Hepatitis C: Can we eliminate a cause of CKD?

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TORONTO CENTRE FOR LIVER DISEASE

Disclosures: J Feld

- Research support: Abbvie, Gilead, Janssen, Merck
- Consulting: Abbvie, Gilead, Merck
- Speaking: None

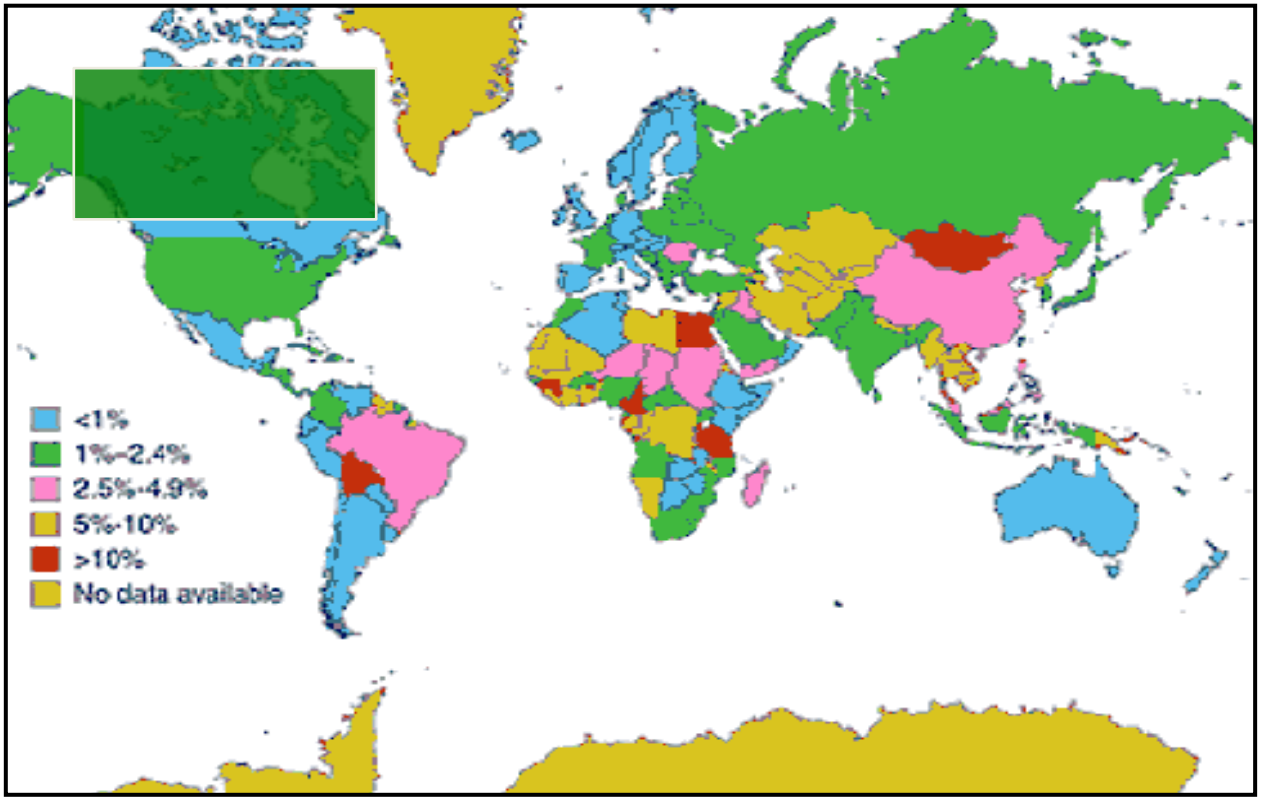
Objectives

1. Appreciate the burden of illness cause by hepatitis C in the renal and non-renal populations
2. Recognize the significant advances in antiviral therapy for patients with hepatitis C and particularly for those with renal disease
3. Understand the remaining challenges in the road to elimination of hepatitis C

Outline

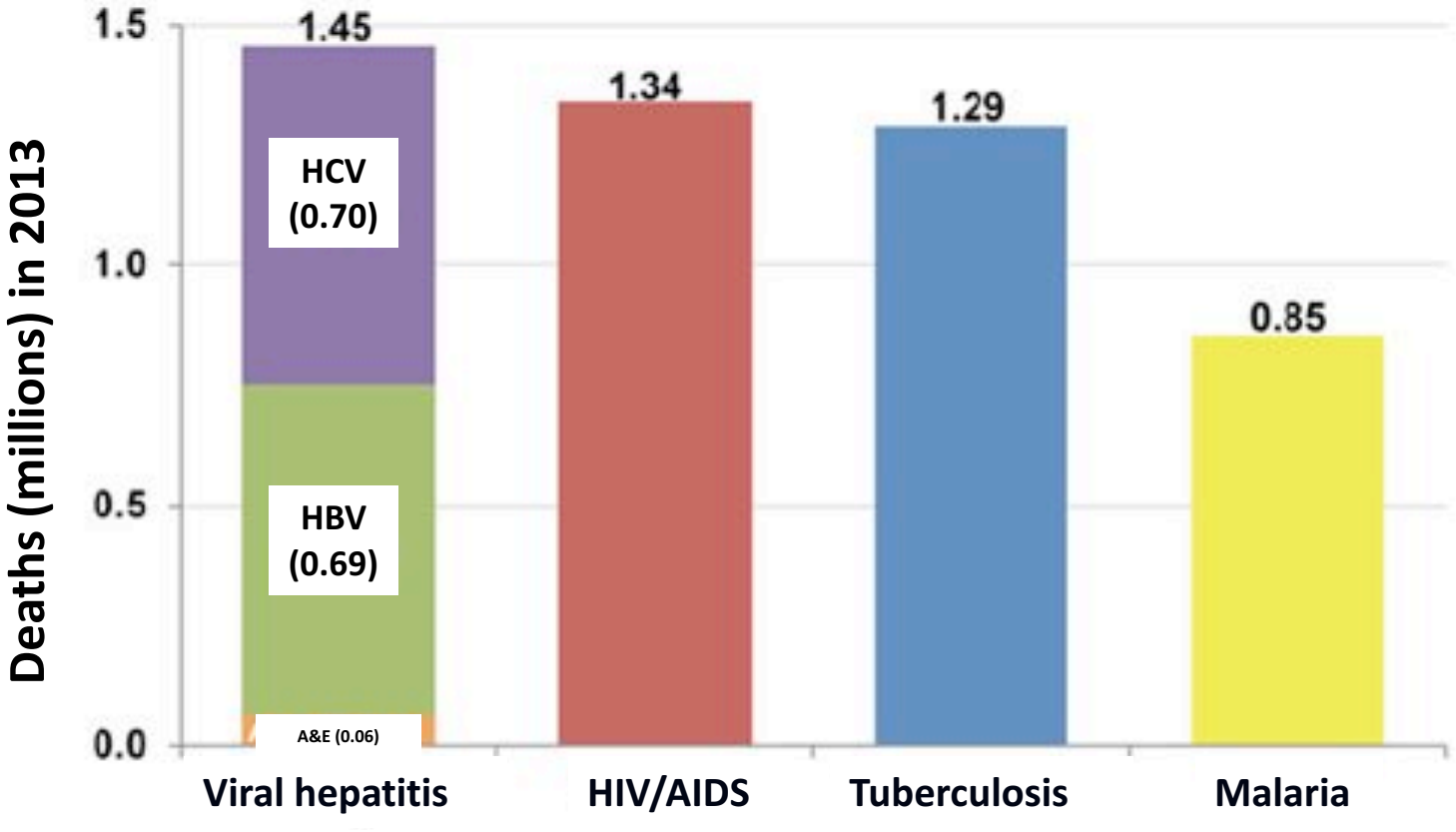
- Background on HCV
- HCV & CKD
  - Risk of HCV in CKD and CKD in HCV
- Treatment
  - Genotype 1
  - Other genotypes…controversies remain
  - Cryo-related renal disease
- The transplant conundrum

HCV is a MAJOR global public health problem



- ~71 million people infected
- No vaccine
- Leading indication for liver transplant

Should the big 3 be the big 4?



Global Burden of Disease Study 2013, Lancet 2015

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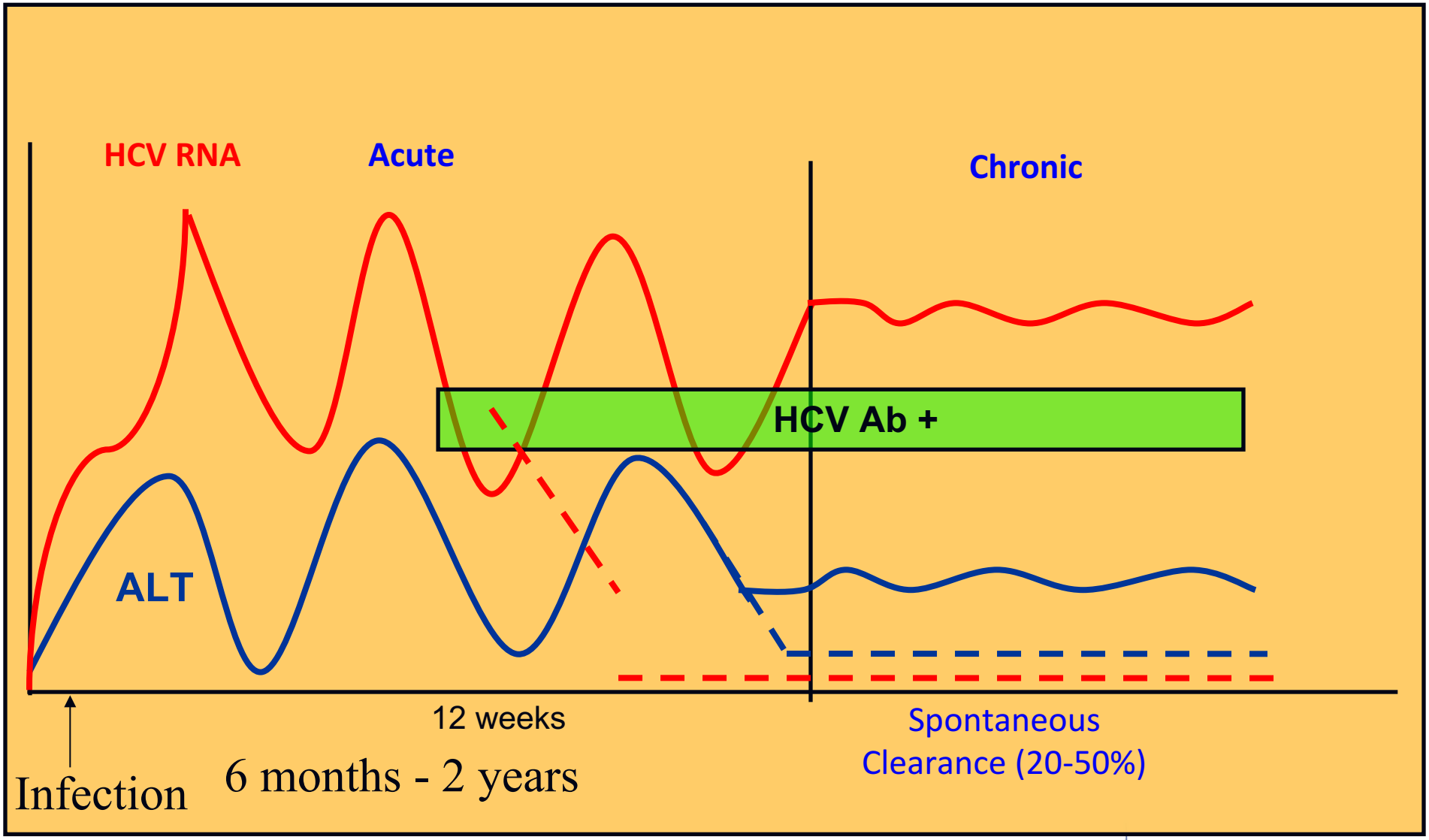
Natural History

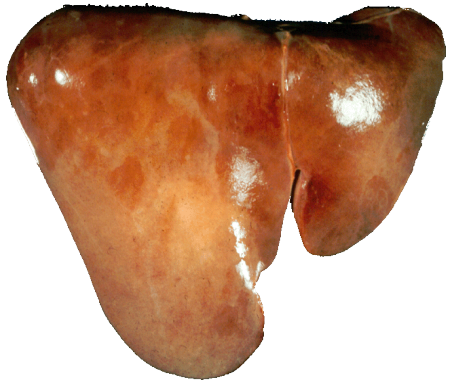


Implications of Spontaneous Clearance

- Profile
  - Anti-HCV Ab +ve, HCV RNA –ve
  - Repeat to confirm but likely true clearance vs. false +ve
- True ***cure*** of infection
- No liver or non-liver related increased morbidity or mortality → NO clinical significance to +ve test
- (Surrogate for risk behaviours????)
- Will remain anti-HCV +ve lifelong, no risk of relapse but not protected from reinfection

Potential consequences of HCV

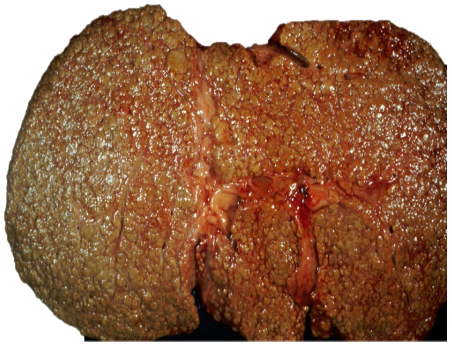
Healthy Liver



Cirrhosis

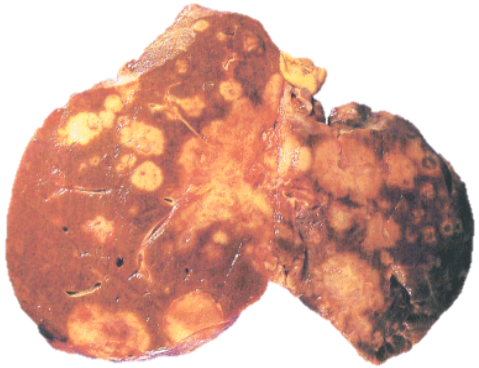
20%

(at 20 yrs of infection)



Liver Cancer

1-4%/yr

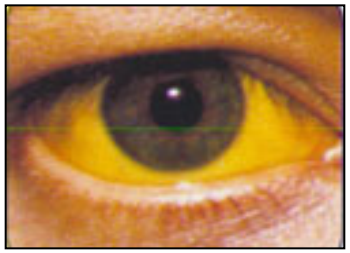


Slowly progressive over decades of infection

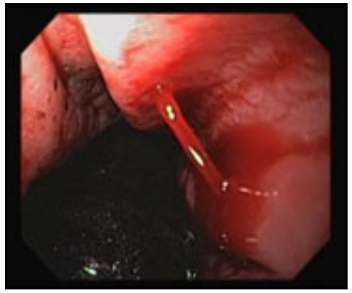
No!

