Update on The Liver

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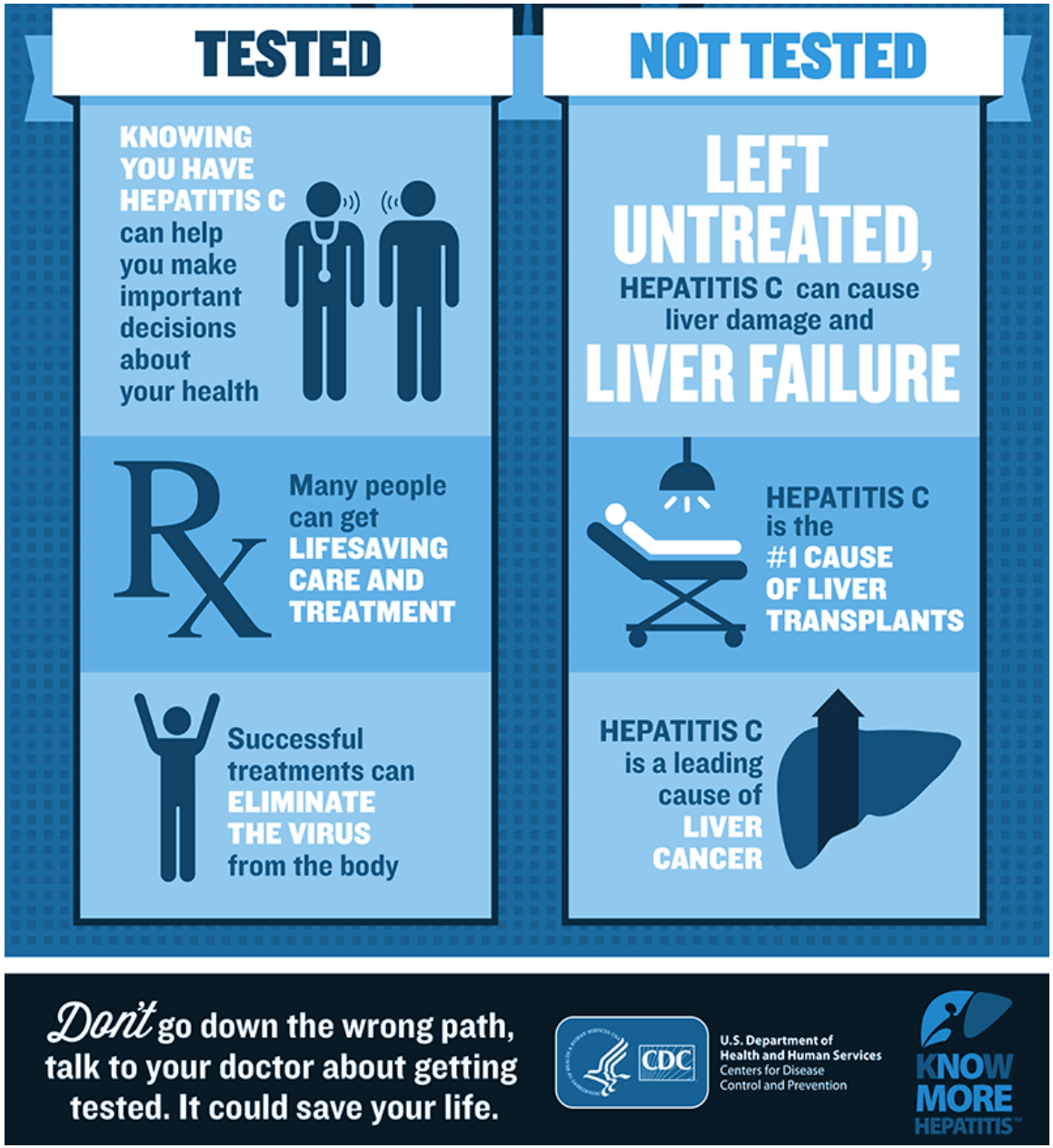
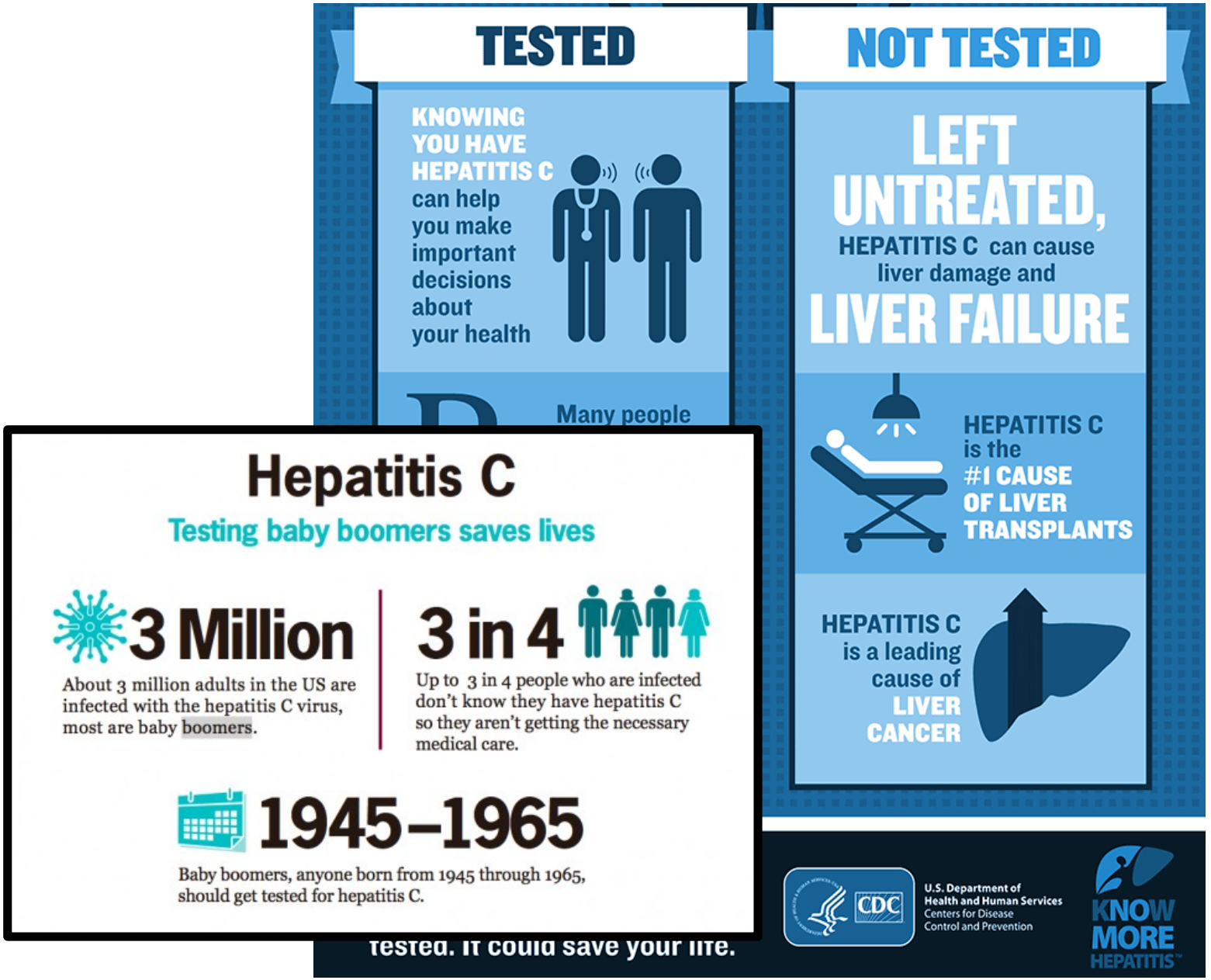
Update on the Liver

