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Office of AIDS Research

DC Partnership for HIV/AIDS Progress Clinical Division

The Intersection of HIV and Hepatitis C

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DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NIH National Institute of Allergy and Infectious Diseases
Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.

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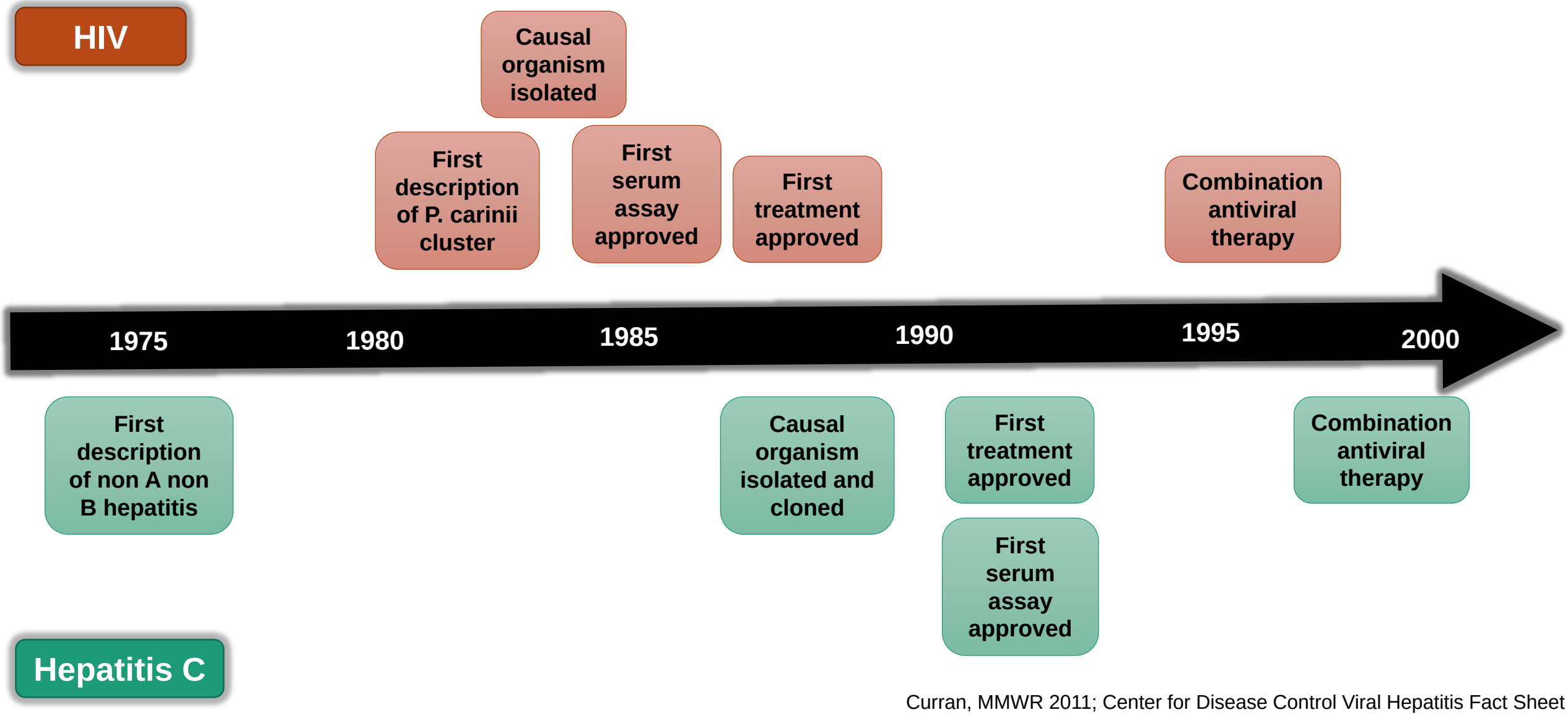
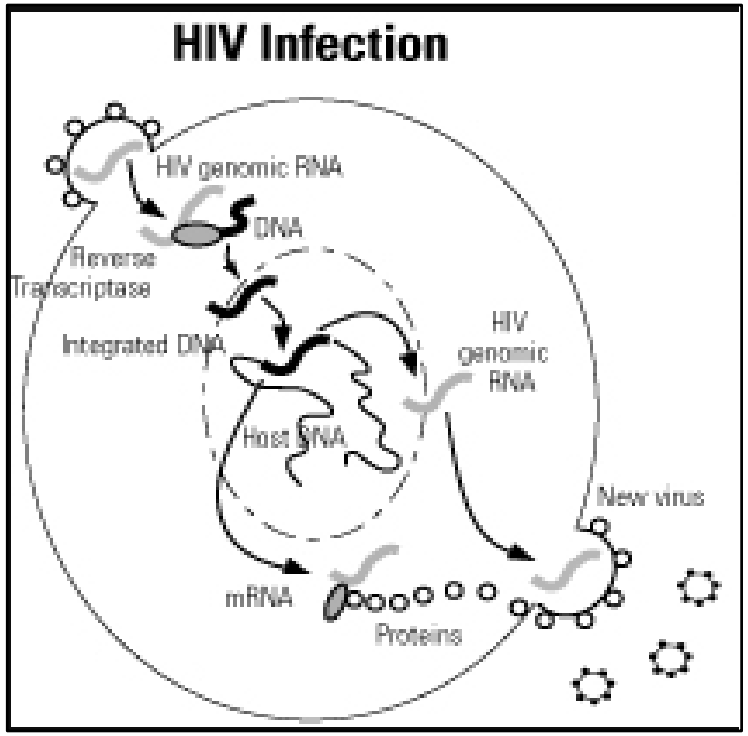
UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

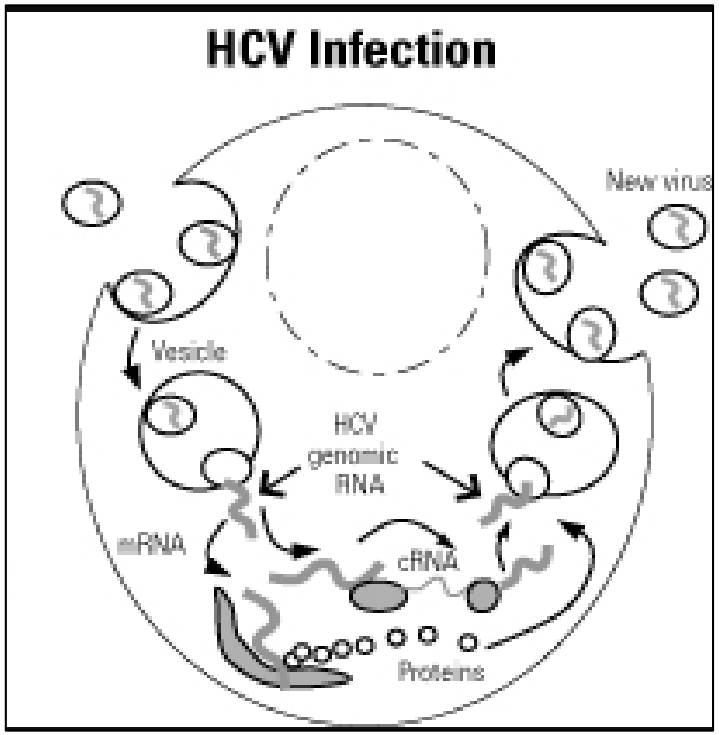
Major Historical Milestones in HIV and HCV



