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Optimization of Screening Strategies for Viral Hepatitis

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Optimization of Hepatitis C Screening

- Strategic information
- Policy development
- Financial planning (budgetary, cost- effectiveness)
- Feasible/ effective implementation
- Technology

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Criteria to Guide Public Health Screening

1. The condition sought should be an important health problem.
2. There should be an accepted treatment
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process

Wilson Junger, WHO 1968. www.who.int

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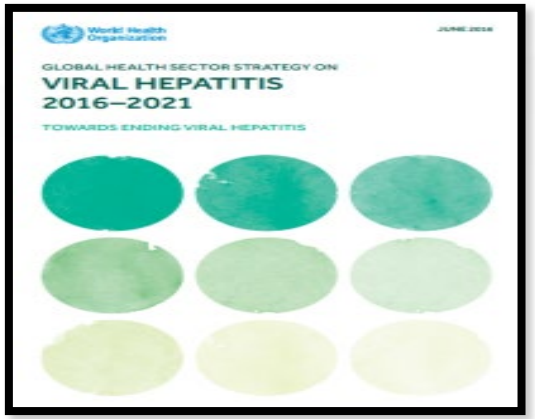
In response to the growing threat, the World Health Assembly set goals for reductions in transmission and mortality for 2030

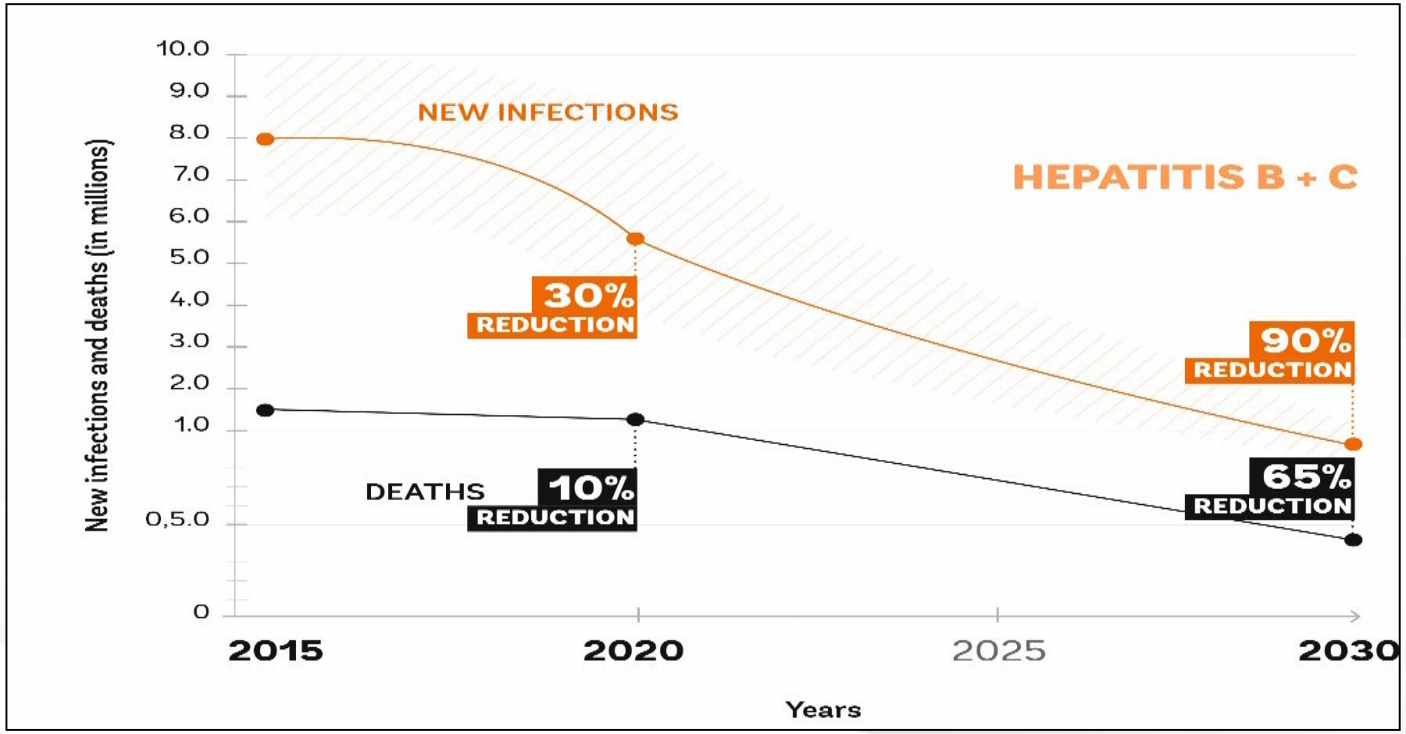


Global Health Sector Strategy on Viral Hepatitis, 2016-2021

Goal: *Eliminate viral hepatitis as a major public health threat by 2030*

Health outcome targets:

- Reduce the incidence from 1.75 M cases of chronic HCV infection to less than 200,000 infections by 2030
- Reduce the annual deaths from chronic hepatitis from 400,000 to less than 150,000 deaths by 2030



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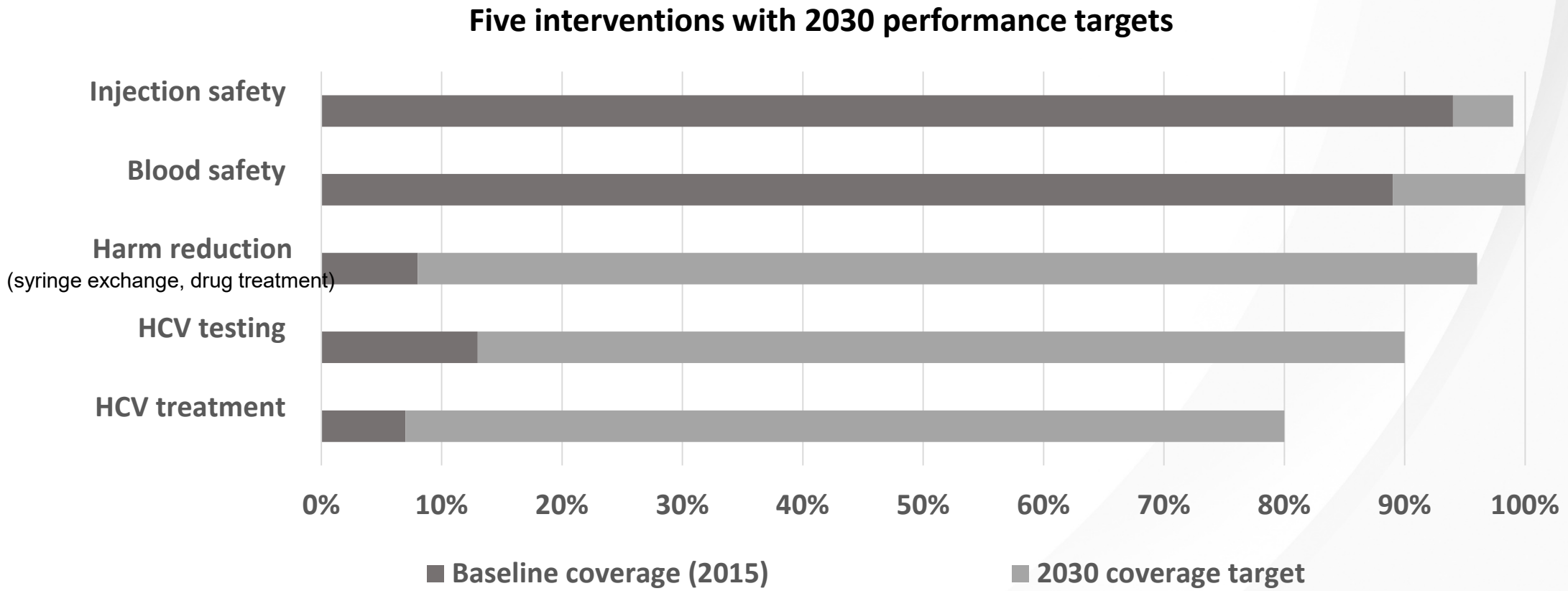
There are five key interventions to reach HCV elimination



