Is global HCV eradication realistic?

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Antonio Craxi: disclosures

Ad Board and grants: Abbvie, BMS, Gilead, MSD, Intercept

Speaker: Abbvie, BMS, Gilead, MSD, Intercept

Slide credits

Observatory POLARIS

Hepatitis B and C Public Policy Association

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Fighting an infection: the semantics

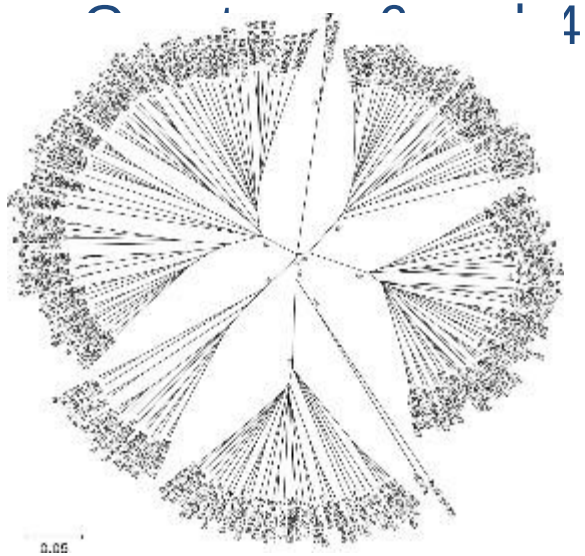
- **Eradication:** permanent reduction to zero of the worldwide incidence of infection; intervention measures no longer needed
  - Only 1 example: smallpox
- **Elimination:** reduction to zero of incidence in a defined geographical area as a result of deliberate efforts; continued intervention measures required
- **Control:** reduction in the incidence, prevalence, morbidity, or mortality of an infectious disease to a locally acceptable levels; continued intervention measures required

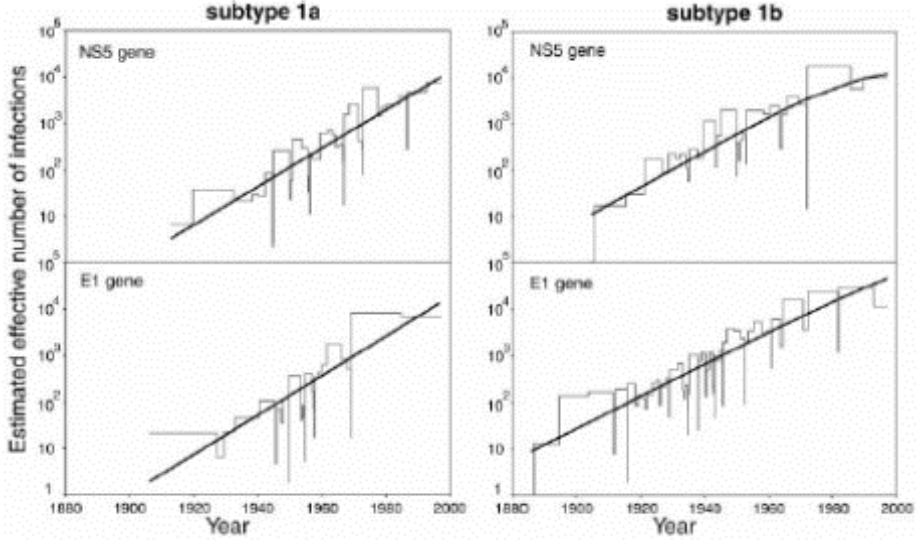
Molyneux DH, et al. Trends Parasitol. 2004;20:347-351.

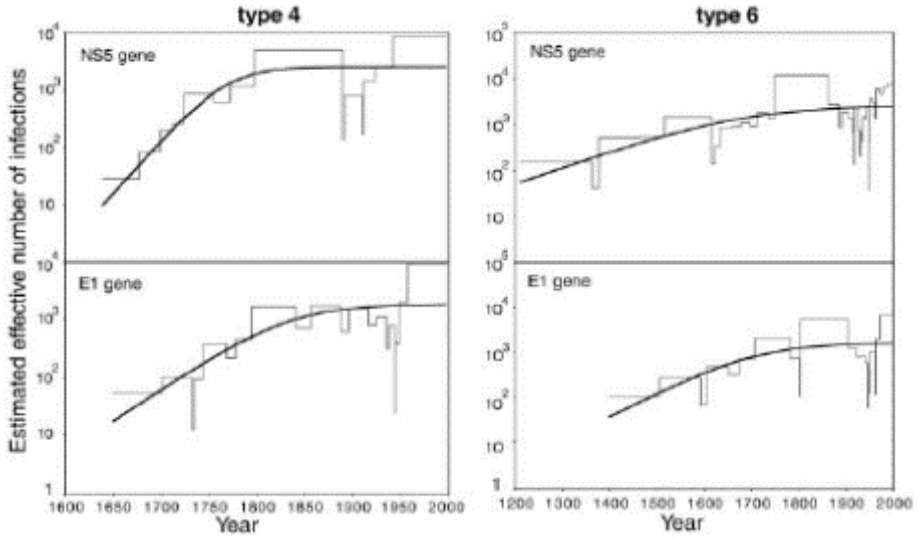
HCV: an old foe

- The origin of primate Flaviviridae is as ancient (35 million years) as the differentiation of primate species
- HCV co-evolved with human populations migratiNG out of Africa within the past 100-150,000 years
- The HCV genotype / subtype hierarchy encompassing at least 86 classified subtypes is much more recent

Genotypes 2 and 4 originated 700 years and 350 years ago, and subtypes 1a and 1b < 100





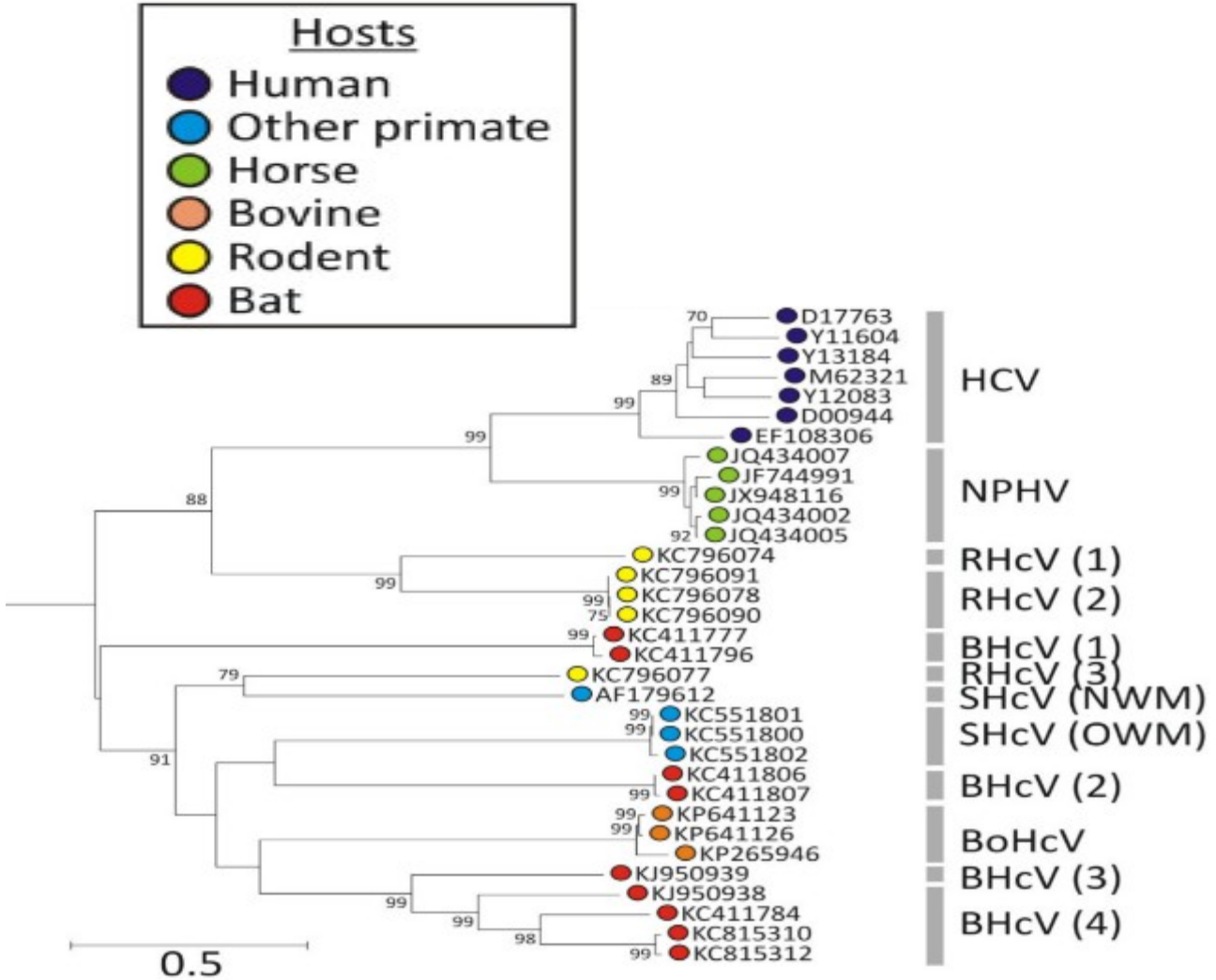


1: Smith DB, Bukh J, Kuiken C, Muerhoff AS, Rice CM, Stapleton JT, Simmonds P. Expanded classification of hepatitis C virus into 7 genotypes and 67 subtypes:updated criteria and genotype assignment web resource. Hepatology. 2014;59:318-27.

2: Pybus OG, Charleston MA, Gupta S, Rambaut A, Holmes EC, Harvey PH. The epidemic behavior of the hepatitis C virus. Science. 2001; 292:2323-5.

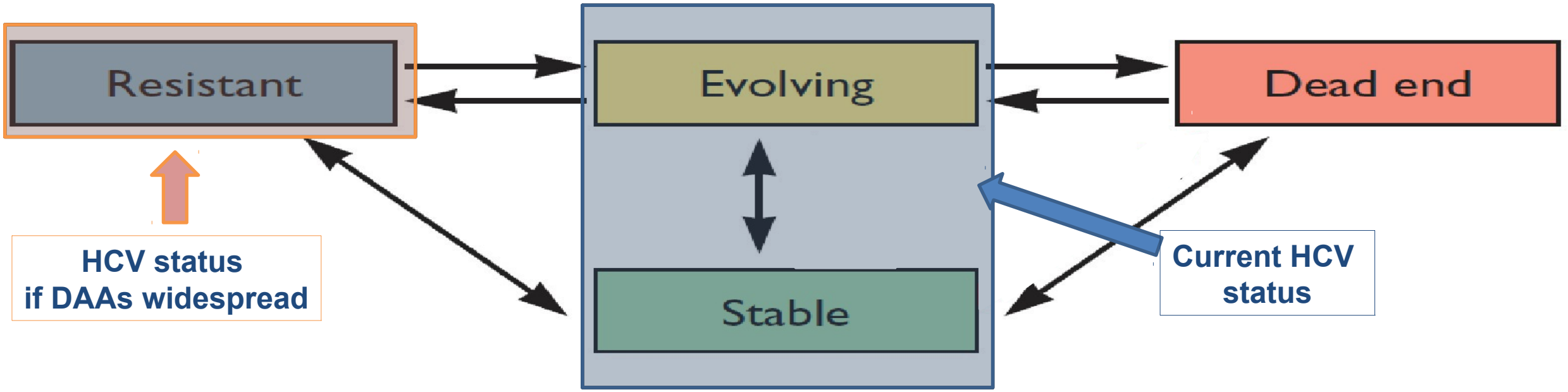
The expanded *Hepacivirus* genus

- Highly diverse variants
  - Several candidate new species
  - Variable and highly erratic distribution in different mammalian species
- No association between host and virus phylogenies
  - Evidence for cross-species transmission
- Limited species barriers consistent with a zoonotic origin of HCV in humans



1: Scheel TK, Simmonds P, Kapoor A. Surveying the global virome: identificationand characterization of HCV-related animal hepaciviruses. Antiviral Res. 2015Mar;115:83-93.

General interactions of hosts and viruses

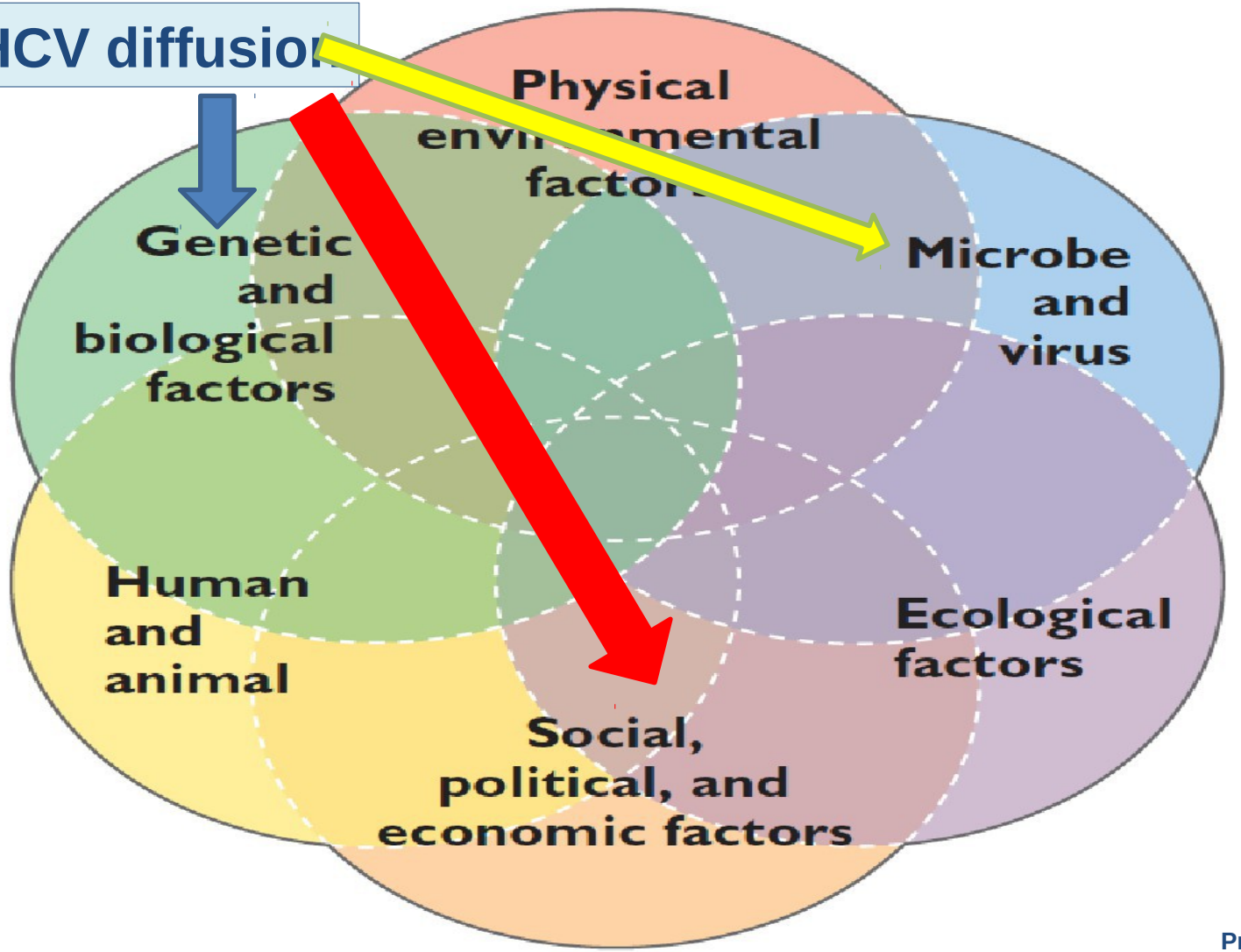


- Stable: maintains virus in ecosystem
- Evolving: passage of virus to naive population
- Dead---end: one way to different species
- Resistant host: infection blocked

Principles of Virology, ASM Press

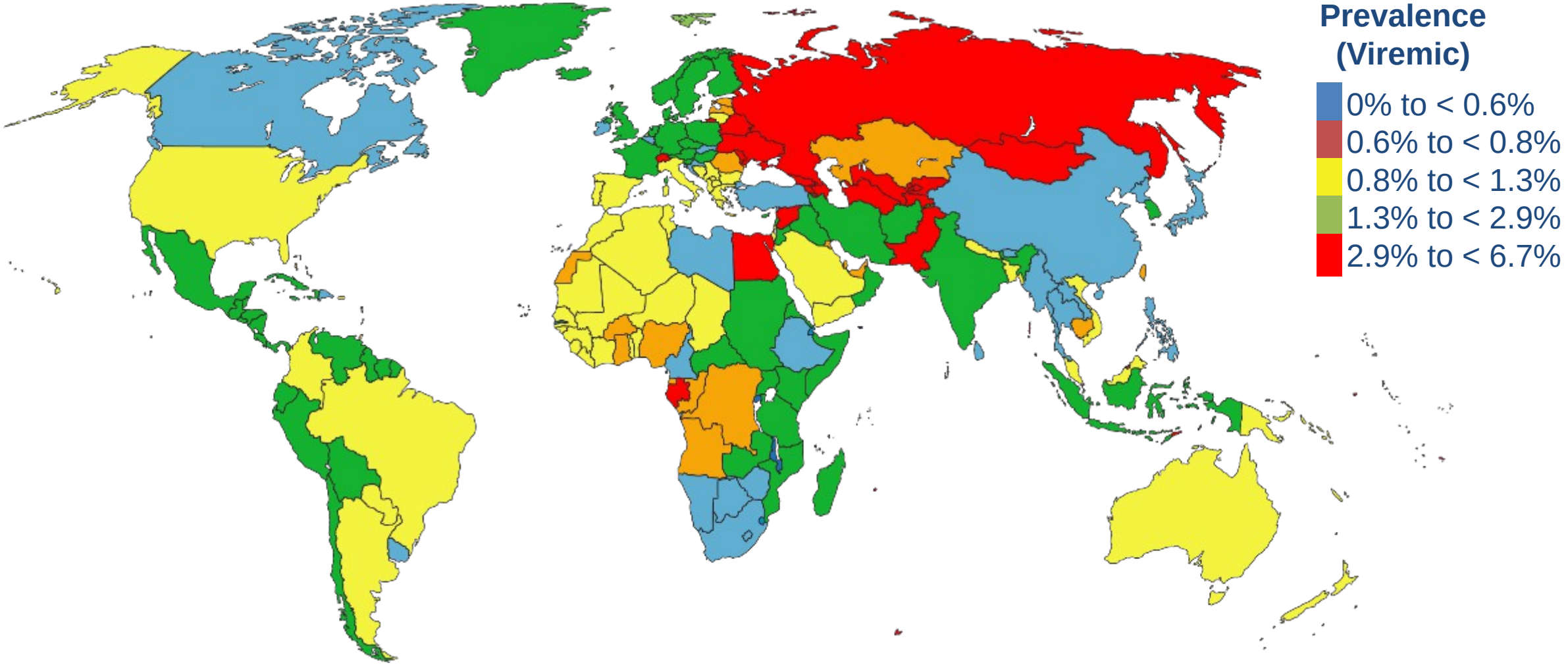
Regulators of viral epidemiology in a human population