Curran, MMWR 2011; Center for Disease Control Viral Hepatitis Fact Sheet

Viral Characteristics





- Retrovirus
- Double stranded
- RNA → DNA→RNA

- Flavivirus
- Single stranded, positive sense
- RNA→ RNA

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Viral Characteristics

	HIV	Hepatitis C
Target Host Cell	CD4+ T Cell	Hepatocyte
Replication	Latent	Active
Population	1 million	5 million
Mutation Rates	Very high	Very high
Virions/Day	10^{10}	10^{12}
Genetic Archive	Yes	No

Adapted from Soriano et al, JAC 2008

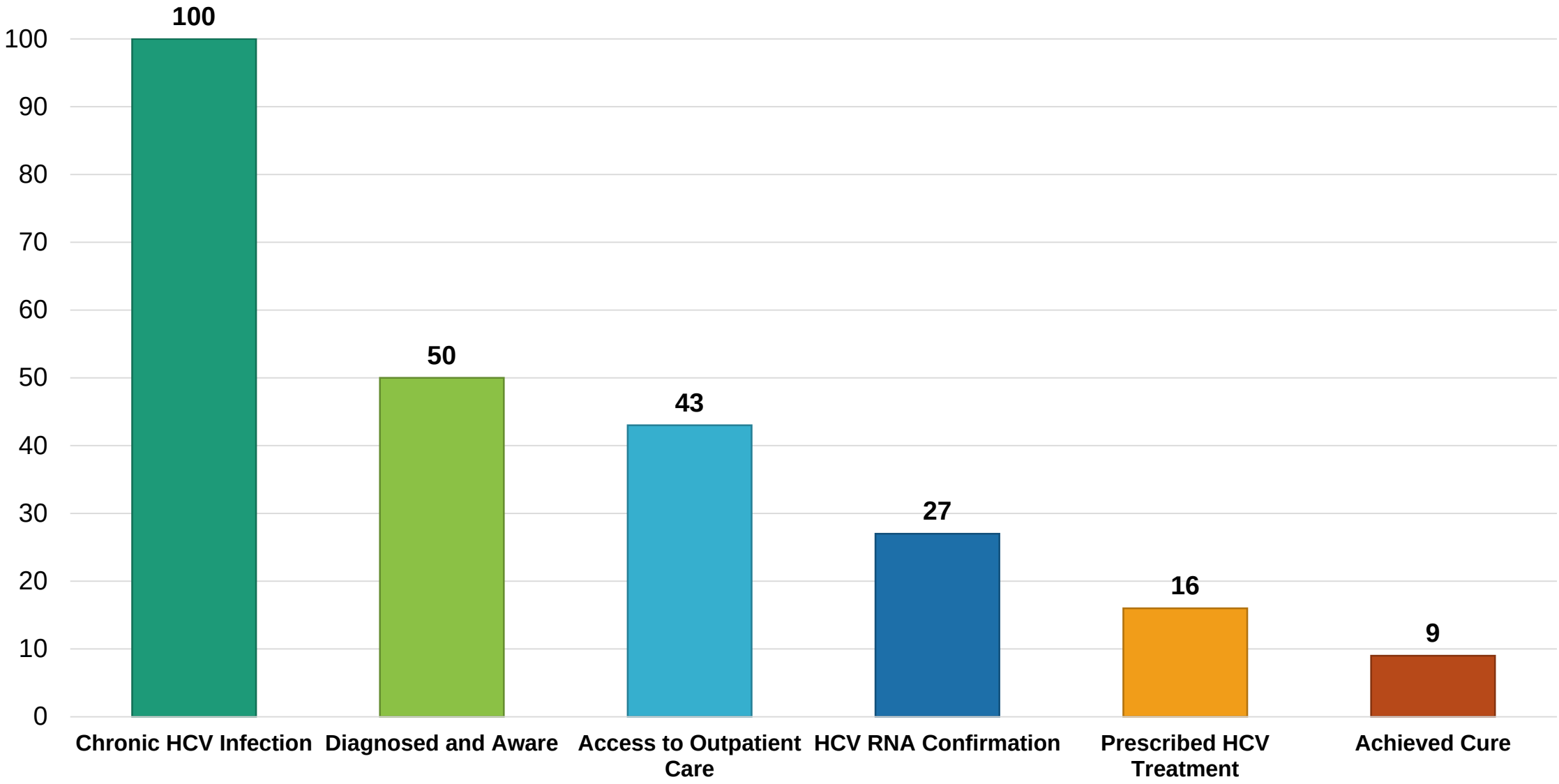
Current Directly Acting Antivirals

REGIMEN	Genotypes	Duration	SVR (%)
SOF/RBV	ALL	12-24 WKS	70-100
LDV/SOF	1 & 4	12-24 WKS[#]	>95
SOF/VEL	ALL	12 WKS[#]	>99
DAC/SOF	ALL	12-24 WKS[#]	>95
PRO-D/TECHNIVIE[@]	1 & 4	12-24 WKS	>90
GRZ/ELB	1 & 4	12-16 WKS[$]	>95

[#] RBV to be added for decompensated cirrhosis
[@]Dasabuvir has no activity against genotype 4
[$] RBV to be added for those with baseline NS5A mutations

AASLD-IDSA HCV Guidance (hcvguidance.org)

