
Diagnosis and treatment of acute HCV in an interferon free era: Does it really matter?

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What is 'acute HCV'?

Diagnosing acute HCV

Traditionally defined as the *first 6 months* after infection

1. Documented HCV antibody seroconversion
2. Clinical illness with jaundice (15-20%)
3. New rise in ALT without alternate cause and positive HCV RNA
4. Low $<10^4$ or fluctuating >1 log HCV RNA

NEAT consensus paper 2011

- Preferred criteria (Grade A, Level II)
 - (1) Positive antibody in the presence or absence of a positive HCV RNA and a documented negative antibody or HCV RNA in the previous 12 months
- Alternative criteria (Grade B, Level III)
 - Positive HCV RNA with: (1) A) an acute rise in ALT $> 10x$ ULN or an acute rise in ALT $> 5x$ ULN, with documented normal ALT within 12m and (2) and exclusion of other causes of acute hepatitis.

Potential duration of infection up to 1 year

Australian Trial in Acute Hepatitis C (I/II)

Recent HCV infection as defined by:

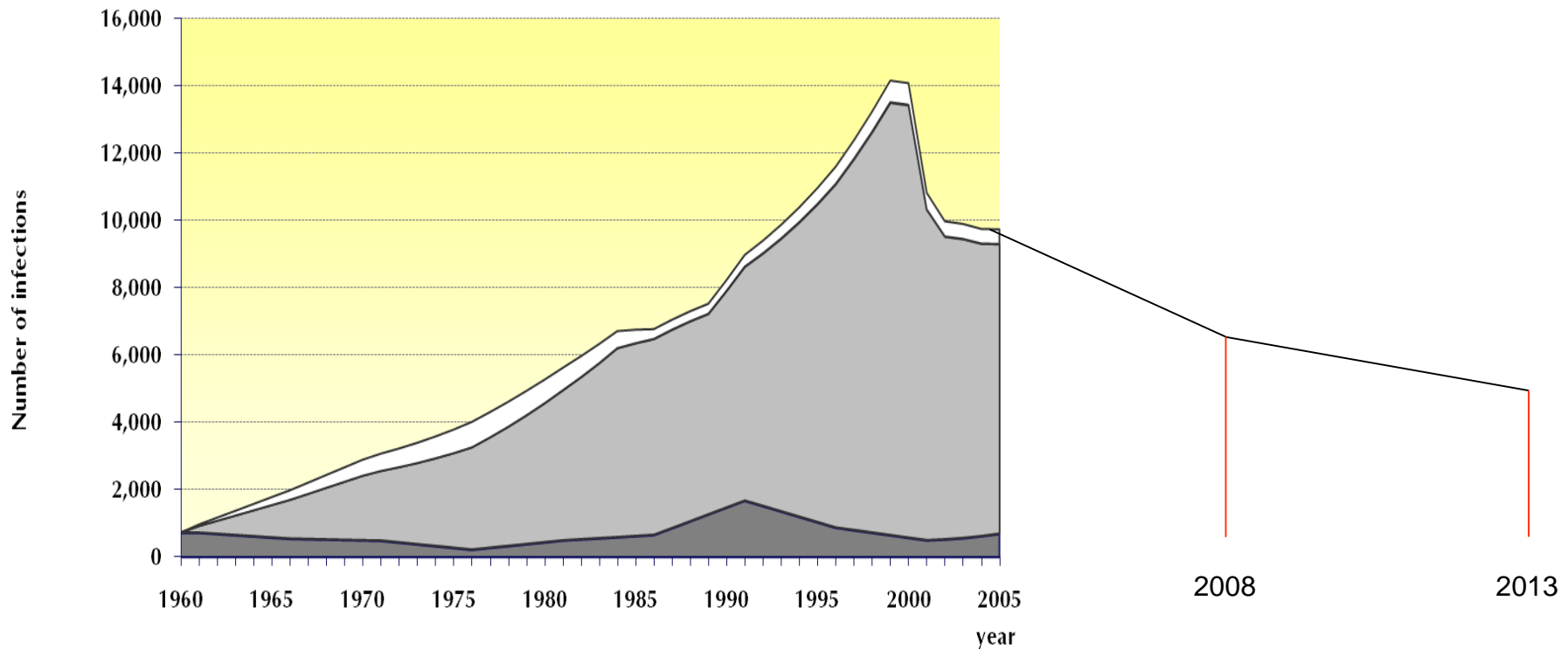
- an initial positive anti-HCV antibody within 6 months of enrolment and either:
 - (i) a negative anti-HCV antibody in the 2 years prior to the initial positive anti-HCV antibody; or
 - (ii) acute clinical hepatitis C (jaundice or ALT level $> 10\times$ ULN) within 12 months of the initial positive anti-HCV antibody

Maximal estimated duration of infection 18 months
Potential duration of infection up to 2.5 years

~~ACUTE~~

RECENTLY ACQUIRED

Australia: estimated incidence of HCV



Currently approximately 5-6,000 new HCV infections pa

Diagnoses of recent HCV by exposure category

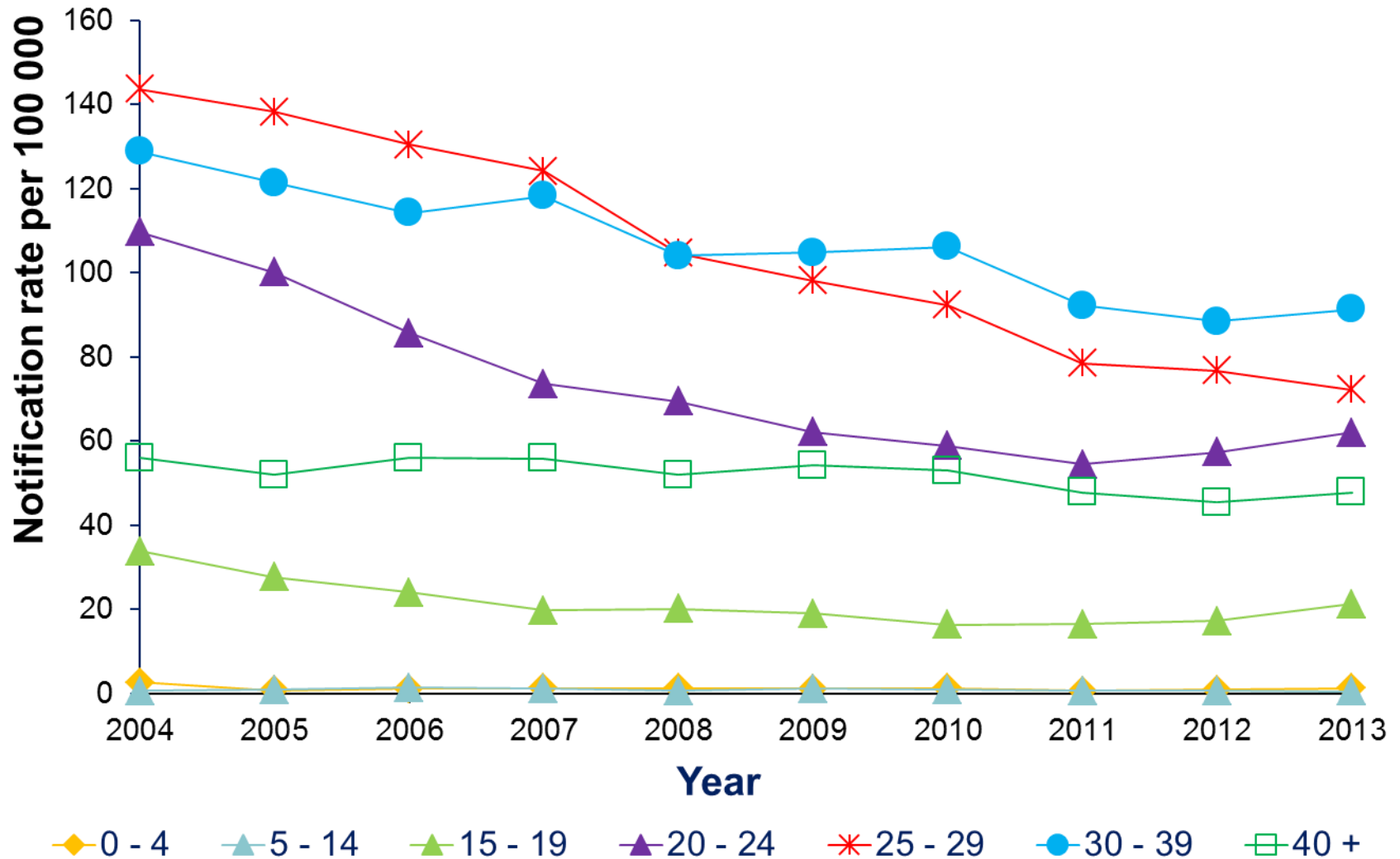
Table 2.1.13 Number of diagnoses of newly acquired hepatitis C infection, 2008 – 2012, by exposure category, year and sex