Main drivers of HCV diffusion



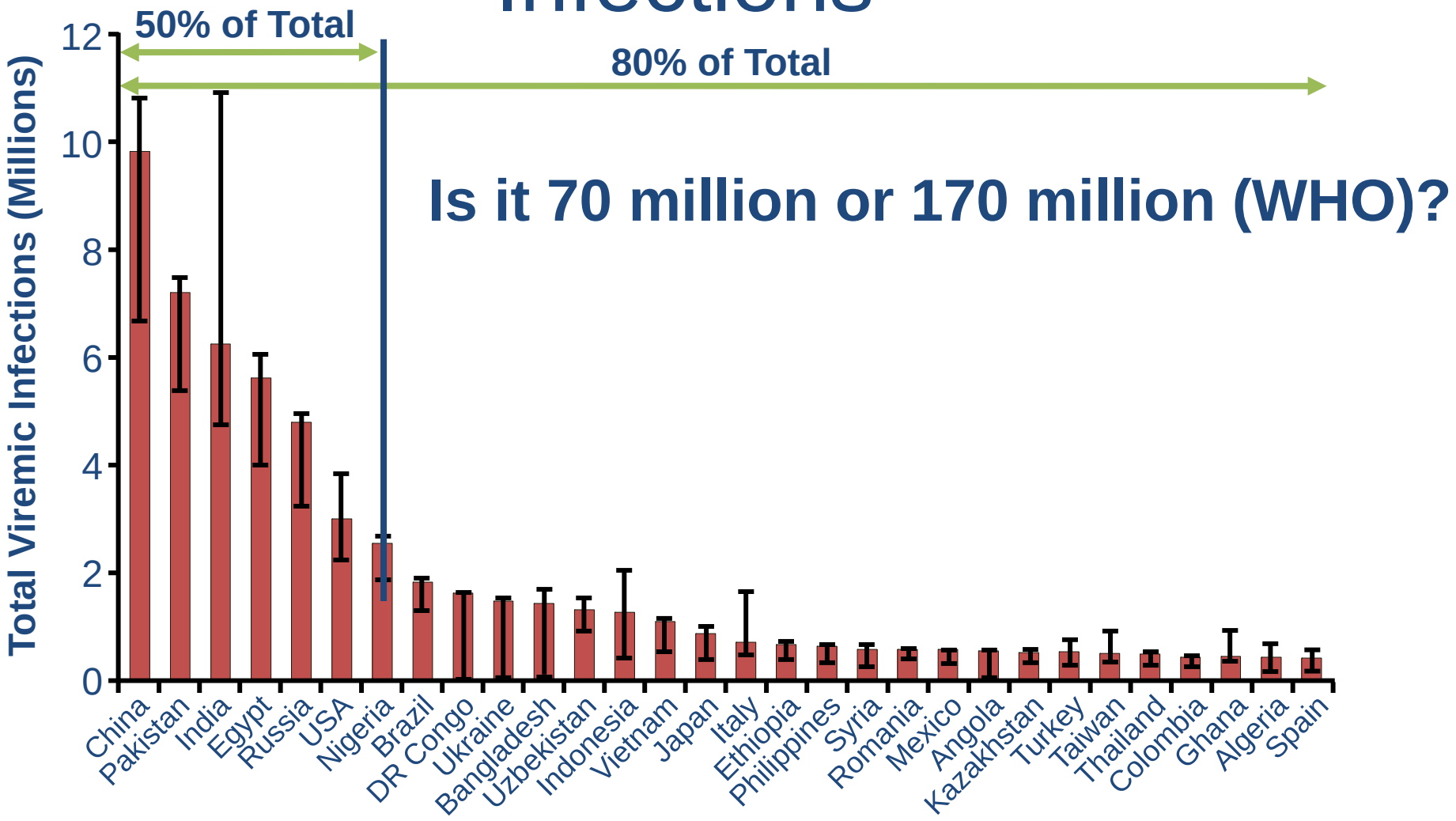
Principles of Virology, ASM Press

Estimated 70 Million Persons Living With HCV



Polaris Observatory HCV Collaborators. Lancet Gastroenterol Hepatol. 2017;2:161-176.

30 Countries Account for 80% of HCV Infections



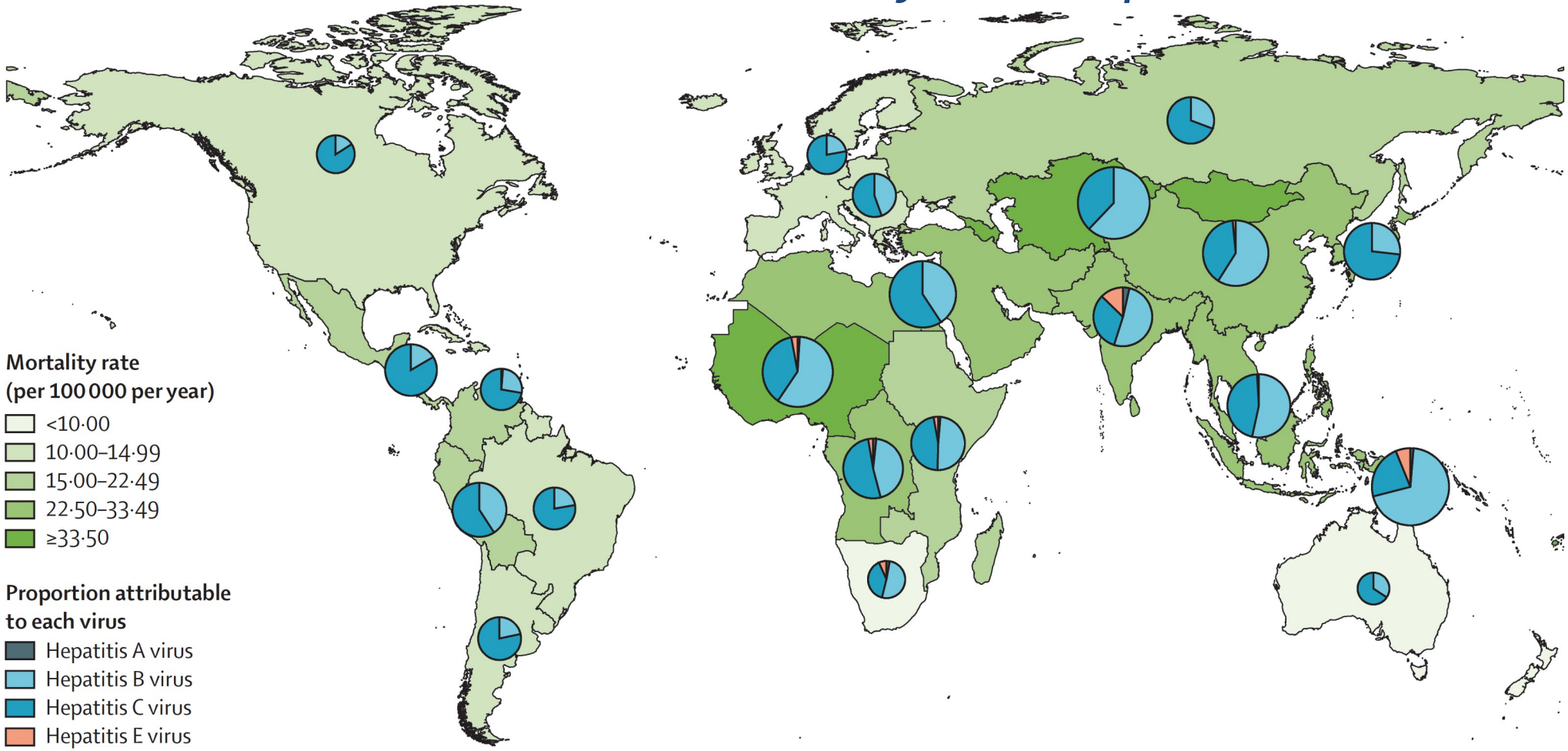
Is it 70 million or 170 million (WHO)?

Polaris Observatory HCV Collaborators. Lancet Gastroenterol Hepatol. 2017;2:161-176.
Blach S, et al. AASLD 2016. Abstract 753.

In 2013 HCV infection caused an estimated 700,000 deaths

vs 1990: 67% higher cirrhosis and 291% HCC

Regional distribution of deaths shown by size of pie charts



Stanaway, Lancet 2016; GBD Lancet 2015

The evolution of HCV therapy

Sofosbuvir/Velpatasvir/
Voxilaprevir
(DAA failures, all
genotypes)

Sofosbuvir/
Velpatasvir
(all genotypes)

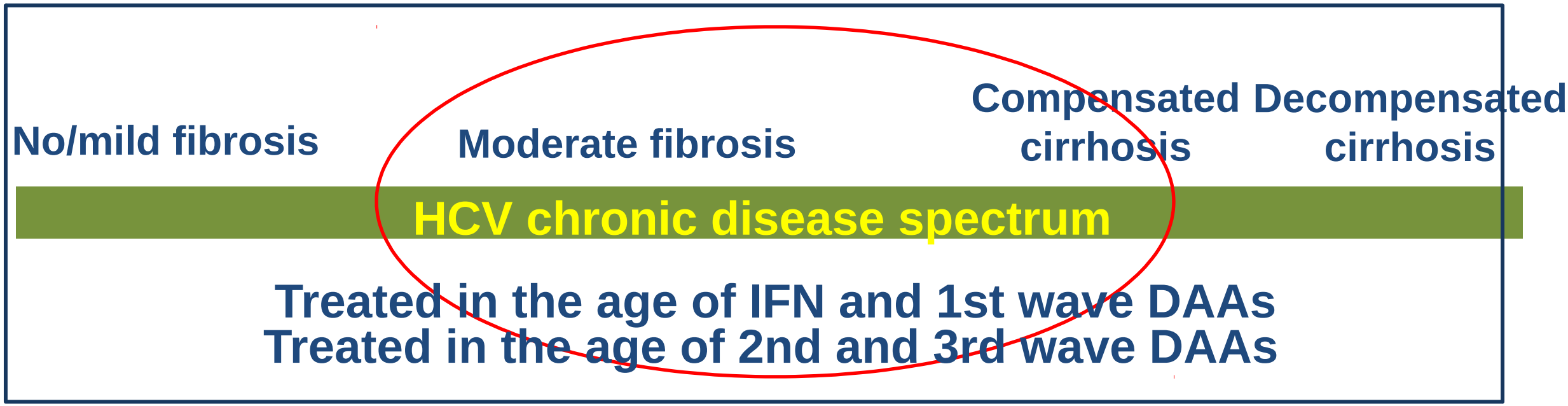
2017

?

Glecaprevir/
Pibrentasvir
(all genotypes)

evir/
GT1,4)

Current DAAs allow treating all HCV patients



- by enrolling patients at all stages of disease and comorbidities (CKD, HIV)
- by pangenotypic/subtypic activity
- by lifting restrictions due to tolerability and DDIs

Third (and last) wave HCV drugs

- GLE: pangenotypic **NS3/4A** protease inhibitor
- PIB: pangenotypic **NS5A** inhibitor
- **GLE/PIB:** once daily, oral, fixed-dose combination (300/120 mg) for GTs 1-6

All third wave compounds are more potent and have a higher barrier to resistance as compared to former DAAs

- **SOF/VEL/(VOX):** once daily, oral, fixed-dose combination (400/100/(100 mg) for GTs 1-6

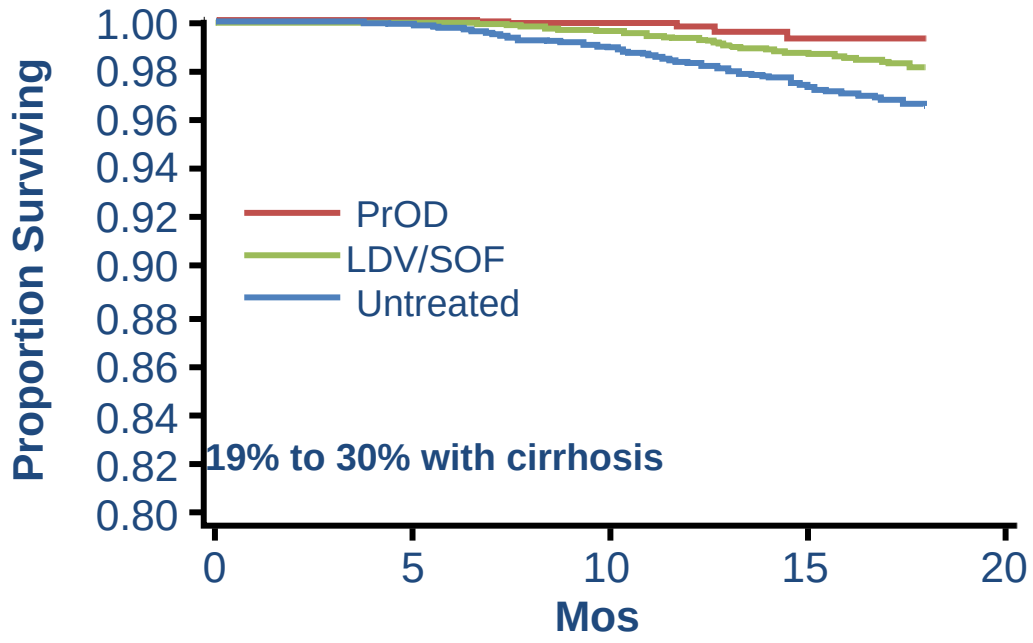
Pangenotypic, RBV-free DAAs for 8-12 weeks available for most HCV patients

Setting	EMA indications for pangenotypic, RBV-free regimens		
	GLE/PIB	SOF/VEL	SOF/VEL/VOX
Treatment naive	GT1-6 ▪ No cirrhosis: 8 wks ▪ Compensated cirrhosis: 12 wks	GT1-6 ▪ No cirrhosis or compensated cirrhosis: 12 wks	GT1-6 ▪ No cirrhosis 8 wks ▪ Compensated cirrhosis: 12 wks (8 weeks may be considered in GT3 pts)
IFN/RBV * experienced	GT1, 2, 4, 5, 6 ▪ No cirrhosis: 8 wks ▪ Compensated cirrhosis: 12 wks GT3 ▪ No cirrhosis or compensated cirrhosis: 16 wks	GT1-6 ▪ No cirrhosis or compensated cirrhosis: 12 wks	GT1-6 ▪ No cirrhosis 8 wks ▪ Compensated cirrhosis: 12 wks (8 weeks may be considered in GT3 pts)
DAA experienced	▪ Not indicated	▪ Not indicated	GT1-6 ▪ No cirrhosis or compensated cirrhosis: 12 wks

*Includes PR ± SOF for GLE/PIB and PR ± BOC, SMV, or TVR for SOF/VEL.

Mortality Reduction Achieved by HCV Cure

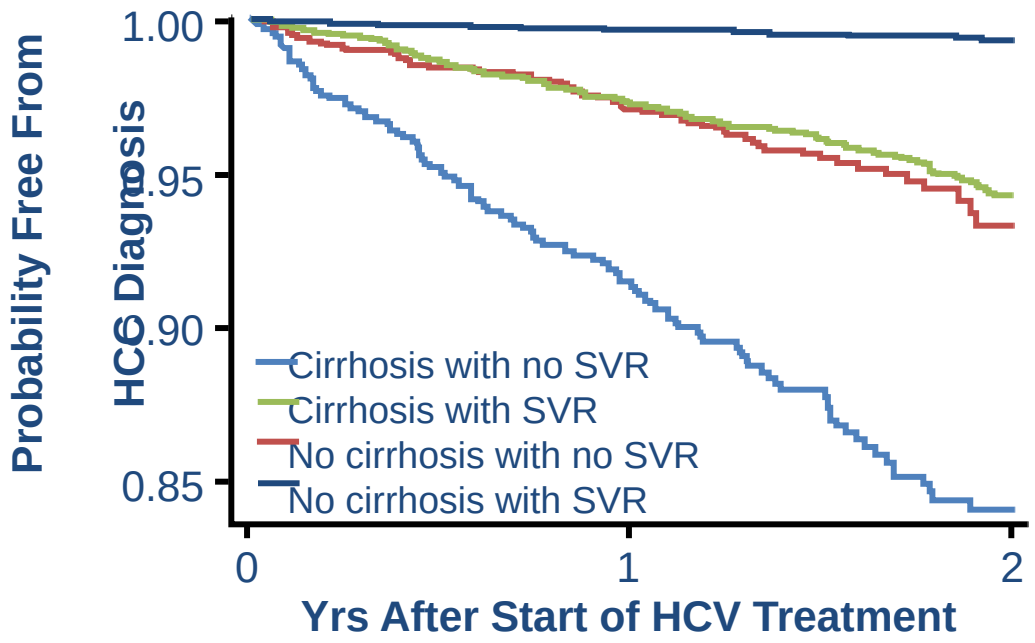
Survival in ERCHIVES Veterans (N = 13,940*†)[1]



DAA-induced SVR is associated with a 43% reduction in mortality

*For 18 mos of follow-up.
†BL cirrhosis: PrOD, 24.9%; LDV/SOF, 29.4%; untreated, 19.4%.

