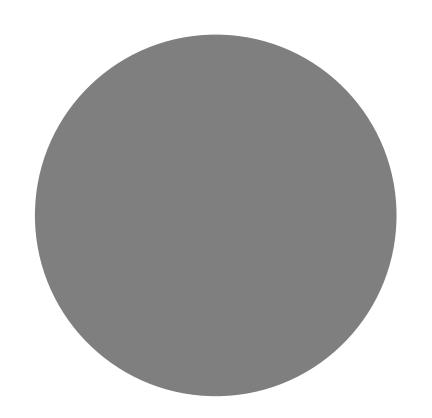
Update in hepatitis C virus infection

Eoin Feeney
Consultant in Infectious Diseases

St. Vincent's University Hospital



Overview

Natural history

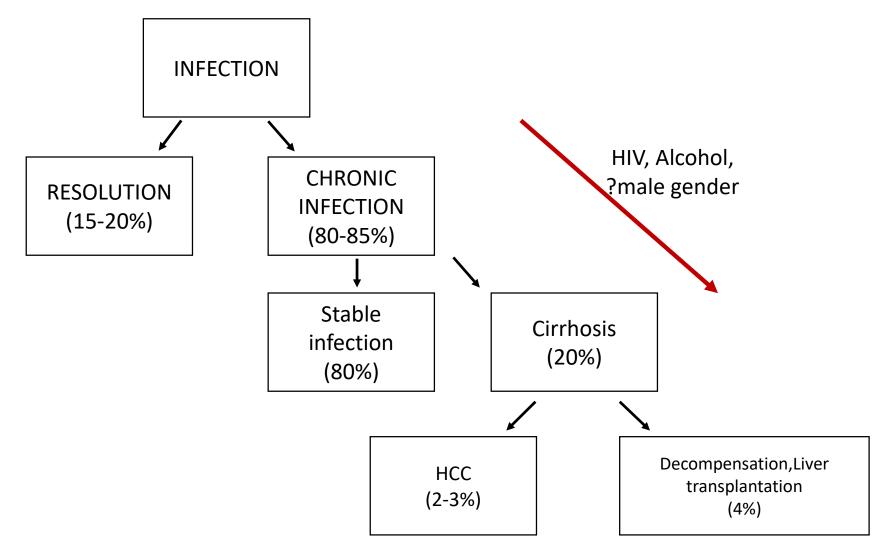
• Diagnosis, screening, staging

Management

Barriers going forward

Natural History, Diagnosis and Staging

Natural history



Diagnosis

- HCV antibody Serum sample
 - Positive in almost everyone infected
 - Positive after successful treatment or spontaneous clearance
- HCV antigen Serum sample
 - Confirms ongoing infection
- HCV viral load
 - Detects HCV RNA in the blood. Confirms ongoing infection. Allows genotype to be determined

- Those who have ever injected drugs
- Those who have used unprescribed or illicit drugs by a route other than injecting (non-injecting drug use (NIDU)), if there is a possibility of transmission of infection by the route of administration
- Prisoners or former prisoners
- Homeless people who have a history of engaging in risk behaviours associated with HCV transmission, or who have had a potential HCV risk exposure
- Migrants from a country with an intermediate and high prevalence of HCV (anti-HCV ≥ 2%*)
- People who are HIV positive
- Infants of HCV-RNA positive women
- Men who have sex with men.
- People on renal dialysis or who have had a kidney transplant
- Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested
- Recipients of anti-D immunoglobulin in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 to 18th February 1994 who have not yet been tested
- Recipients of plasma derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested

Strong
recommendation
- Screening
should be offered

- Those with a tattoo, particularly those who received tattoos a number of decades ago, in non-professional settings, prisons, countries with a high prevalence of HCV, or in circumstances where infection control was poor
- Household contacts of a person who is HCV positive in circumstances where household transmission is more likely to have occurred
- Recipients of solid organ transplants in Ireland prior to the introduction of routine screening
- Recipients of blood components and blood products overseas in any country where a quality assured blood donor screening programme may not have been in place
- People who have received medical or dental treatment in countries where HCV is common (anti-HCV prevalence ≥ 2%*) and infection control may be poor
- Sexual partners of known HCV cases:
 - o If the case or contact is also HIV positive
 - o If the HCV-infected case is an injecting drug user
- Sexual contacts of persons who inject drugs, but where HCV status is unknown or where there is evidence of resolved infection
- Commercial sex workers

Weak
recommendation
- Screening
should be
considered

Rapid screening



Oral Fluid

Fingerstick

Venipuncture Whole Blood

Serum/Plasma

Simple Testing Procedure

Oral Fluid

Step 1 - Collect sample.



Swab between the teeth and upper and lower gum once.

Step 2 - Insert the device into the buffer.



Step 3 - Read between 20 and 40 minutes.



Non-Reactive Line in the C Zone



Reactive Line in the C and T Zones



WP 7 - HEPCHECK- OVERVIEW

	DUBLIN	LONDON	BUCHAREST	SEVILLE	TOTAL
1. No. of individuals offered/screened	712/569	-/310	-/469	657/401	1,749
Proportion of individuals with positive HCV antibody on screening	137/569 24%	123/310 39%	166/469 35%	133/401 33%	559
3. No. of individuals screened (Ab only, bloods only, both Ab and bloods)	Pending	Pending	Ab + bloods 104 365 Ab	Ab + bloods: 21 Ab: 264 Bloods:116	-
 No. of HCV Ab+ individuals (either new or previously diagnosed) attending specialist appointment for HCV assessment. 	Pending	106	65	51	



Recommendation 24

- 24.1. Serum and plasma are the preferred specimen types for screening and diagnostic testing for HCV infection using quality assured assays.
- 24.2. Screening and diagnostic testing for HCV infection should not be performed on oral fluid samples due to the low sensitivity and low positive predictive value.
- 24.3. Dried blood spot testing can be considered for screening for HCV in special circumstances, such as mass screening initiatives e.g. in prisons.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines **Strength of recommendation:** strong

Staging

- Bloods
 - Screening for HIV, hepatitis B
 - FBC, U&E, LFTs (including AST), INR