1. Hep C Updates
2. Common Medication Myths: Debunked!

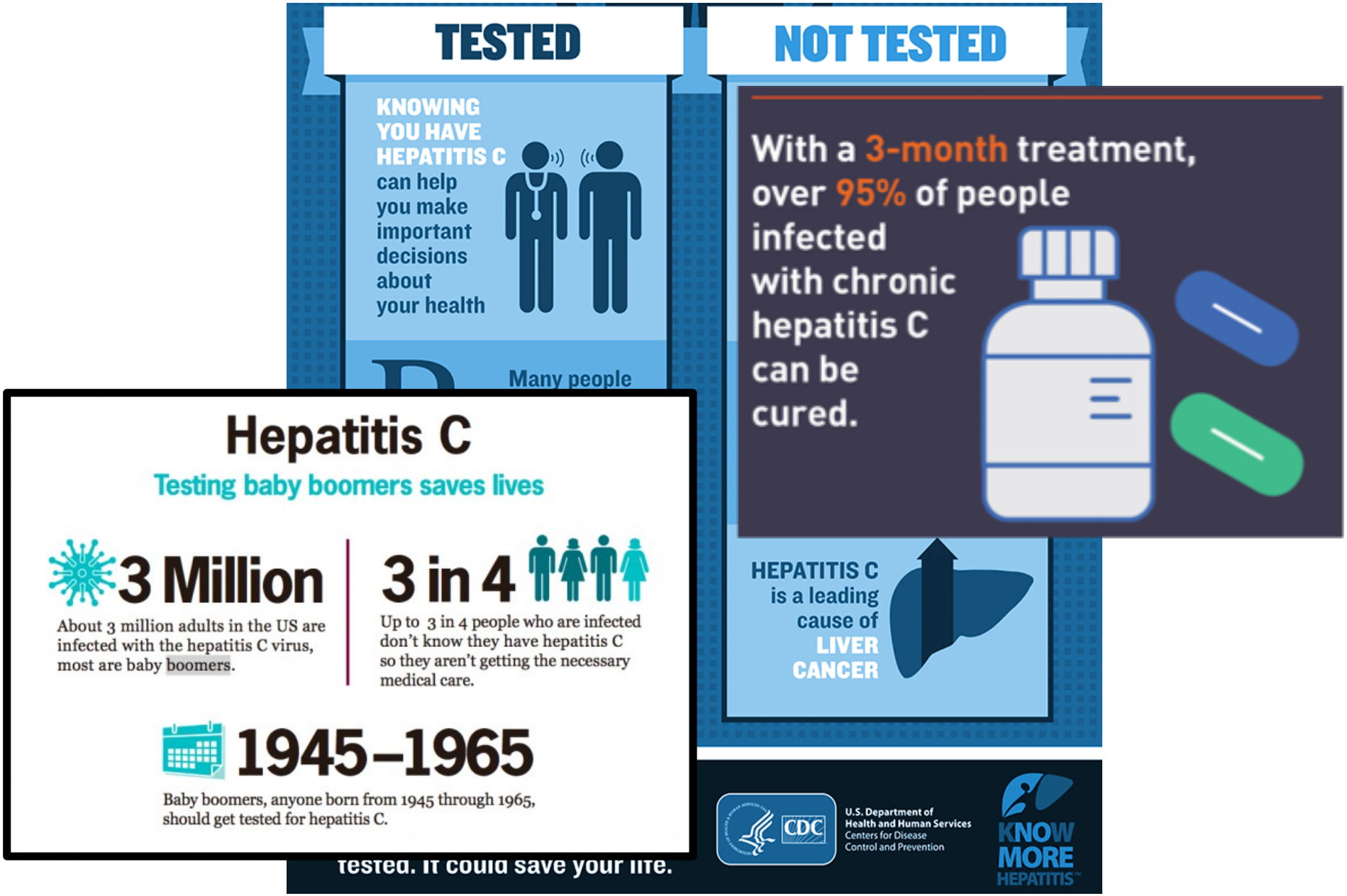
Hepatitis C: an easily curable disease!