Only 20% of people living with HCV have been diagnosed and 7% treated

Source: WHO Global Health Sector Strategies: Roadmaps to Elimination, 2016-2021

All-oral, curative HCV therapies are a medical breakthrough and have evolved to allow for simple delivery of care and treatment

✓ **Transformational medicine:**

- Cure > 95 % with 1-3 pills/day/8-12 wks
- Excellent safety profile
- 75%-80% reduction in mortality risk
- Treatment as prevention reduces transmission risk

✓ **Allow for public health approach:**

- Delivery can be co-located in high prevalence settings (e.g. HIV, TB) and primary care
- Shift management to mid–level providers (e.g., pharmacists)

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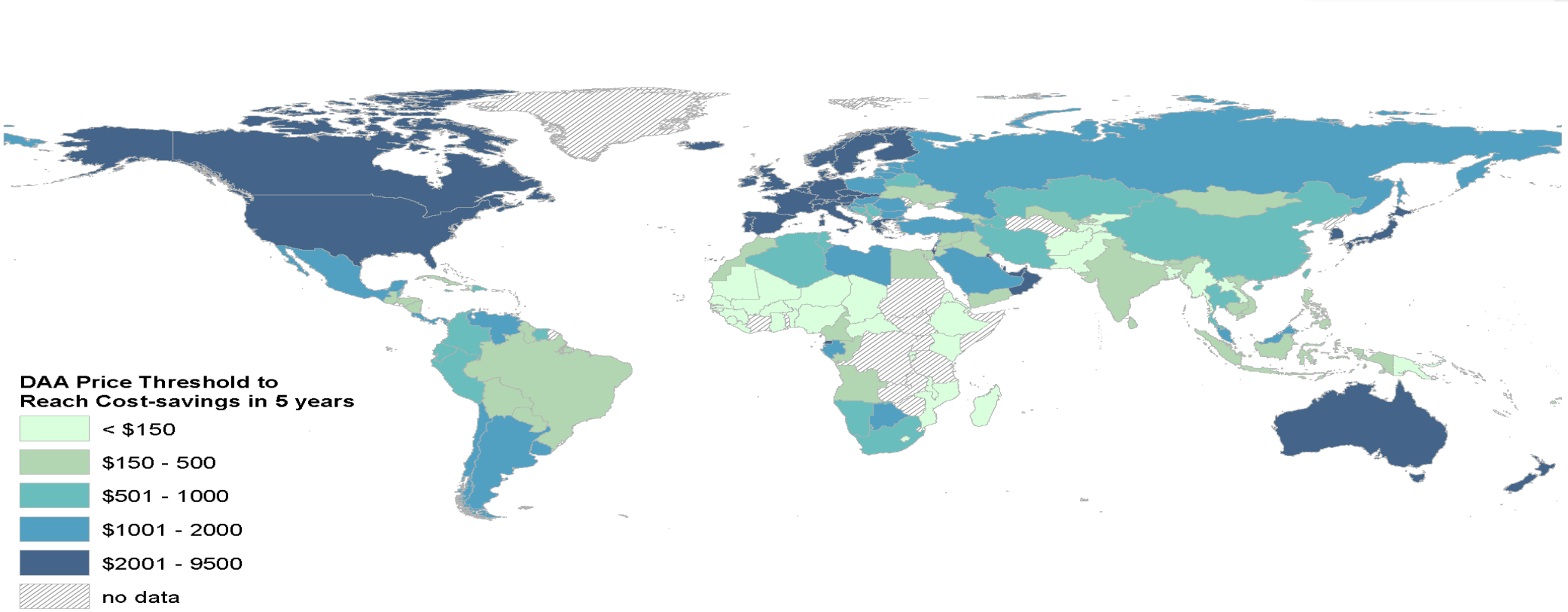
Cost of HCV treatment is no longer the major barrier to elimination



62% of persons with HCV live in countries with access to HCV medication < $150

Chhatwal J, unpublished data, Who Global Hepatitis Report 2017

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Scaling up HCV testing limits access to curative treatment across settings

HCV testing challenges	
Algorithm	• Current two step testing – anti-HCV (exposure) + viral testing (PCR)
Utilization	• Central lab requires patient or specimen transport • Point of care (e.g., Genexpert PCR) improves access; 92% of TB, HIV programs use < 50% of Genexpert capacity • Lack of policies to guide testing • Lack of data to monitor test volume and results
Cost	• Varied costs $5-200 (PCR)– because of diverse procurement mechanisms, lack of price transparency, and uncertain purchase volumes • Volume as reaching health targets will require near universal screening
Technology	• **Research priority: Move from two step to a single test to diagnose HCV infection** • **Prime candidate- HCV core-antigen test**

Source: CHAI and FIND. Diagnostics landscape. (2017)

