



HCC:
Screening,
Imaging &
Therapy



החברה הישראלית
לחקר הכבד
Israel Association for the
Study of the Liver



29.3.2016 • מלון דן פנורמה תל אביב

כנס החורף של

החברה הישראלית לחקר הכבד בשיתוף עם
איגוד הרדיולוגים בישראל

From Podium to Practice: HCV SAL 2016



Prof. Rifaat Safadi
Director of The Liver Unit



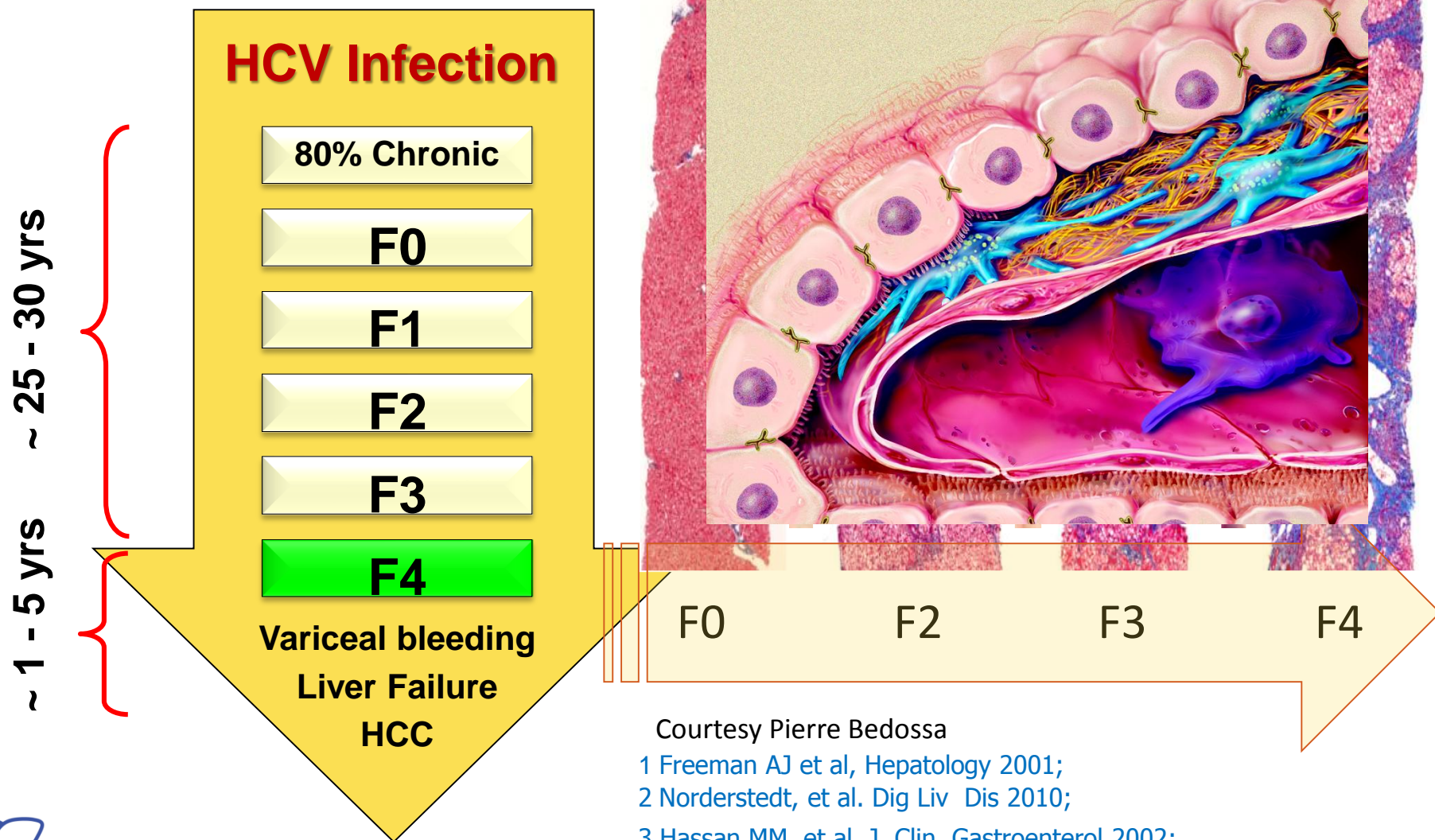
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HCV is Asymptomatic for > 90%



