Treatment for hepatitis C infection in the UK Collaborative HIV cohort (UK CHIC) study

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Background

- The aim of treatment for hepatitis C virus (HCV) is a sustained virological response (SVR): negative HCV-RNA 6 months after treatment has ceased
- SVR is associated with a reduction in the risk of liver-related events and it may reverse fibrosis and cirrhosis caused by HCV infection
- Treatment with Pegylated interferon (Peg-IFN) and ribavirin is long, difficult to tolerate and of low efficacy
  - 24.5% SVR among co-infected patients with genotype 1 or 4[1]
  - 59.4% SVR among co-infected patients with genotype 2 or 3[1]
- New treatment strategies (directly acting agents) are not yet available for everyone and regimens may still include Peg-IFN

[1] Davies et al, 2013, PLOS One

Aims and objectives

Aim:

- To describe patterns of treatment for HCV among a cohort of HIV/ HCV co-infected individuals in the UK

Objectives:

1. To identify factors associated with receiving any HCV treatment
2. To characterise the treatment received with regard to drugs included and time on treatment
3. To identify factors associated with treatment failure defined as a positive HCV-RNA test in the one year after stopping treatment

Methods 1

UK CHIC

- Observational longitudinal study of HIV-positive adults
- 11 centres contributed additional data on HCV co-infected individuals seen for care from 2004 onwards including data on liver disease outcomes and HCV treatment

Inclusion/exclusion criteria

- All individuals included in the expanded data collection with a positive HCV-RNA test at any time during follow-up
- No evidence of HCV treatment before entry into the cohort
- Among treated individuals, at least one HCV RNA test in the year after stopping treatment

Methods 2

- Cox proportional hazards models used to identify independent predictors of each outcome

Outcome	Follow-up	Censoring
1. Starting HCV treatment	**From**: Earliest of cohort entry or first positive HCV test **Until:** Starting treatment; date of death; last date of follow-up	Evidence of spontaneous HCV clearance
2. Treatment failure	**From**: Date of stopping treatment **Until:** A positive HCV-RNA test; death; last date of follow-up	Evidence of a subsequent course of HCV treatment

Results: Treatment received

- 929/2272 (40.9%) co-infected individuals received any HCV treatment
- 114/929 (12.3%) received > one course of treatment

Drugs included in regimen	Number of individuals (%)		
	1st episode of treatment	2nd episode of treatment	3rd episode of treatment
Peg IFN/IFN alone	43 (4.6)	3 (2.6)	0 (0.0)
Peg IFN/IFN + Ribavirin	836 (90.0)	91 (79.8)	12 (85.7)
Regimens including DAAs[1]	50 (5.4)	20 (17.5)	2 (14.3)

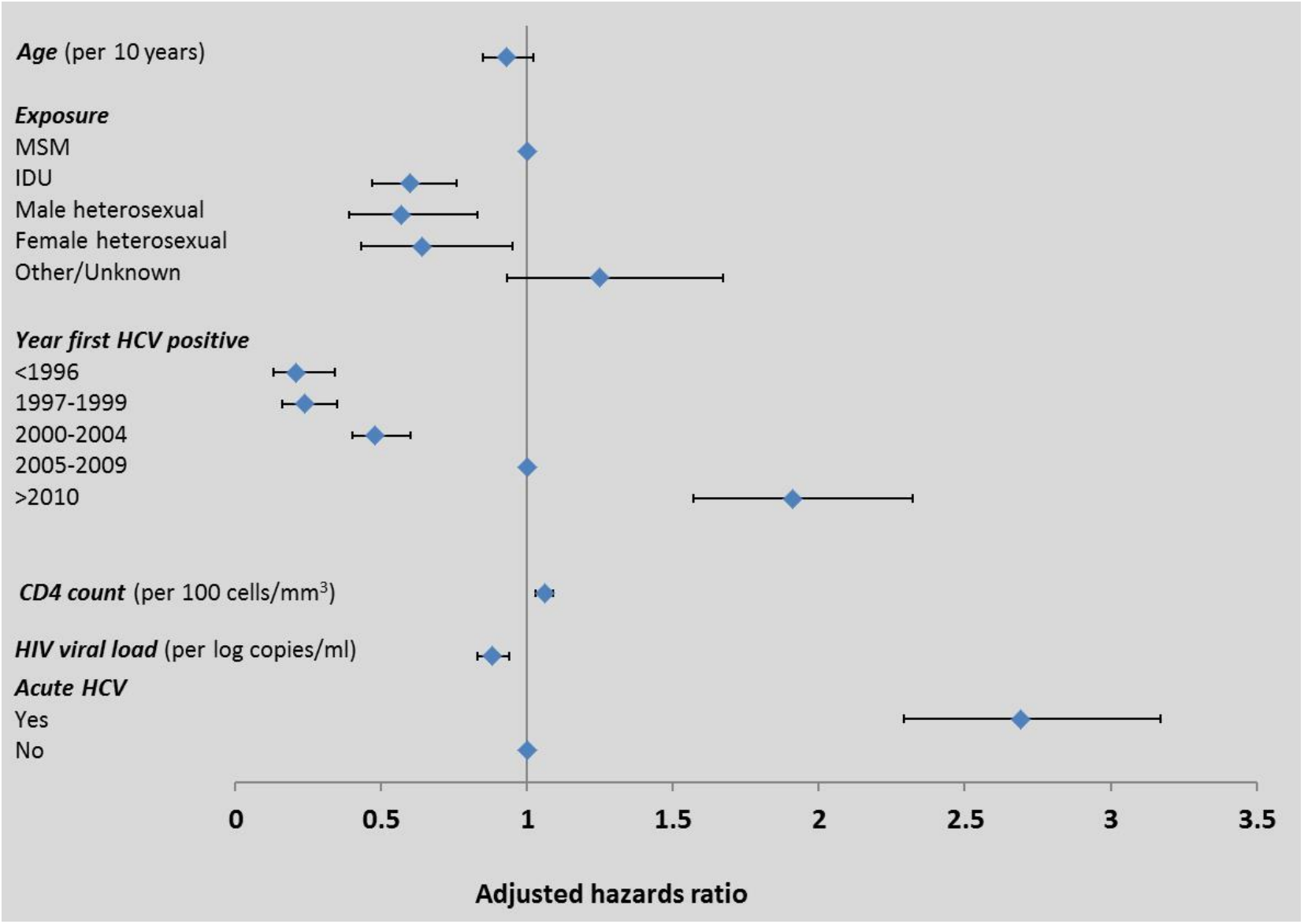
[1]Regimens included: Peg-IFN and ribavirin plus either telaprevir or boceprevir; sofosbuvir plus ribavirin and sofosbuvir alone