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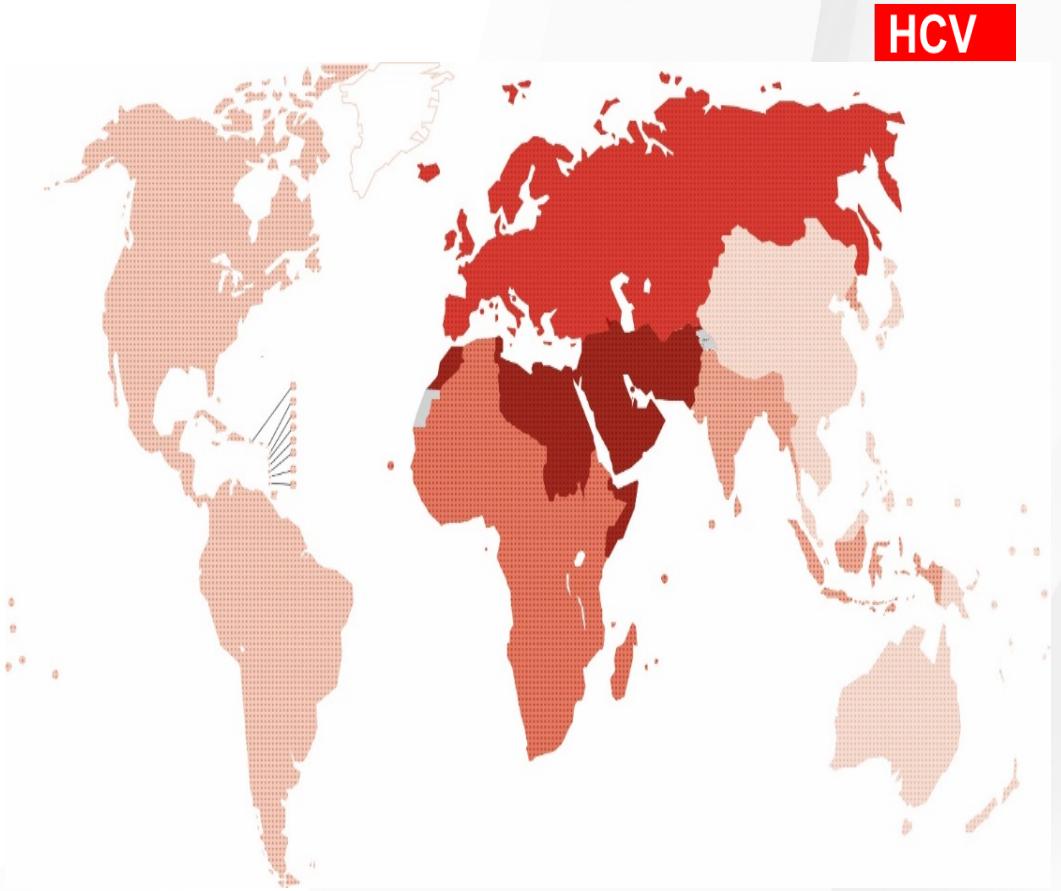
WHO Recommendations for HCV Testing and Treatment

- Testing
  - All blood donors- 95% of donors globally
  - Risk populations- exposures, clinical illness
  - Sub-population- i.e. birth cohorts
  - General population- > 2% or > 5% prevalence

- Treat all persons with HCV



www.WHO.org

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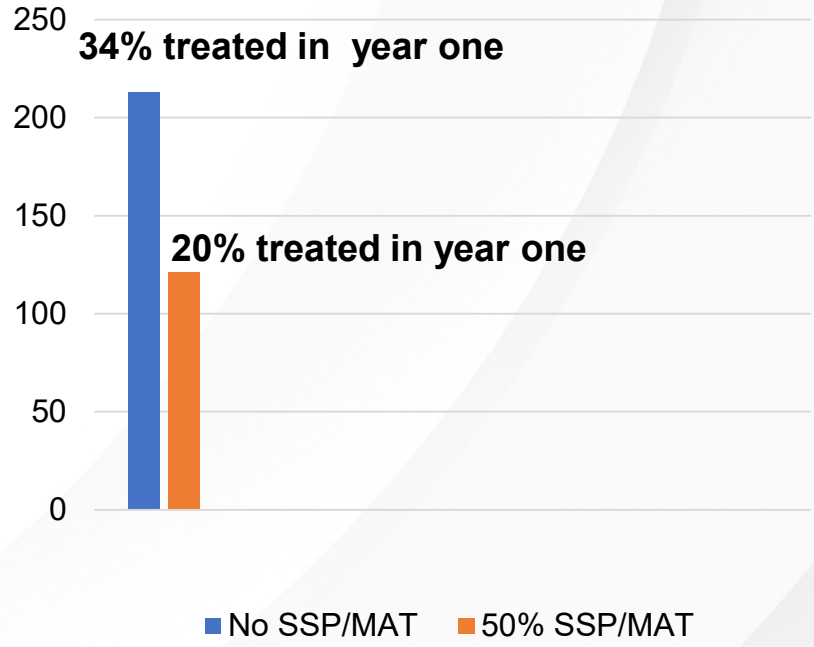
Risk-based Testing
HCV Testing for Persons Who Inject Drugs

- Global prevalence 60%
- Drug treatment, syringe services programs reduce risk by 71%
- Addition of HCV testing/ treatment reduces risk by 90%
- In US HCV testing 79% of syringe service programs
  - 88% of drug treatment programs offer
  - Linkage to car is the issue
- HCV treatment
  - Good adherence and response to therapy
  - Reinfection is relatively low 0.0. to 6.4 /100 person years
- Routine testing (annual)

90% reduction in HCV incidence by 2030



Ward, J, Gastroenterology 2019, . Cochrane Database Syst Rev. 2017, Fraser H, Addiction. 2018 Frazier H, Addiction 2017

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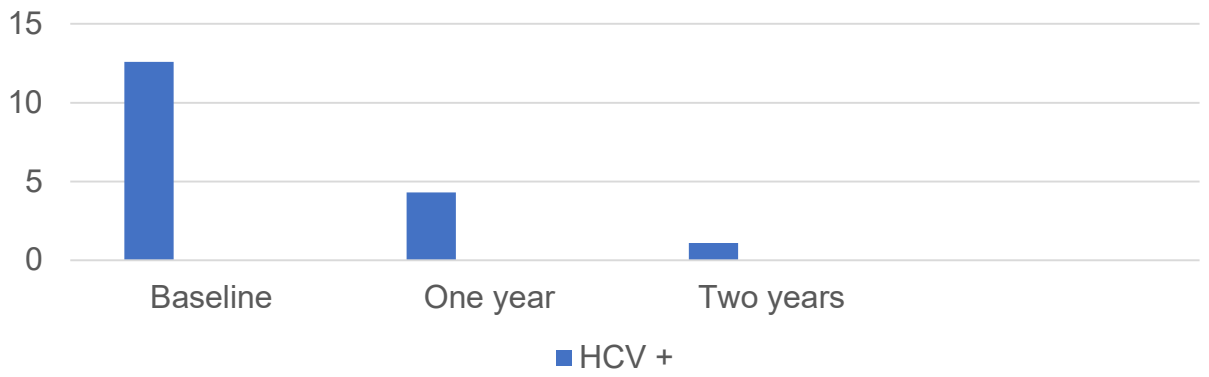
Risk-based Testing Incarcerated Populations

