Pricing of Drugs and Formulary Placement: Making Sense of Hepatitis C Treatment

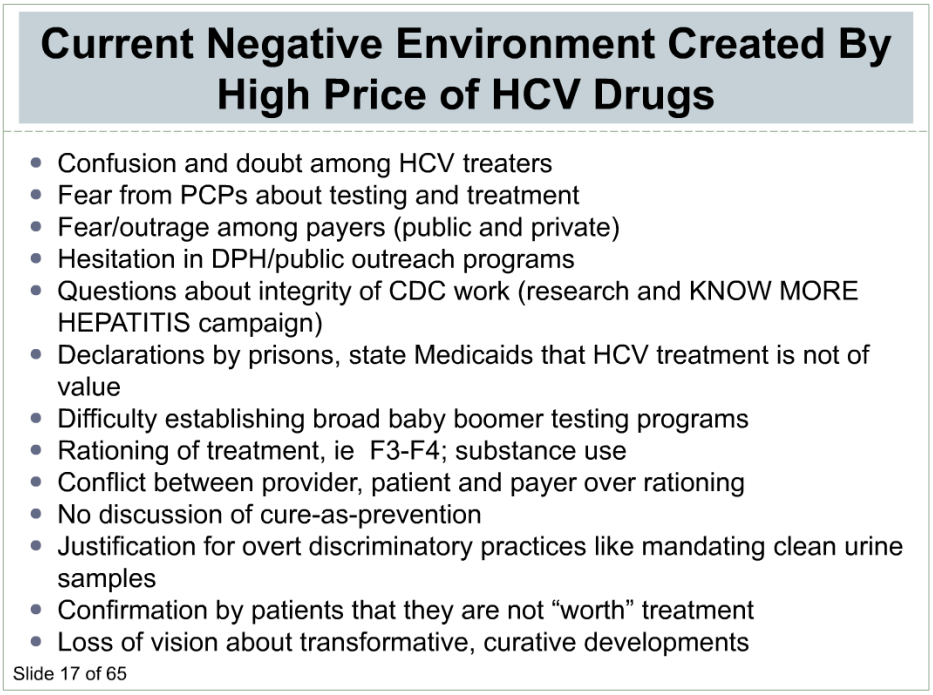
Camilla S. Graham, MD, MPH
Co-Director, Viral Hepatitis Center, Division of Infectious Disease
Beth Israel Deaconess Medical Center and Harvard Medical School
Boston, Massachusetts

Tuesday, March 31, 2015

GOLD SUPPORTERS
Bristol-Myers Squibb
AbbVie
Gilead Sciences, Inc

SILVER SUPPORTER
Merck & Co, Inc

https://www.iasusa.org/content/pricing-of-drugs-and-formulary-placement-webinar-2015
https://iasusa.adobeconnect.com/_a1090822362/p2h0yk85lmq/?launcher=false&fcsContent=true&pbMode=normal
(ok to skip the first 5-7 minutes of the presentation)



Confusion and doubt: Who should we be treating?
Fear of testing: Why make people anxious and not be able to treat them?
Public health programs stymied because why find people and then not be able to treat them?
Deliberate rationing
Vulnerable patient population already stigmatized, now experiencing overt discrimination, in effect telling patients they aren't worthy of being treated.

Landscape is complex and changing quickly.

How did we get ourselves into this mess?

Payer Landscape

- Commercial insurance coverage
  - >600 total insurance companies and many plans in US
  - Large national companies (United, Anthem)
  - Regional companies
  - Closed companies (Kaiser, Geissenger)
  - May manage employer based plans
  - May negotiate prices on own or use PBM
- Medicaid
  - Every state Medicaid is different (!)
  - Fee for service
  - Managed Care Medicaid
  - Medicaid expansion plans under ACA
  - Automatic 23.1% rebate off “best price” for FFS plans under ACA

Slide 19 of 65

Landscape is overwhelmingly incredibly more complicated than in any other nation on Earth.