Exposure category	Year of diagnosis															
	2008			2009			2010			2011			2012			T
	M	F	T	M	F	T	M	F	T	M	F	T	M	F		
Injecting drug use	160	95	255	164	95	259	158	103	261	173	62	236	165	96	261	
Sexual contact	6	8	14	7	8	15	8	3	11	6	7	13	6	3	9	
Blood/tissue recipient	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Skin penetration procedure	6	4	10	4	4	8	5	5	10	13	2	15	4	2	6	
Healthcare exposure	2	3	5	1	11	12	4	38	42	1	5	6	0	0	0	
Household contact	1	0	1	0	2	2	2	1	3	1	1	2	0	0	0	
Other	14	9	23	27	12	39	22	6	28	19	6	25	19	7	26	
Undetermined	30	27	57	38	23	65	24	18	42	70	46	116	112	52	164	
Total	219	146	365	241	155	400	223	174	397	283	129	413	306	160	466	

1 Totals include diagnoses in people whose sex was not reported.

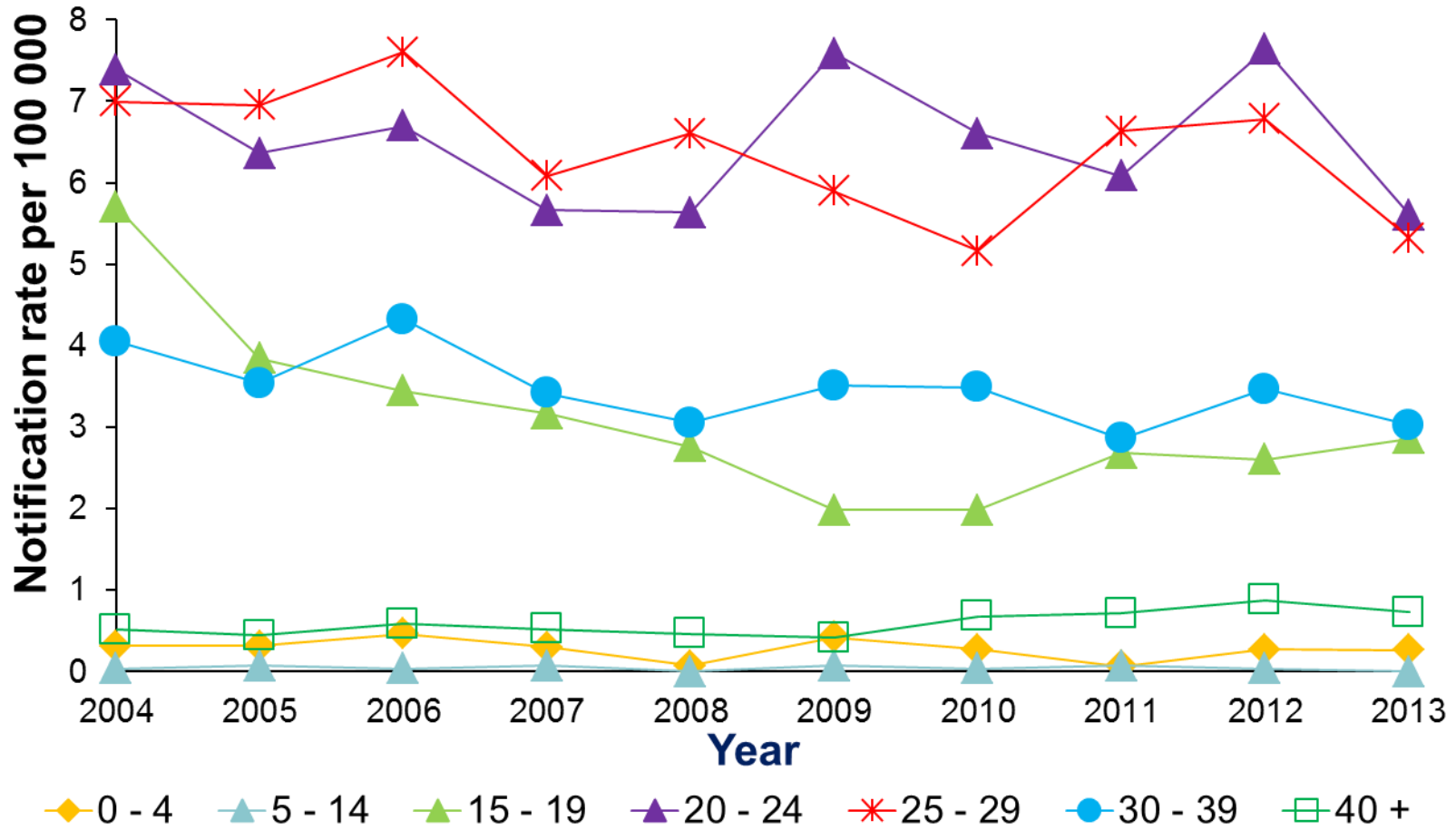
Source: National Notifiable Diseases Surveillance System