HCC Risk in DAA-Treated Veterans (n = 25,424‡)[2]



DAA-induced SVR is associated with a 71% reduction in HCC risk

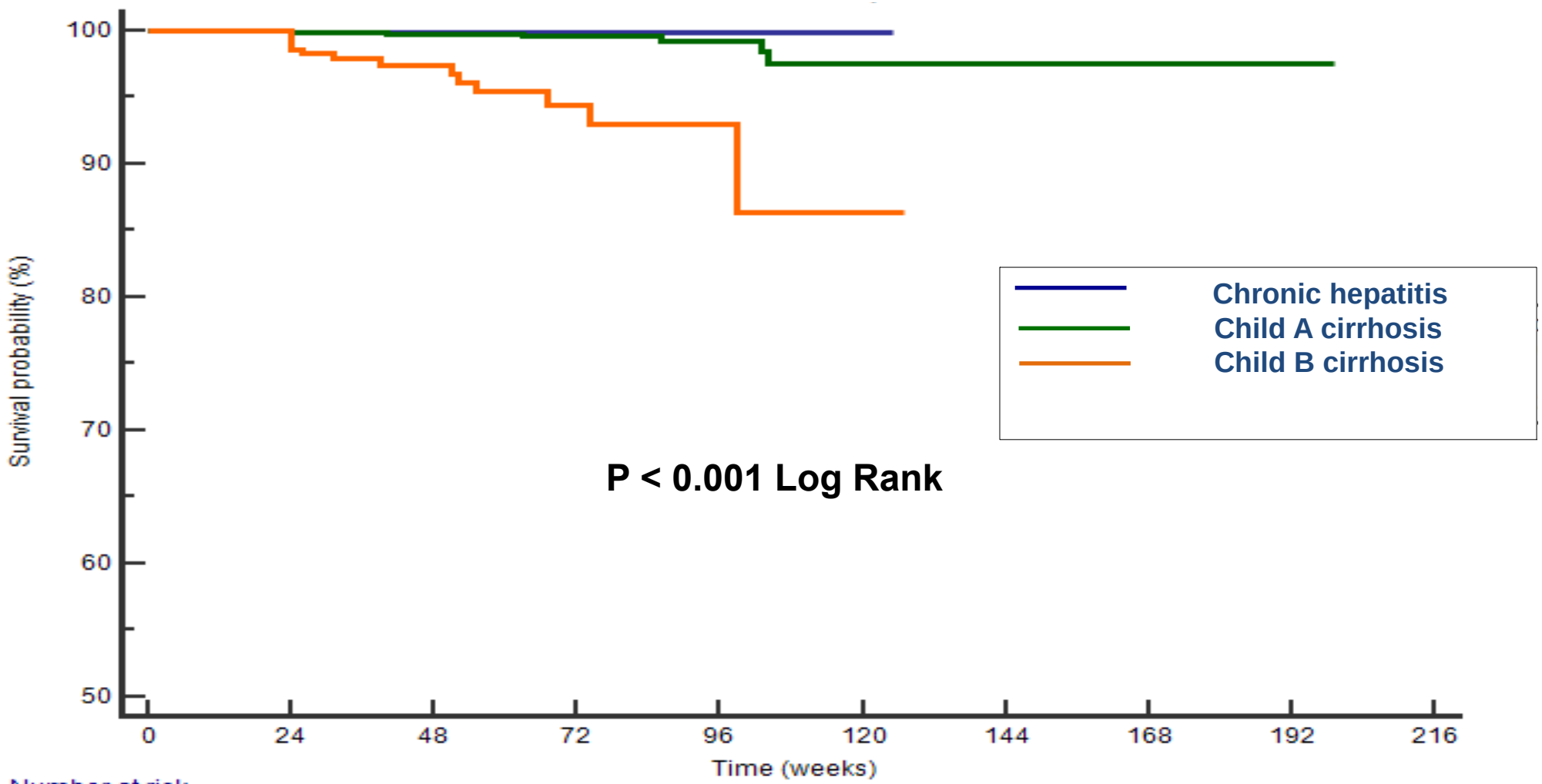
‡For 38,204 pt-yrs of follow-up.

1. Butt AA, et al. Clin Infect Dis. 2017:65:1006-1011.
2. Ioannou GN, et al. J Hepatol. 2017;[Epub ahead of print].

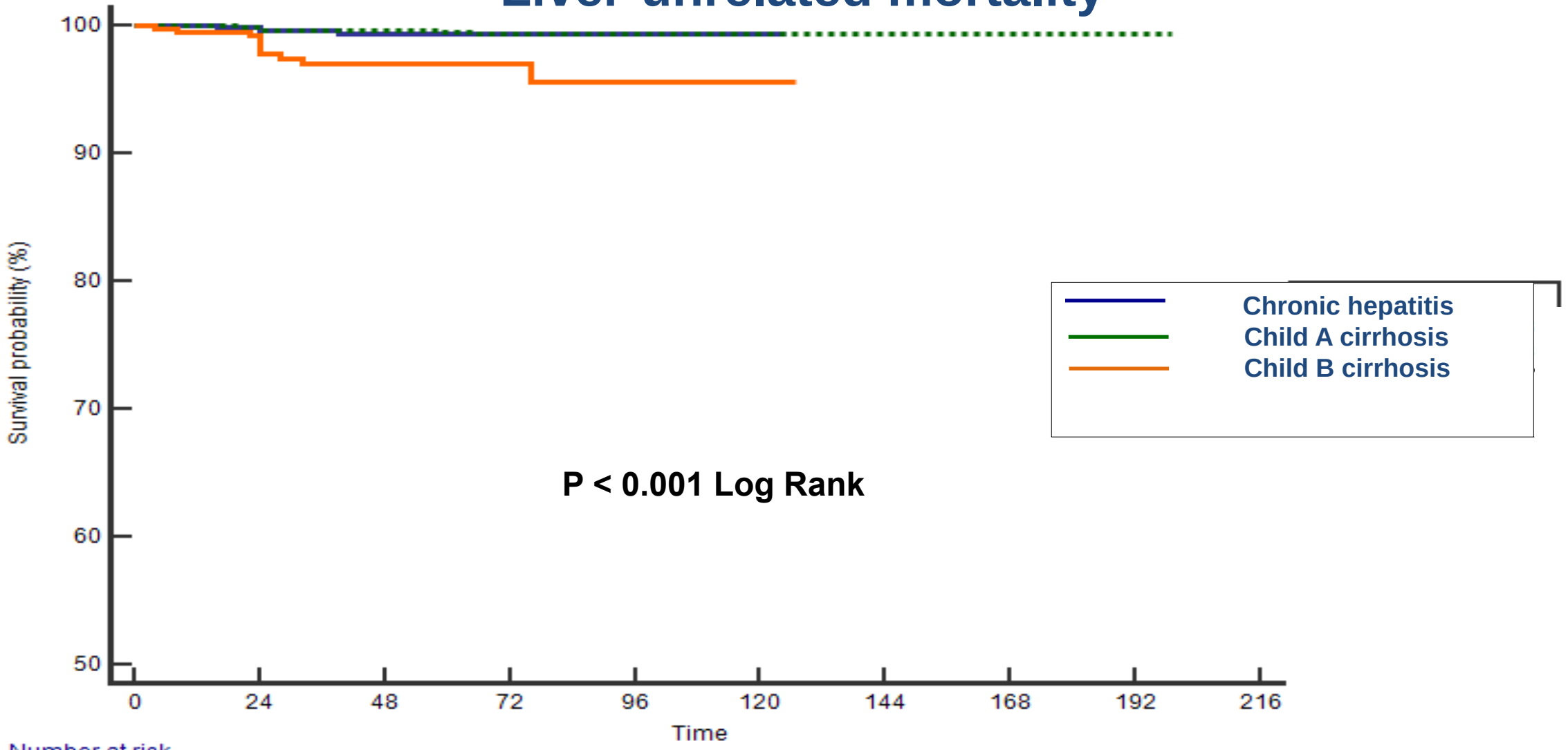
Features and outcomes of 4.147 patients included in RESIST-HCV cohort and treated with DAAs

	Mean age	Gender Males %	Liver Complication	SVR % 3766(90.8%)	Death	Liver related	Liver unrelated
Chronic hepatitis 934 (22.5%)	62.2 ±12.7	533(57.1)	0	834 (89.3)	6 (0.6)	1 (0.1)	5 (0.5)
Cirrhosis Child-Pugh A 2851 (68.7%)	66.8±10.9	1646(57.7)	95 (3.3%)	2643 (92.7)	24 (0.8)	10(0.4)	14(0.5)
Cirrhosis Child-Pugh B 362 (8.7%)	65.5±11.9	208(57.5)	50 (13.8%)	289 (79.8)	25 (6.9)	14(3.9)	11(3.0)
P	< 0.001	0.94	< 0.001	<0.001	<0.001	<0.001	<0.001

Liver-related mortality



Liver-unrelated mortality

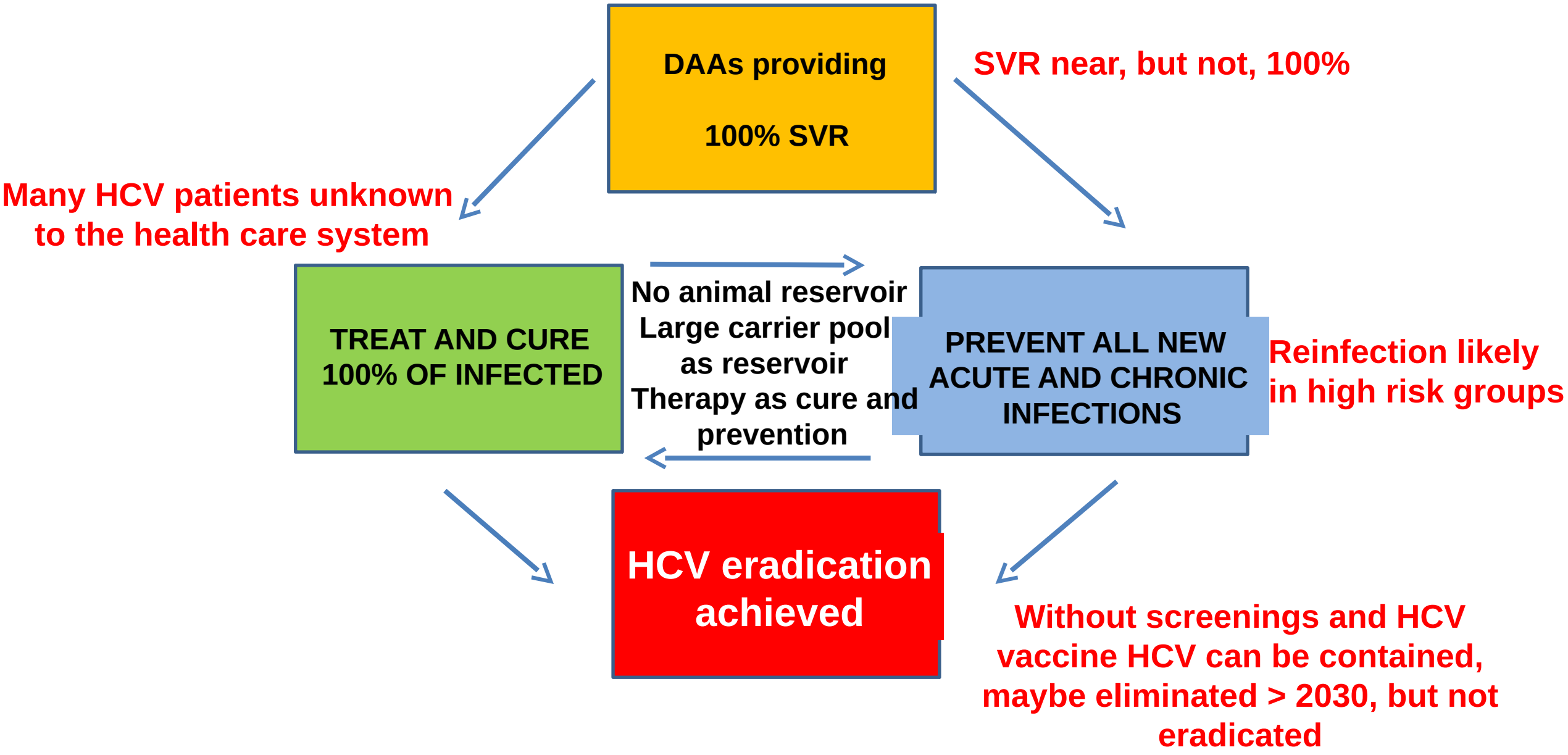


P < 0.001 Log Rank

Number at risk

Group: Chroni hepatiis									
934	760	361	123	25	3	0	0	0	0
Group: Child A cirrhosis									
2851	2513	1262	617	163	31	1	1	1	0
Group: Child B cirrhosis									
362	318	157	75	15	2	0	0	0	0

Disease Eradication vs Elimination vs Control



WHO: Elimination of HCV as a Public Health Threat

- Defined as achievement of measurable global targets in relation to infection and burden of disease
- Intensity of interventions required will vary by setting
  - Setting-specific model required to determine what is necessary to achieve the impact targets

- **2030 Targets**
  - **90% Diagnosed**
  - **80% Treated**
  - **65% Reduced Mortality**

WHO. Global health sector strategy on viral hepatitis 2016-2021. 2016.

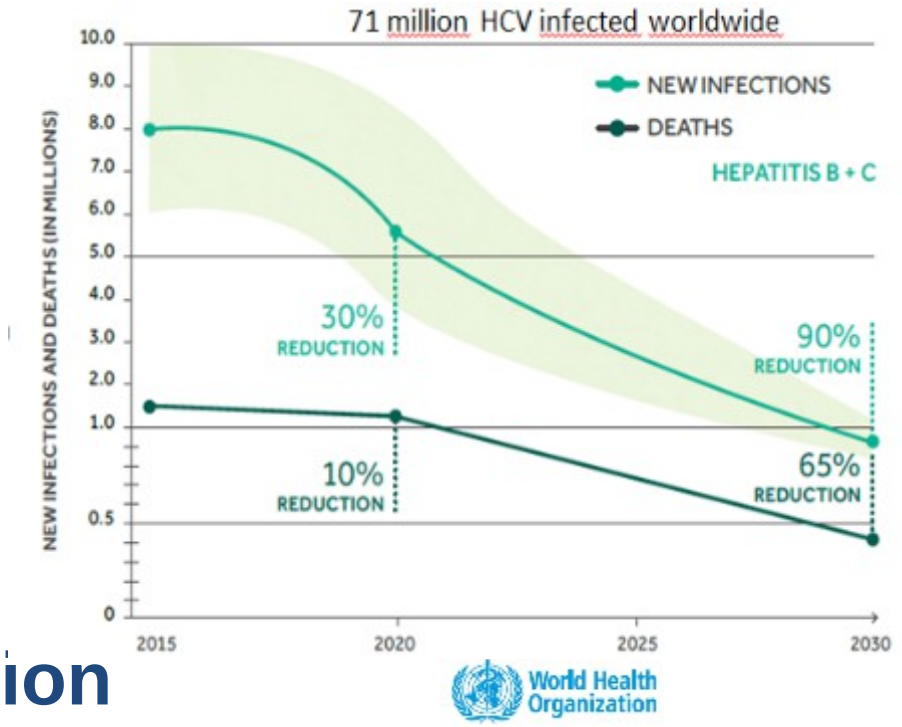
Treatment of chronic Hepatitis C: new horizons

n at individual level

ishing liver disease progression
ression of the hepatic damage
ucing liver and non-liver complications

n at community level

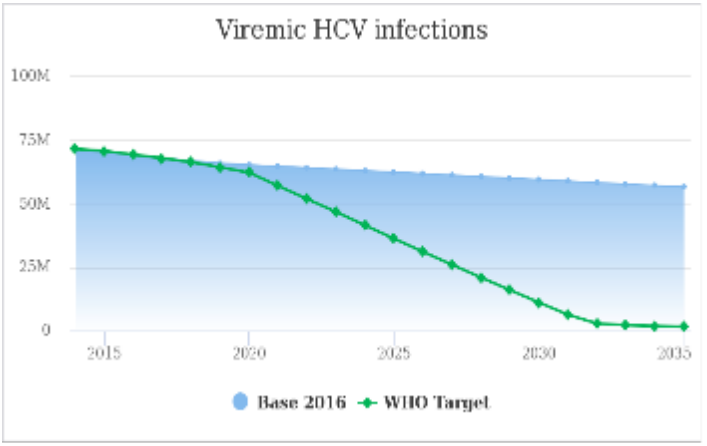
duce (abolish) the spread of HCV infection
duce direct and indirect costs

