Liver fibrosis regression measured by transient elastography
in people living with HIV successfully treated for hepatitis C using direct acting antivirals

J. Young [1], S. Wang [1], R. Sacks-Davis [2], A. Stewart [2], D. Van Santen [2], M. van der Valk [3], J. Doyle [2], G. Matthews [4], J. Berenguer [5], L. Wittkop [6], K. Lacombe [7], A. Rauch [8], M. Stoové [2], M. Hellard [2], M. Klein [1]

[1] Research Institute of the McGill University Health Centre, Montreal, Canada, [2] Burnet Institute, Melbourne, Australia, [3] Amsterdam University Medical Centre, Amsterdam, Netherlands, [4] The Kirby Institute, Sydney, Australia, [5] Gregorio Marañón General University Hospital, Madrid, Spain, [6] Inserm Research Center, Bordeaux Population Health, Bordeaux, France, [7] Sorbonne University, Paris, France, [8] Bern University Hospital, Bern, Switzerland

Background

- Successful treatment for hepatitis C virus (HCV) is known to reduce liver fibrosis.
- Unlike indexes based on serum biomarkers (FIB-4, APRI and ELF), **transient elastography (TE)** has been shown to capture true fibrosis regression after successful HCV treatment, once inflammation abates.
- It is not clear how fibrosis changes in the medium term after a successful treatment, particular for those with advanced fibrosis or cirrhosis prior to starting treatment.

Methods

- TE measurements were collected in eight of the 11 cohorts in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC). Cohorts providing data were from Australia, Canada, France, the Netherlands, Spain and Switzerland.
- We selected individuals successfully treated for a primary HCV infection using all oral direct acting antivirals and with at least one TE measured within a year prior to starting treatment. This baseline measurement was used to create subgroups according to fibrosis stage when starting treatment (F0-F1<7.2, F2-F3≥7.2-<14.6, F4≥14.6 KPa).
- For those selected, all TE measurements after successful treatment were included in our generalised additive modelling, provided the individual was not re-infected with HCV. The model was fit in R using the mgcv package written by Prof Simon Wood.
- Our model included a random intercept allowing for repeated measures from the same individual and an adaptive spline representing the change in mean fibrosis over time. The model also included covariates for: cohort, sex, age when starting treatment, and a time dependent indicator of a detectable HIV viral load.

Results

- TE measurements were included from 1718 individuals (Table 1); 523 had a measurement after treatment ended (227 F0-F1, 204 F2-F3, 92 F4) with a median follow-up of 0.9 years (0.8 F0-F1, 1.1 F2-F3, 1.2 F4). Figure 1 shows the data available for each fibrosis subgroup and the placement of the knots when constructing an adaptive spline for the mean response.
- For those with advanced fibrosis (F2-F3) or cirrhosis (F4), the mean response shows a gradual rise leading up to treatment; then a rapid decline in stiffness during treatment as inflammation abates.
- After the treatment period, those with advanced fibrosis regress towards normal (F0-F1) with the mean response falling below 7.2KPa; those with cirrhosis show little regression and the mean response never falls below the threshold for cirrhosis (Figure 2).

Discussion

- Estimates of change in fibrosis (Table 2) suggest that those with advanced fibrosis reach maximal improvement within 2.5 years of successful treatment. A TE measurement 2 years after treatment may be useful clinically to establish the level of residual fibrosis.
- The mean response after treatment ends (Figure 2) suggests that those with cirrhosis show very little, if any, improvement in TE measures once inflammation abates, suggesting that reversibility of true fibrosis is minimal.

Table 1 Participant characteristics

Participant characteristics (n=1718)	**Fibrosis stage when starting treatment**		
Median or percent (% missing)	**F0-F1** <7.2 KPa (n=873)	**F2-F3** ≥7.2-<14.6 KPa (n=595)	**F4** ≥14.6 KPa (n=250)
Female, %	20 (2)	18 (3)	20 (4)
When starting treatment			
Age, years	49 (0)	52 (0)	51 (0)
BMI	23 (31)	24 (26)	24 (32)
APRI	0.5 (29)	0.7 (30)	1.4 (39)
FIB-4	1.1 (29)	1.6 (30)	2.9 (39)
Undetectable HIV viral load, %	93 (6)	91 (4)	93 (10)
Hepatitic C infection			
Age at infection, years	38 (24)	37 (22)	36 (14)
Duration of infection, years	8 (23)	13 (22)	15 (13)
Genotype 3, %	17 (18)	19 (21)	22 (20)
Infected through injection drug use, %	38 (4)	48 (3)	64 (2)