Payer Overview

- Medicare
  - Complicated Part D plans (“donut hole”)
  - Government prohibited from negotiating prices with pharmaceutical companies
- Veterans Administration
  - Usually obtains substantial Federal discount on price (>40%)
- Corrections
  - Federal prisons receive federal discount; state and local jails and prisons more fragmented systems

Slide 20 of 65

VA negotiates not only for themselves but also for military (DoD), IHS, and Federal prisons (Federal supply schedule).
Results of all negotiations are secret.
Most imprisoned people (in “corrections”) are in state prisons and have essentially no care.

Payer Overview (con't)

- Pharmacy benefits managers (PBM)
  - Companies such as Express Scripts, CVS Health
  - Manage formularies and engage in contract negotiations on behalf of plans
  - Due to large volume of lives covered, can often negotiate better terms than smaller plans could on their own
- Specialty Pharmacies
  - May be preferred-providers by specific plans
  - Receive payments in exchange for delivery of services (should not just be filling prescriptions)

Slide 21 of 65

Specialty pharmacies should be providing adherence support, etc.

Price and Cost

- Price of a drug/regimen is set by the pharmaceutical company
  - Reported as Wholesale Acquisition Cost (WAC)
- Wholesale distributors add a mark-up
  - Average Wholesale Price (AWP)
  - This is typically the benchmark on which reimbursement is based
- PBMs (and some insurance plans) negotiate rebates, which determine actual cost
  - These have competitive implications and are confidential
- Mandated discounts with Federal plans

Slide 22 of 65

http://www.nhpf.org/library/issue-briefs/IB775_AWP_6-7-02.pdf

Payer Actions

- May create own cost-effectiveness and budget impact models
- Treatment guidelines
  - Usually derived from existing guidelines
- Formulary placement
- Reimbursement/contracting
- Prior authorization criteria
- Can contact the medical director and pharmacy director responsible for these activities

Slide 23 of 65

Pharma Pricing Strategies

- Cost-effectiveness models
- Budget impact models
- Benchmarking against similar regimens
- Surveys and focus groups with payers (commercial and public insurance, PBMs) to understand what market will bear
- Expectations of shareholders
- Cost of investment in drug development
- Cost of manufacturing and marketing

Slide 24 of 65

Costs of investments in drug development, manufacturing, and marketing play a relatively small role in pricing decisions. They're usually irrelevant considerations.

Let's Pretend We Are the Team Helping Set Ledipasvir/Sofosbuvir Price

Factor	Price Implication
Lifetime cost of not treating anyone[1]	$100.3 billion
Cost-effectiveness vs no treatment at $50,000/QALY[1]	$139,000
Benchmark (WAC 2013): Telaprevir+Peg-IFN+RBV x 24 weeks	$97,680
Real-world all cost-per-cure PI/Peg-IFN + RBV [2]	$125,915 – $302,070
Benchmark (WAC 2014): Sofosbuvir+Peg-IFN+RBV	$94,421
Cost-per-cure of drugs: SOF+P+R (90% SVR)	$104,912
Maximum market will bear (WAC; 2014): Sofosbuvir+Simeprevir x 12 weeks	$150,000
Premium for all-oral regimen (difference in cost-per-cure for Peg-IFN + RBV versus SOF + R in genotype 2)	$42,000
Premium for one-pill-once-a-day	$1,000
Cost-per-cure ledipasvir/sofosbuvir x 12 weeks (if 95% SVR)	X + 5%
Price for ledipasvir/sofosbuvir for 12 weeks	???

Slide 25 of 65

[1]Rein, CID 2015; [2]Sethi, AASLD 2013; 1847

CDC estimates that hepatitis C will cost $100 billion for all the people currently infected if we do nothing about it. Price at which hepatitis C treatment is cost-effective is $139,000 (according to Rein *et al*.).

(assumes cost of peg/riba x 12 weeks = $13,680?)

