european hiv hepatitis co-infection

EUROPEAN
HIV HEPATITIS CO-INFECTION (EHHC)
CONFERENCE

10–11 December 2015

QEII Centre · London

Pre-conference Nurses' Course

european hiv hepatitis co-infection

Dr Emma Thomson

University of Glasgow Centre for Virus Research, UK

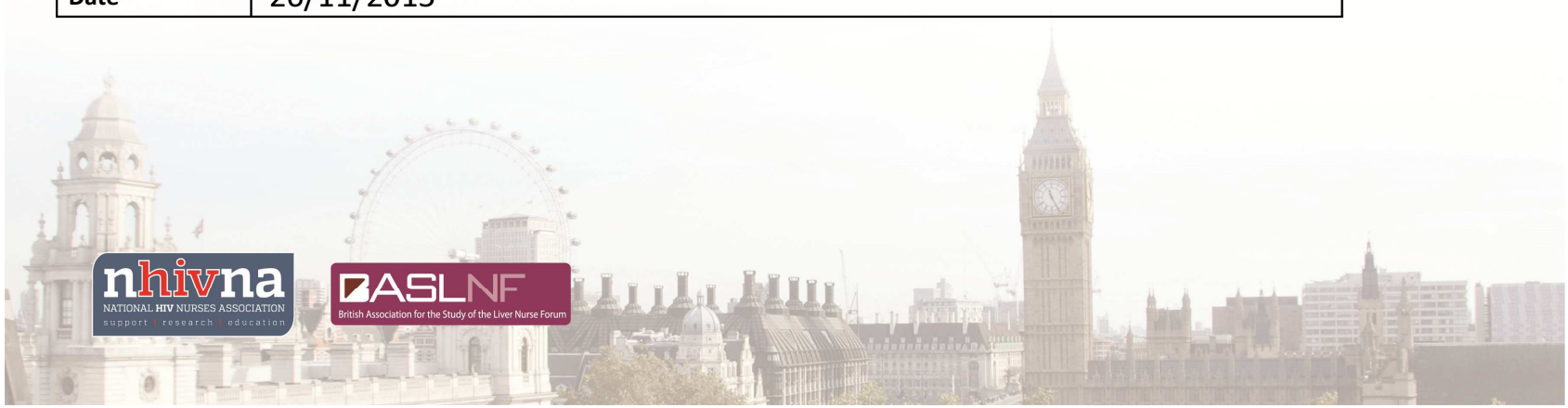
Pre-conference Nurses' Course

eHHC european hiv hepatitis co-infection

Dr Emma Thomson

University of Glasgow Centre for Virus Research, UK

COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:	
Speaker Name	**Statement**
Emma Thomson	I have no competing interests. I am funded by the Wellcome Trust (as a fellow) and by the MRC.
Date	26/11/2015



The arguments for treating promptly vs waiting for eligibility for DAAs

Dr Emma Thomson

EHHC 2015

MRC Medical Research Council

University of Glasgow

A tale of two cities…

London

Glasgow

Treat promptly or wait for DAAs

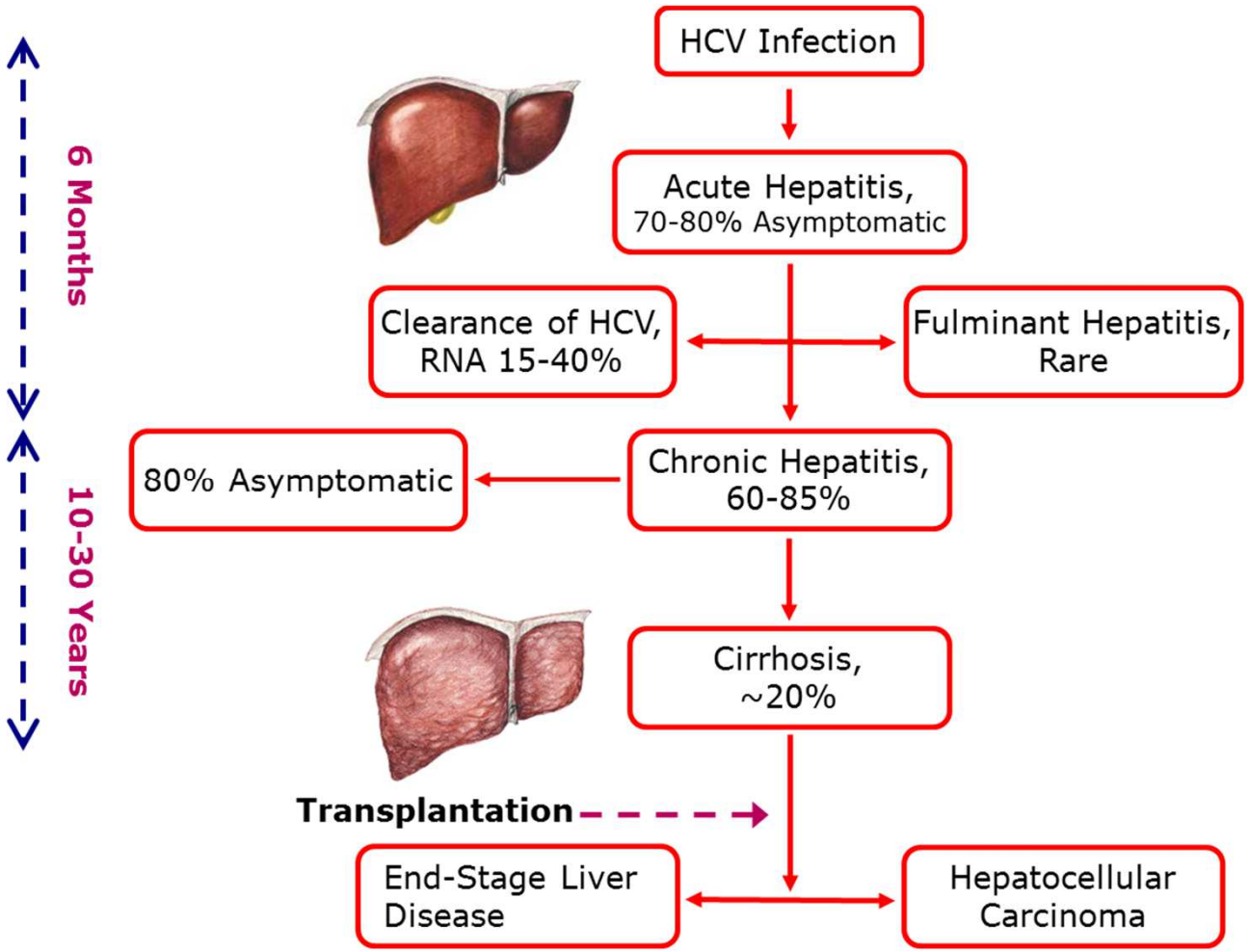
Early

- Treat early and avoid **disease**
- If **HIV** co-infected outcome is worse
- **Resistance** – RAVs have more impact in late infection
- Reduce **secondary** cases
- **Cost** – IFN is cheaper
- Treat early – **loss to follow-up**

Delayed

- Not everyone progresses to severe **disease - cost**
- IFN is **toxic** so wait for DAAs
- Address behaviours first – may need to treat multiple times for **reinfection**
- Delay – **spontaneous clearance** may occur (early infection)

