Enabling hepatitis C cure for individuals experiencing homelessness

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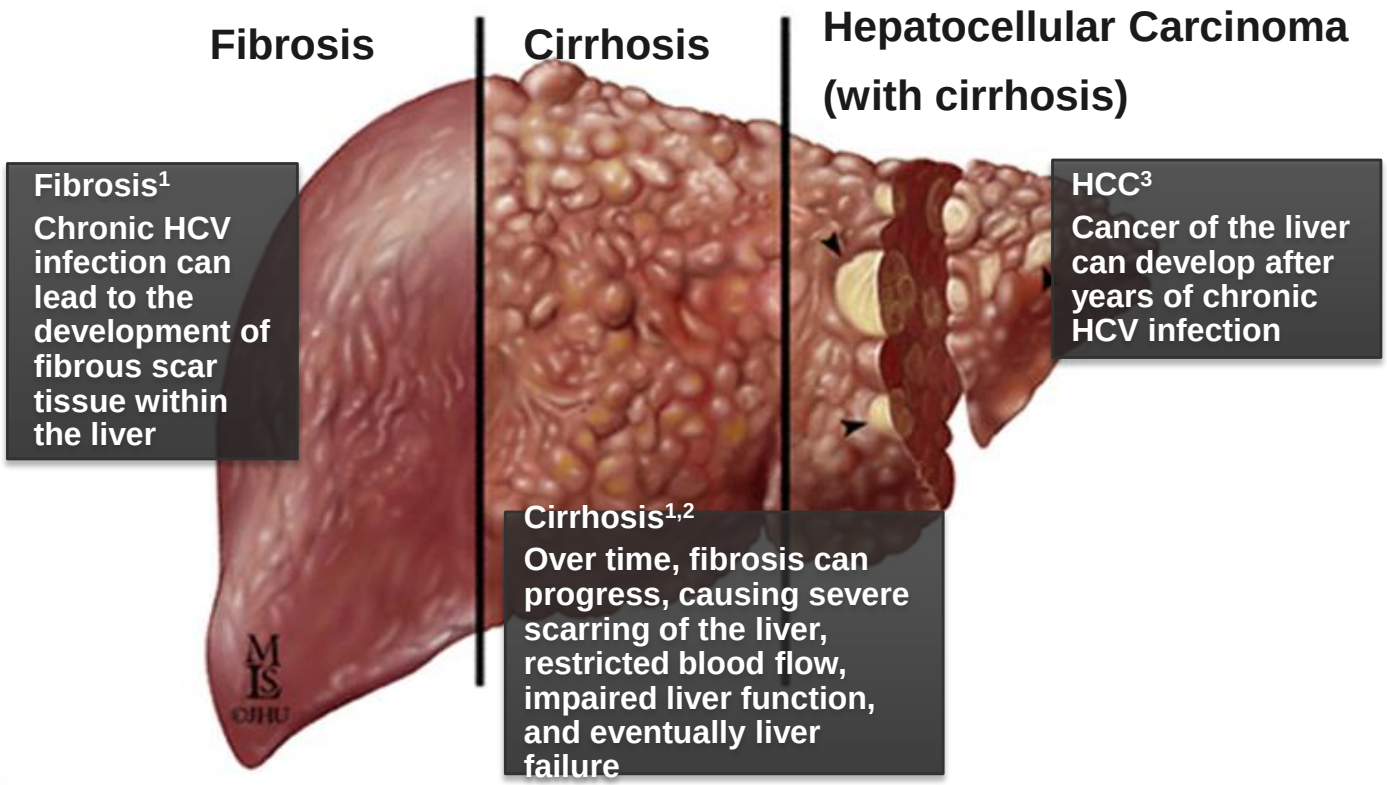
Boston Health Care for the Homeless Program
6/2/16

- I have no disclosures
- Off-label use of hepatitis C medications may be discussed

Outline

- Scope of HCV-related morbidity and mortality
- Strategies to assess HCV-related health in HCH programs
  - Screening
  - Liver fibrosis
  - Enhanced RHM for advanced fibrosis
- Strategies for successful treatment
  - Benefits of HCV cure
  - Team model
  - Tools and Pearls