Examples for Treatment of Genotype 1, Naïve, Non-Cirrhotic Patients

Regimen	SVR rates	WAC Price	Cost per SVR
Telaprevir + PegIFN + Ribavirin x 24 weeks[2]	75%	$86,843	$115,791
Sofosbuvir + PegIFN + Ribavirin x 12 weeks	90%	$94,421	$104,912
Sofosbuvir/Ledipasvir x 8 weeks	94%	$63,000	$67,021
Sofosbuvir/Ledipasvir x 12 weeks	99%	$94,500	$95,454

Slide 26 of 65

Package inserts for products

Cost-Effectiveness of HCV Treatment

Study	Key Findings
Leidner, Hepatology 2015	For 55 y/o treated with $100,000 regimen and SVR = 90%, treating at F2 compared to waiting until F3 had CE = $37,300/QALY Threshold cost for treating at F0 versus waiting until F1 to yield $50,000/QALY = $22,200
Rein, CID 2015	Ledipasvir/sofosbuvir and ombitasvir/paritaprevir/r + dasabuvir tablets compared to no treatment yields $32,000 to $35,000/QALY Compared to no treatment, threshold cost for treating F0 with all-oral regimen = $47,000
Najafzadeh, Annals Int Med 2015	Compared to no treatment in genotype 1, costs per additional QALY gained for ledipasvir/sofosbuvir = $25,291 and Peg-IRN + RBV = $24,833 If ledipasvir/sofosbuvir <$66,000/treatment course, would be cost saving
Chhatwal, Annals Int Med 2015	Average ICER for sofosbuvir-based treatment compared to prior SOC = $55,378/QALY Range = $9,703/QALY for naïve, cirrhotic geno 1 to $410,548 for treatment experienced, geno 3 without cirrhosis

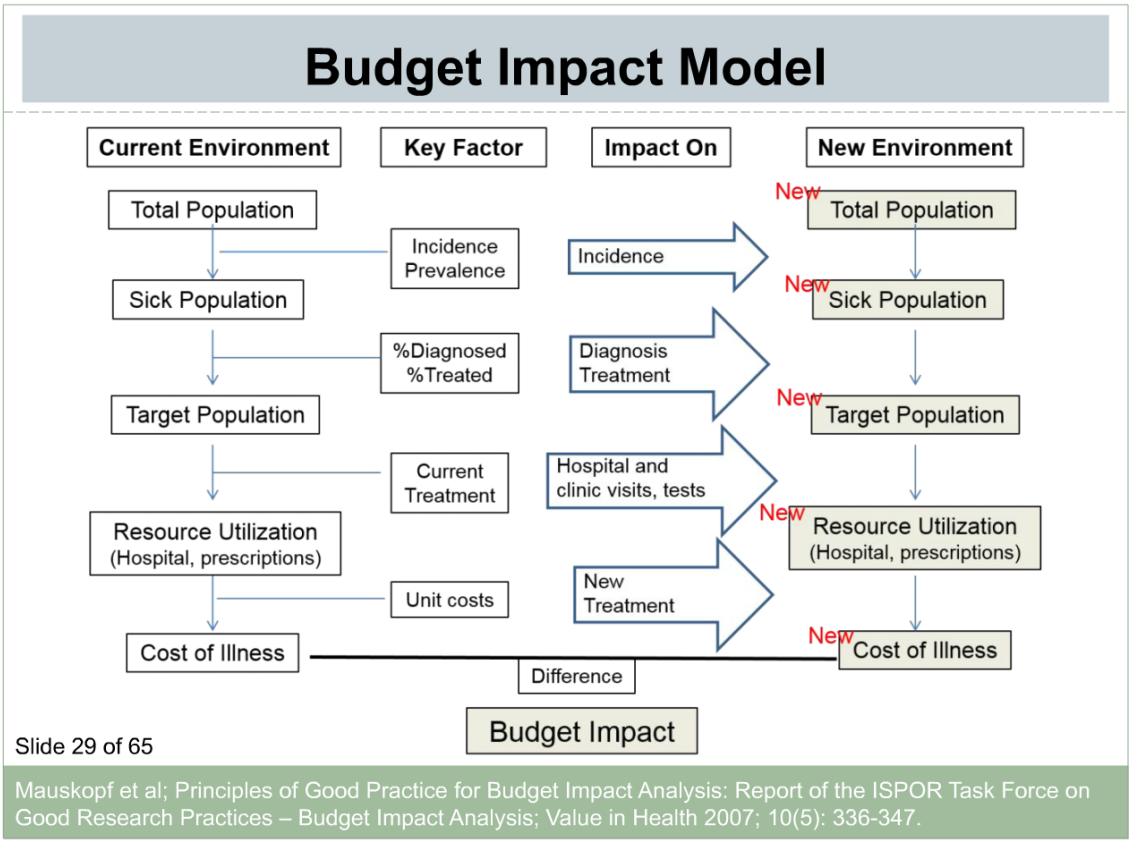
Slide 27 of 65

also Linus *et al*. Annals geno 2 and 3

Why are People Still Hysterical About HCV Drug Prices?