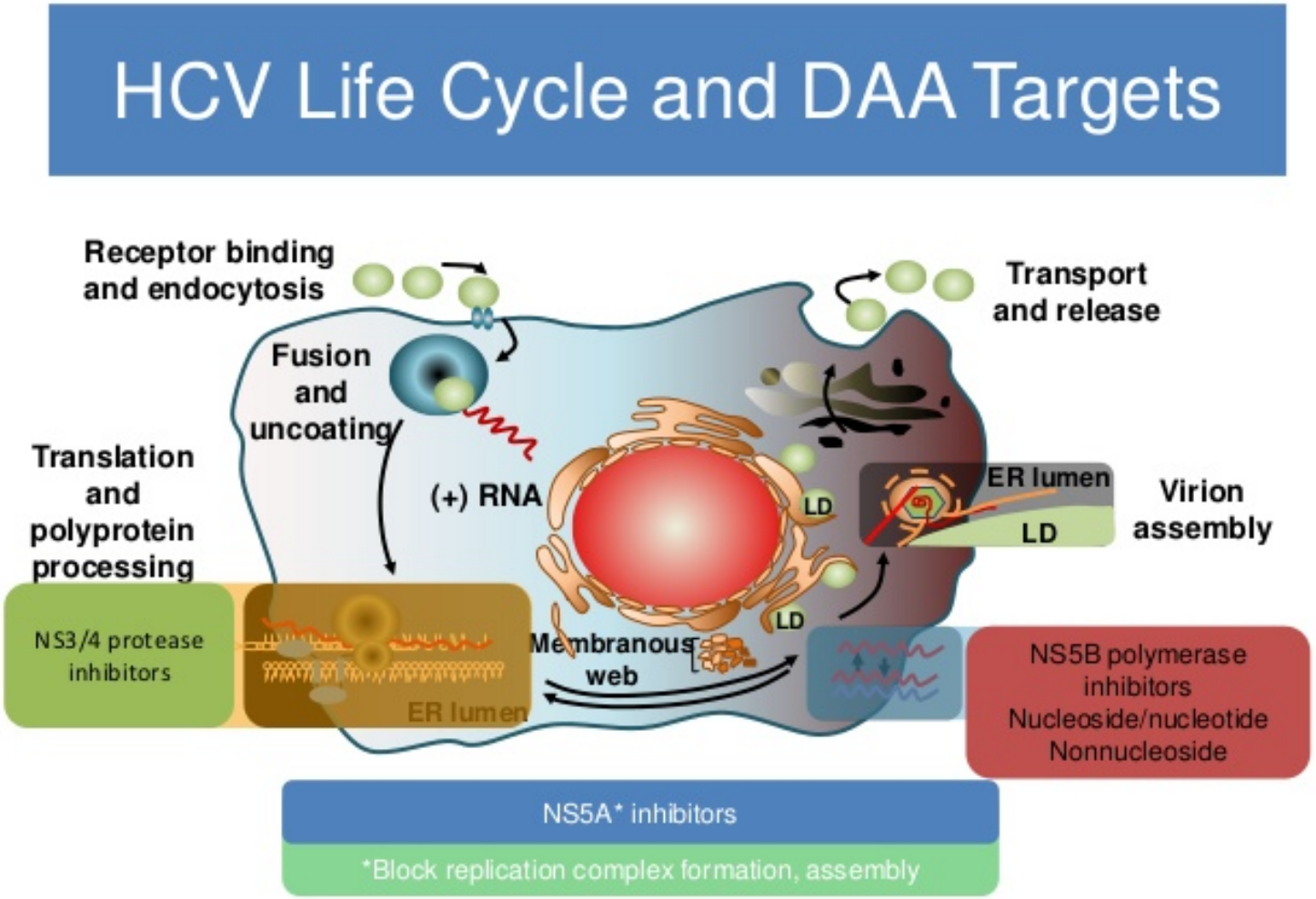
Hepatitis C: an easily curable disease!



Hepatitis C: an easily curable disease!



Direct Acting Antivirals



Ref: Manns MP, et al. Nat Rev Drug Discov. 2007;6:991-

NS5A inhibitors:

- Ombitasvir
- Daclatasvir
- Ledipasvir
- Elbasvir
- Velpatasvir
- Pibratenasvir

NS5B polymerase inhibitors:

- Sofosbuvir

NS3/4a protease inhibitors:

- Telaprevir
- Boceprevir
- Simeprevir
- Paritaprevir
- Grazoprevir
- Voxilaprevir
- Glecaprevir

Need help finding a treatment regimen for your pt?

hcvguidelines.org

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Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis[a]		
RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[b] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c]	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs[b] for elbasvir	16 weeks	IIa, B

Hepatitis C Treatment: DAA

- DAA (Directing Acting Antivirals) → new hep C meds
  - e.g. harvoni, epclusa, zepatier, mavyret, vosevi
- So many excellent regimens to choose from!
- Many of the newest DAAs are pangenotypic (less confusing)
- All oral (no more injectable IFN, usually no more anemia-causing ribavirin)
- Well tolerated: HA, fatigue, diarrhea, nausea
- Most are 8-12 weeks
- SVR12 (cure) rates> 95% for most populations, including those with compensated cirrhosis

Treatment naïve patients

Geno	Regimen	Duration of treatment (weeks)	
		No cirrhosis	Compensated cirrhosis
1	Glecaprevir/pibrentasvir (mavyret) Sofosbuvir/velpatasvir (epclusa) Ledipasvir/sofosbuvir (harvoni) Elbasvir/grazoprevir (zepatier)	8 12 12 (8 if RNA<6M) 12	12 12 12 12
2/3	Glecaprevir/pibrentasvir (mavyret) Sofosbuvir/velpatasvir (epclusa)	8 12	12 12
4	Glecaprevir/pibrentasvir (mavyret) Sofosbuvir/velpatasvir (epclusa) Ledipasvir/sofosbuvir (harvoni) Elbasvir/grazoprevir (zepatier)	8 12 12 12	12 12 12 12
5/6	Glecaprevir/pibrentasvir (mavyret) Sofosbuvir/velpatasvir (epclusa) Ledipasvir/sofosbuvir (harvoni)	8 12 12	12 12 12

