Akershus universitetssykehus

UNIVERSITETET I OSLO

RECOMMENDATION FOR THE MANAGEMENT OF HEPATITIS C VIRUS INFECTION AMONG PEOPLE WHO INJECT DRUGS

The International Network on Hepatitis in Substance users (INHSU)

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Oslo

Grebely J et al Int J Drug Policy

HELSE SØR-ØST

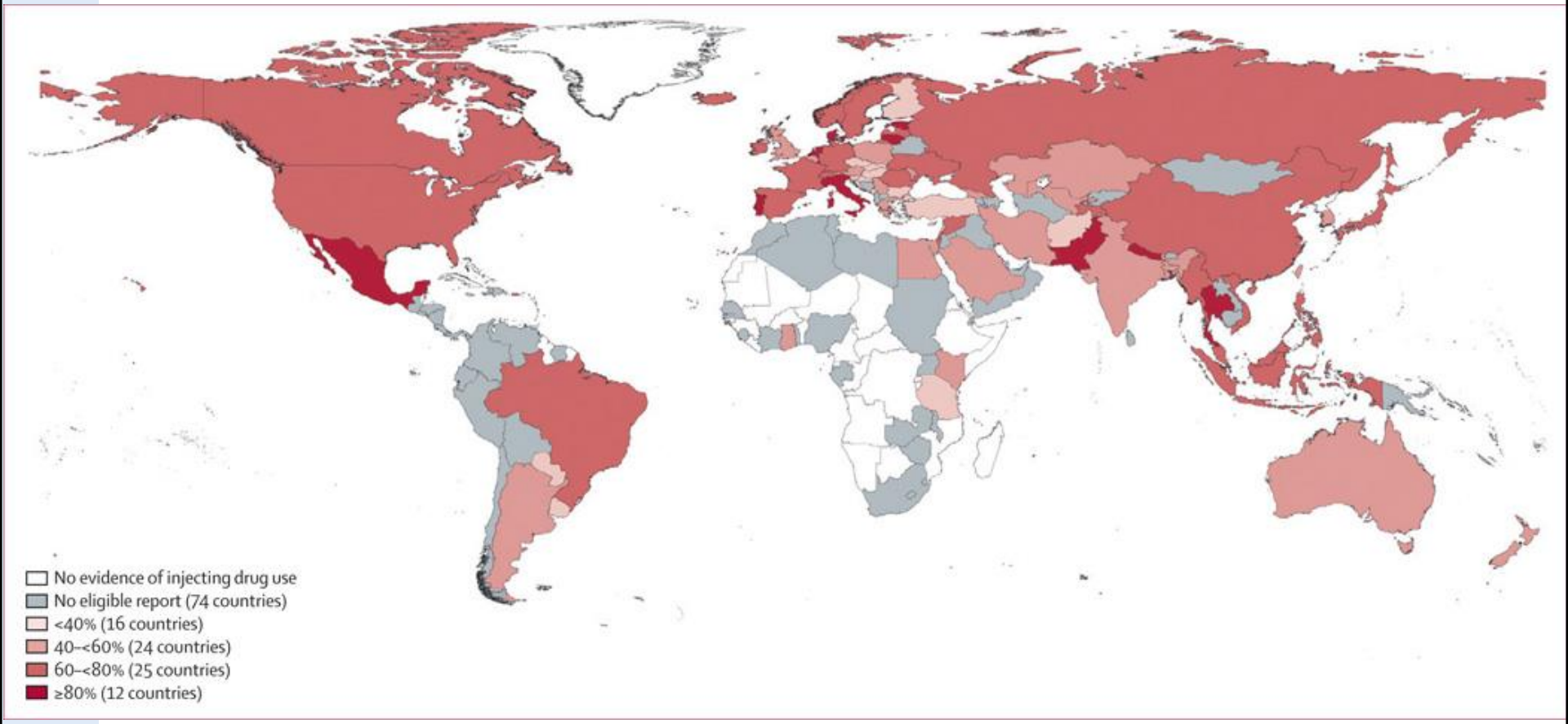
International Network on Hepatitis in Substance Users (INHSU)

- An international organisation devoted to the epidemic of HCV among substance users

- The aim of INHSU is to advance research of pathogenesis, prevention, and treatment of hepatitis among substance users.