Chronic HCV Infection



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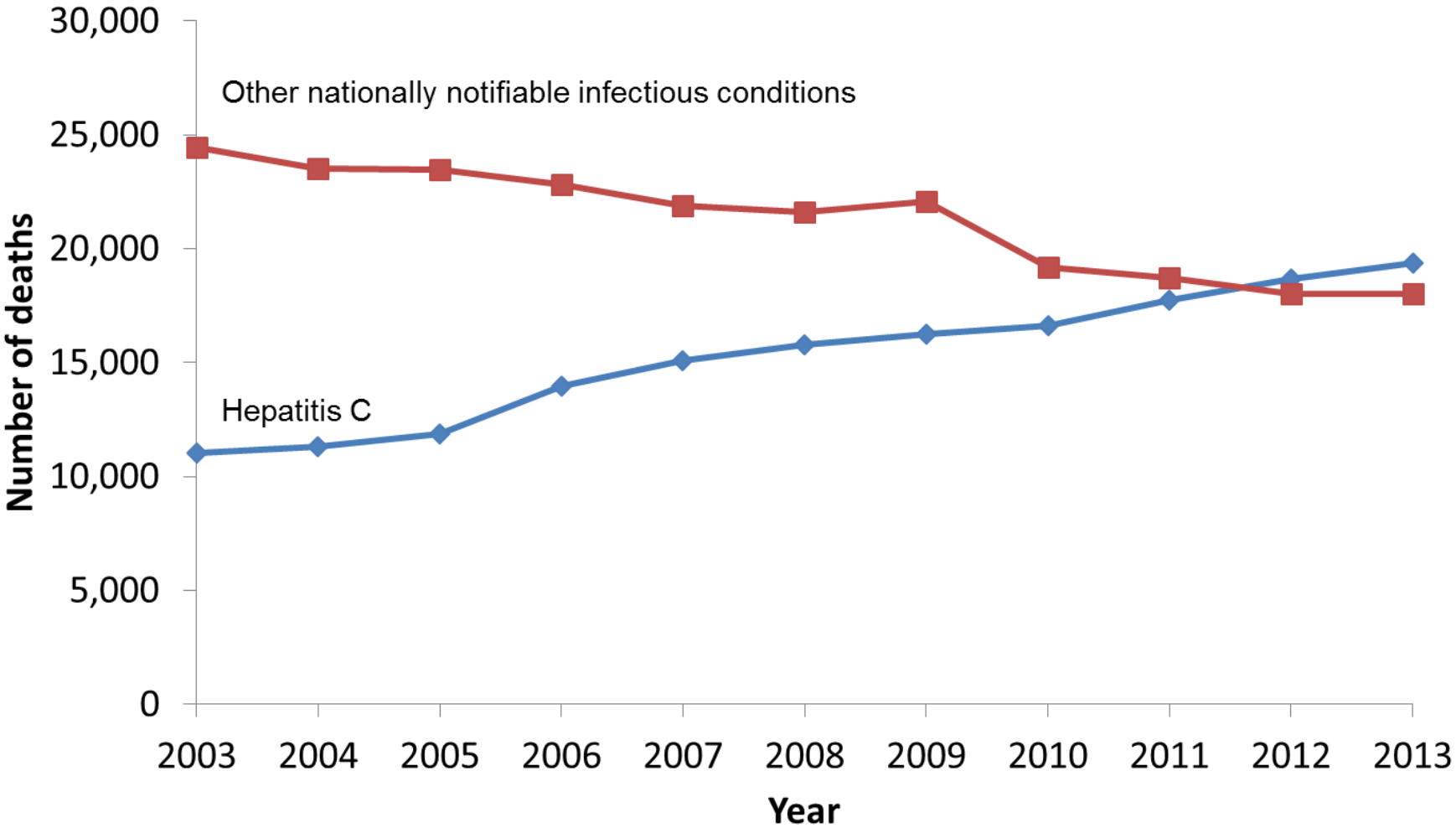
Chronic liver disease includes fibrosis, cirrhosis, and hepatic decompensation; HCC=hepatocellular carcinoma.

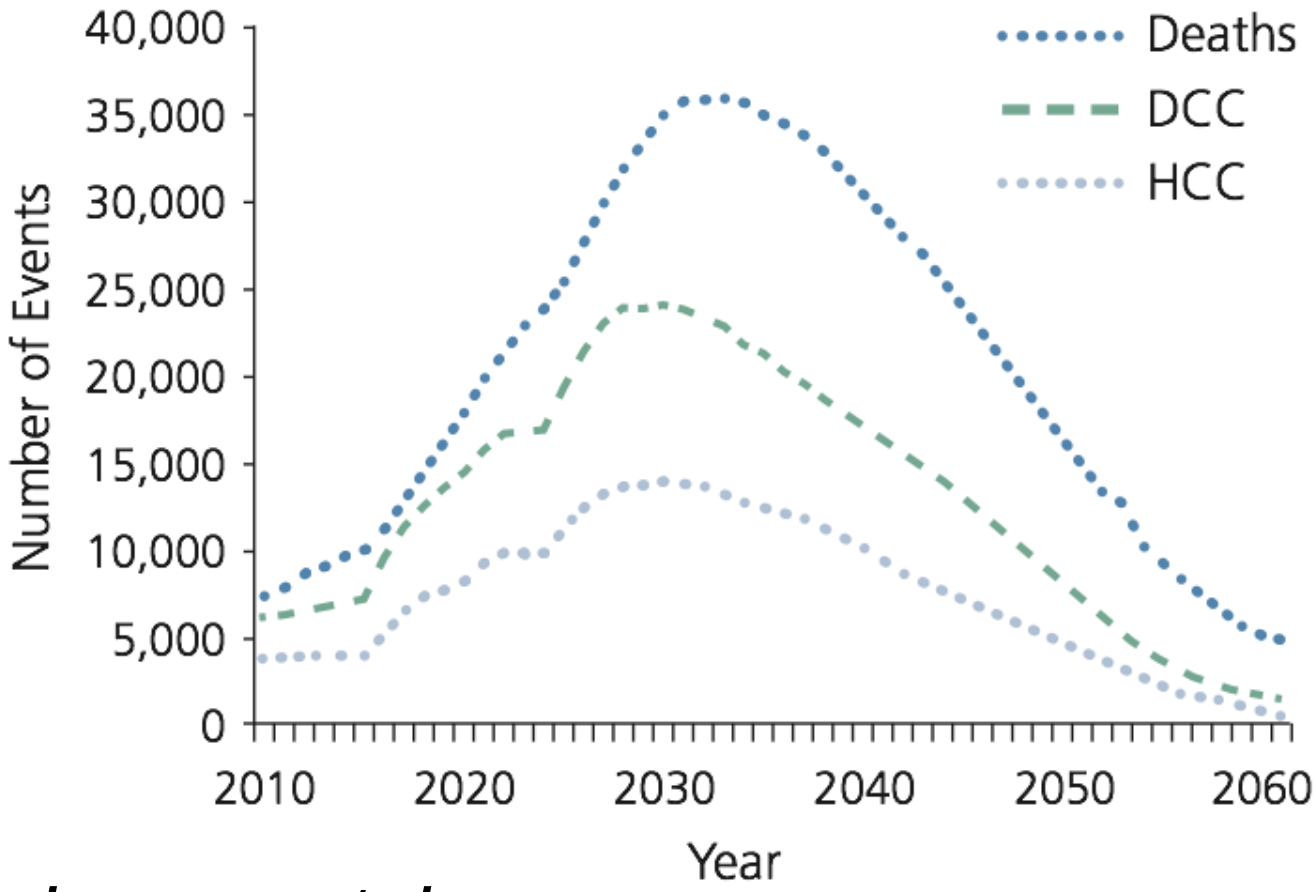
1. Highleyman L. Hepatitis C Support Project. http://www.hcvadvocate.org/hepatitis/factsheets_pdf/Fibrosis.pdf. Accessed August 18, 2011
2. Bataller R et al. *J Clin Invest*. 2005;115:209-218
3. Medline Plus. http://www.nlm.nih.gov/medlineplus/enxy.article/000280.htm. Accessed August 28, 2012; 4. Centers for Disease Control and Prevention. http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm. Accessed May 8, 2012.