All SVR ≥ 95%

Treatment naïve patients

Geno	Regimen	Duration of treatment (weeks)	
		No cirrhosis	Compensated cirrhosis
1	**Glecaprevir/pibrentasvir (mavyret)**	8	12
	Sofosbuvir/velpatasvir (epclusa)	12	12
	Ledipasvir/sofosbuvir (harvoni)	12 (8 if RNA<6M)	12
	Elbasvir/grazoprevir (zepatier)	12	12
2/3	**Glecaprevir/pibrentasvir (mavyret)**	8	12
	Sofosbuvir/velpatasvir (epclusa)	12	12
4	**Glecaprevir/pibrentasvir (mavyret)**	8	12
	Sofosbuvir/velpatasvir (epclusa)	12	12
	Ledipasvir/sofosbuvir (harvoni)	12	12
	Elbasvir/grazoprevir (zepatier)	12	12
5/6	**Glecaprevir/pibrentasvir (mavyret)**	8	12
	Sofosbuvir/velpatasvir (epclusa)	12	12
	Ledipasvir/sofosbuvir (harvoni)	12	12

All SVR ≥ 95%

HBV reactivation with DAA

- Prevalence of HBV/HCV co-infection
  - *Chronic* HBV infection (sAg +) = 1.5-6%
  - *Resolved* HBV infection (sAg-, cAb +) = 35-62%
- Believed that HCV suppresses HBV replication
  - Risk of HBV reactivation with treatment of HCV with DAA
- Incidence rate of HBV reactivation with DAA → Rare!
  - 62,290 vets who underwent DAA, none had HBV ppx
  - Reactivation:
    - *Chronic HBV infection* (sAg +) → 8/377 (2%)
    - *Resolved HBV infection* (sAg -, cAb +) → 1/7200 (0.01%)

Bini EJ, et al. Hepatol 2010;51:759-766.
Belperio PS et al. Hepatol 2017;66:27-36

HBV reactivation with DAA

WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV

See full prescribing information for complete boxed warning.

Hepatitis B virus (HBV) reactivation has been reported, in some cases resulting in fulminant hepatitis, hepatic failure, and death. (5.1)

- AASLD/EASL/IDSA: recs screening all HCV patients for HBV prior to DAA treatment
  - HBsAg, HBcAb, HBsAb

What about my pt with Hep C and…

1. *CKD/ESRD on HD* → Glecaprevir/Pibrentavir (mavyret) x 8 weeks (no cirrhosis) or 12 weeks (cirrhosis)
   - SVR 98%
2. *Failed DAA* → Velpatasvir/Sofosbuvir/Voxilaprevir (vosevi) x 12 weeks
   - SVR 97%
3. *Decompensated cirrhosis* → sofosbuvir/velpatasvir (epclusa) + riba 600 mg daily x 12 weeks
   - SVR >90%
   - No protease inhibitors with Child B/C (no mavyret, vosevi)!
4. *Post liver transplant* → Glecaprevir/Pibrentavir (mavyret) x 12 weeks
   - SVR 96% (no cirrhosis)

Can you as GI nurses do this???

Expansion of Treatment for Hepatitis C Virus Infection by Task Shifting to Community-Based Nonspecialist Providers:

A Nonrandomized Clinical Trial

SVR, by Subgroup

Subgroup	Patients, *n*/*N*	SVR (95% CI), %
Overall	516/600	86.0 (83.0–88.7)
Provider type		
NP	134/150	89.3 (83.3–93.8)
PCP	139/160	86.9 (80.6–91.7)
Specialist	243/290	83.8 (79.0–87.8)
Provider type mixed		
NP	120/134	89.6 (83.1–94.2)
PCP	135/155	87.1 (80.8–91.9)
Specialist	240/287	83.6 (78.8–87.7)
NP/specialist	17/19	89.5 (66.9–98.7)
PCP/specialist	4/5	80.0 (28.4–99.5)

Ann Intern Med 2017;167:311-318

Can you as GI nurses do this???