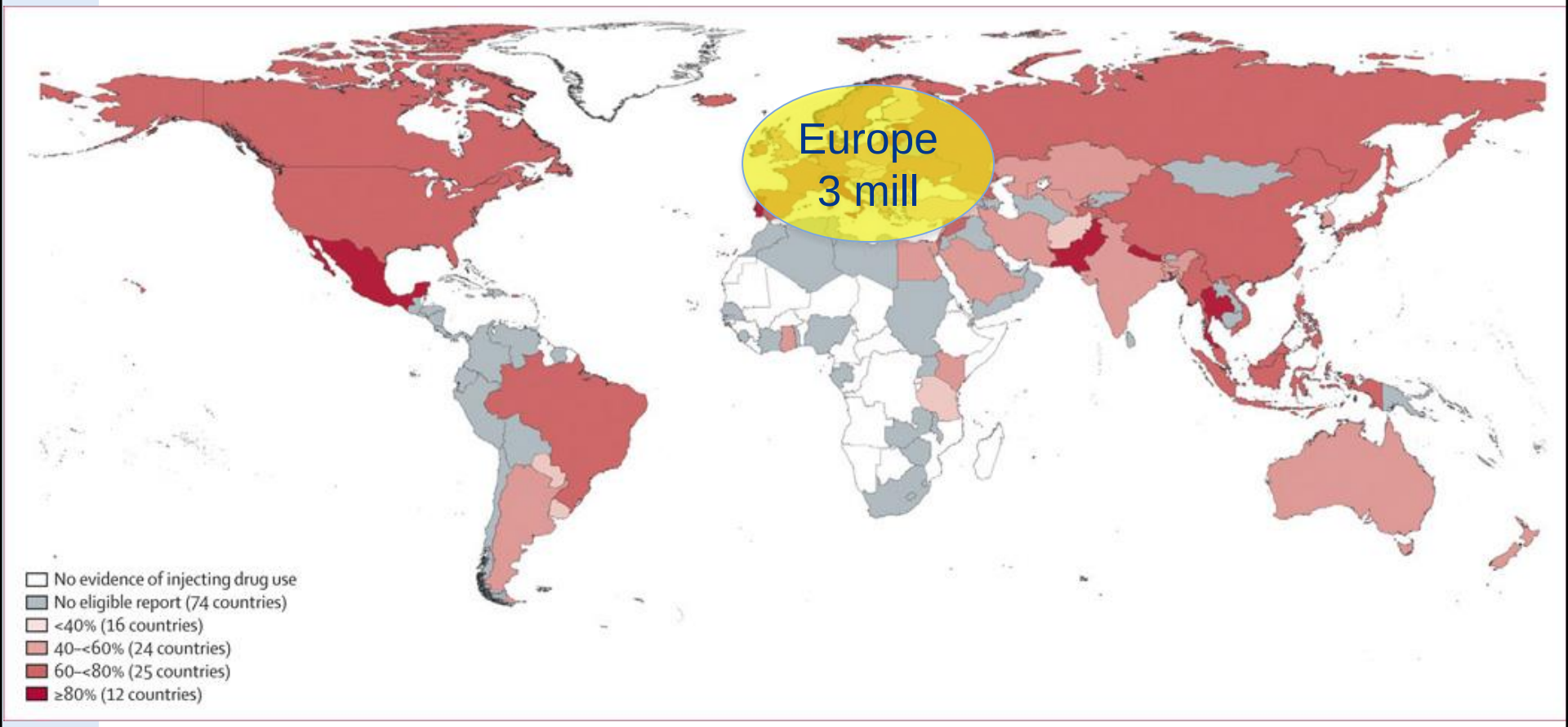
EPIDEMIOLOGY AND PREVENTION

Prevalence hep C in PWID



Nelson PK Lancet 2011

Prevalence hep C in PWID



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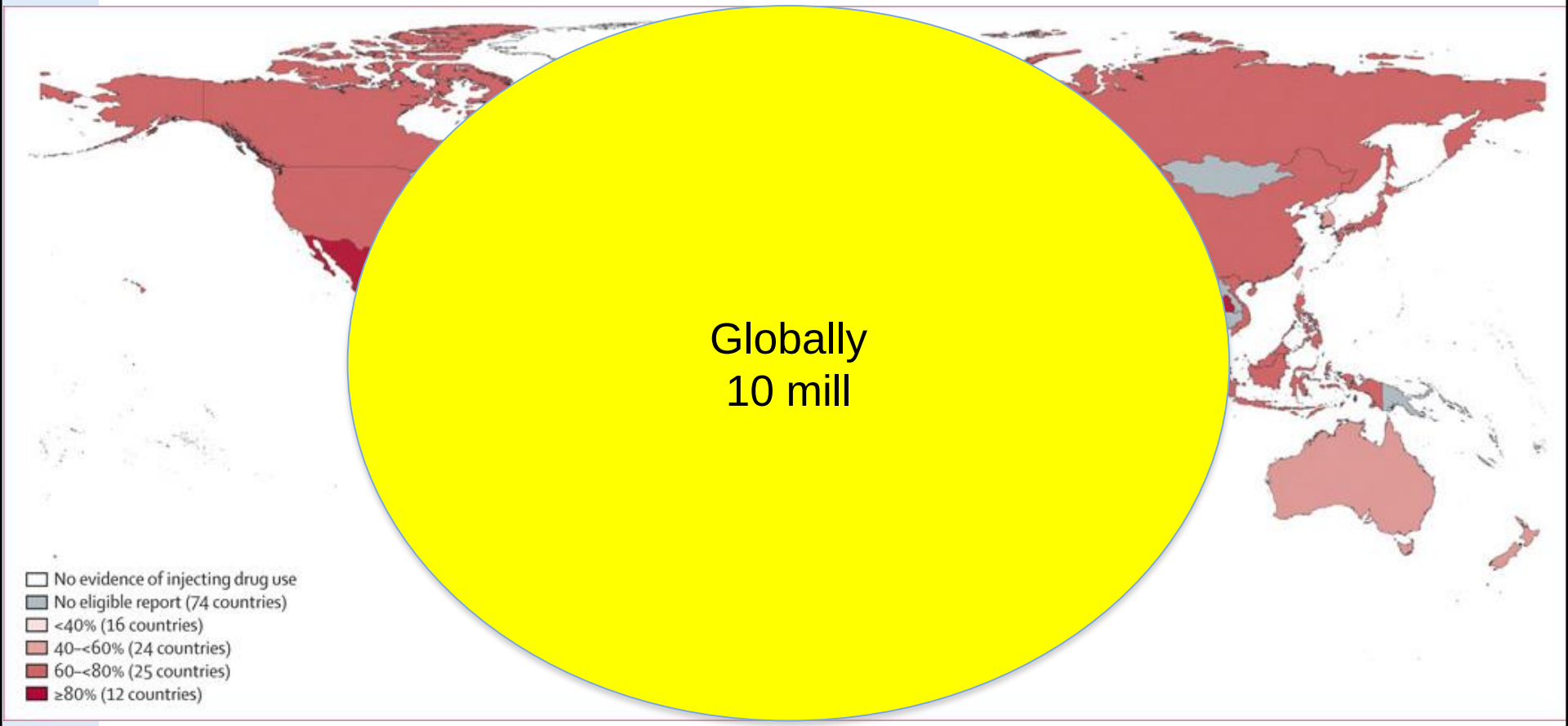
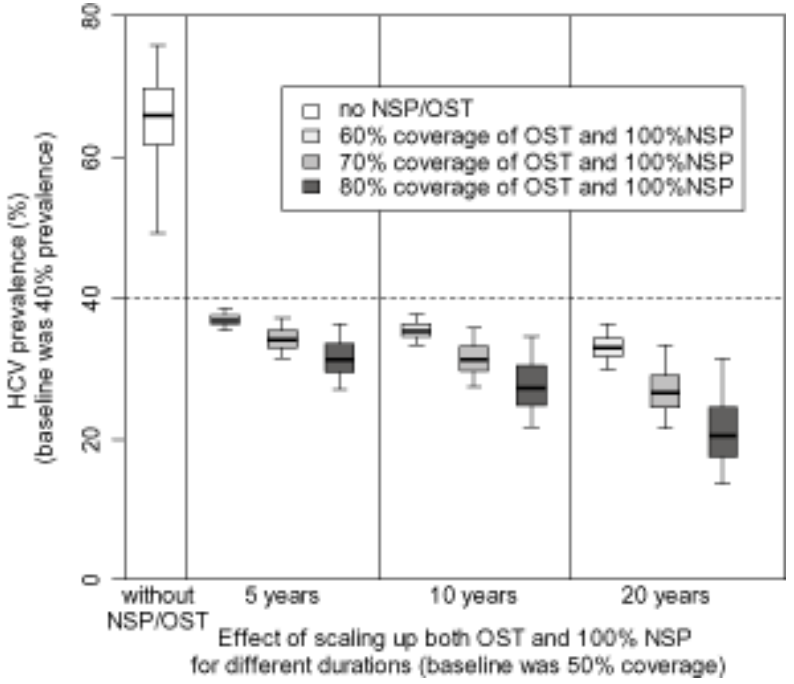
Prevalence hep C in PWID