Cirrhosis risk 41% at 30 yrs…lifetime risk 50-60% or higher

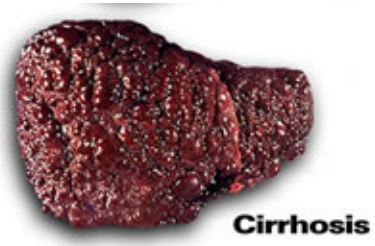
What we're trying to prevent

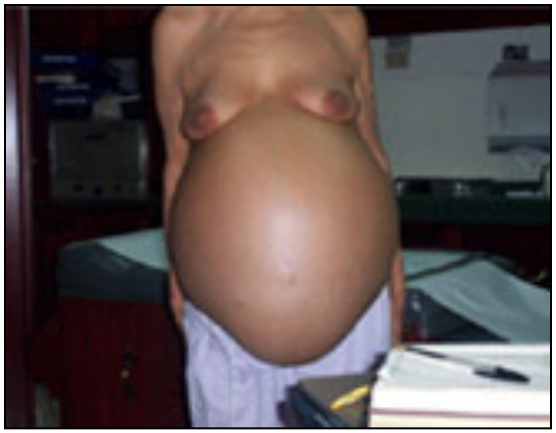


Jaundice

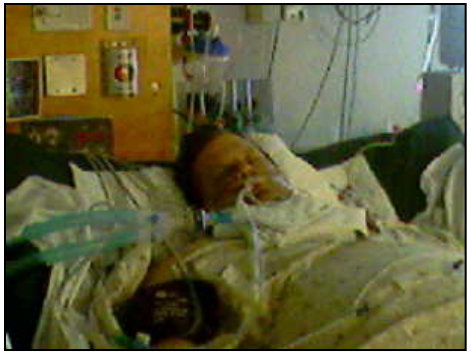


Esophageal Varices

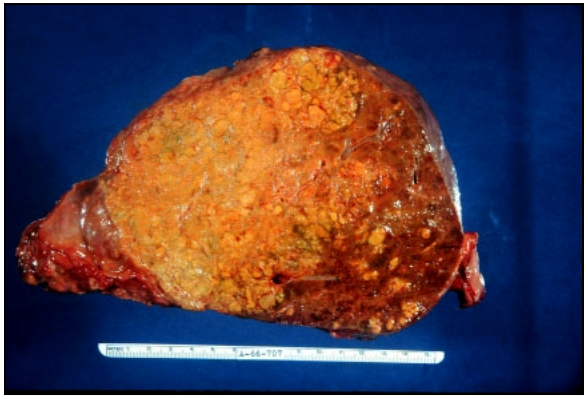




Fluid Retention
Ascites

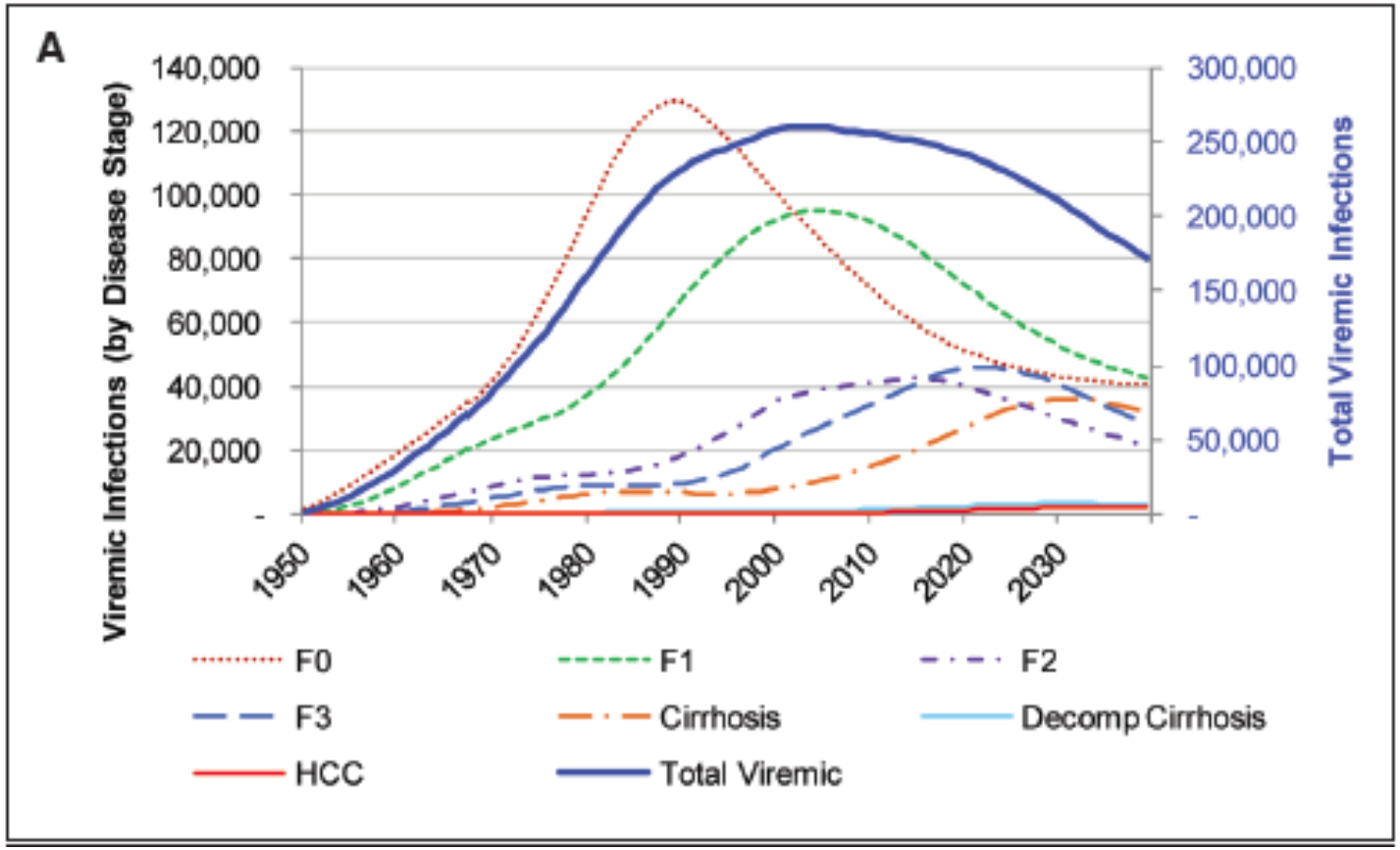


Hepatic Encephalopathy



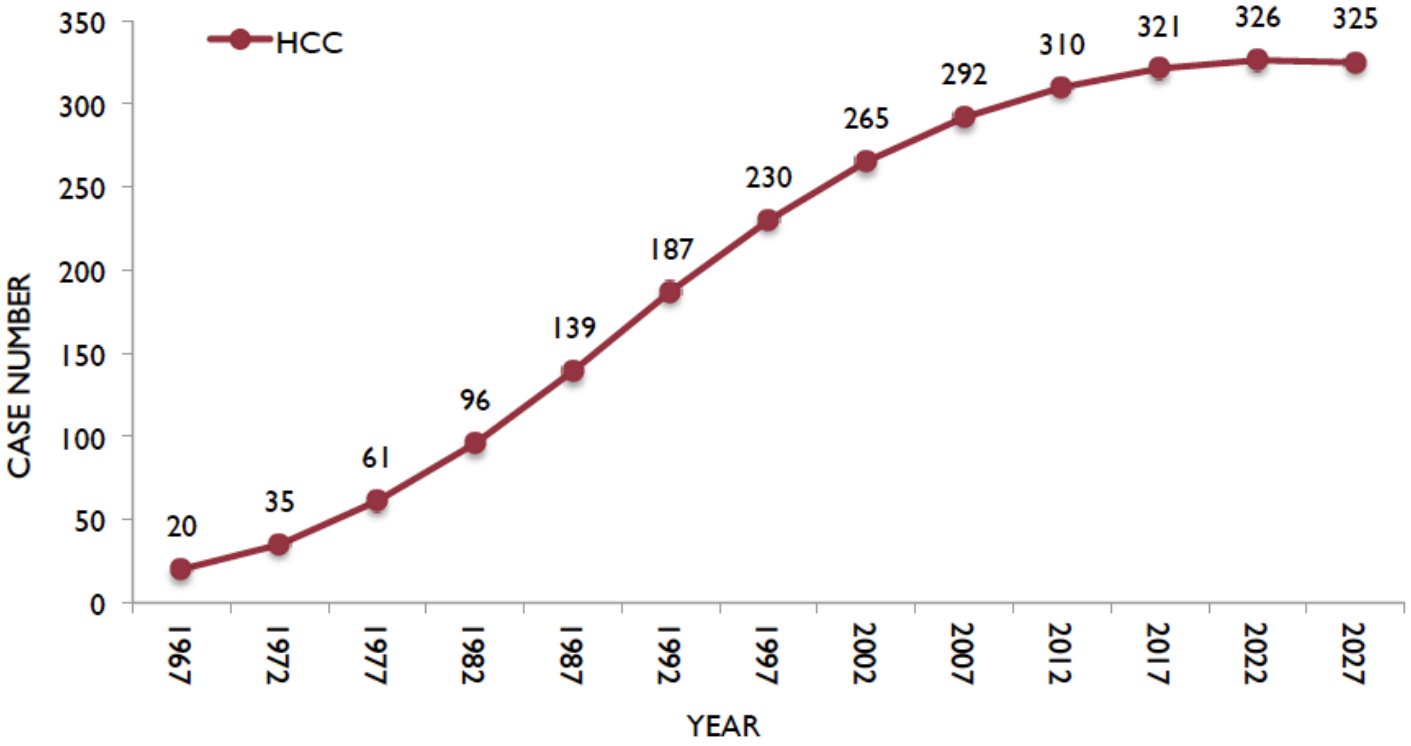
Liver Cancer

The complications are just beginning



- Rising rates of cirrhosis, liver failure, liver cancer

Liver cancer rates increasing



Increasing rates of liver cancer until 2027

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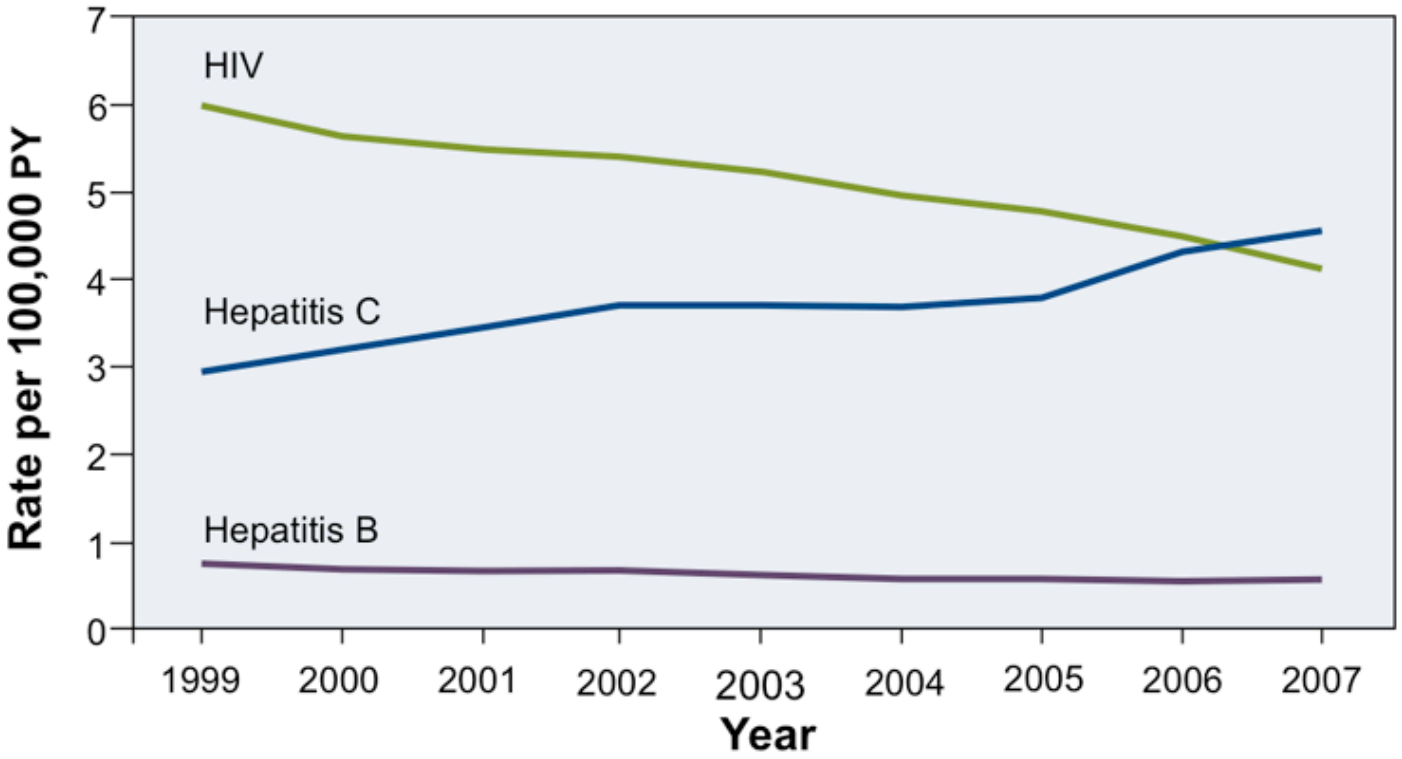
Increasing HCV and decreasing HIV mortality



Ly Ann Int Med 2012 CDC

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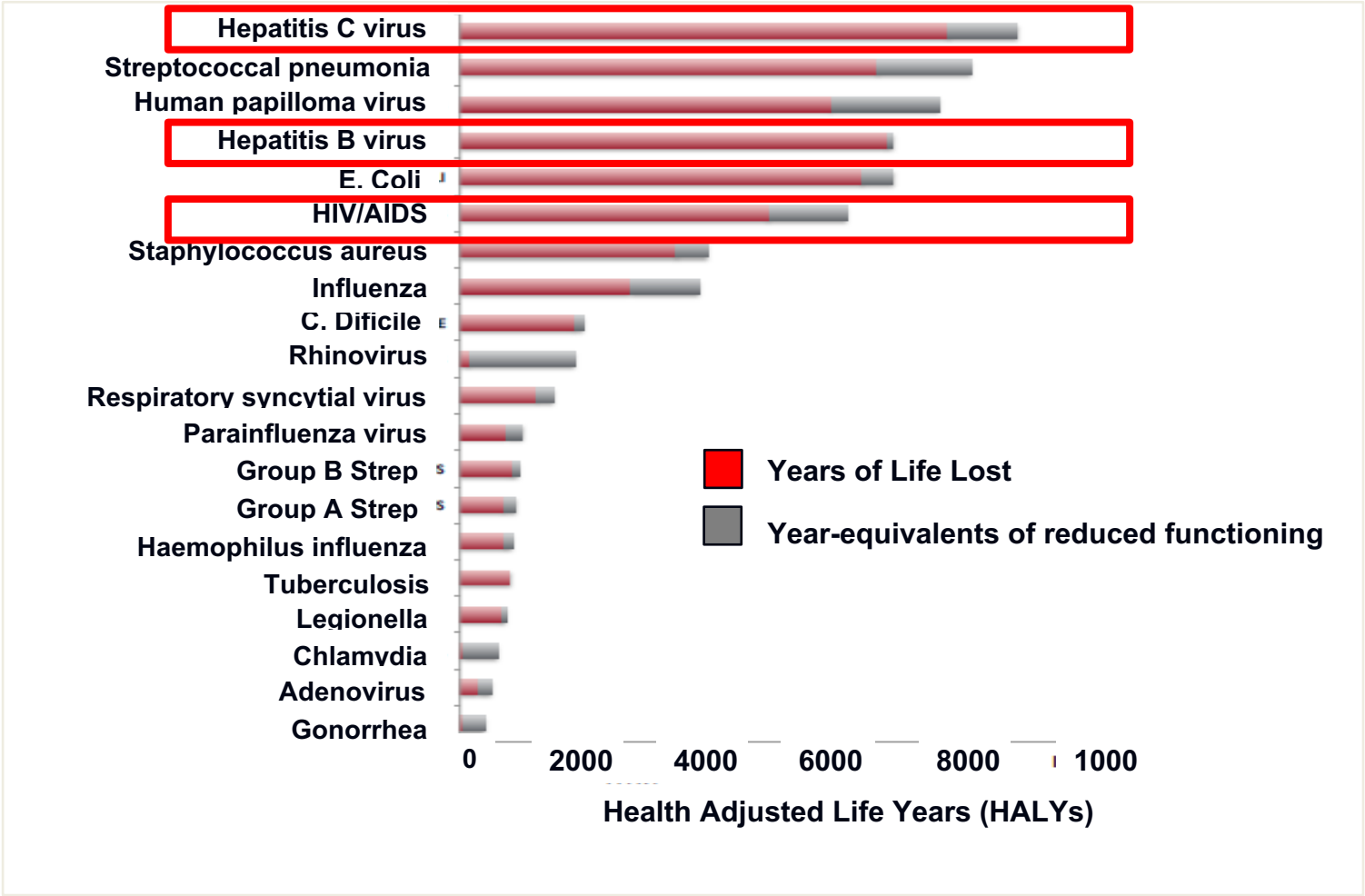
Hepatitis is a MAJOR health problem in Canada



Kwong et al PLoS One 2012

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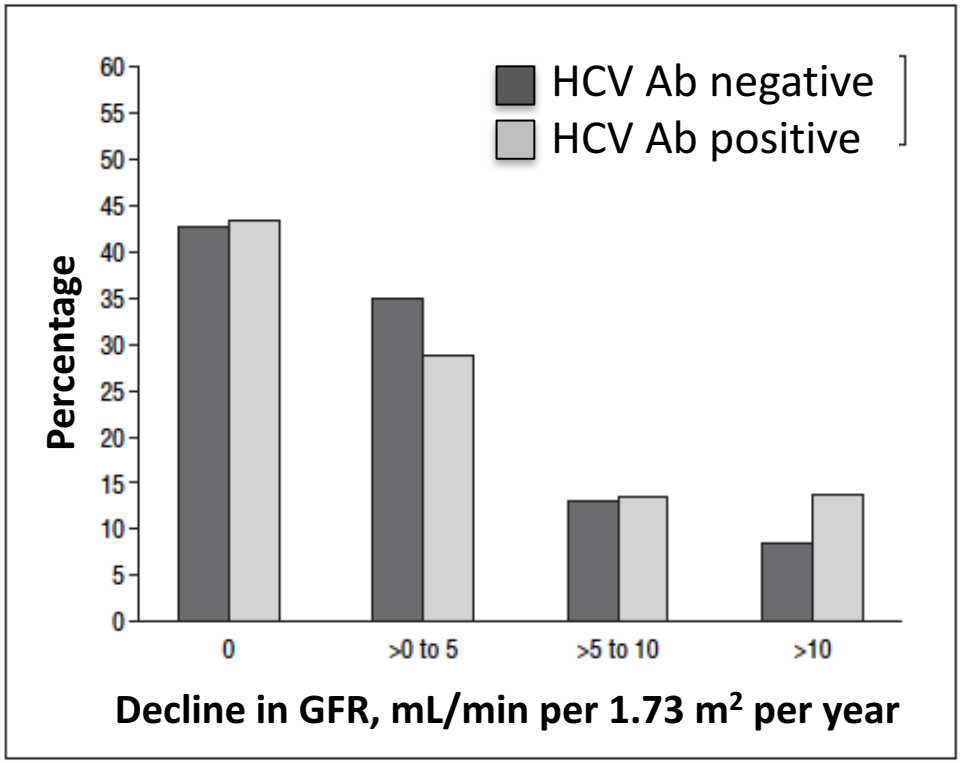
Outline

- Background on HCV
- **HCV & CKD**
  - **Risk of HCV in CKD and CKD in HCV**
- Treatment
  - Genotype 1
  - Other genotypes…controversies remain
  - Cryo-related renal disease
- The transplant conundrum

HCV increases the risk of CKD

474,369 from the VA – 52,874 with HCV followed for 4 years – change in GFR and incidence of ESRD



Higher adjusted risk
- All age strata (to 70)
- All strata of baseline GFR

- Etiologies similar but more
  - DM
  - GN

- Rate of ESRD: HCV +ve 4.26 vs HCV –ve: 3.05 per 1000 pt-yrs
- Recent meta-analyses: aHR 1.23 to 1.46 of ESRD if HCV +ve

Tsui Arch Int Med 2007, Fabrizi Dig Dis Sci 2015, Park JVH 2015

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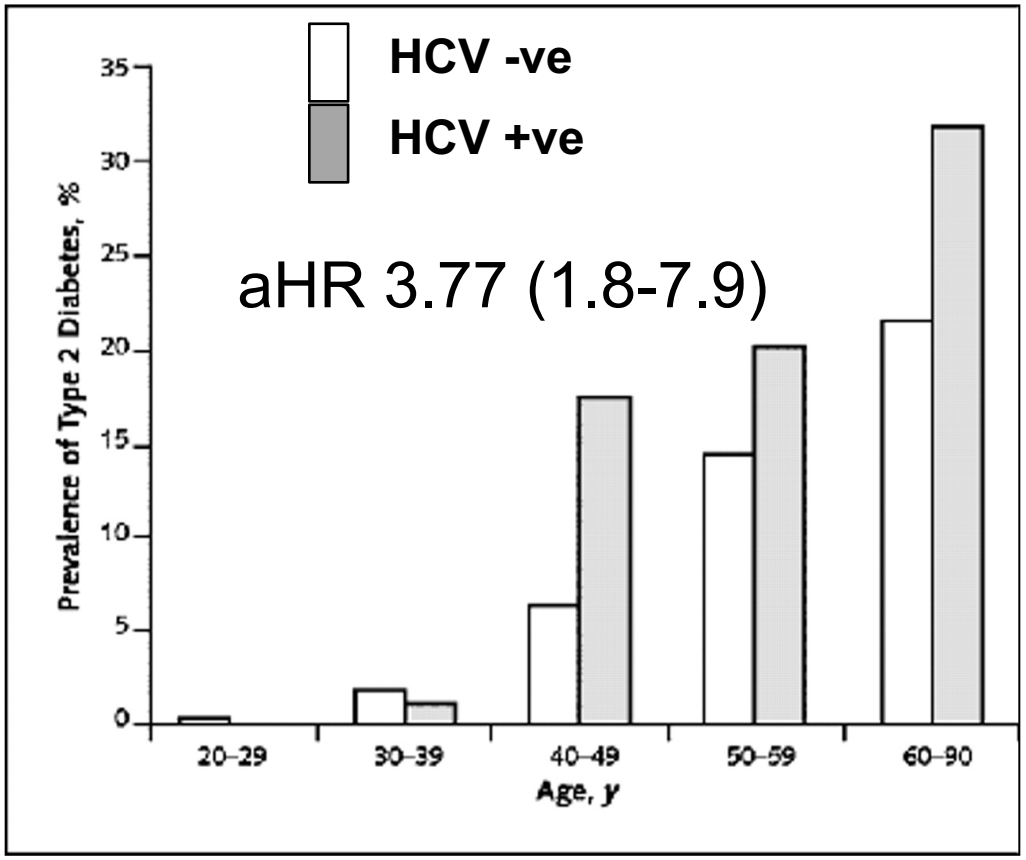
An indirect cause of CKD

NHANES 9,841 patients – Prev of DM & HCV



HCV interferes with glucose/lipid metabolism → IR → DM

Mehta Ann Int Med 2000

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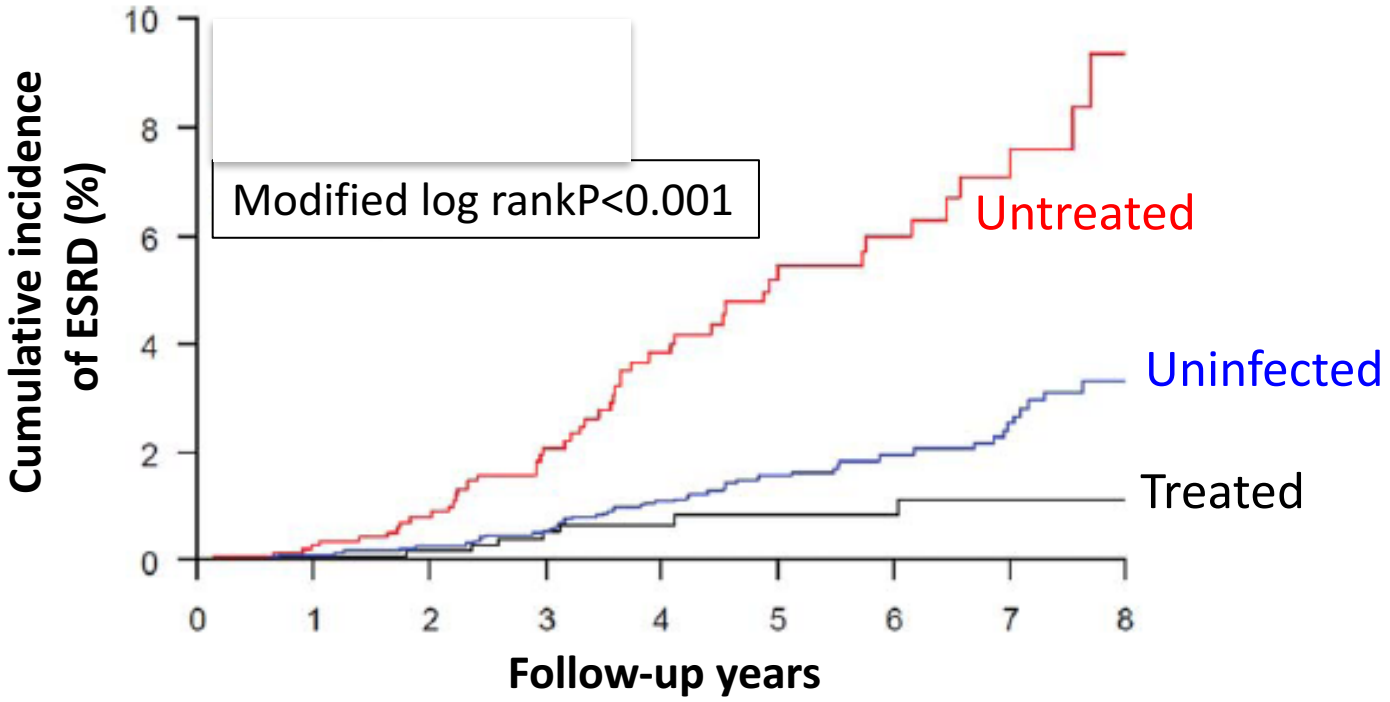
Effect of HCV on DM to ESRD