Hepatitis C notifications, 2004 – 2013, by year and age group



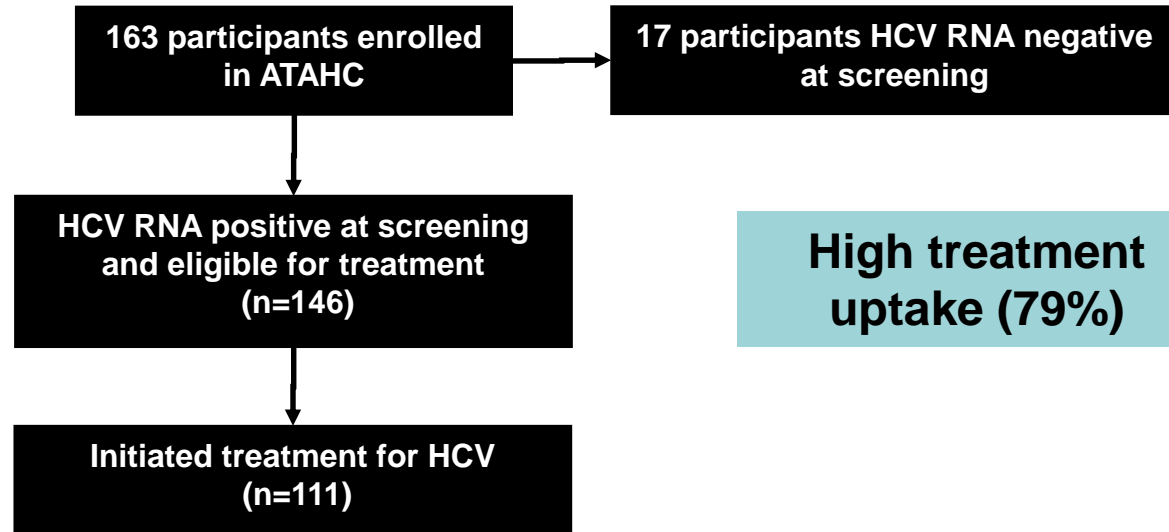
Source: National Notifiable Diseases Surveillance System

Newly acquired hepatitis C notifications, 2004 – 2013, by year and age group



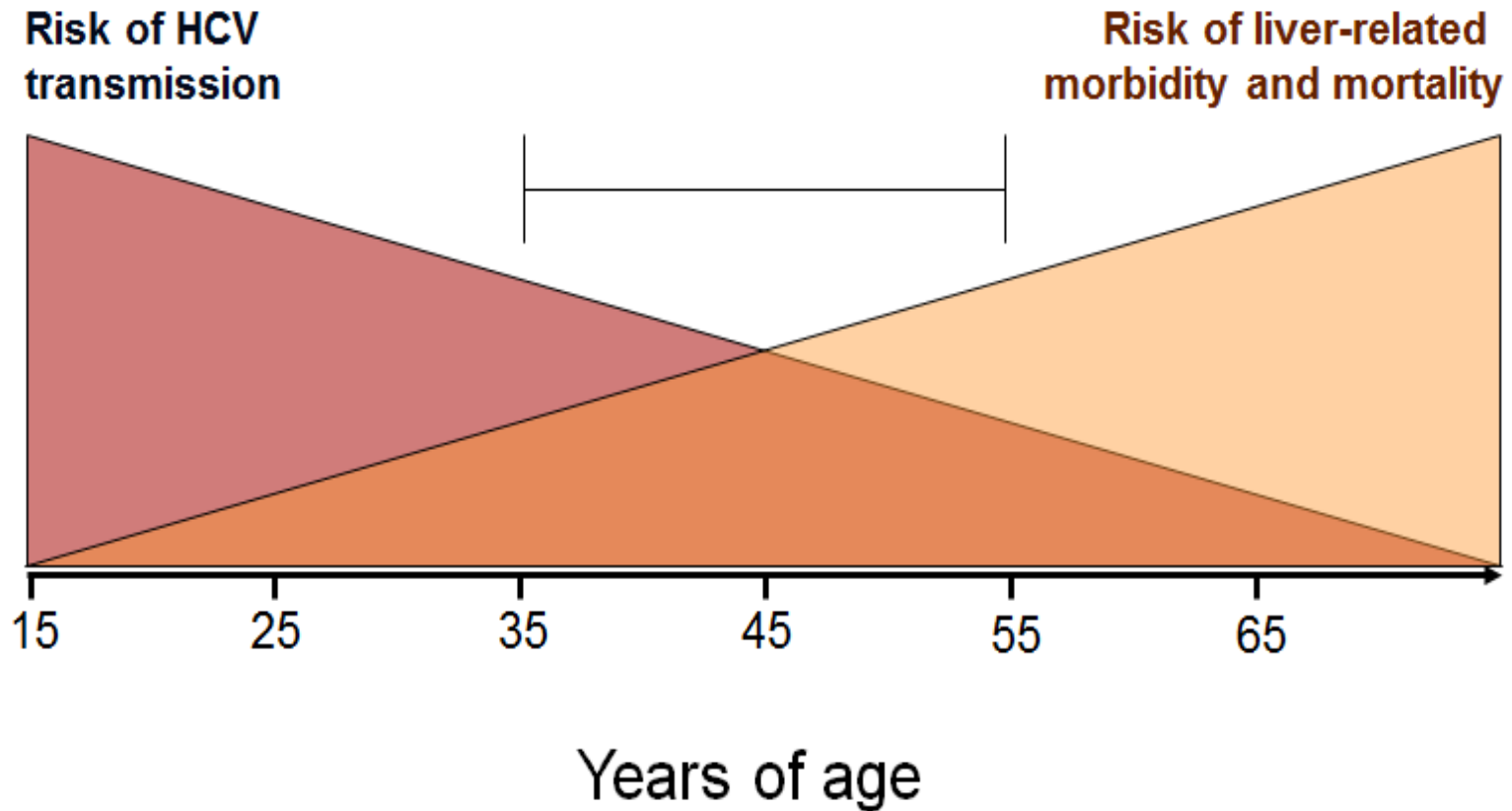
Source: National Notifiable Diseases Surveillance System

Does diagnosis of recent HCV matter?