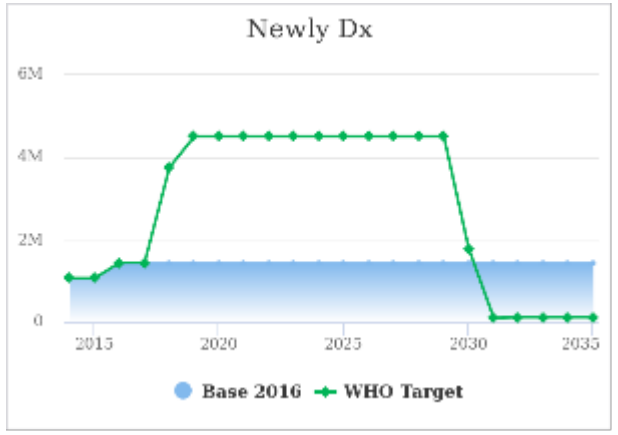


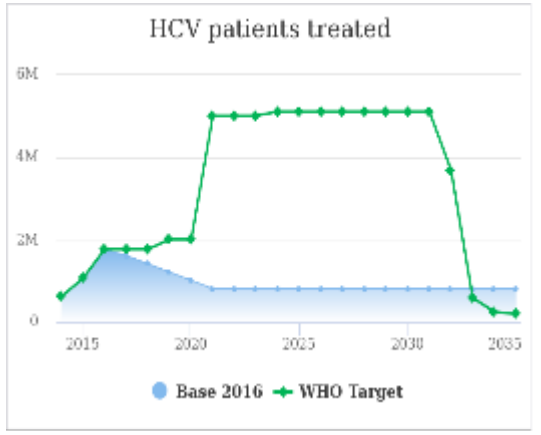
At individual level: treat infection/ liver disease

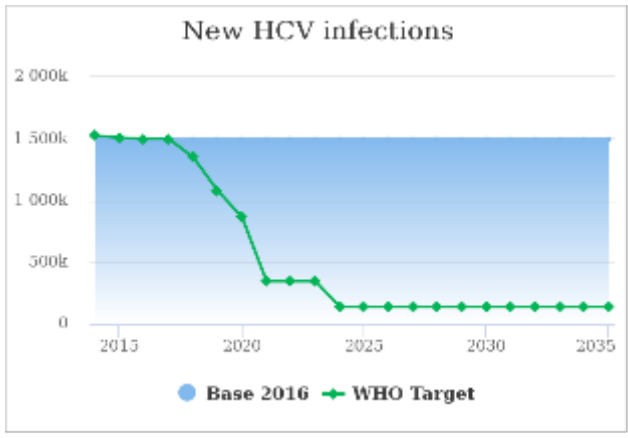
At community level: treating infection; those with high potential for transmission; reduce desease burden

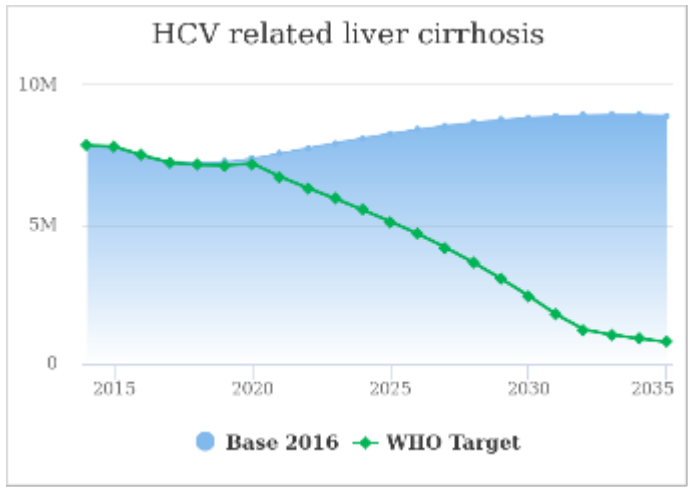
Current and future HCV global scenario

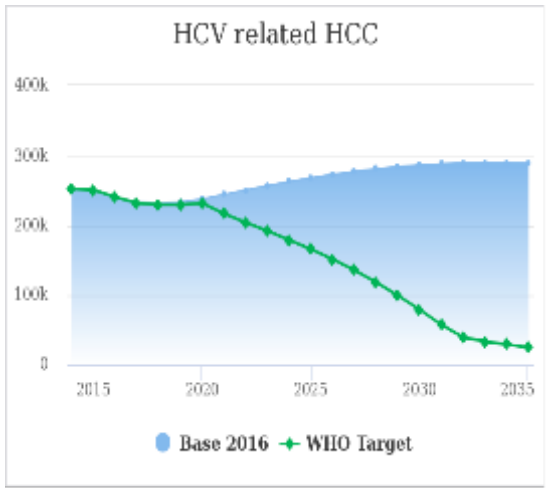


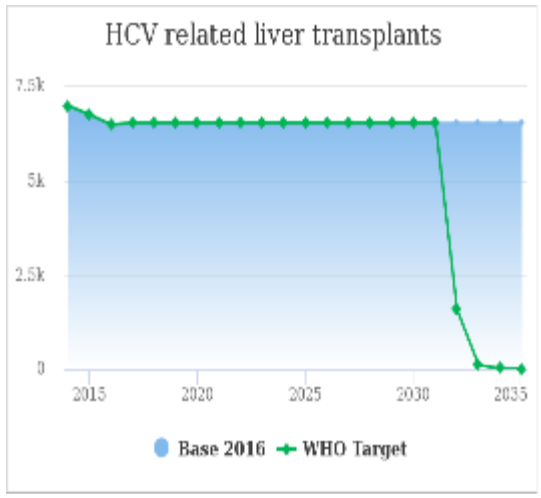


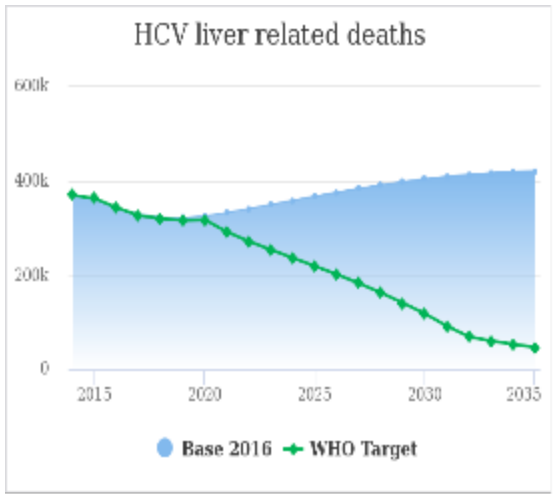












http://polarisobservatory.org/polaris_view/hepC.htm accessed Jan 11, 2018

Progress Toward HCV Elimination Goals by Countries

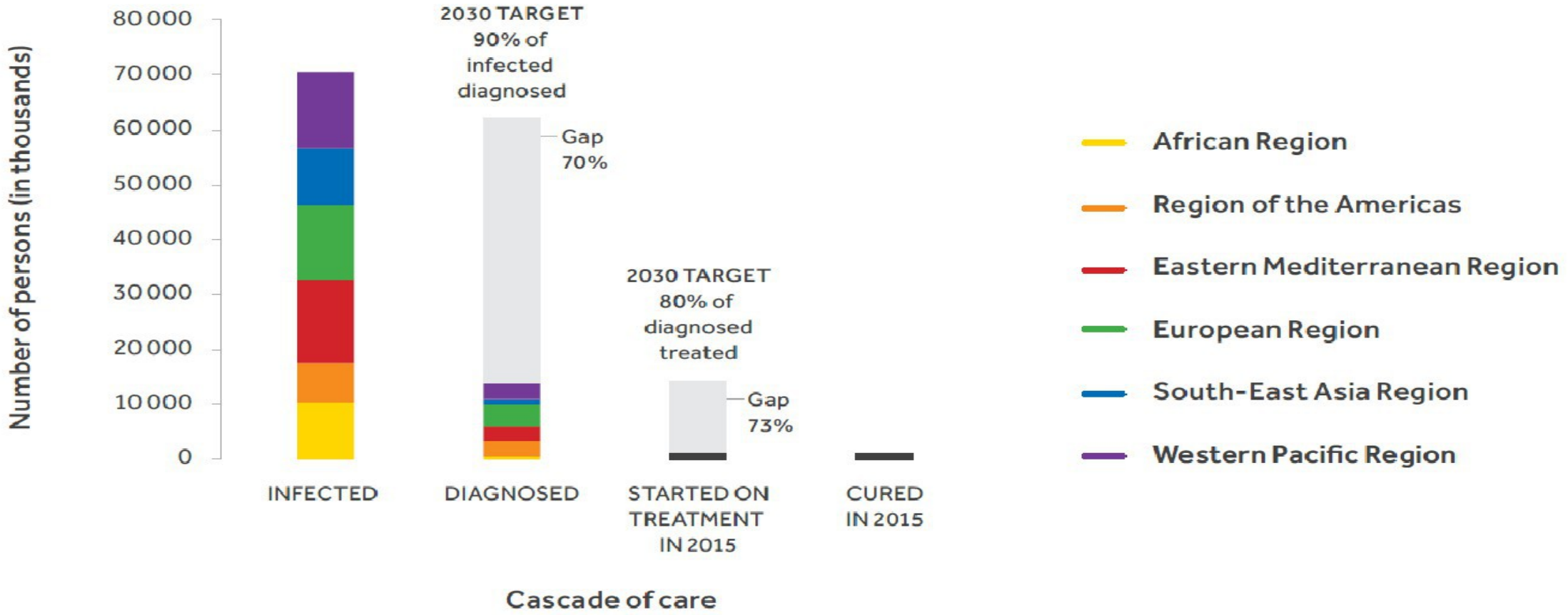
2016

On Track for WHO Elimination Targets	Working Towards Elimination	Elimination Unachievable Given Present Policy	
Iceland	United States	Ireland	Kyrgyzstan
Qatar	Spain	Hungary	Croatia
Australia	Austria	Saudi Arabia	Venezuela
Georgia	Sweden	Latvia	Kazakhstan
Japan	Malta	Morocco	Viet Nam
Netherlands	UK	Switzerland	Jordan
Egypt	Korea	Denmark	Bulgaria
France	Luxembourg	Pakistan	Argentina
Germany	Brazil	Hong Kong	UAE
	Mongolia	India	Ethiopia
	Norway	Chile	Cuba
	Estonia	Belgium	Burundi
	Portugal	Romania	Malaysia
	Canada	Israel	Colombia
	Lithuania	Czech Republic	Russia
	Lebanon	Finland	Azerbaijan
	New Zealand	Algeria	Philippines
	Italy	China	Mexico
	Slovenia	Oman	Cambodia
	Poland	Slovakia	Indonesia
	Iran	Tunisia	Panama
	Uzbekistan	Peru	Turkey
		Bahrain	El Salvador
		Puerto Rico	South Africa
		Greece	Nigeria
		Iraq	Afghanistan
		Papua New Guinea	Ghana
		Libya	Yemen
		Taiwan	Syria
		Cameroon	Madagascar
		Dominican Republic	Kenya
		Thailand	

On Track Working Towards

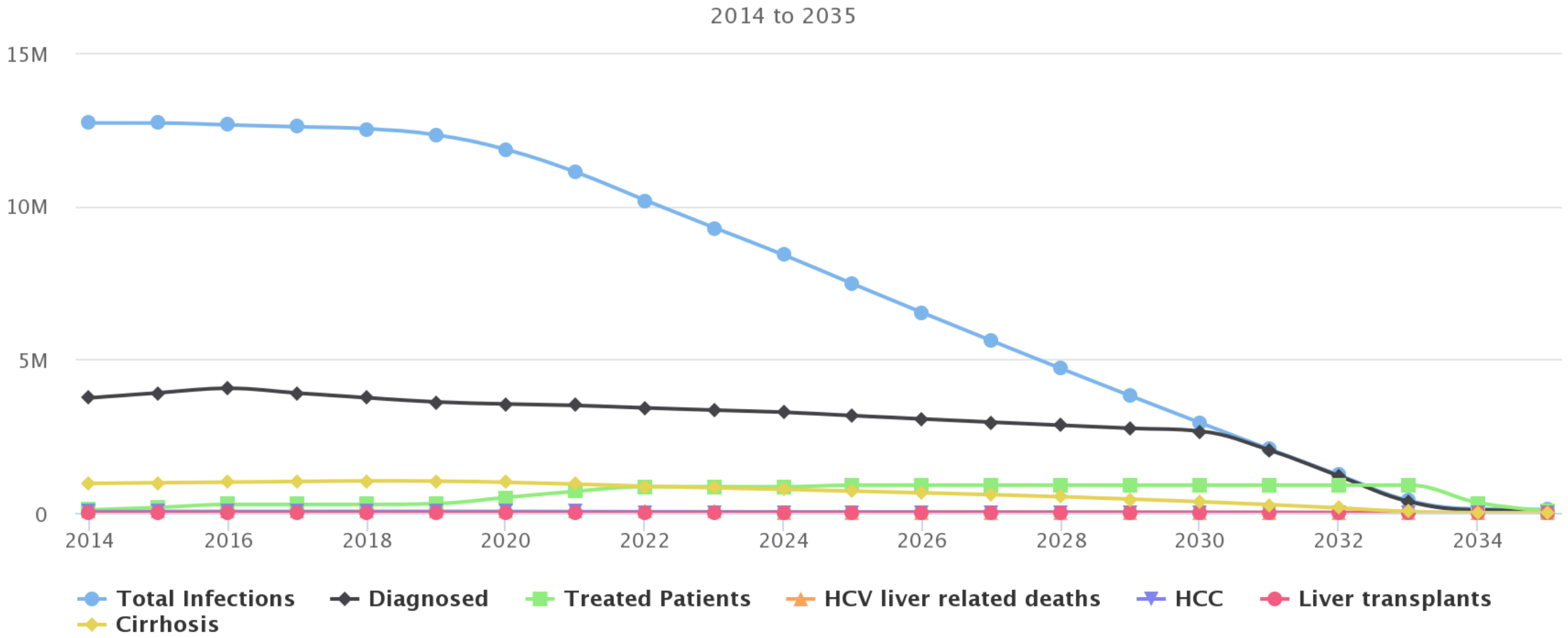
http://polarisobservatory.org/polaris_view/hepC.htm accessed Jan 11, 2018

Cascade of care for HCV infection, by WHO region, 2015



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

Current and future HCV scenario: Europe



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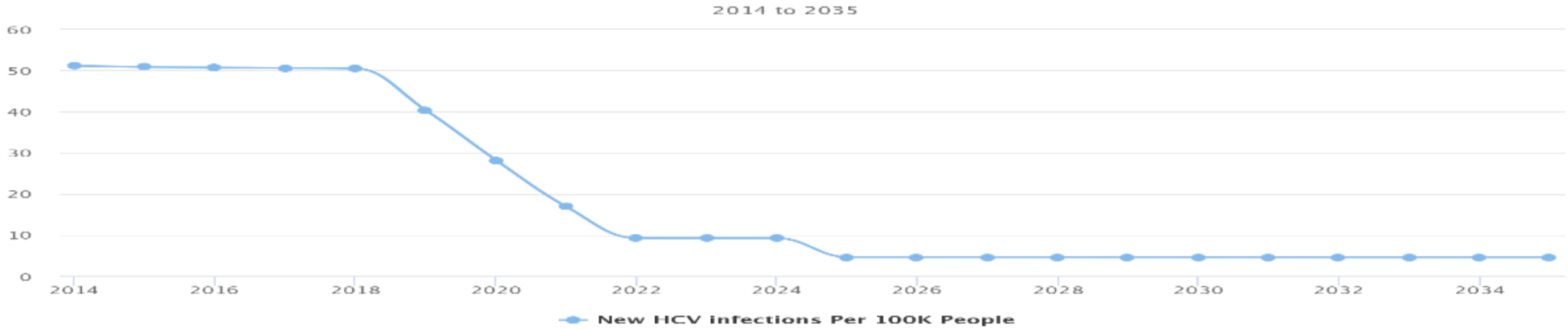
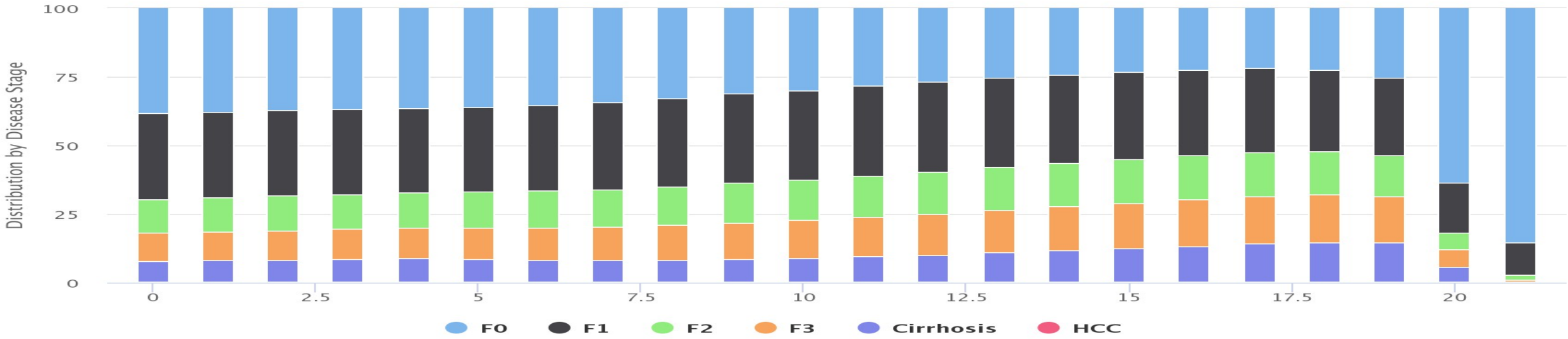
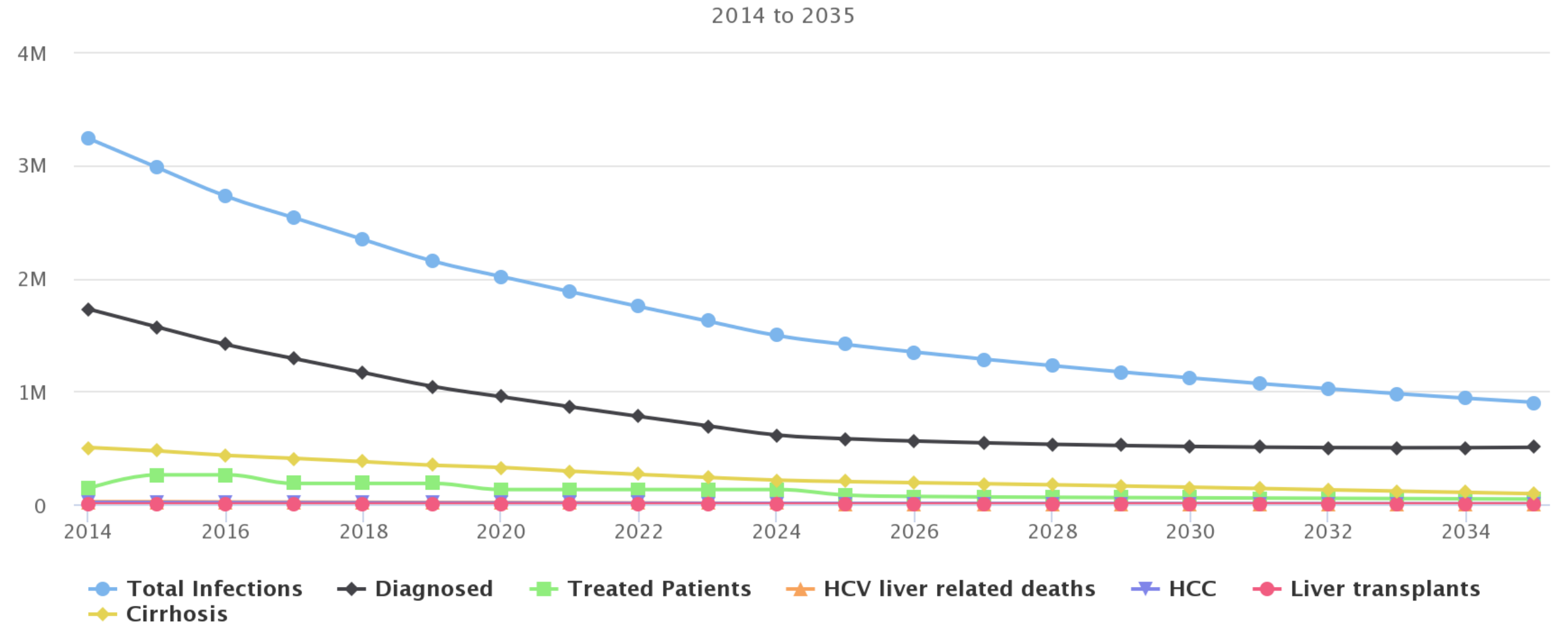
Current and future HCV scenario: Europe