HCV prevalence
Lotus Glen Correctional Center



Global: 13% have HCV (8-95%)

North America – 15%

Europe 18-23%

Opportunity to Test, Cure and eliminate HCV

Micro-elimination program demonstrate the feasibility of HCV elimination

Routine testing

Education

Treatment on site

Barriers include cost, systematic and jurisdictional issues

Bartlett S, Clin infect Dis 2018 Larney S, Hepatology 2013

Risk-based Testing
Persons with HIV

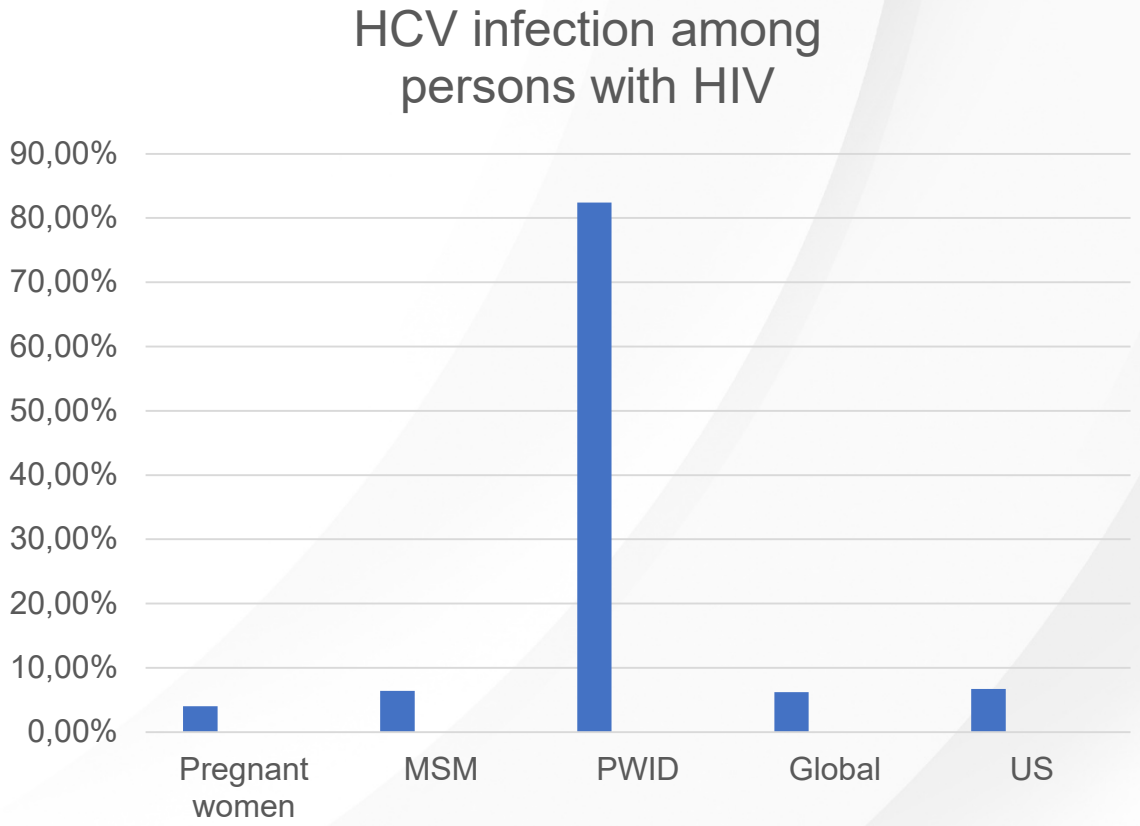
Global 2.3M (6.4%) persons with HIV/HCV; 1.4M PWID

HIV accelerates HCV disease progression

Liver disease leading cause of death for HIV+ persons

For MSM, HCV incidence 19X greater if HIV+

- HCV cure decreases mortality risk for HIV+ persons
- Integrate care- set “micro- elimination” targets



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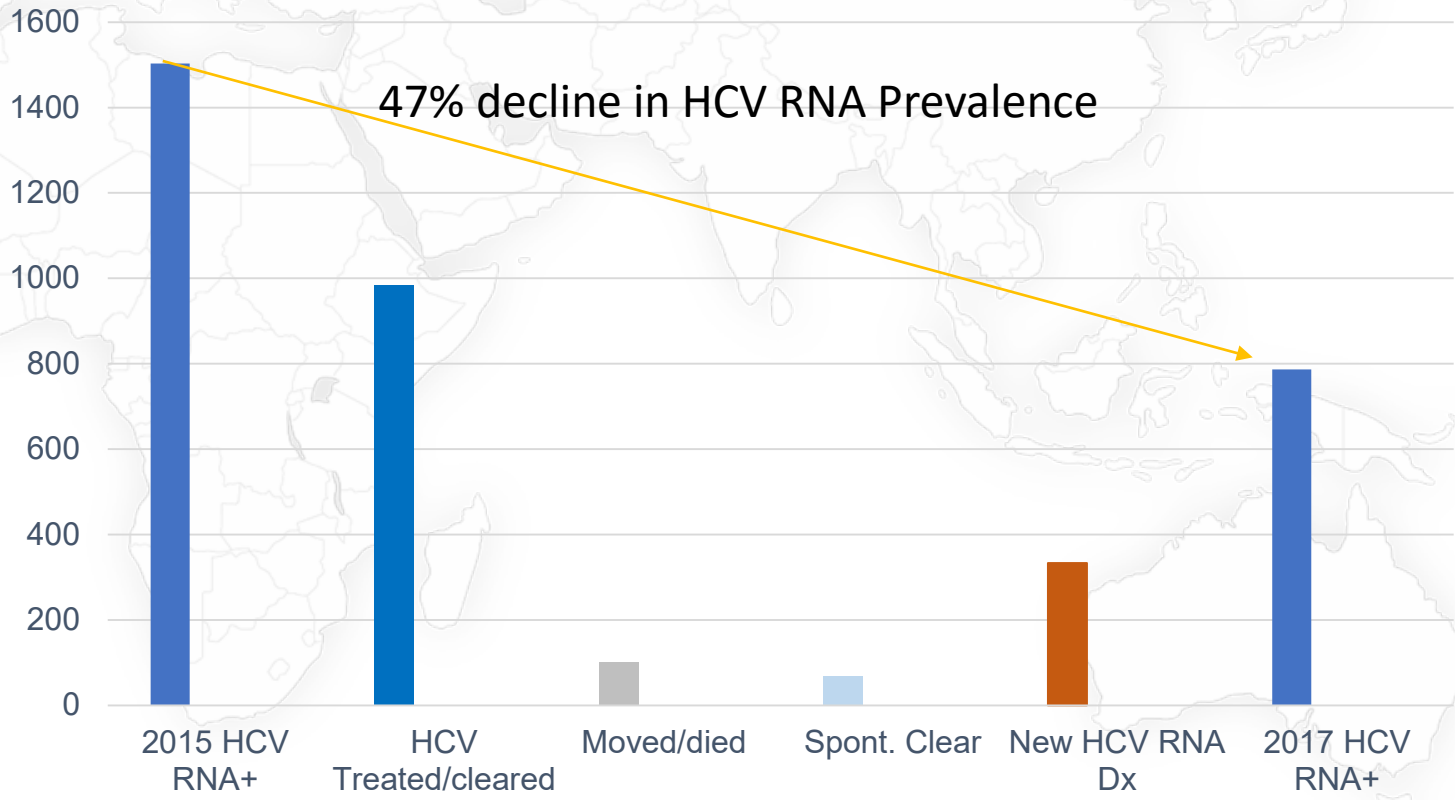
Risk- based Testing with Linkages to Care
Spain -2015-2017