	OR	95% CI	<i>P</i>	AOR	95% CI	<i>P</i>
Tertiary education or greater, n (%)						
Yes	1.00	-	-	1.00	-	-
No	0.41	0.17-0.96	0.037	0.43	0.17-1.08	0.071
Full-time or part-time employment, n (%)						
Yes	1.00	-	-	1.00	-	-
No	0.39	0.17-0.91	0.030	0.44	0.18-1.10	0.080
Current depression, n (%)						
No	1.00	-	-	1.00	-	-
Yes	0.29	0.11-0.78	0.014	0.40	0.14-1.17	0.093
Estimated duration of infection (wks)	1.02	1.00-1.05	0.063	1.03	1.00-1.06	0.035
Log₁₀ HCV RNA (IU/L)	1.90	1.34-2.68	<0.001	1.92	1.36-2.73	<0.001

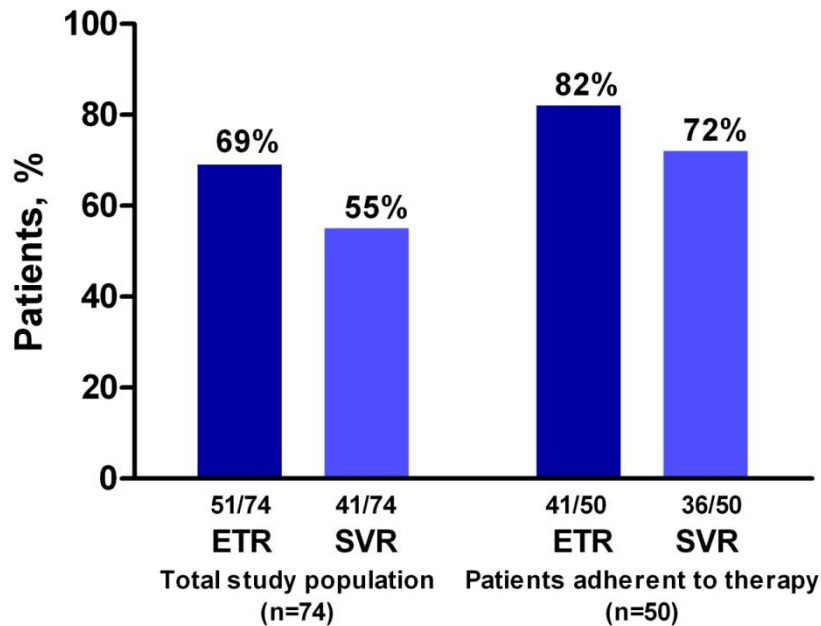
Does diagnosis of recent HCV matter?



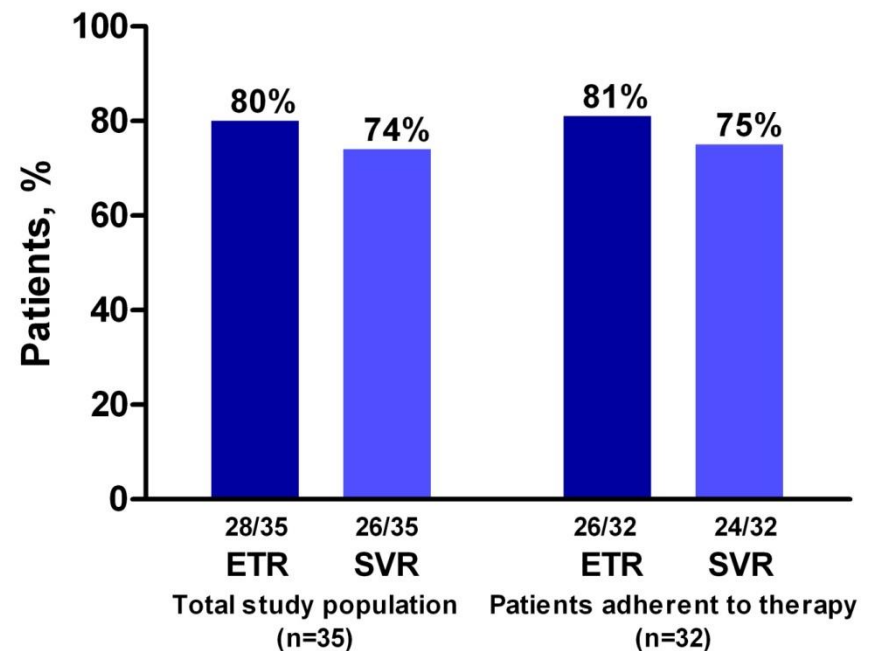
-
- Is diagnosing recent HCV important? ✓
 - Is treating recent HCV important?

Treatment for recent HCV traditionally shortened

ATAHC : 24 weeks PEG (+RBV for HIV positive)