Figure 1 Mean response over time in each fibrosis subgroup

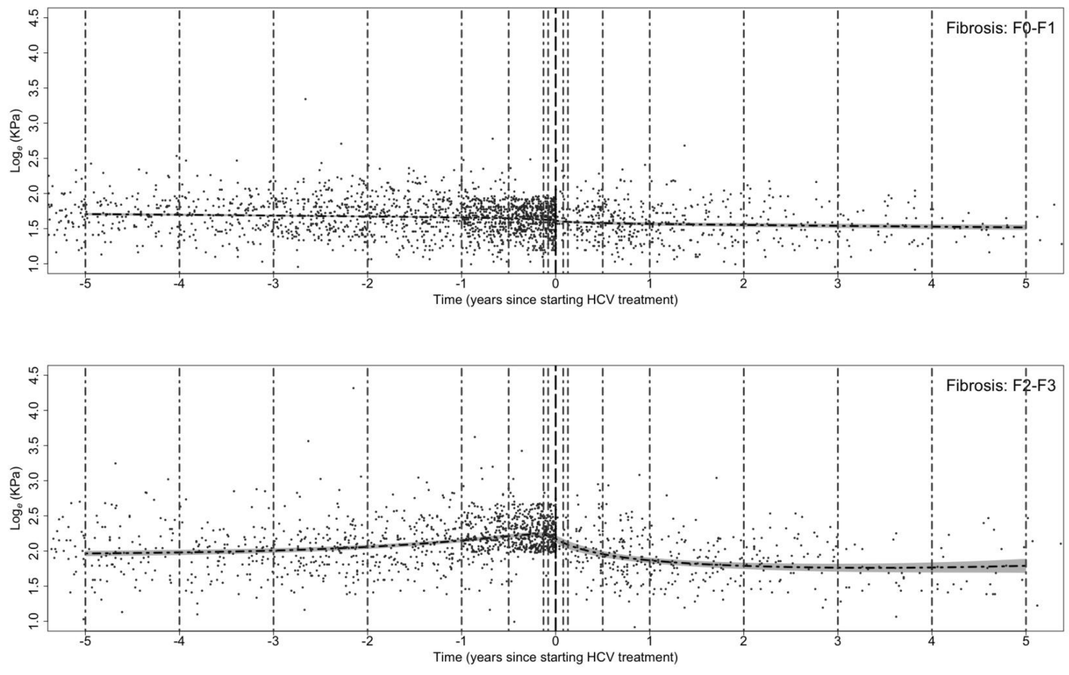

Figure 2 Comparing fibrosis subgroups - mean responses over time

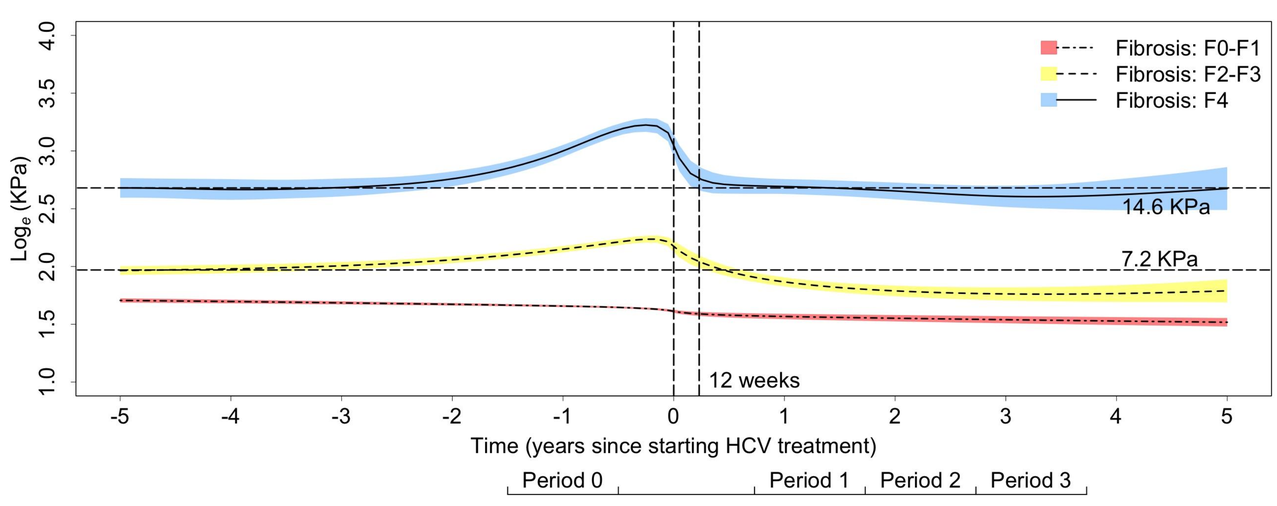

Table 2 Estimated annual change in fibrosis over different periods

Change in KPa (95% credible interval)	**Fibrosis stage when starting treatment**		
Period (see Figure 2)	**F0-F1** <7.2 KPa	**F2-F3** ≥7.2-<14.6 KPa	**F4** ≥14.6 KPa
0: 1.5 to 0.5 years before treatment starts	-0.1 (-0.1 to -0.1)	0.9 (0.5 to 1.3)	6.0 (4.0 to 8.8)
1: 0.5 to 1.5 years after treatment ends	-0.1 (-0.1 to -0.1)	-0.6 (-1.0 to -0.3)	-0.4 (-1.5 to 0.7)
2: 1.5 to 2.5 years after treatment ends	-0.1 (-0.1 to 0.0)	-0.2 (-0.4 to 0.0)	-0.6 (-1.6 to 0.2)
3: 2.5 to 3.5 years after treatment ends	-0.1 (-0.1 to 0.0)	0.0 (-0.2 to 0.2)	-0.1 (-1.1 to 1.1)

Conclusions

- **Successful HCV treatment with DAAs leads to meaningful fibrosis regression in those with advanced fibrosis (F2-F3).**
- **Those with cirrhosis (F4) remain cirrhotic and need continued surveillance.**

Presented at IAS 2023, the 12th IAS Conference on HIV Science

Contact
james.young2@mcgill.ca

InCHEHC is funded by the Australian Government National Health and Medical Research Council (GNT1132902 and GNT2020121).

IAS 2023 23–26 July