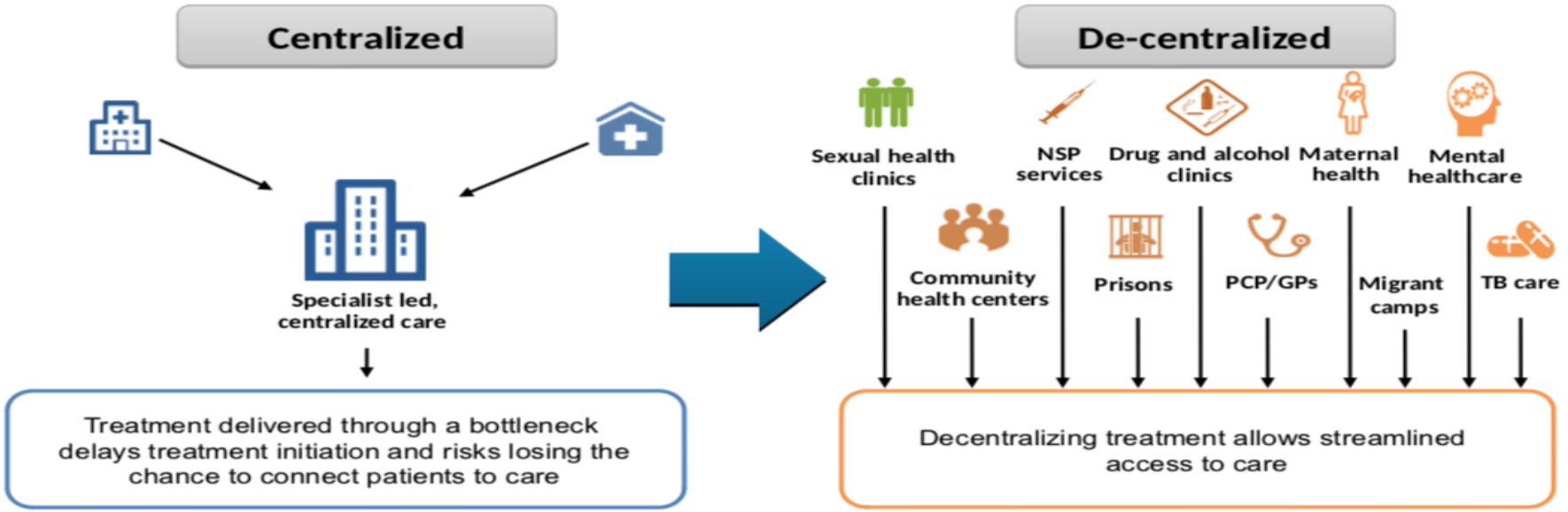
Table 1: Educational materials used for awareness raising and public education[28]



Gamal Shiha et AL An educate, test, and treat programme towards elimination of hepatitis C infection in Egypt: a community-based demonstration project www.thelancet.com/gastrohep Published online July 17, 2018

"De-centralize" screening and care in communities

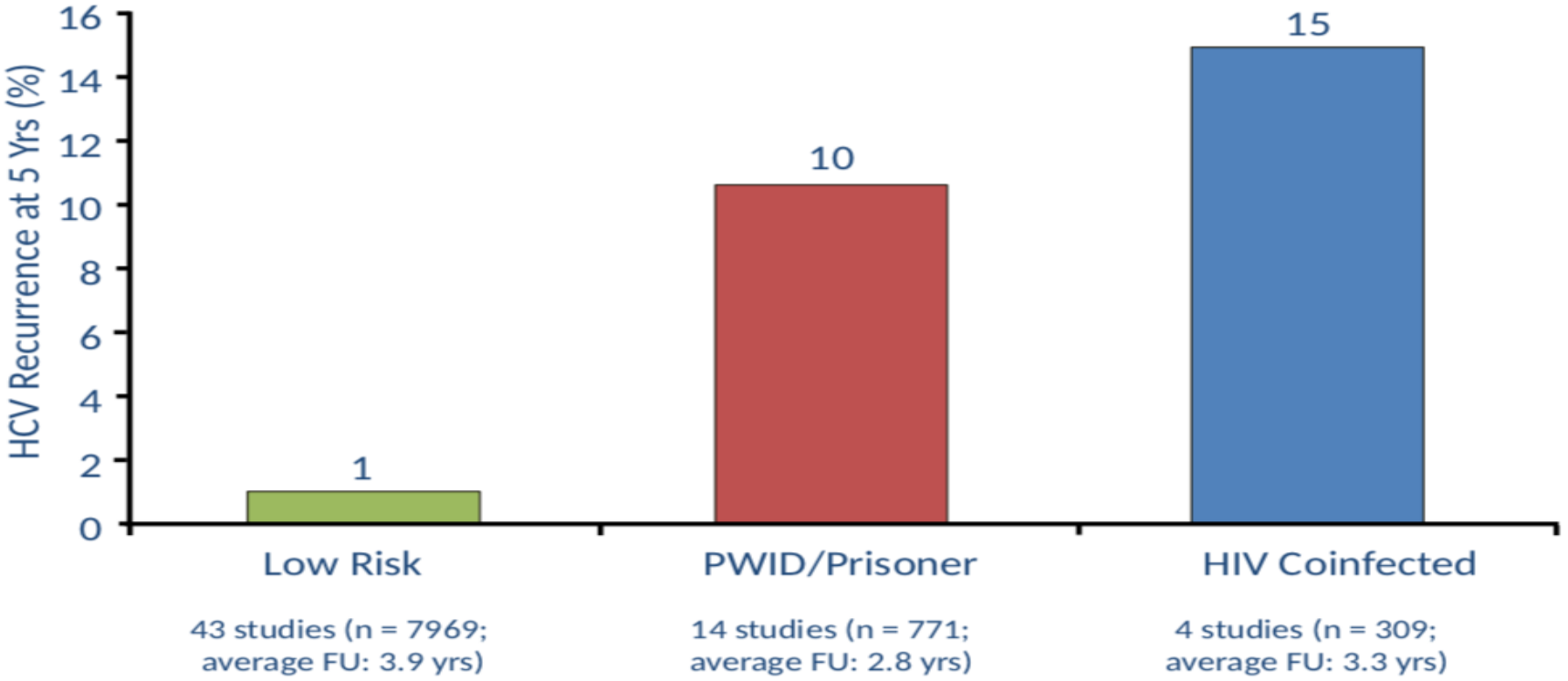
Patients may face difficulties in accessing testing and treatment facilities. Different populations have differing needs and require specific settings and measures in place to access treatment