- Up until the approvals of sofosbuvir and simeprevir, payers relied on the inability/refusal of most patients to take interferon-alfa as the mechanism to keep HCV drug expenditure down
- With the combinations of sofosbuvir+ribavirin and sofosbuvir +simeprevir, nearly all patients with HCV infection theoretically could be treated
- How appropriate is this concern about pricing with recently announced reductions in cost?

Slide 28 of 65



Mauskopf et al; Principles of Good Practice for Budget Impact Analysis: Report of the ISPOR Task Force on Good Research Practices – Budget Impact Analysis; Value in Health 2007; 10(5): 336-347.

also Linus *et al*. Annals geno 2 and 3

Institute for Clinical and Economic Review: "The Comparative Clinical Effectiveness and Value of Simeprevir and Sofosbuvir in the Treatment of Chronic Hepatitis C Infection" for the California Technology Assessment Forum

Factor	Result
Enrollee plan	1 million enrollees
1.7% prevalence HCV infection	17,000 enrollees
50% undergo treatment in one year	8,500 enrollees
Estimated HCV treatment cost (per 1 enrollee)	$70,588
Total treatment (8,500 x $70,588)	$600 million
Cost of HCV treatment per enrollee ($600 million/1 million enrollees)	$600/year
Cost per member per month	$50

Conclusion: Simeprevir and sofosbuvir are superior in terms of clinical effectiveness compared to 1st generation PIs + Peg-IFN/RBV, but of "low value" due to high cost

Slide 30 of 65

Cost per member per month = cost for each person covered by the plan to pay
$50/member/month (for every single person covered to pay for hepatitis C treatment alone) is outrageous and completely impossible.

Unique Aspects of Hepatitis C

- Relatively common disease
- Majority of people infected 20 – 40 years ago (75% in 1945-1965 birth cohort)
- Peak of severe liver complications expected to occur over this next decade, so urgency to identify and treat people soon
- Everyone who has >1 year life expectancy is theoretically a treatment candidate
- Pricing more similar to treatments for rare diseases

Slide 31 of 65

Payer Dilemmas

- Most payers had no idea how much they were actually spending per treated patient (or per cure) in the interferon era
  - PI/Peg-IFN + RBV in cirrhotic patients ~ $266,000 per cure[1]
- Pharmacy budgets often separate from medical budgets
  - Pharmacy budgets don't get "credit" for avoidance of medical costs
  - Annual budgets
    - "Is it cost effective?" (off-sets over the long term)
    - "Is it affordable?" (costs over one year)

Slide 32 of 65

[1]Sethi, AASLD 2013

Being cost-effective (in the long term) doesn't make it affordable (in the short term).

Negotiating Prices

- Press releases and conference calls give a glimpse into this world:
  - Gilead reveals a 46% gross-to-net discount compared to 22% in 2014
  - Veterans Administration given >50% discount
  - ADAP Crisis Task Force negotiates "voluntary discounts for ombitasvir/paritaprevir/r + dasabuvir tablets that are significantly lower than the WAC"
  - Payers and PBMs representing 60% of covered lives – 80% have access to ledipasvir/sofosbuvir

Slide 33 of 65

We have had "mind-blowing" progress in price negotiation in recent months.
Gilead's "46%" discount – I think this is wrong – it was their prediction for 2015, not actual in 2014, averaged over all payers (incl. VA).

What Does This Mean for HCV Regimens?