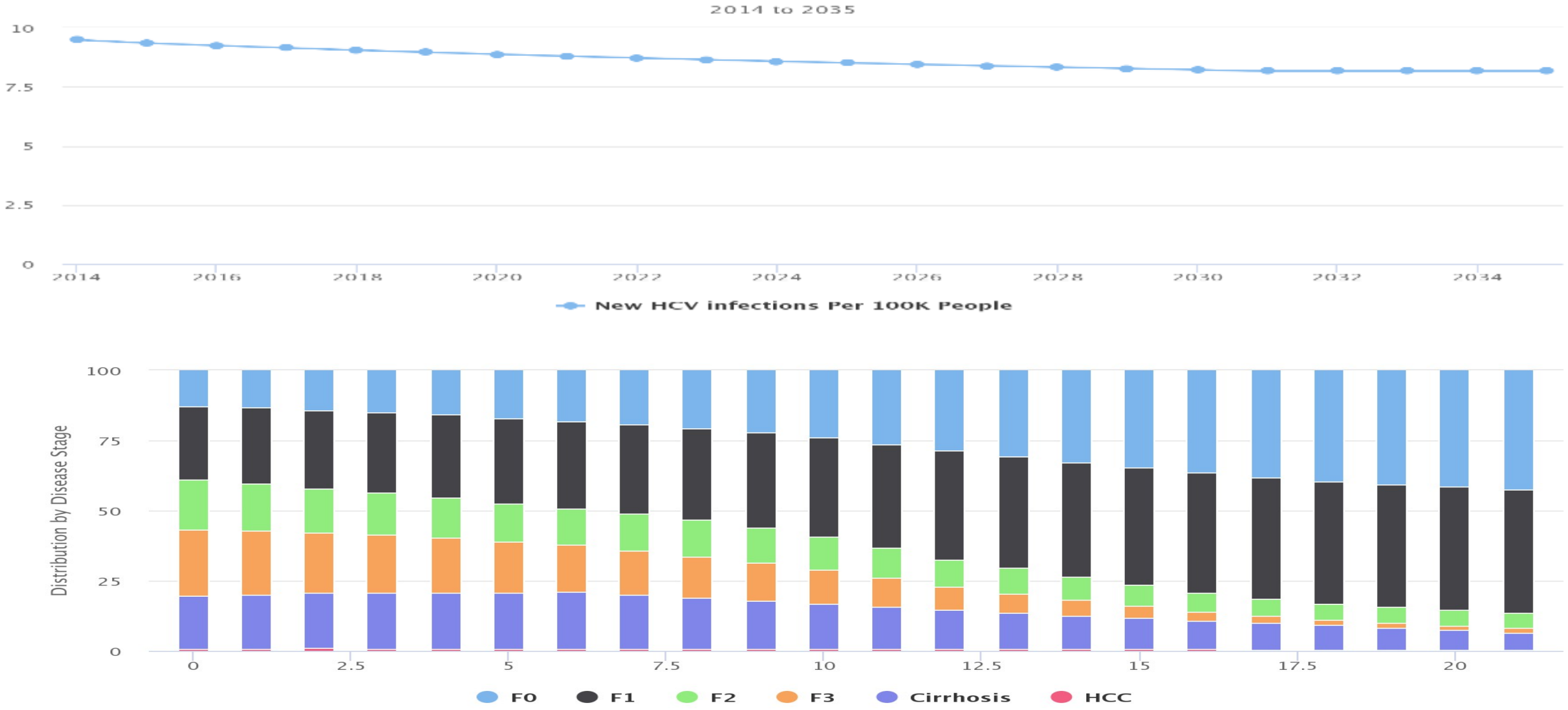
http://polarisobservatory.org/polaris_view/hepC.htm accessed Jan 11, 2018

Current and future HCV scenario: USA



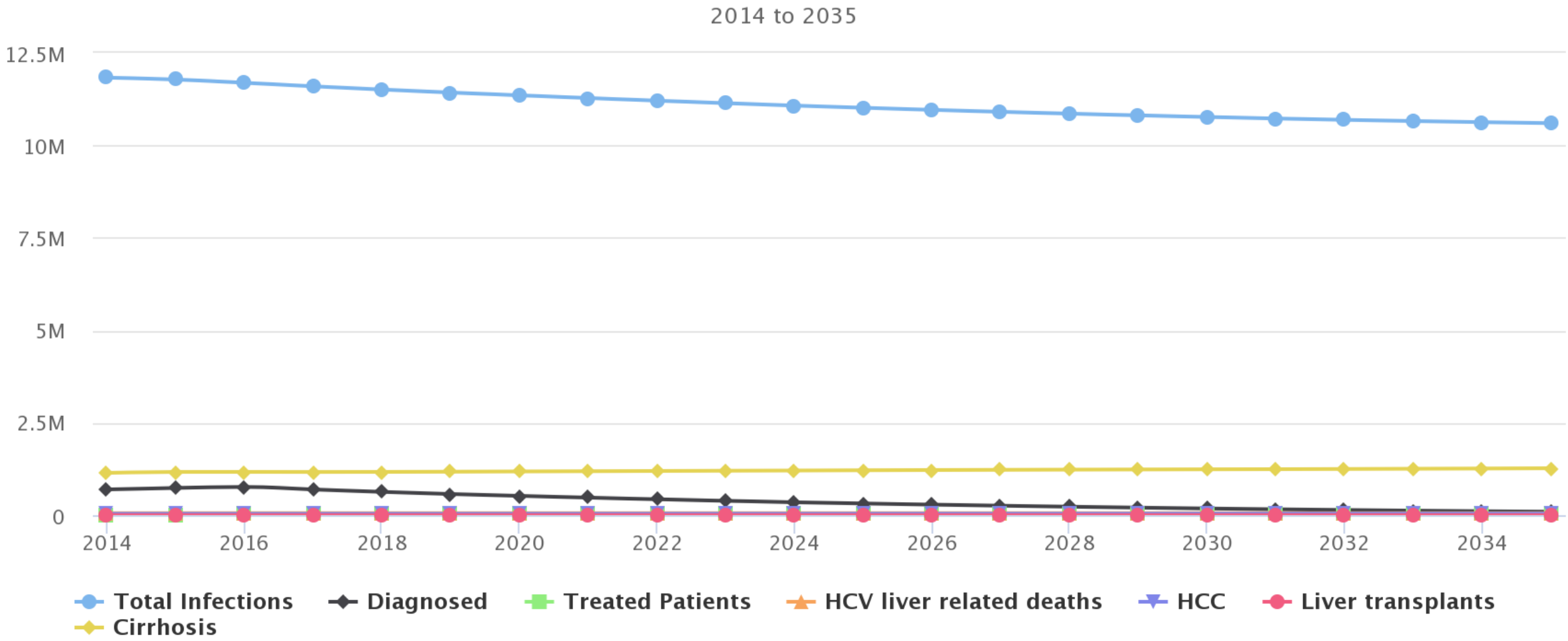
http://polarisobservatory.org/polaris_view/hepC.htm accessed Jan 11, 2018

Current and future HCV scenario: USA



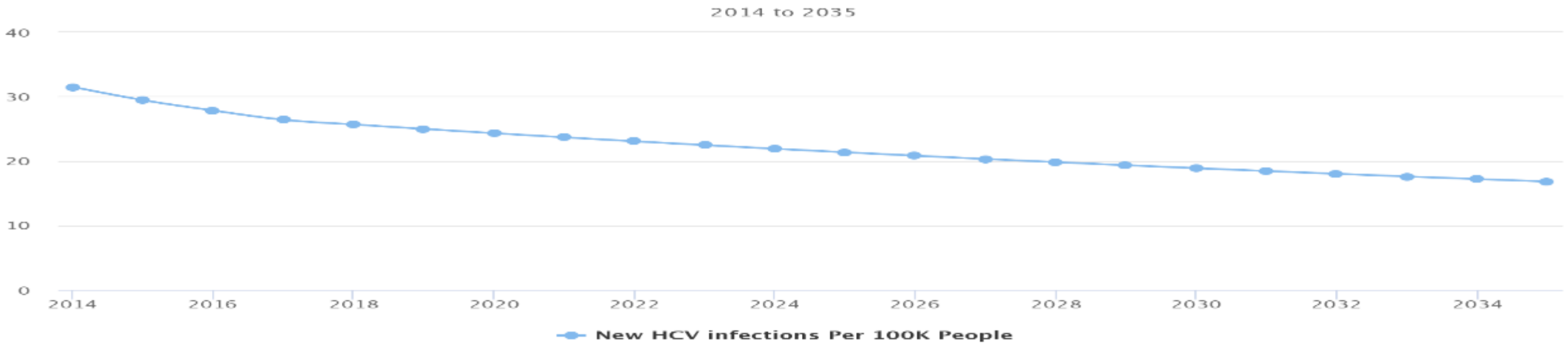
http://polarisobservatory.org/polaris_view/hepC.htm accessed Jan 11, 2018

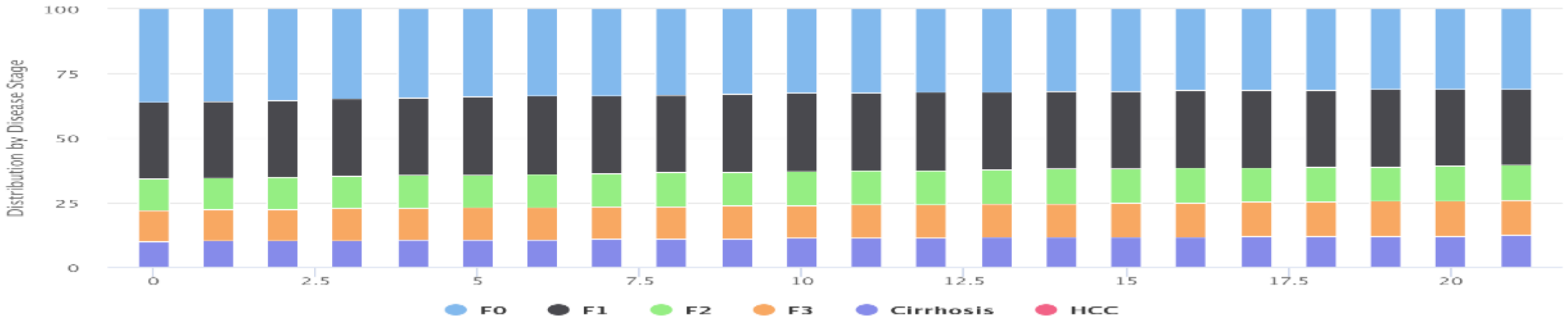
Current and future HCV scenario: Africa



http://polarisobservatory.org/polaris_view/hepC.htm accessed Jan 11, 2018

Current and future HCV scenario: Africa





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Disease Eradication vs Elimination vs Control

DAAs providing

100% SVR

SVR near, but not, 100%

DAAs make their job

Efficacy - >95%

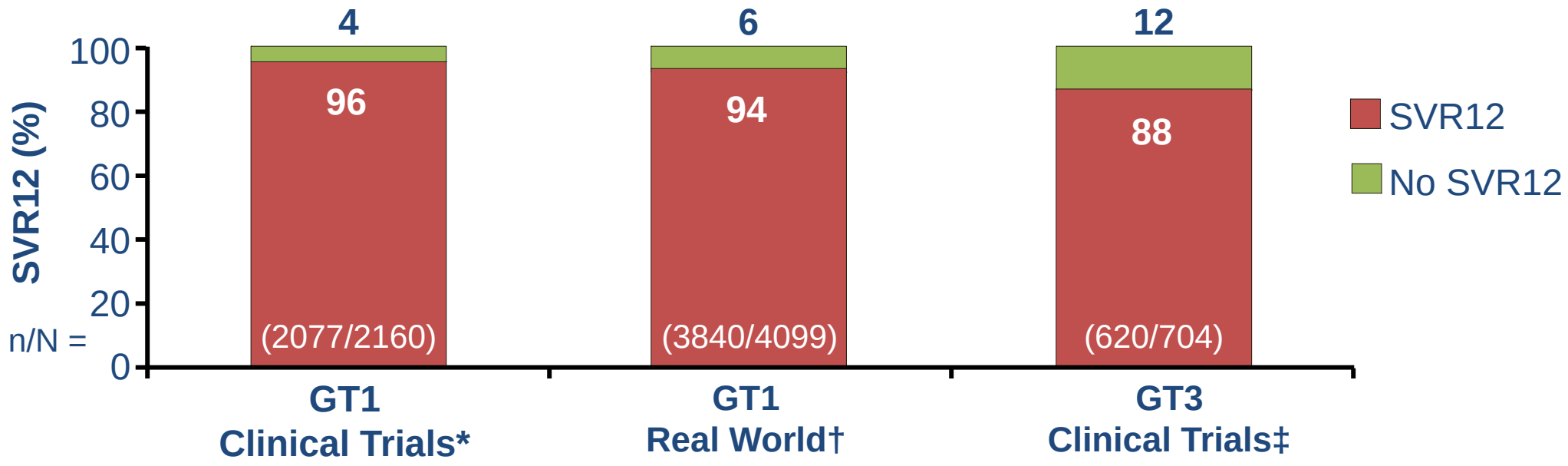
Safety – very few serious AE; low rates of discontinuati

Simplification

- **Short treatment duration**
- **Once daily dosing**
- **No baseline resistance testing**
- **No or minimal AEs**
- **Kidney friendly**
- **Pangenotypic**

Costs are decreasing and availability increasing

Failures mostly occur with 1st and 2nd wave DAA regimens (*but some also with 3rd wave….*)



*Clinical trials with GZR/EBR, PTV/RTV/OBV + DSB, SOF + DCV ± RBV, SOF/LDV, SOF + SIM ± RBV, SOF/VEL.[1-11]
†Data from the HCV TARGET study; pts treated with varied regimens that included ≥ 2 DAAs.[12]
‡Clinical trials with SOF + DCV, SOF + RBV, SOF/VEL.[13,14]

1. Kwo P, et al. Gastroenterology. 2017;152:164-175.
2. Ferenci P, et al. N Engl J Med. 2014;370:1983-1992.
3. Feld JJ, et al. J Hepatol. 2016;64:301-307.
4. Luetkemeyer AF, et al. Clin Infect Dis. 2016;62:1489-1496.
5. Afdhal N, et al. N Engl J Med. 2014;370:1889-1898.
6. Afdhal N, et al. N Engl J Med. 2014;370:1483-1493.
7. Kowdley KV, et al. N Engl J Med. 2014;370:1879-1888.
8. Kwo P, et al. Hepatology. 2016;64:370-380.
9. Lawitz E, et al. Lancet. 2014;384:1756-1765.
10. Feld JJ, et al. N Engl J Med. 2015;373:2599-2607.
11. Sulkowski MS, et al. EASL 2017. Abstract SAT-229.
12. Nelson DR, et al. Hepatology. 2015;61:1127-1135.
13. Foster GR, et al. N Engl J Med. 2015;373:2608-2617.

Decompensated Cirrhosis

- Treatment options are more limited than for pts without cirrhosis or with compensated cirrhosis
  - SVR rates are generally lower; treatment remains controversial
  - **Protease inhibitors are not recommended for CPT B or C**
- Continuing role for ribavirin, extended treatment duration
  - No options for **CPT B or C** patients with severe renal impairment

Regimen	Duration/RBV Inclusion	
	RBV Eligible	RBV Ineligible
SOF/VEL	**12 wks + RBV†**	**24 wks**

Initial RBV dose: 600 mg/day, increase as tolerated. †Weight-based RBV; low initial dose for CPT C.