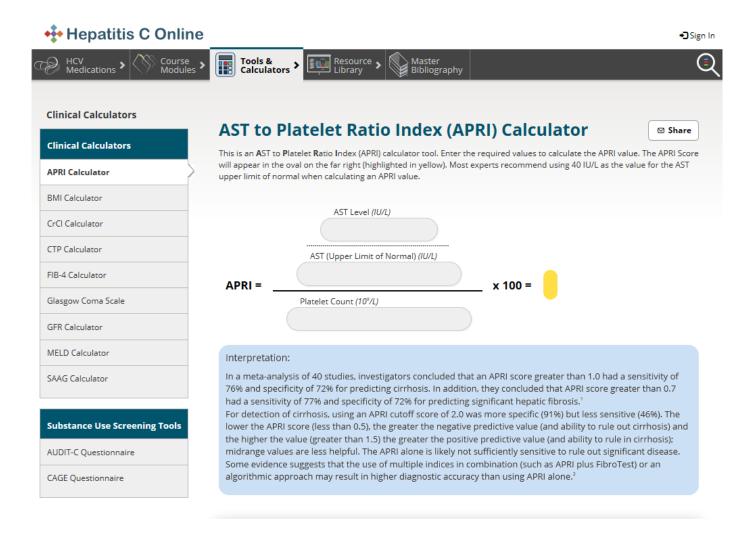
- HCV Genotype
 - Currently required for treatment decisions
 - 6 genotypes, predominantly 1 and 3 in Ireland
- Fibrosis assessment

Fibrosis Assessment

- Clinical exam
 - Signs of cirrhosis
 - Highly specific (75-98%), low sensitivity (15-68%)

- Liver biopsy
 - Gold standard
 - Highest risk
 - Takes long
 - Patient fear +++

Non invasive



Fibroscan





Table 1 Recommended values for different stage of fibrosis

Disease	F0–F1 (Kpa)	F2 (Kpa)	F3 (kpa)	F4 (kpa)
Hepatitis B	≤6.0	≥6.0	≥9.0	≥12.0
Hepatitis C	≤7.0	≥7.0	≥9.5	≥12.0
HCV-HIV coinfection	≤7.0	≤10	≥11.0	≥14.0
Cholestatic liver disease	≤7.0	≥7.5	≥10.0	≥17.0
NAFLD/NASH	≤7.0	≥7.5	≤10	≥14.0

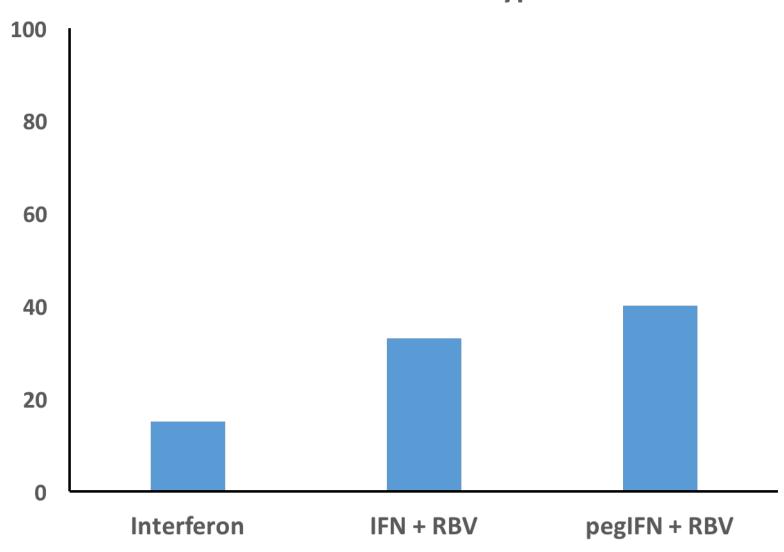
Treatment – "Interferon Era"

- Pegylated interferon
 - Weekly subcutaneous injection
 - "Flu-like" side effects

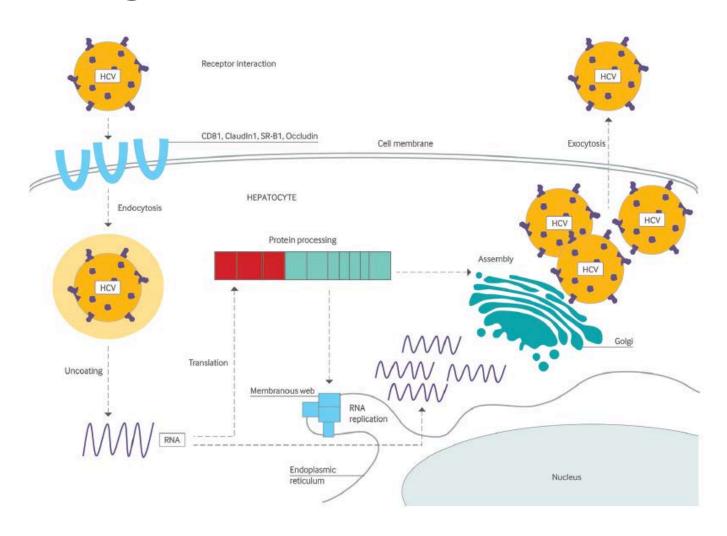
- Ribavirin
 - Oral medication, twice daily
 - Marrow suppression, sleep disturbances, teratogenic

Combined for 24-48 weeks

Treatments for HCV Genotype 1 2010



Direct acting antivirals



Current 1st line regimens for HCV Ireland

	GENOTYPE 1	GENOTYPE 2	GENOTYPE 3	GENOTYPE 4
Non cirrhotic	Viekirax ii OD Exviera i BD GT1a + RBV - 12 weeks GT1b 8 weeks	Sofosbuvir+ Daclatasvir 12 weeks	Sofosbuvir+ Daclatasvir 12 weeks	Viekirax ii OD RBV 12 weeks
Cirrhotic	Viekirax ii OD	Sofosbuvir/Velpatasvir	Sofosbuvir/Velpatas	Viekirax ii OD
	Exviera GT1a +RBV 12-24 weeks	12 weeks	vir+RBV	RBV
	GT1b 12 weeks		12 weeks	12 weeks

HCV DAA treatment landscape Ireland

• 2014 – Early access programme – Cirrhosis, decompensated

 2015 – Cirrhosis (Fibroscan >12.5kPa), State-infected, Liver transplants

• 2016 – Fibrosis (Fibroscan >8.5kPa), all the above

2017 – Open access (up until June)

Hepatitis C patients unable to get drugs due to funding problems

Funding freeze blamed on 'significantly increased and unpredicted' number of claims