Indicator- HCV RNA + prevalence

- HCV testing- risk based- ~ 26,000/yr.
- HCV all oral treatment

HCV Prevalence

- 1960s birth cohort- 52% of cases
- HIV- 19%
- HCV Rate change from 2.4 to 1.3/1000 (2015-2017)



Juanbeltz R, et al. PLoS One. 2018

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General Population Screening

1945-1965 Birth Cohort Strategy in the United States

- 81% of the HCV infected population
- ~3% anti-HCV prevalence (2010)
- 50% moderate severe liver disease
- 50% reported no risks- health care and drug use exposures in the distant past
- Non-stigmatizing
- Cost-effective $32000 per QALY
- Baby boomer cohort a recognized entity to public
- Policy intended to be time limited

Recommendation for all adult testing (18-79yrs) pending
Potential impact: identify 256,000 additional HCV cases, 280,000 additional cures and 4,400 fewer cases of hepatocellular carcinoma in same time period as current recommendation(1)

Smith B, MMWR, 2012, Rein D, Ann int Med, 2012

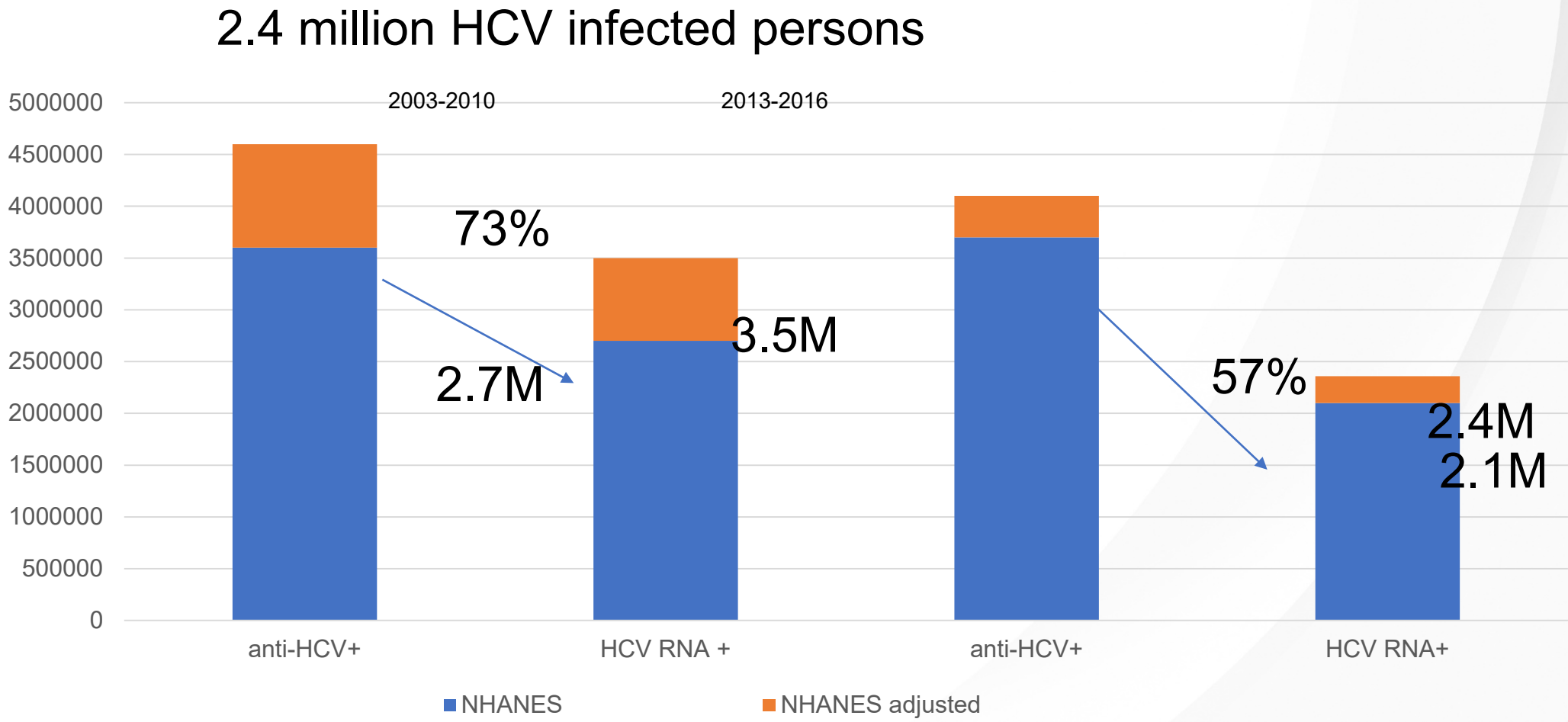
Strategies that Expand Access to HCV Testing- United States

- Policy
- Provider education
- Clinical decision tools (table)
- Reflex RNA testing
- Performance indicators/incentives
- Case management
- Co-localization of HCV and primary care
- Accessible HCV therapies

	Study	Strategy	Increase in testing	Total tested
	Primary care	BPA- Best practice alert	Two fold Increase	71%
	Primary care	BPA	15 fold increase	11%
	Health system	BPA and clinical support	Two fold increase	10%

AJPH 2017, B Reilly MMWR, 2016, Kanwal F,
Gastroenterol Hepatol 2012, Coyle, C, MMWCancer Epidemiol Biomarkers Prev. 2018 R 2015, Mera, MMWR 2016, Canary L, Ann Int Med 2
CDC unpublished data; Klonerman , Hepatology 2017; Kasting M, Can Epid and Biomarkers 2018

Declines in HCV Prevalence- United States



Hofmeister M, Hepatology 2018

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General Population HCV Testing
Essential components of effective elimination programs: Egypt

Political commitment

- 10 yrs of small-scale program
- External assistance obtained (e.g., USCDC, World Bank, industry)
- President launches HCV campaign to test all persons 18-59 yrs.