Regimen	WAC Price	46% Discount
SOF + LDV x 8 wks	$63,333	$34,200
3D + RBV x 12 wks	$85,820	$46,343
SOF + LDV x 12 wks	$95,000	$51,300
SOF/LDV + RBV x 12 wks	$97,500	$52,650
SOF + SMV x 12 wks	$150,000	$81,000
3D + RBV x 24 wks	$171,640	$92,686
SOF + LDV x 24 wks	$190,000	$102,600
SOF + SMV x 24 wks	$300,000	$162,000

Slide 34 of 65

With a 46% discount, sof/ldv is $34,200-$51,300 for an 8-12 week course.

Recommended regimens for patients with HCV genotype 1a or 1b infection who have compensated cirrhosis, in whom prior PEG-IFN and RBV treatment has failed

	Cost (with discount)
• **Daily fixed-dose combination of ledipasvir/sofosbuvir for 24 weeks** **Rating:** Class I, Level A	**$102,600**
• **Daily fixed-dose combination of ledipasvir/sofosbuvir + weight-based RBV for 12 weeks…** **Rating:** Class I, Level B	**$52,650**
• **Daily fixed-dose combination of paritaprevir/ritonavir/ombitasvir + twice-daily dosed dasabuvir and weight-based RBV for 24 weeks is recommended for patients with HCV genotype 1a…** **Rating:** Class I, Level A	**92,683**
• **Daily sofosbuvir plus simeprevir with or without weight-based RBV for 24 weeks…** **Rating:** Class IIa, Level B	**$162,000**

Slide 35 of 65

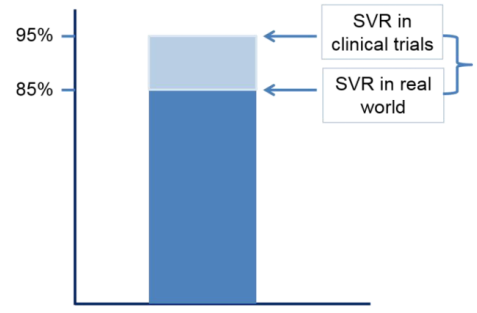
Adapted from www.hcvguidelines.org

HCV Providers Collaborating with Payers

- Share your understanding and concern about the budget impact of HCV treatments
- Efficacy and safety will not be compromised (non-negotiable)
- Express responsibility for our shared resources:
  - For reasonably equivalent treatment options, include cost as a factor
  - Optimize adherence and AE management
  - Prioritize reducing re-infection rates
  - Minimize other causes of liver damage like alcohol

Slide 36 of 65

Hypothetical Costs of Not Optimizing SVR Rates in Clinical Practice



10% difference in SVR rates for a $100,000 regimen result in:

- $12,384 "loss $ per unachieved cure" for each patient
- Cost of retreating all patients who did not achieve SVR
- Costs of liver complications (decompensation, liver cancer, etc.) in those who are not cured and progress

Slide 37 of 65

Prioritization Versus Rationing

- Prioritization involves determining and balancing:
  - Medical needs
    - Immediacy of patient suffering
    - Risk of increasing medical complexity of management
    - Future costs of complications (or not intervening)
    - Public health risks
  - Resource constraints
    - Provider capacity (eg, MA has ~150,000 patients with hepatitis C infection and ~250 HCV providers)
    - Distribution of providers
    - Financial limits (payer horizon typically ~1 to 3 years)
  - Most of us can accept prioritization

Slide 38 of 65

At the rate we are going in Massachusetts it will take us about 10 years to treat everybody.

Rationing

- Limiting access to medical care
- Often non-attributable in US
  - Lack of or under insurance
  - Lack of access to appropriate providers
  - High co-pays
- Frank denial of medication coverage by payers
  - Usually when a less expensive, "equivalent" alternative is available
- Much of EU, Canada, Australia ration medicine based on urgency of medical needs and anticipated clinical benefit
- Can be based on bias/discrimination

Slide 39 of 65

Rationing is usually done when there is a less expensive "equivalent" alternative. I can't think of another situation in which we are told that a person with a treatable disease has zero treatment options.