O Mon, Jul 31, 2017, 01:00

Paul Cullen



SVUH Data

DAA tx 8/10/2017	Nos completed	Cirrhotics completed tx	Nos SVR 12 data available	No of Cirrhotics (>12kPa) with SVR 12 data (%)	Relapsed	SVR 12 results (%)
Total completed	351 Excludes 7 who didn't complete; see table below	154	259	140 (54.0)	9 8 cirrhotic	250 (96.5)
G1a	117	55	81	46 (56.7)	1 Non cirrhotic OLT	80 (98.7)
G1b	112	40	92	37 (40.2)	1 cirrhotic	36 (98.9)
G1 no subtype	3	3	3	3 (100)	0	3 (100)
Geno 2	11	5	6	4 (66.6)	0	6 (100)
Geno 3	97	53	70	44 (62.8)	6	64 (91.5)
Geno 4	12	7	9	6 (66.6)	1 After SVR 12	8 (89.9)
Transplants treated	65	??40	61		2 1 cirrhotic G3 1 non cirrhotic 1a	96.7

The Problem

The numbers

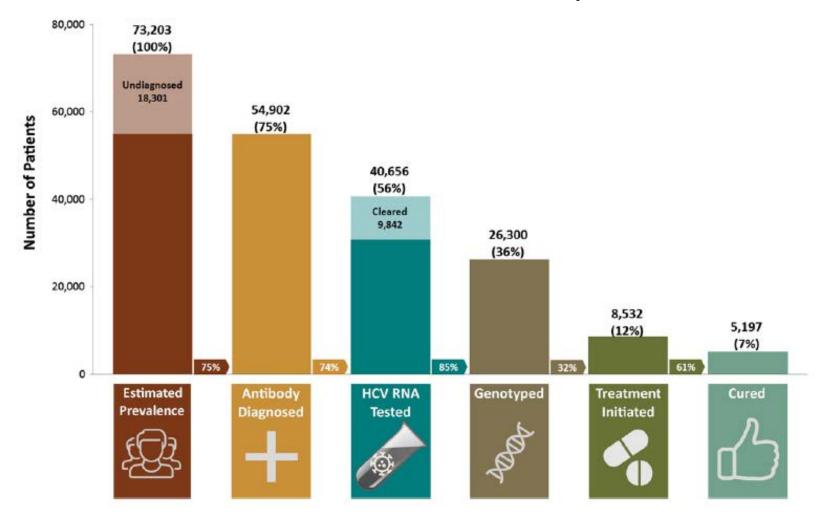
• 2006 – estimated 20,790 heroin users in Ireland

August 2016 – 9,652 patients receiving OST (not including prisons)

HCV prevalence in PWID reported as 62-81% ~ 2003

Globally 5.6 million HCV infections related to PWID

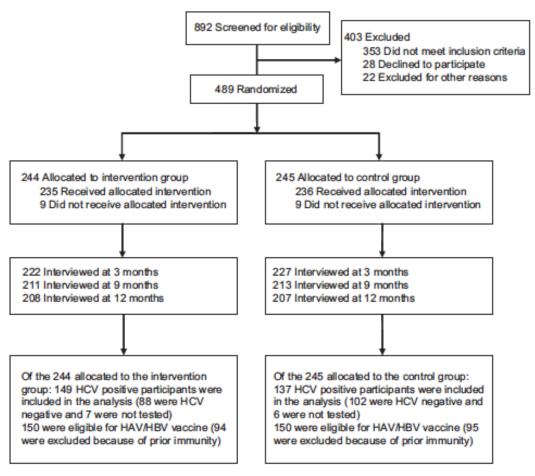
The cascade of care – HCV (BC, Canada)



Why don't PWID attend for treatment?

- Alcohol and drug use
- Fear of HCV treatment

- Fear of liver biopsy
- Distance to hospital
- Early morning appointments



Note. HAV - hepatitis A virus, HBA - hepatitis B virus; HCV - hepatitis C virus.

FIGURE 1—Allocation of participants in study to promote linkage to hepatitis services: San Francisco, CA, and New York City, February 2008–June 2011.

TABLE 3—Effects of Intervention Condition on Adherence to HCV Clinical Evaluation in Study to Promote Linkage to Hepatitis Services: San Francisco, CA, and New York City, February 2008–June 2011

Variable	OR (95% CI)
Intervention condition	
Hepatitis care coordination	4.10** (2.35, 7.17)
Control (Ref)	1.00
Recruitment location	
San Francisco	3.21** (1.73, 5.95)
New York City (Ref)	1.00
Gender	
Female	0.83 (0.46, 1.49)
Male (Ref)	1.00
Race/ethnicity	
White (Ref)	1.00
African American	0.93 (0.46, 1.86)
Hispanic	0.79 (0.40, 1.57)
Other	2.33 (0.65, 8.33)
Education, y	
≥ 12	1.10 (0.64, 1.91)
< 12 (Ref)	1.00
HIV status	
Positive	8.02** (2.81, 22.95)
Negative (Ref)	1.00
Homeless past 6 mo	
No	2.28* (1.25, 3.33)
Yes (Ref)	1.00

Note. CI = confidence interval; HCV = hepatitis C virus; OR = odds ratio.

^{*}P<.01; **P<.001.

ECHO study

Table 2. Sustained Virologic Response According to Genotype and Site of Treatment.*					
Difference between ECHO Sites and UNM HCV Genotype ECHO Sites UNM HCV Clinic HCV Clinic P V					
	no. of patients with response/total no. (%)		percentage points (95% CI)		
All genotypes	152/261 (58.2)	84/146 (57.5)	0.7 (-9.2 to 10.7)	0.89	
Genotype 1	73/147 (49.7)	38/83 (45.8)	3.9 (-9.5 to 17.0)	0.57	
Genotype 2 or 3	78/112 (69.6)	42/59 (71.2)	-1.5 (-15.2 to 13.3)	0.83	

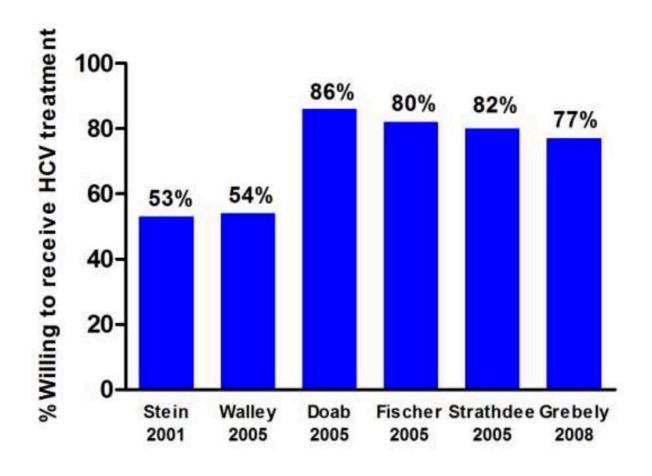
^{*} The rates of sustained virologic response are not reported separately for six patients with genotype 4 or genotype 6. ECHO denotes Extension for Community Healthcare Outcomes, HCV hepatitis C virus, and UNM University of New Mexico.