GP, general practitioner; NSP, needle and syringe program; PCP, primary care practitioner; TB, tuberculosis.

1. EMCDDA Hepatitis C Among Drug Users in Europe. Available at: http://www.emcdda.europa.eu/system/files/publications/2740/att_212353_EN_EMCDDA_POD_2013_Hep%20C%20treatment.pdf (accessed December 2018).
2. WHO Implementing Comprehensive HIV and HCV Programmes with People Who Inject Drugs. Available at: http://www.who.int/hiv/pub/idu/IDUIT_2017.pdf?ua=1. (accessed December 2018)
3. WHO Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Available at https://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/ (accessed December 2018) .

HCV reinfection over 5 years



Simmons B, et al. Clin Infect Dis. 2016:62:683-694.

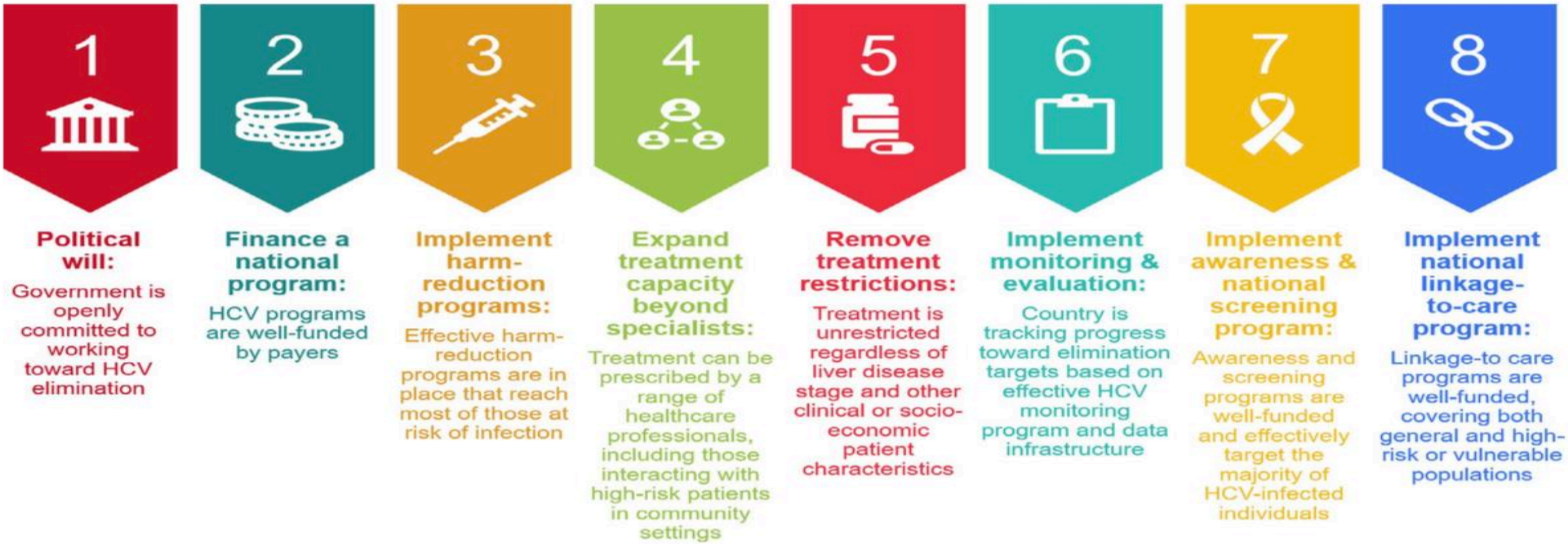
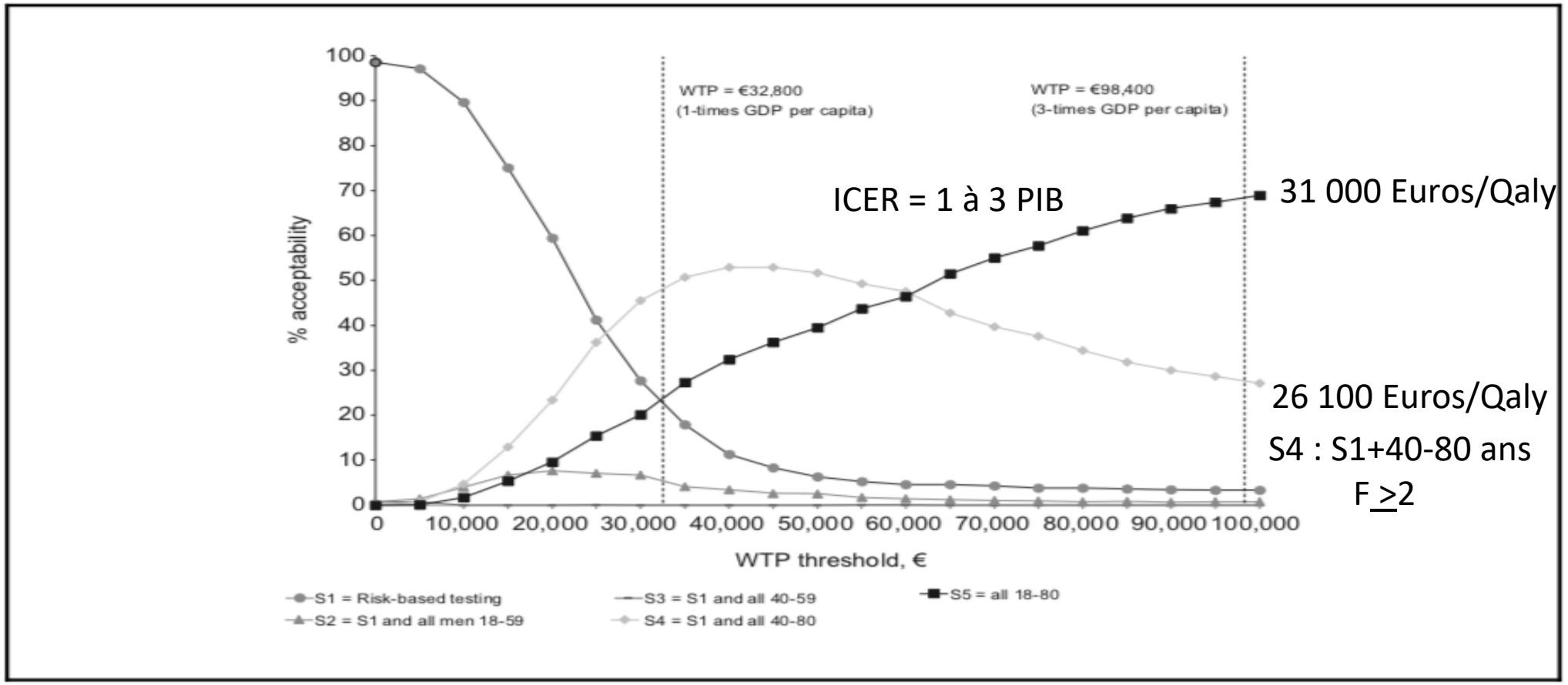