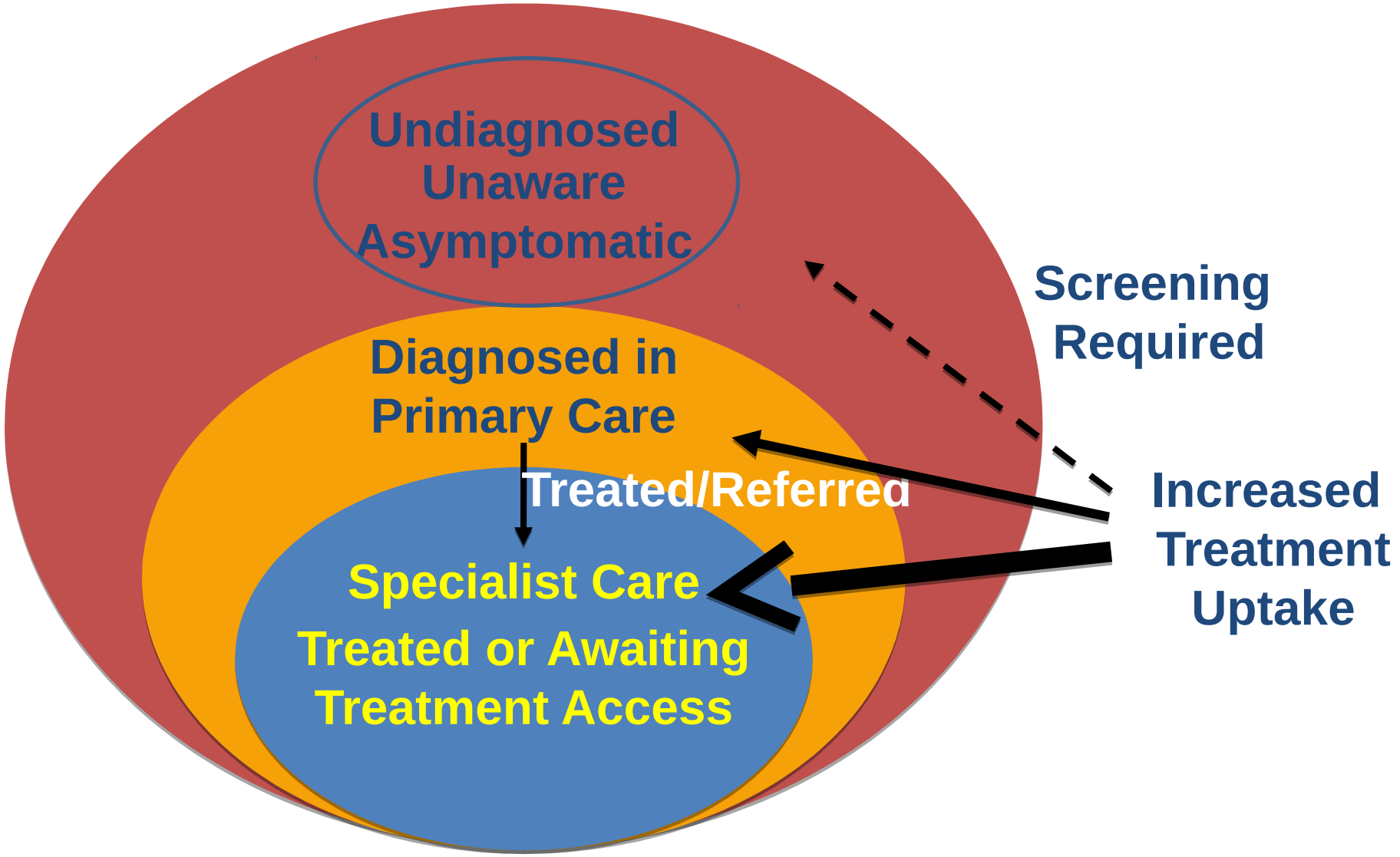
Third wave regimens not relevant in this setting

Disease Eradication vs Elimination vs Control

Many HCV patients unknown to the health care system

TREAT AND CURE 100% OF INFECTED

HCV Population



Screening Approaches

- **Risk-based**
  - Identify and test only those with risk factors
- **Pros:**
  - High yield
  - Cheaper
- **Cons:**
  - Contact with HC system
  - **Must k**now & discuss risk factors
  - Test **may be** stigmatized
  - **Miss those without RFs**

- **Population-based**
  - Test a segment of the population eg. baby boomers, immigrants
- **Pros:**
  - High coverage rate
  - Easy to implement
- **Cons:**
  - Need to choose the pop'n
  - Low yield, expensive
  - May be stigmatizing to pop'n – eg. immigrants

Not mutually exclusive

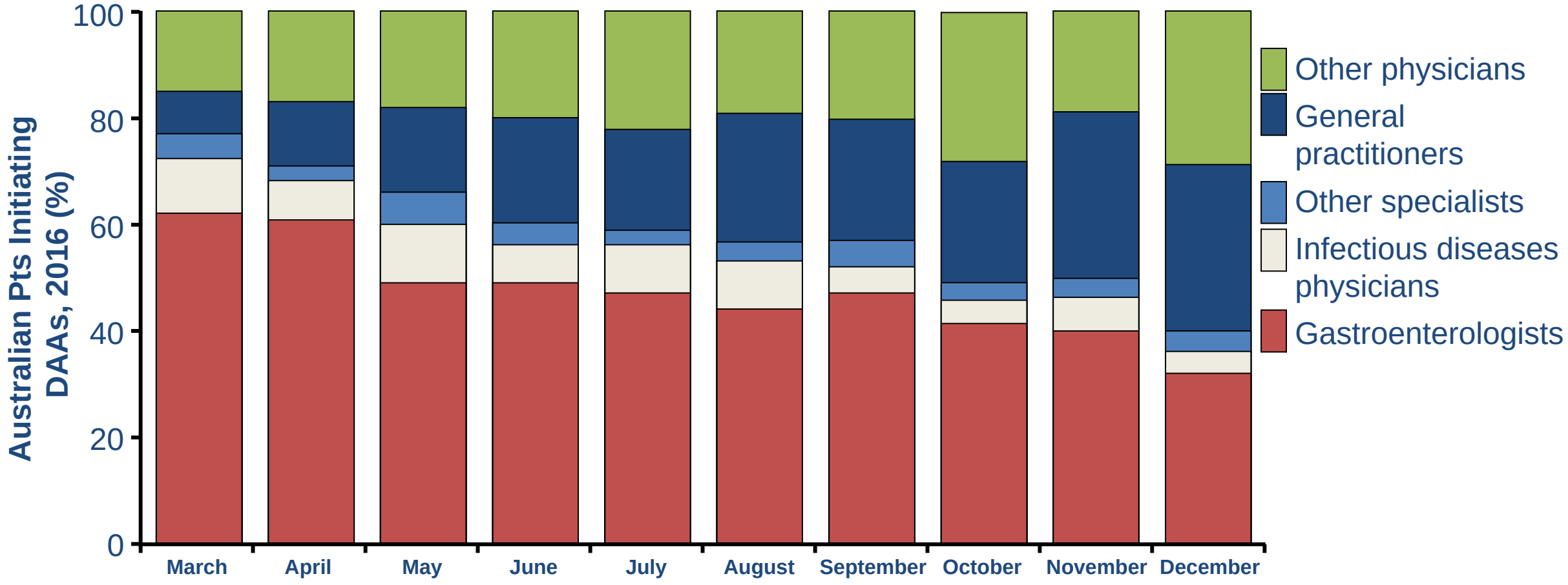
Improving screening - New technologies

Saliva or blood rapid antibody test

Point-of-care PCR test

Dried Blood Spot

Nonspecialists Can Effectively Treat HCV



Dore G - Kirby Institute 2017 (http://kirby.unsw.edu.au/research-programs/vhcrp-newsletters)

The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia (Issue 7). Available at: https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-7-july-2017.

Cirrhosis Determination Feasible in Primary Care

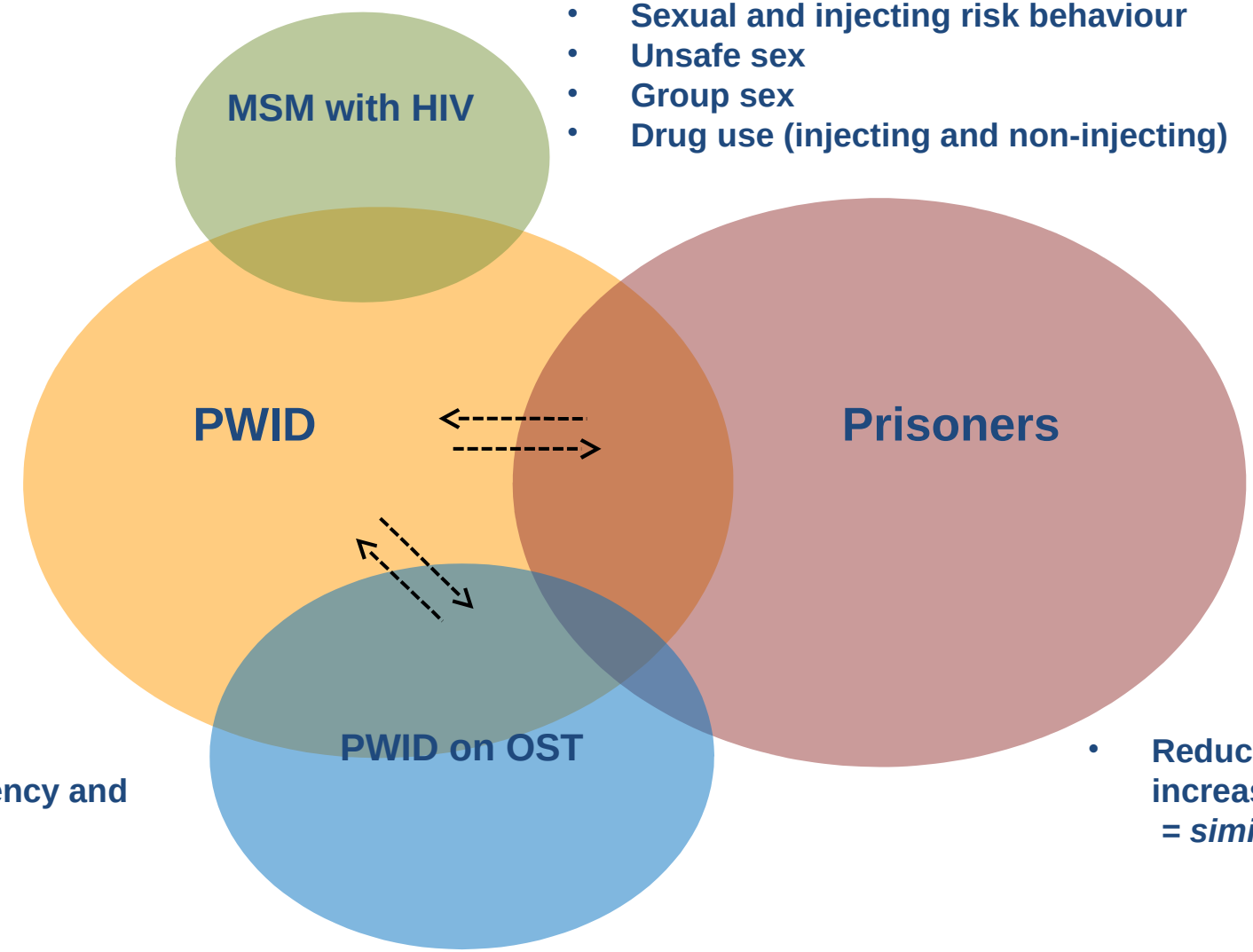
- AAR (AST/ALT ratio):
  - AST/ALT
- APRI (AST platelet ratio index) score:
  - (AST/upper limit of normal)/platelet count (expressed as platelets x 109/L) x 100
- Modified APRI score:
  - [Age (yr) x (AST/upper limit of normal)]/ [serum albumin (g/dL) x platelet count (expressed as platelets x 109/L) x 100]
- FIB-4:
  - Age (yr) x AST (IU/L)/[platelet count (x 109/L) x √ALT (IU/L)]

Critical to assess for advanced fibrosis or cirrhosis

- **I**nforms when specialist referral needed
- **Indicates n**eed for post-SVR HCC monitoring
- Affects HCV regimen selection

High risk populations for HCV

- Younger age
- Female gender
- Injecting frequency
- Needle sharing
- Lack of NSP
- Lack of OST
- Public injecting

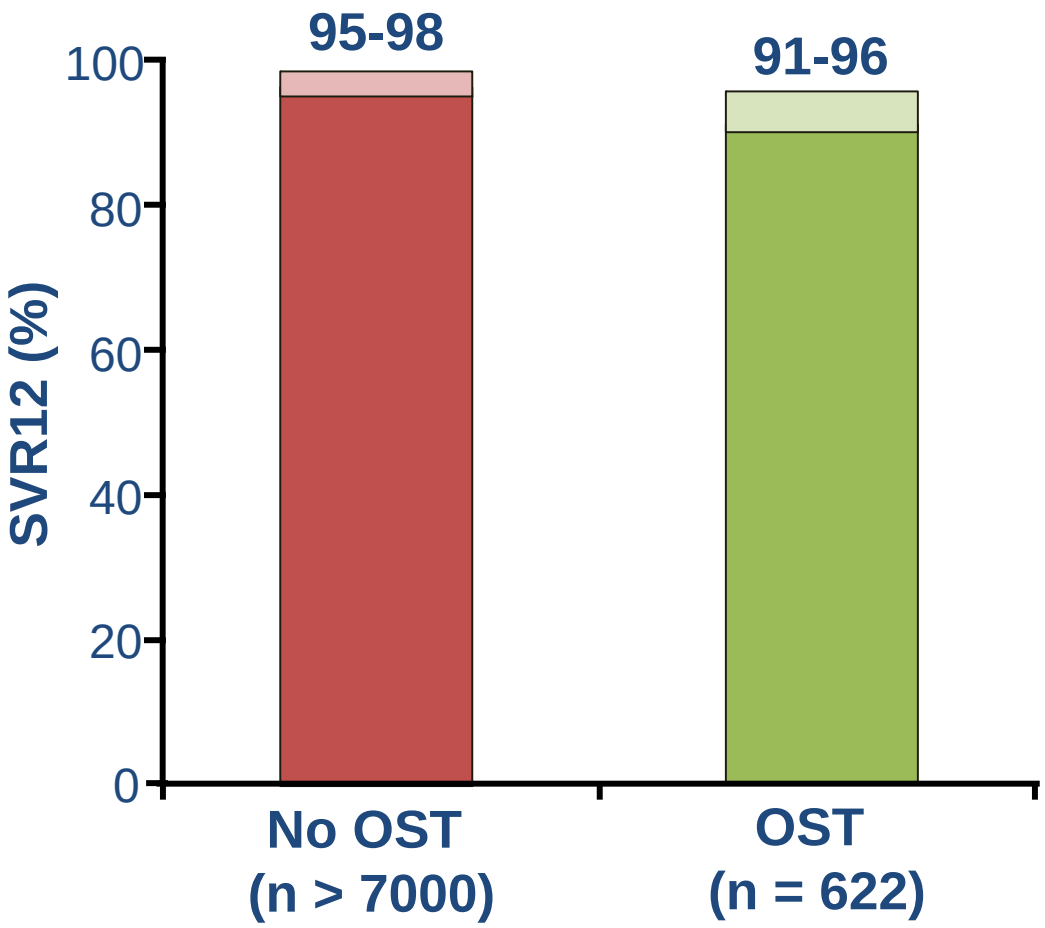


- Sexual and injecting risk behaviour
- Unsafe sex
- Group sex
- Drug use (injecting and non-injecting)

- Reduced inj. frequency and reduced sharing
  = *reduced risk*

- Reduced inj. frequency but increased sharing
  = *similar risk*

HCV DAA Therapy Highly Effective in PWIDs



SVR12 rates also > 90% among pts with current/recent IDU

- 90.4% in C-EDGE CO-STAR (n = 136)
- 94% in SIMPLIFY (n = 102)
- 98% in pooled analysis from 6 phase III trials (mITT; n = 63)

1. Feld JJ, et al. N Engl J Med. 2014;370:1594-1603.
2. Puoti M, et al. AASLD 2014. Abstract 1938.
3. Grebely J, et al. EASL 2017. Abstract FRI-236.
4. Grebely J, et al. Clin Infect Dis. 2016;63:1405-1411.
5. Grebely J, et al. Clin Infect Dis. 2016;63:1479-1481.
6. Zeuzem S, et al. Ann Intern Med. 2015;163:1-13.