Results: Individuals starting treatment

- 2163 individuals included in analysis[1], 820 of whom started treatment (37.9%):
  - Median age 37 (IQR 32, 43) years
  - 83.5% (1806/2163) of white ethnicity;
  - 61.1% (1322/2163) men who have sex with men (MSM)
  - 27.7% (601/2163) diagnosed with HCV in the acute stage
- Median time between first positive test and starting first HCV treatment: 11.2 months (IQR 3.7, 46.6 months)
- Median time on treatment: 47.7 (IQR 24, 48) weeks

[1] Excluding n=49 whose date of starting first episode of treatment was unknown; n=58 who started HCV treatment before their first recorded positive test; and n=2 individuals whose first treatment was before entry into the cohort

Results: Predictors of starting treatment



Results: Treatment failure

- Treatment episodes which included DAAs were excluded from the analysis
- There were 417 separate episodes of treatment where at least 1 HCV-RNA test result was recorded in the year after stopping treatment
- 138/417 (33.1%) episodes of treatment showed evidence of failure in the year after treatment ended
- No association was found between treatment failure and age, ethnicity, HIV exposure group, year of starting treatment, CD4 count, HIV viral load, HAART or treatment episode number

Results: Predictors of treatment failure

		Crude Odds ratio (95% CI)	P value	Adjusted Odds ratio (95% CI)	P value
Acute HCV	No	1	-	1	-
	Yes	0.70 (0.50-0.97)	0.03	0.61 (0.41-0.92)	0.01
HCV viral load[1]	(per log copies/ml)	1.26 (1.04-1.53)	0.02	1.26 (1.12-1.42)	0.0001
HCV genotype	1 or 4	1	-	1	-
	2 or 3	0.42 (0.23-0.78)	0.01	0.34 (0.15-0.81)	0.01
	Other/unknown	1.32 (0.90-1.94)	0.15	1.67 (1.04-2.69)	0.04
HBV co-infection	No	1	-	1	-
	Yes	1.06 (0.65-1.73)	0.82	1.31 (0.74-2.31)	0.36
	Unknown	1.74 (1.10-2.75)	0.02	1.65 (0.85-3.30)	0.16
Time on treatment	(per week)	0.85 (0.78-0.92)	<0.0001	0.73 (0.66-0.80)	<0.0001

[1] HCV viral load was unknown for 91 individuals

Limitations

- Limited post-treatment HCV-RNA test results
- Unable to assess end of treatment response or SVR
- Determining acute HCV infection
- No information on HCV reinfection

Summary and conclusions

- A significant group of co-infected individuals have not received treatment or have failed treatment for HCV infection
- These individuals remain at risk of developing liver disease and would benefit from access to new treatment strategies
  - In particular, those who are not diagnosed within the acute stage; those who with genotype 1 or 4 infection and those who remain on treatment for shorter period
- Further work should concentrate on collection of data which can be used to assess treatment outcomes more thoroughly as new drugs become used more regularly

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