Courtesy Pierre Bedossa

1 Freeman AJ et al, Hepatology 2001;

2 Norderstedt, et al. Dig Liv Dis 2010;

3 Hassan MM, et al. J Clin, Gastroenterol 2002;

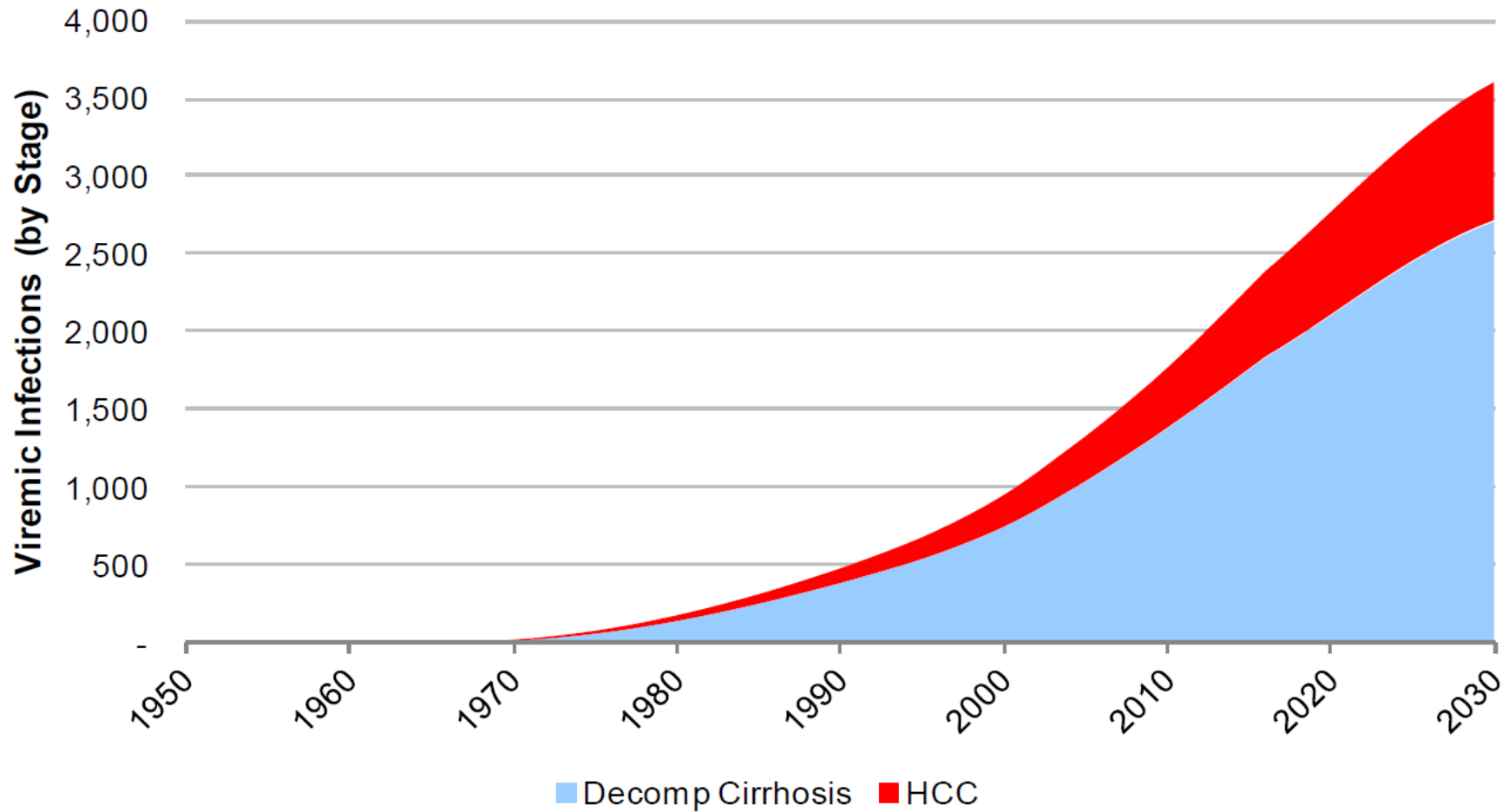
4 Rein et al, Dig Liver Dis 2011; Am J Epidemiology 2002;