HCV is not a benign disease: Natural history of infection



Progression to cirrhosis accelerated in HIV coinfection

Extra-hepatic manifestations of disease

CNS

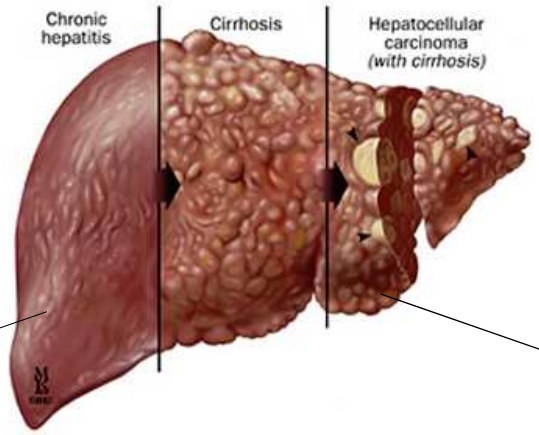
Joints

Skin

Kidneys

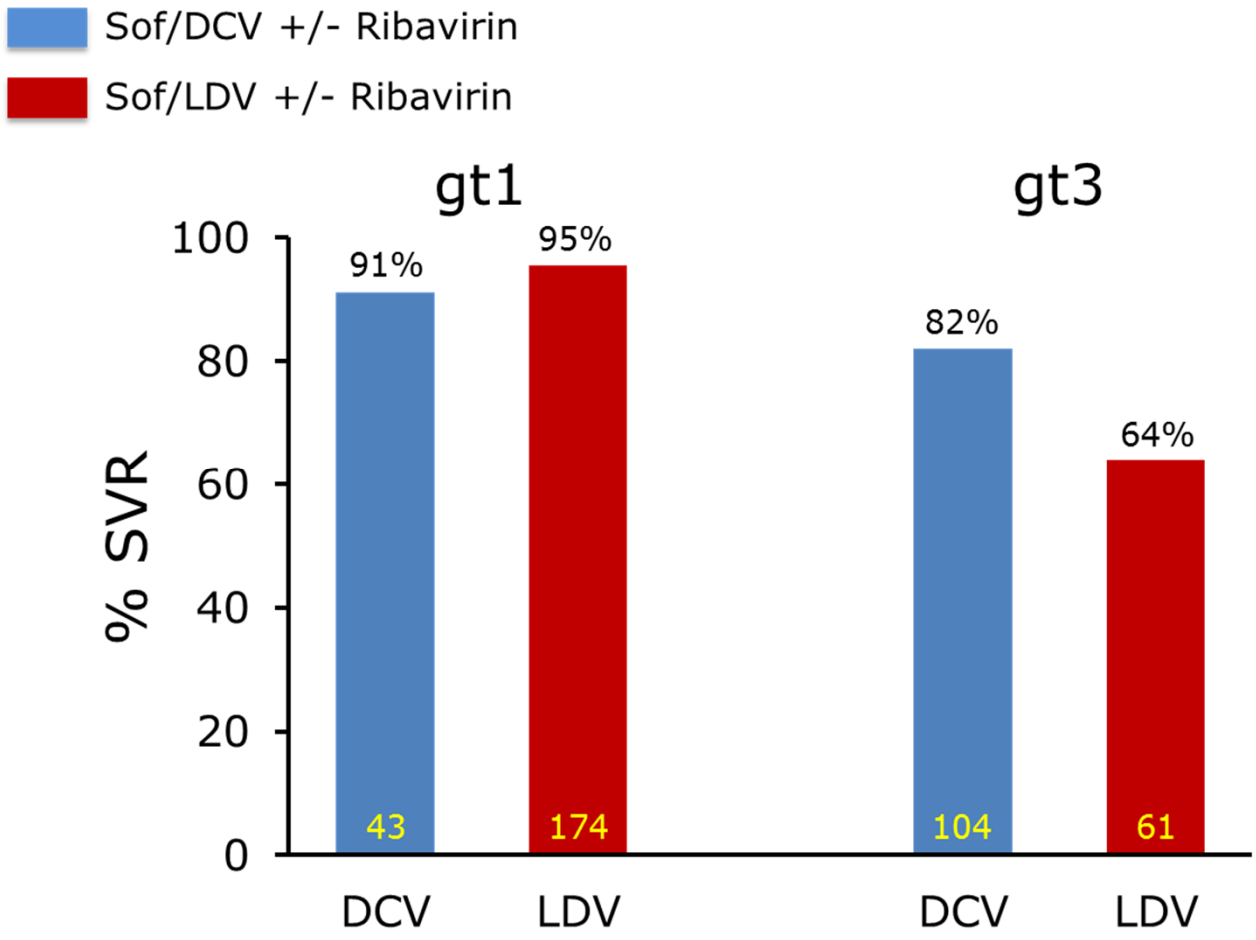
Immune system

Early treatment is more effective and less toxic than late treatment

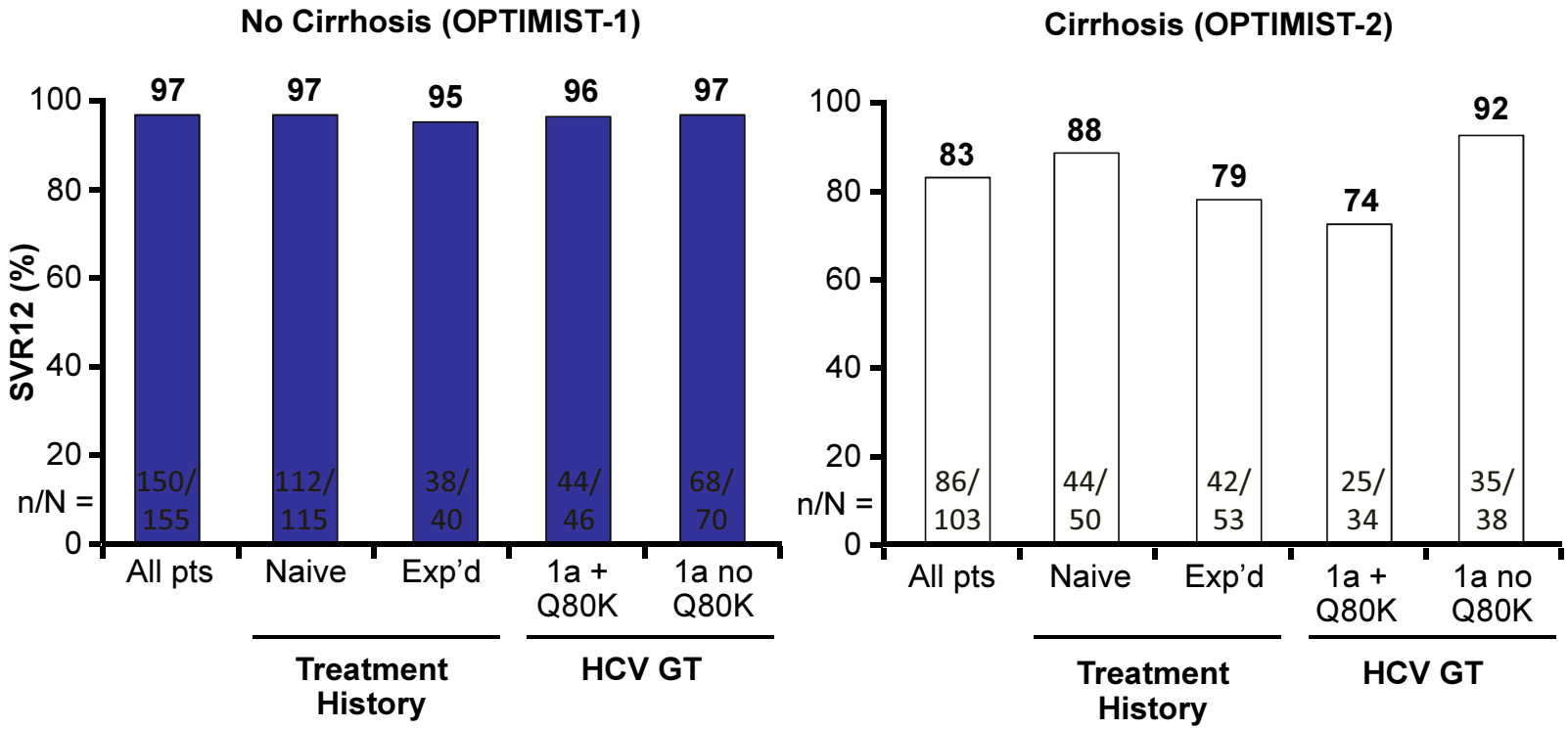


Patients with mild-moderate fibrosis	Patients with cirrhosis
SVR rates >90%	SVR rates lower, especially in genotype 3
RAVs have very little impact	Impact of RAVs higher
Shorter duration (8 weeks in eligible patients)	Longer duration (12-24 weeks)
No need for RBV	RBV may be used to maximise likelihood of SVR

Early Access Programme –treatment in cirrhosis results in lower SVR rates

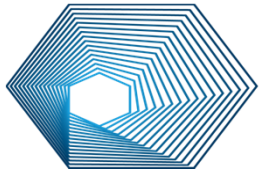


Impact of RAVs is worse in patients with cirrhosis
OPTIMIST: Baseline NS3 Q80K mutation lowers SVR rates in cirrhotic patients treated with SIM/SOF



Kwo P, et al. EASL 2015. Abstract LP14; Lawitz E, et al. EASL 2015. Abstract LP04.