Negotiating affordable diagnostics/ medications

	Prices in US $	
	2017	2018 (Campaign)
HCV antibody Elisa	5	0.7
HCV antibody rapid test	5	0.56
HCV RNA RT-PCR	20	4.8
Treatment (12 weeks (sofosbuvir + daclatasvir)	80	42

Decentralization: Broad-based screening & treatment

- Testing in clinical and community (mobile) settings
- No co-pays
- Network of 60 treatment centers

Source: Egyptian national HCV program data courtesy of Dr. Imam Waked

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General HCV Testing
Pakistan is a High Burden Country Beginning Development of an HCV Elimination Program

Achievements to date

commitment

- Recent political commitment
- National plan
- Local coalition of stakeholders

Phase 2: Set the foundation

- Negotiated affordable HCV medications <US$ 40 per cute
- Field studies of HCV testing and treatment
- Identified effective screening and treatment strategies (modeling)

Phase 3: Challenges to achieving scale

-Test 25 m /year
-Treat 700,000 year

This scale-up could lead to…

- Only with point-of-care anti-HCV and PCR

Potential impact of reaching 2030 targets

	Baseline	2030
Prevalence	8.27M	89,000
Incidence	281,000	9200
Mortality	93,300/ yr	323,000 (averted)
DALYs	60.74M total	13M (averted)
Cost	$684M/yr	**$2.6b (saved)***

Challenges for phase 1 and 2 persist

- Strategic information for planning
- Provincial-level government buy-in
- **Need policy of one time HCV testing of all adults**
- Limited partnerships to date (except CDC)

- Monitoring and accountability system
- **Negotiate affordable diagnostic costs**
- Reduce or eliminate costs for patients
- Health promotion campaign

Chhatwal JAMA Online 2019,
Saeed Hamid, personal communication

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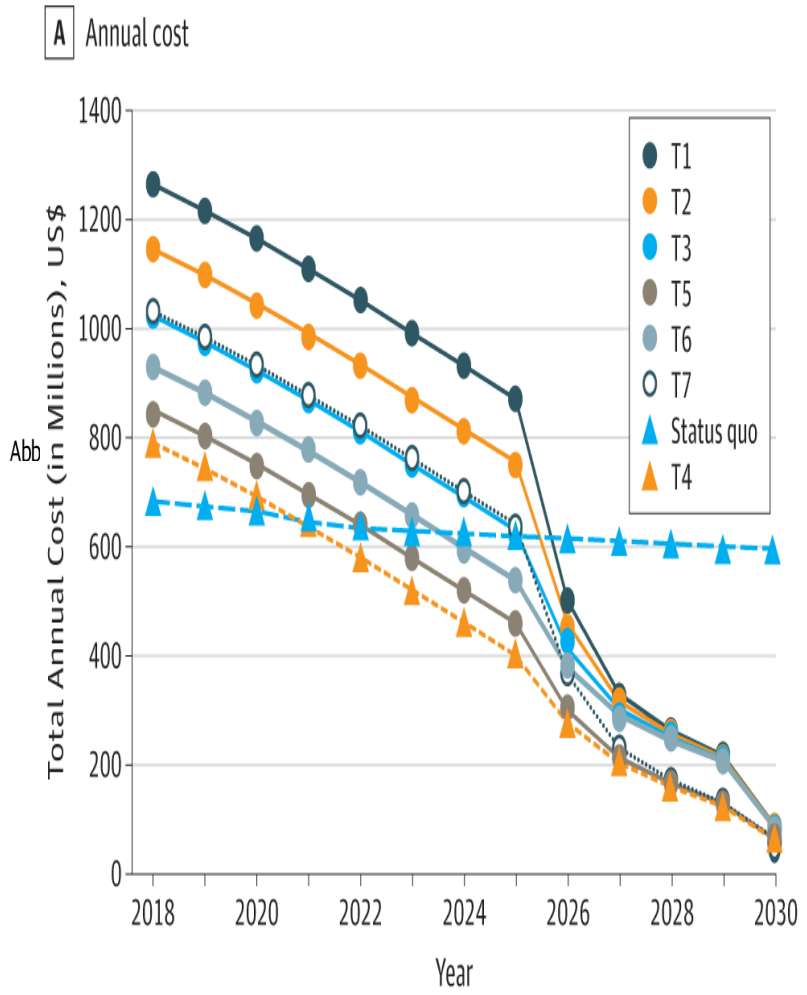
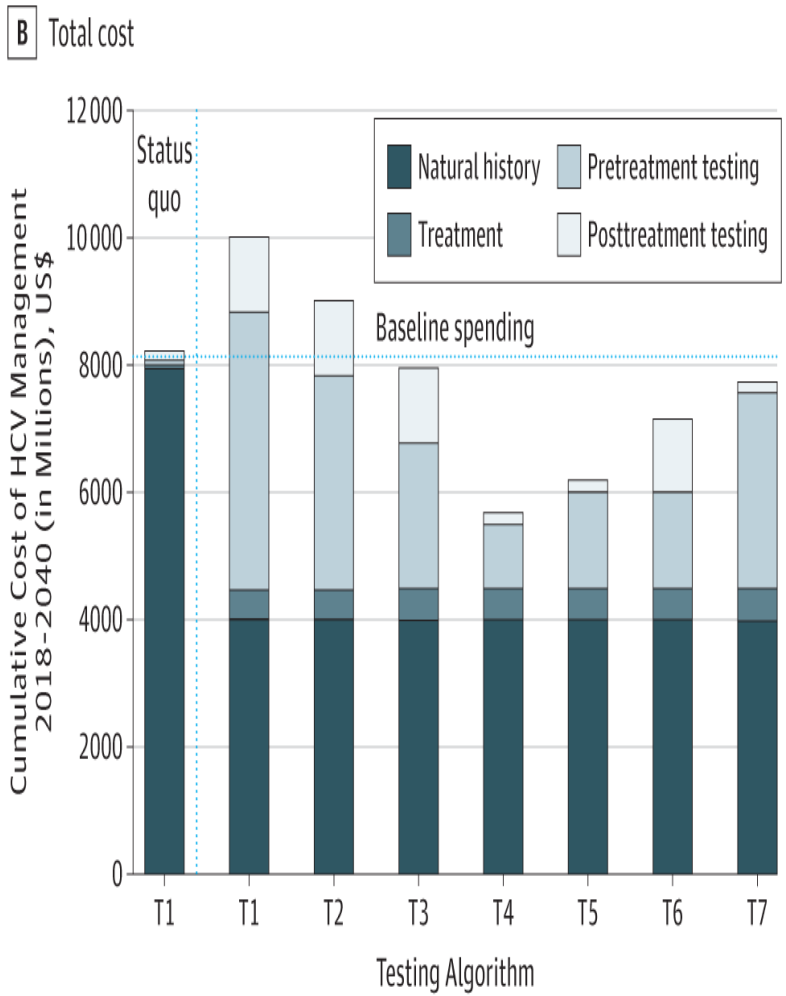
Models can Guide Selection of Cost-effective Testing Strategies Pakistan