Propensity score matched risk of ESRD among Taiwanese patients with DM with untreated (n=1, 411), treated (n=1,411) or no HCV (n=5,644)



Treatment of HCV reduces the risk of ESRD among patients with DM

HCV in patients with ESRD

- Increased risk → historically very high prevalence in HD populations due to transfusion + HD transmission
- Increased risk of chronicity with exposure

- **Wealthy countries** → decreasing risk
  - US 1985 - 10.4% to 2002 – 7.8% → likely much lower now
  - Europe – 13.5% 1991 to 6.8% in 2000
  - Ongoing transmission 0.2% per year
  - No recommendation for isolation of HCV patients but universal precautions & test every 6-12 months

- **Developing countries**
  - Very variable but up to 80% in single centre studies & up to 15% per year transmission

Finelli Sem Dial 2005, Jadoul Nephrol Dial Transplant 2004

Clinical aspects in ESRD

- Clinical effects may be a bit more subtle
- Lower ALT
  - Screen everyone! Not just those with high ALT
  - Must continue to screen for HCV over time – ongoing transmission risk
- HCV RNA
  - Lower levels post HD
- Fibrosis assessment
  - Biopsy challenging – platelet dysfunction
  - Non-invasive tools

Liu Clin J Am Soc Neph 2011, Varaut Transplantation 2005,
Canbakan Neph Clin Prac 2011, Liu J Gastro Hep 2011

Assessment of Fibrosis Critical

1. Determines degree of liver damage

– (fibrosis ≠ cirrhosis)

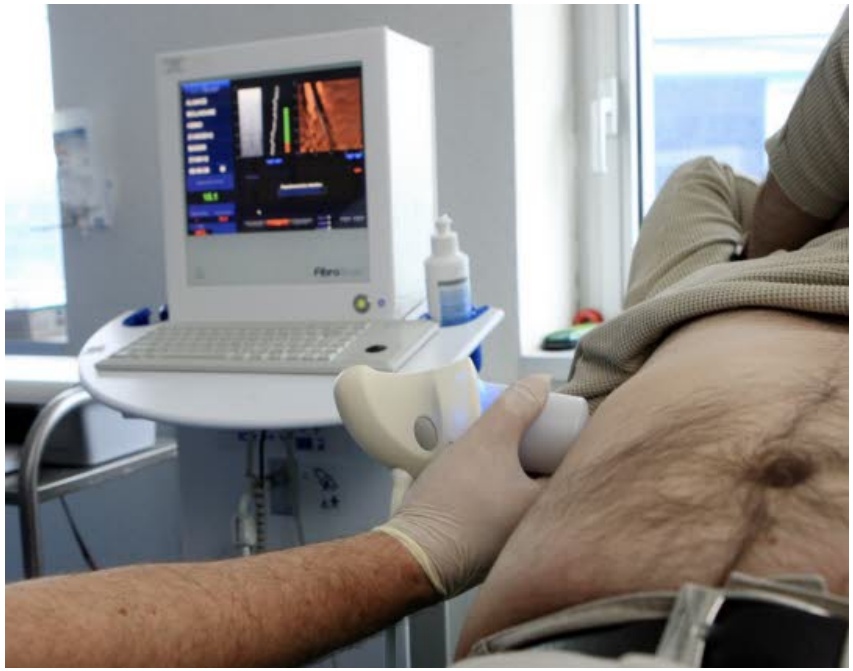
2. Determines need for therapy
3. Determines management

- Affects response rate
- Affects duration of therapy
- Affects follow-up (need for HCC screening)
- May affect choice of treatment

- All patients should have an assessment of fibrosis
- If cirrhosis obvious – no need

New Tools

Transient Elastography (Fibroscan)



- Ultrasound-based technique
- Determines liver 'stiffness'
- Correlates well with fibrosis
- No ceiling ie. increases with worsening cirrhosis → predicts complications (eg. varices)
- Simple to use – minimal training

Caveats: Fails in up to 20% (especially obese) – improved with XL probe
Influenced by inflammation – falsely elevated
Not effective with ascites - with PD??? Lower values in CKD?

Liu J Gastro Hep 2011

Serum Panels

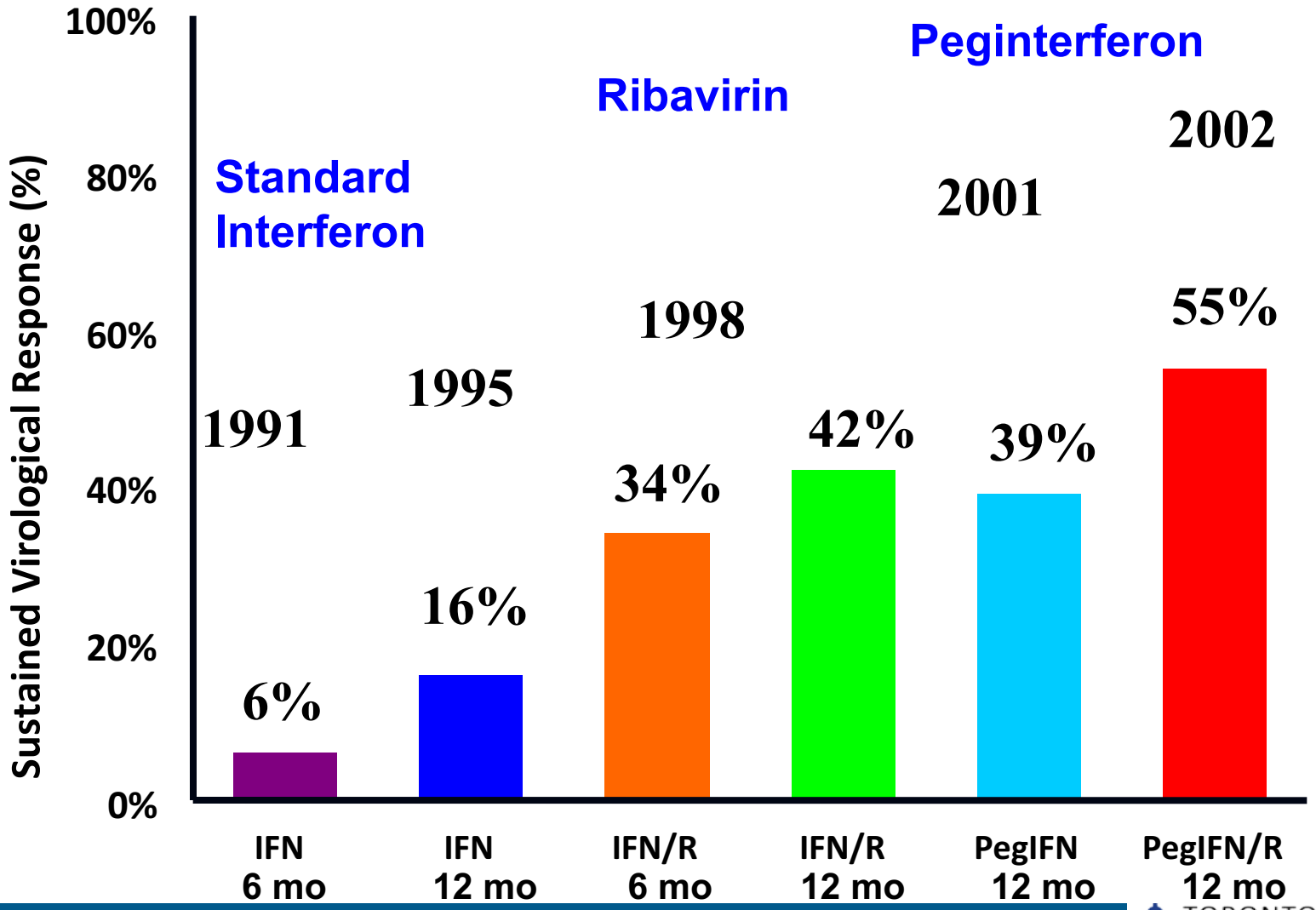
- APRI – AST:Platelet Ratio Index
  - (AST/ULN) / (Plt/ULN)
  - <0.5 98% NPV for cirrhosis, <1.0 93% NPV
  - >2 80% PPV (more useful for ruling out cirrhosis)

- Fibrotest
  - GGT, Bilirubin, Haptoglobin
  - Alpha-2-macropglobulin, apo-lipoprotein-A1
  - ?No data in CKD…levels may be affected

- HCV is bad for kidneys and ESRD is bad for HCV…can we do anything about it?

What about treatment?

The good news



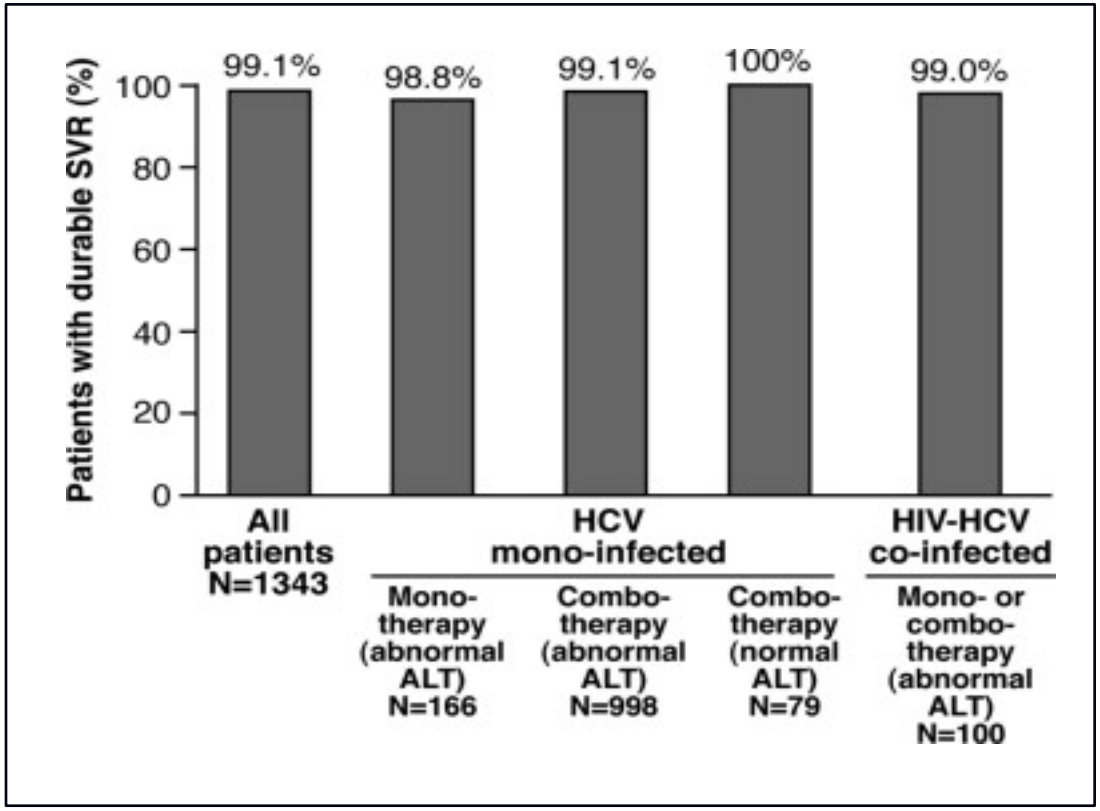
Treatment

- HCV is a **CURABLE** infection

- No small feat – first curable chronic viral infection

SVR is a durable endpoint

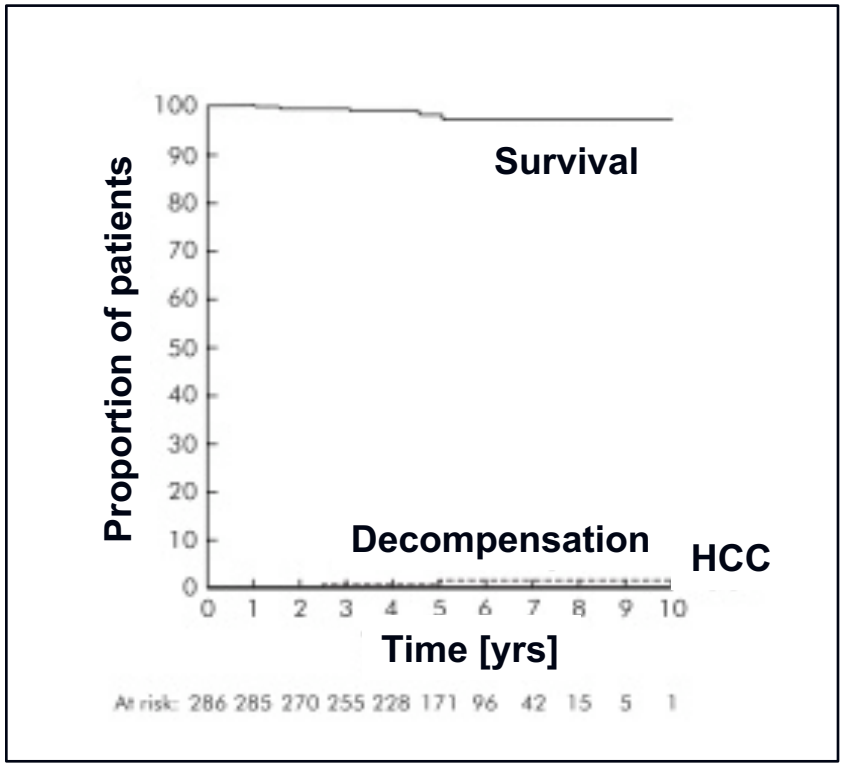
1,343 patients who achieved SVR followed for mean 3.9 yrs

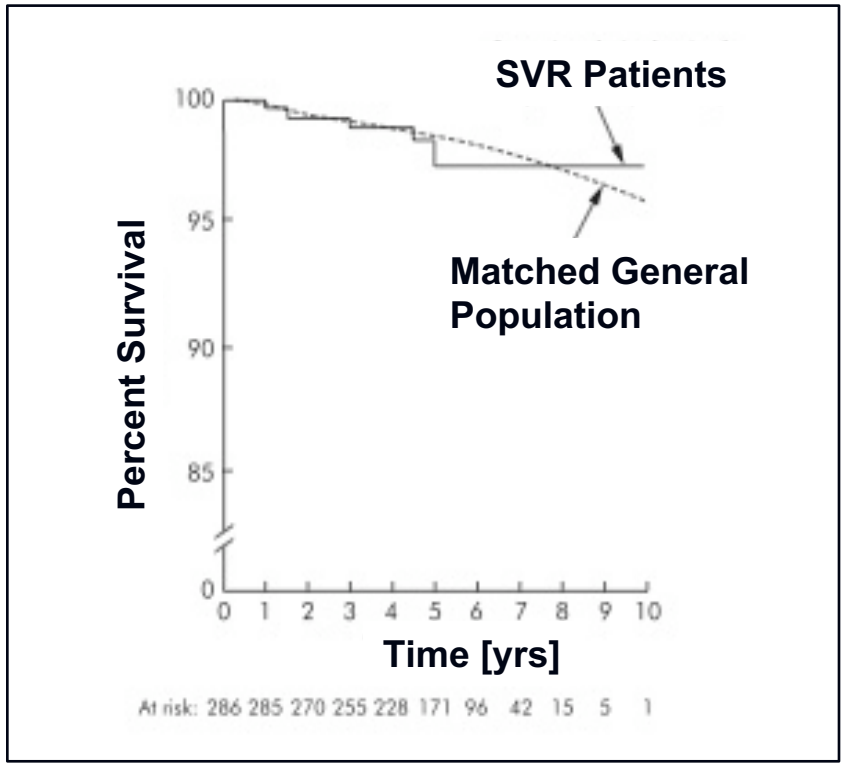


- Late relapse is extremely rare
- **SVR is truly a virological cure**

Is SVR a cure of liver disease

286 pts with mild fibrosis and SVR after IFN therapy





- SVR stops progression of liver disease
- Normal survival in those with mild disease

Veldt Gut 2002

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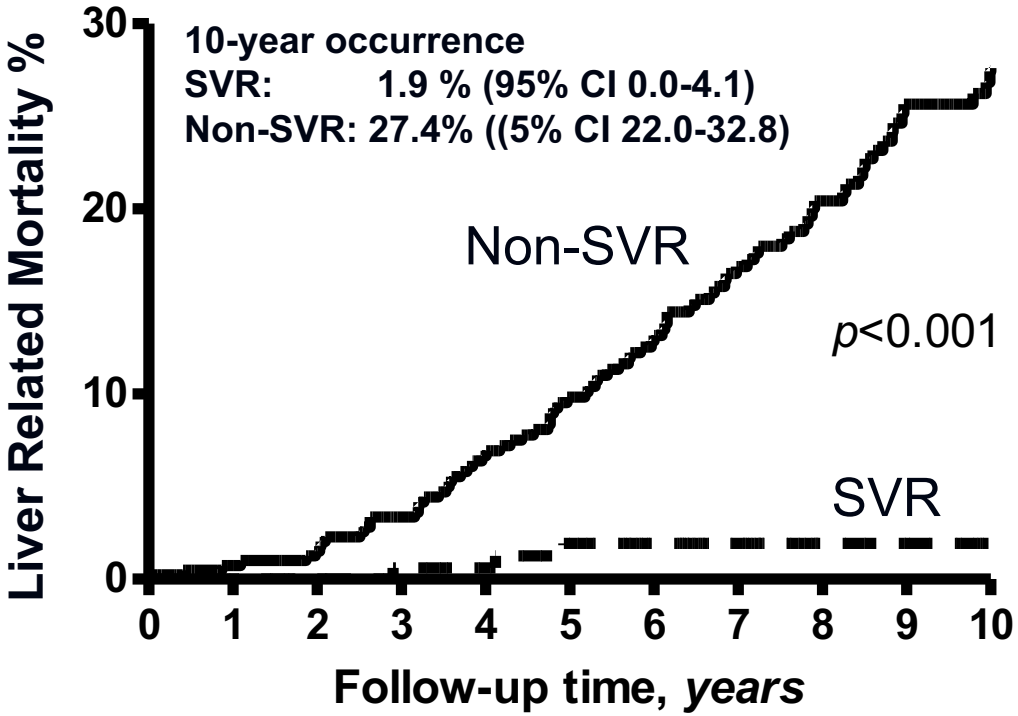
What about with advanced disease?