Modified from Poynard



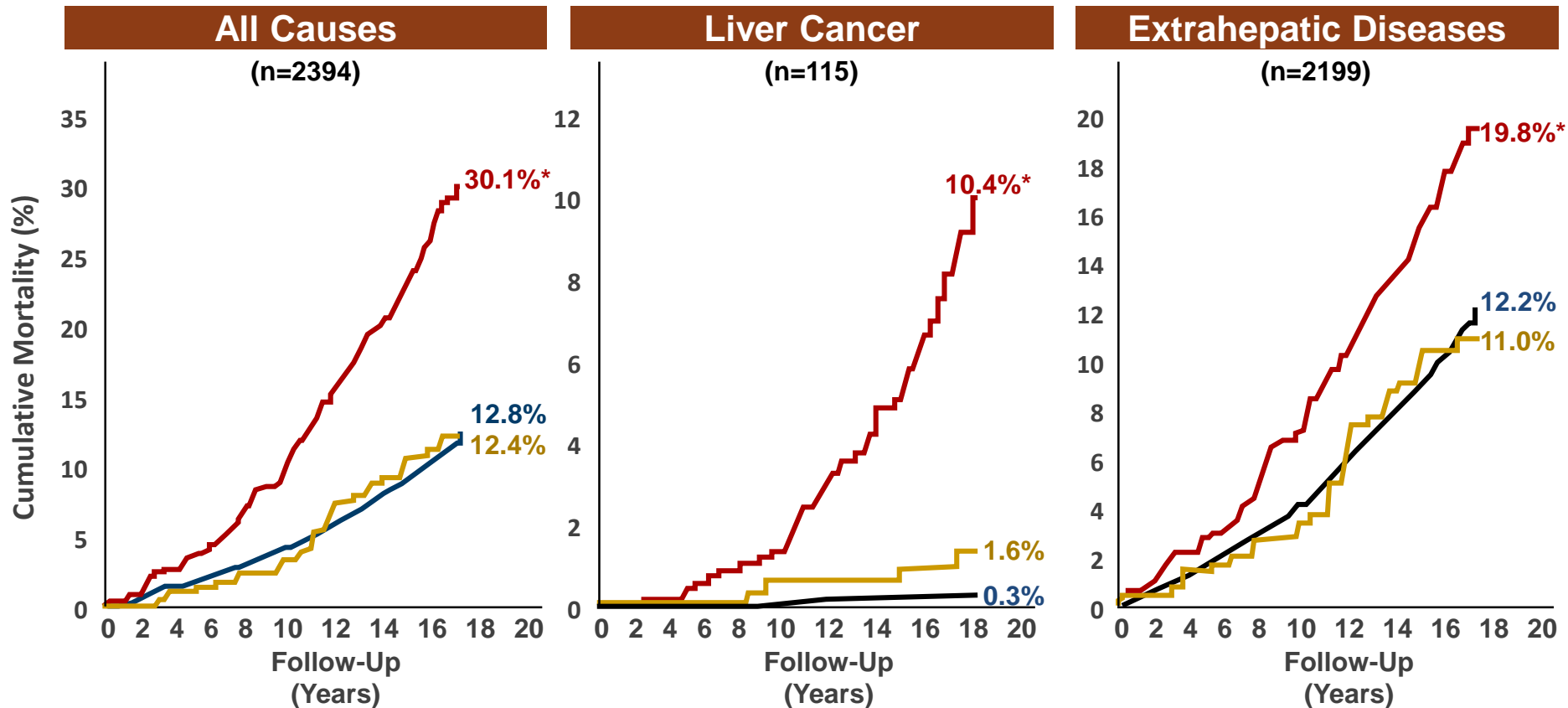
The present and future disease burden of HCV infections with today's treatment paradigm

Israel



HCV Viremia Was Associated With Increased Mortality in a Prospective Taiwanese Cohort Study

— Anti-HCV+, HCV RNA detectable — Anti-HCV+, HCV RNA undetectable — Anti-HCV—



REVEAL HCV: Risk Evaluation of Viral Load Elevation and Associated Liver Disease/Cancer (1991-2008).

Anti-HCV seronegative (n=18,541); anti-HCV seropositive (n=1095; detectable HCV RNA: 69.4%). Average follow-up: 16.2 years.

Among extrahepatic causes of death, 68.5% and 69.3% were noncancer deaths for HCV seronegative and seropositive, respectively.

* $P < .001$ for comparison among all 3 groups and $P < .001$ for HCV RNA detectable vs undetectable.