FIGURE 3 Key success factors for HCV elimination, a conceptual framework. HCV, hepatitis C virus

Razavi et Al .Liver International. 2020;40:522–529.



ICER = 1 à 3 PIB

31 000 Euros/Qaly

26 100 Euros/Qaly

S4 : S1+40-80 ans

F ≥2

Deuffic-Burban S et al. Assessing the cost-effectiveness of hepatitis C screening strategies in France. J Hepatol (2018), https://doi.org/10.1016/j. jhep.2018.05.027

TABLE 3 Direct medical 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			5463		–	–	
GHSS Targets	2020	Graduated screening 1	5974	1968-1987	144 000	3552	3552
	2023	Graduated screening 2	6028	1948-1967	125 000	4532	[a]
		Screening 1948-1977	6081		142 000	4349	[a]
		Screening 1958-1977	6083		128 000	4831	[a]
		Universal screening	6441		145 000	6758	562 855

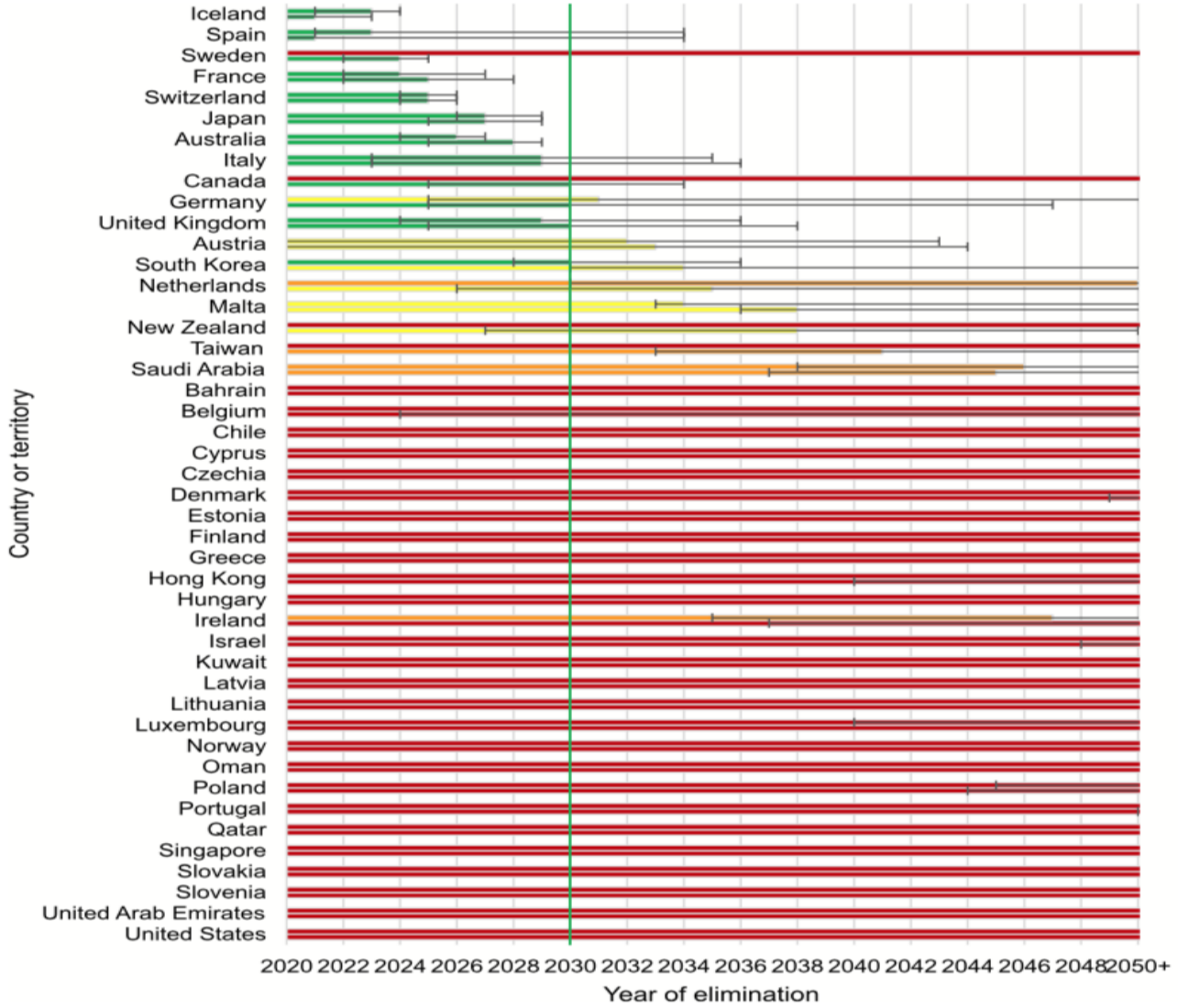
Note: Values have been rounded, so ICERs may not be reproducible using table values.