Long-term follow-up of 534 patients with F3/F4 post-treatment



SVR eliminates liver failure & liver-related death

Van de Meer et al JAMA 2012

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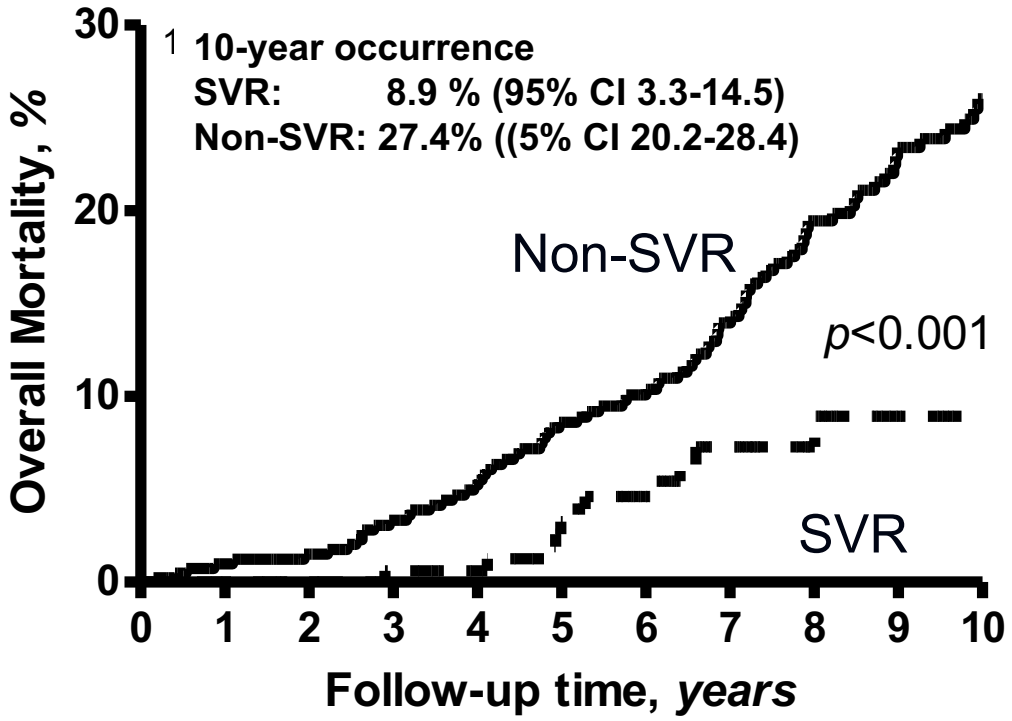
SVR reduces *All-Cause* Mortality

Long-term follow-up of 534 patients with F3/F4 post-treatment



SVR is not a surrogate = reduced ***all-cause*** mortality

Van de Meer et al JAMA 2012

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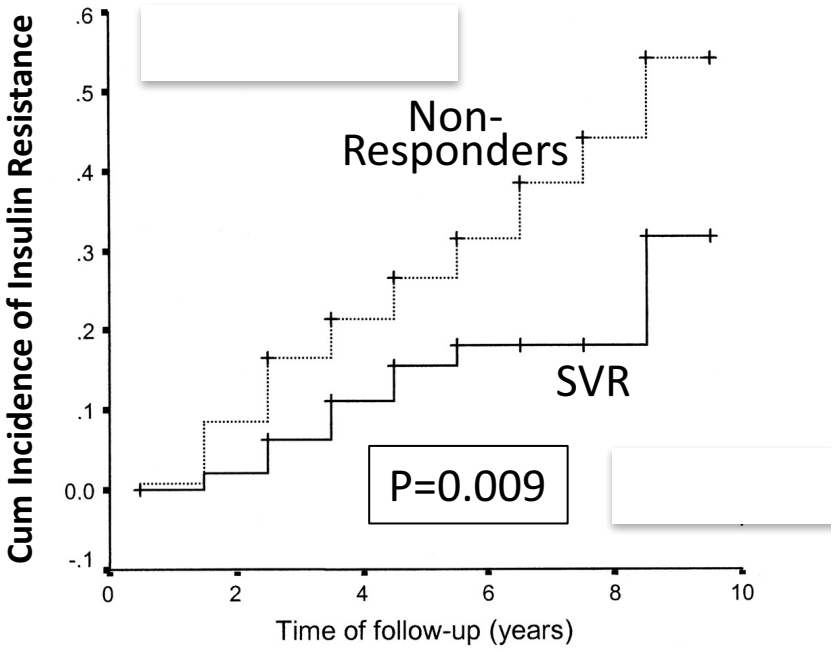
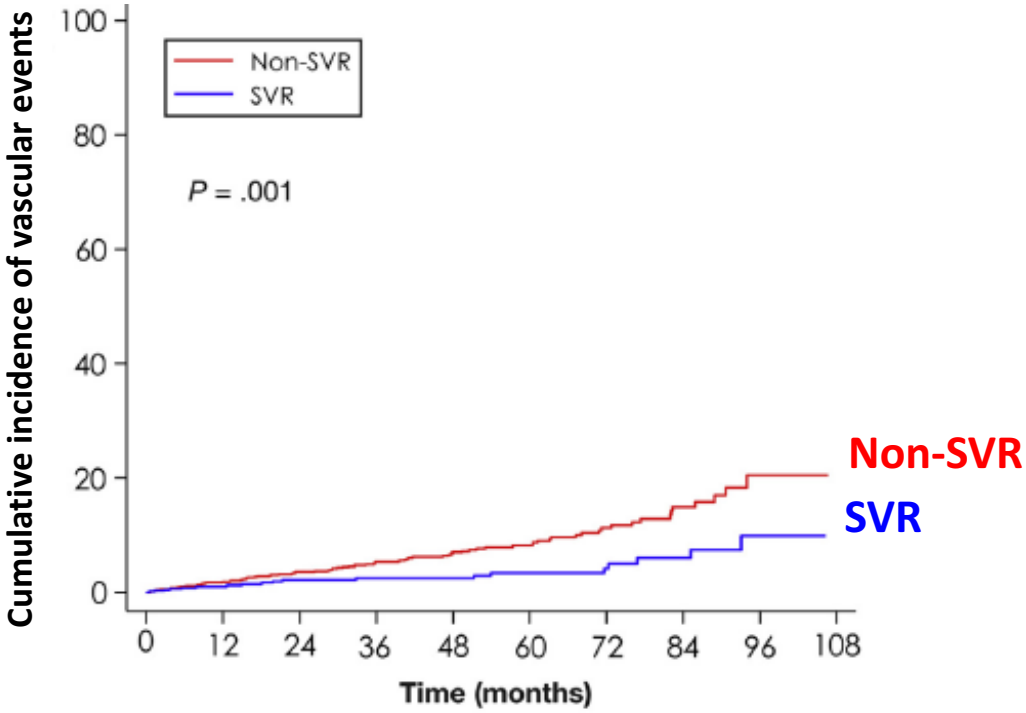
Benefits beyond the liver

Risk of Insulin Resistance/DM



Cardiovascular Disease



SVR may reduce diabetes and CVD!

Guiltinan Am J Epi 2008, Nahon Gastro 2017

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Effective but difficult

Lots of side effects

- Flu-like symptoms
- Fatigue
- Depression
- Anemia
- Neutropenia
- Injection site reactions
- Hair thinning
- Skin rash
- Autoimmune reactions
- Many others…

Try dealing with this for a whole year!

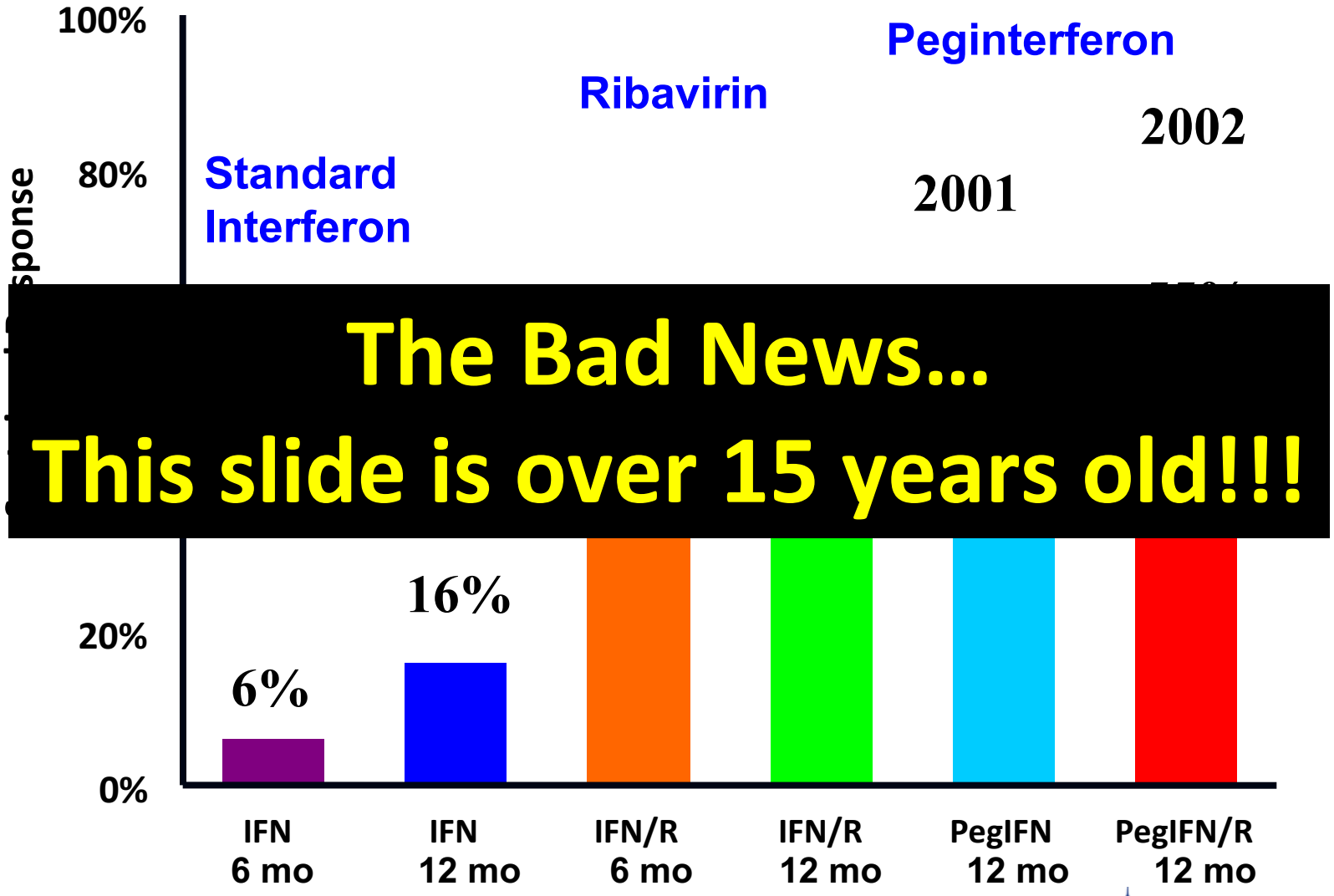
Treatment in CKD – the old paradigm

- Indications for treatment similar
  - Preferably before transplant
  - Post-transplant – IFN risk of graft loss
- Very difficult with Peg/RBV → anemia
  - 1% treatment uptake among 4,735 HCV pts on HD
- Many small studies – poor results
  - SVR ~33% with peg monotherapy
  - D/C rates 18-30%
  - Add low dose RBV → increase SVR to ~50%, but D/C rate to ~25%

But now we have DAAs…everything has changed right?

Goodkin Am J Nephrol 2013, Liu Ann Int Med 2013

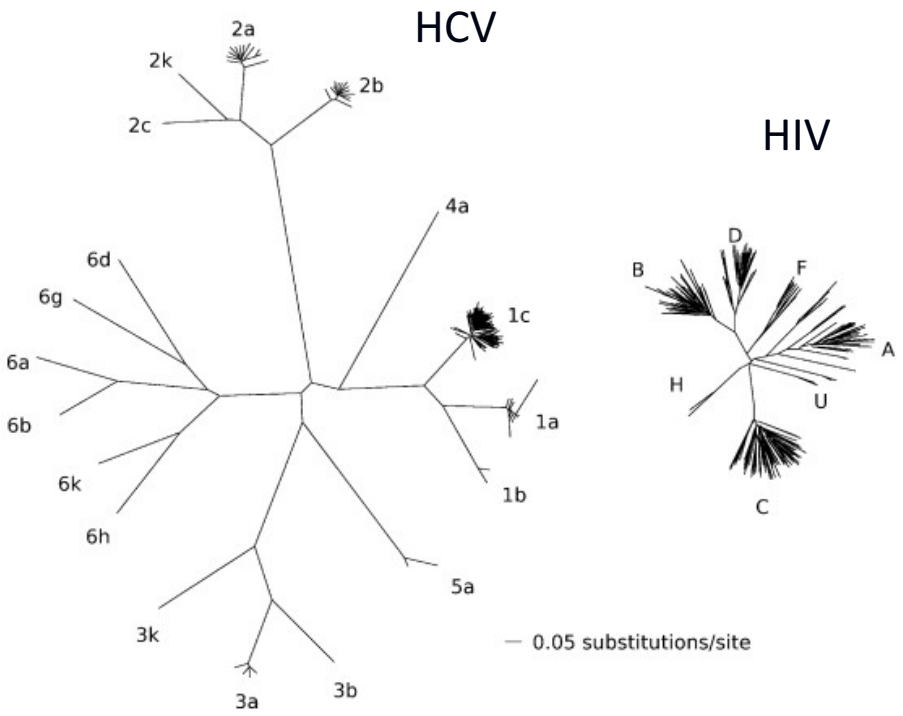
The Good News



The Bad News…

This slide is over 15 years old!!!

Why did it take so long?



Remarkable Diversity

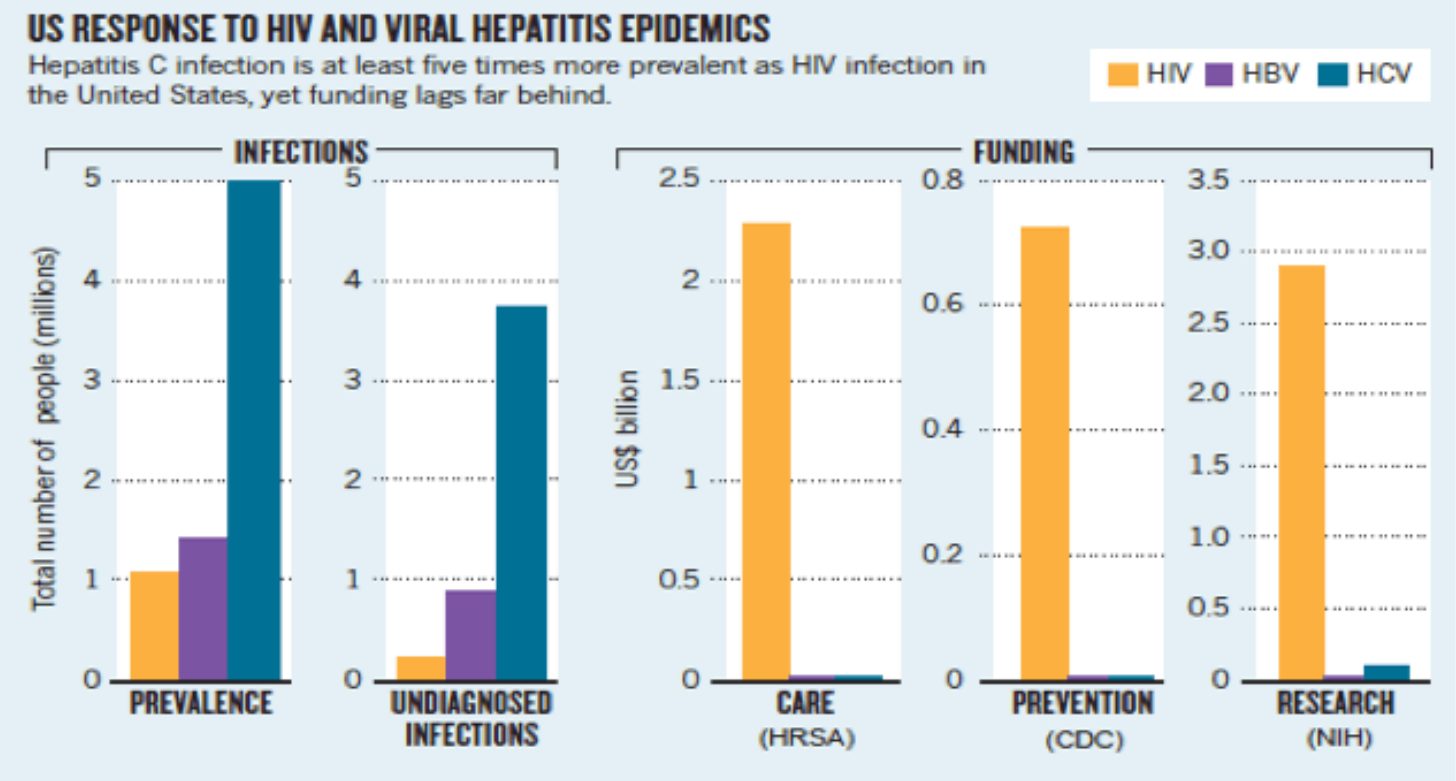
Toxicity of Early DAAs

The real reason…

HIV Lobby

HCV Lobby

Not just a theory….



Edlin Nature 2012

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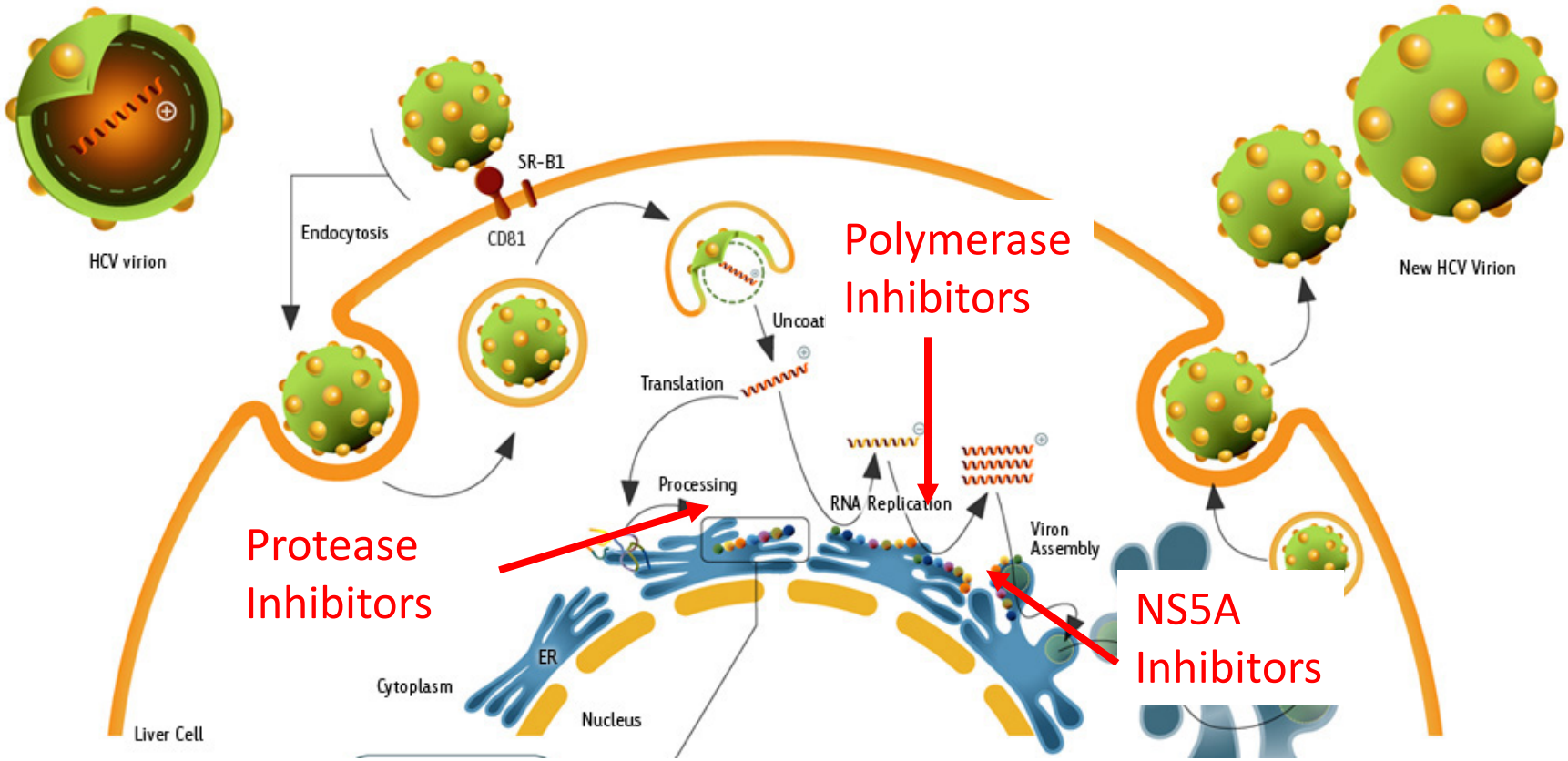
Fortunately…there has been progress