HCV deaths exceed those from 60 infectious conditions (including HIV, pneumococcus)



Ly et al. CID 2016

Without intervention, HCV deaths may reach total of 897,000 in the United States



DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma

Rein et al. Dig Dis Sci 2011
John Ward, Topics in Antiviral Medicine 2013

- What are you seeing in your programs?
- Are you screening?
- Are you finding new HCV infections?
- Are you managing cirrhosis? In the shelters? On the streets?
  - Are you finding cancer?
- Do you have support for this specialized work?

Prevalence in HCH programs

	Location	Prevalence
Denniston et al., 2014	NHANES household surveys	1%
Gelberg et al., 2012	Los Angeles	26.7%
Strehlow et al., 2012	8 HCH sites (LA, Phoenix, Denver, Albuquerque, Des Moines, Milwaukee, Birmingham, Providence)	31%
Bharel, et al., 2013	Boston	23%

Patients at BHCHP with HCV had significantly increased health care utilization compared to BHCHP patients without HCV (Bharel, et al. 2013)

Homeless men at BHCHP suffered excess mortality burden from liver cancer than the general MA male population (Baggett, et al. 2015)

Screening considerations in HCH programs

- CDC Guidelines

Who Should Be Tested for Hepatitis C?

New: Anyone born between 1945 and 1965 should be tested once, regardless of risk factors

In addition, patients with the following risk factors:

- Elevated ALT (even intermittently)
- A history of illicit injection drug use or intranasal cocaine use (even once)
- Needle stick or mucosal exposure to blood
- Current sexual partners of HCV infected persons
- Received blood/organs before 1992
- Received clotting factors made before 1987
- Chronic hemodialysis
- Infection with HIV
- Children born to HCV-infected mothers

Why Test People Born Between 1945-1965?

- 76% of the ~4 million people with HCV infection in the US are baby boomers
- In the 1945-1965 cohort:
  - All: 1 out of 30
  - Men: 1 out of 23
  - African American men: 1 out of 12
- Up to 75% do not know they have HCV
- 73% of HCV-related deaths are in baby boomers (Smith BD et al 2012)

- Same for HCHPs?
- Implementation
  - Who does the testing?
  - EMR prompts

Primary care management and monitoring

- Confirmatory testing
- Related screenings
- Lab monitoring
- Fibrosis assessment
- RHM for cirrhotics

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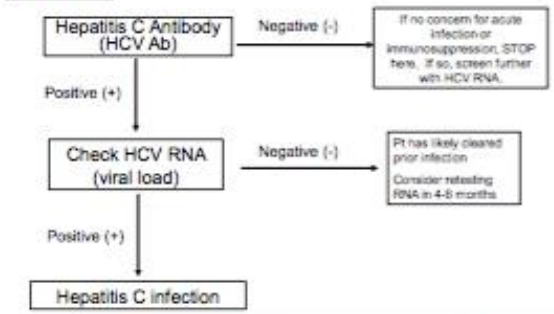
Primary care management for patients with hepatitis C

Diagnosis



If you suspect acute HCV infection refer to liver or ID specialist

Preventive Screening

- Hepatitis A and B
  - Screen and vaccinate as needed
- HIV Antibody

Preventive Immunizations

- Influenza vaccination
- Pneumococcal vaccination

Alcohol Use→ Brief Intervention/Referral if indicated

Chronic HCV monitoring labs

	Baseline	Q6mo ***cirrhosis only	Annualy	only w/symptoms
HCV viral load (RNA)	X			
HCV genotype	X			
CBC/diff	X	X	X	
PT/INR	X	X	X	
BMP/LFTs	X	X	X	
Abd U/S	X	X		
Cryoglobulins				X
Fib-4 index	X		X	
HIV Antibody	X		X if risk factors	
HAV screening	X			
HBV screening	X			
Endoscopy	At time of cirrhosis diagnosis- FU based on results			

Cirrhosis Management- Consider Fib-4 scores >3.25 highly suggestive of cirrhosis and implement cirrhosis monitoring by:

- Screen for HCC with abdominal u/s q6 months
  - AFP testing lacks adequate sensitivity/specificity to be an effective surveillance tool and is no longer recommended
- Screen for esophageal varices with endoscopy
  - Frequency of FU based on findings
- Recommend referral to GI for management of complications r/t decompensated cirrhosis
  - Ascites
  - esophageal varices
  - portal hypertension
  - coagulopathy

Liver Fibrosis Assessment

- Goal - to determine fibrosis stage and diagnose cirrhosis

Fib-4 index- a validated calculation to predict fibrosis

- <1.45= highly suggestive of minimal fibrosis (F0-F1)
- >3.25=highly suggestive of advanced fibrosis (F3-F4)
- 1.46-3.24= indeterminate level of fibrosis

Fibroscan (transient elastography) is preferred secondary fibrosis assessment

- > 12kPa = F4 (cirrhosis)

Reference: Metavir scale of fibrosis

- F0 = no fibrosis.
- F1 = portal fibrosis w/o septa.
- F2 = few septa.
- F3 = numerous septa w/o cirrhosis
- F4 = cirrhosis.

Patient education

Harm reduction counseling

Tx considerations

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Guidance for Patients

HCV Infection is a blood-borne virus that affects the liver and, for some people, can cause scarring, cirrhosis and liver cancer over the course of many years.