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; GHSS: Global Health Sector Strategy.

[a]Strongly dominated scenario (costlier and less effective than another scenario).

Kondili et Al. Optimization of hepatitis C virus screening strategies by birth cohort in Italy *Liver International.* 2020;40:1545–1555.

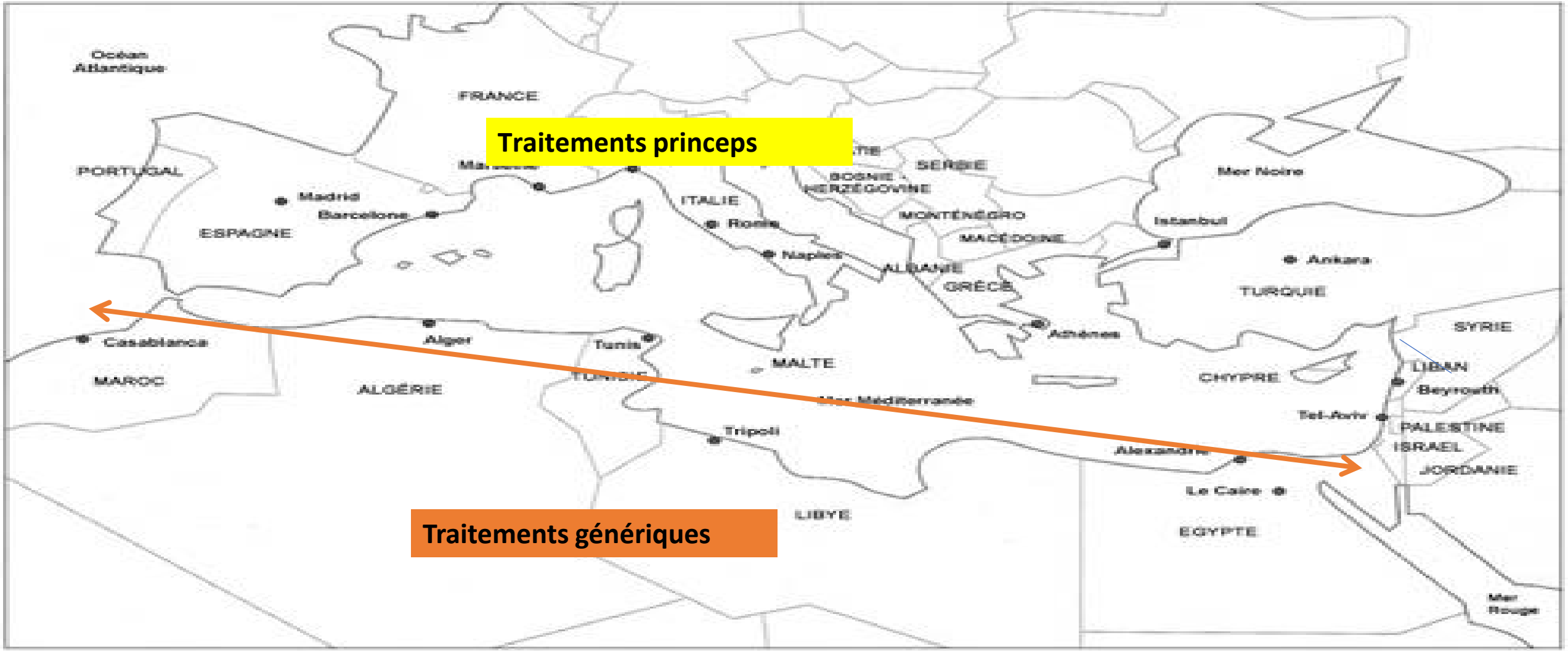
Global timing of hepatitis C virus elimination in high-income countries



- High income mediterrannean countries

GAMKRELIDZE Et AL.
Liver International. 2021;41:456–463.