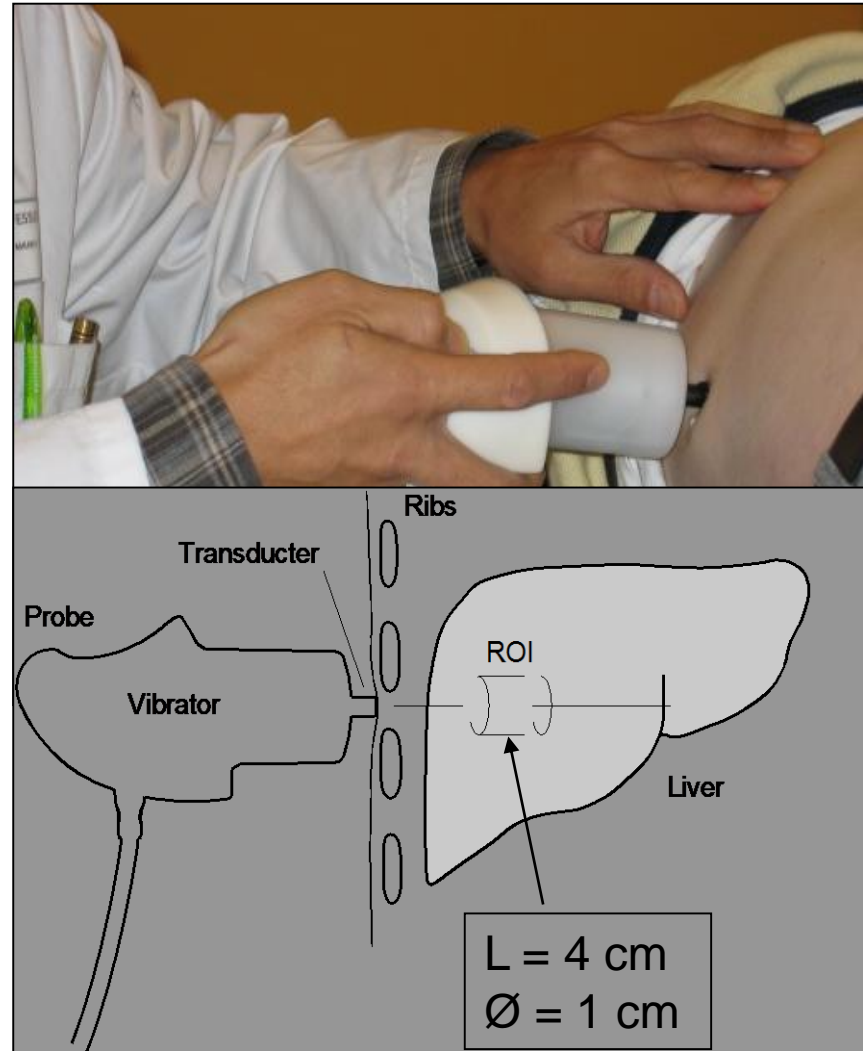
סל 2016



טיפול בזיהום מסוג Clostridium difficile (C difficile associated diarrhea) בחולים הסובלים מהישנות המחלה.	Fidaxomicin	Dificlir
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 1 עם דרגות פיברוזיס F3-F4	Sofosbuvir + Ledipasvir	Harvoni
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 1 עם דרגות פיברוזיס F3-F4	Grazoprevir + Elbasvir	MK-5172/8742
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 2 עם דרגות פיברוזיס F3-F4	Daclatasvir	Daklinza
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 3 עם דרגות פיברוזיס F3-F4	Daclatasvir	Daklinza
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 4 עם דרגות פיברוזיס F3-F4	Daclatasvir	Daklinza
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 2 עם דרגות פיברוזיס F3-F4	Sofosbuvir	Sovaldi
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 3 עם דרגות פיברוזיס F3-F4	Sofosbuvir	Sovaldi
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 4 עם דרגות פיברוזיס F3-F4	Sofosbuvir	Sovaldi
טיפול בהפטיטיס C כרונית בחולים עם גנוטיפ 4 עם דרגות פיברוזיס F3-F4	Paritaprevir + Ritonavir + Ombitasvir	Viekirax



Fibroscan



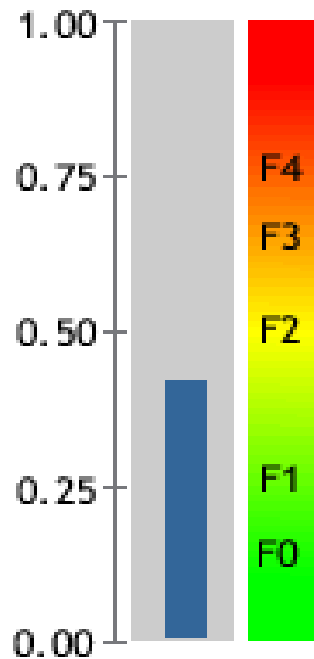
Courtesy of M. Ziol

Guha et al, Gut 2006



FibroTest ActiTest

FibroTest

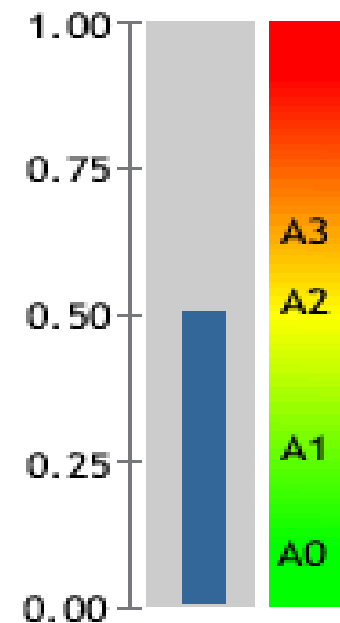


Score : 0.42
(F1-F2)

Five Serum Markers:

- ✓ α 2Macroglobulin
- ✓ Total Bilirubin
- ✓ γ GT
- ✓ Apolipoprotein A1
- ✓ Haptoglobin