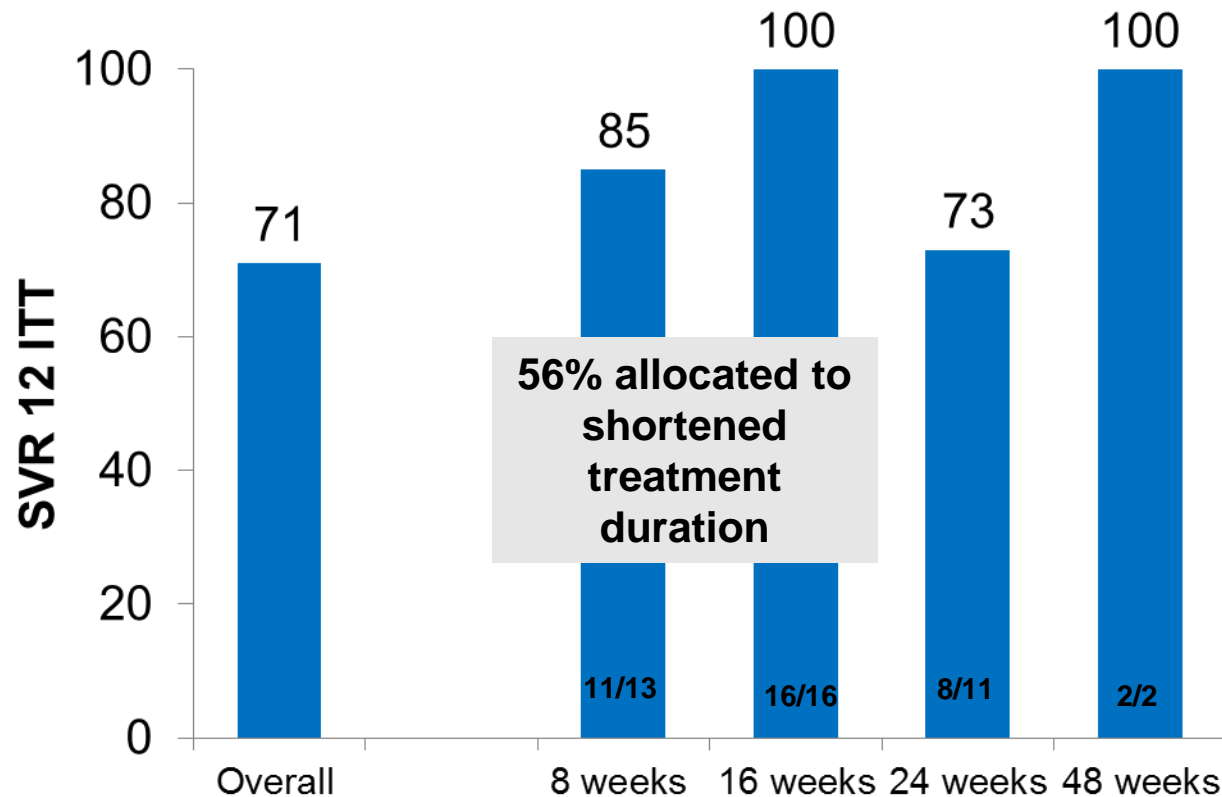
HIV negative



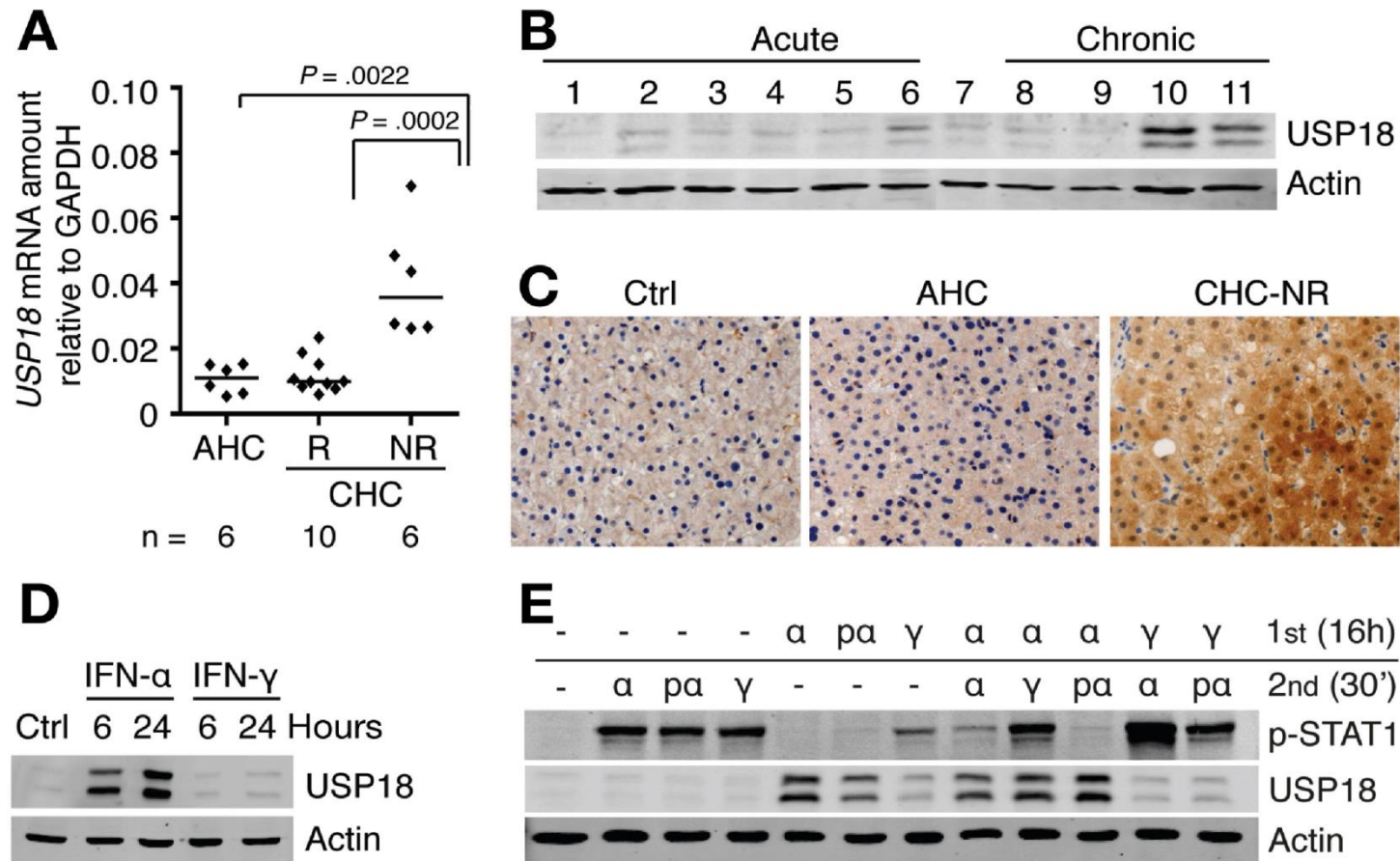
HIV positive

Treatment for recent HCV traditionally shortened

ATAHC II : Response guided PEG +RBV



ISG pattern is different in AHC versus CHC



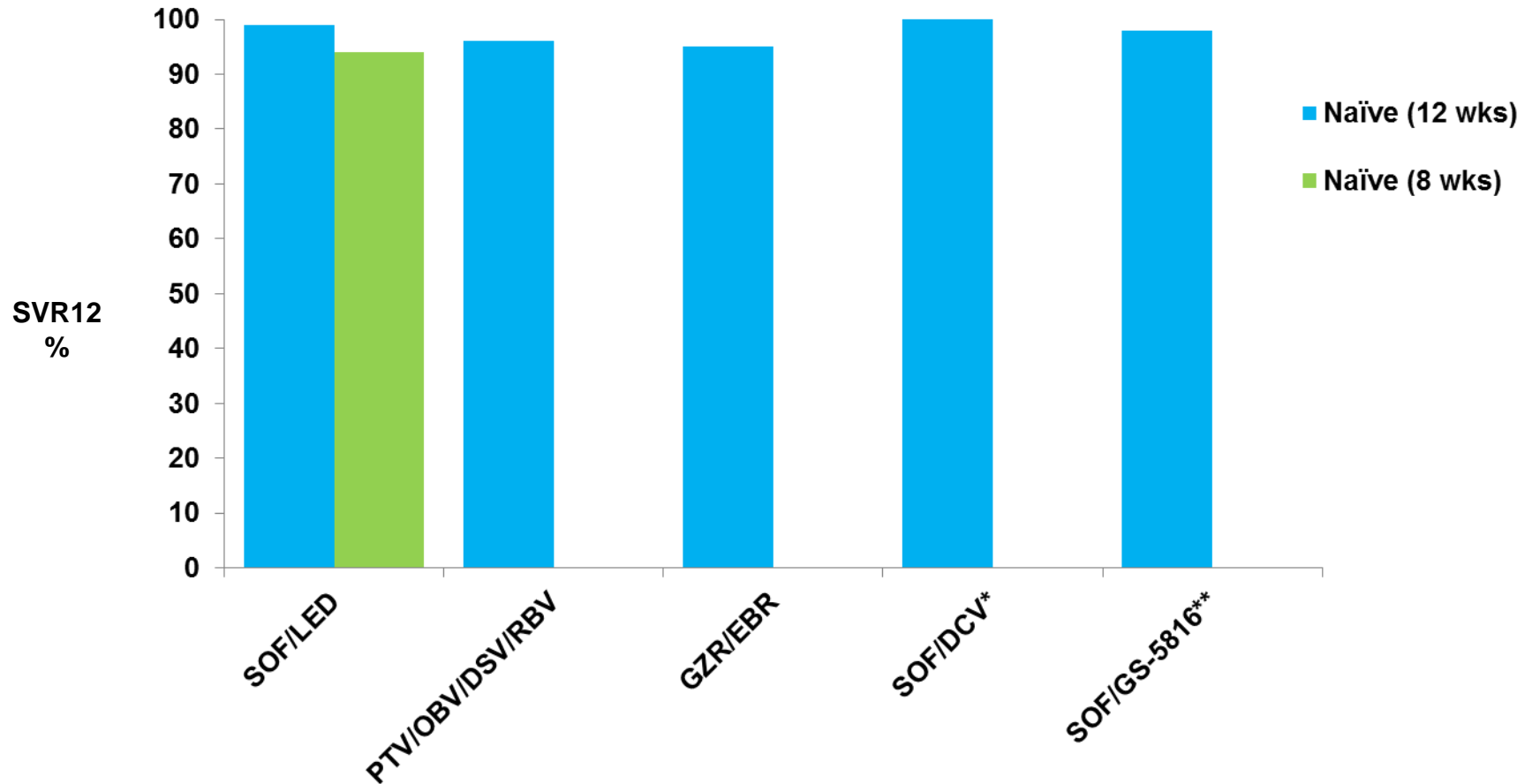
Can treatment for recent HCV be shortened in
the era of IFN-free DAA therapy?