Traitements

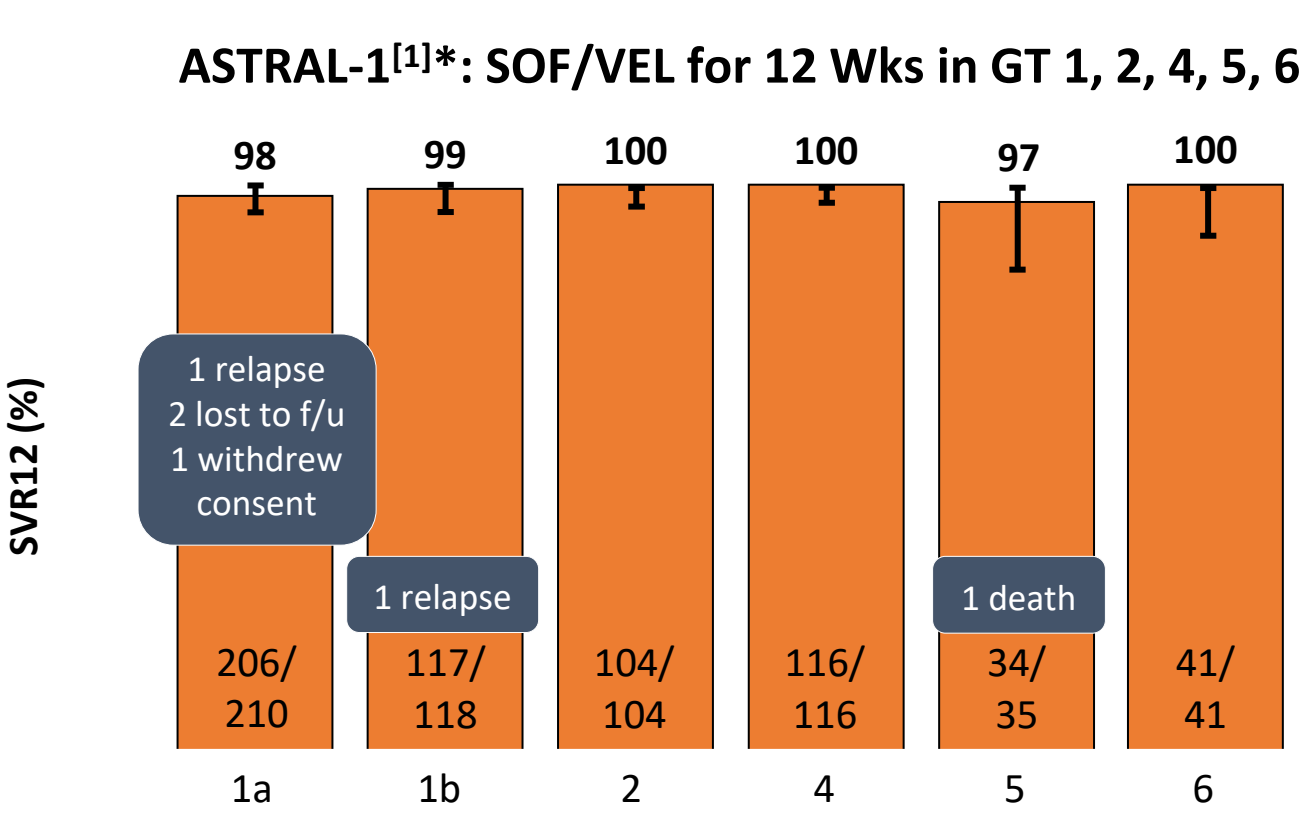


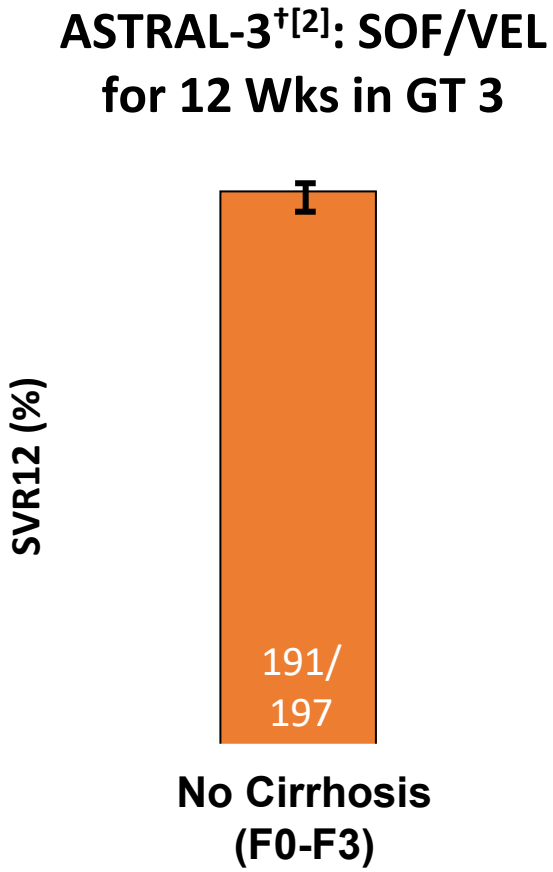
Recommended Treatment Regimens

- **Genotype-specific**
  - Elbasvir/Grazoprevir: GT 1, 4
  - Ledipasvir/Sofosbuvir: GT 1, 4, 5, 6
- **Pangenotypic**
  - Sofosbuvir/Velpatasvir – GT 1-6
  - Glecaprevir/Pibrentasvir – GT 1-6
  - Sofosbuvir/Velpatasvir/Voxilaprevir – GT 1-6 (reserved for salvage therapy)

AASLD/IDSA. HCV Guidance. 2018.