Hepatitis C Care Continuum



Adapted from Yehia et al PLOS One 2015

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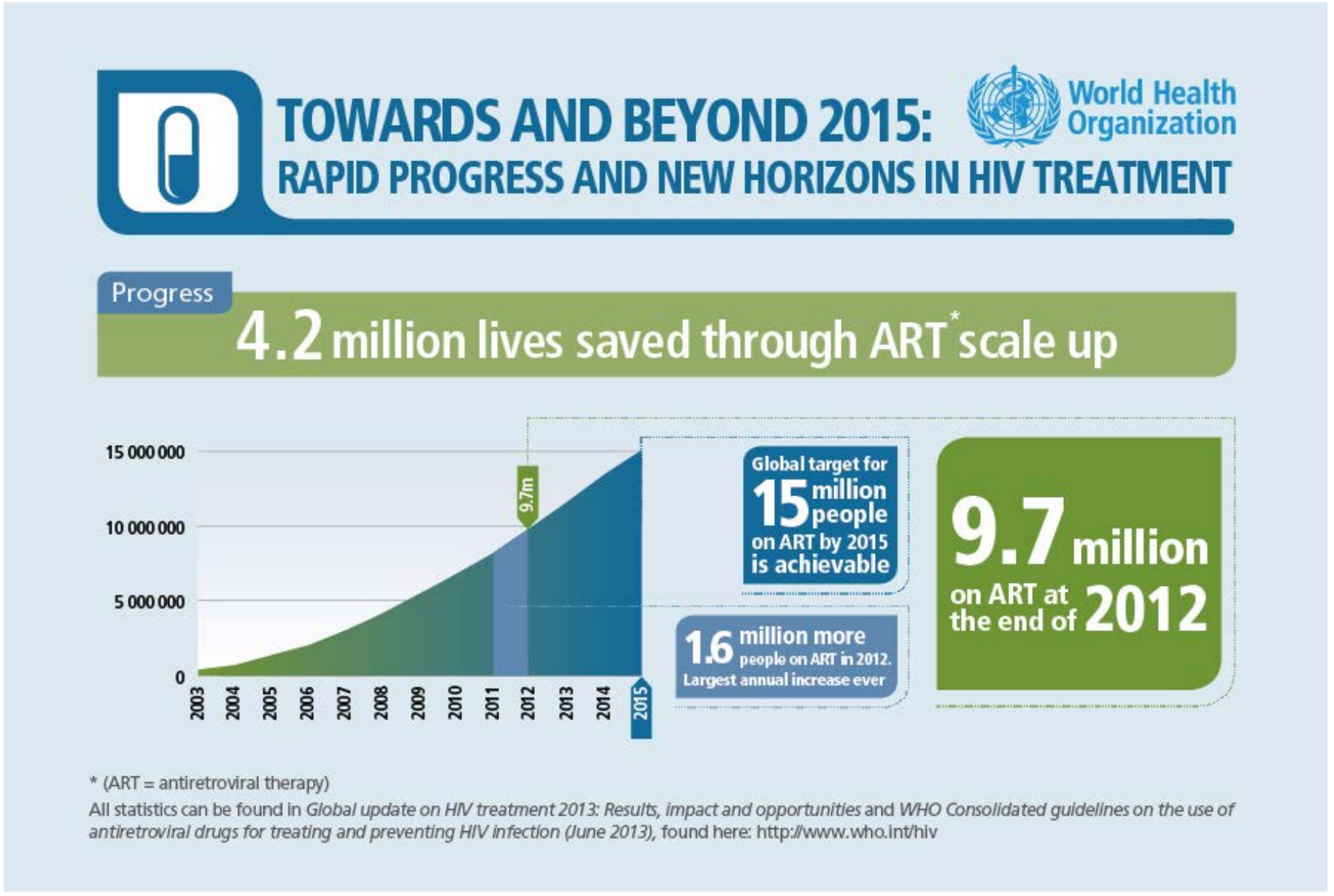
Where does the HCV field go from here?

Dramatic Progress in HIV Treatment



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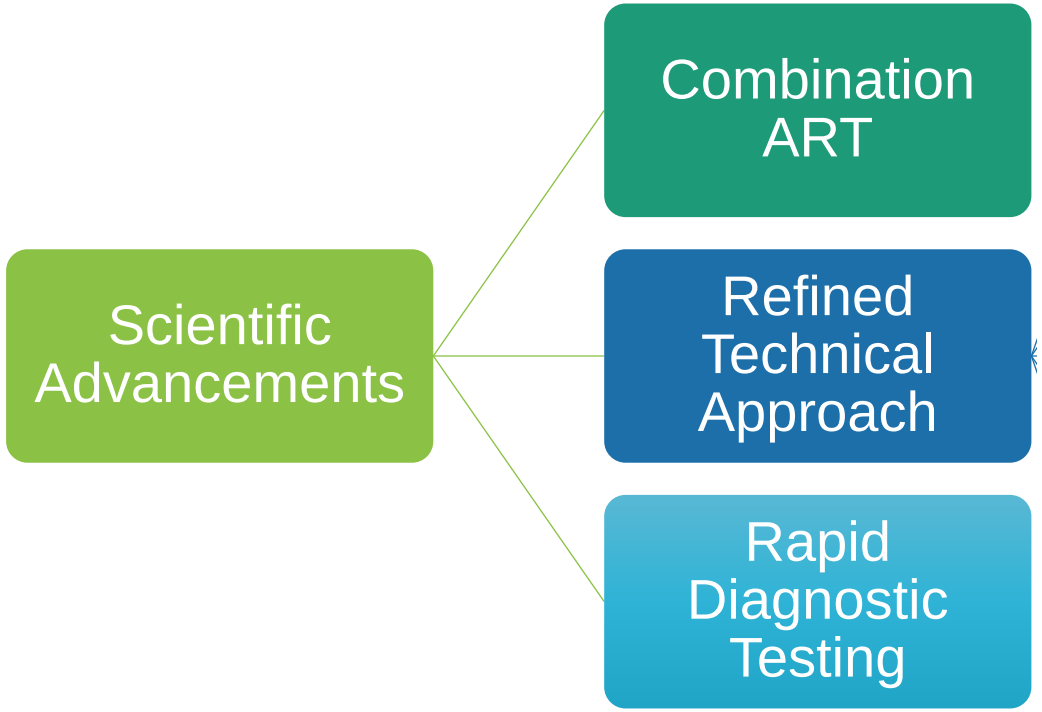
Key Factors in HIV Treatment Implementation



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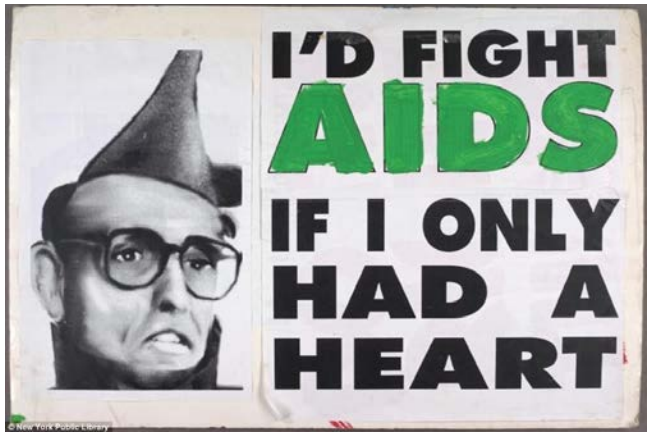
Key Factors in HIV Treatment Implementation