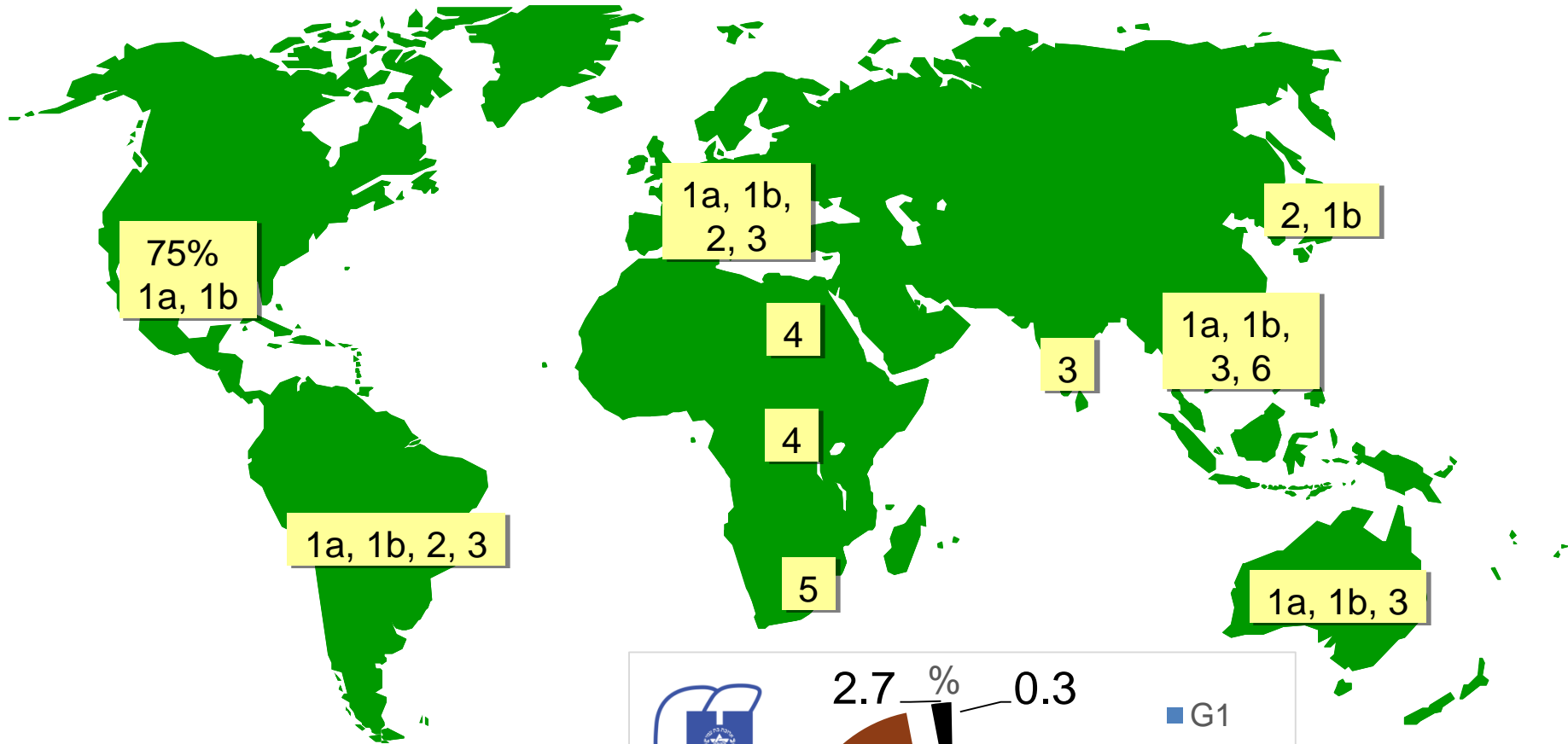
ActiTest



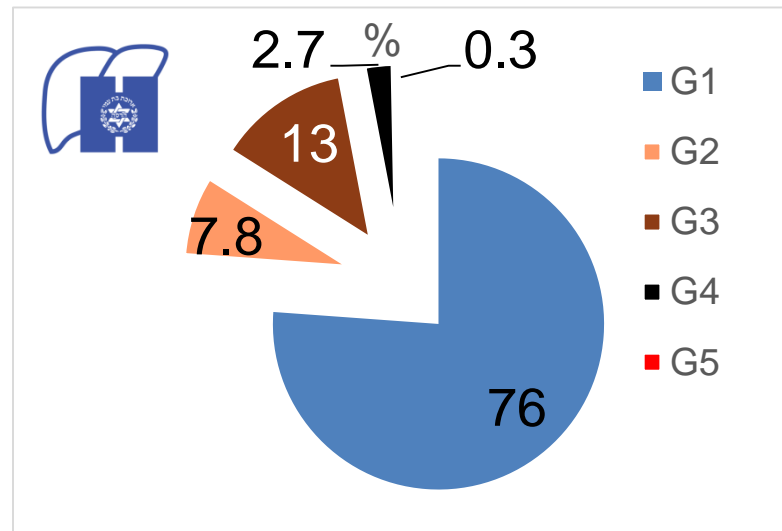
Score: 0.50
(A1-A2)



Genotype prevalence & Distribution

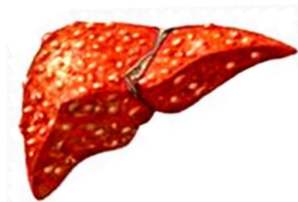


1. Hoofnagle J. Hepatology 2002; 36: S21
2. Zein N. Clin Microbiol Rev 2000; 13: 223
3. Alter M, et al. N Engl J Med 1999; 341: 556



GT1 ±HIV TN &TE without cirrhosis

Patients	Zepatier	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 1a	12-16 wk, with RBV	No	8-12 wk, without RBV	12 wk with RBV	No	12 wk without RBV	12 wk without RBV
Genotype 1b	8-12 wk, Without RBV		12 wk without RBV	12 wk without RBV			