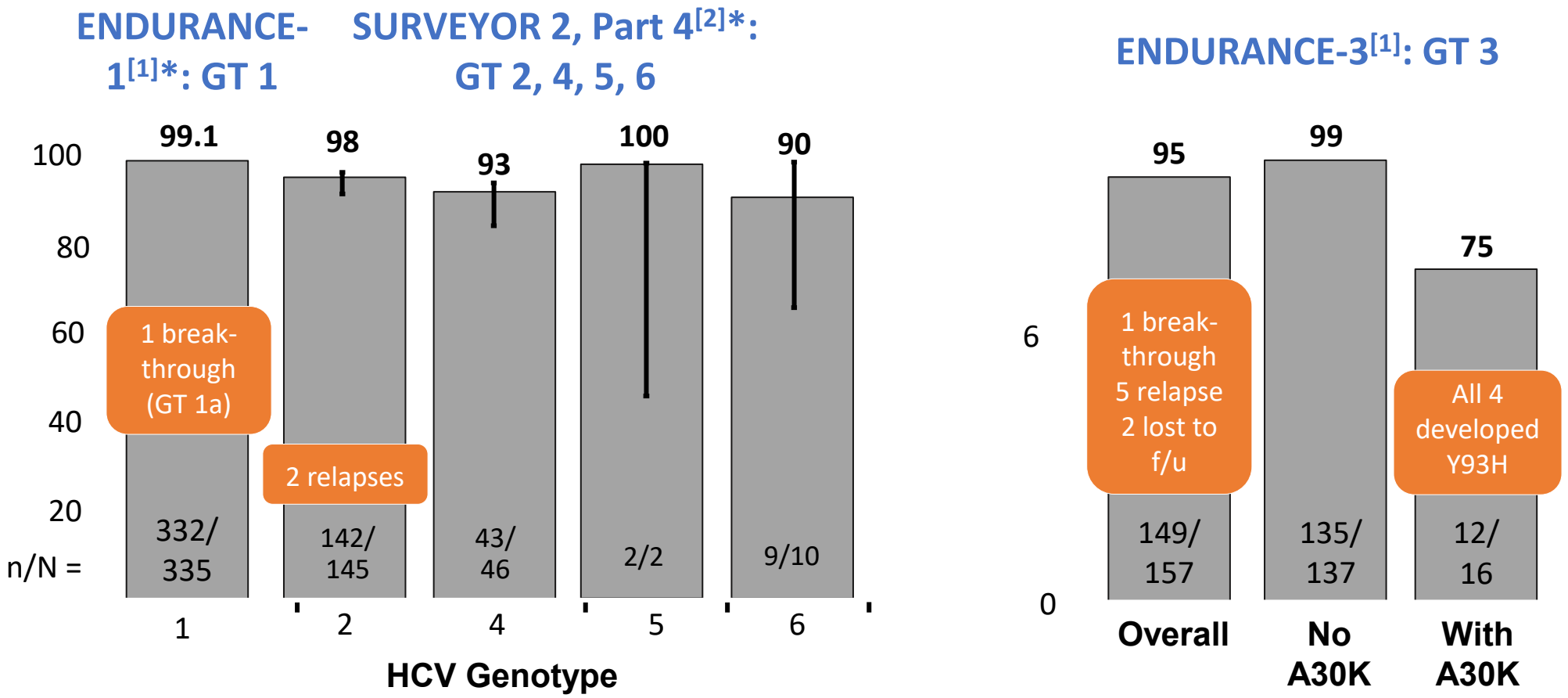
Pangenotypic Regimens: SOF/VEL for 12 Wks





1. Feld. NEJM. 2015;373:2599. 2. Foster. NEJM. 2015;373:2608.

Pangenotypic Regimens: GLE/PIB for 8 Wks in Patients Without Cirrhosis



*Includes treatment-naive and treatment-experienced patients.

1. Zeuzem. NEJM. 2018;378:354. 2. Asselah. Clin Gastro Hepatol. 2018;16:417.

HCV DAAs: Prices in USA and India versus Target

Drug	Current US price (lowest)	Current lowest Indian market price	Target price
Sofosbuvir	$49,680	$324	$62
Daclatasvir	$50,653	$153	$14
SOF+LDV	$56,700	$507	$96
SOF+VEL	$74,760	-	$181-216

Gotham D, Barber M, Fortunak J, Pozniak A, Hill A. Rapidly falling costs for new hepatitis C direct-acting antivirals (DAAs): potential for universal access. Abstract number A-792-0516-01639, presented at AIDS2016, Durban.

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Bioequivalent pharmacokinetics for generic and originator Hepatitis C Direct Acting Antivirals

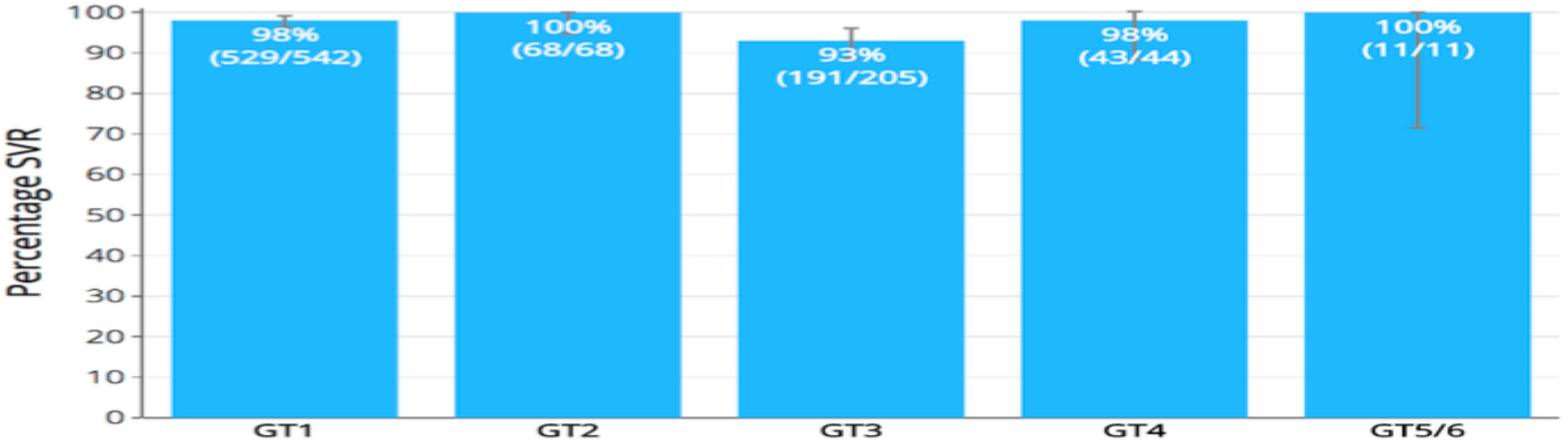
Andrew M. Hill[1], Loai Tahat[2], Mohammed Khalil Mohammed[3], Sanjay Nath[4], Rabab Fayez Tayyem[3], James A. Freeman[5], Ismahane Benbitour[7], Sherine Helmy[6]; [1]Department of Translational Medicine, University of Liverpool, Liverpool, United Kingdom; [2]Pharmaceutical Research Unit, Amman, Jordan; [3]ACDIMA BioCentre, Amman, Jordan; [4]Faculty of Medicine, Imperial College London, London, United Kingdom; [5]GP2U Telehealth, Hobart, TAS, Australia; [6]R&D Project Innovations, Pharco, Cairo, Egypt; [7]BEKER Laboratories, Algiers, Algeria