Nelson PK Lancet 2011

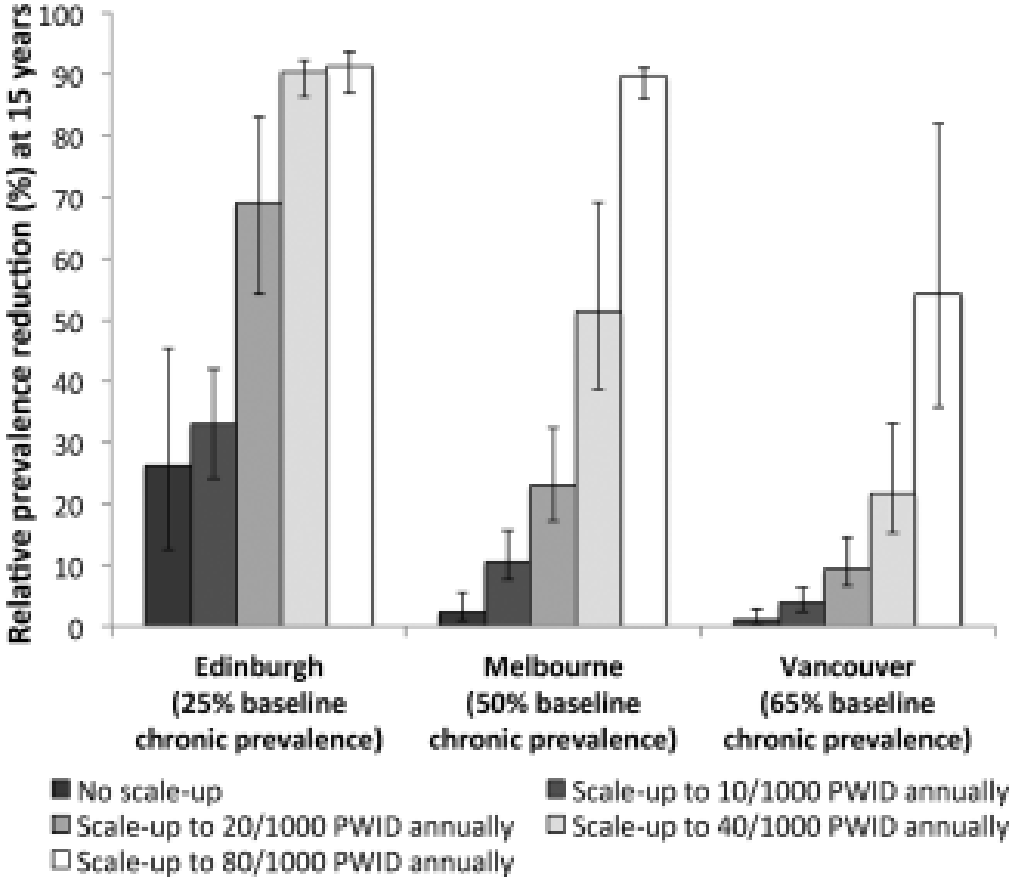
Epidemiology and prevention

- The effect of scaling up opiate substituton treatment in a setting of 100% coverage of needle/syringes program on HCV prevalence.



Addiction
Volume 107, Issue 11, pages 1984-1995, 12 JUL 2012 DOI: 10.1111/j.1360-0443.2012.03932.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2012.03932.x/full#add3932-fig-0004

Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals



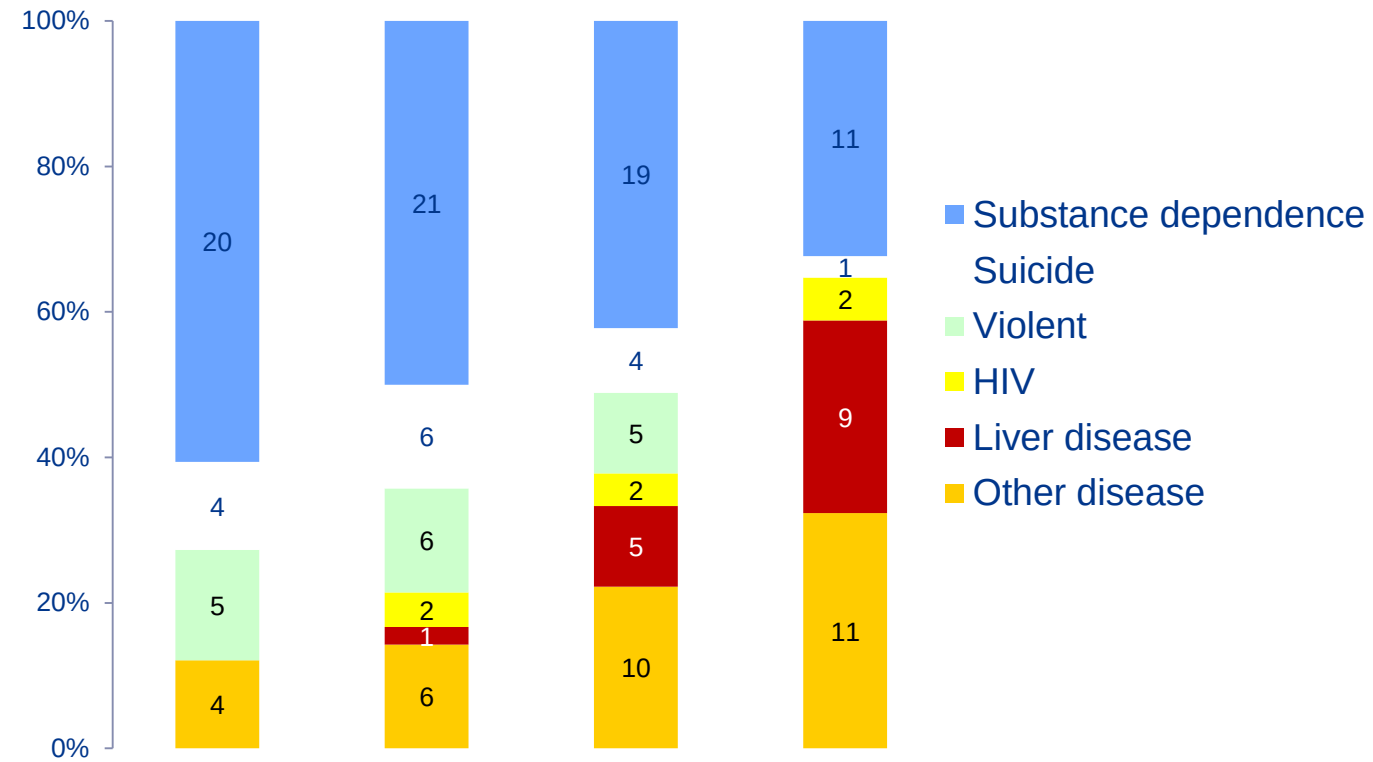
Hepatology
Volume 58, Issue 5, pages 1598-1609, 26 AUG 2013 DOI: 10.1002/hep.26431
http://onlinelibrary.wiley.com/doi/10.1002/hep.26431/full#hep26431-fig-0003