If we treat early, ribavirin can be avoided

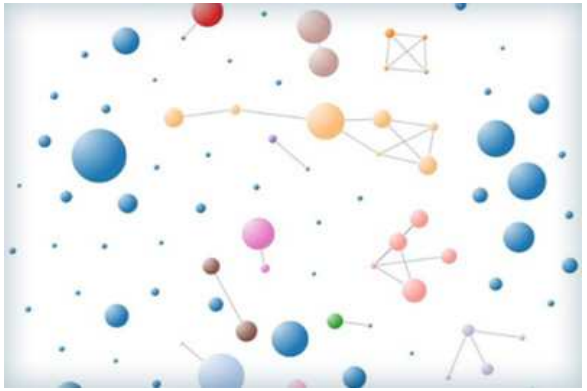


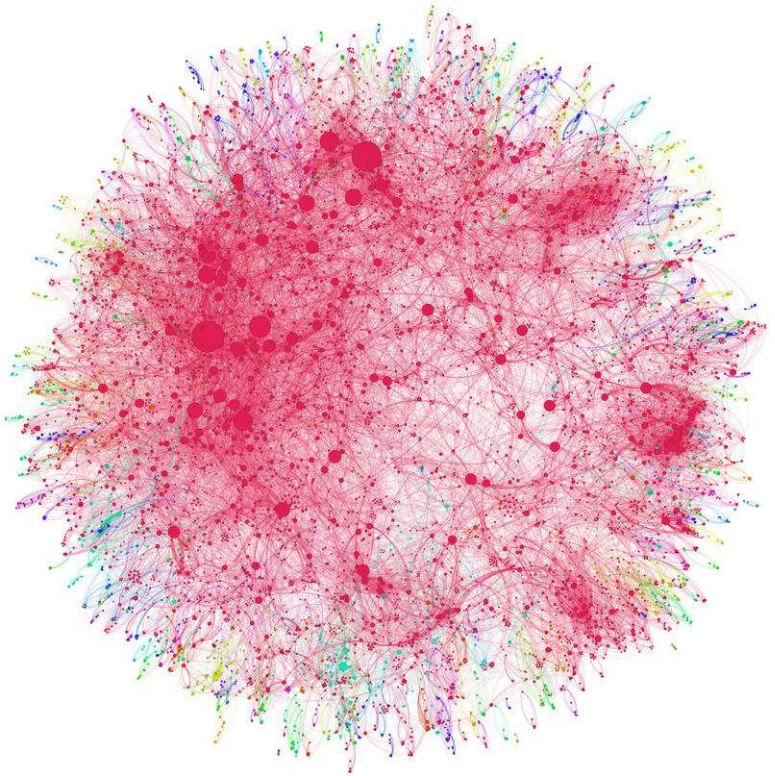
CVR
Medical Research Council
University of Glasgow
Centre for Virus Research

SVR12, %	Total (N = 513)	Treatment Naive (n = 161)	Treatment Experienced (n = 352)
Overall	96	98	95
12 wks ± RBV	95	97	94
24 wks ± RBV	98	99	98
Without RBV	95	96	95
With RBV	97	99	96
12 wks without RBV	92	96	90
12 wks with RBV	96	98	96
24 wks without RBV	98	97	98
24 wks with RBV	100	100	100

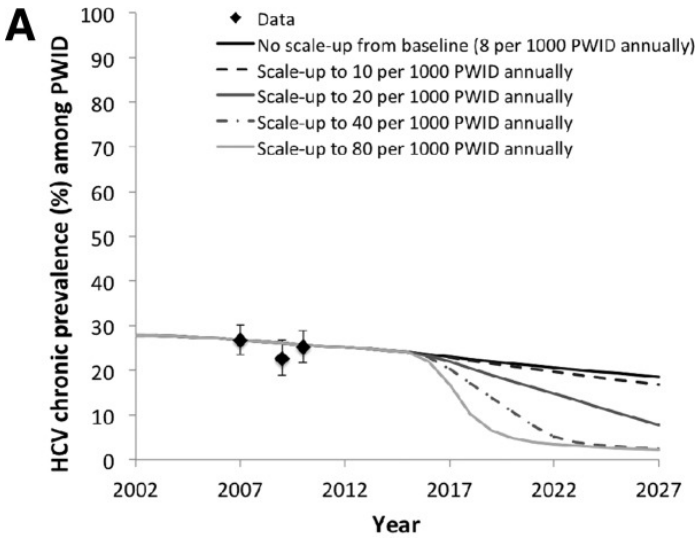
Reddy KR, et al. Hepatology. 2015;62:79-86.