Why don't doctors treat PWID?

- They don't want it
- They're not going to take it
- It's not going to work
- They're just going to reinfect again afterwards
- It will have no benefit

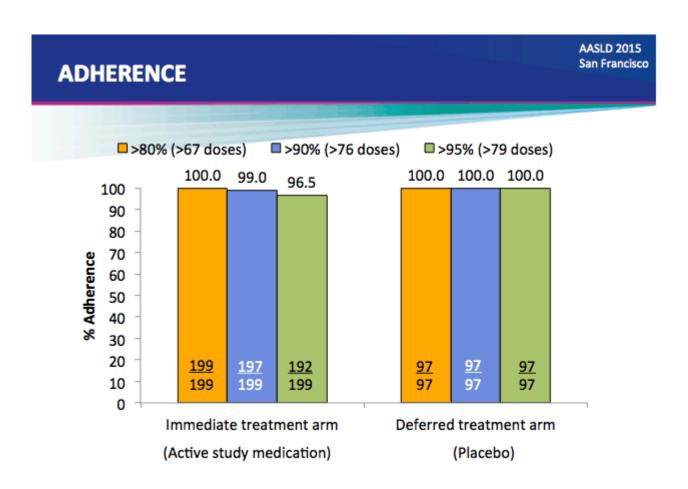
They don't want it

"They don't want it" — IFN era data



They're not going to take it

C-EDGE CO STAR



PREVAIL study

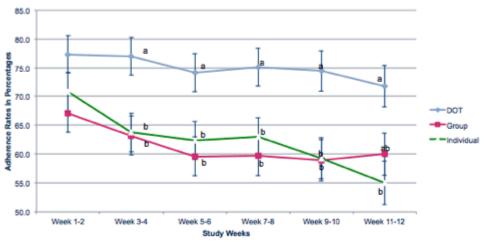
Randomized, controlled trial

- Individual arm (control arm): subjects self-administer all HCV medications.
- <u>DOT arm</u>: subjects receive observed oral doses by nursing staff at same time as receive methadone or buprenorphine. Weekly directly administered IFN injections (if applicable).
- Group arm: subjects attend weekly treatment group.
 Weekly directly administered IFN injections (if applicable).

Montefiore

Adherence higher in DOT vs. both Individual (p=0.0008) and Group (p=0.0003)





Overall adherence: DOT (75.0%) vs. Group (61.4%) vs. Individual (62.4%)

Montefiore

PREVAIL study

SVR12 high in all 3 arms (p=0.24)

Study Arm	ETR	SVR12
DOT	98.0% (50/51)	98.0% (50/51)
Group	93.8% (48/51)	93.8% (48/51)
Individual	96.1% (49/51)	90.2% (46/51)
Total	96.0% (144/150) (95% CI 92% - 99%)	94.0% (141/150) (95% CI 89% - 97%)