NO DATA YET!

Registered clinical trials for DAAs in recent HCV infection

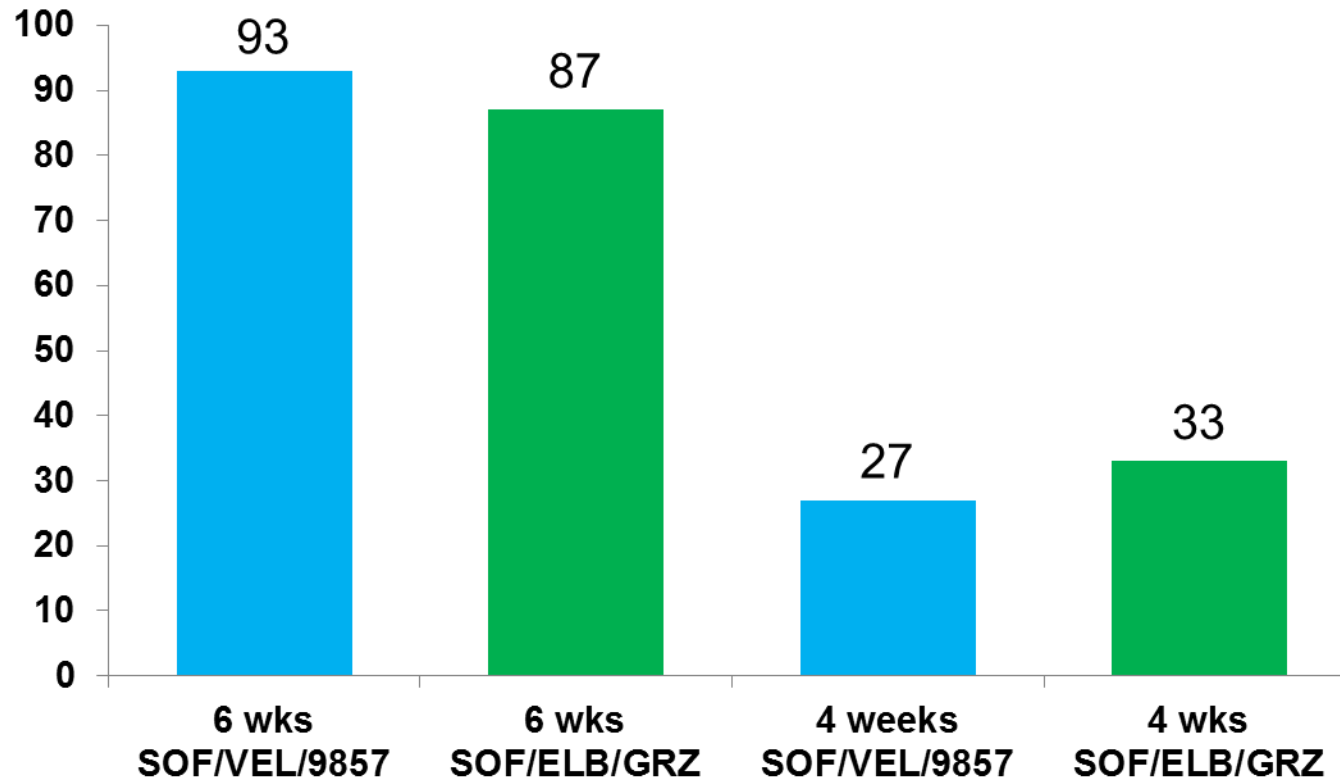
Principal investigator and/or study group	Country, year commenced	Title	Duration of infection (months)	Study population	Estimated enrolment (n)	Regimen	Treatment duration (weeks)
Matthews G	Australia 2012	DARE-C I	6-18	HCV GT 1; HIV+ and PWID eligible	15	PEG-IFN, RBV, TVR	8, 12 or 24
Rijnders B	Netherlands 2013	DAHHS	≤6	HCV GT 1 and HIV+; PWID eligible	60	PEG-IFN, RBV, BOC	12
Nelson M	UK 2014	CHAT	≤6	HCV GT 1 and HIV+; PWID eligible	20 (per arm)	PEG-IFN, RBV +/- TVR (1:1)	Response guided
Matthews G	Australia, New Zealand 2014	DARE-C II	≤12	GT 1-6; HIV+ and PWID eligible	20	Results to be presented at AASLD 2015	
Naggie S; AIDS Clinical Trials Group	US 2014	SWIFT-C	≤6	HCV GT 1-6 and HIV+; PWID eligible	44		
Manns MP; HepNet	Germany 2014	HepNet Acute HCV IV	≤4	HCV GT 1; HIV+ and PWID ineligible	20		