Risk factors for disease progression include alcohol consumption, HIV coinfection, concomitant liver disease, obesity, age, genetic factors

Patient Education

- Avoid sharing toothbrushes and dental or shaving equipment and cover any cut or sore in order to prevent contact of their blood with others.
- Stop using illicit drugs. Get treatment for substance abuse. **Those who continue to inject drugs should avoid reusing or sharing syringes, needles, water, cotton or other paraphernalia**; use only sterile syringes from a reliable source (e.g., pharmacy, needle exchange); use a new sterile syringe to prepare and inject drugs; use sterile water to prepare drugs – otherwise use clean water from a reliable source (e.g. tap); clean the injection site with a new alcohol swab; and dispose of syringes and needles after one use in a safe, puncture-proof container.
- Do not donate blood, body organs, other tissue, or semen.
- If the patient has high risk sexual behavior (including multiple sex partners, anal sex or rough sex/fisting), recommend barrier precautions (e.g., latex condoms or gloves) and "safer" sex. Otherwise, the risk of sexual transmission of HCV is low, and the infection itself is not a reason to change sexual practices (i.e., those in long-term relationships need not start using barrier precautions).
- To protect the liver from further harm: do not drink alcohol; do not start any new medicines, including over-the-counter and herbal medicines, without checking with their provider.

Treatment - Who is appropriate for treatment?

- HCV treatment is recommended for all individuals living with HCV whose life expectancy is > 1 year
- Individuals with advanced fibrosis are the highest priority for treatment, but all individuals with HCV should be considered possible treatment candidates
- Successful HCV treatment does not protect against reinfection so harm reduction counseling must be included in the treatment continuum
- **Refer to BHCHP HCV Consult Service for education, treatment evaluation and initiation**

Baden, R., Graham, C. (2013). *Hepatitis C Update* [PowerPoint Slides].

Bruix, J., Sherman, M. (2011). Management of hepatocellular carcinoma: an update. *Hepatology* 53(3): 1020-22.

Sulkowski, M.S., Cheever, L.W., Spach, D.H. (2011). A guide for evaluation and treatment of hepatitis C in adults coinfected with HIV: A quick reference guide for clinicians in the diagnosis, evaluation and treatment of HCV in the setting of HIV primary care. DHHS/HRSA. Last updated January 14, 2011.

SFGH Chronic HCV Primary Care Guideline. 2/11/13.

www.hcvguidelines.org. 4/29/16

Fibrosis Assessment

Selected Noninvasive Systems to Assess Liver Fibrosis in Chronic Hepatitis C

Marker	Description	Performance
AST to platelet ratio index (APRI)	(AST level/ULN x 100)/ platelet count	Threshold of 0.7 has a sensitivity of 77% and specificity of 72% for significant fibrosis (Metavir stage 3 or 4)[13]
FIB-4 index	**(Age (yrs) x AST (IU/mL))/(platelets (x 1000) x ALT (IU/mL)$^{1/2}$)**	**Index of > 3.25 has PPV of 82% with a specificity of 98% for significant fibrosis (Metavir stage 3 or 4)[14]**
FibroTest	Calculation including age, haptoglobin, alpha-2-macroglobulin, apolipoprotein A1, GGT, and total bilirubin	Sensitivity of 75% and specificity of 85% to detect Metavir stage 2 or greater[15]
FibroScan	Ultrasound device that uses transient elastography to assesses liver shear wave velocity (meters/second) that is converted to equivalent liver stiffness (kilopascals) at 50 Hz, which correlates with hepatic fibrosis stage	Threshold for diagnosis of cirrhosis 12.5 KPa with sensitivity of 87% and specificity of 91%[16,17]

18

In the interest of applying an accurate, easily administered, cost-effective measure that enables BHCHP to identify the highest risk patients for morbidity and mortality to the large population of patients with HCV at BHCHP, the Fib-4 index is chosen as the preferred fibrosis staging instrument.

Fib-4 index =(age (yrs) x AST (Iu/mL)/(platelets (x1000) x ALT (IU/mL)$^{1/2}$)

Liver Fibrosis Assessment

- Goal - to determine fibrosis stage and diagnose cirrhosis

Fib-4 index- a validated calculation to predict fibrosis

- <1.45= highly suggestive of minimal fibrosis (F0-F1)
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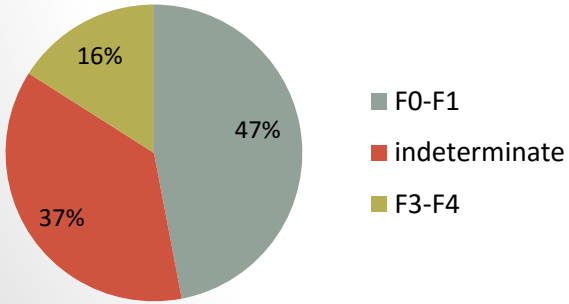
- > 12kPa = F4 (cirrhosis)

FIB-4 results n=1480



Order Medication Problem

Primary Care | Treatment

Most Recent Test Results — Include test results in note

HCV AB:	Positive (01/22/2010)
HCV VL:	No data on record
HCV GENOTYPE:	No data on record
HCV GENOTYPE LiPA:	No data on record

Fibrosis 4 Calculation — Last score: No data on record — Include last Fib 4 score in note

Most Recent Lab Results

Patient Age: 40 — Click 'Update' to record newer lab results

Platelet Count:	210	Update
AST:	46	Update
ALT:	53	Update

Calculate Score

Score: 1.20

Interpretation: Highly suggestive of minimal fibrosis (F0-F1)

Other Fibrosis Assessments

	Interpretation	Date:	
Fibroscan:			Record
Fibrosure:			Record
Hepascore:			Record