Treat early and stop transmission

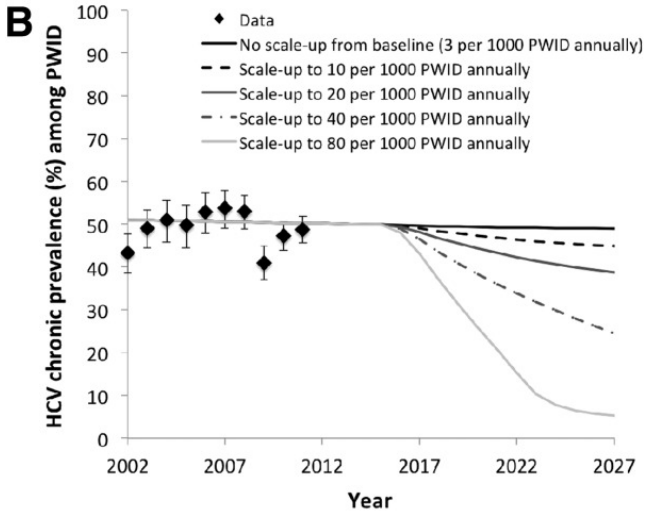




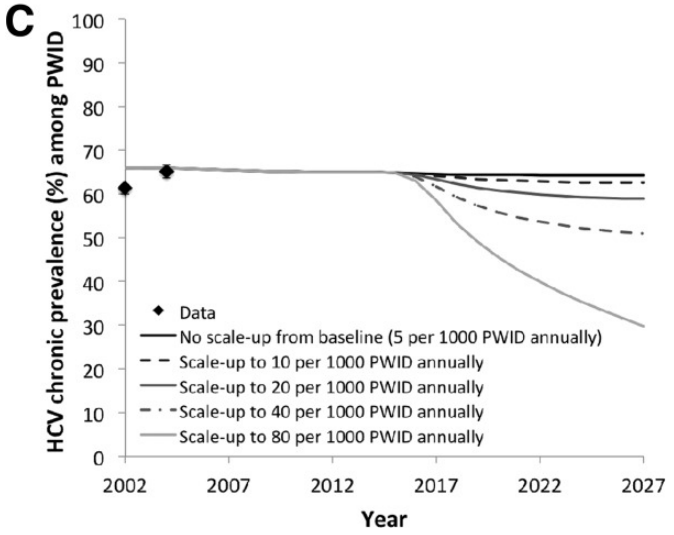
Treatment prevents onward transmission



Edinburgh

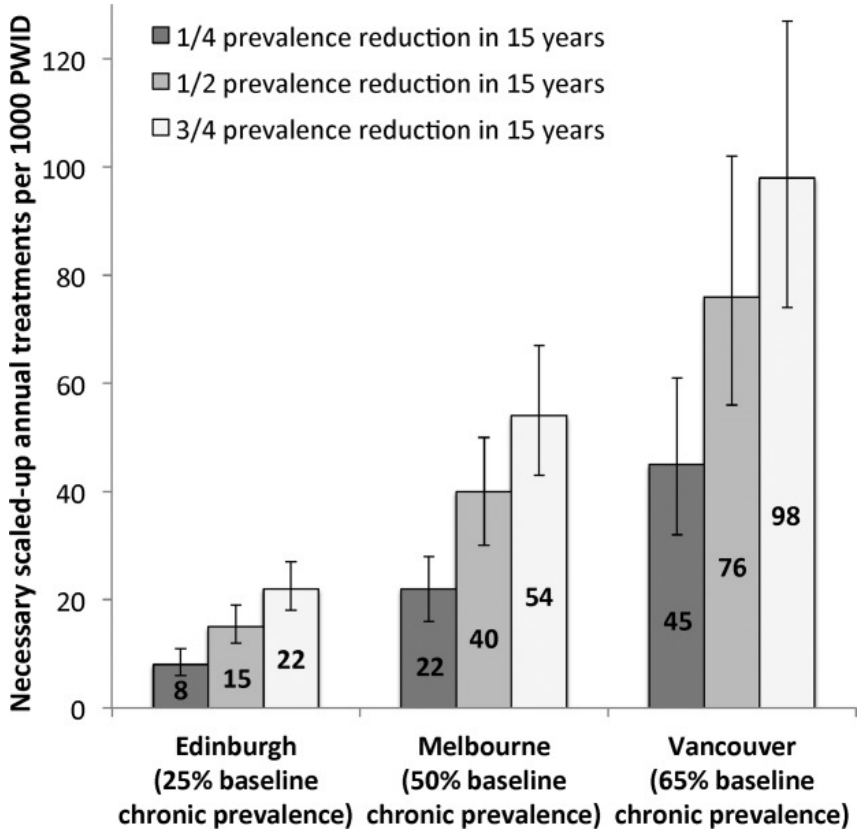


Melbourne



Vancouver

Treating a small number of patients reduces prevalence



What about treating very early infection?

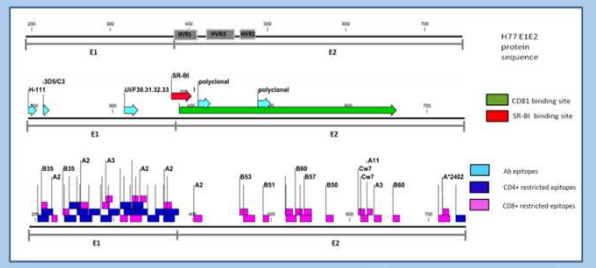
Acute HCV UK
T cell-mediated immunity to HCV

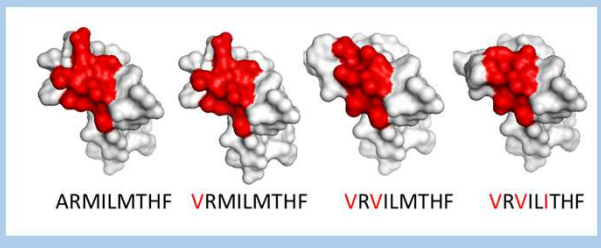
Acute HCV UK cohort

Wellcome Trust £1M

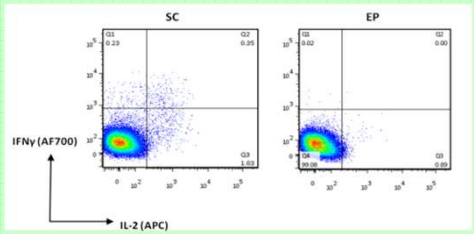
200/500 patients
2000 samples
PBMCs and plasma

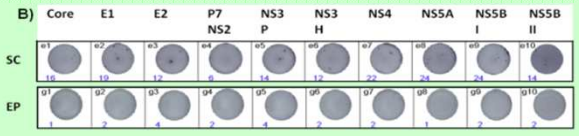
Whole genome sequencing

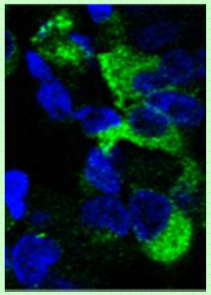


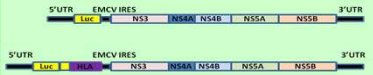


Functional T cell assays









Acute HCV in HIV-positive men: an emerging epidemic

UK August 2004 *STI*

Increased numbers of acute hepatitis C infections in HIV positive homosexual men; is sexual transmission feeding the increase?

R Browne, D Asboe, Y Gilleece, M Atkins, S Mandalia, B Gazzard, M Nelson

St Stephens Centre, Chelsea and Westminster Hospital, 369 Fulham Road, London, SW10 9NH, UK

Germany March 2005 *JViralHep*

Treatment of acute hepatitis C infection in HIV-infected patients: a retrospective analysis of eleven cases

M. Vogel,[1] B. Bieniek,[2] H. Jessen,[3] C. K. Schewe,[4] C. Hoffmann,[5] A. Baumgarten,[6] A. Kroidl,[7] J. R. Bogner,[8] U. Spengler[1] and J. K. Rockstroh[1]

Netherlands January 2004 *Ned TijdschrGeneeskd*

Sexual transmission of hepatitis C in homosexual men

Ruys TA, den Hollander JG, Beld MG, van der Ende ME, van der Meer JT

France July 2004 *HIV Medicine*

Acute hepatitis C in HIV-infected men who have sex

France January 2006 *AIDS*

Sexually transmitted acute infection with a clustered genotype 4 hepatitis C virus in HIV-1-infected men and inefficacy of early antiviral therapy

Jeanne Serpaggi[a,b], Marie-Laure Chaix[c], Dominique Batisse[d], Caroline Dupont[e], Anaïs Vallet-Pichard[a,b], Hélène Fontaine[a,b], Jean-Paul Viard[f], Christophe Piketty[d], Elisabeth Rouveix[e], Christine Rouzioux[c], Laurence Weiss[d] and Stanislas Pol[a,b]

USA January 2006 *JAIDS*

Clinical Presentation and Course of Acute Hepatitis C Infection in HIV-Infected Patients

USA September 2008 *JID*

Liver Fibrosis during an Outbreak of Acute Hepatitis C Virus Infection in HIV-Infected Men: A Prospective Cohort Study

Daniel S. Fierer,[1] Alison J. Uriel,[2] Damaris C. Carriero,[2] Arielle Klepper,[2] Douglas T. Dieterich,[2] Michael P. Mullen,[1] Swan N. Thung,[3] M. Isabel Fiel,[3] and Andrea D. Branch[2]

Netherlands June 2005 AIDS

A cluster of acute hepatitis C virus infection among men who have sex with men – results from contact tracing and public health implications