Current standard duration DAA therapy in naïve patients



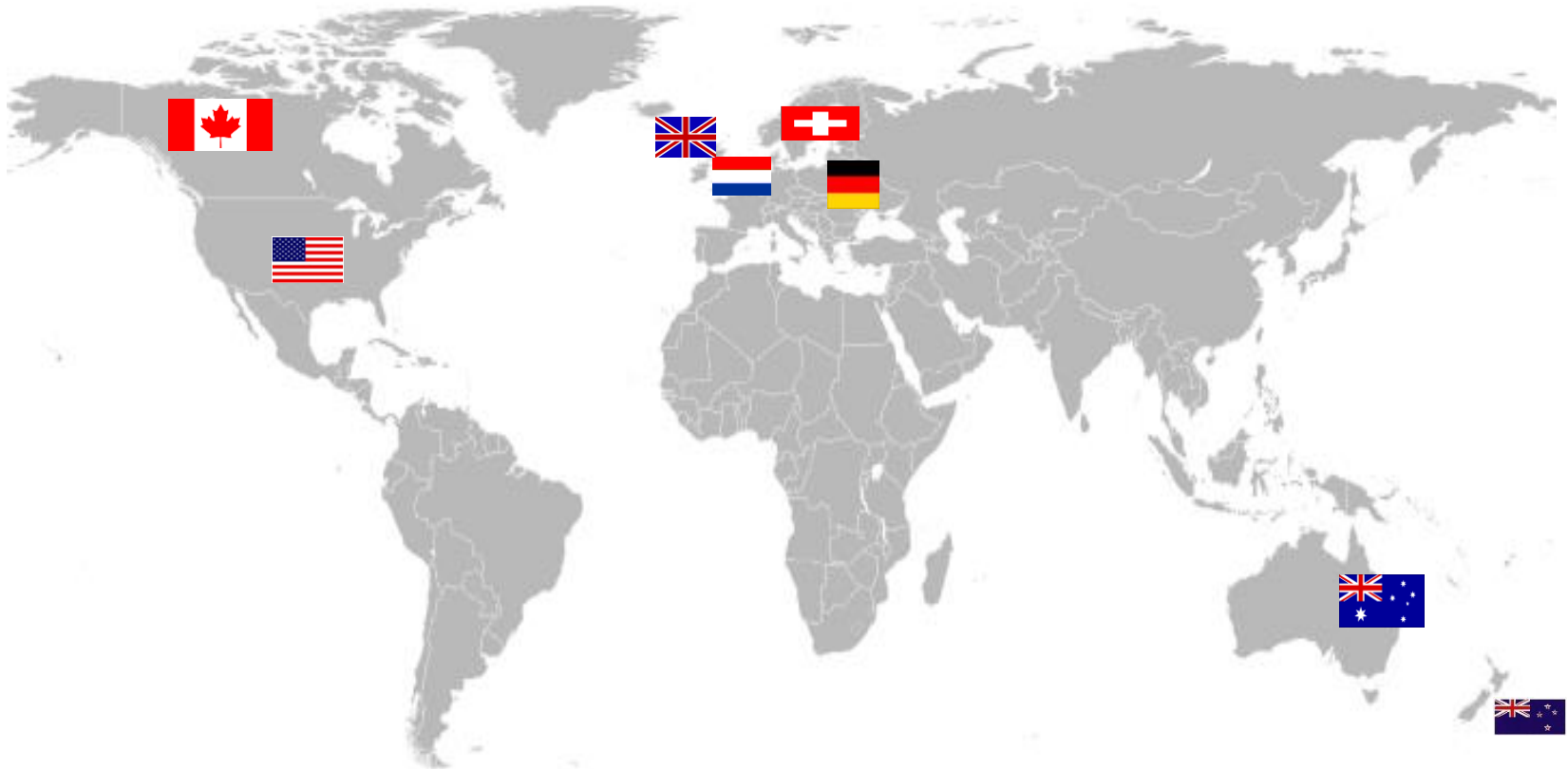
Can therapy go shorter?

Triple NA/NS5A/PI: treatment naive, F0-3



REACT

A Randomised Controlled trial of IFN-free therapy for HEpatitis C during Recent infection)