Cirrhosis

Does this patient have cirrhosis? Yes No

Most Recent AUDIT-C Score — Include AUDIT-C Score in note

AUDIT-C Score: 4 (10/21/2013)

Consider annual screening for alcohol use / misuse — Go to Risk Factors

Primary Care Management for Patients with Hepatitis C: Guideline — Open Guideline

CTP Calculator for Classification of Cirrhosis Severity — Open CTP Calculator

Enhanced RHM for cirrhotics

- Screening
  - HCC
  - Varices
- Monitoring
  - Labs Q3-6 mos
    - INR, Alb, plts
  - Decompensation
    - Ascites
    - Encephalopathy
    - Hepatorenal
    - Hepatopulmonary

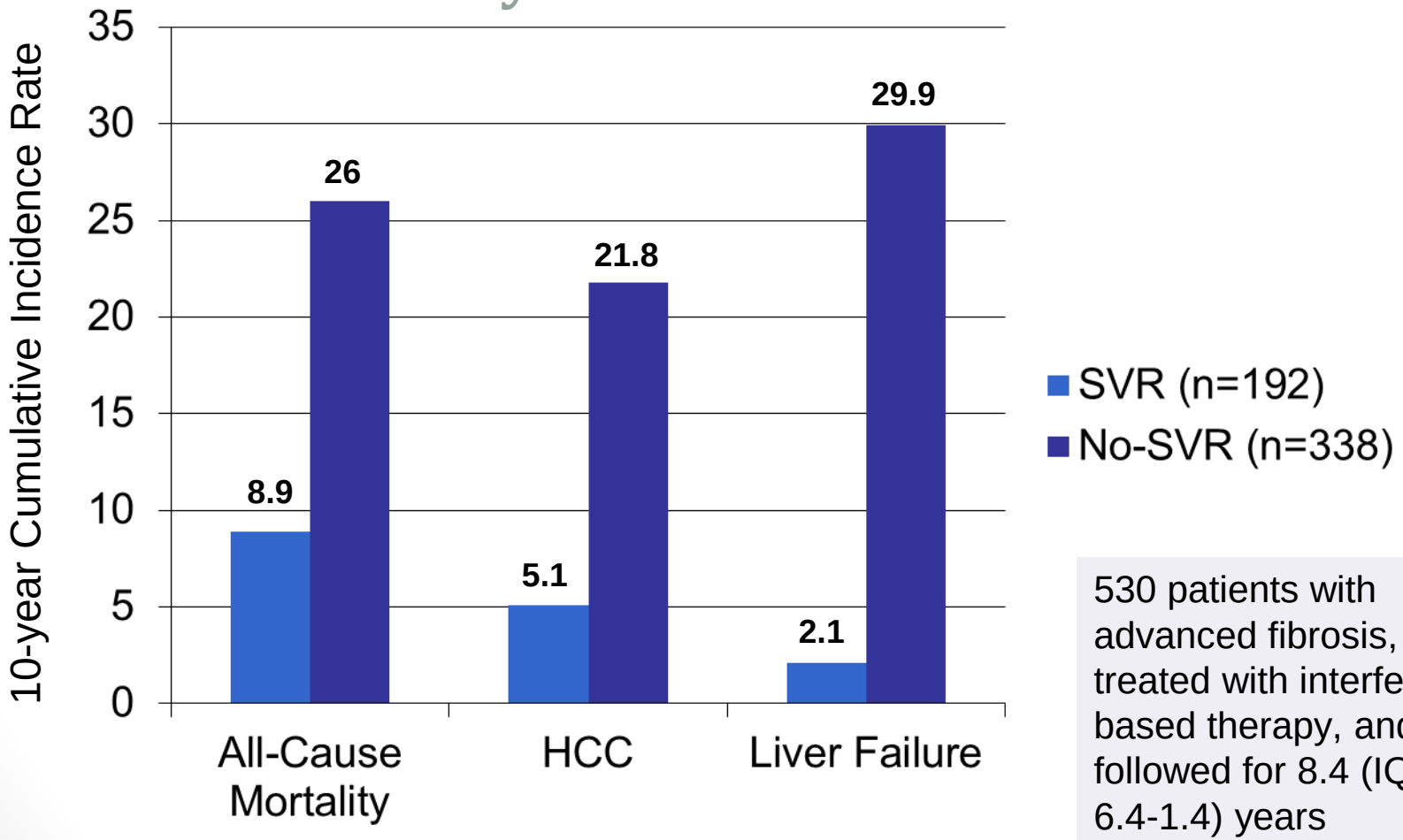
HCV Treatment

- www.hcvguidelines.org
- Multiple highly efficacious HCV treatment regimens
  - sofosbuvir/ledipasvir (Harvoni)
  - paritaprevir/ritonavir/ombitasvir and dasabuvir +/- ribavirin (Viekira)
  - elbasvir/grazoprevir (Zepatier)
  - sofosbuvir (Sovaldi) and daclatasvir (Daklinza)
  - simeprevir (Olysio) and sofosbuvir (Sovaldi)

  - sofosbuvir/velpatasvir (Epclusa?) – PDUFA 6/28/16

- **Most importantly for patients experiencing homelessness**
  - **>95% cure rate**
  - **Highly tolerable**
  - **Low pill burden**

SVR (Cure) Associated with Decreased All-Cause Mortality



530 patients with advanced fibrosis, treated with interferon-based therapy, and followed for 8.4 (IQR 6.4-1.4) years

