Identity transformations and other unexpected benefits of HCV treatment:
a review of the evidence and reflections for the DAA era.

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Acknowledgements & disclosures

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Introduction: conceptualising treatment benefit & 'cure'

I always used to say we eliminate the virus but we also cure the patients, which are two different things and the new treatments will carry on eliminating the virus but may not cure the patient, and I think we have to look into how we replace that role, and that is going to be difficult. (London Hepatologist)

DAA promise: clinical cure - viral elimination

The interferon era: evidence of non-clinical cure

Cure & care in action: a London case study

Implications of DAA provision for non-clinical benefits?

The promise of DAAs: >SVR + democratised access = elimination

- HCV treatment traditionally provenance of specialist / tertiary sector
  - Complexity of interferon side effects, monitoring requirements etc.
- DAA efficacy, simplicity & safety: facilitate primary provision (GPs, DTS, NSP etc)

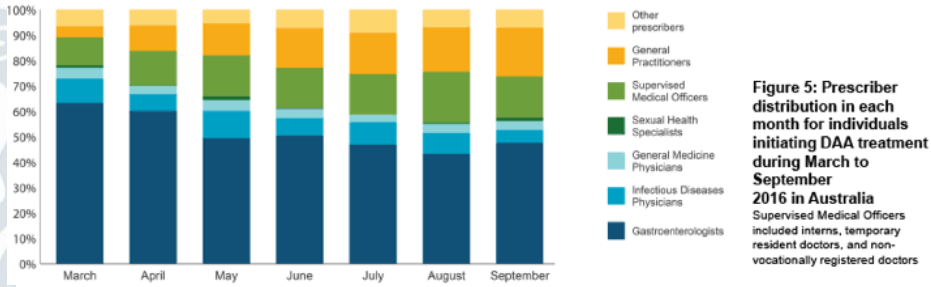


Figure 5: Prescriber distribution in each month for individuals initiating DAA treatment during March to September 2016 in Australia
Supervised Medical Officers included interns, temporary resident doctors, and non-vocationally registered doctors

Hajarizadeh, B. et al., 2017, EASL.

- Reducing barriers to access (hospital system inaccessibility/stigma)

➡ Enabling scale up for PWID ➡ Elimination (*'as a public health threat by 2030'*)

Access in action: Australia

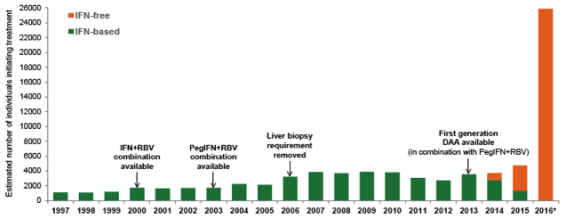


Figure 1: The estimated number of individuals initiating HCV treatment annually from 1997 to 2016 in Australia
* March to September 2016; IFN: Interferon; RBV: Ribavirin; PegIFN: Pegylated Interferon

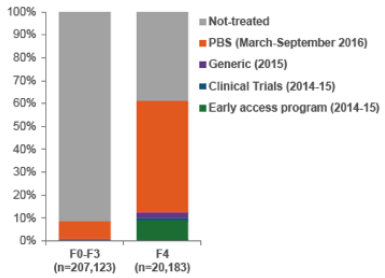


Figure 4: Distribution of DAA therapy uptake from 2014 to September 2016 in Australia, by liver fibrosis stage

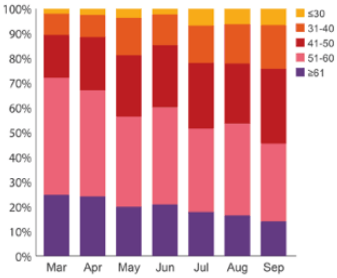


Figure 3: Age distribution of individuals initiating DAA treatment in each month during March to September 2016 in Australia

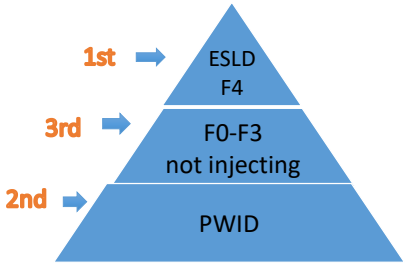
Hajarizadeh, B. et al., 2017, EASL.