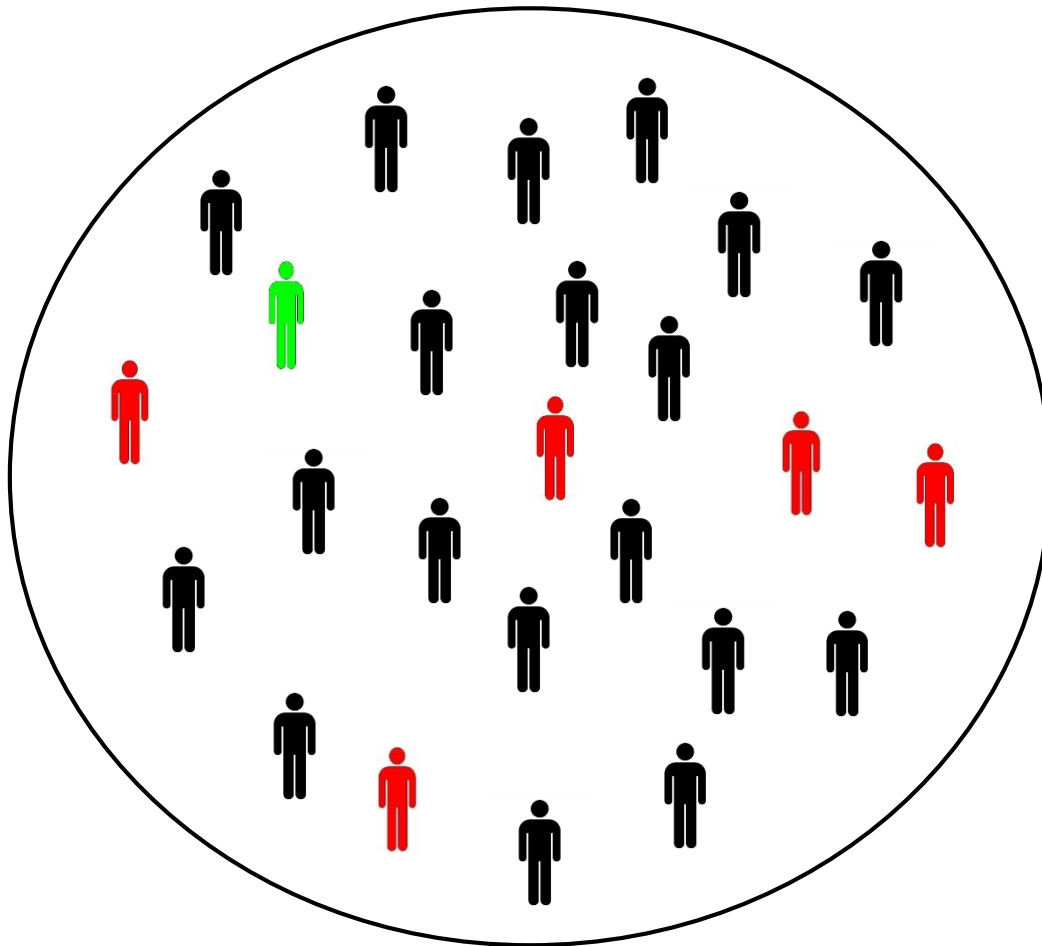
250 patients, 8 countries

Standard vs short duration or rolling very short duration cohorts

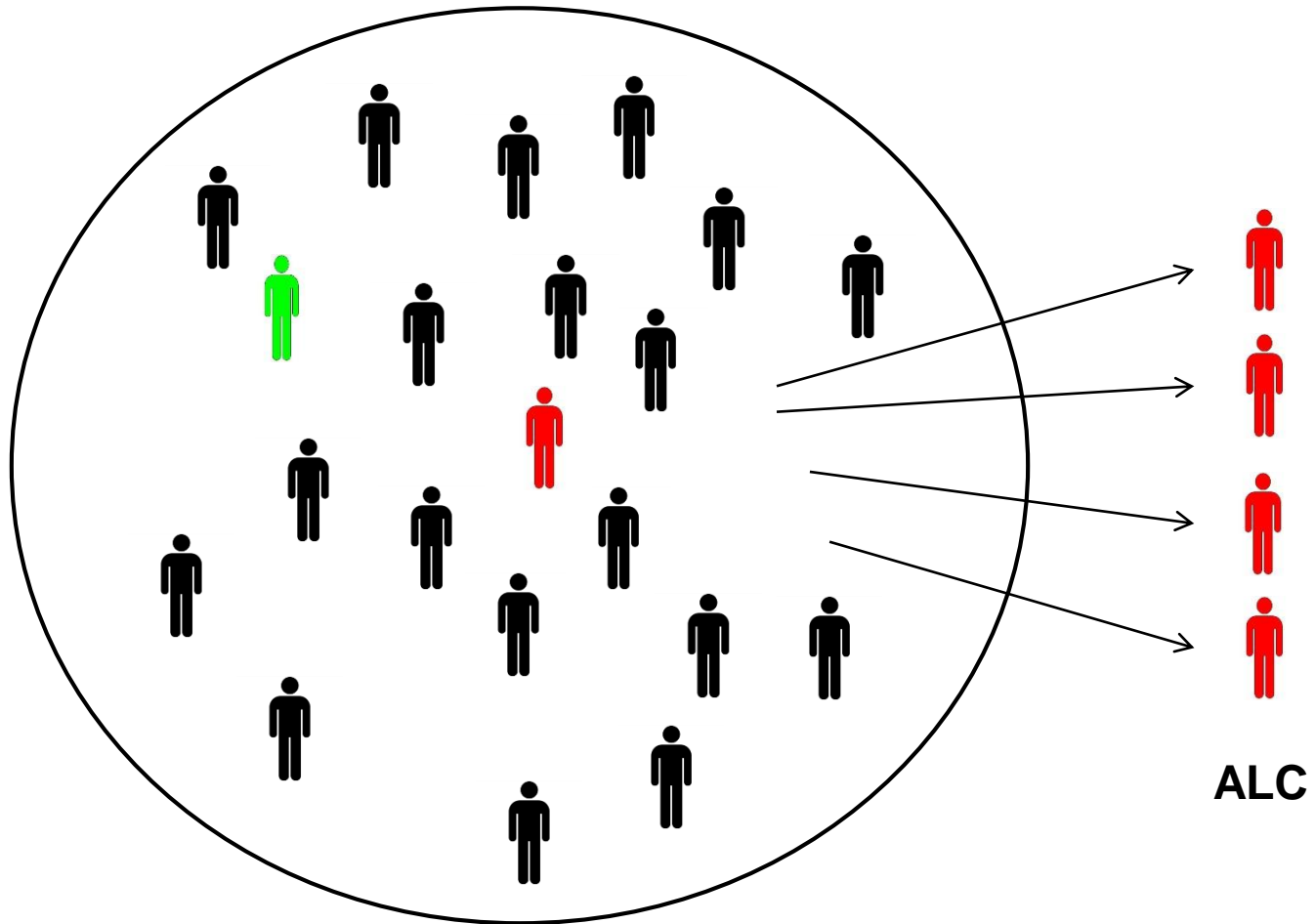
Adherence, risk behaviour, reinfection

-
- Is diagnosing recent HCV important? ✓
 - Is treating recent HCV important? ✓

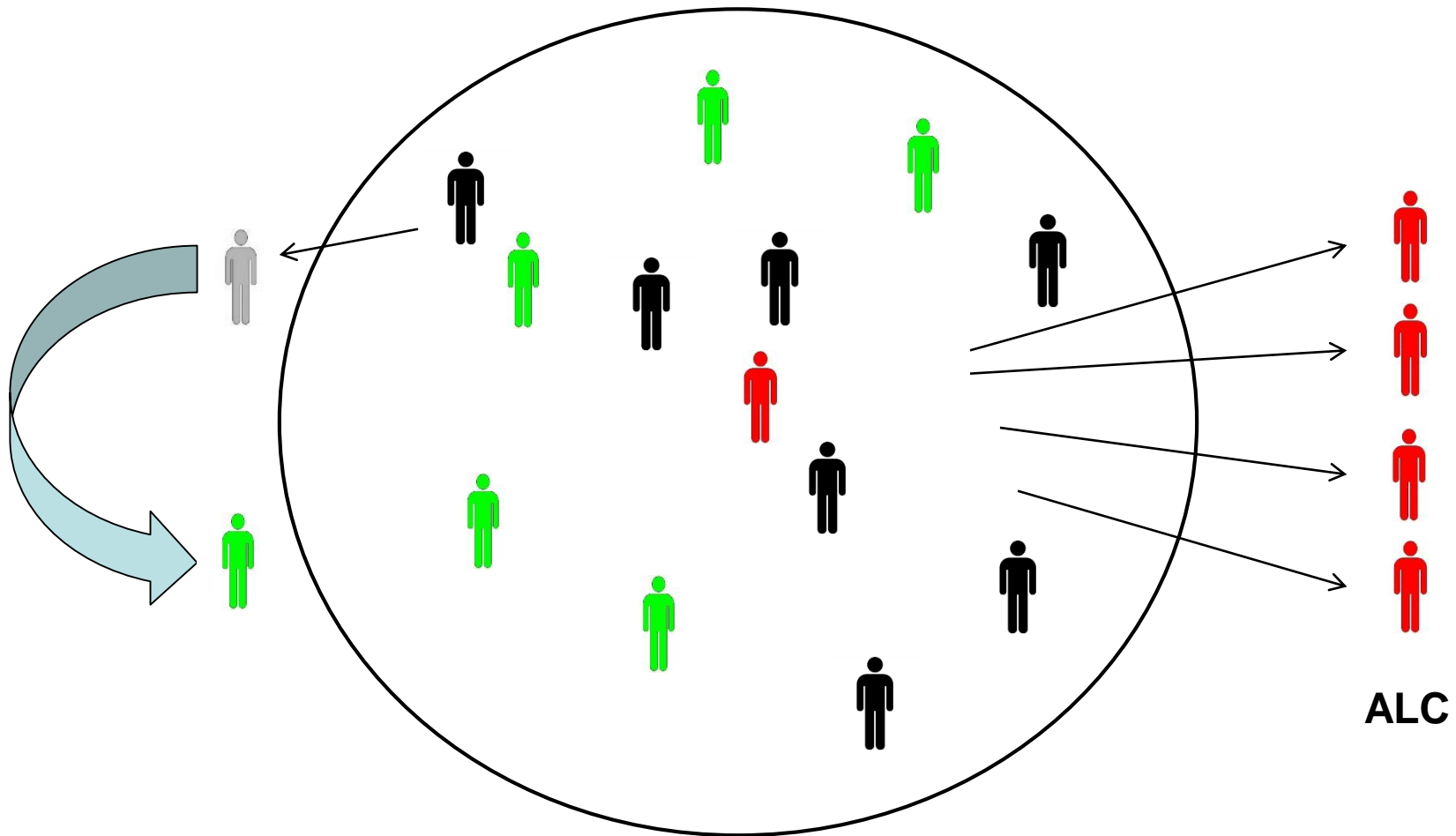
Why recent infection is still important?



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Why recent infection is still important?



The future: test and treat