It's not going to work

Interferon era

Pegylated IFN plus RBV Mauss et al (2004) [41] Prospective enrollment of IDUs in a stable methadone maintenance program; for each IDU, a control patient was matched for sex, age, HCV genotype, and HCV RNA level Non-IDUs (no IDU or substitution therapy and abstained from drug use for at least 5 years before initiation of treatment) Schaefer et al (2007) Prospective enrollment; recruitment source not clear Schaefer et al (2007) [42] Prospective enrollment through multiple veterans' health care medical centers Non-IDUs Neri et al (2007) [44] Prospective enrollment; IDUs enrolled through hospital detoxification department Neri et al (2007) [44] Prospective enrollment through multiple clinics Prospective enrollment through multiple clinics Treatment IDUs (currently receiving all all 33 (72.2) No substitution therapy; ongoing users excluded) Former IDUs (history of addiction; ongoing users excluded) Non-IDUs Thomson et al (2007) [44] Prospective enrollment through multiple clinics Prospective enro						
ble methadone maintenance program; for each IDU, a control patient was matched for sex, age, HCV genotype, and HCV RNA level Schaefer et al (2007) [42] Schaefer et al (2007) [42] Prospective enrollment; recruitment source not clear Seal et al (2007) [43] ^d Prospective enrollment through multiple veterans' health care medical centers Non-IDUs (history of IDU; IDU) Non-IDUs (history of IDU; IDU) Within 6 months before initiation of treatment) Former IDUs (currently receiving users excluded) Non-IDUs Seal et al (2007) [43] ^d Prospective enrollment through multiple veterans' health care medical centers Non-IDUs Non-IDUs Non-IDUs Prospective enrollment; IDUs enrolled through hospital detoxification department Treatment IDUs (former heroin users abuse of other drugs; currently receiving users excluded) Non-IDUs Non-IDUs Non-IDUs Treatment IDUs (former heroin users abuse of other drugs; currently receiving substitution therapy) Non-IDUs Non-IDUs Non-IDUs (history of addiction; ongoing users excluded) Non-IDUs (history of IDU; IDU) Within 6 months before enrollment was usually considered to be an exclusion criterion, although this could be overruled by individual doctors) Non-IDUs Non-IDUs (history of alcoholism or abuse of other drugs; currently receiving substitution therapy) Non-IDUs (IDU probably risk factor for acquisition of hepatitis C)	Pegylated IFN plus RBV					
apy for at least 5 years before initiation of treatment) Schaefer et al (2007) Prospective enrollment; recruitment source not clear Prospective enrollment; recruitment promption of treatment promption of treatment (2007) [42] Prospective enrollment through multiple veterans' health care medical centers promption of the prospective enrollment; IDUs (bistory of IDU; IDU probably risk factor for acquisition of treatment) Nori et al (2007) [44] Prospective enrollment; IDUs enrolled through hospital detoxification department promptions of the prospective enrollment through multiple clinics Prospective enrollment; IDUs enrolled through department promptions of the prospective enrollment through multiple clinics Prospective enrollment; IDUs enrolled promption of treatment IDUs (former heroin users without history of alcoholism or abuse of other drugs; currently receiving substitution threapy) Non-IDUs Prospective enrollment through multiple clinics	Mauss et al (2004) [41]	ble methadone maintenance pro- gram; for each IDU, a control patient was matched for sex, age, HCV ge-	tution therapy and abstained from drug use for at least 6 months before treatment initiation)			No
source not clear substitution therapy; ongoing users excluded) Former IDUs (history of addiction; ongoing users excluded) Non-IDUs Seal et al (2007) [43] ^d Prospective enrollment through multiple veterans' health care medical centers Non-IDUs Prospective enrollment through multiple veterans' health care medical centers Non-IDUs Prospective enrollment; IDUs enrolled through hospital detoxification department Prospective enrollment; IDUs enrolled through hospital detoxification department Prospective enrollment; IDUs enrolled through this tory of alcoholism or abuse of other drugs; currently receiving substitution therapy) Non-IDUs Prospective enrollment through multiple clinics IDUs (IDU probably risk factor for acquistion of hepatitis C)		notype, and HCV RNA level	apy for at least 5 years before initia-	50	28 (56.0)	
Seal et al (2007) [43] ^d Prospective enrollment through multiple veterans' health care medical centers Non-IDUs Seal et al (2007) [43] ^d Prospective enrollment through multiple veterans' health care medical centers Promer IDUs (history of IDU; IDU veterans' health care medical centers) Within 6 months before enrollment was usually considered to be an exclusion criterion, although this could be overruled by individual doctors) Non-IDUs Non-IDUs Prospective enrollment; IDUs enrolled through hospital detoxification department Prospective enrollment; IDUs enrolled without history of alcoholism or abuse of other drugs; currently receiving substitution therapy) Non-IDUs Prospective enrollment through multiple clinics Prospective enrollment through multiple clinics IDUS (IDU probably risk factor for acquisition of hepatitis C)			substitution therapy; ongoing users	18	13 (72.2)	No
Seal et al (2007) [43] ^d Prospective enrollment through multiple veterans' health care medical centers Promer IDUs (history of IDU; IDU within 6 months before enrollment was usually considered to be an exclusion criterion, although this could be overruled by individual doctors) Non-IDUs Neri et al (2007) [44] Prospective enrollment; IDUs enrolled through hospital detoxification department Prospective enrollment; IDUs enrolled through department Prospective enrollment through multiple clinics Prospective enrollment through multiple clinics Former IDUs (history of IDU; IDU within 6 months before enrollment was usually considered to be an exclusion criterion, although this could be overruled by individual doctors) Non-IDUs Treatment IDUs (former heroin users without history of alcoholism or abuse of other drugs; currently receiving substitution therapy) Non-IDUs Former IDUs (history of IDU; IDU 447 81 (18.1) No 107 67 (62.6) Not tested Testement IDUs (former heroin users without history of alcoholism or abuse of other drugs; currently receiving substitution therapy) Non-IDUs Thomson et al (2008) Prospective enrollment through multiple clinics IDUs (IDU probably risk factor for acquisition of hepatitis C)			going users excluded)			
veterans' health care medical centers within 6 months before enrollment was usually considered to be an ex- clusion criterion, although this could be overruled by individual doctors) Non-IDUs 345 62 (18.0) Neri et al (2007) [44] Prospective enrollment; IDUs enrolled through hospital detoxification department Treatment IDUs (former heroin users without history of alcoholism or abuse of other drugs; currently re- ceiving substitution therapy) Non-IDUs 52 40 (76.9) Thomson et al (2008) Prospective enrollment through multiple clinics IDUs (IDU probably risk factor for acqui- sition of hepatitis C)			Non-IDUs	39	21 (53.8)	
Neri et al (2007) [44] Prospective enrollment; IDUs enrolled through hospital detoxification department Prospective enrollment; IDUs enrolled without history of alcoholism or department abuse of other drugs; currently receiving substitution therapy) Non-IDUs Thomson et al (2008) Prospective enrollment through multiple clinics Prospective enrollment through multiple clinics Prospective enrollment through multiple clinics Prospective enrollment through multiple sition of hepatitis C)	Seal et al (2007) [43] ^d		within 6 months before enrollment was usually considered to be an ex- clusion criterion, although this could	447	81 (18.1)	No
through hospital detoxification without history of alcoholism or department abuse of other drugs; currently receiving substitution therapy) Non-IDUs Thomson et al (2008) Prospective enrollment through multiple clinics Prospective enrollment through multiple clinics IDUs (IDU probably risk factor for acquisation of hepatitis C) Thomson et al (2008) Prospective enrollment through multiple clinics			Non-IDUs	345	62 (18.0)	
Thomson et al (2008) Prospective enrollment through multiple IDUs (IDU probably risk factor for acqui- 205 120 (58.5) No [45] clinics sition of hepatitis C)	Neri et al (2007) [44]	through hospital detoxification	without history of alcoholism or abuse of other drugs; currently re-	107	67 (62.6)	
[45] clinics sition of hepatitis C)			Non-IDUs	52	40 (76.9)	
Non-IDUs 142 86 (60.6)				205	120 (58.5)	No
			Non-IDUs	142	86 (60.6)	

PrOD

• Post-hoc analysis of 12 phase 2/3/3b studies of PrOD

• 4747 GT1 patients, 149 (3%) were on OST

Measured adherence and SVR12

PrOD

HCV TREATMENT ADHERENCE AND COMPLETION

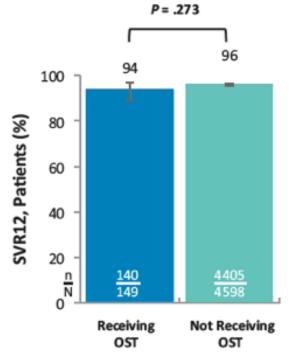
- Adherence to overall HCV treatment was lower in patients receiving OST vs those not receiving OST (Table 2)
- Adherence to both OBV/PTV/r + DSV and RBV was lower in patients receiving OST vs those not receiving OST
- In both patient groups, adherence to RBV was lower than adherence to OBV/PTV/r + DSV
- The proportion of patients completing HCV treatment was similar between those receiving OST and those not receiving OST (Table 2)

Table 2. HCV Treatment Completion and Adherence

	Receiving OST	Not receiving OST	<i>P</i> -value
Treatment completion, n/N (%)	144/149 (97)	4510/4598 (98)	.211
Treatment adherence, n/N (%)			
Overall treatment	105/149 (70)	4057/4598 (88)	<.001
DAA + RBV			
DAA	114/138 (83)	2855/3071 (93)	
RBV	101/138 (73)	2699/3071 (88)	
DAA only			
DAA	11/11 (100)	1437/1527 (94)	

DAA, direct-acting antiviral (ombitasvir/paritaprevir/ritonavir and dasabuvir); OST, opioid substitution therapy.