Van der Meer et al. JAMA 2012; 308:2584

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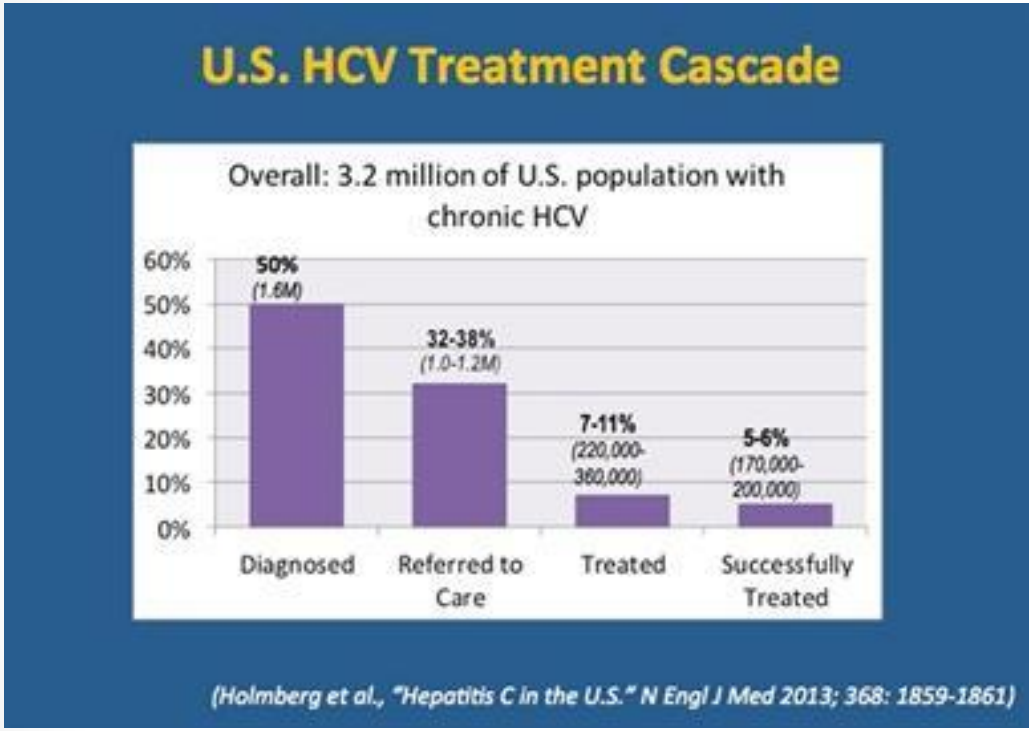
So why are there still barriers?



- COST
- Access
- Expertise
- Stigma*
- Competing priorities

*Ideally, treatment of HCV-infected persons who inject drugs should be delivered in a multidisciplinary care setting with services to reduce the risk of reinfection and for management of the common social and psychiatric comorbidities in this population. Regardless of the treatment setting, recent and active IDU should not be seen as an absolute contraindication to HCV therapy. There is strong evidence from various settings in which persons who inject drugs have demonstrated adherence to treatment and low rates of reinfection, countering arguments that have been commonly used to limit access to this patient population. www.hcvguidelines.org

BHCHP HCV Consult Service

- Started in January 2014 by NP, MD and RN with experience in HCV treatment
  - FT Americorps member added in 9/14
  - 3nd clinician added 5/15
  - Formal budgetary provisions 7/15

- Key elements
  - Specialty back-up
    - ID/GI/pharmacy
  - Administrative buy-in
  - Insurance expertise
  - Adherence support
    - Med storage
    - Frequent and flexible patient check-ins
    - Care coordinator as adherence champion and PA navigator

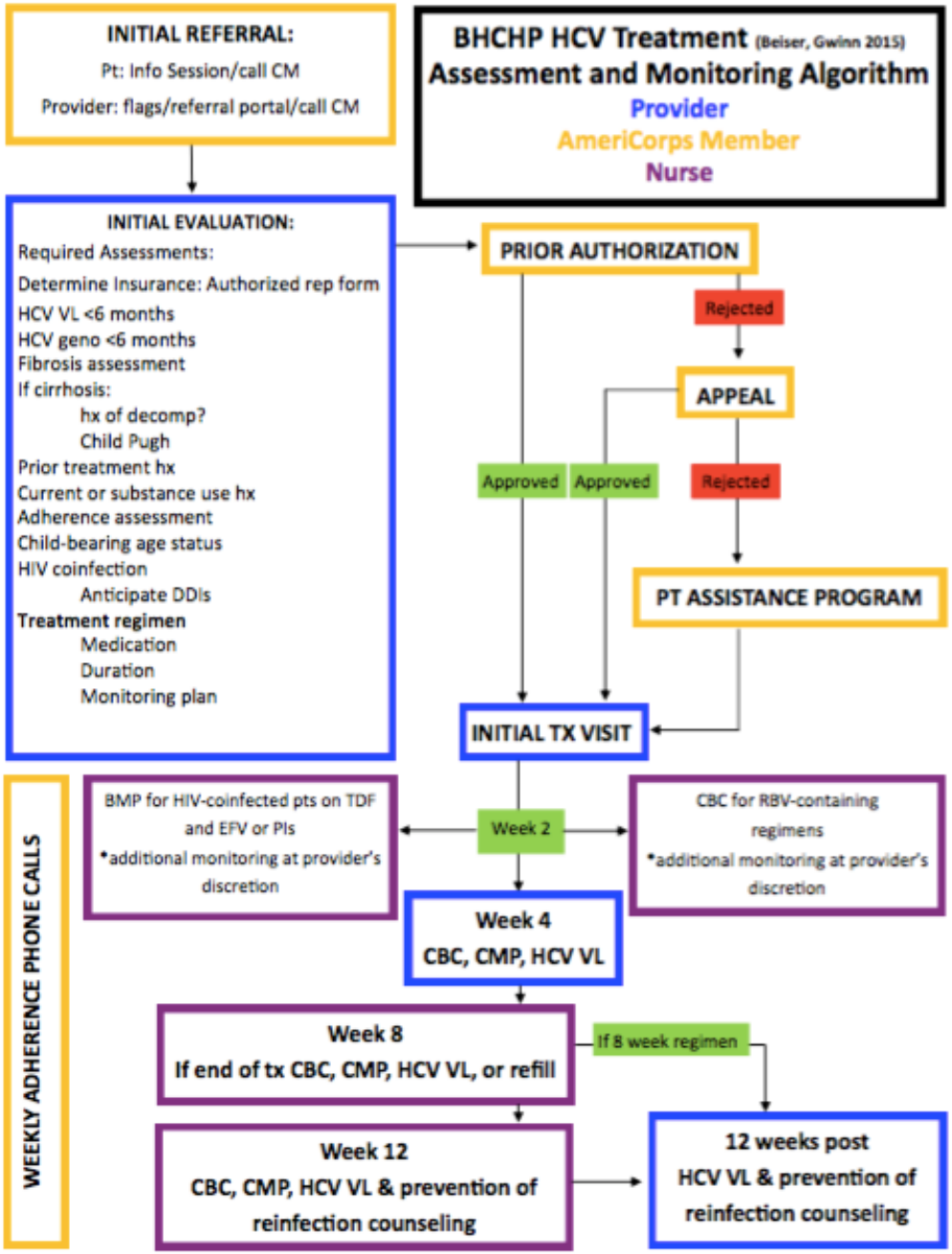
395 patients evaluated for treatment since 1/14