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Hep C Updates: Summary

- HCV is a curable disease!
  - Even in difficult populations like ESRD, comp and decomp cirrhosis, DAA treatment failures, post-liver transplant, HIV/HCV coinfection
  - > 95% chance of cure in most pts
    - 3 mo, once daily pill, minimal side effects
  - It's easy… PCPs, general GI, and especially GI nurses can treat and cure!
- hcvguidelines.org
- If using DAA, screen for HBV → sAg, cAb, sAb
- Screen baby boomers (1945-1965)

Common Medication Myths: Debunked!

- Case 1: PPI and Cirrhosis
- Case 2: Statins and Liver Disease
- Case 3: Tylenol (and NSAIDs) and Liver Disease

PPI and Cirrhosis?

- Case 1: 32 yo F with EtOH cirrhosis c/b well controlled ascites (lasix/spironolactone) complains of epigastric pain.
  - Trial PPI?

PPI and Cirrhosis?

- 865 pts with cirrhosis and ascites, 1 yr
  - 39% used PPI at baseline
  - 189 new HE
  - 86 new SBP
- PPI use associated with:
  - 88% increased risk of HE
  - 72% increased risk of SBP

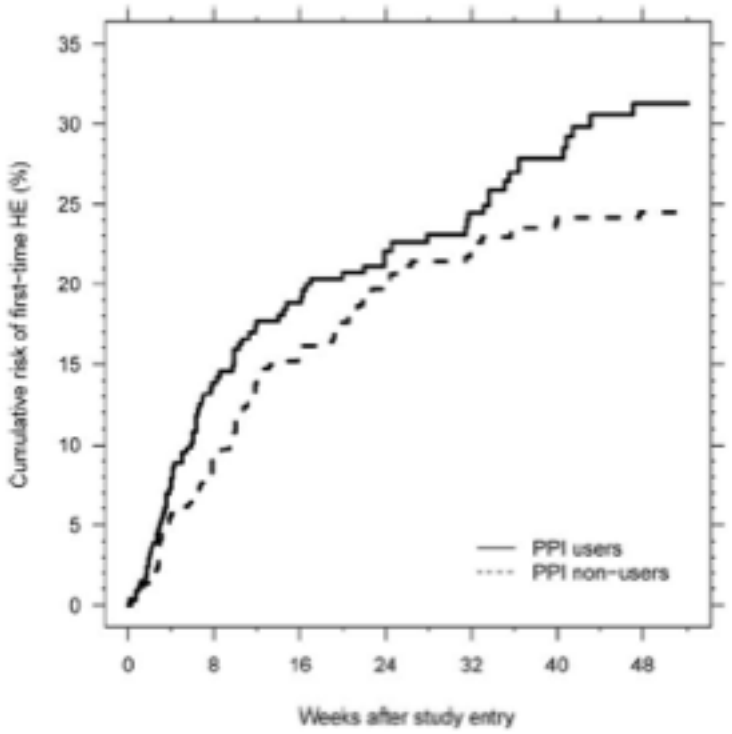


FIG. 3. Cumulative risk of first-time HE in patients who did (N = 340) or did not (N = 525) use PPIs at the time of study entry.

Dam G. Hepatology. 2016 Oct;64(4):1265-72.

PPI and Cirrhosis?

- Case 1: 32 yo F with EtOH cirrhosis c/b ascites controlled with lasix/spironolactone complains of epigastric pain.
  - Trial PPI?

- Recs: in pts with Cirrhosis (esp if ASCITES)
  - Would not empirically trial PPI
  - Investigate etiology
  - If PUD→ weigh pro/con

Statins and Liver disease?

- Case 2: 58 yo M with obesity, DM, HTN, hyperlipidemia with mildly elevated LFTs (2-3 x ULN). On atorvastatin x 2 years
  - Consult: etiology of elevated LFTs and d/c atorvastatin?

- RF for liver disease:
  - EtOH: none
  - No fam hx liver disease, No known herb/supplement use
  - Metabolic syndrome:
    - Obesity (BMI 35; 20# wt gain over past 2 yr)
    - DM
    - HTN
    - Hyperlipidemia

Statins and Liver disease?

- Workup:
  - Plt 161
  - TSH 1.8
  - HgA1c-5.6
  - % transferrin satn 50%
  - Ferritin 261
  - NL SPEP (no reduced A1 glob; no elevated gamma glob)
  - ANA neg; ASMA neg
  - Ceruloplasmin 21

- Ultrasound: hepatic steatosis, no cirrhosis, normal spleen

Statins and Liver disease?

Does this pt have Statin-induced hepatoxicity?