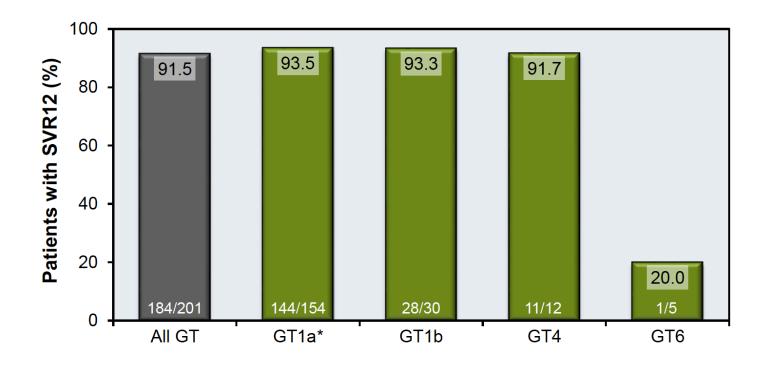
Figure 1. SVR12 by Receipt of OST



OST, opioid substitution therapy; SVR12, sustained virologic response at post-treatment Week 12.

C-EDGE CO-STAR

- HCV GT1, 4 or 6, receiving OST for >3 months and keeping >80% of appointments
- Allowed cirrhosis (20%) and HIV (8%)
- 12 weeks EBV/GZP
- 5 reinfections



ASTRAL

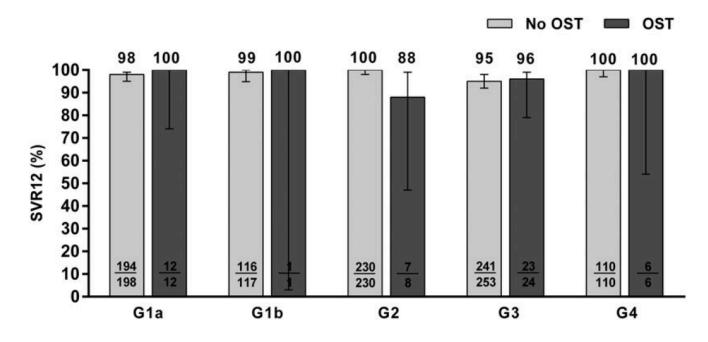


Figure 1. Sustained virologic response (SVR) in patients with chronic hepatitis C virus genotypes 1–4 receiving and not receiving opioid substitution therapy (OST) and sofosbuvir/velpatasvir in the ASTRAL 1–3 studies.

1480 • CID 2016:63 (1 December) • BRIEF REPORT

SIMPLIFY

 HCV infection, recent injecting drug use (last 6 months)

12 weeks of SOF/VEL

Table 1: Baseline characteristics (n=103)

	SOF/VEL (12 weeks) n=103, n (%)
Age <40 years	25 (24)
Female sex	29 (28)
OST and injecting drug use (in the last month)*	
No OST, no injectina	12 (12)
No OST, injecting	33 (32)
OST, no injecting	15 (15)
OST, injecting	43 (42)
HCV genotype	
1	36 (35)
2	5 (5)
3	60 (58)
4	2 (2)
Fibrosis stage (METAVIR)**	
F0-F1	59 (62)
F2-F3	27 (28)
F4	9 (9)

[&]quot;At study screening; ""Missing data in eight participants

SIMPLIFY

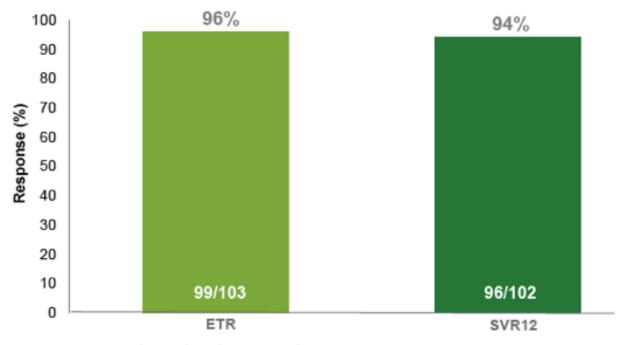


Figure 2: Proportion of the study population who achieved ETR and SVR12. ITT analysis includes all patients who should have reached the SVR12 time-point by data extraction (n=102).

□ No cases of virological failure and one case of virological relapse/reinfection has been observed to date (undergoing sequencing to confirm) They're going to reinfect

Table 1. Overview of Studies on Hepatitis C Virus Reinfection Following Treatment Among People Who Inject Drugs

Study	Country	Study Design	Geno- typing	Sequence Analysis	No.	Median Age at Treatment Start, y	% Male	IDU Pretreatment <6 mo	IDU Post treatment	Follow-up, Median (IQR)	PY Ever PWID/ PWID Who Continue	No. of Re- infections	Reinfection Rate (95% CI) per 100 PY Ever PWID/PWID Who Continue
Backmund et al, 2004 [8]	Germany	Pros	Yes	No	18	32	61	NA	9	Mean 2.8 (SD 0.8–5.1)	50.8/23.8	2	3.94 (0.48-14.22)/ 8.4 (1.02-30.36)
Dalgard et al, 2002 [11]	Norway	Pros	Yes	No	27	30	66	0	9	5.4 (1.1–6.8)	125.0/40.0	1	0.8 (0-5)/2.5 (0-14)
Currie et al, 2008 [10]	US	Pros	No	No	9	46 (mean)	88	NA	2	3.6 (3.2–6.0)	38.0/3.5	1	2.63 (0.07-14.66) 28.57 (0.72-159.19)
Grebely et al, 2010 [13]	Canada	Pros	Yes	Yes	35	44 (mean)	86	19	16	2.0 (0.4–5.0)	62.5/37.7	2	3.20 (0.39–11.56)/ 5.30 (0.64–19.16)
Bate et al, 2010 [9]	Australia	Pros	Yes	No	57	NA	NA	NA	NA	NA	NA	5	NA
Grady et al, 2012 [12]	Netherlands	Pros	Yes	Yes	42	51	73	5ª	11	2.5 (1.6-3.7) ^b	131.6/32.3	1	0.76 (0.04-3.73)/ 3.42 (0.17-16.90)
Grebely, 2012 [14]	Australia	Pros	Yes	Yes	88	36	72	33ª	NA	1.2 (0.1-3.0) ^b	108	5	4.7 (1.9–11.2)

Abbreviations: CI, confidence interval; IDU, injection drug use; IQR, interquartile range; NA, specific information was not available; Pros, prospective; PWID, people who inject drugs; PY, person-years.

^a During treatment.

b Follow-up from end of treatment.

Table 2. Incidence estimates of hepatitis C virus reinfection after sustained virological response and applied methods in studies among people who inject drugs and men who have sex with men.