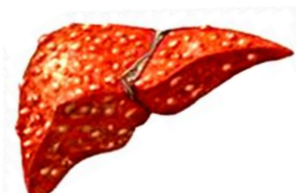
GT1 ±HIV TN &TE with CHILD-A cirrhosis

Patients	Zepatier	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 1a	12-16 wk, with RBV	No	12 wk with RBV, or 24 wk without RBV, or 24 wk with RBV if negative predictors of response	24 wk with RBV	No	12 wk with RBV, or 24 wk without RBV	12 wk with RBV, or 24 wk without RBV
Genotype 1b	8-12 wk, Without RBV		12 wk with RBV	12 wk with RBV			



GT2 ±HIV TN &TE without cirrhosis

Patients	PegIFN-α, RBV and sofosbuvir	PegIFN-α, RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 2	12 wk	No	12 wk	No	No	No	No	12 wk without RBV



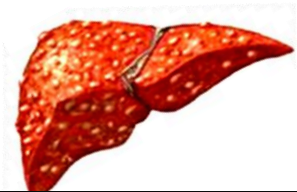
GT2 ±HIV TN &TE with cirrhosis

Patients	PegIFN-α, RBV and sofosbuvir	PegIFN-α, RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 2	12 wk	No	16-20 wk	No	No	No	No	12 wk without RBV



GT3 ±HIV TN &TE without cirrhosis

Patients	PegIFN- α , RBV and sofosbuvir	PegIFN- α , RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 3	12 wk	No	24 wk	No	No	No	No	12 wk without RBV



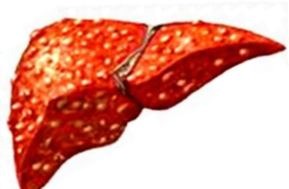
GT3 ±HIV TN &TE with cirrhosis

Patients	PegIFN- α , RBV and sofosbuvir	PegIFN- α , RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 3	12 wk	No	No	No	No	No	No	24 wk with RBV



GT4 ±HIV TN &TE without cirrhosis

Patients	PegIFN- α RBV and sofosbuvir	Zepatier	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 4	12 wk	12 wk, Without RBV	No	12 wk without RBV	No	12 wk with RBV	12 wk without RBV	12 wk without RBV



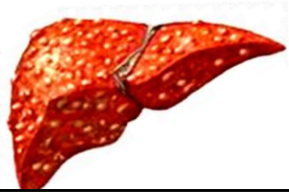
GT4 ±HIV TN &TE with cirrhosis

Patients	PegIFN- α RBV and sofosbuvir	Zepatier	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 4	12 wk	12 wk, Without RBV	No	12 wk with RBV, or 24 wk without RBV, or 24 wk with RBV if negative predictors of response	No	24 wk with RBV	12 wk with RBV, or 24 wk without RBV	12 wk with RBV, or 24 wk without RBV



GT5/6 ±HIV TN &TE without cirrhosis

Patients	PegIFN- α , RBV and sofosbuvir	PegIFN- α , RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 5 or 6	12 wk	No	No	12 wk without RBV	No	No	No	12 weeks without RBV



GT5/6 ±HIV TN &TE with cirrhosis

Patients	PegIFN- α , RBV and sofosbuvir	PegIFN- α , RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 5 or 6	12 wk	No	No	12 wk with RBV, or 24 wk without RBV, or 24 wk with RBV if negative predictors of response	No	No	No	12 wk with RBV, or 24 wk without RBV



Re Treat HCV±HIV who fail prior therapy containing ≥1 DAA(s)

Failed treatment	Genotype	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
PegIFN-α, RBV and either telaprevir or boceprevir	Genotype 1	12 wk with RBV	No	No	No	12 wk with RBV
Sofosbuvir alone, in combination with RBV or in combination with PegIFN-α and RBV	Genotype 1	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
	Genotype 2 or 3	No	No	No	No	12 weeks with RBV or 24 weeks with RBV if F3 or cirrhosis
	Genotype 4	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
	Genotype 5 or 6	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
PegIFN-α, RBV and simeprevir	Genotype 1 or 4	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
PegIFN-α, RBV and daclatasvir	Genotype 1	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No
	Genotype 2 or 3	No	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
	Genotype 4	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No
	Genotype 5 or 6	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
Sofosbuvir and simeprevir	Genotype 1 or 4	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis

Re Treat HCV±HIV who fail prior therapy containing ≥1 DAA(s)

Failed treatment	Genotype	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Sofosbuvir and daclatasvir or Sofosbuvir and ledipasvir	Genotype 1	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No
	Genotype 2 or 3	No	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
	Genotype 4	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No
	Genotype 5 or 6	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Genotype 1	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis
Ritonavir-boosted paritaprevir and ombitasvir	Genotype 4	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	No	No	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis	12 wk with RBV or 24 wk with RBV if F3 or cirrhosis

Currently, there is limited data to firmly support these retreatment recommendations, which are based on indirect evidence and consideration of HCV genotype, known resistance profiles of the previously administered drugs, number of drugs used, use of ribavirin, treatment duration. Thus, these recommendations are subject to change when more data become available.