Key Factors in HIV Treatment Implementation

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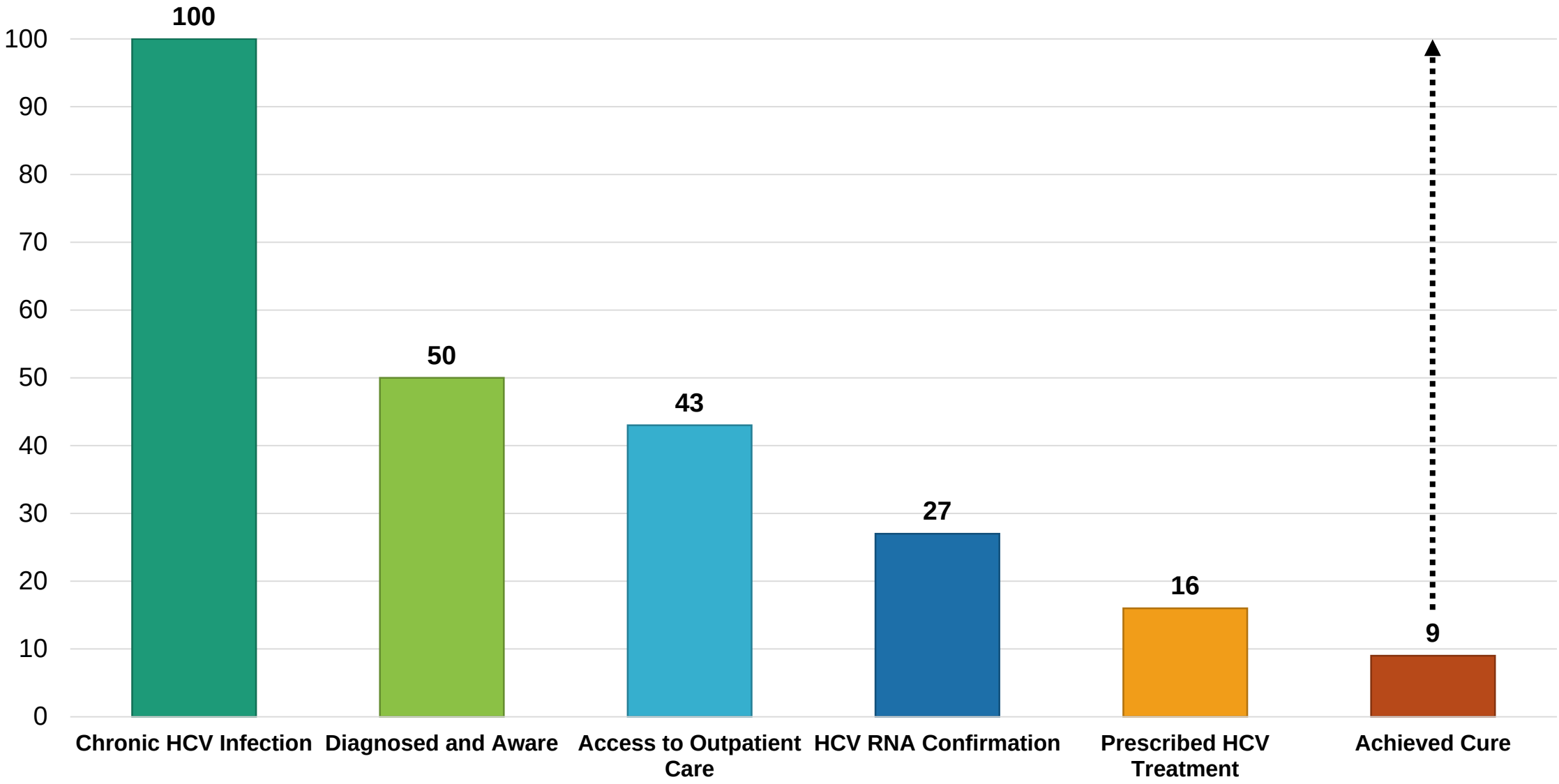
Hepatitis C Care Continuum



Adapted from Yehia et al PLOS One 2015

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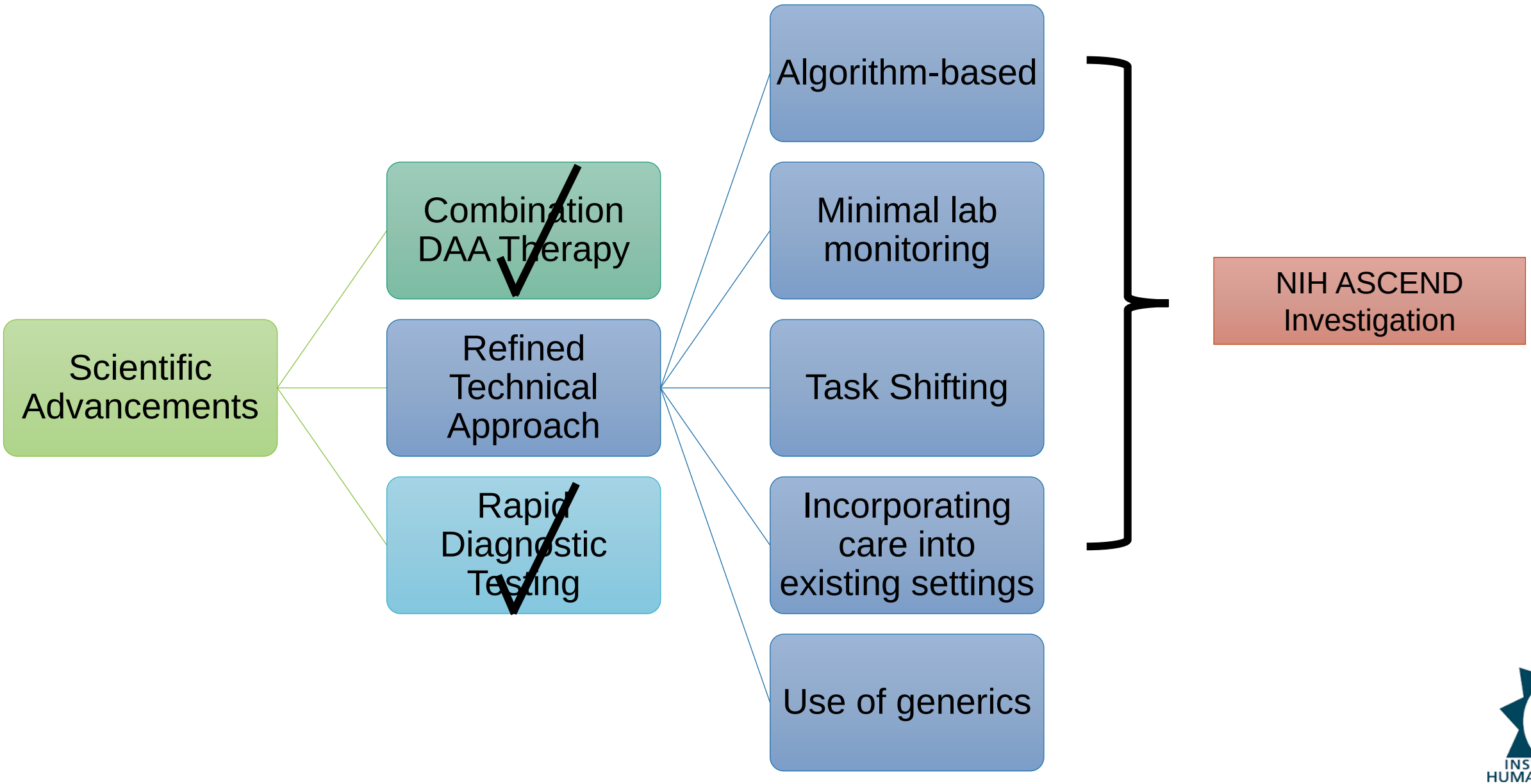
HCV Treatment Implementation