Study	Population	SVR	FU, mean yr	PYFU/PYFU post-SVR risk	Method	Testing interval, yr	Reinfections	Incidence (overall/post- SVR risk), per 100 PY
Dalgard et al. 2002 [118]	PWID	27	5.4	118/40	Genotyping Risk factors	1-7	1	0.8/2.5
Backmund <i>et al.</i> 2004 [119]	PWID	18	2.8	51/24	Genotyping Risk factors	1	2	3.9/8.4
Currie et al. 2008 [120]	PWID	9	3.6	38/3.5	HCV RNA Risk factors	0.5	1	0.56/1.89
Grebely et al. 2010 [121]	PWID	35	2.0	63/38	Genotyping Risk factors	1	2	3.2/5.3
Grady et al. 2012 [122]	PWID	42	2.5	132/32	Sequencing	0.5-1	1	0.8/3.4
Grebely et al. 2012 [123]	PWID	67	1.1	140/56	Sequencing Risk factors	0-2	5	12.3/7.3
Hilsden et al. 2013 [124]	PWID	23	1.8	36/n.r.	HCV RNA	n.r.	1	2.8/n.r.
Pineda et al. 2015 [125]	PWID	84	2.8	330/n.r.	Sequencing Risk factors	0.5	4	1.2/8.7
Midgard et al. 2016 [126]	PWID	94	7.1	593/206	Sequencing Risk factors	0.5-8	10*	1.7/4.9
Weir et al. 2016 [127]	PWID	277	4.5	410/n.r.	Genotyping Risk factors	n.r.	7	1.7/5.7
Bate et al. 2010 [128]	Prisoners	53	3.4	n.r.	Genotyping	n.r.	5	n.r.
Marco et al. 2013 [129]	Prisoners	119	1.4	171/n.r.	Genotyping Risk factors	1	9	5.3/n.r.
Lambers et al. 2011 [98]	MSM	55	1.3	72/n.r.	Sequencing Risk factors	0.25	11	15.2/n.r.
Martin et al. 2013 [7]	MSM	114	1.6	224/n.r.	HCV RNA	n.r.	27	9.6/n.r.
Vanhommerig et al. 2014 [130]	MSM	31	4.0	n.r.	Sequencing	0.5	8	n.r.

^{*}Persistent reinfections.

PWID, people who inject drugs; MSM, men who have sex with men; SVR, sustained virological response; FU, follow-up; PYFU, person-years of follow-up; PY, person-years; n.r., not reported.

Table 3. Differences in hepatitis C epidemiology among people who inject drugs and men who have sex with men.

	PWID	MSM
HCV prevalence	High	Low*
Proportion of total HCV population	Large	Small
Access to HCV care	Poor	Good
Treatment of acute HCV infection	Rare	Common
Risk behaviours post-SVR	Variable	Prevalent
Transmission networks	Local	International
Reinfection rates	2-6/100 PY	10-15/100 PY

^{*}Mainly limited to HIV-infected.

PWID, people who inject drugs; MSM, men who have sex with men; SVR, sustained virological response; PY, person-years.

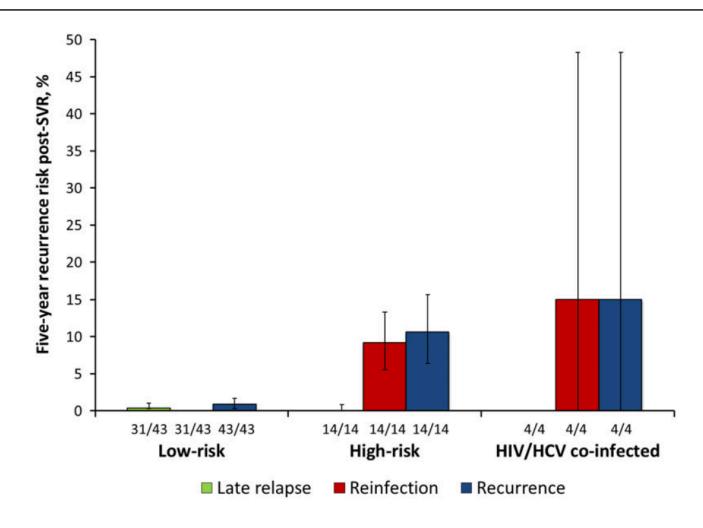
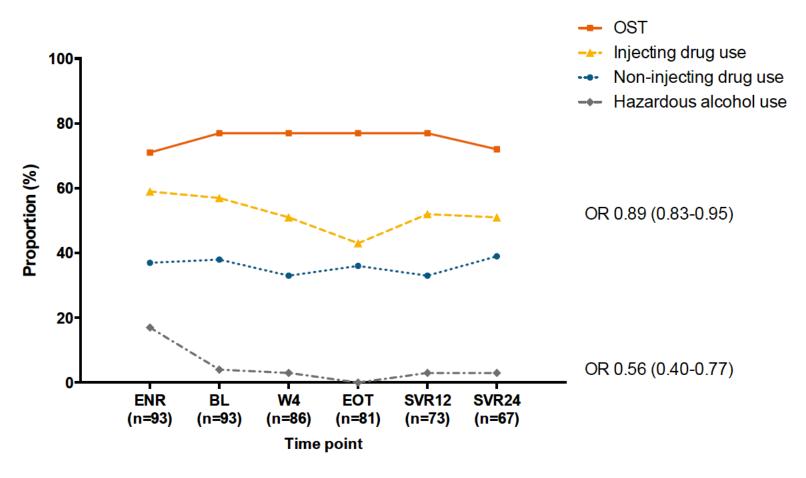


Figure 2. Summary 5-year risk (95% confidence interval) of recurrence post-sustained virological response (SVR), by risk group. Presented are the pooled estimates for the 5-year risk of recurrence after achieving an SVR. Also shown are the number of studies that were included to derive each estimate. Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus.

It will have no benefit



ENR, enrolment; BL, baseline; W4, treatment week 4; EOT, end of treatment; SVR12,12 weeks post-treatment follow-up; SVR24, 24 weeks post-treatment follow-up.

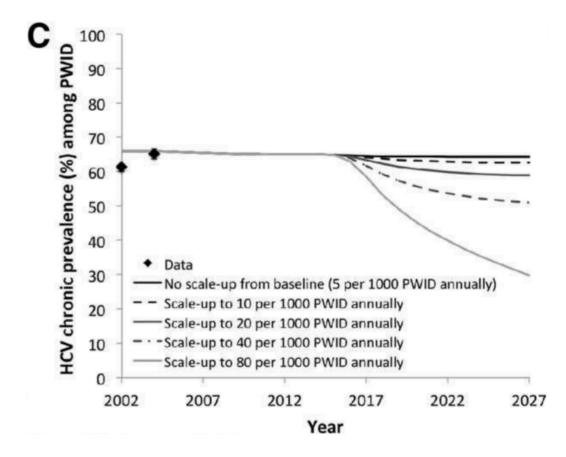


Fig. 2. Chronic prevalence over time in (A) Edinburgh, (B) Melbourne, and (C) Vancouver. Simulations show no scale-up from baseline, or scale-up to 10, 20, 40, or 80 per 1,000 PWID treated annually. We assume no treatment prior to 2002, a linear scale-up to baseline treatment rates during 2002-2007, and baseline treatment rates during 2007-2012. A linear scale-up from baseline to scaled-up rate during 2015-2017 was modeled. HCV prevalence data points shown for comparison with 95% confidence intervals.