RECOMMENDATIONS

- Provide access to OST and clean drug injecting equipment as part of widespread comprehensive harm reduction programs, including in prisons
- Offer HCV treatment

NATURAL HISTORY OF HCV AND EFFECTS OF DRUGS ON THE LIVER

CAUSES OF DEATH AMONG PWID (n=327)



Age at death	<30	30-39	40-49	50+
Number of deaths	33	42	45	34

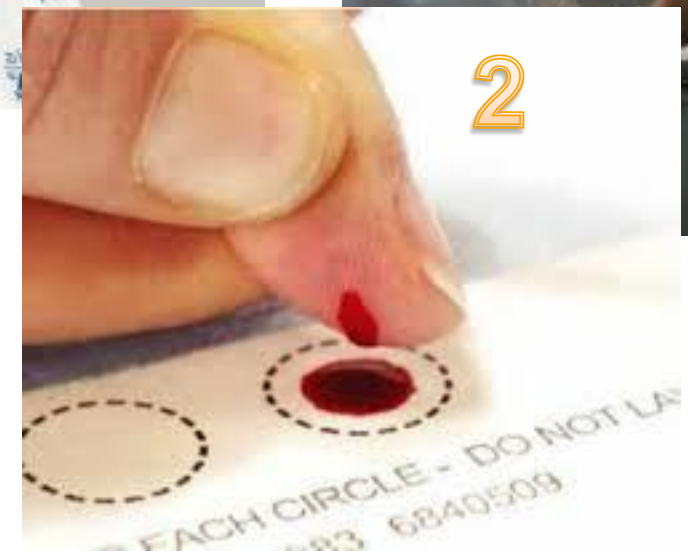
Modified from Kielland KB J Hepatol 2013

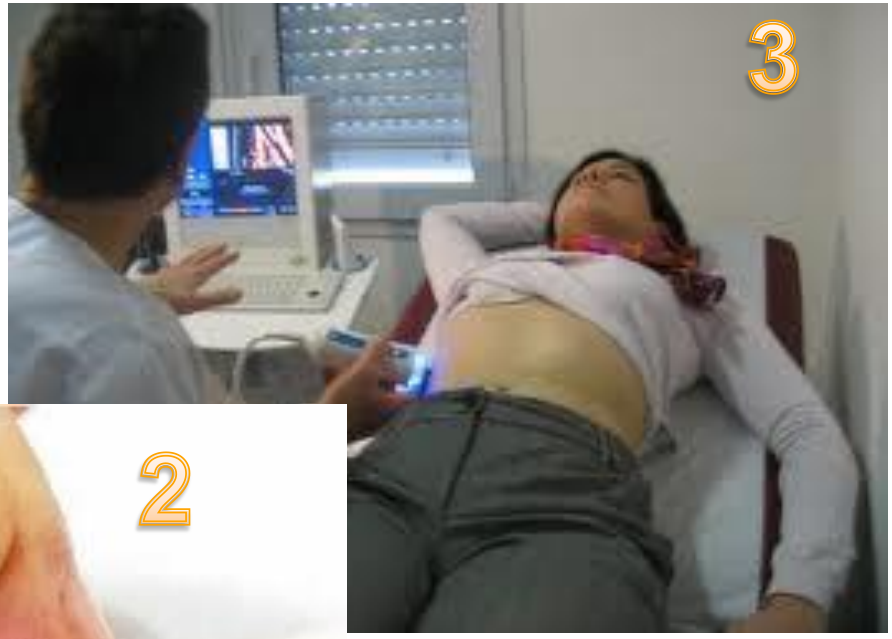
RECOMMENDATIONS

- Counsel to moderate alcohol intake, or abstain if evidence of advanced liver disease.
- Cessation of injecting is not required to limit HCV disease progression

TESTING OF HCV INFECTION

Testing of HCV infection





RECOMMENDATIONS

- Test for anti-HCV, and if the result is positive, current infection should be confirmed by a sensitive RNA test.
- PWID who are anti-HCV antibody negative should be routinely and voluntarily tested for HCV antibodies/RNA and if negative, every 12 months.
- Testing should also be offered following a high risk injecting episode
- PWID who are anti-HCV antibody positive and HCV RNA negative (through spontaneous or treatment-induced clearance) should receive regular HCV RNA testing, every 12 months or following a high risk injecting episode