Table. Different Hepatitis C Virus Testing Algorithms Evaluated to Scale Up Interventions in Pakistan[a]

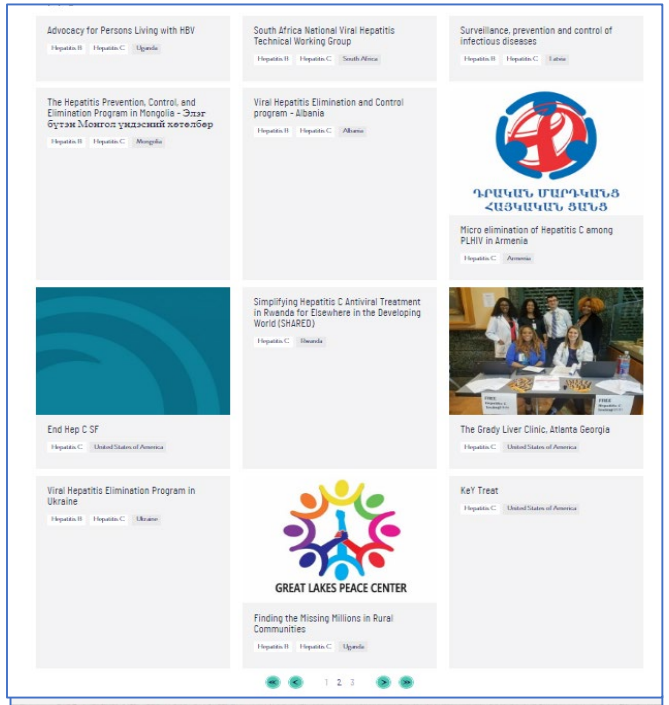
Testing Algorithm	Screening Test	Detection of Viremia	Assessment of Hepatitis C Treatment Response
T1 (base case)	Laboratory based	Nucleic acid test	Nucleic acid test
T2	Laboratory based	HCVcAg test	Nucleic acid test
T3	Point of care	Nucleic acid test	Nucleic acid test
T4	Point of care	GeneXpert	GeneXpert
T5	Point of care	HCVcAg test and nucleic acid test if HCVcAg test result is negative	HCVcAg test
T6	Point of care	HCVcAg test and nucleic acid test if HCVcAg test result is negative	Nucleic acid test
T7	Laboratory based	GeneXpert	GeneXpert

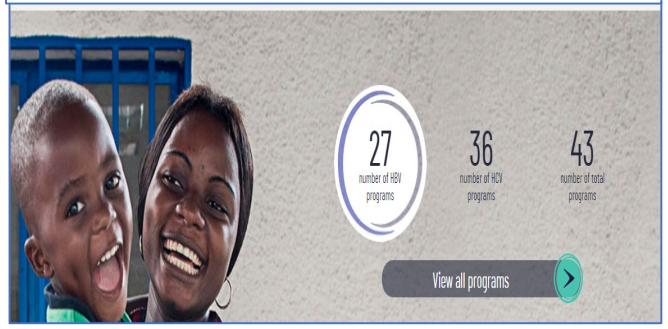


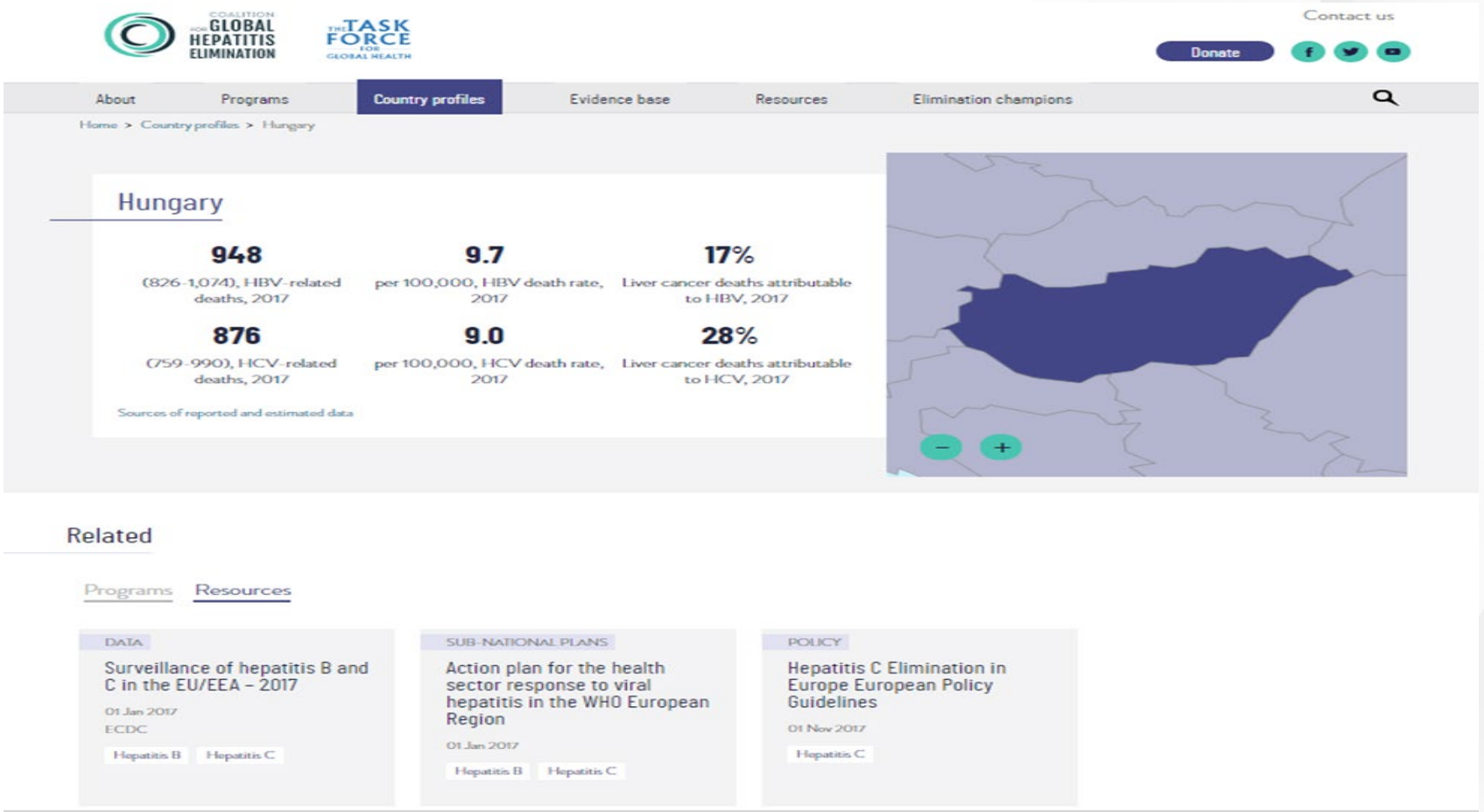


Chhatwal J, JAMA NETW OPEN 2019

Coalition for Global Hepatitis Elimination
A community of practice to improve information sharing and assist future actions