182 patients treated since 1/14

110/115 of those achieved SVR

5 reinfections

BHCHP HCV team model



HCV care team roles

Care coordinator	Nurse	Provider
Take referrals from providers and patients	Preliminary visit- labs, education	Treatment evaluation
Pre-tx adherence assessment	Pre-tx adherence assessment	Pre-tx adherence assessment
Outreach education to programs, shelters, health fairs, support groups, etc	Pharmacy coordination	Consultation with specialists prn
Adherence- phone calls, home/shelter visits	Adherence- pillboxes, DOT, home/shelter	Adherence support
Prior authorizations- insurance management		
Coordinate and escort to fibroscans		
Manage tracking documents		
Appointment reminders		

“My favorite part of this role is meeting a patient for the first time during one of my hep C info sessions, coordinating their treatment with the HCV team, working with them all the way to their SVR date, and providing the news that they have cleared their infection and have been cured.”

“Patients can have very emotional responses to the news that they have been cured. I have talked to several patients that express gratitude for the opportunity to be cured, which is a big deal for a patient that may have experienced significant trauma in his or her life and has lived with a stigmatizing disease for decades, maybe even having been denied treatment in the past because he or she was ‘not sick enough’.”

-Molly

All patients seen for HCV evaluation

Seen By	Name	DOB	Date of visit	HIV?	Geno	Fib-4	Notes
Carlo	***	***	7/31/13	Y	1	1.86	Fibroscan ordered
Beiser	***	***	11/5/13	Y	1	2.9	
Beiser	***	***	12/12/13	Y	1a or 1	1.04	
Beiser	***	***	12/30/13	N	1	4.03	no longer in care at BHCHP
Beiser	***	***	1/6/14	Y	1	2.6	
Beiser	***	***	1/13/14	Y	1a or 1	2.94	contact when new meds out
Carlo	***	***	1/13/14	Y	1a or 1	2.35	Fibroscan ordered,change insurance
Beiser	***	***	1/27/14	N	2		
Beiser	***	***	2/3/14	N	1	5.73	
Beiser	***	***	2/4/14	Y	1	1.03	
Beiser	***	***	2/6/14	Y	1	1.02	not seen recently by practice
Carlo	***	***	2/7/14				
Beiser	***	***	2/10/14	Y	1	2.36	
Beiser	***	***	2/10/14	Y	2	1.31	
Beiser	***	***	2/10/14	N	1	1.83	deferred d/t F0 and insurance issues

On treatment tracking

Name: *** DOB: *** best phone number *** Start Date: 3/3/16 Harvoni BHCHP	Week 1	10-Mar	yes, at night	little tired	no	
	Week 2	17-Mar				
	Week 3	24-Mar				
	Week 4	31-Mar				yes
	Week 5	7-Apr	yes, doing well			
	Week 6	14-Apr	yes		no	
	Week 7	21-Apr				
	Week 8	28-Apr				yes
	Week 9	5-May				
	Week 10	12-May				
	Week 11	19-May				
	Week 12	26-May				
Name: *** DOB: *** best phone number ***	Week 1	10-Mar				
	Week 2	17-Mar	yes	no	no	
	Week 3	24-Mar				
	Week 4	31-Mar				yes
	Week 5	7-Apr				
	Week 6	14-Apr				

Outcomes tracking

Seen By	Name	DOB	HIV?	Geno	Fib-4	Tx initiation date	Projected Tx completion date	SVR date	SVR achieved?	Reinfection?
Beiser	***	***	N	2	2.16	2/4/14	4/29/14	7/30/14	N	
Beiser	***	***	N	1	5.73	3/14/14	6/6/14	8/29/14	Y	
Beiser	***	***	Y	1	3.98	3/25/14	6/17/14	9/9/14	Y	
Beiser	***	***	Y	1a	3.35	5/6/14	7/29/14	10/21/14	Y	
Beiser	***	***	Y	1b	1.95	5/6/14	7/29/14	10/21/14	Y	
Beiser	***	***	Y	2	1.31	2/20/14	5/15/14	11/4/14	Y	Y
Carlo	***	***	Y	1a	6.3	5/16/14	8/8/14	11/14/14	Y	
Carlo	***	***	Y	1a	2.47	7/21/14	10/12/14	1/5/15	Y	Y
Beiser	***	***	N	1a	1.35	11/4/14	12/30/14	3/24/15	Y	
Beiser	***	***	N	1	1.36	11/10/14	1/5/15	3/30/15	Y	
Beiser	***	***	Y	1b	3.75	10/24/14	1/8/15	4/2/15	Y	
Carlo	***	***	N	1a	1.32	11/13/14	1/8/15	4/2/15	Y	

Pearls

Readiness

- Adherence to appointments
- Thorough substance use hx
  - Harm reduction/reinfection risk
- Partners, possible co-tx
- Determine outstanding legal issues/other major medical plans