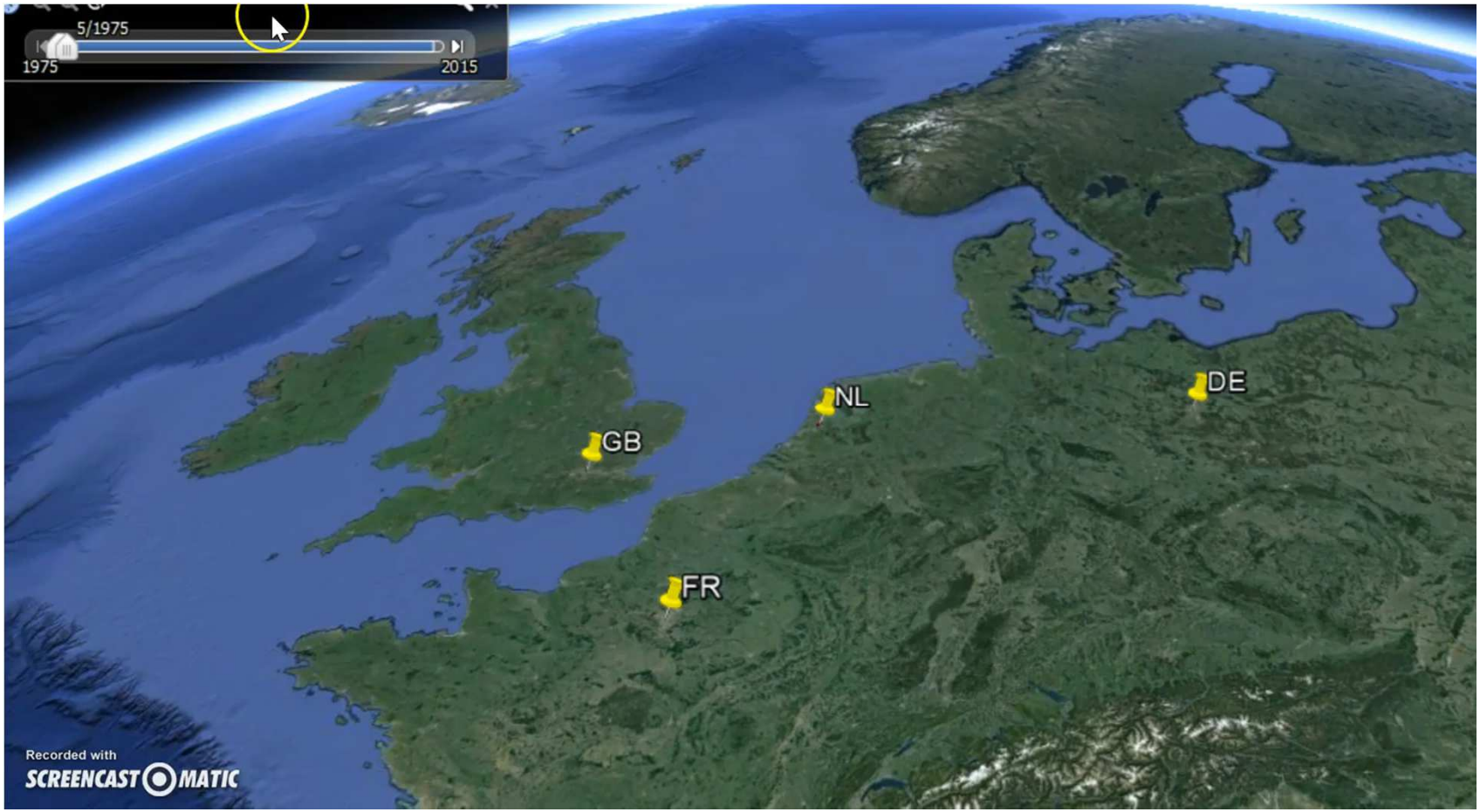
Hannelore M. Götz[a], Gerard van Doornum[b], Hubert G.M. Niesters[b], Jan G. den Hollander[c,e], H. Bing Thio[d] and Onno de Zwart[a]

Australia January October 2007 *Int J Drug Policy*

Recruitment and follow-up of injecting drug users in the setting of early hepatitis C treatment: Insights from the ATAHC study

Oanh K. Nguyen[a,*], Gregory J. Dore[b,1], John M. Kaldor[b,1], Margaret E. Hellard[a,2], on behalf of the ATAHC Protocol Steering Committee

Emergence of genotype 4d in HIV infected MSM



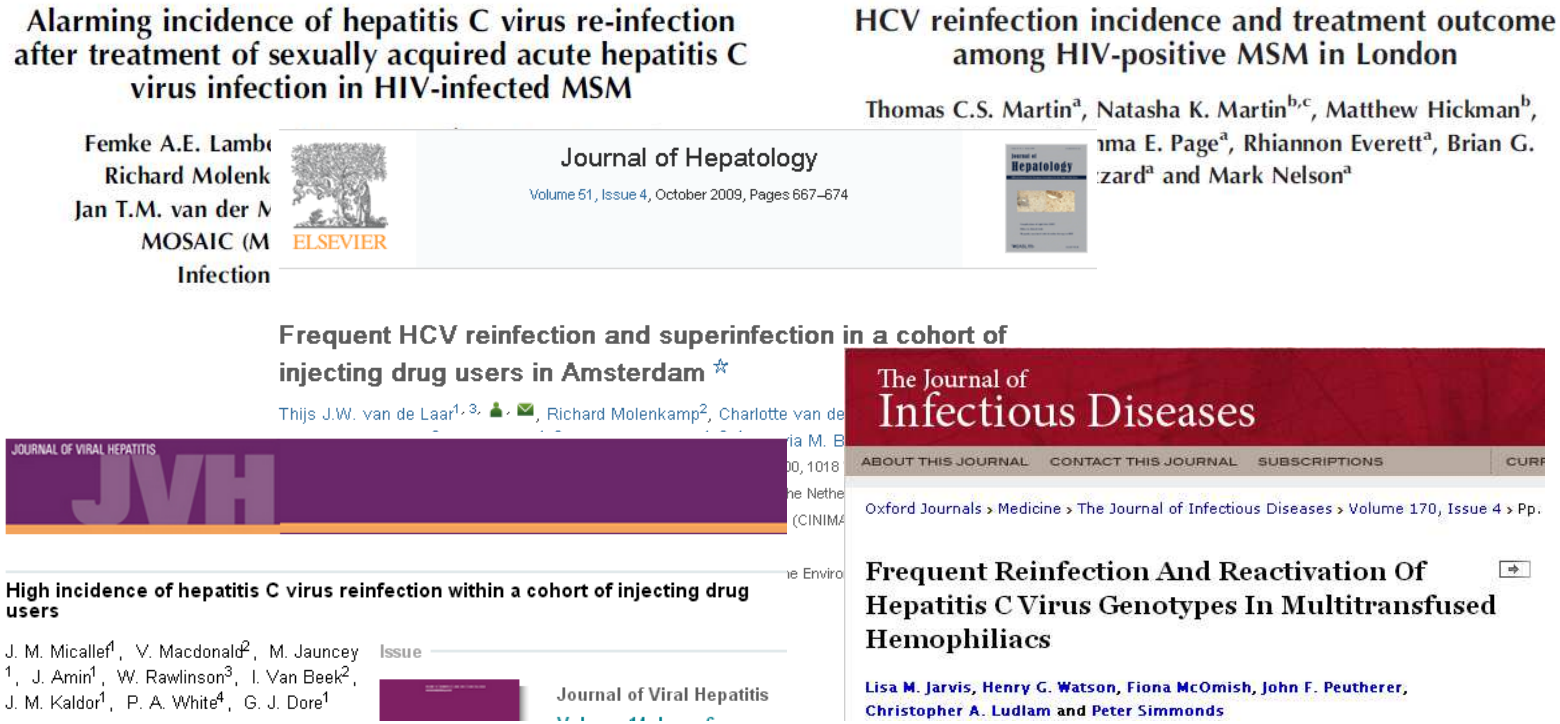
Acquisition of acute HCV is often associated with high risk behaviours