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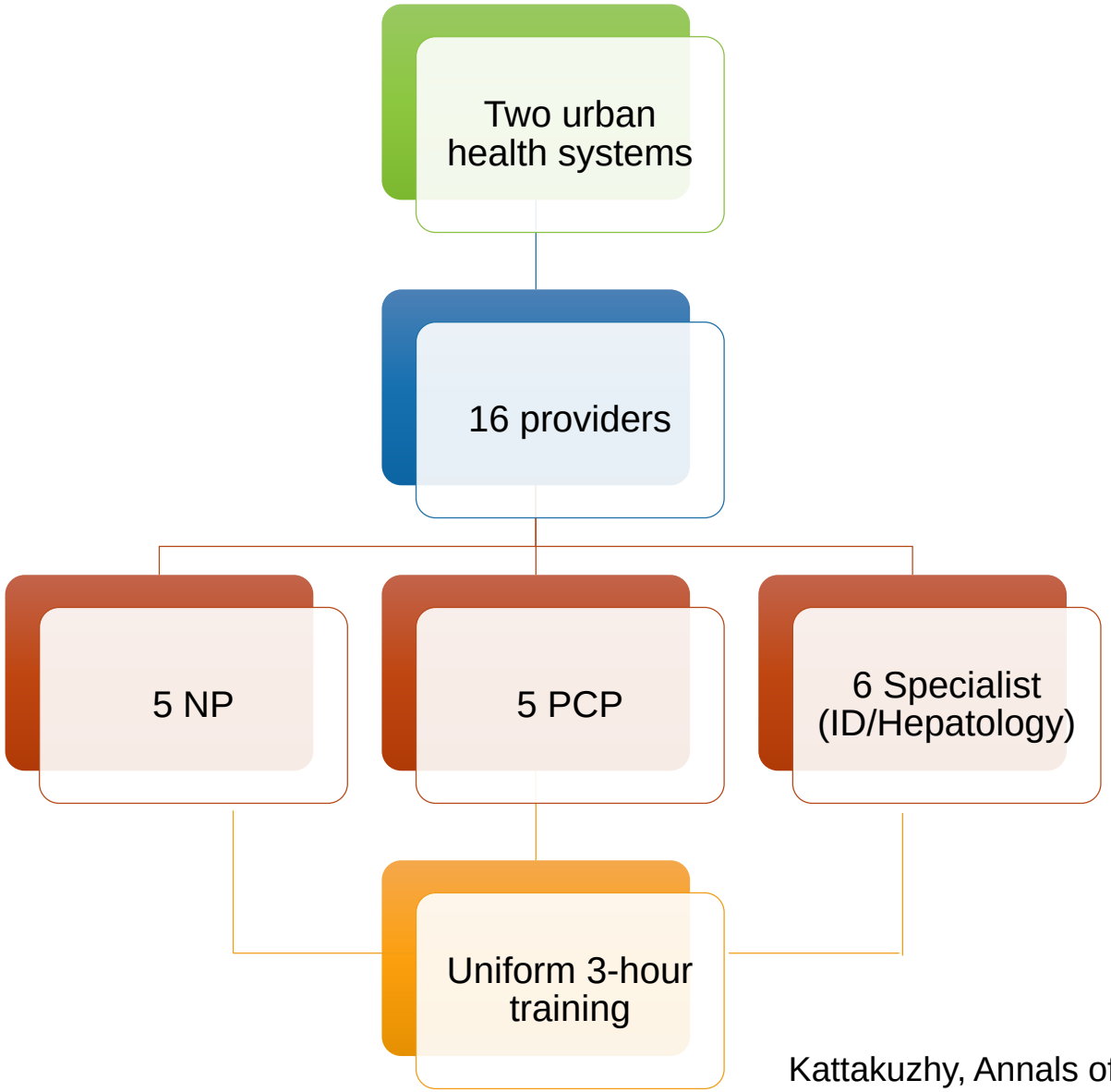
Study Design



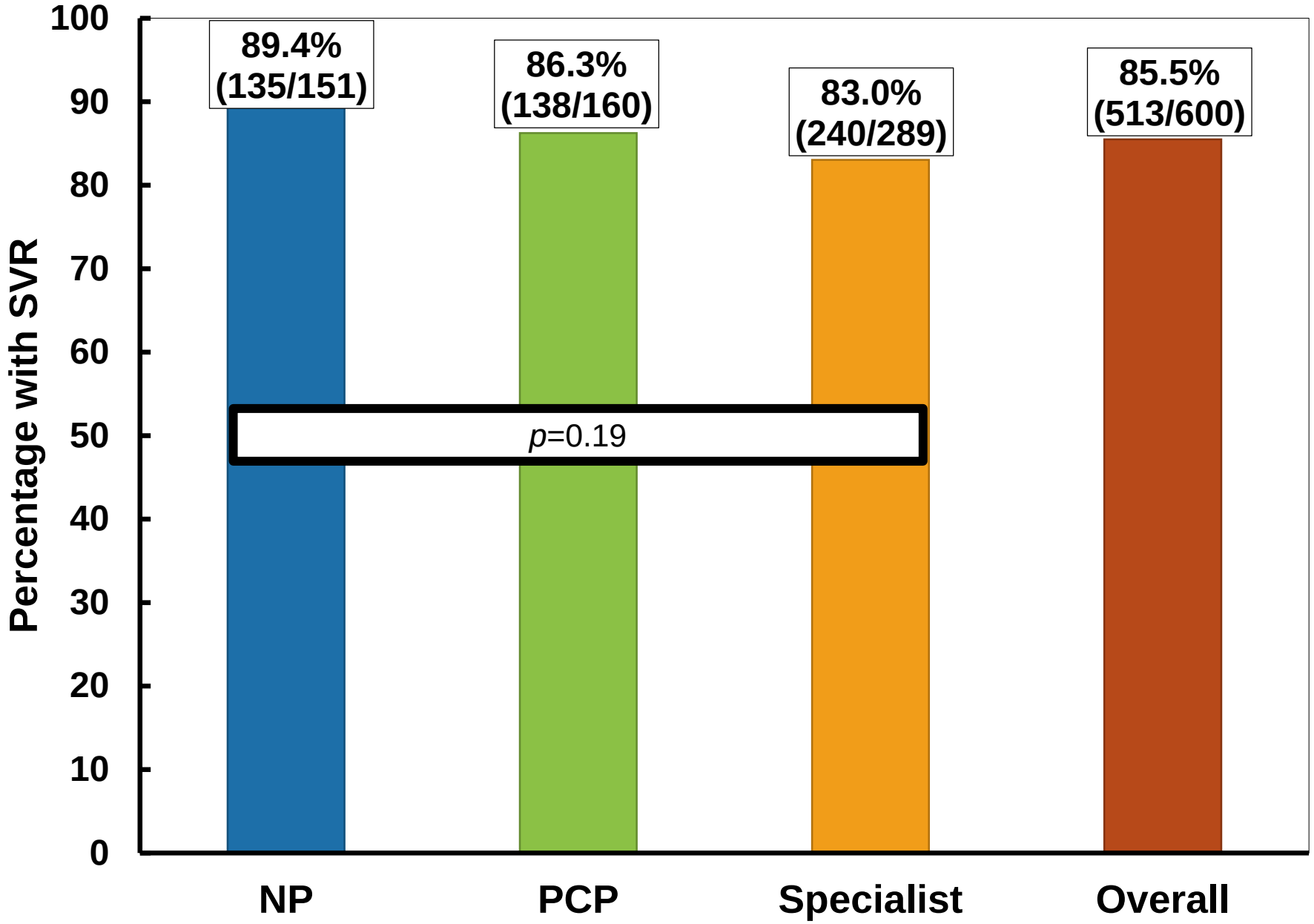
Kattakuzhy, Annals of Internal Medicine 2017