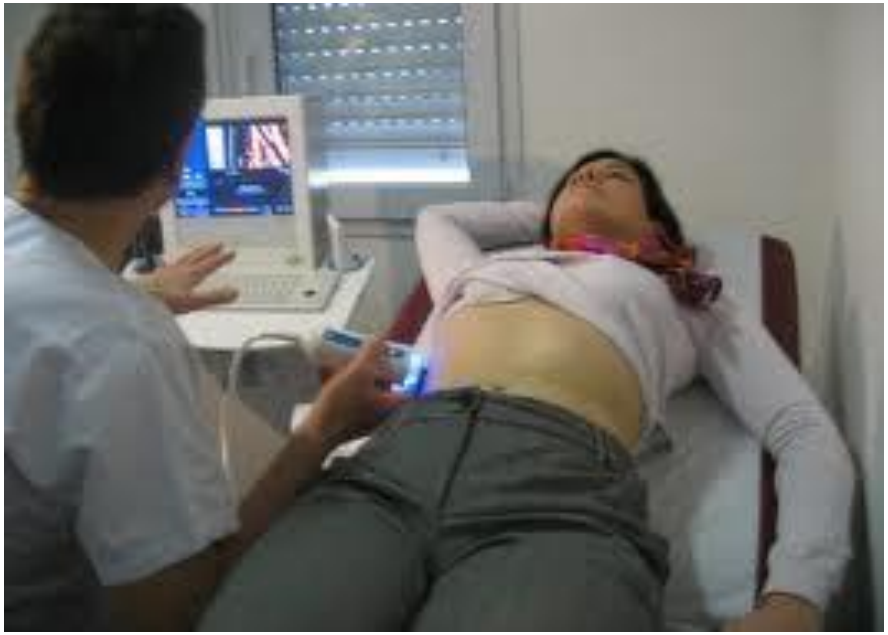
NON-INVASIVE LIVER FIBROSIS ASSESSMENT

Non-invasive liver fibrosis assessment

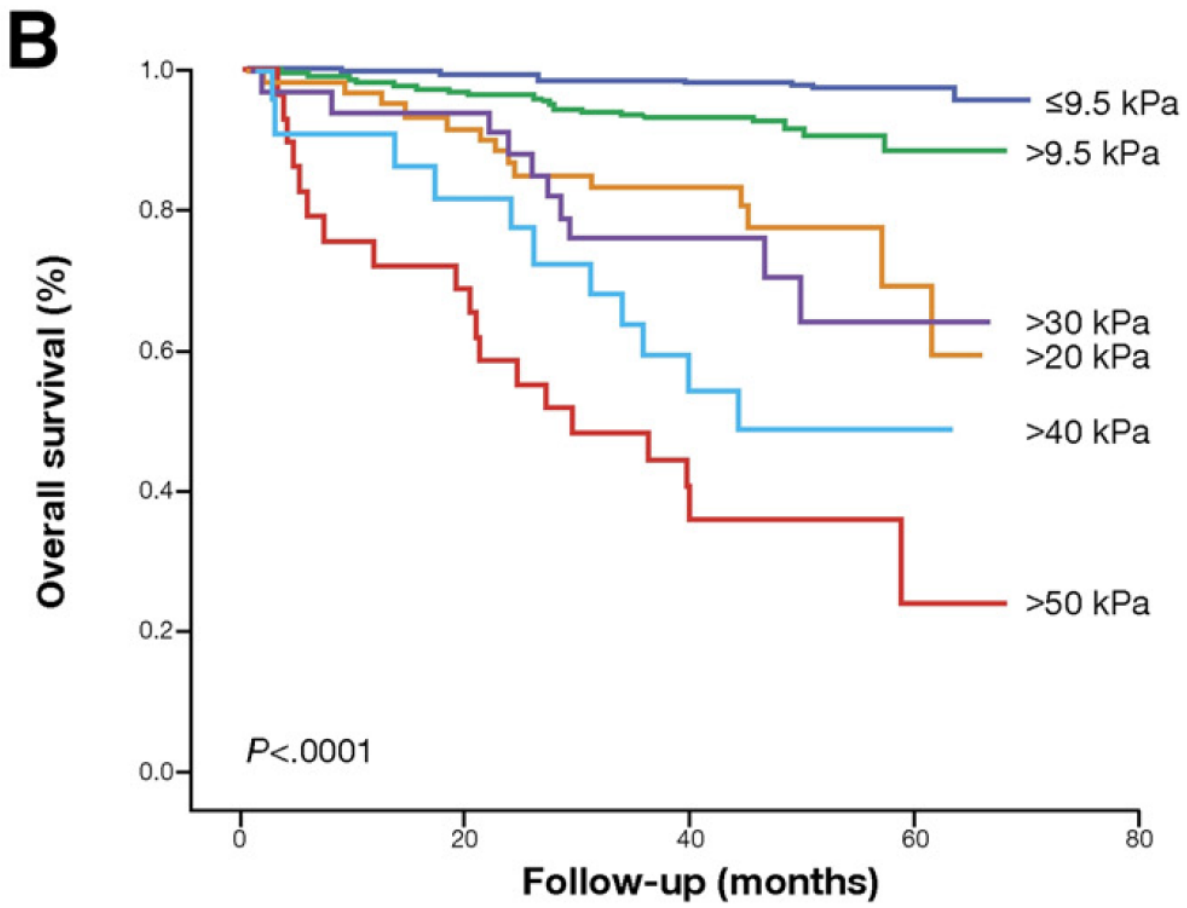
- Leverelastisity
  - –Fibroscan®

  < 7 kPa:
    - No or minimal liver fibrosis

  >12.5 kPa
    - Cirrhosis



TE – survival(n=1457)



Vergniol et al. Gastroenterology 2011

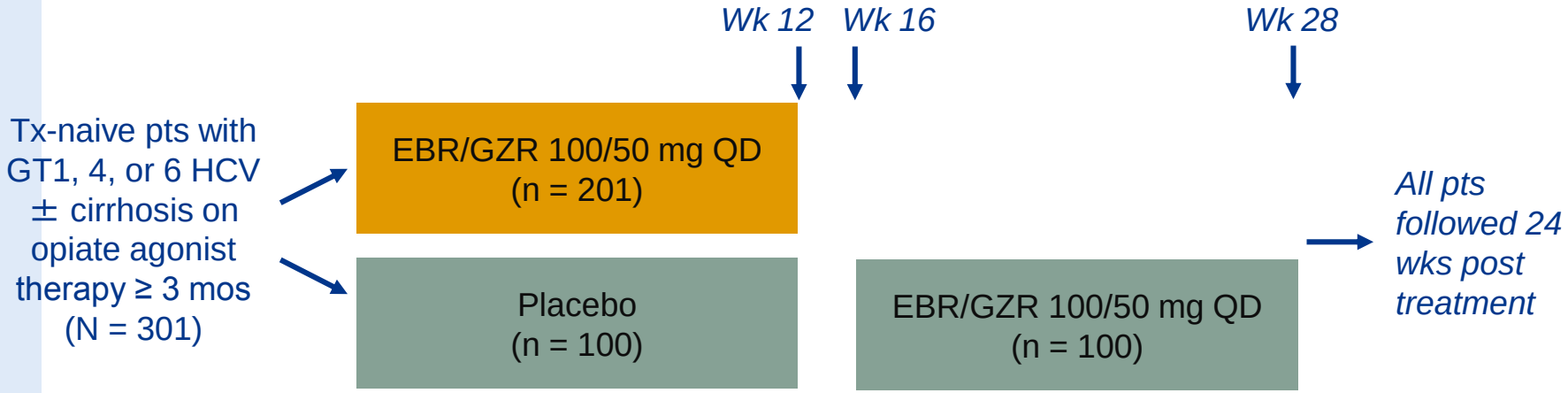
RECOMMENDATIONS

- Non-invasive assessments should be offered, if available.
- Combining multiple non-invasive assessments is recommended.