- Rare: ALT elev > 3# ULN occur in 1% of pts
  - No different than placebo (mevacor, scandanavian trial)
  - ALT elevations transient
- FDA 2012: revised labels to remove need for monitoring LFTs (FDA safety announcement in Feb, 2012)
  - FDA recommends with statin initiation:
    - Pretreatment liver chemistries
    - Routine periodic LFT monitoring not effective in detecting or preventing serious liver injury with statins
    - Liver chemistry monitoring should be implemented only "as clinically indicated"
- Patients with NAFLD are not at an increased risk of statin hepatotoxicity
  - But… they are increased risk of ACS

Statins and Cirrhosis: Helpful?

- Decreased risk of hep decompensation
  - Retrospective review of 1350 pts with cirrhosis
  - Statin users matched through propensity scores
  - Decreased risk of decompensation, death, HCC ($p<0.001$)

- Decreased development of HCC

Statin Use	OR of new HCC
Never	1
Ever	0.4
6m-1yr	0.56
1-2yr	0.41
> 2yr	0.30

Chang et al. Hepatol 2017; 66
Kim et al. J of Hepatol 2018;68:476.

Statins and Liver disease?

- Case 2: 58 yo M with obesity, DM, HTN, hyperlipidemia mildly elevated LFTs (2-3 x ULN). On atorvastatin x 2 years
  - Consult: d/c atorvastatin?

- Recs:
  - Would not discontinue atorvastatin
    - Higher risk of ACS than hepatoxicity!
  - Elevated LFTs are likely due to NAFLD
    - Wt loss, diet, exercise…
    - Repeat LFT in 3 months

Tylenol and Cirrhosis?

- Case 3: 55 yo M with ALD cirrhosis (still drinks) seeing you for routine followup. He has knee pain after fall. His PCP said no Tylenol, so pt has been taking Motrin 800 mg TID for past week.
  - Good pain plan?

Tylenol and Cirrhosis?

- Large doses > 10-15 grams/d (20-30 XS Tylenol) can cause ALF
- If taken in acceptable amounts, safe pain med for pts with cirrhosis
  - Cirrhosis or active etoh use < 2gram/24 hr
  - Liver disease without cirrhosis (NAFLD) < 4 gram/24 hr

- OTC meds that contain acetaminophen
  - Nyquil, Alka-seltzer Plus, Tylenol Cold and Flu, Theraflu
- Opioid medications that contain acetaminophen
  - Percocet, Vicodin, Norco
  - 2011: FDA limit to 325 mg/tablet

Larson AM. Clin Liver Dis. 2007;11:525-48

NSAIDs and Cirrhosis

- NSAIDs→
  - Bleeding from PUD, varices, GAVE, PHG
    - Retrospective review of 4876 cirrhotics
      - Adj OR for UGIB (var, non var) = 1.87 with NSAID use
  - Thrombocytopenia
  - Decreased renal perfusion → ARF
  - Sodium retention

Rostram A et al. Clin Gastroenterol Hepatol 2007;5:818-28
Lee YC et al. Liv International 2012;32,859-866

Tylenol and Cirrhosis?

- Case 3: 55 yo M with ALD cirrhosis (still drinks) with knee pain after fall, taking Motrin 800 mg TID for past week.
  - Good pain plan?

- Recs:
  - D/C NSAIDs
  - Advise acetaminophen max 2 grams/24 hr, ice, PT
  - Educate re OTC (and opioids) that contain acetaminophen