Treatment Priority Per AASLD/IDSA/IAS–USA HCV Guidance

1. Patients with highest risk for severe complications
   - Advanced fibrosis or compensated cirrhosis
   - Organ transplant
   - Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (ie, vasculitis)
   - Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

Treatment Priority Per AASLD/IDSA/IAS–USA HCV Guidance

2. Patients with high risk for complications
   - Stage 2 fibrosis
   - HIV coinfection
   - HBV coinfection
   - Other coexistent liver disease (ie, NASH)
   - Debilitating fatigue
   - Type 2 diabetes mellitus (insulin resistant)
   - Porphyria cutanea tarda

These people should be treated when capacity allows.

No one ever implied that these people shouldn't be treated. That's insanity.

Treatment Priority Per AASLD/IDSA/IAS–USA HCV Guidance

3. Persons with high transmission risk
   - MSM with high-risk sexual practices
   - Active injection drug users
   - Incarcerated persons
   - Persons on long-term hemodialysis

Payer Decisions to Limit Access to HCV Treatment

- Medical need restrictions
- Insurance restrictions
- Prescriber restrictions
- Specialty pharmacy restrictions
- Insurance termination / switch during treatment

Medical Need Restriction

- Advanced fibrosis (Metavir F3-F4)
  - Evidenced by liver biopsy, transient elastography, FibroSure, APRI or FIB-4 score, radiological imaging consistent with cirrhosis, physical findings or clinical evidence consistent with cirrhosis as attested by the prescribing physician

Response to Restricting Treatment to F3/F4

- Cannot require liver biopsy (may be highest risk of death in HCV care with all-oral regimens)
- Since no test can perfectly distinguish F2 from F3 or F3 from F4, limiting access to F3/F4 really means directing treatment to cirrhotic patients
- If we wait until advanced fibrosis, need to do life-long screening for HCC every six months even if cured (expense, logistics, patient anxiety)
- Prioritization of F2-F4 unless other compelling urgency may align with provider capacity

Restrictions Based on Current or History of Substance Use

- Prescriber assessment and documentation
  - 3 to 12 months sobriety/abstinence from EtOH/drug use
  - Completion or enrollment in a treatment center
  - May require drug testing results
- Participate in counseling services
- Engage in care with an addiction specialist

Compare: Department of Veterans Affairs (VA) Guidelines for PWID

"There are no published data supporting a minimum length of abstinence as an inclusion criterion for HCV antiviral treatment. Patients with active substance- or alcohol-use disorders should be considered for therapy on a case-by-case basis and care should be coordinated with substance-use treatment specialists."

- http://www.hepatitis.va.gov/provider/guidelines/2014hcv/special-groups.asp

Slide 47 of 65

Center for Health Law and Policy Innovation of Harvard Law School

Discussing Substance Use Restrictions with Payers

- Address potential impact on adherence
  - Many people with substance use issues able to remain adherent
  - Data from peg-IFN/RBV treatment shows good adherence with adequate support
- Concern about reinfection
- Legal medical marijuana use
  - May improve adherence via management of side effects
- Most DAA clinical trials allow methadone +/- buprenorphine – not a concern with adherence
  - Need programs that integrate HCV treatment into opiate replacement centers
- Inability to study cure-as-prevention
- Ask: Would we limit treatment in someone with XX disease?

Slide 48 of 65

Would we tell cancer patients you can't have chemotherapy until you demonstrate 6 months of abstinence from drugs and alcohol. It would be unthinkable.

Prescriber Restriction

- Medication has to be prescribed by:
  - Hepatologist
  - Gastroenterologist
  - Infectious disease specialist (not allowed in some states)

This is demeaning to our colleagues in internal medicine.

It also exacerbates the shortage of providers, and we need to address the shortage of providers.

IDSA Response

- Letter explaining why infectious disease physicians are well-positioned to provide HCV care
  - Most experience with HIV/HCV coinfection
  - Experience with clinical trials; on FDA committees
- ECHO/Telemedicine programs pair specialists with our primary care colleagues who provide HCV care