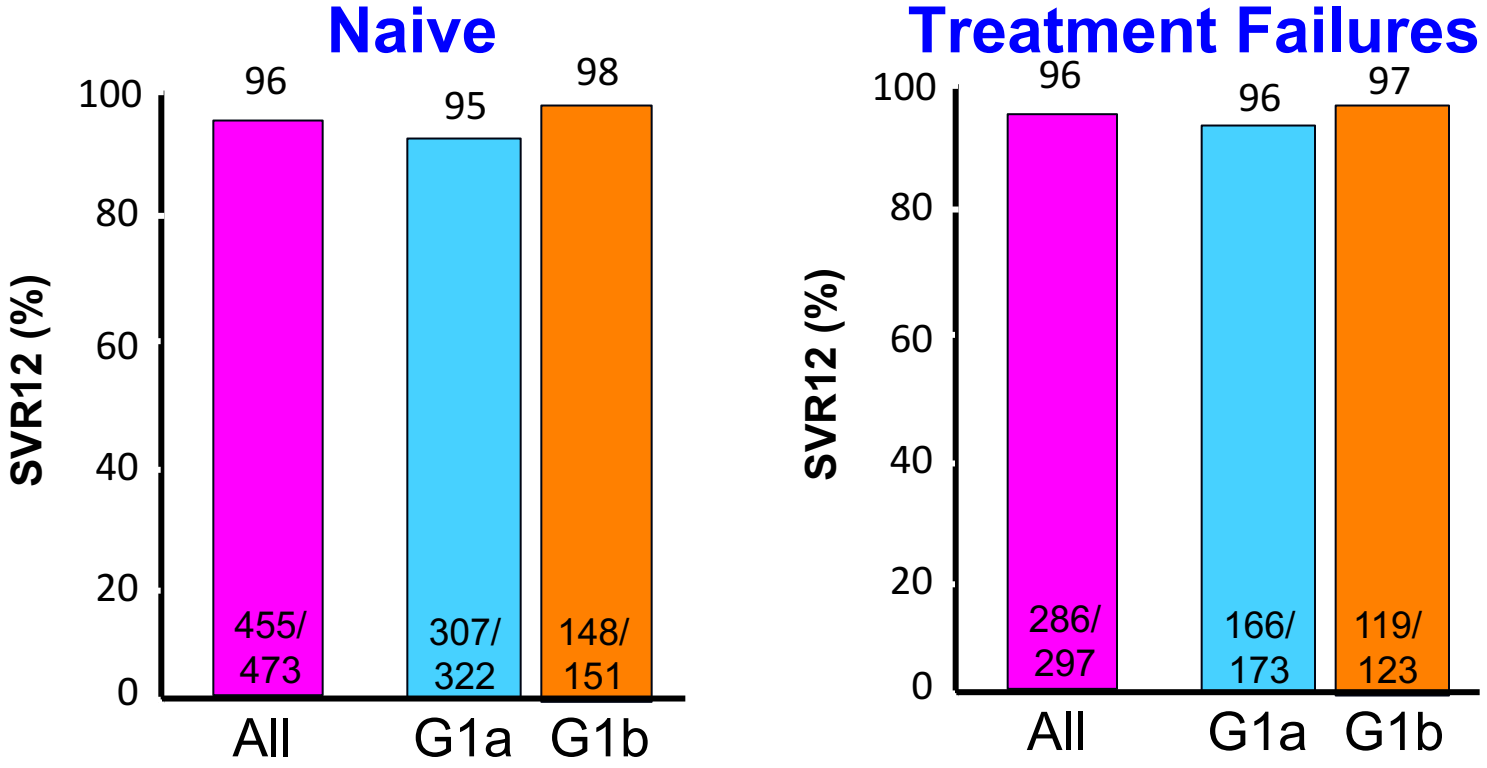


Manns Nat Rev 2007

23 HCV Trials in NEJM since 2012

Combination therapy

Paritaprevir/r (PI) + Ombitasvir (NS5A) + Dasabuvir (NNI) + RBV x 12 wks



- 5 drugs (3 pills) BUT 12 wks, 1 size fits all
- Very well tolerated (vs. placebo), few virologic failures

Feld J NEJM 2014, Zeuzem NEJM 2014

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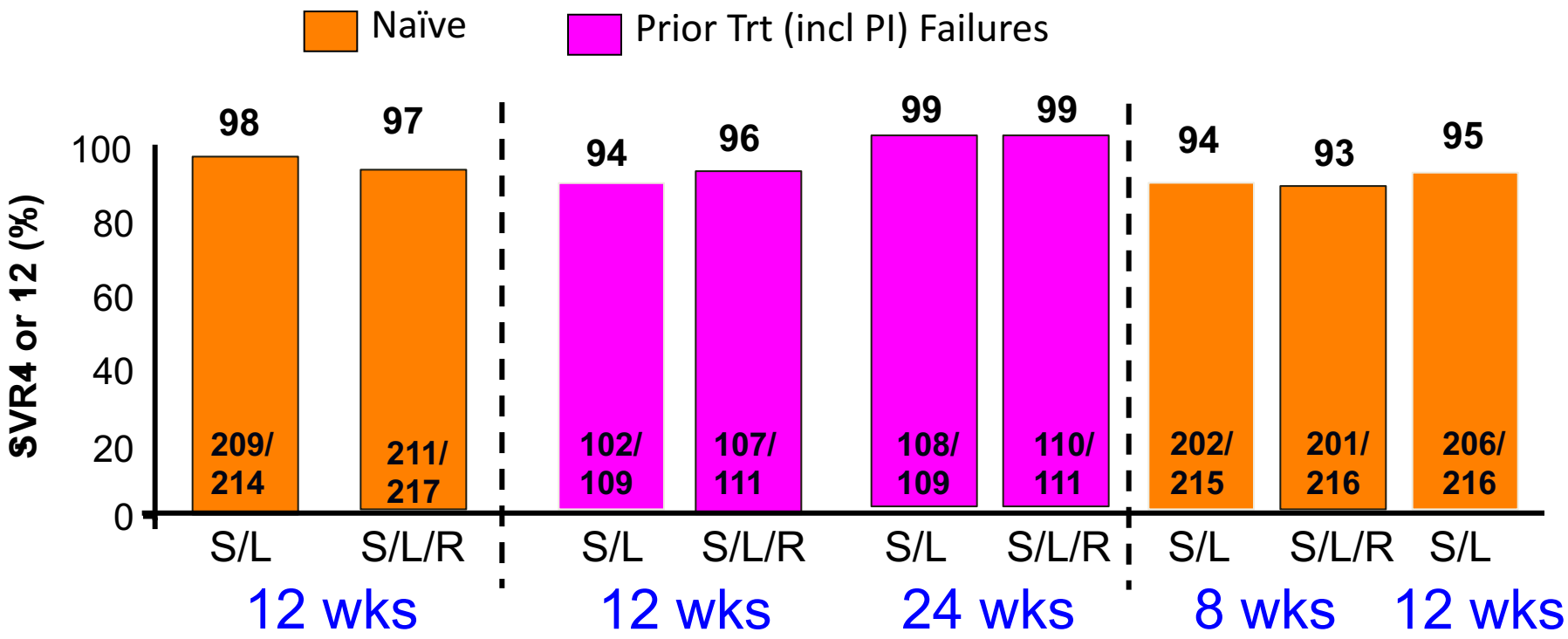
How about a single pill?

ION 1, 2 & 3: Sofosbuvir (Nuc) + Ledipasvir (NS5A) FDC +/- RBV



- Highly effective single-tablet regimen
- No issues with resistance

Afdahl NEJM 2014, Afdahl NEJM 2014, Kowdley NEJM 2014

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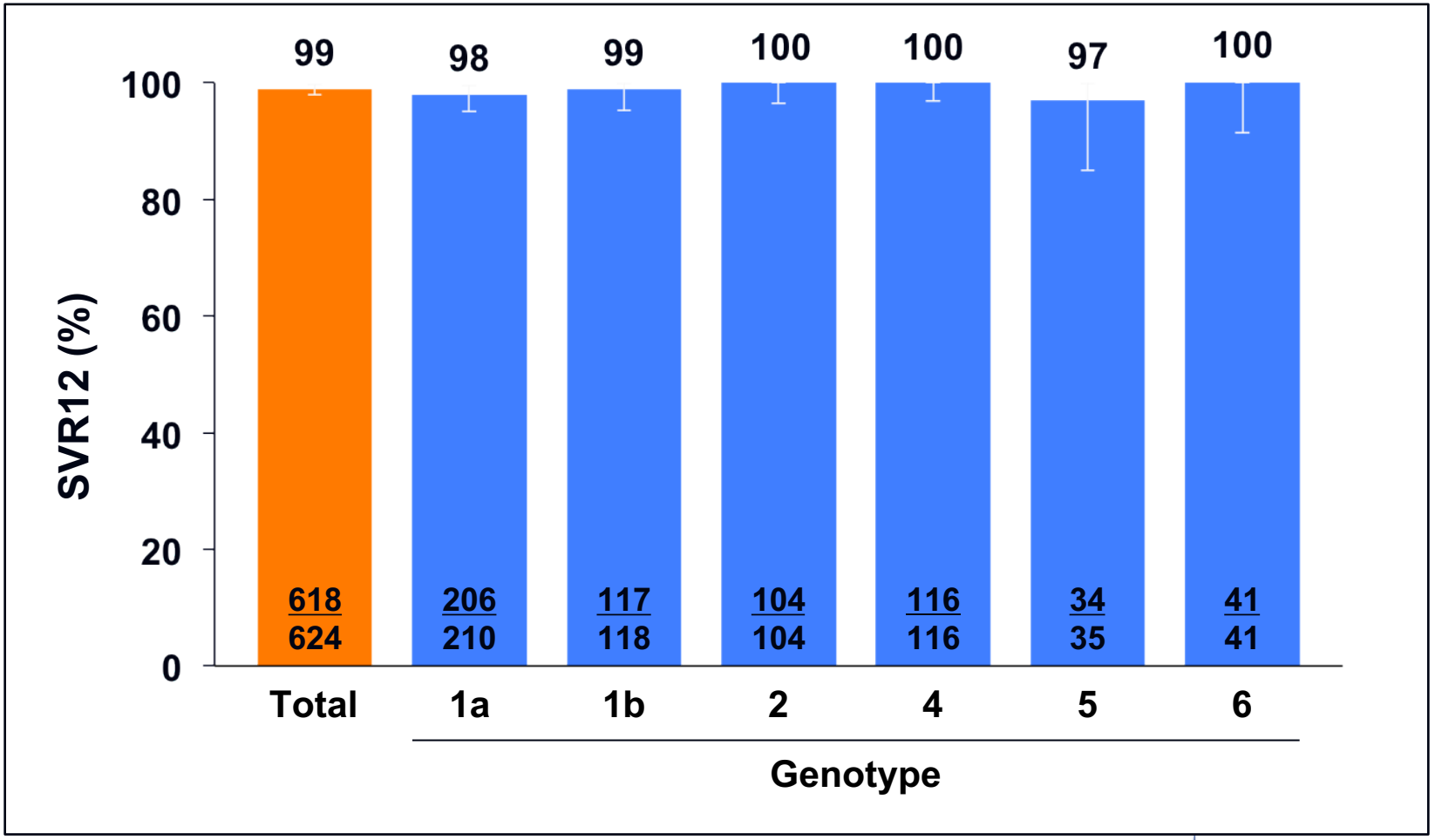
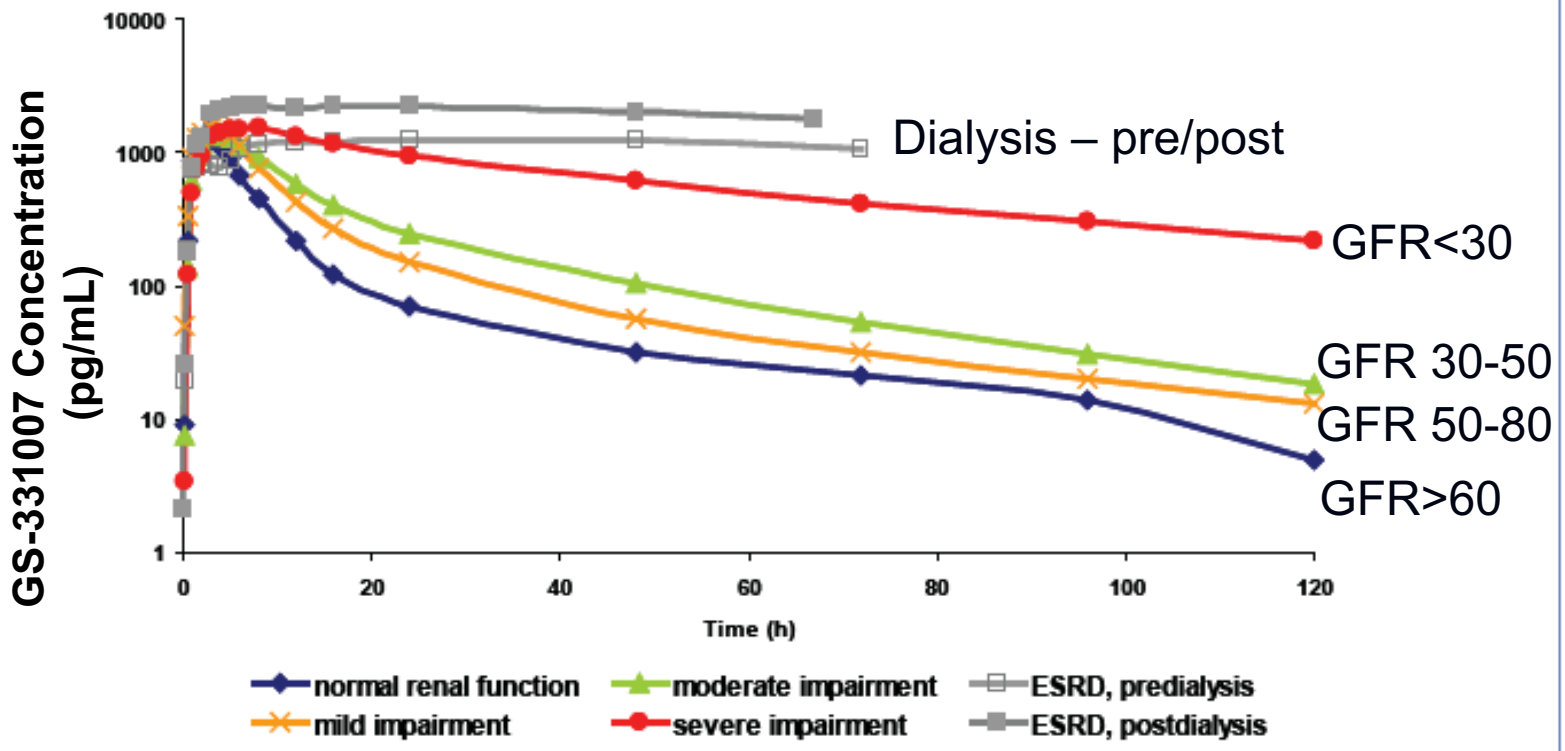
Pretty close to perfectovir!

SOF + Velpatasvir (NS5A) x 12 wks in
G1, 2, 4, 5, 6 – Naïve/Experienced +/- cirrhosis



Sofosbuvir in renal disease



- Metabolite accumulates – unclear clinical significance
- Based on this – approved in all but severe renal impairment

Cornpropst M, et al. EASL 2012. Abstract 1101.

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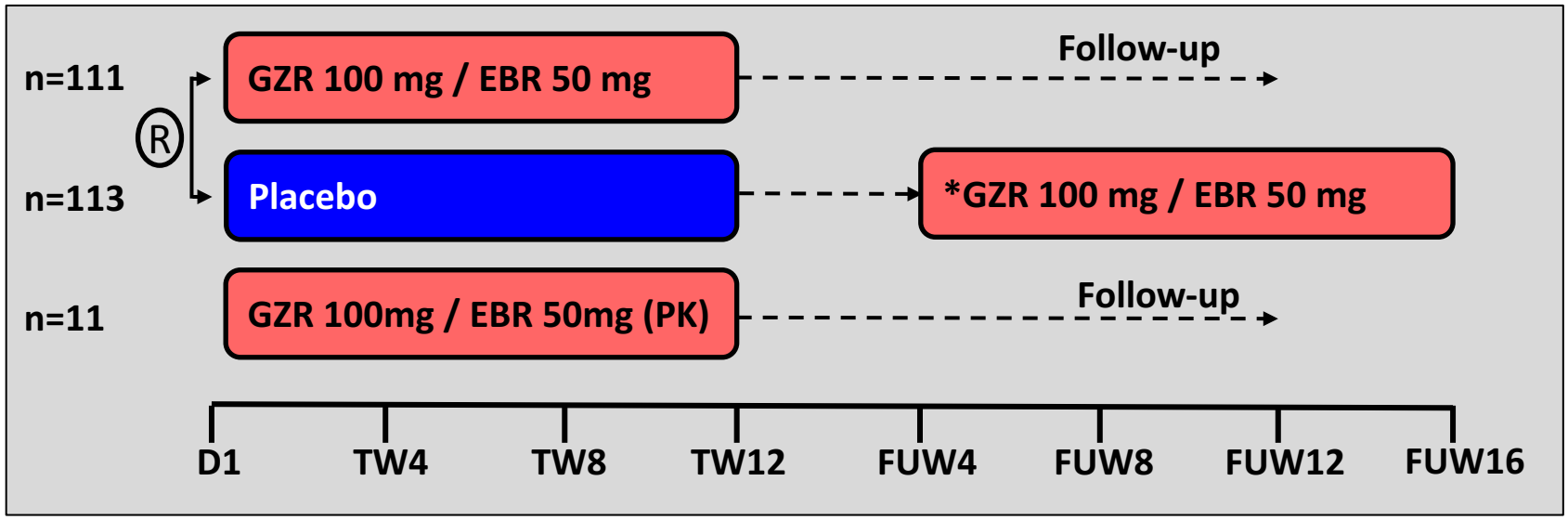
What about those with advanced CKD?