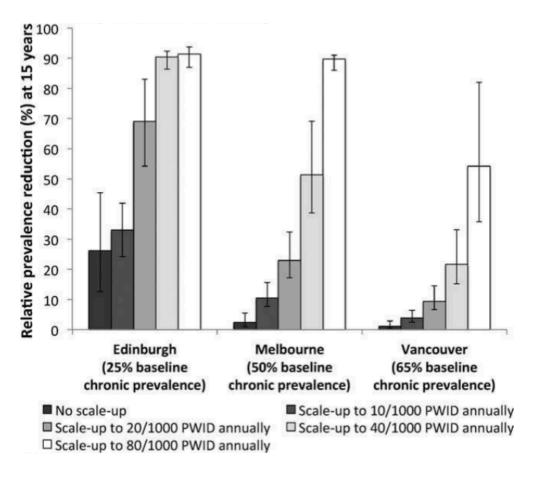


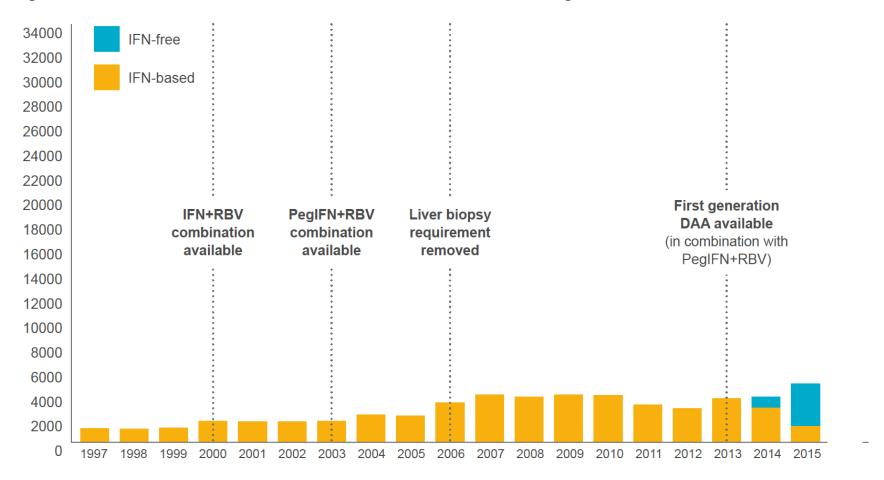
Fig. 3. Relative prevalence reductions at 15 years (by 2027) with no treatment scale-up (8 per 1,000 PWID annually in Edinburgh, 3 per 1,000 PWID annually in Melbourne, and 5 per 1,000 PWID annually in Vancouver) and four treatment rate scenarios (10, 20, 40, and 80 per 1,000 PWID annually). Bars indicate the mean relative prevalence reductions, with whiskers representing the 95% Crl for the simulations.

SVUH Data

DAA treatments completed By year	Nos completed total 351	Cirrhotics completed tx Total 154	Relapsed Total 9	Attending Addiction Centres Patrick St/Bray/Baggot St
Nov 2014 to Dec 2015	113	91	7	1 (0.8%)
2016	100	36	2	3 (3.0%)
2017 Jan to June	138	27	0	32 (23.0%)

The Australian experience -2016

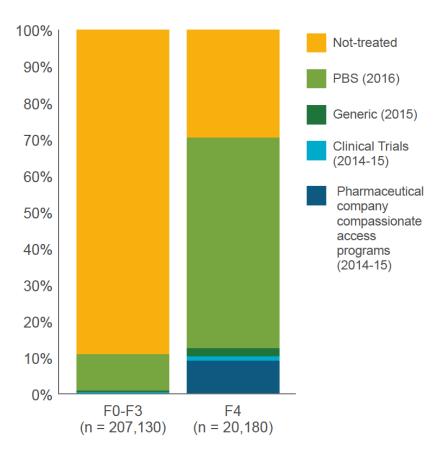
Figure 1: Estimated annual number of individuals with chronic HCV infection initiating HCV treatment from 1997 to 2016 in Australia.



IFN: interferon; PegIFN: pegylated interferon; RBV: ribavirin; DAA: Direct acting antiviral

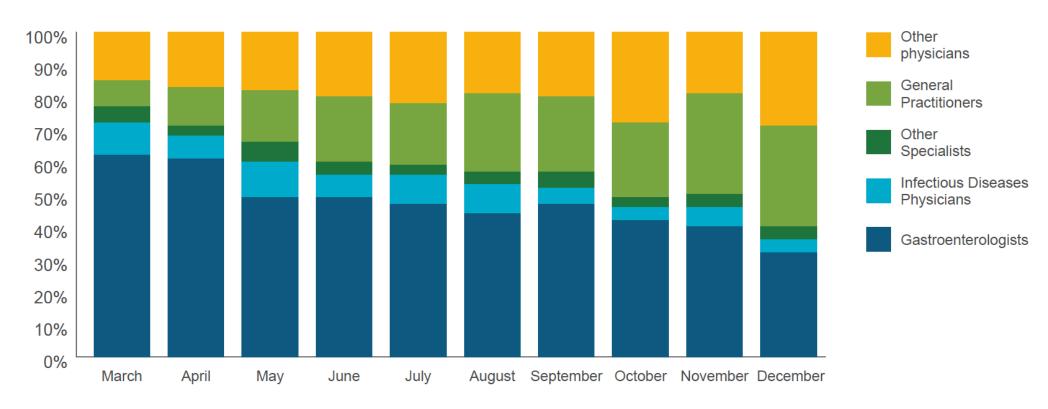
The Australian experience - 2016

Figure 2: The estimated proportion of individuals living with chronic HCV infection in Australia who initiated DAA treatment between 2014 and 2016, by liver fibrosis stage



The Australian experience - 2016

Figure 10: Distribution of prescriber types in each month for individuals initiating DAA treatment in 2016 in Australia



Other physicians included supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, and non-vocationally registered doctors.

Discussion

Screening/ diagnosis and staging

Referral

Treatment