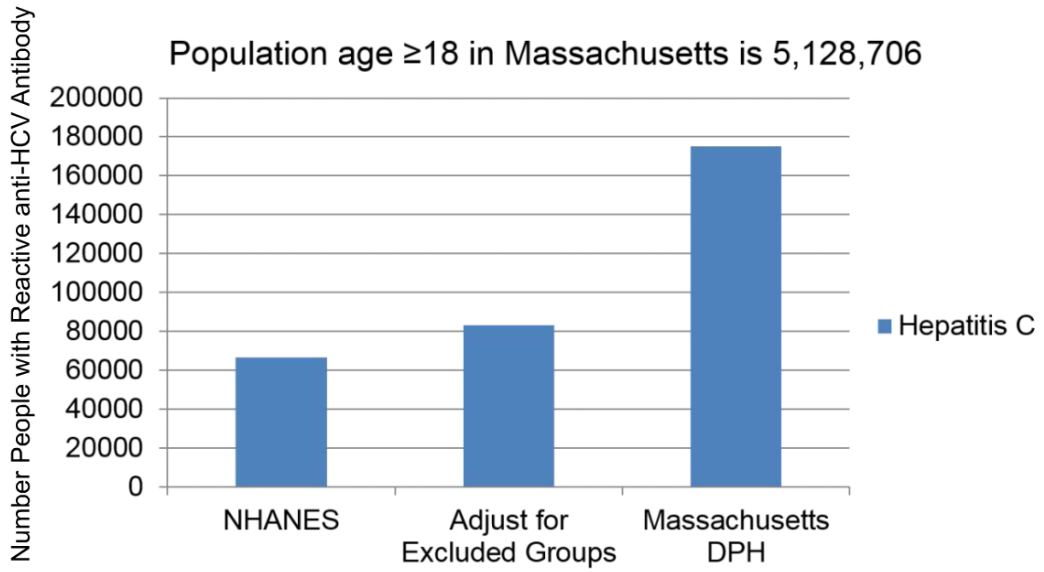
Insufficient Information to Determine Allocation of Resources in Hepatitis C

- Inadequate funding for state-level HCV surveillance
  - Difficult to determine who has HCV and trends in incident infection rates
- Inadequate understanding of HCV treater capacity issues
  - Difficult to design linkage to care programs

Importance of State-Specific HCV Epidemiology Data to Develop an Advocacy Base

- Education of primary care providers:
  - Personalize the importance of hepatitis C as a disease they will see and manage
  - Increase interest in implementation of HCV screening programs in their health systems
- Increase awareness with policy makers
  - Advocate for legislation
  - Mobilize resources for local and state departments of public health
- Encourage community awareness and advocacy

Estimates of People with Hepatitis C in Massachusetts

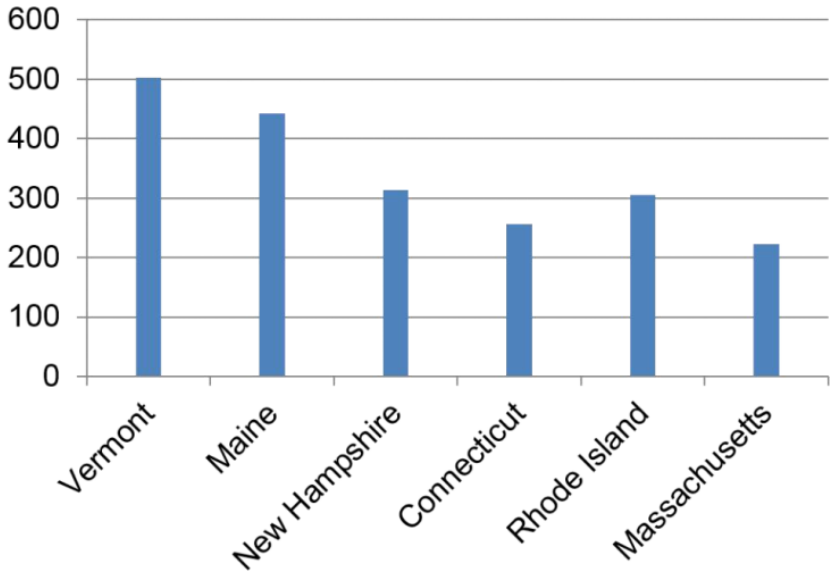


Slide 53 of 65

United States Census Bureau 2010: Age and Sex Compositions (http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf; accessed 7/23/14); Ditah et al. J Hepatology 2014; 60:691 - NHANES HCV survey found 1.3% prevalence anti-HCV in US population age >18; Chak et al. Liver International 2011; 31:1090 - Adjustment for groups excluded from NHANES including homeless, incarcerated, active military and nursing home residents. **www.nvhr.org**

110,000 patients have ***already been reported*** to MA DPH with hepatitis C.