C-SURFER

Second generation PI (Grazoprevir) + NS5A (Elbasvir)



- 75% Dialysis
- 45% Black
- 52% G1a
- 83% Trt naive
- 6% cirrhosis

Roth Lancet 2015

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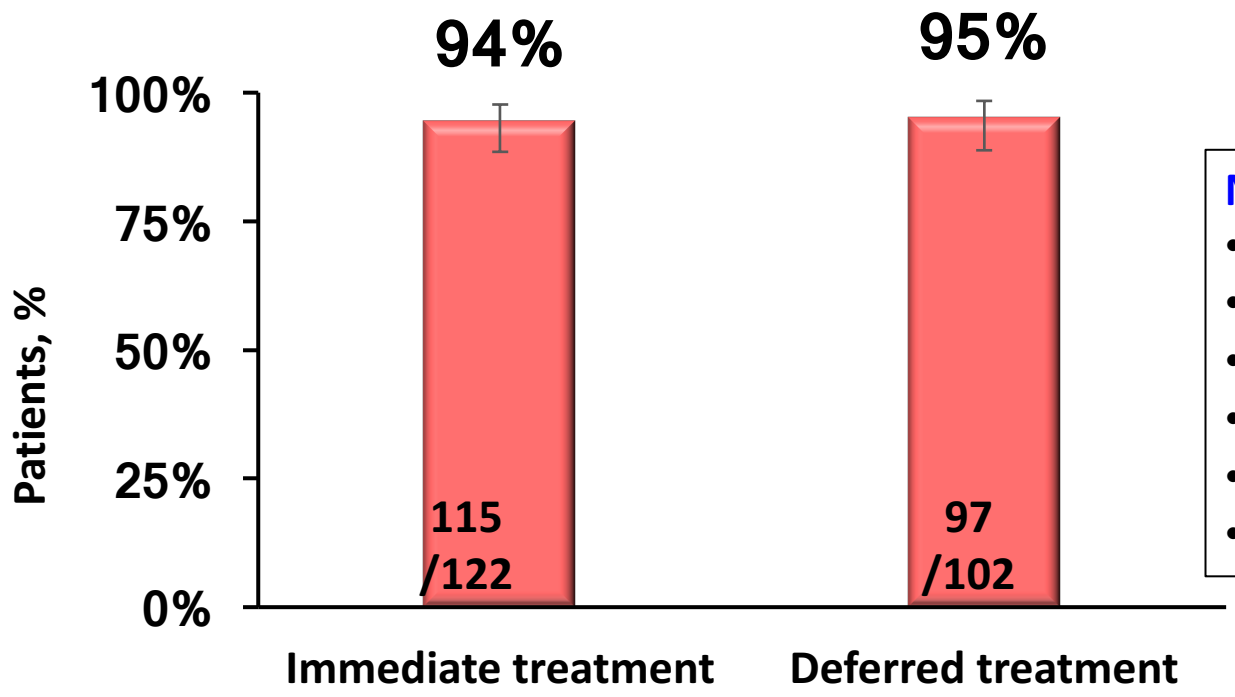
SVR12



Non-Virological Failure

- 1 AE
- 2 LTFU
- 1 Non-compliance
- 2 death (unrelated)
- 2 w/d by subject
- 1 w/d by MD

Relapse	**1**	**2**
D/C unrelated to Tx	**6**	**3**

* 1 SVR12 in placebo group – no treatment taken…

Roth Lancet 2015,Roth ASN 2015

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Safety

	GZR/EBR (ITG) (n = 111)	GZR/EBR (DTG) (n = 102)	Placebo (DTG) (n = 113)	Difference in % Estimate ITG vs placebo (95% CI)
AEs,[a] n (%)	84 (75.7)	61 (59.8)	95 (84.1)	–8.3 (–18.9, 2.2)
Headache	19 (17.1)	7 (6.9)	19 (16.8)	0.3 (-9.6, 10.4)
Nausea	17 (15.3)	10 (9.8)	18 (15.9)	–0.6 (–10.3, 9.1)
Fatigue	11 (9.9)	9 (8.8)	17 (15.0)	–5.1 (–14.1, 3.7)
Insomnia	7 (6.3)	2 (2.0)	12 (10.6)	–4.3 (–12.2, 3.2)
Dizziness	6 (5.4)	5 (4.9)	18 (15.9)	–10.5 (–19.1, -2.6)
Diarrhea	6 (5.4)	5 (4.9)	15 (13.3)	–7.8 (–16.1, -0.2)
Serious AEs, n (%)	16[b] (14.4)	13[c] (12.7)	19 (16.8)	–2.4 (–12.1, 7.3)
Discon due to an AE, n (%)	0 (0)	3 (2.9)	5 (4.4)	–4.4 (10.0, -1.0)
Deaths,[d] n (%)	1 (0.9)	0 (0)	3 (2.7)	–1.8 (–6.7, 2.5)

Fewer AEs in delayed treatment group
Fewer AEs and SAEs than in placebo group

Summary Grazoprevir/Elbasvir

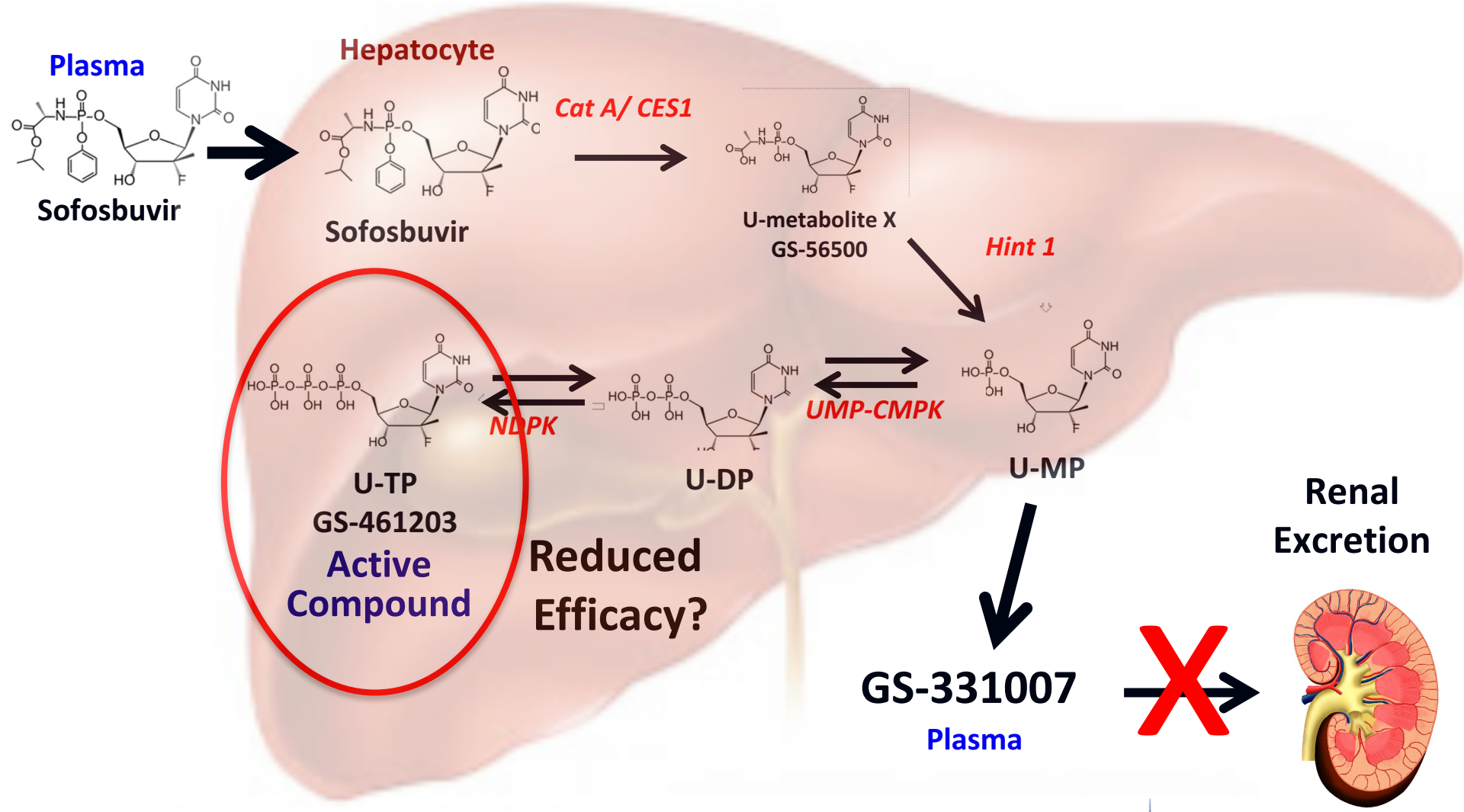
- Highly effective for G1 and G4 with CKD
- Safety similar to placebo
- But what about those with other genotypes?

What about SOF?

8.6 Renal Imp

No dose adjust with mild or moderate renal impairment. T en established in patients with severe rena tage renal disease (ESRD) requiring he for patients with severe renal impairment o nd Clinical *Pharmacology (12.3)]*. Refer als cribing information for patients with CrCl <5

Can we just lower the dose?

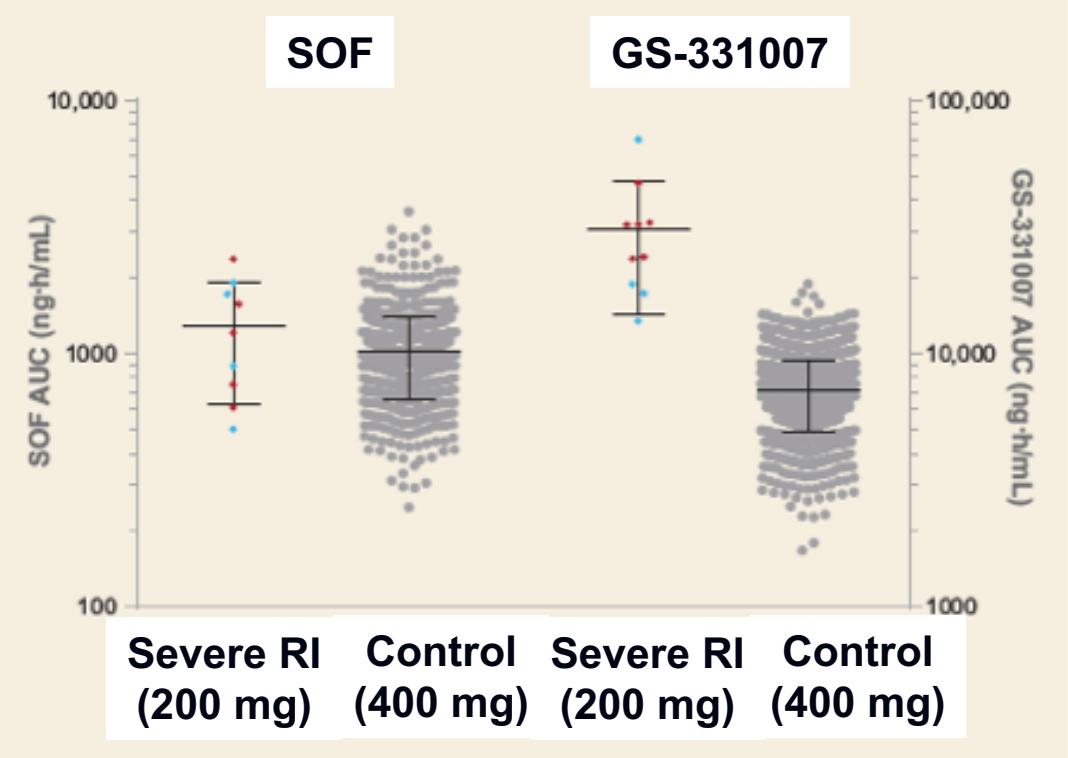


Modified from Murakami JBC 2010

TORONTO CENTRE FOR LIVER DISEASE

Reduced SOF Dosing

SOF 200 mg + RBV 200 mg OD x 24 wks vs historical control (400 mg)



- Dose reduction lowers exposures but early studies suggested 200 mg dose less effective…alternate days likely similar
- Viral kinetics similar in this pilot study but probably not ideal esp for G3

Gane EJ, et al. AASLD 2014. Abstract 966.

What happens when clinicians ignore the label?

SOF in CKD – HCV TARGET

	eGFR ≤30* (N=19)	eGFR 31-45 (N=63)	eGFR 46-60 (N=168)	eGFR >60 (N=1,643)	p-value
Age ≥ 65	5 (26)	18 (29)	55 (33)	292 (18)	<0.01
Cirrhosis	8 (42)	43 (68)	95 (57)	844 (51)	0.03
History of Decompensation	6 (32)	30 (48)	55 (33)	382 (23)	<0.01
MELD ≥ 10	5 (26)	26 (41)	33 (20)	227 (14)	<0.01
Liver Transplant	7 (37)	34 (54)	57 (34)	136 (8)	<0.01
Kidney Transplant	3 (16)	5 (8)	9 (5)	12 (1)	<0.01
Diabetes	7 (37)	30 (48)	48 (29)	358 (22)	<0.01

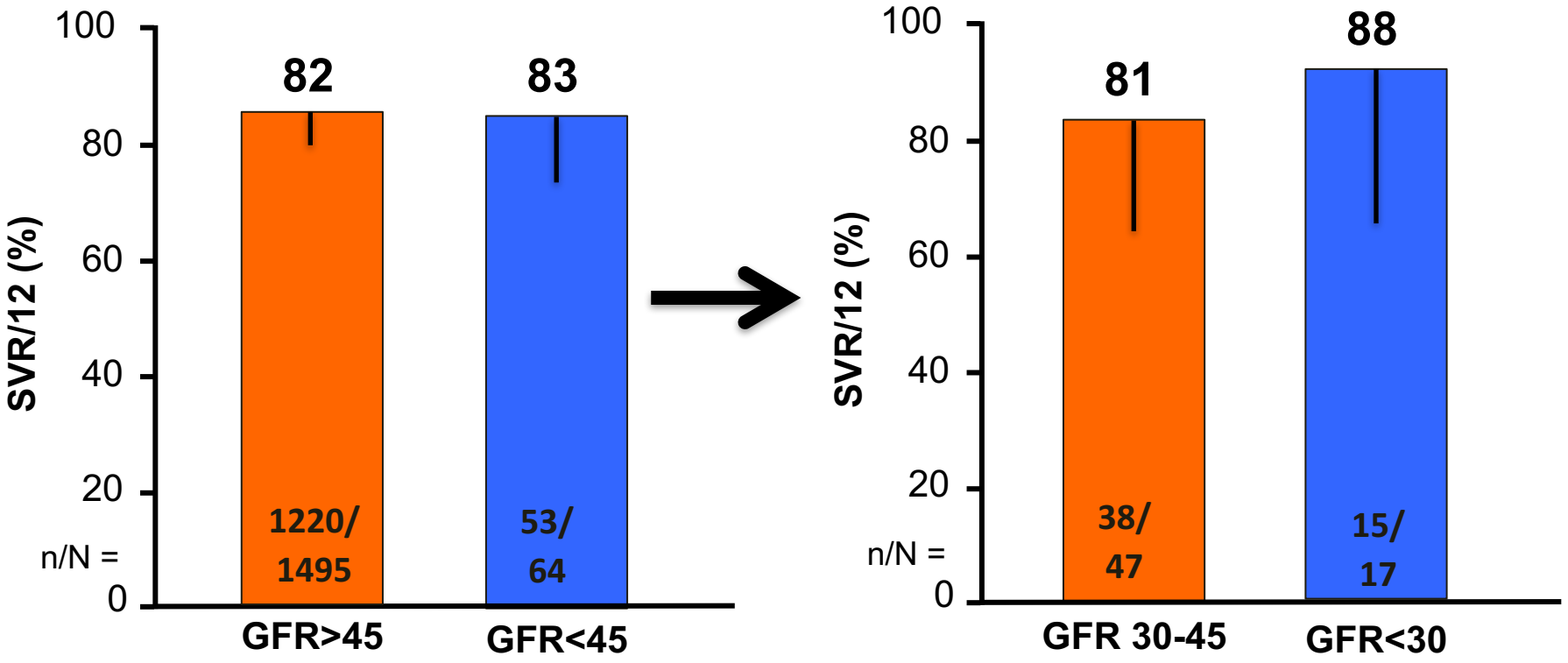
CKD in older pts with DM, cirrhosis, history of decomp & post-Tx

Saxena EASL 2015, Liver International 2016

TORONTO CENTRE FOR LIVER DISEASE

Response unaffected by GFR

Different SOF-containing regimens: SOF/PR, SOF/RBV, SOF/SIM



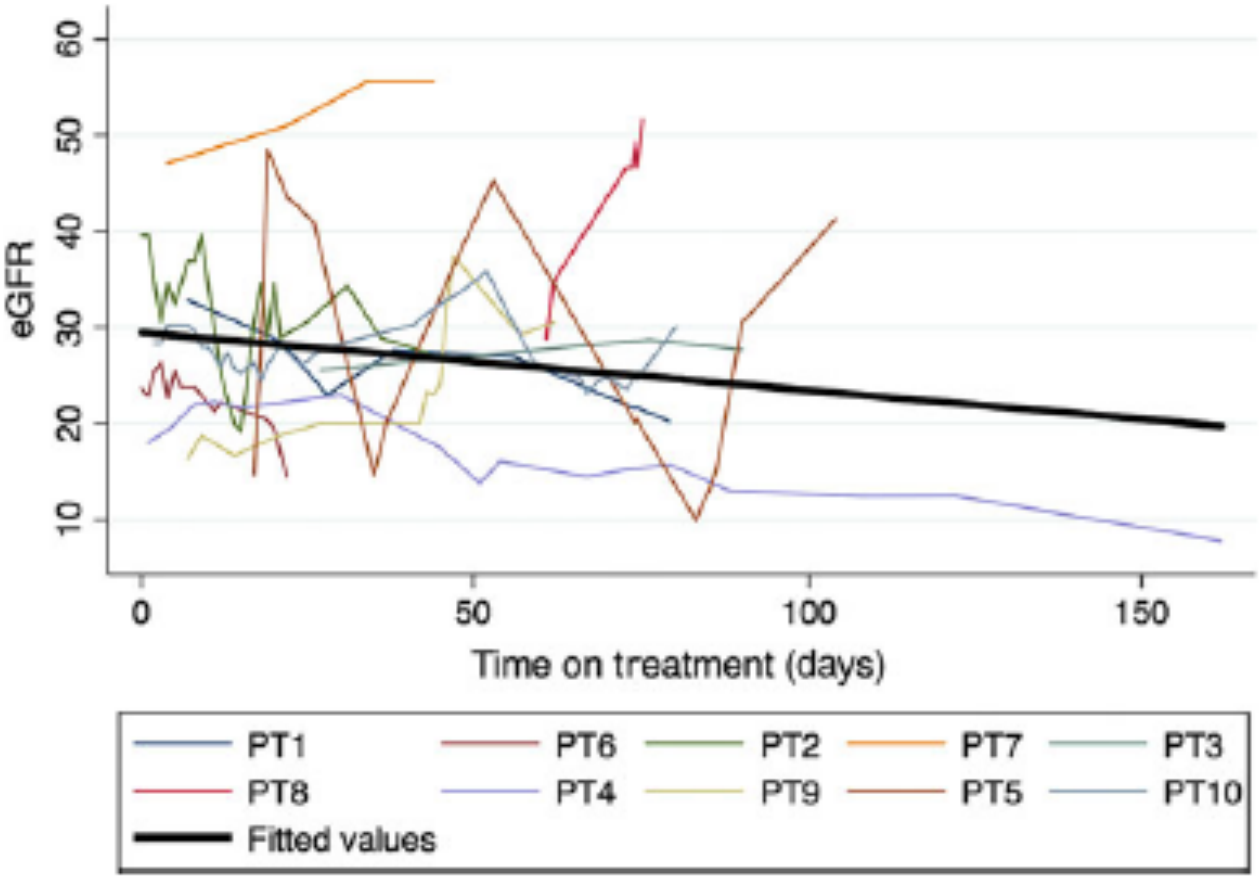
What about safety?

	eGFR ≤ 30 (N=17)	eGFR 30-45 (N=56)	eGFR 46-60 (N=157)	eGFR>60 (N=1,559)	p-value
Common SOF AEs					
Fatigue	3 (18)	19 (34)	56 (36)	543 (35)	0.54
Headache	1 (6)	9 (16)	19 (12)	274 (18)	0.24
Nausea	3 (18)	8 (14)	33 (21)	247 (16)	0.39
Anemia AE	**6 (35)**	**16 (29)**	**37 (24)**	**246 (16)**	**<0.01**
Required Transfusion(s)	**2 (12)**	**5 (9)**	**3 (2)**	**31 (2)**	**<0.01**
Received Erythropoietin	**0 (0)**	**6 (11)**	**13 (8)**	**46 (3)**	**<0.01**
RBV					
Dose reduction for anemia	**3 (43)**	**8 (30)**	**33 (42)**	**185 (19)**	**<0.01**
RBV Discontinuation	**0 (0)**	**4 (15)**	**1 (1)**	**12 (1)**	**<0.01**
Worsening Renal Function	**5 (29)**	**6 (11)**	**4 (3)**	**14 (1)**	**<0.01**
Renal or Urinary System AEs	**5 (29)**	**6 (11)**	**13 (8)**	**84 (5)**	**<0.01**
Serious AEs	**3 (18)**	**13 (23)**	**8 (5)**	**100 (6)**	**<0.01**
Early Treatment Discontinuation	1 (5)	4 (6)	6 (4)	68 (4)	0.60
Early Treatment DC due to AE	1 (5)	2 (3)	4 (2)	39 (3)	0.53
Death	1 (5)	0 (0)	2 (1)	10 (1)	0.11

More anemia and worsening renal function

Saxena Liver International 2016

GFR over time



Overall trend of worsening GFR but very variable individual responses

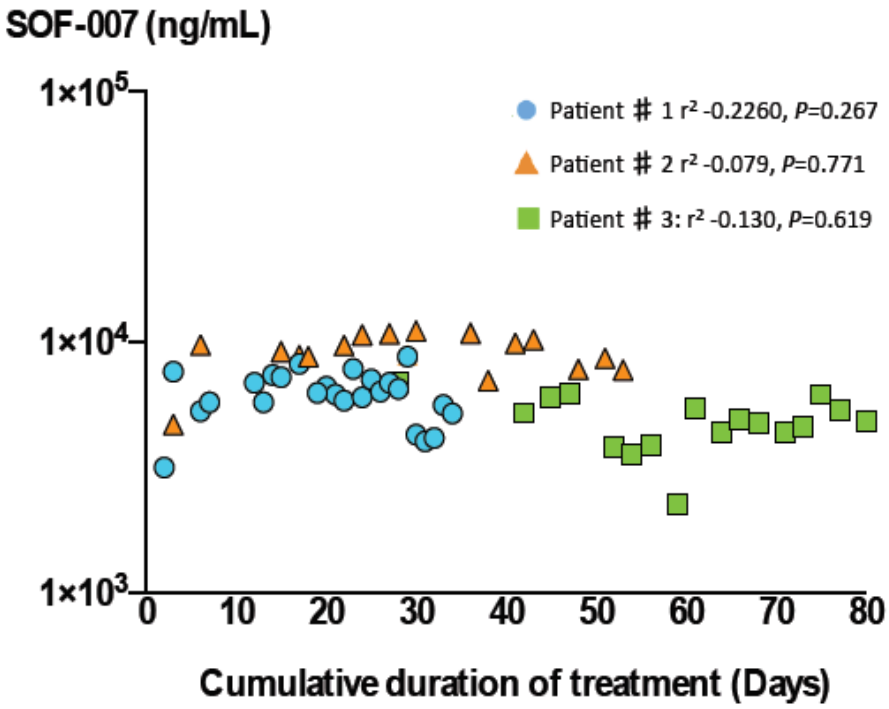
What does this all mean?