	Number participating (%)		
	Controls (%)	Cases (%)	*P*-value*
Sexual practice:			
Active oral sex (no ejaculation)	112 (94.1)	57 (96.6)	0.73
Active oral sex (ejaculation)	56 (47.1)	37 (62.7)	0.07
Active oral sex with condoms (safe)	12 (10.1)	5 (8.5)	0.94
Passive oral sex (no ejaculation)	109 (91.6)	52 (89.7)	0.89
Passive oral sex (ejaculation)	42 (35.3)	30 (50.9)	0.07
Passive oral sex with condoms (safe)	11 (9.2)	2 (3.4)	0.22
Receptive UAI (no ejaculation)	60 (50.4)	53 (89.8)	0.0001
Receptive UAI (ejaculation)	42 (35.3)	46 (78.0)	0.0001
Receptive AI with condoms (safe)	83 (69.8)	44 (74.6)	0.62
Insertive UAI (no ejaculation)	57 (47.9)	49 (83.1)	0.0001
Insertive UAI (ejaculation)	39 (32.8)	34 (57.6)	0.003
Insertive AI with condoms (safe)	82 (68.9)	40 (69.0)	1.00
Passive rimming	92 (77.3)	58 (98.3)	0.0007
Active rimming	92 (77.3)	54 (91.5)	0.03
Insertive fisting	31 (26.3)	44 (74.6)	0.0001
Receptive fisting	15 (12.6)	34 (57.6)	0.0001
Use of sex toys	51 (42.9)	46 (78.0)	0.0001
Lifetime sexually transmitted infection (%)	78 (78)	51 (92)	0.005
Group sex participation (group of >2 individuals):	63 (52.5)	52 (88.1)	0.0001
Group sex practices			
Receptive UAI	26 (41.3)	49 (94.2)	0.0001
Insertive UAI	30 (47.6)	44 (84.6)	0.0001
Receptive fisting	9 (14.3)	29 (55.8)	0.0001
Insertive fisting	10 (15.9)	35 (67.3)	0.0001
Group sex by number of sex practices			
0–1	94 (78.3)	11 (18.6)	
2	14 (11.7)	15 (25.4)	
3–4	12 (10.0)	33 (55.9)	0.0001

*The proportions who have ever had each type of sex were compared using chi-squared tests (or Fisher's exact test if appropriate). anal intercourse (AI)Unprotected anal intercourse (UAI);

AIDS

Treatment failure – reinfection or recrudescence? Should we stop and reduce reinfection risk before treatment



Alarming incidence of hepatitis C virus re-infection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM

Femke A.E. Lamb
Richard Molenk
Jan T.M. van der M
MOSAIC (M
Infection

ELSEVIER

Journal of Hepatology

Volume 51, Issue 4, October 2009, Pages 667–674

HCV reinfection incidence and treatment outcome among HIV-positive MSM in London

Thomas C.S. Martin[a], Natasha K. Martin[b,c], Matthew Hickman[b], ma E. Page[a], Rhiannon Everett[a], Brian G. zard[a] and Mark Nelson[a]

Frequent HCV reinfection and superinfection in a cohort of injecting drug users in Amsterdam ☆

Thijs J.W. van de Laar[1, 3], Richard Molenkamp[2], Charlotte van de

JOURNAL OF VIRAL HEPATITIS JVH

High incidence of hepatitis C virus reinfection within a cohort of injecting drug users

J. M. Micallef[1], V. Macdonald[2], M. Jauncey[1], J. Amin[1], W. Rawlinson[3], I. Van Beek[2], J. M. Kaldor[1], P. A. White[4], G. J. Dore[1]

Issue

Journal of Viral Hepatitis

The Journal of Infectious Diseases

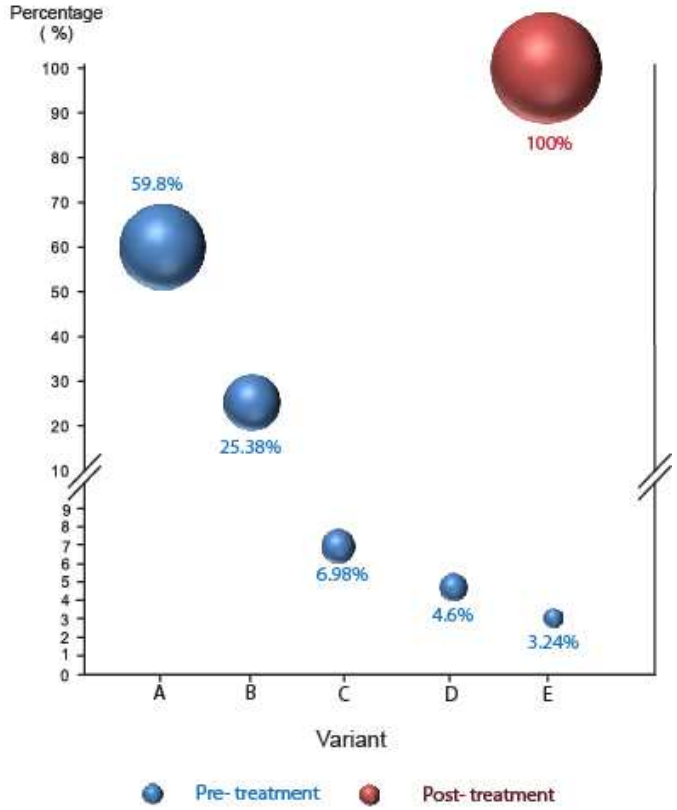
ABOUT THIS JOURNAL CONTACT THIS JOURNAL SUBSCRIPTIONS

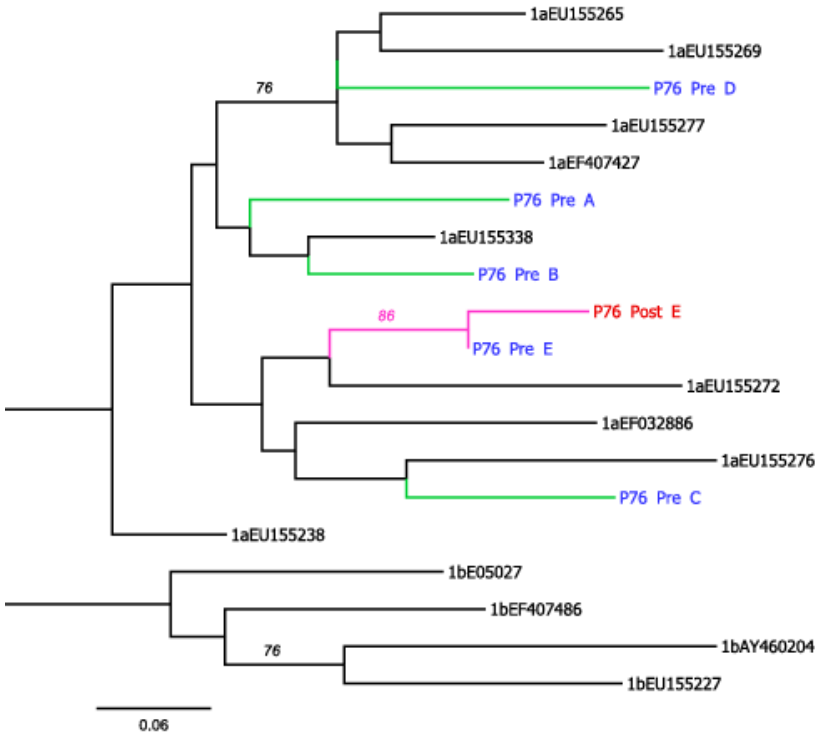
Oxford Journals › Medicine › The Journal of Infectious Diseases › Volume 170, Issue 4 › Pp.