PEG-IFN AND DAA-BASED TREATMENT: TREATMENT RECOMMENDATIONS

C-EDGE CO-STAR: Elbasvir/Grazoprevir for GT1, 4, or 6 HCV in PWID

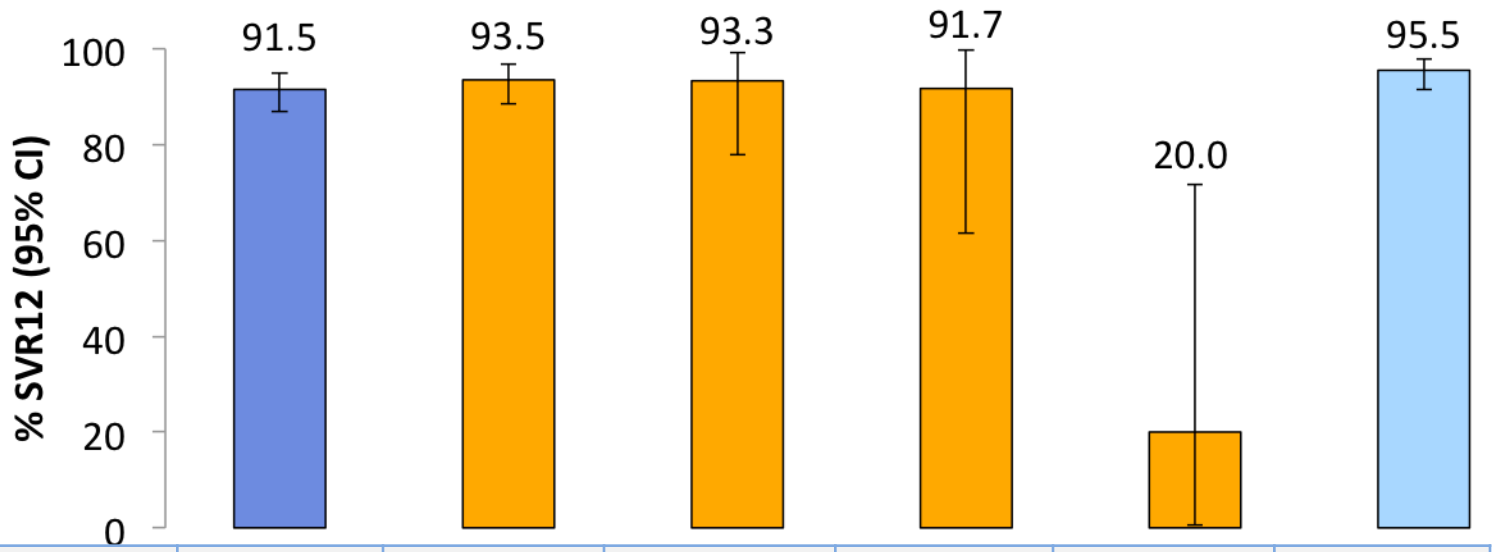
- Randomized, double-blind, placebo-controlled phase III study in PWID on opiate agonist therapy
  - Primary endpoint: SVR12 in immediate treatment arm
  - Study unblinded at Wk 12



Dore G, et al. AASLD 2015. Abstract 40.

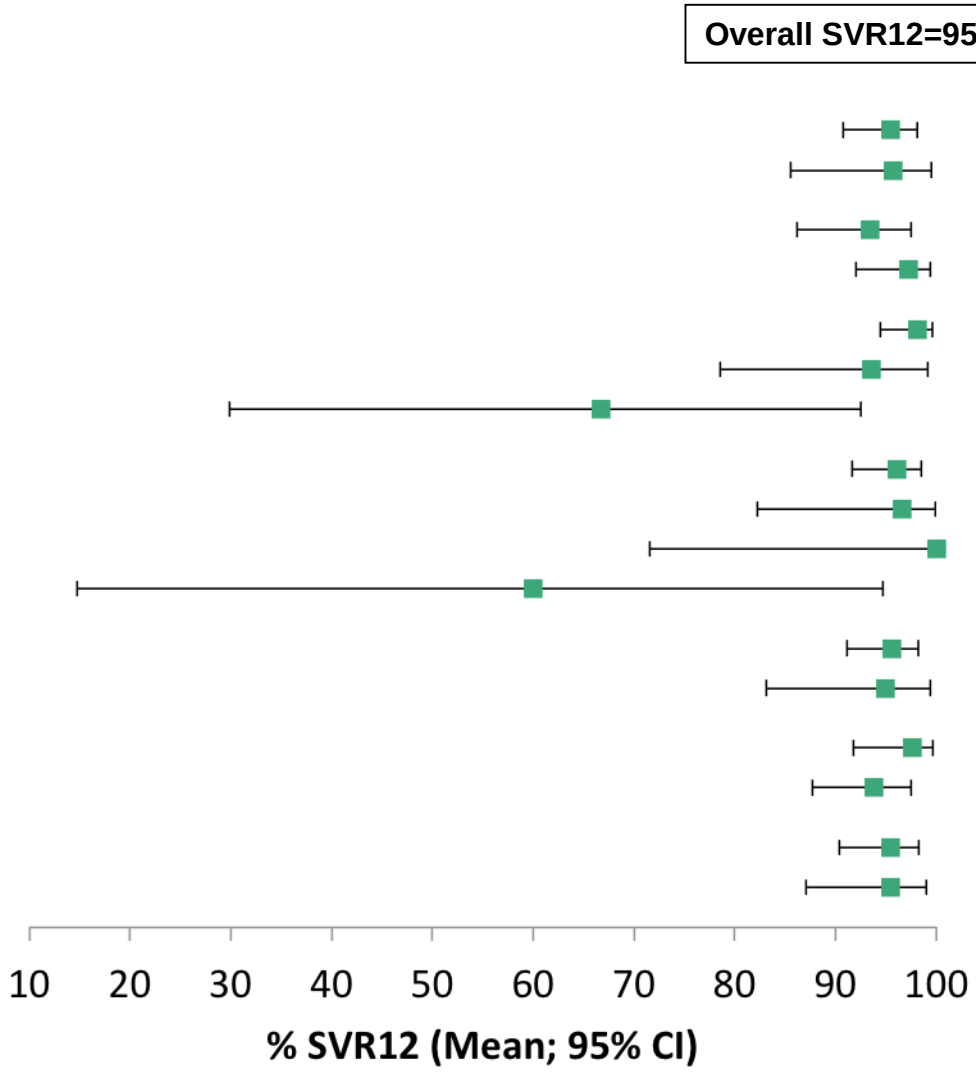
Slide credit: clinicaloptions.com

SVR ITT



	All GT	GT1a*	GT1b	GT4	GT6	mFAS
	184/201	144/154	28/30	11/12	1/5	189/198
Relapse	7	4	1	0	2	7
Reinfection	5	3	0	0	2	--
LTFU or discontinued unrelated to VF†	5	3	1	1	0	2 (excluded)

Dore G et al. AASLD 2015. Abstract 40.