- Kidney injury was based on ‘chart record’ → very variable
  - Could overestimate – not objective
  - Could underestimate – only severe cases noted
  - Transplant, cirrhosis important confounders
  - Consequences unclear
  - No off-treatment ‘recovery’, no control group
  - Relatively small numbers
- Safety data somewhat unclear…
- No effect on SVR

A useful study

- SOF in HD with careful PK
- No SOF accumulation
- Higher 007 levels with qd than TIW BUT…
- HD removed ~53% of 007 but no effect on other DAAs
- No AEs associated with 007 accumulation
- OD dosing – SVR 7/7
- TIW dosing – SVR 5/7

SOF daily or TIW



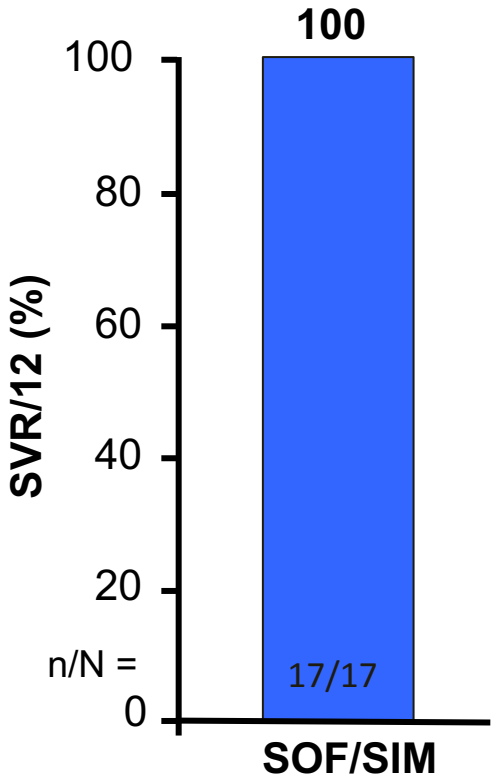
Suggests that full dose of SOF is likely to be safe

Desnoyer J Hep 2016

TORONTO CENTRE FOR LIVER DISEASE

Accumulating safety/efficacy data

- 17 G1 pts with GFR<30 or HD
- Full dose daily SOF/SIM x 12 w
- Advanced liver disease
  - 8 cirrhosis
  - 4 F3
  - 76% G1a
- SVR 100%
- AEs mild + 1 blood transfusion



- Other smaller series with similar results
- Most suggest lower dose/longer interval = reduced SVR

Bottom line on SOF in CKD

To answer the question

We need you…

Our trial

- Sofosbuvir/Velpatasvir in ESRD all genotypes
- 12 weeks of therapy
- HD or PD
- Careful PK and safety monitoring

Please screen your units (again) and send us your non-genotype 1 patients!

We would love to have a renal co-investigator – any takers?

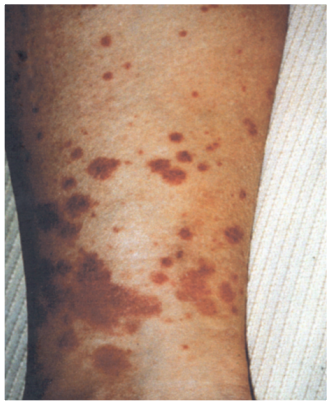
Other therapies coming…

- Glecaprevir (PI) / Pibrentasvir (NS5A)
- Pan-genotypic
- Hepatically cleared – safe in renal disease
- SVR rates 95% +
- Well tolerated
- *Approved but Not reimbursed in Canada!*

What about treatment of HCV-specific CKD?

A case…

- 45 yo woman
- HCV genotype 1a – surgery as an infant
- Presents with:
  - Ascites
  - Severe rash with ulcers on legs & back
- Labs:
  - ALT 35, AST 65 Hb 99 Plt 99 WBC 3.7
  - Bili 12 Alb 32 INR 1.2
  - Cr 130 U/A – 3+ RBC, 3+ Prot, RBCs, cellular casts
  - 24 hr urine – 2.5 g protein + kappa light chains
  - Cryocrit 20%



A case…

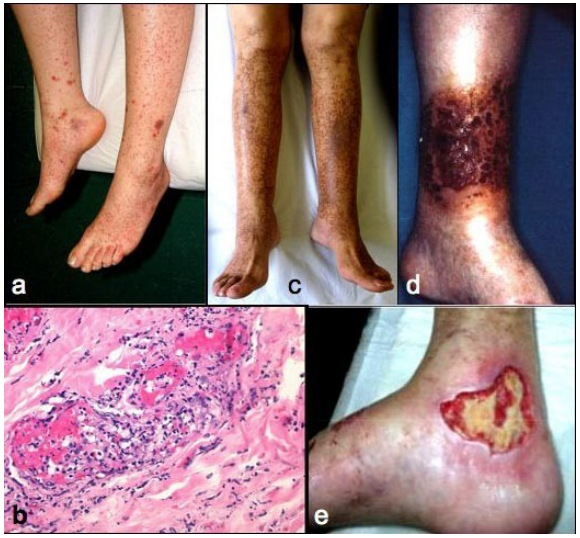
- 2009 - Treated Peg/RBV – seizure – stopped
- 2011 – Ineligible for trials due to co-morbidities
- Desperate for new options…

HCV-related Cryoglobulinemia

- >90% of Type II “Essential” Mixed Cryo are HCV+ve
- Polyclonal IgG + mono/oligoclonal IgM with RF activity

- Found 25-30% of HCV +ve
  - Only 10-15% of total are symptomatic
  - Range mild skin involvement to life-threatening vasculitis

  - Renal involvement
    - Classically MGPN
    - 20% at diagnosis of cryo
    - Overt nephritis 20-25%
    - Nephrotic syndrome 20%
    - ESRD 10-33%



Dammacco NEJM 2013, Ferri Sem Arth Rheum 2004

TORONTO CENTRE FOR LIVER DISEASE

Therapeutic options for HCV-MC

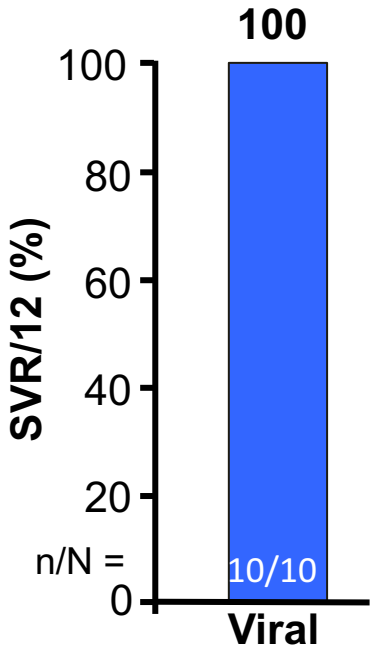
Therapy	SVR	Clinical Response	Relapse	Limiting factors
PEG-IFN + RBV	44-62%	40-67.5%	> 60%	Side effects, Duration of therapy
RTX	Nil	70-80%	Sig. Relapse after 18 months.	Ongoing Tx required
Steroids/ Immunomodulator	Nil	3.5-14%	High	Side effects, efficacy
PLEX	Nil	Minimal Data	Sig. Relapse	Short effect, cost

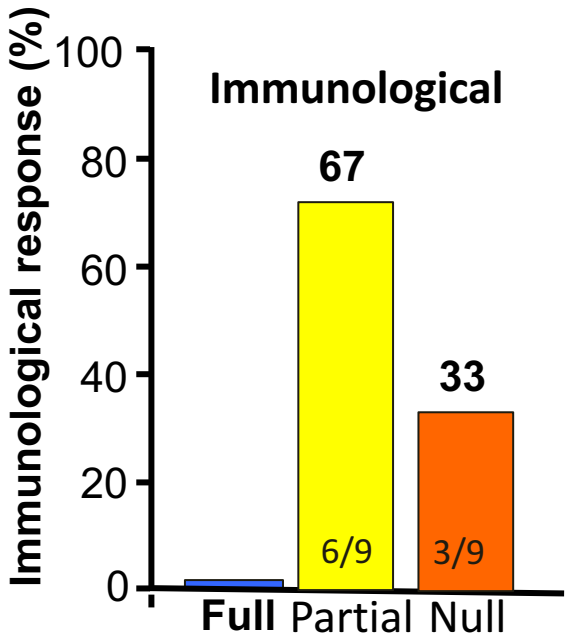
- Antiviral vs immunosuppressive therapy
- Ritux + PR likely best but far from ideal

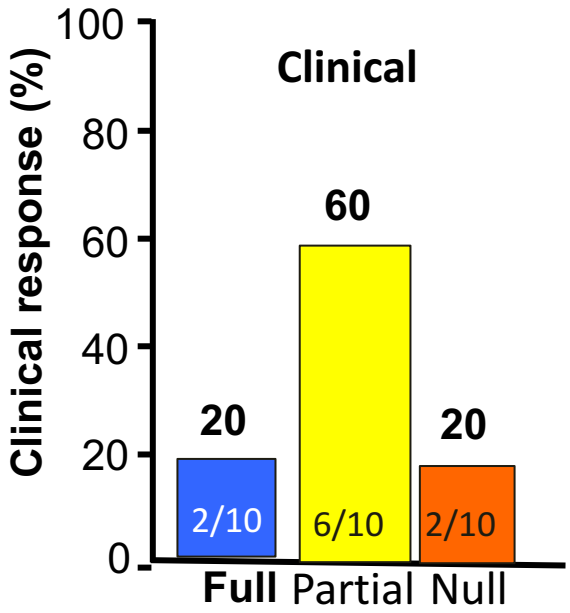
Pietrogrande Autoimmunity Rev 2011, Saadoun Blood 2010

DAAs in HCV-related cryo

- Cohort of 83 with cryo treated with DAAs +/- PR
  - 65 cryo +ve asymptomatic vs 18 with symptoms
  - 10 renal involvement

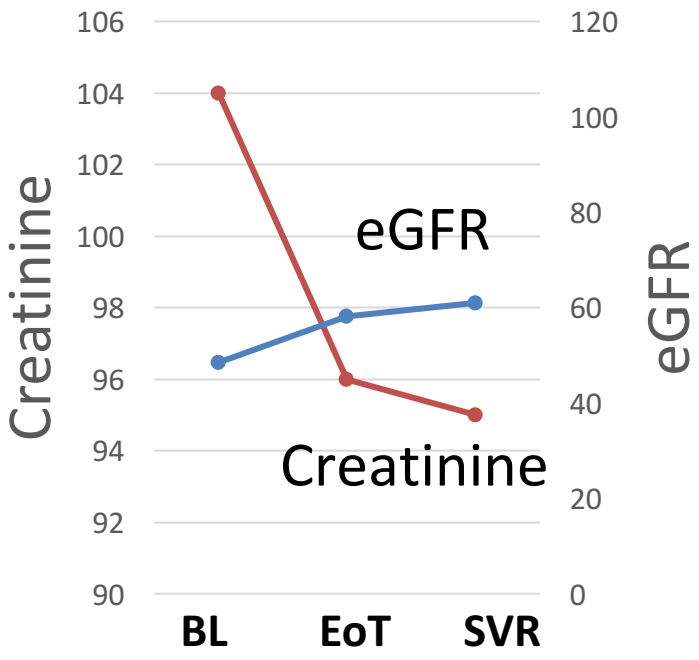


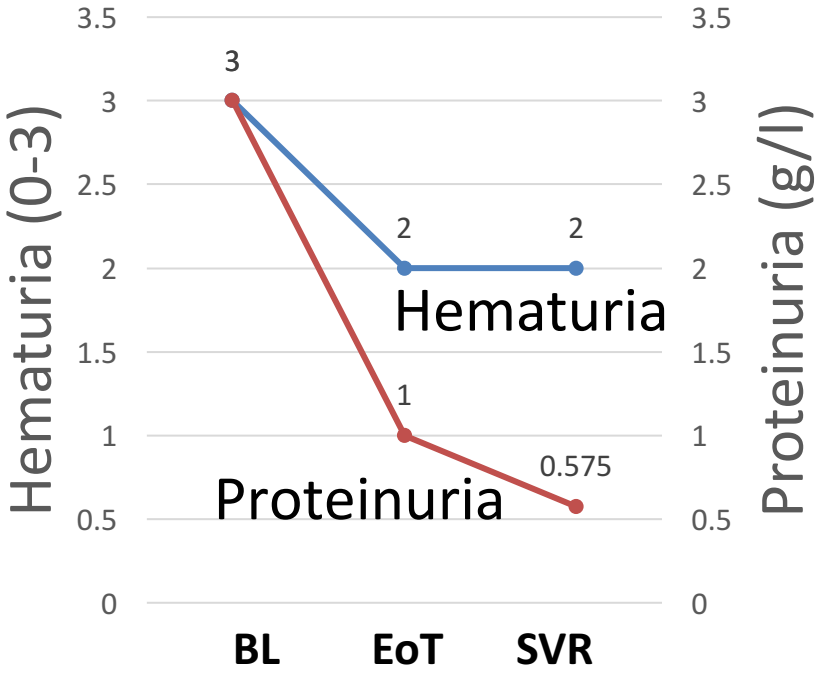




Well tolerated with few AEs with few IFN-free DAAs

Renal parameters during therapy





*2 patients started and 1 remained on HD post-treatment

- Clear improvement in renal function
- Complete clinical and immunological response likely delayed
- Similar results in a study of 7 pts treated with SOF-based tx

Emery Am J Gastro 2016, Sise Hepatology 2016

TORONTO CENTRE FOR LIVER DISEASE

What happened to our patient

- Treated sofosbuvir + simeprevir
  - Symptoms improved with viral suppression
  - Relapsed – symptoms returned!
- Retreated with SOF/ledipasvir
  - SVR
  - Slow resolution of all symptoms
  - Now, no rash, no ascites, GFR 65 cc/min!

Outline

- Background on HCV
- HCV & CKD
  - Risk of HCV in CKD and CKD in HCV
- Treatment
  - Genotype 1
  - Other genotypes…controversies remain
  - Cryo-related renal disease
- **The transplant conundrum**

What about transplant?

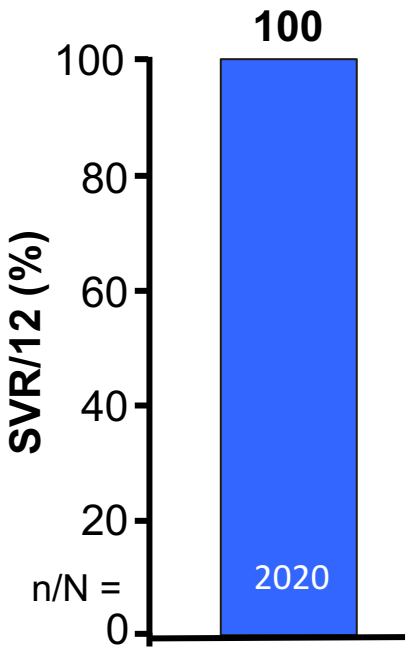
To treat before or after…that is the question

The transplant conundrum…

- Treatment before or after renal transplant?
- IFN dogma
  - Treat before because we can't treat after
- Direct acting antivirals…
  - Treatment after transplant easy → drug interactions but no other issues
  - Are there advantages?

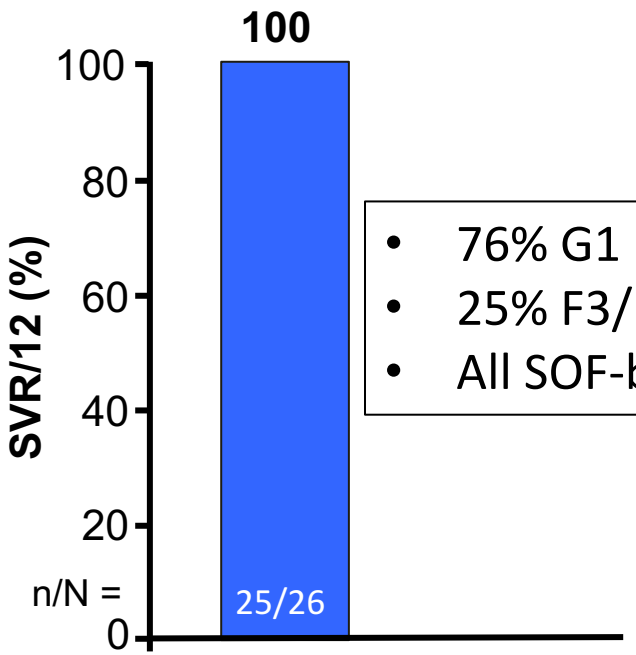
Treatment Post-Transplant

Post Renal transplant (US)



- 85% G1
- 50% F3/F4
- 60% prev Trt
- Primarily SOF/SIM
- **45% CNI dose changes**

Post Renal Transplant (France)



- 76% G1
- 25% F3/F4
- All SOF-based

- Accumulating data…safe & ?easy to treat post transplant
- Only issue is DDIs…manageable but need to be careful

Sawinski Am J Transplant 2015, Kamar Am J Transplant 2015

TORONTO CENTRE FOR LIVER DISEASE

What about HCV +ve donors?