AASLD 2017

DRUG	TRIAL TYPE	COMPANY	NUMBER	CMAX	AUC0-∞
Sofosbuvir	Four-way, four-period, fully replicated, single oral dose	EEPI	36	101.0 (88.1-115.7)	103.0 (97.6-109.7)
Daclatasvir	Two-way, two-period, single oral dose	Dawood	35	106.9 (100.2-114.0)	103.7 (98.3-109.4)
Sofosbuvir	Three-period, two-treatment, three sequence, semi-replicate	Beker	35	95.4 (84.7-107.5)	98.5 (91.6-106.0)
Daclatasvir	Three-period, two-treatment, three sequence, semi-replicate	Beker	35	104.1 (93.1-116.3)	103.0 (94.4-112.4)
Sofosbuvir	Three-period, two treatment, three sequence, partial replicate	Hetero	54	95.7 (87.2-105.2)	100.8 (96.2-105.6)
Sofosbuvir	-	Natco	-	96.1 (81.0-114.0)	100.7 (94.2-107.8)
Daclatasvir	-	Natco	-	94.5 (83.1-107.4)	96.5 (87.1-106.8)
Sofosbuvir	Two-period, two-treatment, single dose	Virchow	22	94.8 (83.3 – 107.9)	95.8 (86.9 – 105.7)

High SVR rates using parallel imported generic DAAs in 1160 patients with Hepatitis C

James Freeman; Nabil Debzi; Giten Khwairakpam; Julia Dragunova; Sergey Golovin;James Wang; Andrew Hill; Vicky Houghton-Price; Rachel Smith; Roxanna Korologou-Linden; John Freeman; Greg Jefferys.



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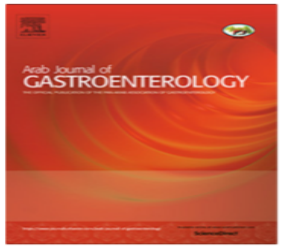
journal homepage: www.elsevier.com/locate/ajg



Editorial

Hepatitis C elimination in Africa: Seizing the moment for hepatitis-C free future

A. Cordie ,R. Mohamed , Mark W. Sonderup ,C. W Spearman , M. A. Medhat , N. Debzi , H. Desalegn , G. Esmat

Hepatitis Can’t Wait

Delaying screening, diagnosis and initiation of DAAs will impact on achieving the WHO 2030 elimination goals.

Table 1. Participation in Screening and HCV Seroprevalence According to Sex.*

Variable	Men	Women	Total
Screening target population — no.†	32,207,165	30,298,399	62,505,564
Participated in screening — no. (%)‡	24,018,428 (74.57)	25,611,891 (84.53)	49,630,319 (79.40)
Previously treated for HCV infection with direct-acting antivirals since 2014 — no. (%)§	692,632 (2.88)	591,739 (2.31)	1,284,371 (2.59)
Screened for HCV antibodies — no. (%)§	23,325,796 (97.12)	25,020,152 (97.69)	48,345,948 (97.41)
HCV seropositive			
No. of adults	1,252,443	976,885	2,229,328
Percent (95% CI)¶	5.37 (5.36–5.38)	3.90 (3.90–3.91)	4.61 (4.61–4.62)

* CI denotes confidence interval, and HCV hepatitis C virus.
† The screening target population included all Egyptian adults 18 years of age or older who had ever been issued a national identification number.
‡ Participation in screening was voluntary. Percentages are relative to the screening target population.
§ Percentages are relative to the number who participated in screening. Persons who had been previously treated with direct-acting antiviral agents were not screened for HCV antibodies.
¶ Percentages are relative to the number screened for HCV antibodies.

I.Waked et al, Special report Screening and Treatment Program to Eliminate Hepatitis C in Egypt
n engl j med 382;12 nejm.org March 19, 2020