Subgroup	n/m	SVR12 % (95% CI)
Male	144/151	95.4 (90.7, 98.1)
Female	45/47	95.7 (85.5, 99.5)
≥ 50 years	85/91	93.4 (86.2, 97.5)
< 50 years	104/107	97.2 (92.0, 99.4)
White	152/155	98.1 (94.4, 99.6)
African-American	29/31	93.5 (78.6, 99.2)
Asian	6/9	66.7 (29.9, 92.5)
GT1a	146/152	96.1 (91.6, 98.5)
GT1b	28/29	96.6 (82.2, 99.9)
GT4	11/11	100 (71.5, 100)
GT6	3/5	60.0 (14.7, 94.7)
Non-cirrhotic	151/158	95.6 (91.1, 98.2)
Cirrhotic	38/40	95.0 (83.1, 99.4)
HCV RNA ≤2 million	83/85	97.6 (91.8, 99.7)
HCV RNA >2 million	106/113	93.8 (87.7, 97.5)
Positive drug screen	127/133	95.5 (90.4, 98.3)
Negative drug screen	62/65	95.4 (87.1, 99.0)

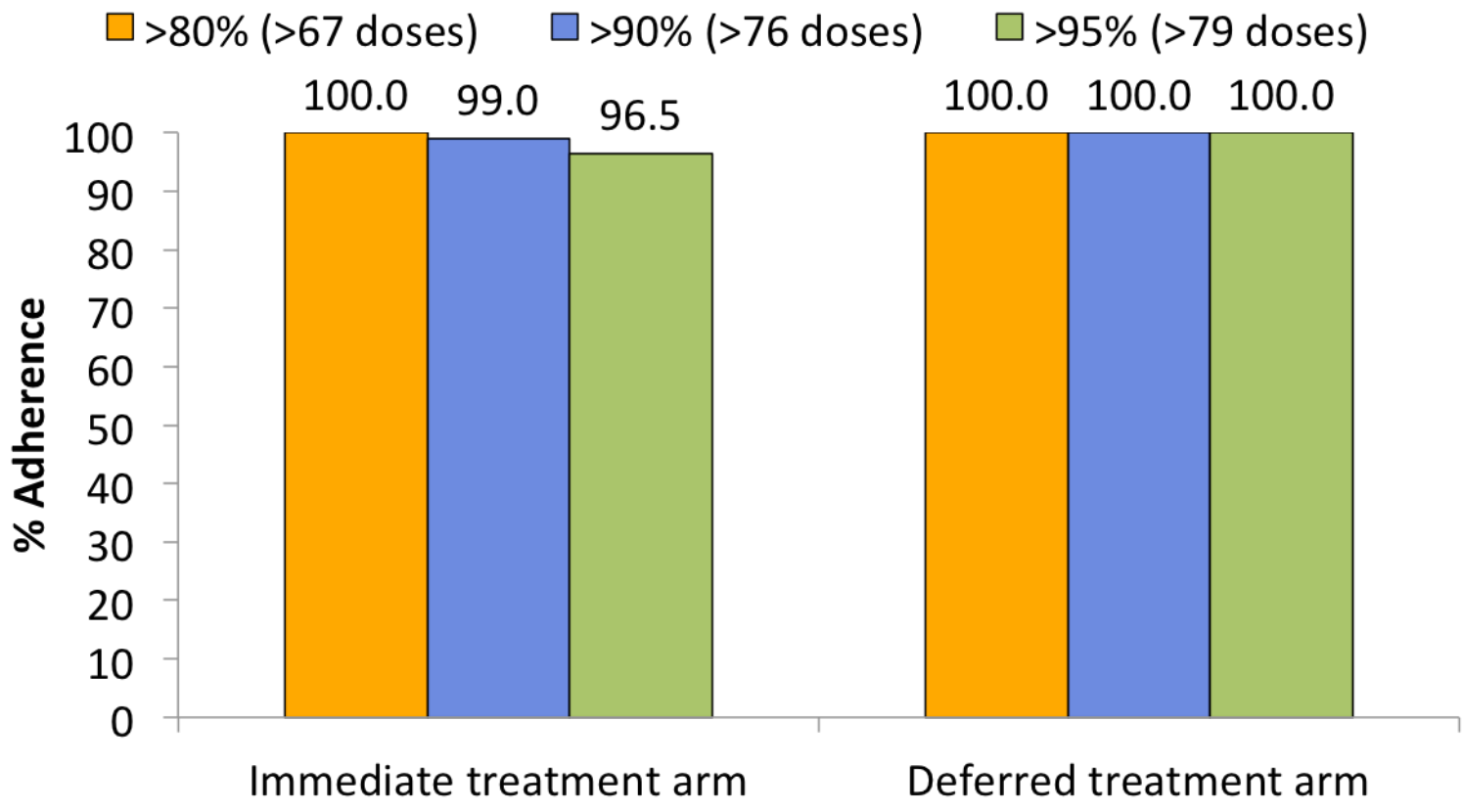
Dore G et al. AASLD 2015. Abstract 40.

RECOMMENDATIONS

- Evaluation of safety and efficacy of interferon-free DAA regimens is required in PWID
- DAAs can be used by those on OST
- PWID with early liver disease should generally be advised to await access to interferon-free DAA regimens.
- Anyone with chronic HCV infection should be considered for DAA therapy
- DAA therapy does not require specific methadone and buprenorphine dose adjustment, but monitoring for signs of opioid toxicity or withdrawal should be undertaken

IMPACT OF DRUG USE ON ADHERENCE AND SVR

Adherence



(Active study medication)

(Placebo)

Dore G et al. AASLD 2015. Abstract 40.

Number (%) of Patients with Number of Missed Doses

Number of missed doses	Immediate treatment arm (n=199)		Deferred treatment arm (n=97)	
0	153 (76.9)		80 (82.5)	
1	23 (11.6)	96.5 %	8 (8.2)	96.9 %
2	8 (4.0)		6 (6.2)	
3	8 (4.0)		0	
4	1 (0.5)		3 (3.1)	
5	0		0	
6	2 (1.0)		0	
7	1 (0.5)		0	
8	1 (0.5)		0	
9	0		0	
10	0		0	