Frequent Reinfection And Reactivation Of Hepatitis C Virus Genotypes In Multitransfused Hemophiliacs

Lisa M. Jarvis, Henry G. Watson, Fiona McOmish, John F. Peutherer, Christopher A. Ludlam and Peter Simmonds

Relapse is not associated with reinfection but is associated with varying dominance of pre-existing strains – we are over-estimating reinfection risk



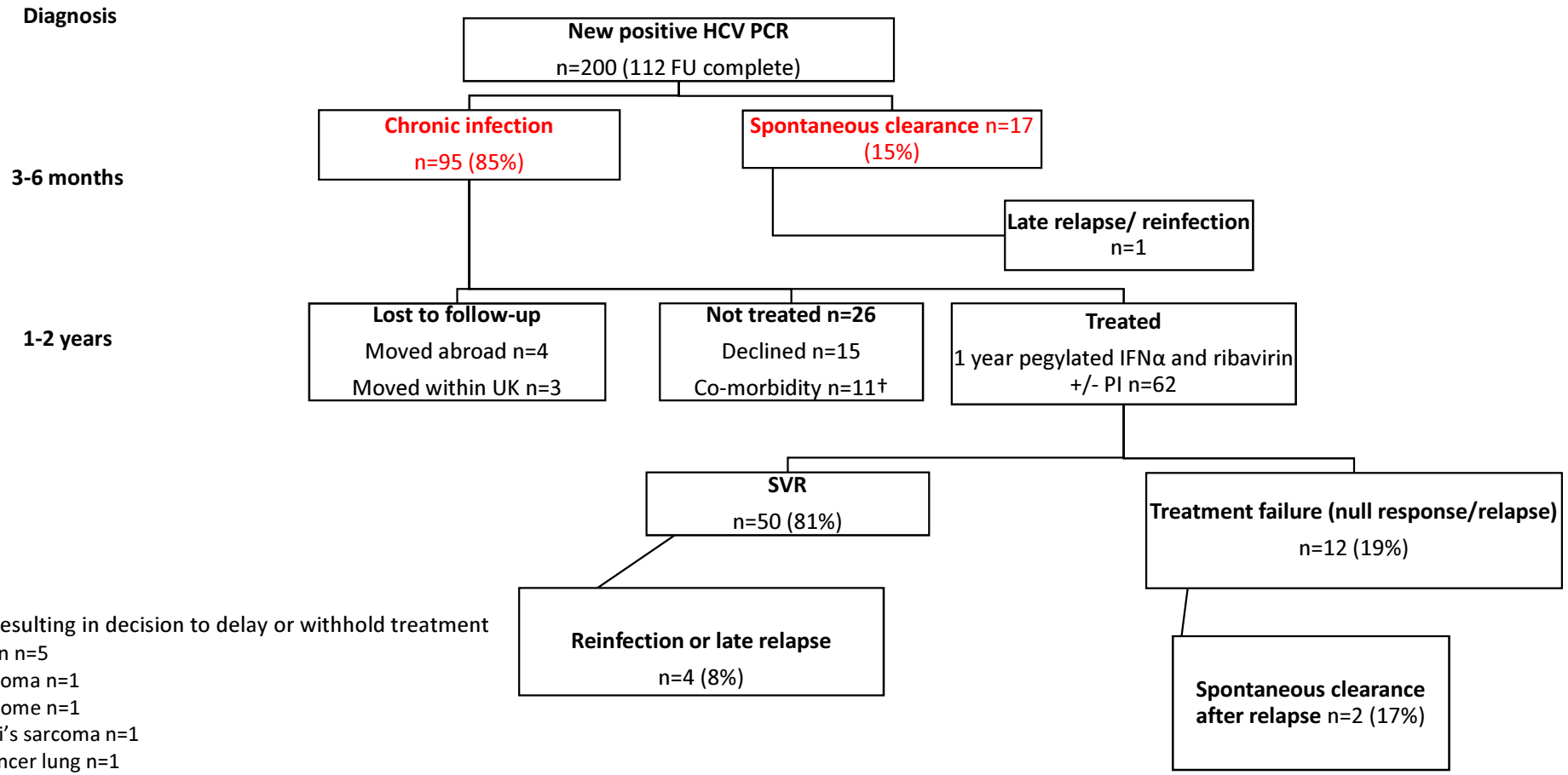


Abdelrahman *et al*, Hepatology 2015

So should we treat early – in acute rather than chronic infection and can we reduce the duration of therapy?

Study	DAA	Genotype	HIV	Duration	SVR
Dutch Acute HCV in HIV Study – DAHHS 57	BOC/IFN/RBV	1	Positive	12 weeks	86% RVR 100% No RVR 50%
Open label (Fierer et al) 36	TEL/IFN/RBV	1	Positive	12 weeks (RVR)	89%
SWIFT-C	SOF/RBV	Any	Positive	12	59%
DARE C II 16	SOF/RBV	Any	Mixed	6	SVR4 – 27%
SLAM C 29	SOF/LED 14 or SOF/SIM 15			4 weeks (SOF/LED) 8 weeks (SOF/SIM)	93% (BOTH ARMS)

Waiting for 3-6 months allows time for spontaneous clearance to occur



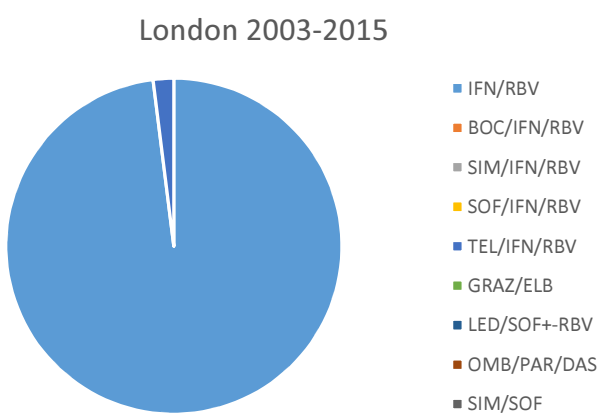
† Co-morbidities resulting in decision to delay or withhold treatment
- Severe depression n=5
- Metastatic melanoma n=1
- Castlemans syndrome n=1
- Pulmonary Kaposi's sarcoma n=1
- Squamous cell cancer lung n=1
- Epilepsy n=1
- Pulmonary tuberculosis n=1