Methods

- No study team involvement after initial visit

- Standardized visit schedule based on AASLD-IDSA guidance
  - Monthly provider visits
  - Week 4 safety labs
  - HCV viral load testing at week 4 and SVR12

Primary Outcome



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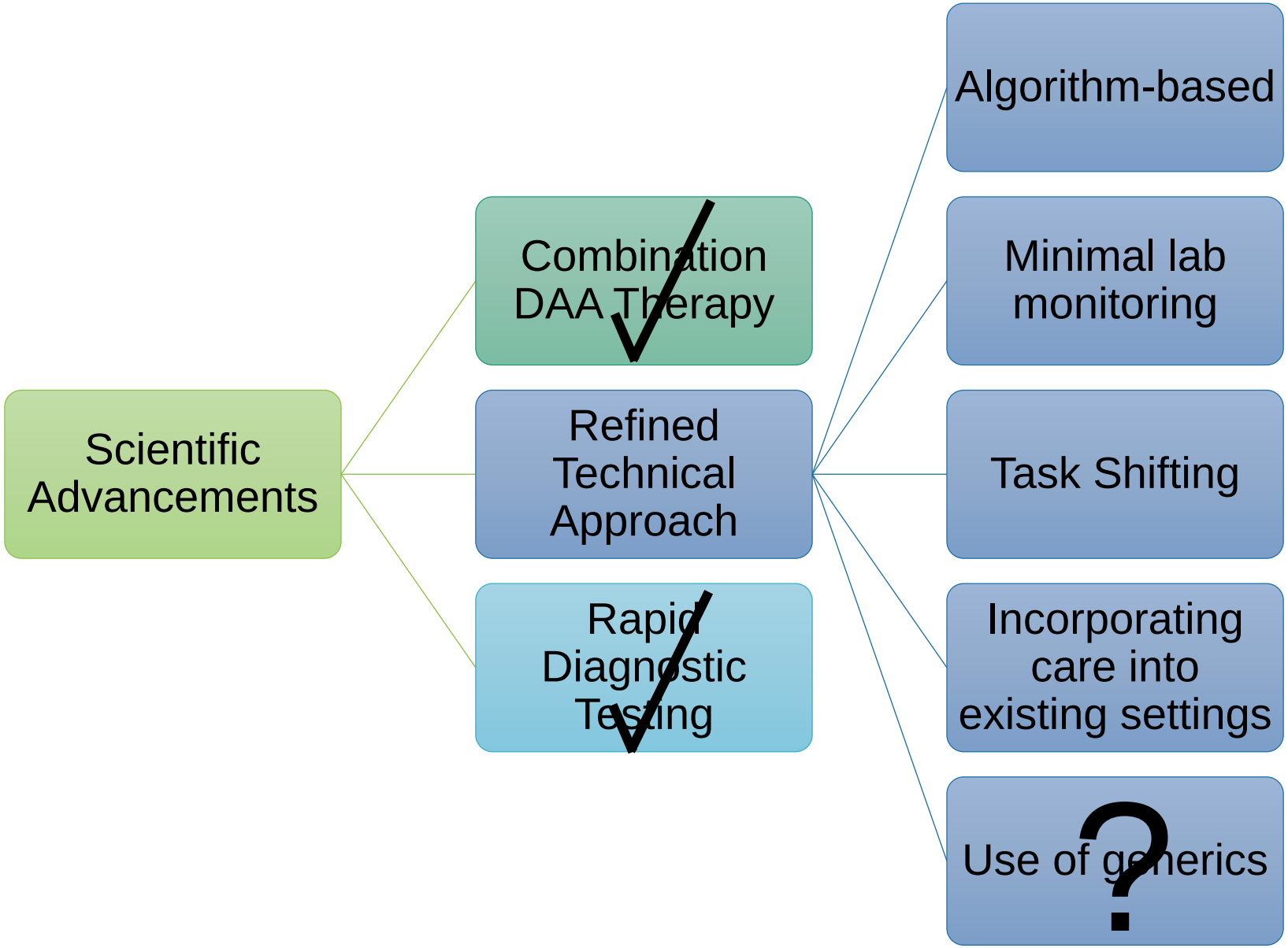
HCV Treatment Implementation



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HCV Medication Cost

Wholesale Acquisition Cost (WAC) of Direct Acting Antiviral Agents used to Treat HCV			
Medication	**Trade Name**	**Manufacturer**	**WAC for 1 Day**
Daclatasvir	*Daklinza*	Bristol-Myers Squibb	$750
Elbasvir-Grazoprevir	*Zepatier*	Merck & Co., Inc.	$650
Ledipasvir-Sofosbuvir	*Harvoni*	Gilead Sciences	$1125
Glecaprevir-Pibrentasvir	*Mavyret*	AbbVie	$417
Ombitasvir-Paritaprevir-Ritonavir	*Technivie*	AbbVie	$912
Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir	*Viekira Pak*	AbbVie	$992
Simeprevir	*Olysio*	Janssen	$790
Sofosbuvir	*Sovaldi*	Gilead Sciences	$1000
Sofosbuvir-Velpatasvir	*Epclusa*	Gilead Sciences	$890
Sofosbuvir-Velpatasvir-Voxilaprevir	*Vosevi*	Gilead Sciences	$890