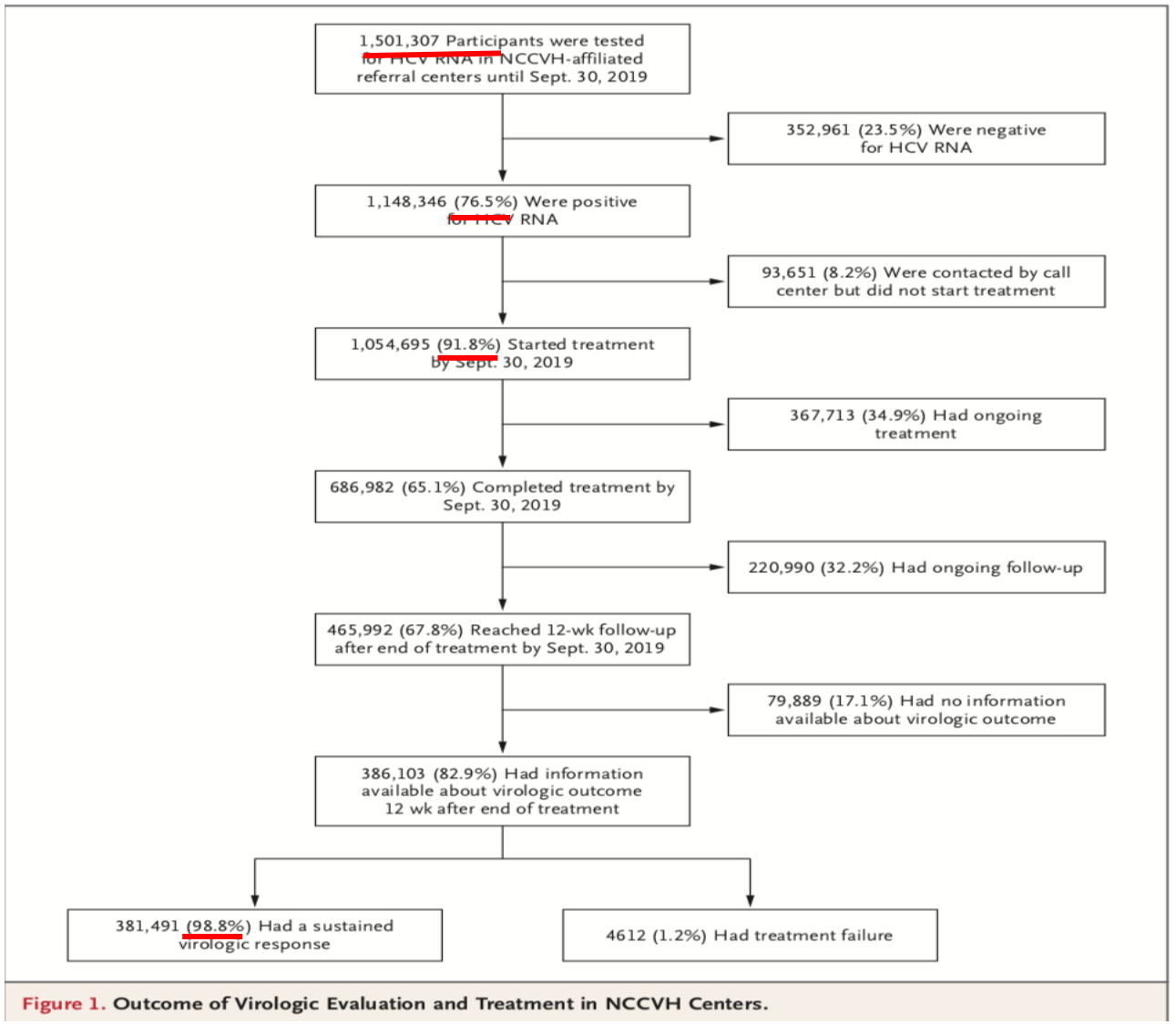


Figure 1. Outcome of Virologic Evaluation and Treatment in NCCVH Centers.

I.Waked et al, Special report Screening and Treatment Program to Eliminate Hepatitis C in Egypt n engl j med 382;12 nejm.org March 19, 2020

Table 3. Cost of the Screening and Treatment Program.*

Variable	Value
Screening	
Staff cost — $	
Medical teams	36,552,528
Administrative staff	15,000
Total	36,567,528
Medical supplies — $	
Rapid diagnostic test for HCV antibodies	27,345,901
Consumables (e.g., gloves, swabs, and staff uniforms)	3,701,062
Total	31,046,963
Information technology and administration — $	4,364,830
Overhead — $	18,787,415
Total cost of HCV screening program — $	90,766,736
No. with HCV seropositivity	2,229,328
Cost of identifying seropositive case — $	40.71
Evaluation	
PCR assay for HCV RNA — $†	14,981,084
Clinical, laboratory, and ultrasonographic evaluation — $‡	31,349,925
Total cost of evaluation — $	46,331,009
No. with viremia	1,605,116
Cost of HCV RNA testing and evaluation per viremic case — $	28.86
Cost of identifying viremic case — $	85.41
Treatment — $	
Total cost of treatment	70,041,432
Cost of treatment per case§	43.64
Total cost	
Total cost of screening, evaluation, and treatment — $	207,139,177
Cure rate — %¶	98.8
Cost of identifying and curing a case — $‖	130.62

* All costs are in U.S. dollars, calculated at the exchange rate at the start of the program in October 2018 (1 U.S. dollar = 17.6 Egyptian pounds). Costs of screening include all costs incurred to screen the 49.6 million persons for HCV antibodies. Costs of evaluation and treatment assume that all seropositive patients were evaluated and that all patients with viremia were treated. PCR denotes polymerase chain reaction.
† Included are the purchase cost per test ($4.80) plus 40% overhead, consumables, and staff, multiplied by the number of HCV-seropositive cases identified in the screening program.
‡ Included are the cost of laboratory tests and ultrasonography, consumables, and staff, multiplied by the number of HCV-seropositive cases identified in the screening program.
§ Included is the cost of a 12-week supply of locally manufactured sofosbuvir plus daclatasvir with or without ribavirin.
¶ Shown is the percentage of patients with a known sustained virologic response in the program.
‖ The result is the cost of screening, evaluation, and treatment for the whole program divided by the number of patients with viremia divided by the cure rate.

200 Millions USD pour 1 million de patients traités en deux années
50 millions à traiter = 10 milliards de dollars
Objectif > 2030

I.Waked et al, Special report Screening and Treatment Program to Eliminate Hepatitis C in Egypt n engl j med 382;12 nejm.org March 19, 2020

CONCLUSION

-Le rendez vous de 2030 sera possible pour les pays à revenu élevé avec une prévalence acceptable de patients virémiques : 20 % d'élus .

-Bassin méditerranéen : 3 pays , France- Italie- Espagne

-Le scénario Égyptien est l'exemple à suivre pour les pays de la rive sud