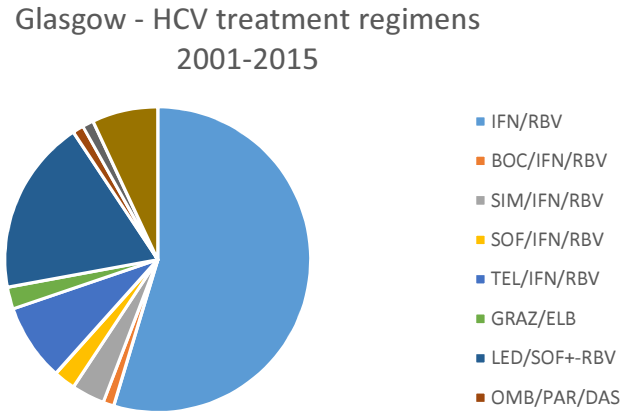
Thomson E *et al*, *Gut* 2011

DAA treatment availability

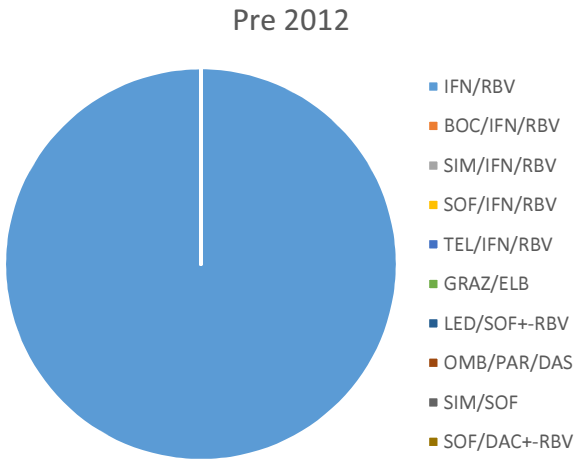
London NICE guidance

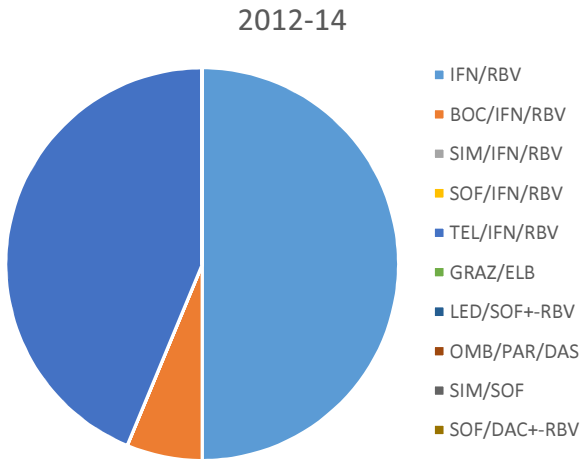
Glasgow SMC guidance

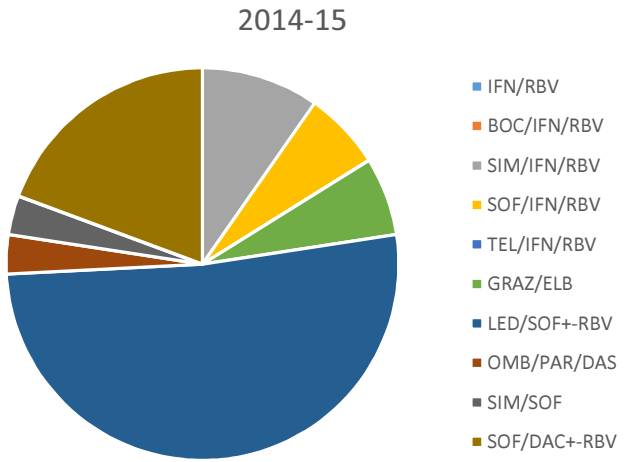




DAA treatment is highly effective in HIV-co-infected patients
The Glasgow Co-infected Cohort (GCC)







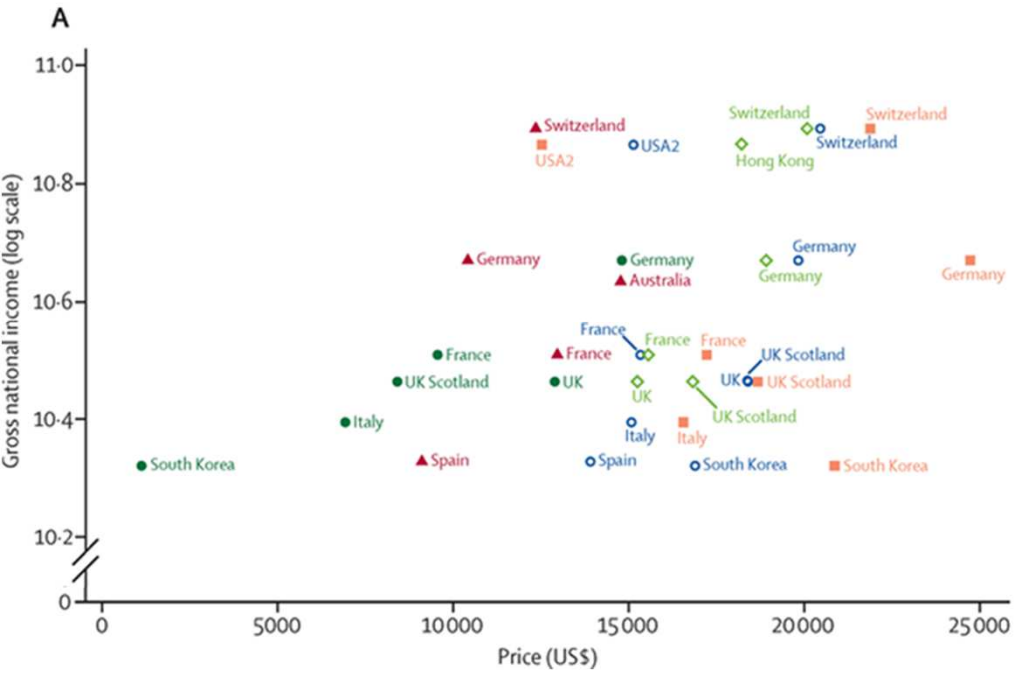
Last prescription of IFN/RBV – 6/11/13

Pre-6/11/13
SVR 74% (n=38)

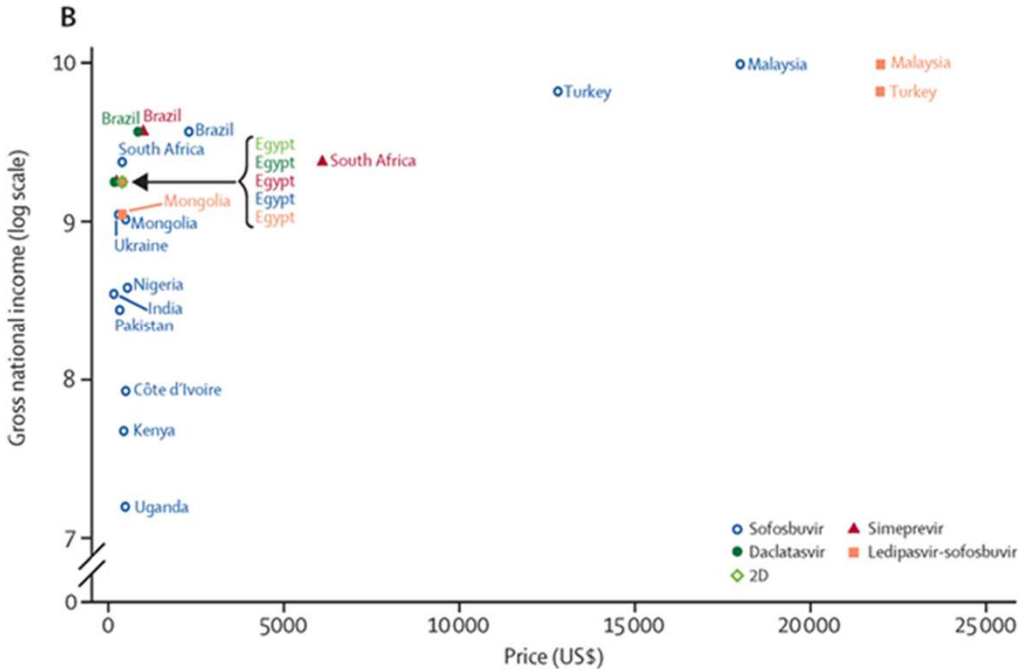
Post-6/11/13
SVR 100% (n=49)

Disparity in market prices for HCV DAAs

High income countries



Middle and low income countries



Andrieux-Meyer *et a*l The Lancet Global Health 2015

Hepatitis C drug maker puts profit ahead of patients US Senate report

BMJ 2015;351:h6573

- Harvoni costs $1000 a pill or $84 000 (£56 000; €79 000)
- Senator Ron Wyden

"Over the eight months Gilead spent determining the price of Sovaldi, the company repeatedly made clear its primary focus was outmaneuvering potential competitors to ensure its drugs had the greatest share of the market, for the highest price, for the longest period of time."

"Gilead pursued a calculated scheme for pricing and marketing its hepatitis C drug based on one primary goal, maximizing revenue, regardless of the human consequences"

- Gilead

"We stand behind the pricing of our therapies because of the benefit they bring to patients and the significant value they represent to payers, providers, and our entire healthcare system by reducing the long-term costs associated with managing chronic HCV. Enabling patient access to Sovaldi and Harvoni is a top priority for Gilead."

- Gilead Company documents – Kevin Young

"Let's not fold to advocacy pressure in 2014 … Let's hold our position whatever competitors do or whatever the headlines."

Conclusions

- We should not have to wait for DAA availability and we should treat now

- Exceptions
  - Previous treatment failure with multiple RAVs
  - Acute HCV

- We need lower drug costs to make this happen – accessibility to treatment is vital