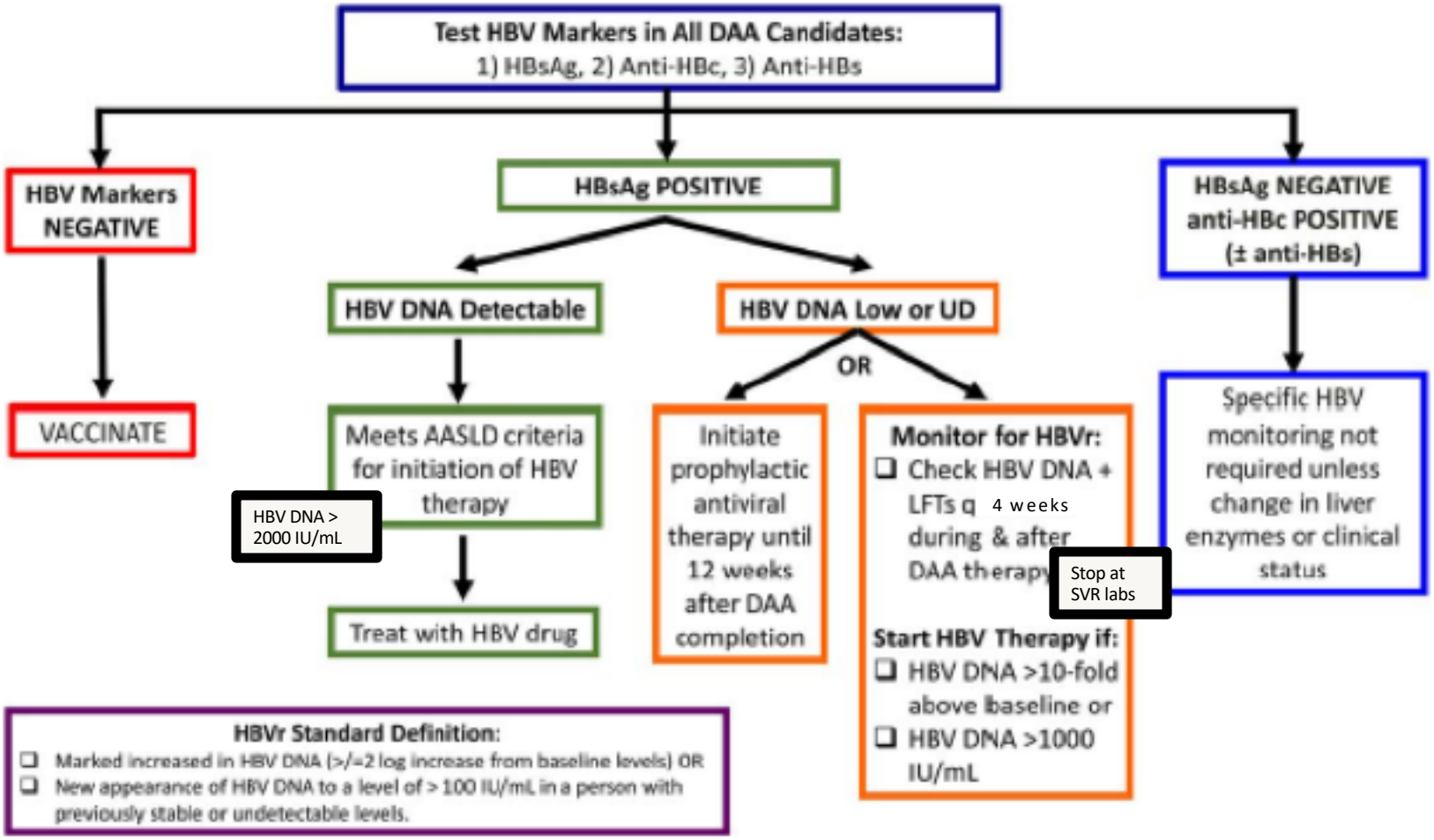
Common Medication Myths: Debunked!

- Avoid PPI (unless needed) in pts with cirrhosis, especially if ascites present
  - Increases risk of HE, infection (SBP)
- Statins are safe for pts with liver disease and cirrhosis
  - Hepatoxicity is rare-- 1% of pts
  - Risk of ACS outweighs risk of hepatotoxicity
  - Might be helpful in pts with cirrhosis
    - Decreased risk of hep decompensation and HCC
- Tylenol is a safe pain med
  - Cirrhosis, active EtOH abuse: < 2 gram/24 hr
  - Non cirrhotic liver disease: < 4 gram/24 hr
- Avoid NSAIDs
  - Increases risk of bleed, ARF, thrombocytopenia, ascites/LE edema

Thank you!!!

QUESTIONS???

HBV reactivation with DAA



Lieber S et al. Clinical Liver Disease 2017;10: 87-92.

IBD: What to do with HBV serology results?

HBV serologies		HBV status	What next?
HBsAg -	HBcAb -	Not infected	Vaccinate Proceed with IBD tx!
HBsAg +	HBcAb +	Overt/chronic infection	• Check baseline HBV DNA • Start HBV ppx (entecavir, tenofovir, TAF) • Begin 7 days prior, or at least at start of IBD immunosuppression • Continue for duration of IBD immunosuppression and for 6 mo after
HBsAg -	HBcAb +	Occult/resolved infection	• Monitor, no ppx needed! (AGA:consider ppx) • Check HBV DNA, LFT, (sAg) q 1-3 months (sAg because rare incidence of seroreversion)

Terrault NA et al. Hepatol 2018;4:1560-1599 Reddy K et al. Gastroenterol 2015;148:215–219