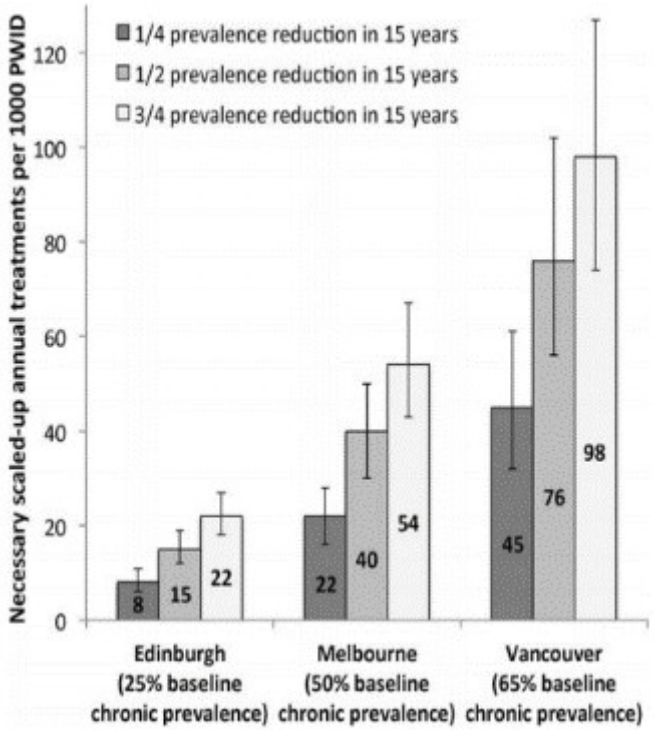
Hard-to-reach groups are also high transmitters of HCV

Key GROUPS

- Prisoners
- MSM
- PWID
- Sex workers
- Migrants

Treatment reluctants

Dedicated screening programs
Counseling
Link to care



Modest rates of HCV treatment among active injecting drug users could effectively reduce transmission

Martin NK, Hepatology 2013; 58:1598-1609

HIV/HCV co-infection in The Netherlands – the outcomes

Patients in care
(N=1420)

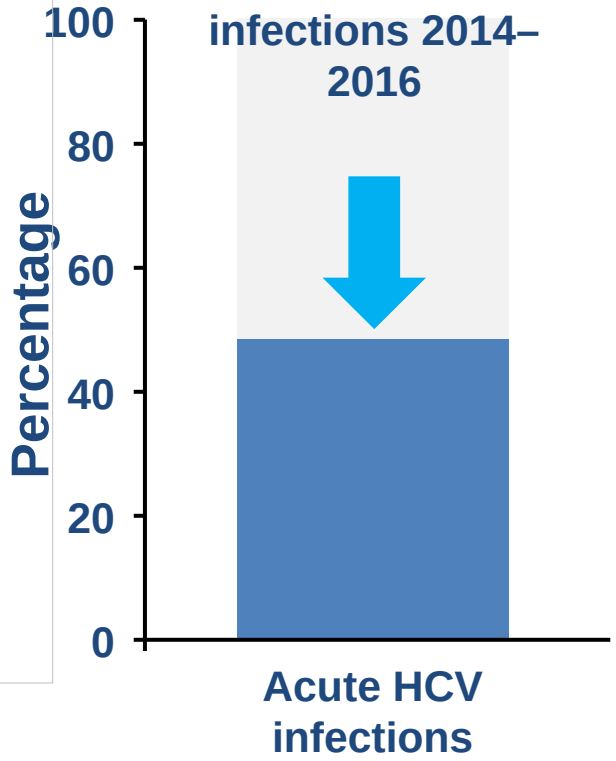
Failed DAA 1%

Treatment ongoing 3%

cured 66%

2/3 of the known HIV/HCV co-infected population have now been cured

51% decrease in acute HCV infections 2014–2016



Treatment as prevention appears effective

- Boerekamps A, et al. CROI 2016; Oral #136; Rijnders B, et al. CROI 2016 Oral #137LB

Road to Cure is Long for People Who Inject Drugs and Prisoners

- ~8,000,000 of 16 million PWID infected
  - 48-92% prevalence
- 1,546,500 of 10 million prisoners infected
  - E. Europe and Central Asia ~20.2%
  - USA and W. Europe ~15.4%
  - ”Able” to test and treat*

***WHO recommendation**

Dolan Lancet 2016; Luhmann Int J Drug Pol 2015

Disease Eradication vs Elimination vs Control

PREVENT ALL NEW ACUTE AND CHRONIC INFECTIONS

Reinfection likely in high risk groups

The 'Anna Karenina principle'

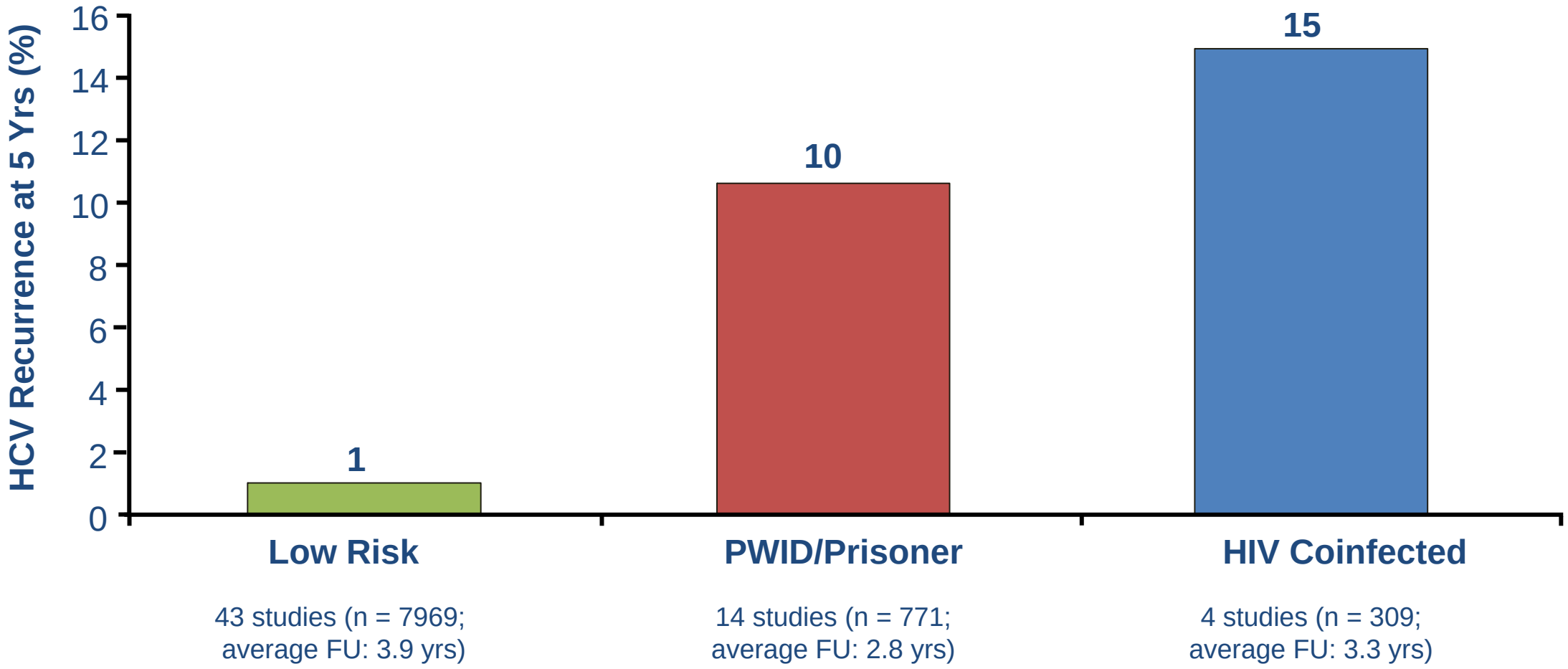
“All happy families look alike; each unhappy family is unhappy in its own way”

Patients with chronic HCV present patterns consistent with Anna Karenina effect

<u>Treated or on treatment</u>
They all showed willingness to be treated, link to care, adherence to treatments

<u>Difficult-to-treat</u>
Heterogeneous group, with poor willingness to be treated and difficult link to care

HCV Reinfection Over 5 Yrs by Study Population



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

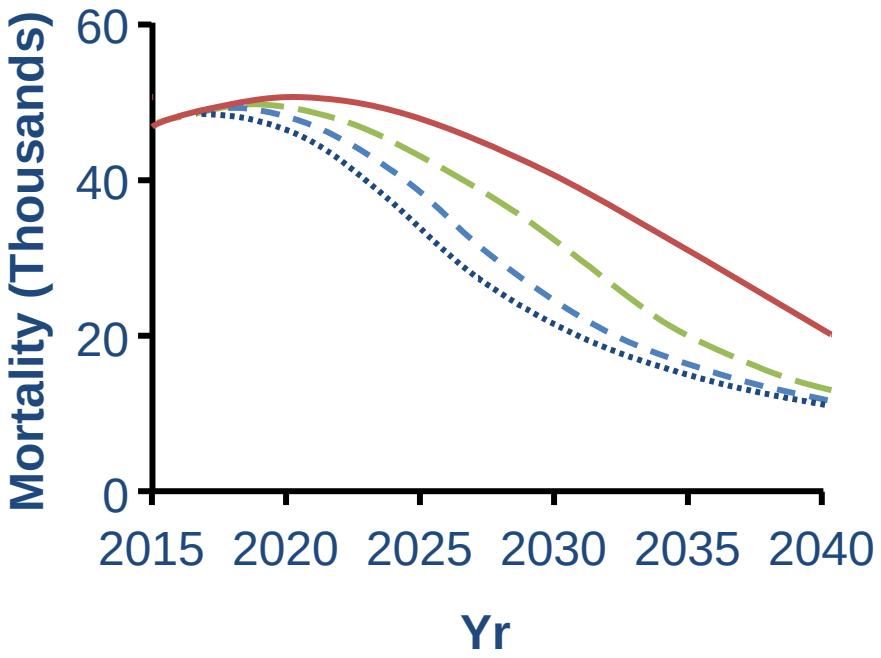
AA polymorphisms and RASs* in 5 patients with acute hepatitis C

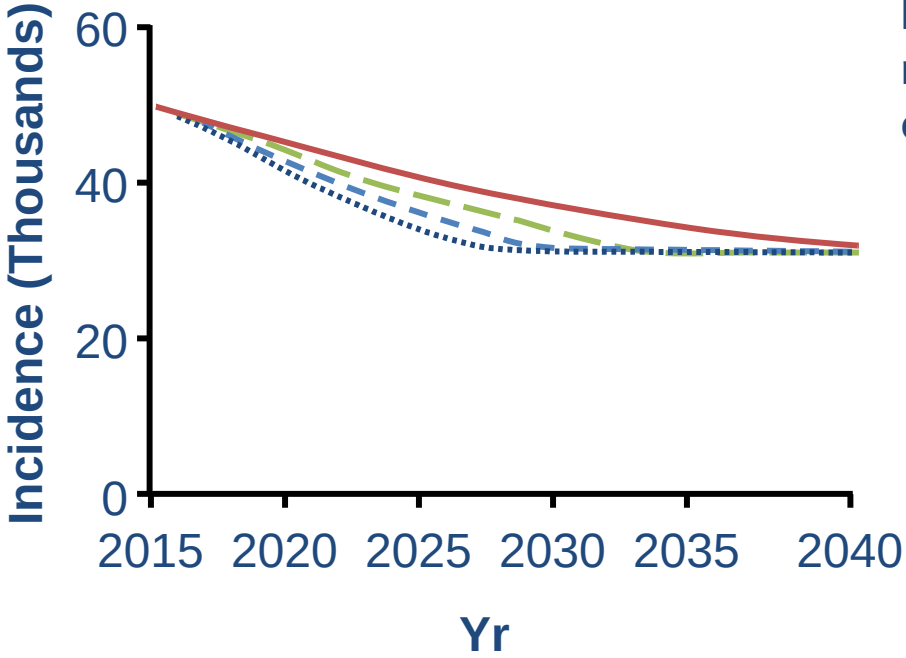
Brancaccio et al.Clin Gastroent Hepatol. In press

		CORE	NS3		NS5A		NS5B	
Pts	SOF/LDV treatment	Natural polymorphisms	RASs	Natural polymorphisms	RASs	Natural polymorphisms	RASs	Natural polymorphisms
Clustered patients								
1	12 weeks	T75A*, T110N*	S122T	S7A, L14F, S61A, T72TI, D103ND, R118RW (1-181aa)	None	G2DG, K6R, S17T, L34V, L37F, T83M, V138I, V164A, V174T, A197T, del-225(1-447aa)	V321I	T19S, L31IV, L36M, L47Q, N117R, R120N, T130N, T132S, F162Y, G198K, E202D, A207T, A210S, A218S, N231S, A300S, E333A, K355Q, Q464E, V499T, R510K, S549G, del-571 (1-592aa)
2	8 weeks	T75A*, T110N*	S122T	S7A, V48I, S61A(1-181aa)	A92T	K6R, S17T, L34V, L37F, T56TI,T83M, T135A, V138I, V164A, V174T, del-187 (1-447aa)	V321I	A16TA, T19S, L36M, L47Q, R98K, N117R, R120N, , T130N, E131EG, T132S, F162Y, G198K, E202D, A207T, A210S, A218S, N231S, C242S, A300S, E333A, K355Q, K441Q, Q464E, V499T, R510K, S549G, del-570 (1-592aa)
3	12 weeks	T75A*, L97LF, T110N*	S122T	S7A, L14F, S61A(1-181aa)	Y93H	K6R, S17T, L34V, L37F, T55TA, T83M, P89PL, H128HY, V138I, V164A, V174T, A197T, del-207 (1-447aa)	V321I	T19S, L36M, L47Q, N117R, R120N, T130N, T132S, G198K, E202D, A207T, A210S, A218S, N231S, A300T, E333A, K355Q, E437KE, Q464E, V499T, R510K, Q514R, S549G, del-580 (1-592aa)
4	8 weeks	T75A*, T110N*	S122T	S7A, L13LF, L14F, S42SF, S61A, S93SF, S133SF(1-181aa)	None	K6R, S17T, L37F,T83M, V138I, V174T, A197T, del-229 (1-447aa)	V321I	A16T, T19S, L36M, L47Q, R98K, N117R, R120N, T130N, T132S, F162Y, T181N, G189K, E202D, A207T, A210S, A218S, N231S, A300S, G328EG, E333A, K335Q, K441Q, Q464E, V499T, R510K, S549G, W574L, L588S, del-589 (1-592aa)
Out cluster patient								
6	12 weeks	K67R, R70Q*, T75A*, L178LF	Y56F	I18V, V48I, I71TI, A87S, A150V, V132I, V170I (1-181aa)	P58PL	K6R, S17T, L37F, K44R,M133I, V164A, K166R, V174T, del-222 (1-447aa)	None	T19S, L31IV, L36M, L47Q, K81KR, V116I, R120N, K124E, E131V, F162Y, A210S, K212KR, N231S, R254KR, A300S, E333A, A338V, K355Q, I412IM, Q461L, R510K, T520N, Q544R, S549G, R566P, del-580 (1-592aa)

Modeling: HCV Elimination in US Requires Enhanced Screening of High-Risk Populations

- Mortality reduction possible with treatment scale-up alone
- Incidence reduction requires **both** treatment scale-up and increased screening



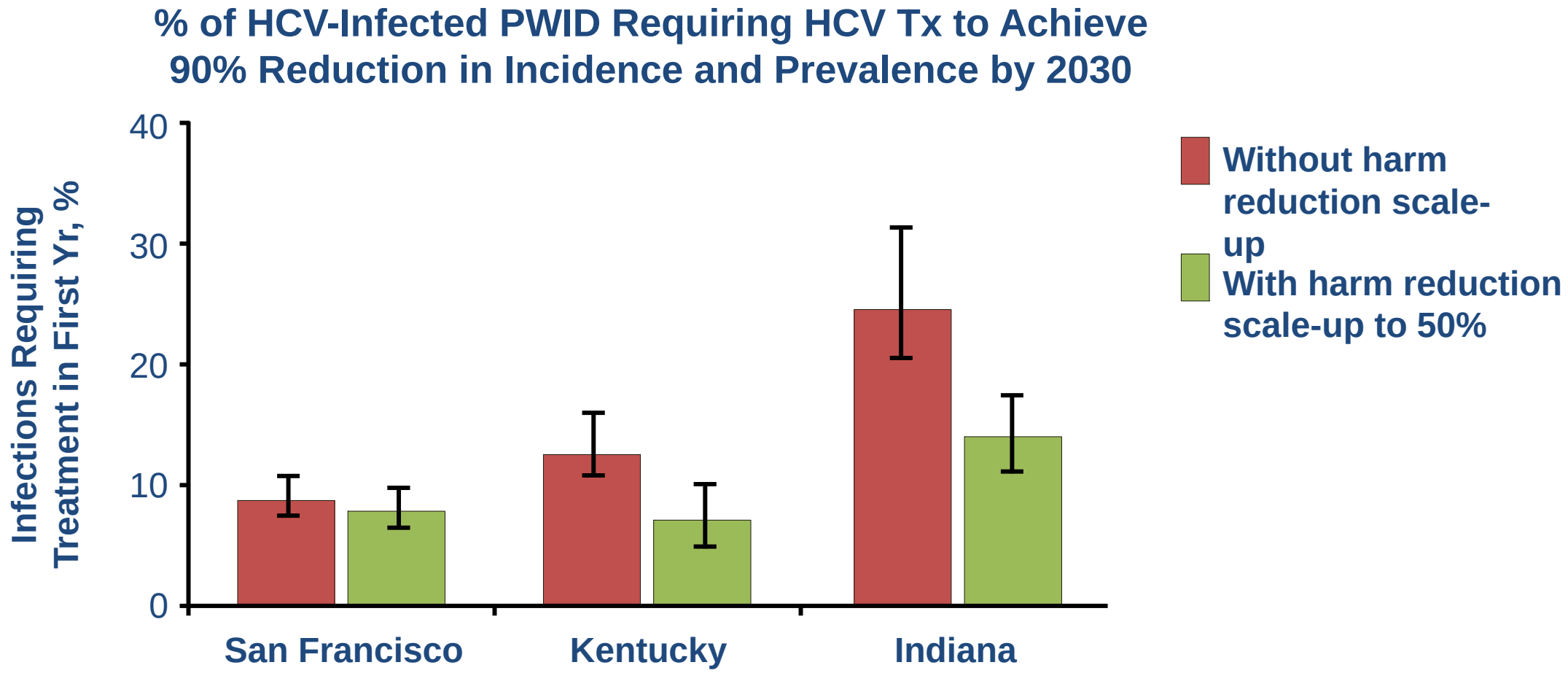


Estimates according to national treatment rates of noninjecting population

- **100,000 pts/yr**
- **200,000 pts/yr**
- **300,000 pts/yr**
- **400,000 pts/yr**

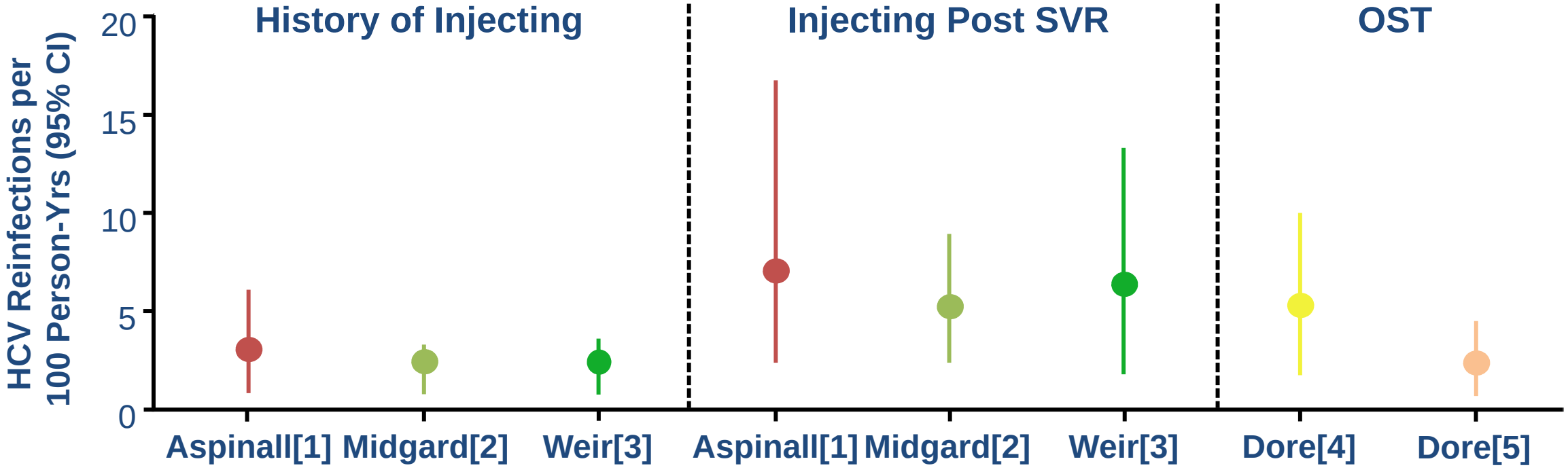
Durham DP, et al. Clin Infect Dis. 2016;62:298-304.