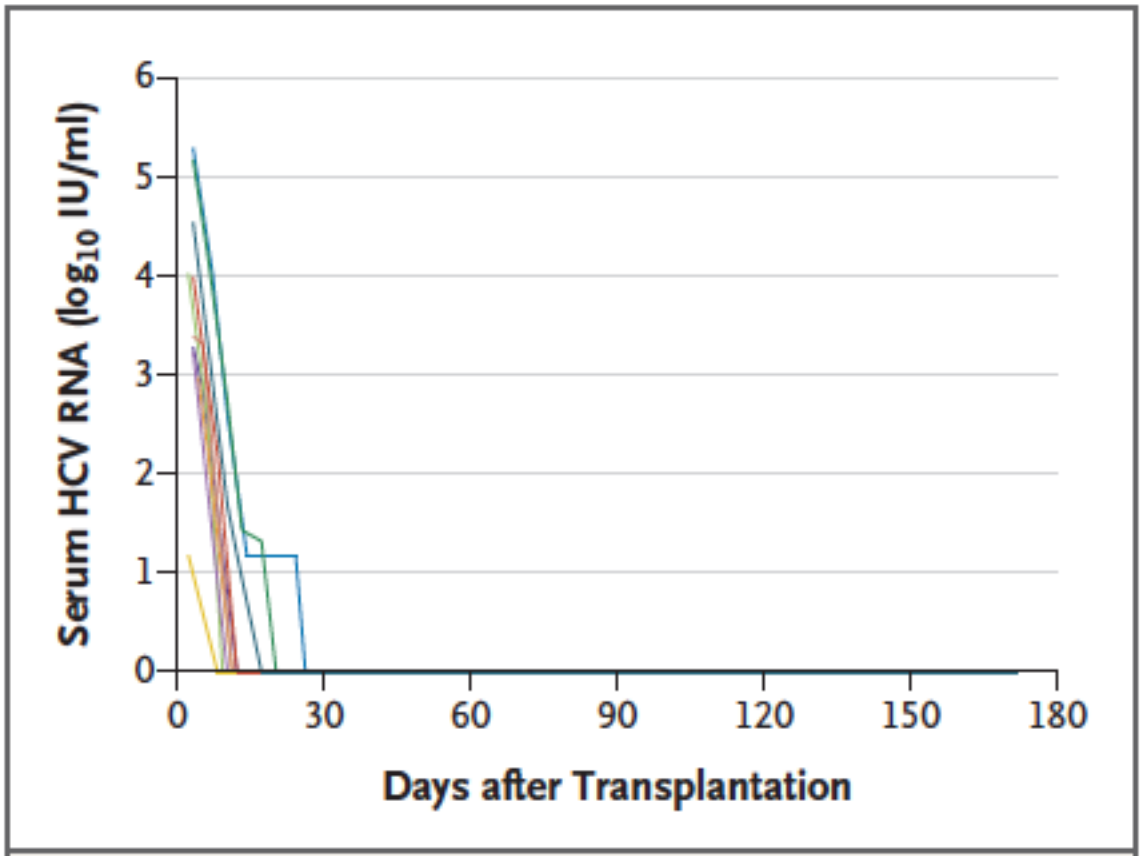
- Shortens waiting time for HCV +ve recipients
  - New York → 7 yrs to 7 mo for cadaveric donor
  - Allows them to receive an HCV-infected kidney…*make sure they are HCV RNA +ve* (not just Ab +ve)
  - If possible, HCV genotype on donor → may affect treatment choices

- Could we even consider it in HCV –ve recipients?
  - Need to be careful – risk of fibrosing cholestatic HCV

Using infected grafts?

The NEW ENGLAND JOURNAL of MEDICINE

Trial of Transplantation of HCV-Infected Kidneys into Uninfected Recipients



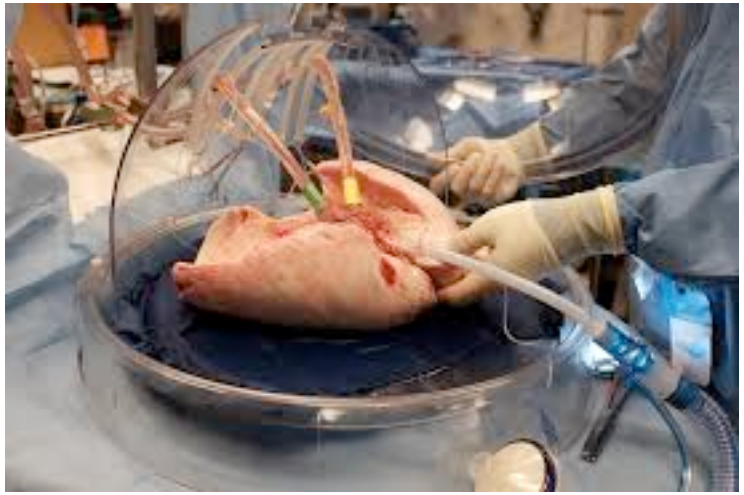
- 10 HCV –ve recipients received HCV +ve kidneys
- All were viremic post-transplant
- All treated elbasvir/grazoprevir
- **100% cure**

Goldberg NEJM 2017

TORONTO CENTRE FOR LIVER DISEASE

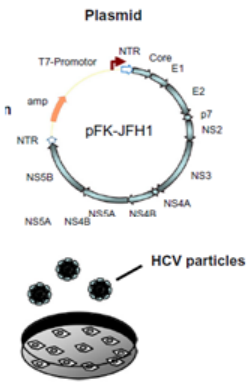
What about in lung transplant?

- With opiate crisis → 20% of eligible lung donors are HCV +ve!
- Ongoing trial of using HCV-infected donors to HCV-negative recipients with ex-vivo lung perfusion



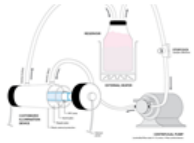
Prevention is better than treatment!

In vitro tests using UVC in the mini-circuit



Transfection of the perfusate

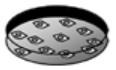
1.5 10^6 copies/mL

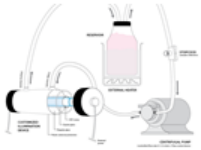


UVC

Treated perfusate

Huh 7.5.1 cell culture transfection

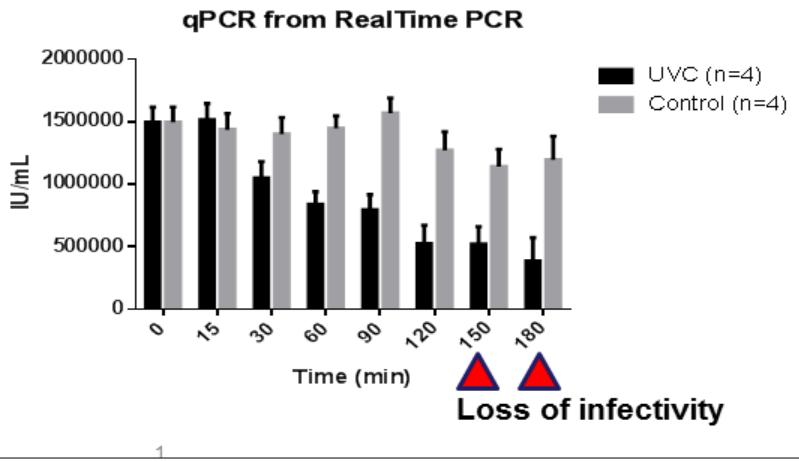


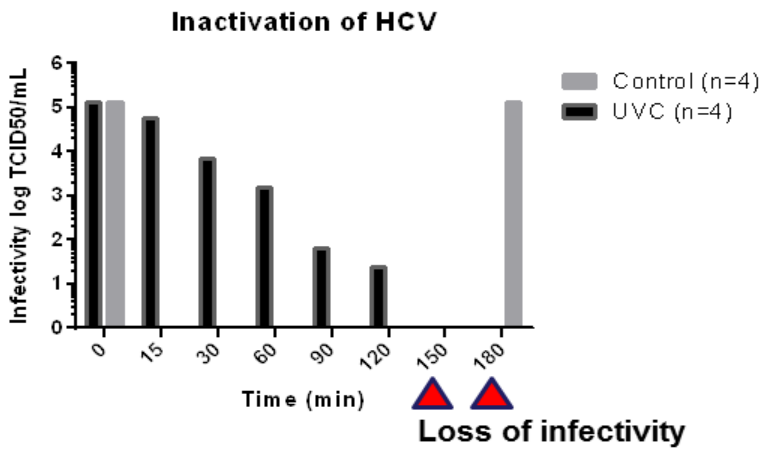


Control

No UVC irradiation

Huh 7.5.1 cell culture transfection





- Treatment with UV light or methylene blue – loss of infectivity…our next study!
- Any interest on the renal front?

Cyprel/Feld Unpublished

TORONTO CENTRE FOR LIVER DISEASE

Summary

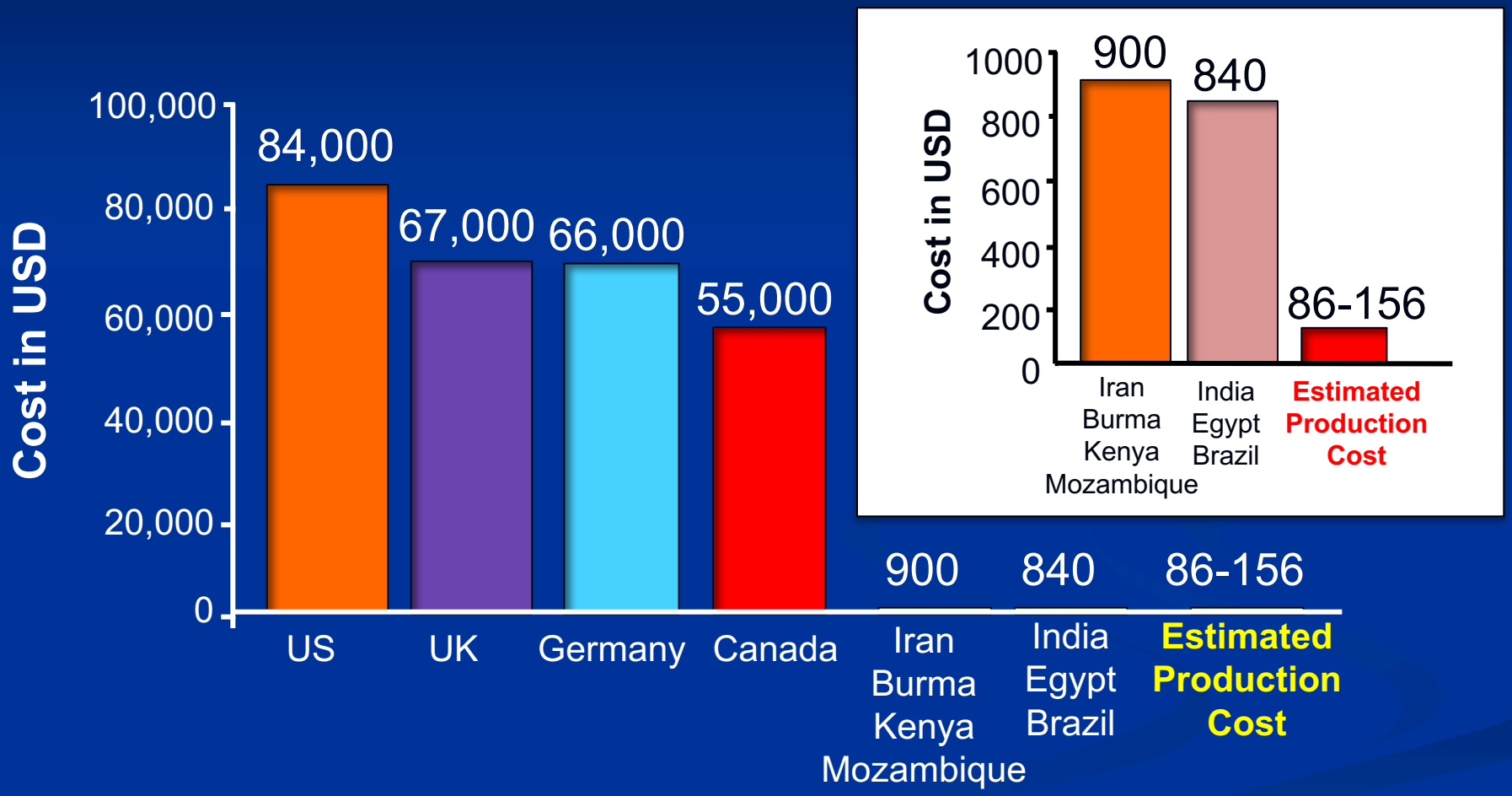
- HCV is a major global AND local public health problem
  - Prevalence and consequences greater in CKD
  - Cause and consequence of CKD/ESRD
  - Still under-diagnosed – screen your patients annually!
- Treatment has improved dramatically!
- Still a challenge for non-genotype 1
  - **Send us your patients for our trial!**
- Cryo-related renal disease
  - Antiviral therapy, immunosuppression
- Approach to transplant still a bit unclear…**interest in a trial of ex-vivo renal perfusion?**

TORONTO CENTRE FOR
LIVER DISEASE

The payers' position

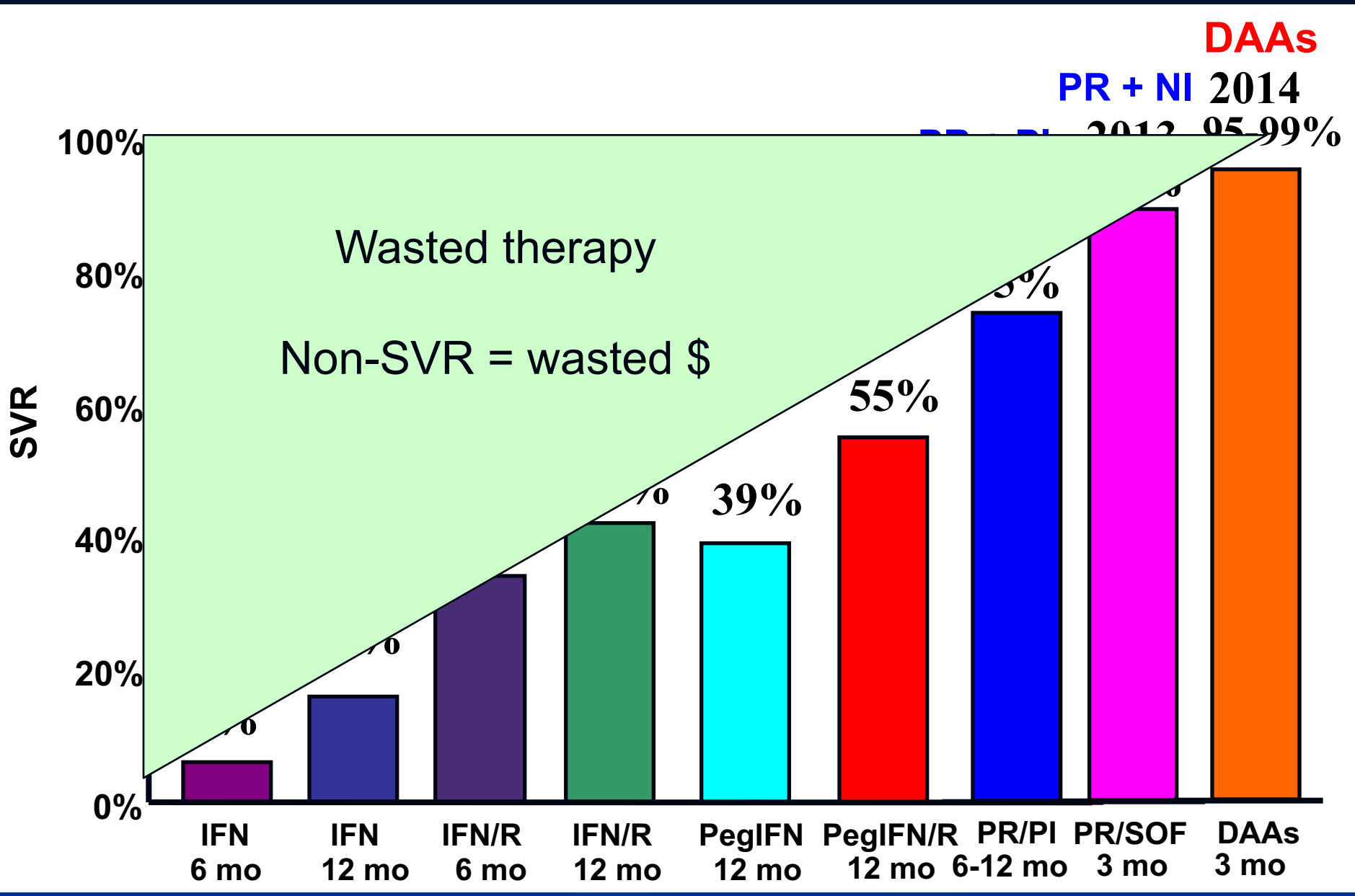
Limitations on access here and in most European countries

Costs for 12 weeks of Sofosbuvir

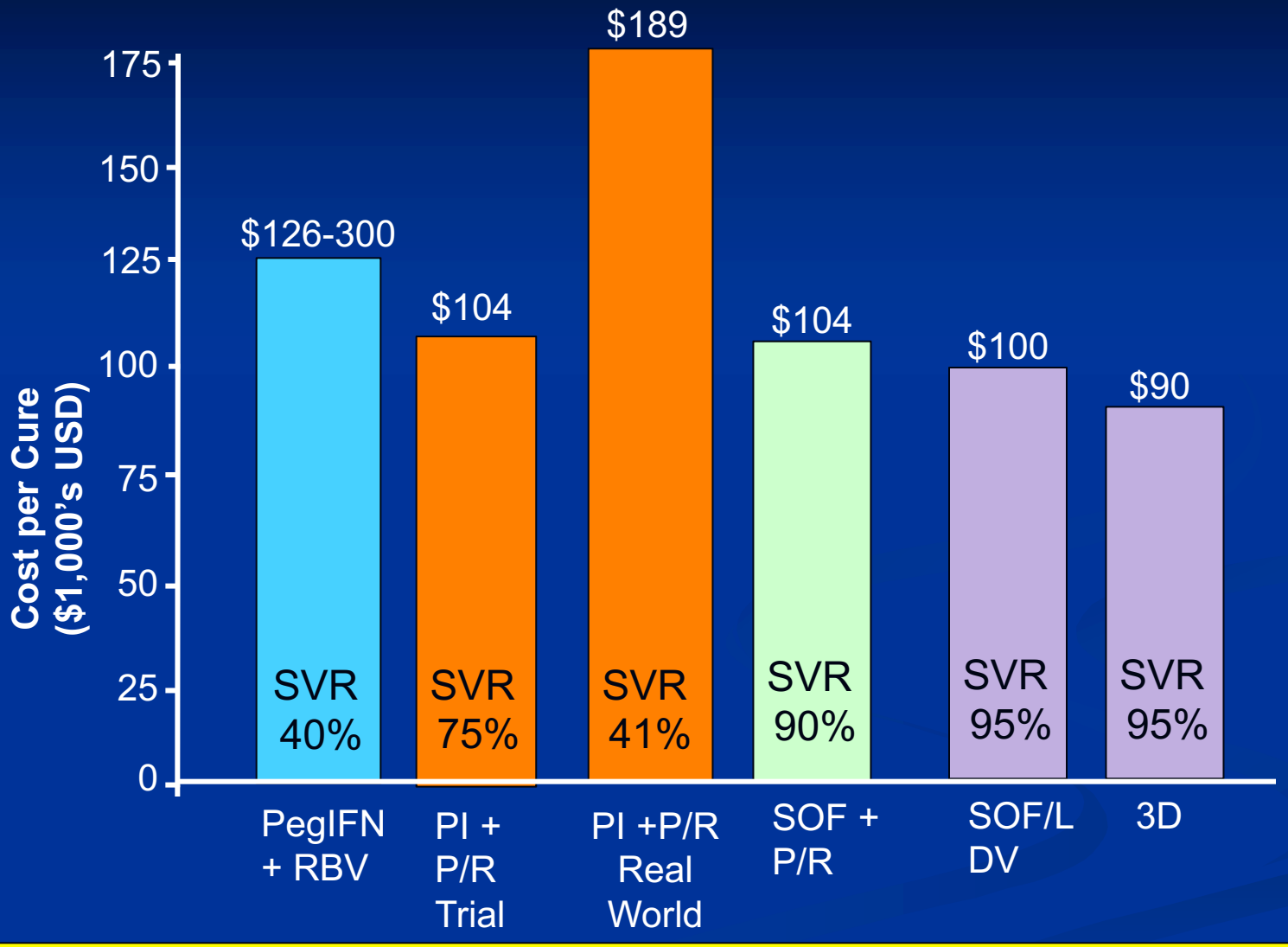


The prices are still much too high!

Hill IAS 2014


DAAs
PR + NI 2014
95-99%
100%
80%
60%
40%
20%
0%
SVR
Wasted therapy
Non-SVR = wasted $
55%
39%
IFN 6 mo
IFN 12 mo
IFN/R 6 mo
IFN/R 12 mo
PegIFN 12 mo
PegIFN/R 12 mo
PR/PI 6-12 mo
PR/SOF 3 mo
DAAs 3 mo

Cost of SVR actually going down



- Lower in Canada – treatment highly cost-effective
- Curative therapy → short-term cost, long-term savings