Adherence Pearls

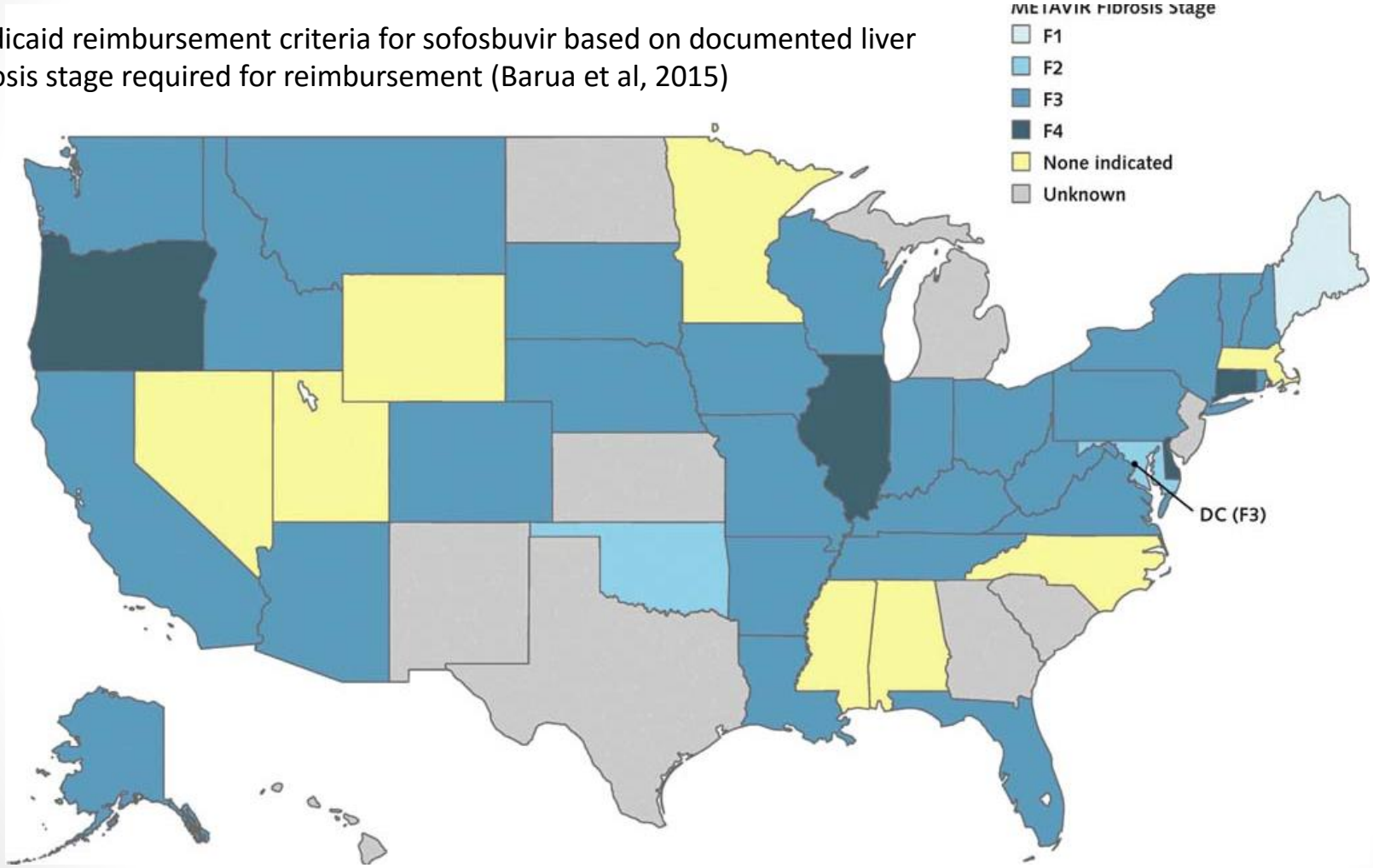
- Weekly med boxes for shelter residents or DOT
- Contact info (many)
- Capacity for outreach
- Pharmacy coordination

Insurance

- Ensure all elements of eval are complete before PA
  - Correct forms
  - Keep copies!
  - Be aware of appeal deadlines
- Address substance use
- Explicitly discuss adherence plan, plan for monitoring
- Language for lower fibrosis
- Provider criteria

Coverage restrictions

Medicaid reimbursement criteria for sofosbuvir based on documented liver fibrosis stage required for reimbursement (Barua et al, 2015)



State by state guide: http://www.chlpi.org/wp-content/uploads/2013/12/Examining_HCV_Treatment_Access_Report.pdf

Patient Assistance Programs

- Designed for uninsured and/or undocumented
- If eligible for insurance must apply and have documented denial
- Proof of residency
- Proof of income
  - Gilead- for uninsured or undocumented patients
    - Proof of income (<500% of the federal poverty level)
    - Copay coupons for insured individuals
    - www.mysupportpath.com
  - Merck
    - <$59,400/yr for an individual
    - Possible copay assistance for insured individuals
    - www.merkhelps/zepatier

Cost-Effectiveness of HCV Treatment

(utilized with permission from Cami Graham, 2015)

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	Harvoni and Viekira Pak 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 Harvoni = $25,291 and Peg-IRN/RBV = $24,833 If Harvoni <$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

Helpful guidance

- AASLD/IDSA guidelines www.hcvguidelines.org
- UW educational modules http://www.hepatitisc.uw.edu/
- State by state review of HCV access issues by Center for Health Law and Policy Innovation at Harvard http://www.chlpi.org/wp-content/uploads/2013/12/Examining_HCV_Treatment_Access_Report.pdf
- CMS letter to state Medicaids on HCV coverage https://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/Rx-Releases/State-Releases/state-rel-172.pdf
- National Viral Hepatitis Roundtable http://nvhr.org/

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