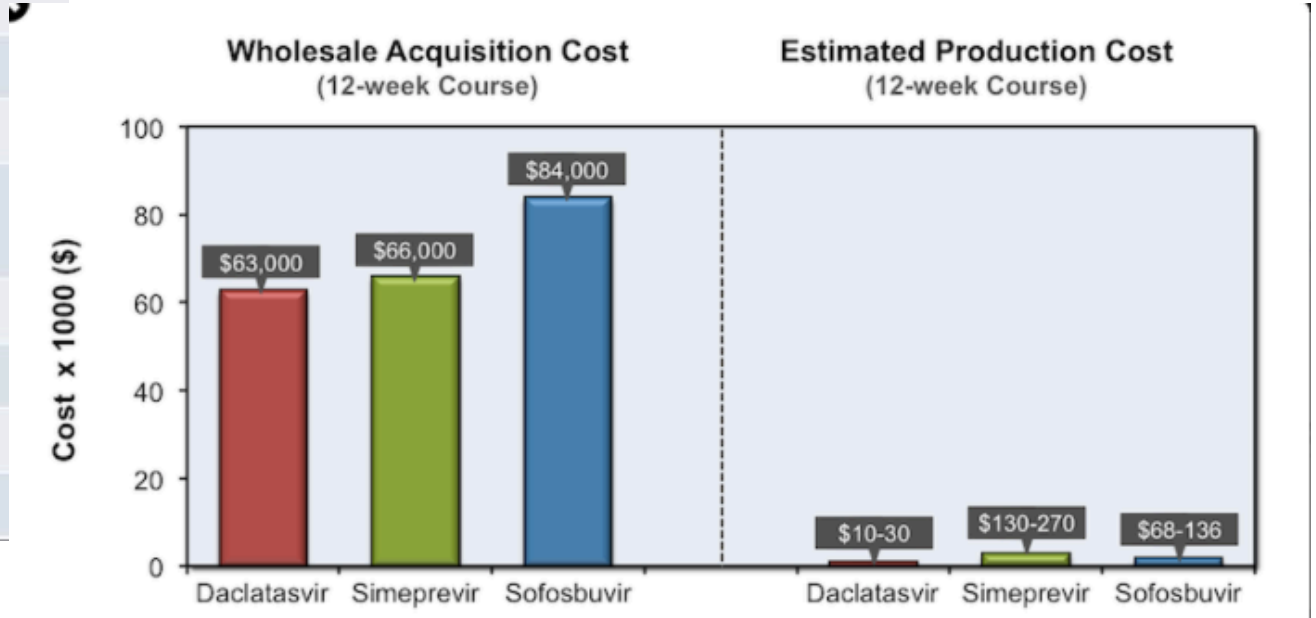

Figure 2 - Wholesale Acquisition Cost versus Estimated Production Cost for DAAs and 12-Week Treatment Course

Source: Hill A, Khoo S, Fortunak J, Simmons B, Ford N. Minimum costs for producing hepatitis C direct-acting antivirals for use in large-scale treatment access programs in developing countries. Clin Infect Dis. 2014;58:928-36.

University of Washington Hepatitis C Curriculum; van de Ven, Hepatology 2015

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HCV Generics

- Gilead License Agreements

- Emerging observational data that licensed generics have equal efficacy

Viral status	Overall *n*/total *n* (%)	SOF/LDV *n*/total *n* (%)	SOF/DCV *n*/total *n* (%)
SVR 12	247/250(99)	104/104(100)	143/146(98)
SVR 24	96/97(99)	30/30(100)	66/67(99)

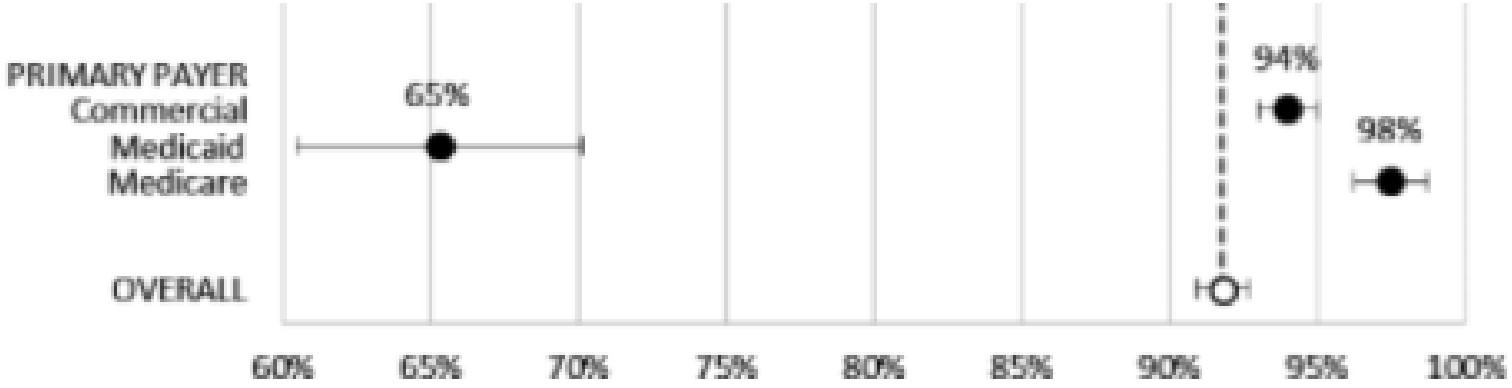
Hill et al, J Virus Erad 2017

Limited Advocacy

Delayed serious outcomes reduce urgency

Unequal access to medications

Disenfranchised populations excluded



Younossi et al, J Viral Hepat 2016

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Limited Government Investment

- Research Funding on HCV is tied to subgroups of political interest, not to disease or implementation needs
- Senate Finance Committee inquiry into Sovaldi pricing December 2015 did not lead to significant price changes
- No PEPFAR or RWCA equivalents
- Medicaid coverage varies state to state and includes non-evidence based restrictions on liver fibrosis stage, substance use, and provider type.

Barua et al, Annals 2015
https://www.finance.senate.gov/ranking-members-news/wyden-grassley-sovaldi-investigation

Where does the HCV field go from here?

- Refine our technical approach through large scale, randomized implementation studies
- Increase advocacy, engaging marginalized populations
- Gain government buy-in
- Obtain access to generic medications