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CGHE Developing a Web-based Tool for Budget Based Planning HCV Testing and Treatment

1 Inputs

Alabama

Prevalence

Number of adults with chronic hepatitis C (in 2015): 31,085

Edit | Update Plots | Reset

Interventions Default Values

Screening | Treatment | Costs

Screening Strategies

Show/Hide Screening Rates

Medicaid: Birth cohort (1945-1965)

Medicare: Birth cohort (1945-1965)

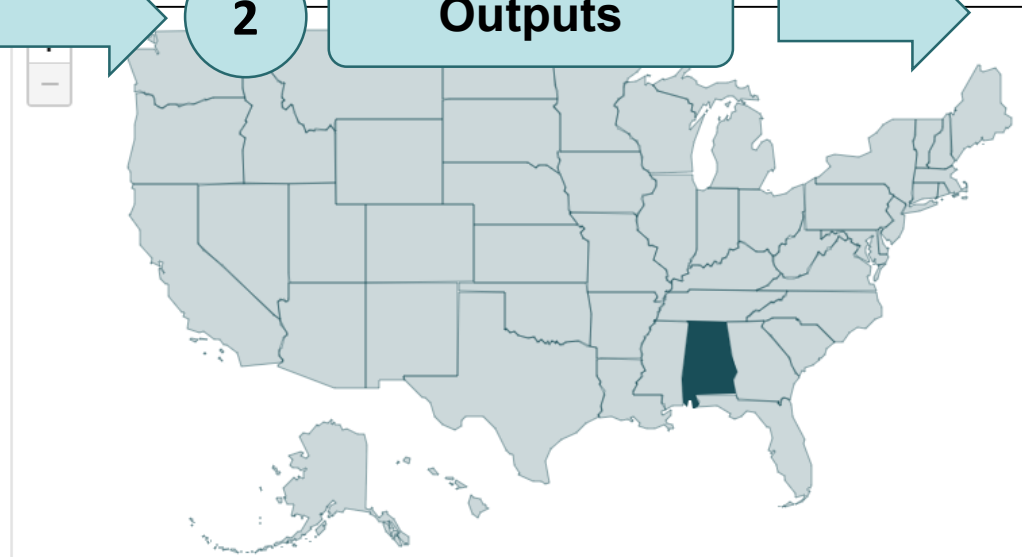
Private: Birth cohort (1945-1965)

Incarcerated: Diagnostic & risk-based

Uninsured: Diagnostic & risk-based

Update Plots | Reset

2 Outputs



Disease Burden | Cost Burden

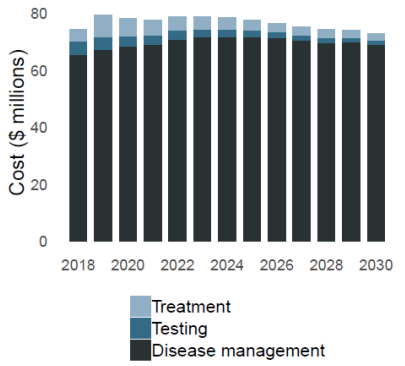
Temporal trends in chronic and cured hepatitis C infections for Alabama

- Estimated number of individuals cured of hepatitis C infections at the end of 2030 is 25,500
- Estimated number of individuals living with diagnosed chronic hepatitis C infections at the end of 2030 is 2,360
- Estimated number of individuals living with undiagnosed chronic hepatitis C infections at the end of 2030 is 11,800

Note: The numbers change, depending on the subpopulations selected. The default includes all subpopulations.

3 Policy brief

Temporal trends in hepatitis C-related costs for Alabama



- Cumulative spending on hepatitis C treatment between 2019 and 2030 is an estimated $49.7 million
- Cumulative spending on hepatitis C screening between 2019 and 2030 is an estimated $31.1 million
- Cumulative spending on hepatitis C disease management between 2019 and 2030 is an estimated $843 million

Note: The results begin in 2019 but the plot includes 2018 as a reference point.

Subpopulations included in plot: Medicaid, Medicare, Private, Incarcerated, Uninsured

Note: The results presented on this slide are from simulated data

Hep C

https://www.hepcsimulator.org/

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High-priority project: core Ag test to enable test and treat approach

Attribute	Current status	
IMPLEMENTATION SETTINGS	Levels 0-1	
PLATFORM FORMAT	Lateral flow	
DETECTION	2 prototypes: 1) Colorimetric (visual readout) 2) Fluorimetric (reader device)	
SENSITIVITY (target 85%)	70%	
SPECIFICITY (target 98%)	95%	
Sample pretreatment	Plans to integrate sample preparation into an easy-to-use, manually actuated rotocol (ongoing)	
Test costs (production costs, estimated)	< 2 US $	< 2 US $

- HCV core antigen level correlates well with HCV RNA level
- HCV core antigen can be used for diagnosis of active infection and to document cure
- A point-of care test could be used to detect HCV and start treatment in single visit
- Main technical challenge: antigen-antibody separation
- high analytical sensitivity requirements unlikely to be met in RDT format

- Project timeline:
  - Design-lock assay: end 2020
  - Regulatory submission Q3 2021

Slide provided by Elena Ivanovar

Optimization of Hepatitis C Screening

- **Strategic information** –
  - Plan- surveillance, serologic surveys, clinical data
  - Evaluate – test volume, results
- **Policy development** – HCV testing policies are needed at national level
  - Target –minimum
  - Scale up to population-based testing as appropriate
- **Financial planning** (budgetary, cost- effectiveness)
  - Negotiate affordable costs
  - Model test options for budget planning
- **Feasible/ effective implementation**
  - Tailor best practices to meet local needs
  - Integrate into existing health systems
- **Technology**
  - Assure quality
  - Efficient use of existing platforms

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