Modeling: Level of Scale-up Needed Depends on Existing Service Levels



Fraser H, et al. Addiction. 2017;[Epub ahead of print].

What About HCV Reinfection in PWID?



Among 28 pts who completed HCV treatment in urban methadone clinic with follow-up viral testing, no reinfections identified through 1 yr posttreatment follow-up[6]

1. Aspinall EJ, et al. Clin Infect Dis. 2013;57(suppl 2):S80-S89. 2. Midgard H, et al. J Hepatol. 2016;64:1020-1026. 3. Weir A, et al. Drug Alcohol Depend. 2016;165:53-60. 4. Dore GJ, et al. Ann Intern Med. 2016; 2016;165:625-634. 5. Dore GJ, et al. AASLD 2017. Abstract 195. 6. Sylvestre DL, et al. AASLD 2017. Abstract LB-18.

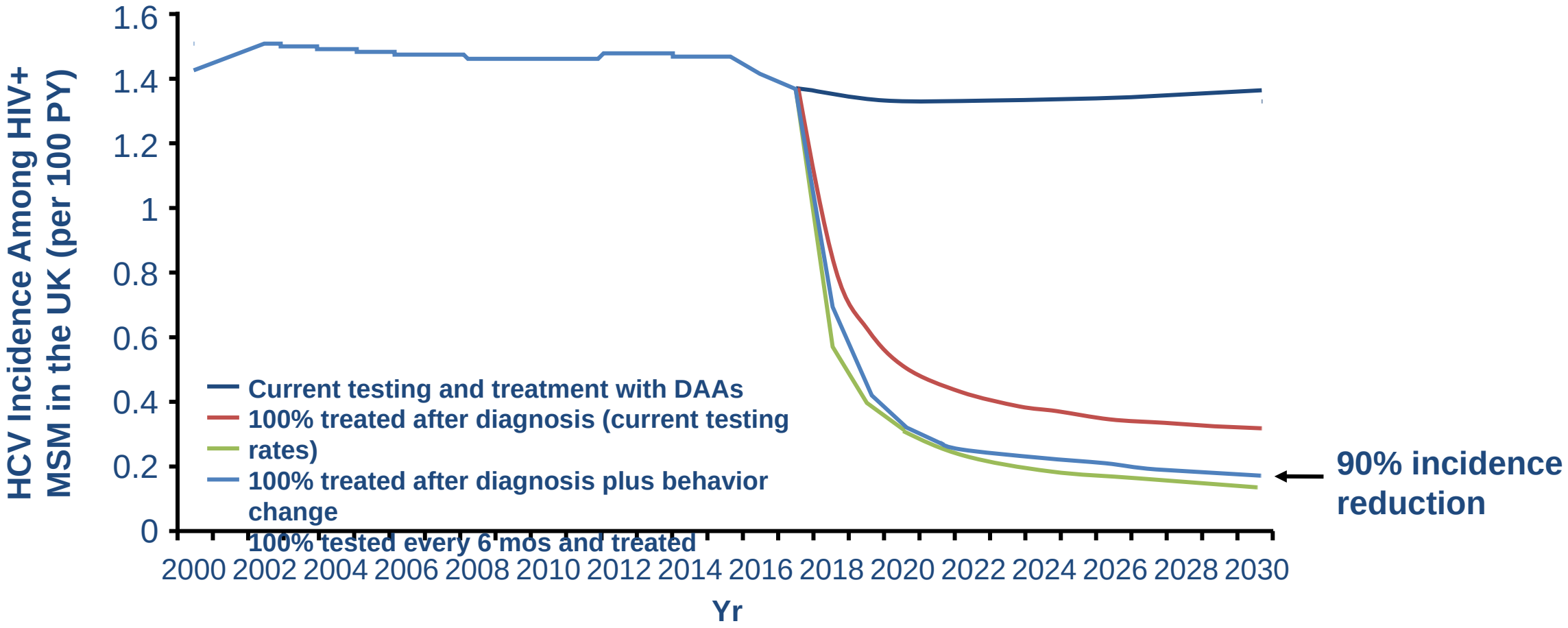
Multiple Prevention Strategies Are Needed

Among PWID: **harm reduction** efficacy estimates against HCV

- Current OST reduces risk of acquiring HCV by 50%
- High-coverage NSP reduces HCV acquisition risk by ~ 21%, although effect was stronger in Europe (56%)
- **In combination, both high-coverage NSP and OST can reduce risk of acquiring HCV by ~ 76%**

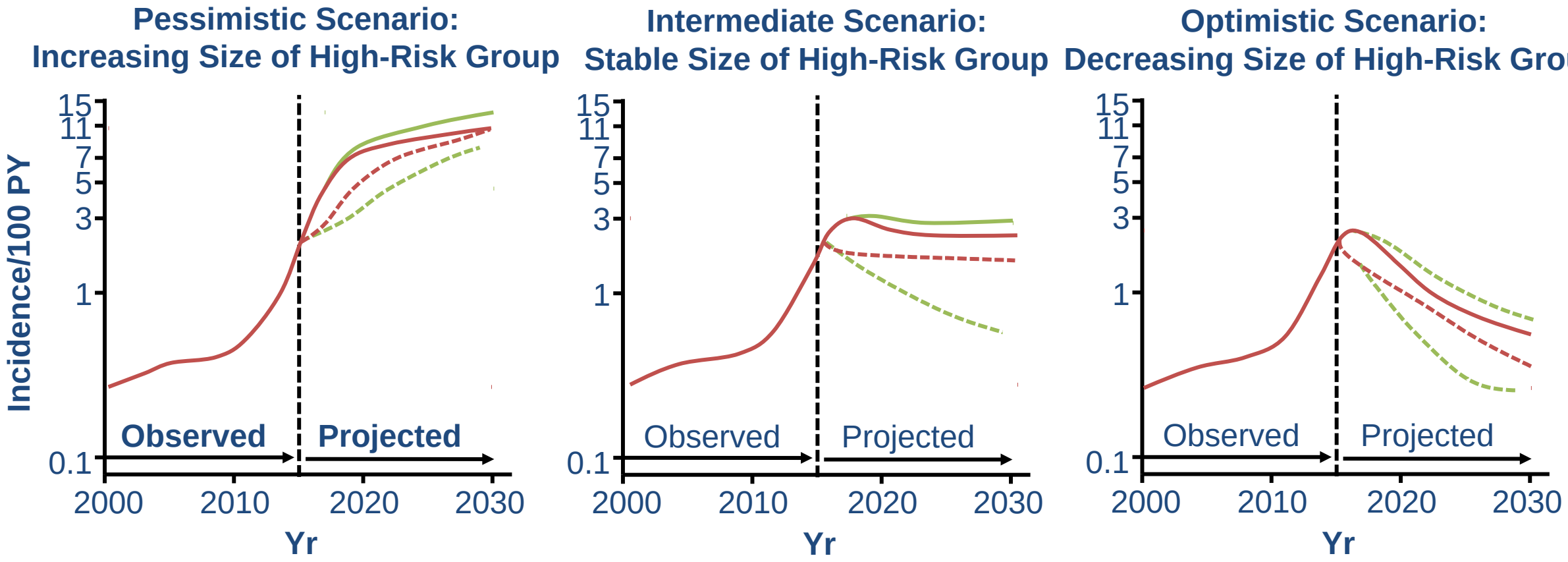
Platt L, et al. Addiction. 2017;[Epub ahead of print].

HIV+ MSM in UK Model: Elimination Will Require High Treatment + More Testing or Harm Reduction



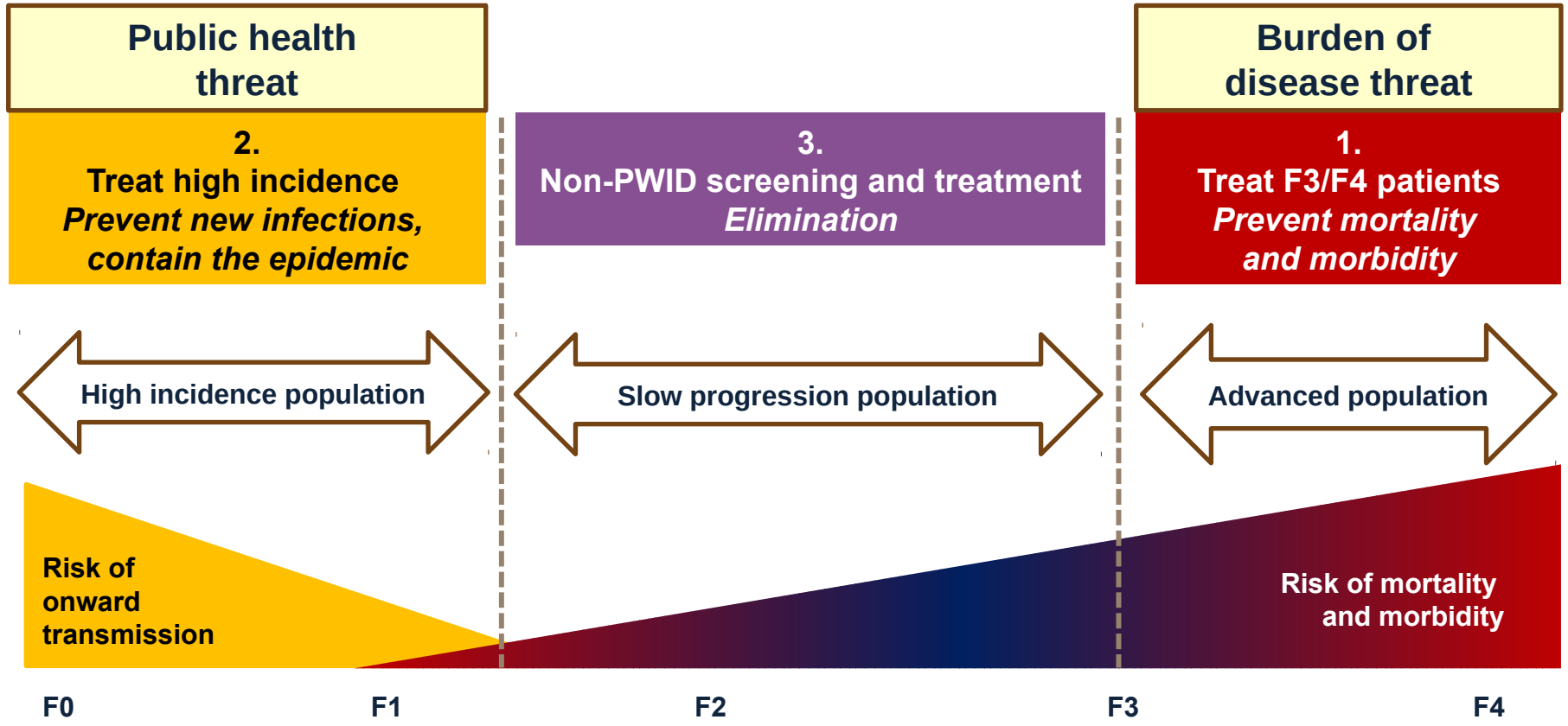
Martin NK, et al. HIV/Viral Hepatitis Coinfection Mtg. Paris, France. 2017.
Martin NK, et al**. Clin Infect Dis. 2016;62:1072-1080.**

HIV+ MSM in Swiss Model: Any Incidence Decrease Not Possible Without Harm Reduction



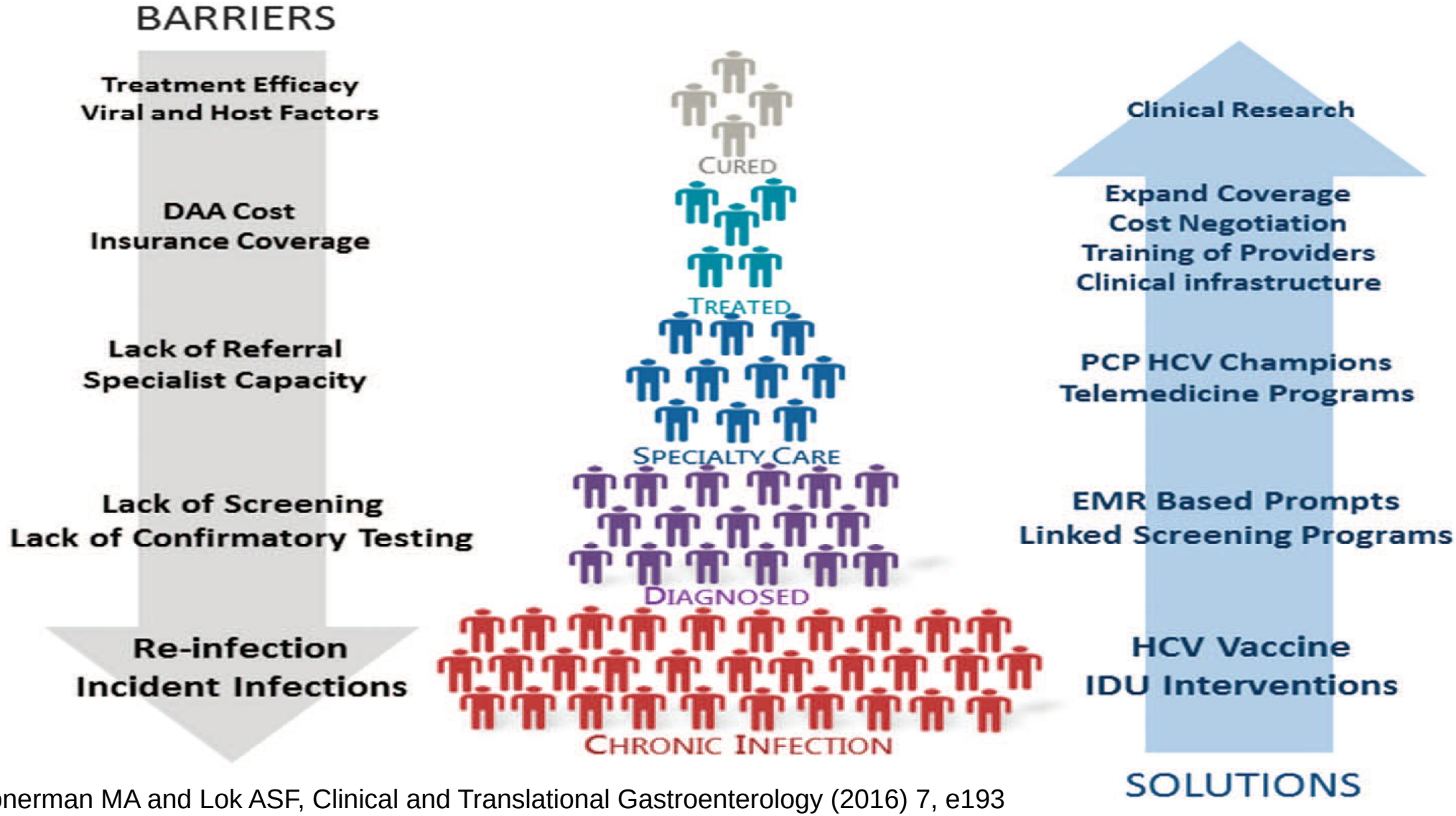
Salazar-Vizcaya L, et al. **Hepatology. 2016;64:1856-1869.**

Use of DAAs to reduce global HCV burden



⇨ **One approach <u>does not</u> fit all**

HCV care cascade and path to disease eradication: barriers and potential solutions



From: Konerman MA and Lok ASF, Clinical and Translational Gastroenterology (2016) 7, e193