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Thank You

Office of AIDS Research

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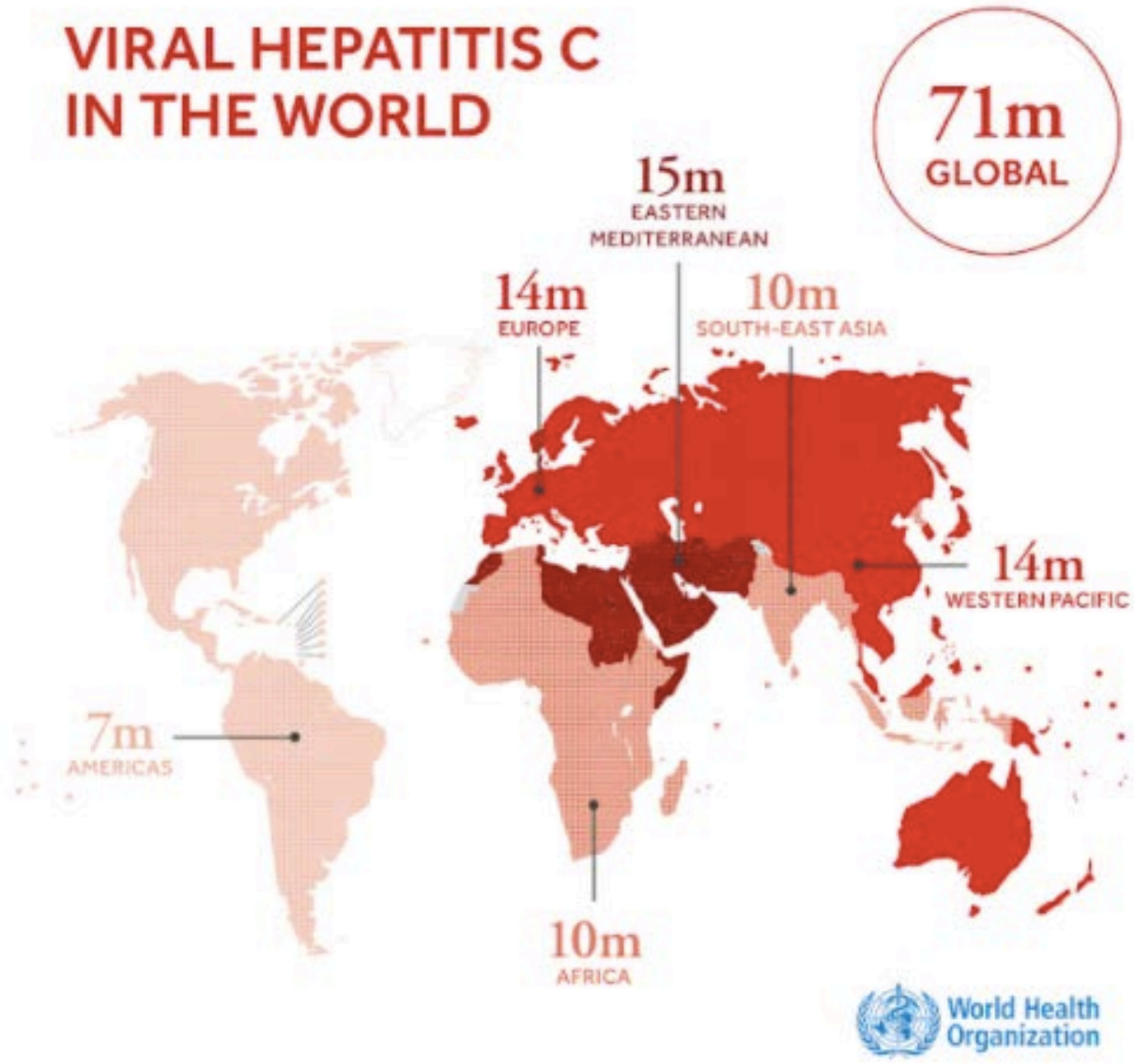
- Poonam Mathur DO

Community Partners

- Unity Healthcare
- Family Medical Counseling Services
- HIPS
- RAP
- DC DOH
- WWH

Patients of the District of Columbia

Hepatitis C: Global Epidemiology



World Health Organization, 2017

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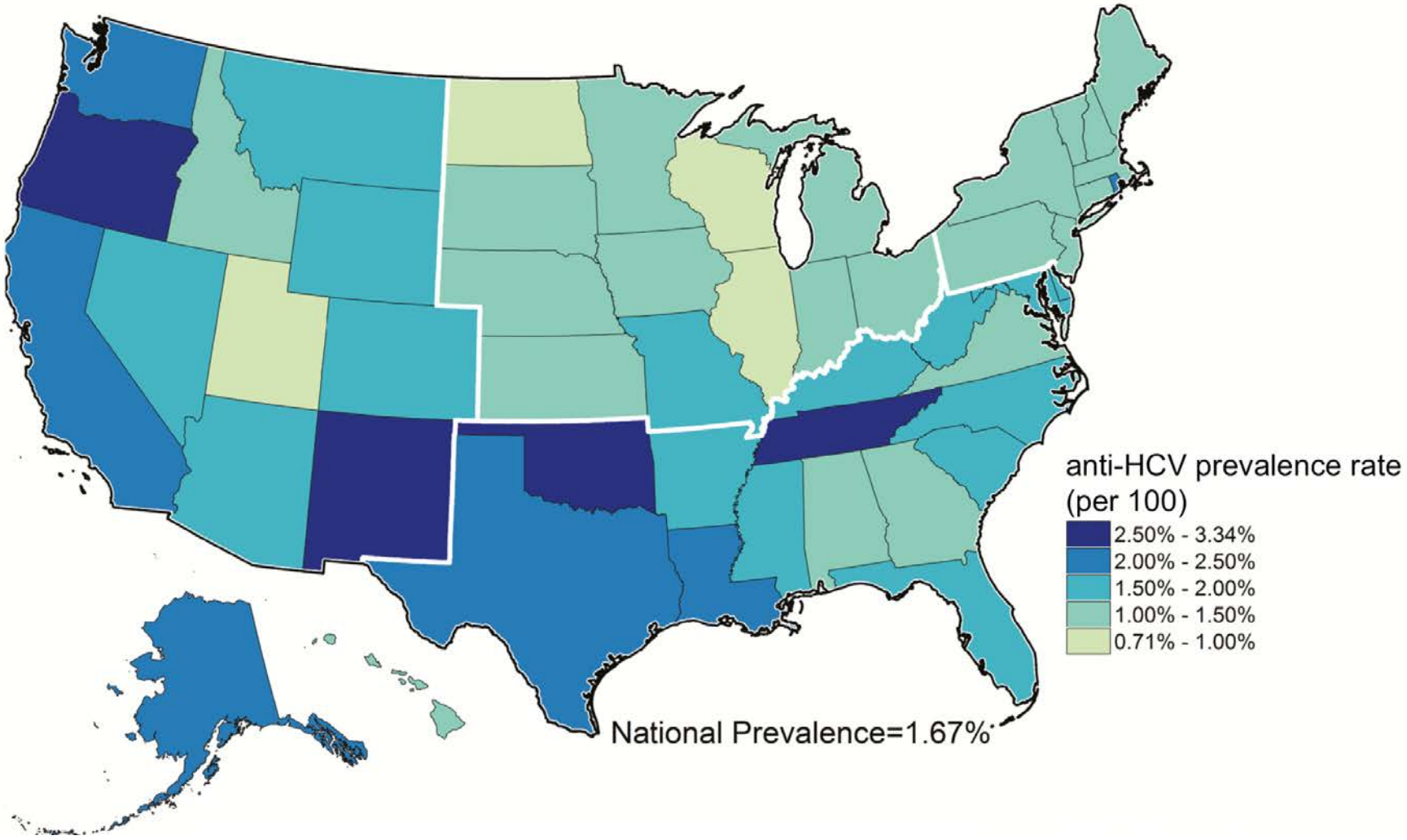
Hepatitis C: National Epidemiology



Clin Infect Dis. 2017;64(11):1573-1581

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Clinical Characteristics

	HIV	Hepatitis C
Transmission	Blood, Sex, Mother to Child	Blood, Sex, Mother to Child
Progression	Slow, ~10 years to fatal disease	Slow, ~20 years to fatal disease in some
Mortality	High in nearly all infected patients if untreated	High in advanced fibrosis patients if untreated
Drug Targets	Multiple	Multiple
Therapy Duration	Lifelong	8-24 weeks
Current Therapeutic Goal	Suppression	Eradication