Drug-drug interactions between HCV DAAs & immunosuppressants

	SIM	DCV	SOF	SOF/ LDV	3D
Azathioprine	•	•	•	•	•
Cyclosporine	•	•	•	•	•
Etanercept	•	•	•	•	•
Everolimus	•	•	•	•	•
Mycophenolate	•	•	•	•	•
Sirolimus	•	•	•	•	•
Tacrolimus	•	•	•	•	•



▪ **Green:** No clinically significant interaction expected.



▪ **Amber:** Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.



▪ **Red:** These drugs should not be coadministered.

www.hep-druginteractions.org (University of Liverpool)

Drug-drug interactions between HCV DAAs and:

HIV antiretrovirals

		SIM	DCV	SOF	SOF/ LDV	3D
NRTIs	Abacavir	•	•	•	•	•
	Didanosine	•	•	•	•	•
	Emtricitabine	•	•	•	•	•
	Lamivudine	•	•	•	•	•
	Stavudine	•	•	•	•	•
	Tenofovir	•	•	•	•	•
	Zidovudine	•	•	•	•	•
NNRTIs	Efavirenz	•	•	•	•*	•
	Etravirine	•	•	•	•	•
	Nevirapine	•	•	•	•	•
	Rilpivirine	•	•	•	•*	•
Protease inhibitors	Atazanavir; atazanavir/ritonavir	•	•	•	•*	•
	Darunavir/ritonavir; darunavir/cobicistat	•	•	•	•*	•
	Fosamprenavir	•	•	•	•*	•
	Lopinavir	•	•	•	•*	•
	Saquinavir	•	•	•	•*	•
Entry/ Integrase inhibitors	Dolutegravir	•	•	•	•	•
	Elvitegravir/cobicistat	•	•	•	•*	•
	Maraviroc	•	•	•	•	•
	Raltegravir	•	•	•	•	•

illicit recreational Drugs

	SIM	DCV	SOF	SOF/ LDV	3D
Amphetamine	•	•	•	•	•
Cannabis	•	•	•	•	•
Cocaine	•	•	•	•	•
Diamorphine	•	•	•	•	•
Diazepam	•	•	•	•	•
Gamma-hydroxybutyrate	•	•	•	•	•
Ketamine	•	•	•	•	•
MDMA (ecstasy)	•	•	•	•	•
Methamphetamine	•	•	•	•	•
Phencyclidine (PCP)	•	•	•	•	•
Temazepam	•	•	•	•	•

lipid lowering Drugs

	SIM	DCV	SOF	SOF/ LDV	3D
Atorvastatin	•	•	•	•	•
Bezafibrate	•	•	•	•	•
Ezetimibe	•	•	•	•	•
Fenofibrate	•	•	•	•	•
Fluvastatin	•	•	•	•	•
Gemfibrozil	•	•	•	•	•
Lovastatin	•	•	•	•	•
Pitavastatin	•	•	•	•	•
Pravastatin	•	•	•	•	•
Rosuvastatin	•	•	•	•	•
Simvastatin	•	•	•	•	•

Drug-drug interactions between HCV DAAs and:

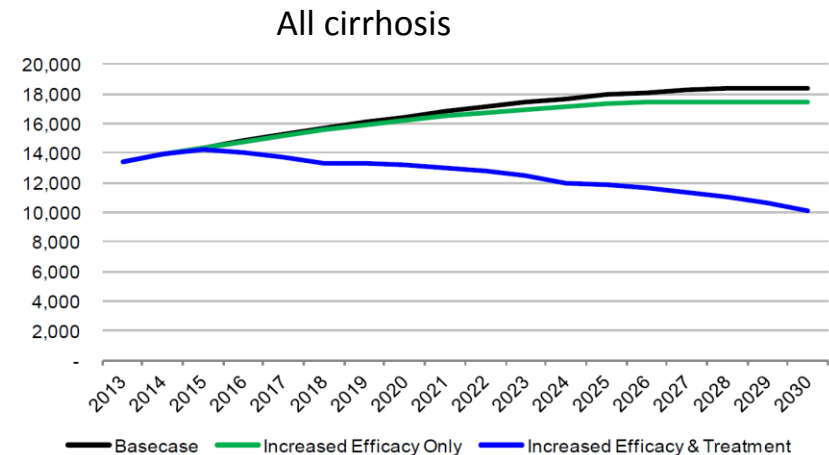
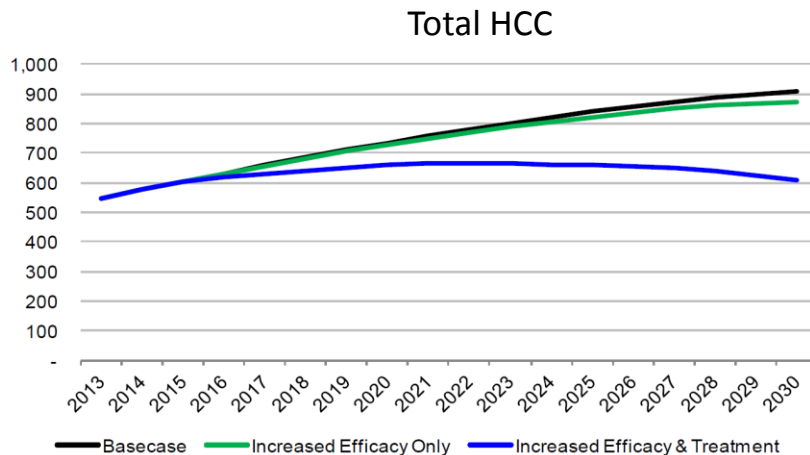
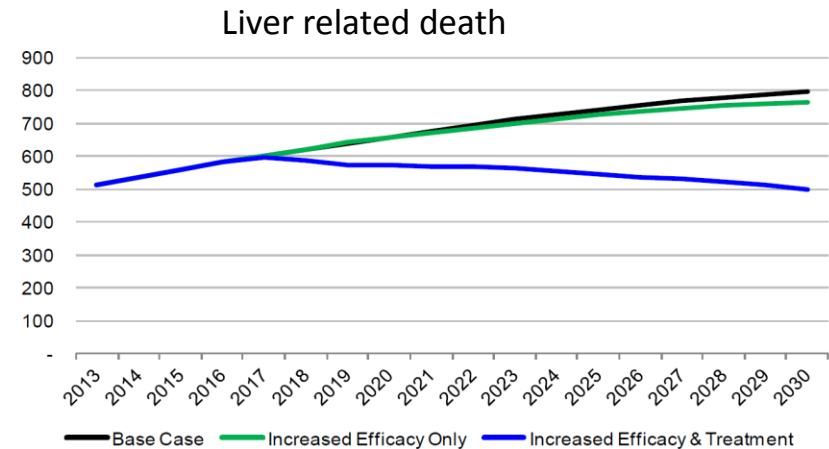
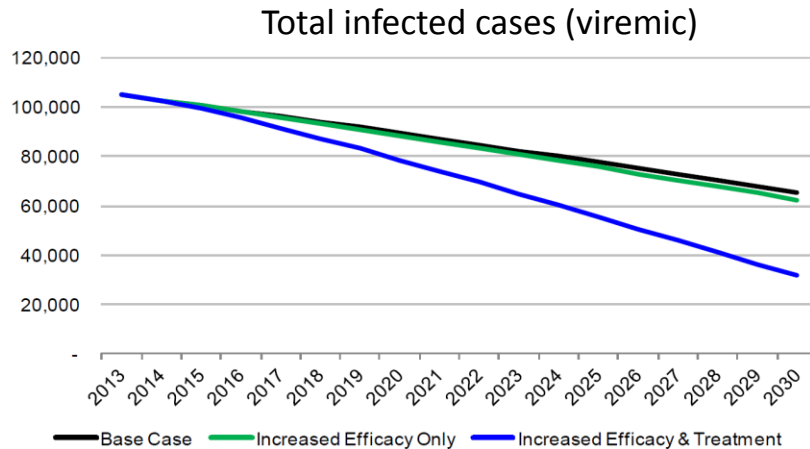
CNS Drugs

		SIM	DCV	SOF	SOF/ LDV	3D
Anti-depressants	Amitriptyline	•	•	•	•	•
	Citalopram	•	•	•	•	•
	Duloxetine	•	•	•	•	•
	Escitalopram	•	•	•	•	•
	Fluoxetine	•	•	•	•	•
	Paroxetine	•	•	•	•	•
	Sertraline	•	•	•	•	•
	Trazodone	•	•	•	•	•
	Trimipramine	•	•	•	•	•
	Venlafaxine	•	•	•	•	•
Anti-psychotics	Amisulpiride	•	•	•	•	•
	Aripiprazole	•	•	•	•	•
	Chlorpromazine	•	•	•	•	•
	Clozapine	•	•	•	•	•
	Flupentixol	•	•	•	•	•
	Haloperidol	•	•	•	•	•
	Olanzapine	•	•	•	•	•
	Quetiapine	•	•	•	•	•
	Risperidone	•	•	•	•	•

CVS Drugs

		SIM	DCV	SOF	SOF/ LDV	3D
Antiarrhythmics	Amiodarone	•	•	•	•	•
	Digoxin	•	•	•	•	•
	Flecainide	•	•	•	•	•
	Vernakalant	•	•	•	•	•
Antiplatelet and anticoagulants	Clopidogrel	•	•	•	•	•
	Dabigatran	•	•	•	•	•
	Warfarin	•	•	•	•	•
Beta blockers	Atenolol	•	•	•	•	•
	Bisoprolol	•	•	•	•	•
	Propranolol	•	•	•	•	•
Calcium channel blockers	Amlodipine	•	•	•	•	•
	Diltiazem	•	•	•	•	•
	Nifedipine	•	•	•	•	•
Hypertension and heart failure agents	Aliskiren	•	•	•	•	•
	Candesartan	•	•	•	•	•
	Doxazosin	•	•	•	•	•
	Enalapril	•	•	•	•	•

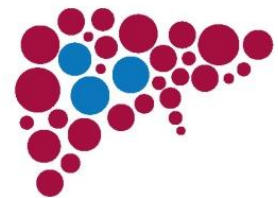
Strategies to manage HCV infection disease burden



Thank You



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