Estimates of the Number of People with Hepatitis C Infection per HCV Provider in New England

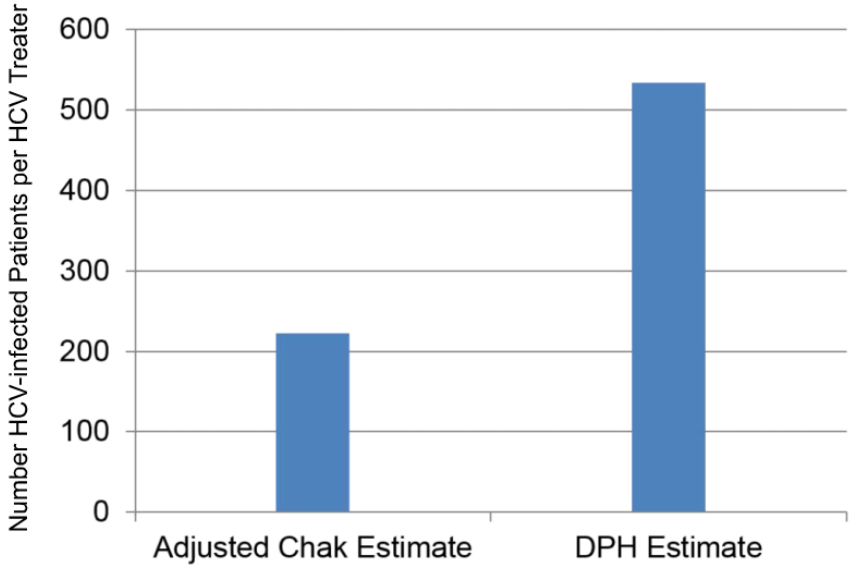


Slide 54 of 65

Chak et al. Liver International 2011; 31:1090 – Estimate 75% of people with anti-HCV antibody reactivity have active hepatitis C infection. Provider data estimated from state-level ribavirin prescription data in 2013-2014. Data kindly provided by IMS. Hepatitis C provider estimate includes everyone who has written at least one prescription for ribavirin. **www.nvhr.org**

and some of these providers probably treat 5-10 patients/year

Estimate of the Number of People with Hepatitis C per HCV Treater in Massachusetts



Slide 55 of 65

Chak et al. Liver International 2011; 31:1090 – Estimate 75% of people with anti-HCV antibody reactivity have active hepatitis C infection. Provider data estimated from state-level ribavirin prescription data in 2013-2014. Data kindly provided by IMS. Hepatitis C provider estimate includes everyone who has written at least one prescription for ribavirin. **www.nvhr.org**

Examples of States Addressing Treatment Access Challenge

- Lynn Taylor, Robert Greenwald and colleagues, Brown University and Center for Health Law and Policy Innovation, Harvard Law School
  - Mapping Medicaid policies for all states
  - Working with CMS on access
- Sheldon Toubman; New Haven Legal Assistance Association
  - Defining legality of restrictions on access to treatment by Connecticut Medicaid
  - May be applicable to other states

Slide 56 of 65

Examples of Approaches to Improve Access to HCV Treatment

- Share successful appeal letters
  - National Viral Hepatitis Roundtable is collecting examples to share (NVHR.org)
- Share stories with media (obtain institutional and patient permission)
- Join local P&T committees
- Educate local payers (public and private) about hepatitis C and the value of treatment
- Consider joining in lawsuits to force access

Slide 57 of 65

This isn't just a story about a $1,000 a pill treatment. These are human being's stories.

Resources

- AASLD/IDSA/IAS–USA HCV Guidance
- Federal guidelines (VA, prison system)
- National Viral Hepatitis Roundtable
  - Collects templates, sample slide presentations, analyses of state and federal policies
  - Program assistance with 1945-1965 birth cohort testing
  - www.NVHR.org

Plus Q and A for another 20 minutes (1:04:30-1:23:53)