Prioritising promise

- Who to treat & first: continued relevance in many contexts
- Prioritisation based on clinical & public health outcomes
- Morbidity /mortality reduction (ESLD) + transmission reduction (PWID)

The challenge for health systems will be whether they can orientate health services to offer therapy to individuals with both advanced fibrosis and PWID in the context of the current high drug prices [1].

- What populations and benefits, are omitted?



Prioritisation Triangle

1. Doyle et al., 2015, *International Journal of Drug Policy*

Redefining benefit?

- Questioning the benefits of SVR for mild disease

"Do high percentages of SVR translate into long term clinical benefit?" [1]

"More realistic expectations may lead to patients making more conservative treatment choices if the benefits on offer are accepted to be modest" [2]

- Conflation of clinical and overall patient benefits

Since most people infected with HCV never develop symptoms and will die from other causes, exposing them to the harms of [DAA] treatment with no possible benefit might outweigh the benefits for the minority who develop end stage liver disease" [1]

- Clinical outcomes ARE patient-important outcomes

"The main concern of patients with HCV is developing end stage liver disease." [2]

1. Koretz et al. 2015, *BMJ.* *2*. Innes et al. (2014). *Gut*

Looking to the literature: non-clinical benefits

- Identity & psychological transformations [1, 2, 5, 6]

Reduced stigma & shame, enhanced self esteem, self care & ability to disclose.
"It was nice to know that somebody actually looked out for Tracy, not just 'Methadone Tracy' [5]
"I didn't want to take care of myself. I didn't care about myself. …Today, I care" [1]

- Behavioural transformations [1, 2, 3, 4, 6]

Reduction in unsafe injecting practices; cessation of drug & alcohol use; healthier lifestyles
"Everything changed. I stopped drug use … I said if I beat the Hep C, I could beat that too." [1]
"I just wanted to get rid of this … This was the incentive to get away from the drinking" [2]

- Social transformations [1, 3, 4, 6]

Improved employment, housing & education opportunities, enhanced altruism
"after SVR, 84% reported permanent housing, 64% finding employment and 56% improved education, all showing significant increase compared to pre-treatment period" [3]

1.Batchelder et al., 2015, *Drug and Alcohol Dependence*. 2. Clark & Gifford, 2015, *Health.*
3. Maticic et al., 2014, *Journal of Hepatology*. 4. Newman et al., 2013, *Canadian Journal of Gastroenterology*.
5. Rance & Treloar., 2014, *Addiction*. 6. Rhodes et al., 2013, *Sociology of Health and Illness.*

Understanding non-clinical benefits

- Overcoming the rigors of interferon therapy [1, 2, 6]

Pride and accomplishment at persevering through the "personal trial" of interferon treatment.

- Breaking symbolic stigma of hepatitis C = illicit drug use [1-6]

"I'm this close to giving up drugs, I don't want to take hepatitis C into my new life." [6]

- Experiencing therapeutic care [1, 4, 5]

Intensive therapeutic relationships; enhanced / holistic engagement: social & practical supports.
"*Looking at [service users] as a whole rather than . . .'you're an opiate addict'" [5]*
"The multidisciplinary treatment team made efforts to stabilize and improve patient incomes" [4]

- Patient citizenship: working to demonstrate 'worth' / selection bias [2, 4, 6]

Displays of responsibility, stability & redemption / the politics of selection
"*Completing the treatment was a demonstration that they had changed for the better and would do the right thing. It was explicitly linked with presentations of new clean and sober selves" [2]*

1.Batchelder et al., 2015, *Drug and Alcohol Dependence*. 2. Clark & Gifford, 2015, *Health.* 3. Maticic et al., 2014, *Journal of Hepatology*. 4. Newman et al., 2013, *Canadian Journal of Gastroenterology*. 5. Rance & Treloar., 2014, *Addicton.* 6. Rhodes et al., 2013, *SHI.*

Impact of DAAs on non-clinical outcomes?