RECOMMENDATIONS

- Adherence should consider missed doses and treatment discontinuation.
- PWID should be counselled on the importance of adherence in attaining an SVR.
- A history of IDU and recent drug use at treatment initiation are not associated with reduced SVR and decisions to treat must be made on a case-by-case basis.
- PWID with ongoing social issues, history of psychiatric disease and those with more frequent drug use during therapy are at risk of lower adherence and SVR and need to be monitored closely during therapy.
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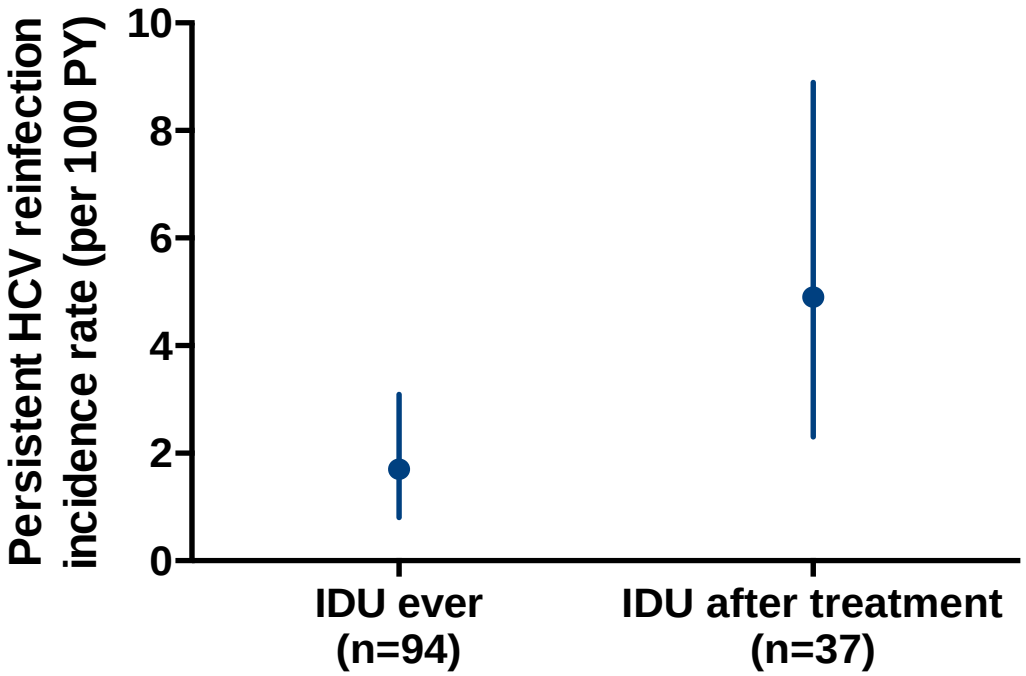
REINFECTION FOLLOWING SUCCESSFUL HCV TREATMENT

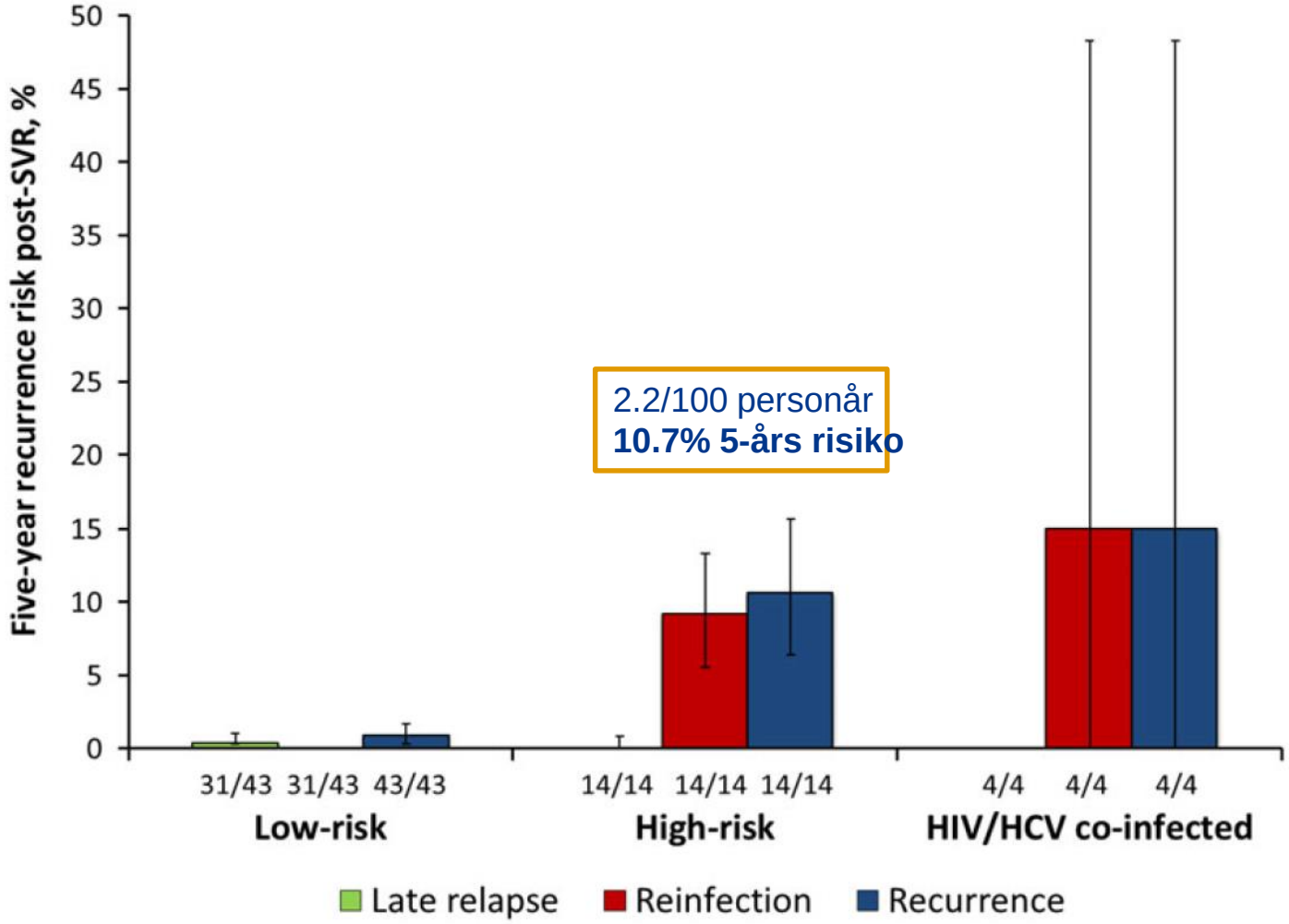
Incidence of persistent reinfection



Time at risk after SVR (PY)	593	206
Persistent reinfections	10	10
Incidence per 100 PY	1.7	4.9
95% CI	0.8–3.1	2.3–8.9

Midgard et al. J Hepatology 2016

HCV reinfection: 5 vears risk



Simmons et al. Clin Infect Dis 2016

RECOMMENDATIONS

- PWID should not be excluded from HCV treatment on the basis of perceived risk of reinfection.
- Harm reduction education and counselling should be provided for PWID in the context of HCV treatment.
- Following SVR, monitoring for HCV reinfection through annual HCV RNA assessment should be undertaken on PWID with ongoing risk behaviour.

Conclusion

- Given the burden of HCV-related disease among PWID, strategies to enhance HCV testing, linkage to care, assessment, and treatment and prevention of HCV reinfection in this group are urgently needed.
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- These recommendations demonstrate that treatment among PWID is feasible and provides a framework for HCV testing, assessment, management and treatment.

Grebely J et al Int J Drug Policy

INHSU 2016

Oslo, Norway • Wednesday 7 - Friday 9 September