We eliminate the virus but we also cure the patients, which are two different things and the new treatments will carry on eliminating the virus but may not cure the patient. (London Hepatologist)

Elimination: SVR

Cure: identity, behavioural and social transformation (irrespective of SVR)

Potential factors informing 'cure'	Interferon era	DAA era
Interferon rigors	YES	NO
Breaking stigmatising associations	YES	YES
Patient citizenship/selection	YES	Perhaps not …
Therapeutic relationships	YES	Perhaps not …

Cure & care in action: a London case study

The Hepatitis C Treatment Journey (2012-2016)

AIM: To longitudinally assess HCV support needs and treatment experiences/outcomes

Sites: 2 London hospitals, 1 drug treatment service

Data generation:

- 1-5 interviews with 28 people with HCV. From referral up to 18mths after tx completior
- Interviews with 8 stakeholders & 10 providers
- 3 focus groups exploring issue of delayed diagnosis (n=16)
- 5 focus groups/workshops targeted at resource production (n= 17)
- 100 hours of clinic observations

NIHR funded.

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Cure: treatment = social transformation

Anticipated

I want to go back for my son. I want back to normal without anything, without drugs, without the hepatitis … Because she [mother] tell me "oh no, you don't see your son, because it's infection". (Ivor)

I found out I got hep C … me life's over, that means women are gone … I'm scared of giving it to them … It was the biggest [treatment incentive] for me. (Ryan)

"I want to sort myself out, and I want to come off methadone as well" (Bobby)

Experienced

"It's amazing . . . I'm clean. I don't feel like a leper anymore" (Bella)

"I'm glowing with happiness, I now have the normal worries of life " (Liam)

None of this would have happened if I hadn't done the treatment, I wouldn't have got fixed, I wouldn't have sorted me drinking out and I wouldn't have had any future. So the treatment has been massive, it's made a big difference. (Ryan)

Care: beyond the biomedical

B has an Xbox mag …. he asks the nurse to read one of the names of a new game to him, then pulls out an envelope – asks her what it means. She reads the letter and explains that it is about National Insurance. She is incredibly patient, going over implications of the letter and assuaging his fears re payments etc. When we later talk she says he is dyslexic and brings all his official letters for her to read. (field notes, 2014)

We write housing letters, we write solicitors letters, many a time I've had solicitors email me and can I have that, you know, housing, DLA but you just do, the key workers as well, they'll phone you and say, do you mind and I say, no, and it's easier for us to do it, we see them on treatment. (London CNS 3)

I feel like we should be providing an holistic service and if I have to fill in someone's benefit application then that's what it is, you know, I'll do that. (London CNS 4)

Care: supporting through difficulty & isolation

I'm just really glad to be with her [nurse]. Unbelievable. I'm so lucky … she's behind you all the way, if she can do anything for you she will, she keeps you good I think. (Bella)

He's brilliant because he talks to me as well, you know "How you feeling mentally, emotionally? How are you coping? Yeah, he's really good (Abel)

She'll always come up to me and say something like "Oh I meant to tell you this" … I'll get an email "I forgot to tell you" or something, she does stay in contact quite a lot …. she's become like my grandma to me, something like that. (Harry)

When I came in here it cheered me up … In a way I used to look forward to the day with catching a bus and meeting someone else. (Bobby)

DAA anticipation: role redundancy?

Once treatments get easier … they're going to say "well why do we justify a team of nurses when treatment is so much easier and, you know, do you need to be so specialist? Can't they just be seen in clinics?" (London CNS 1)

Do I think that things will change, what CNS wise? Oh you won't need us we'll need to find new jobs … I don't think you'll lose us completely but I think we will be halved at the very least … why would you need six nurses when you're giving drugs that are one tablet once a day for 12 weeks with no side-effects, you'll probably do bloods once, why do you need so many CNSs? (London CNS 2)

"When we do get to that regime where it's just one pill a day for 12 weeks, can a GP just prescribe it? Done it" (London CNS 3)

Pharmaceuticalisation

- Comprises a focal shift from "prevention and clinical care" to "access to pharmaceuticals" (Biehl, 2007).
- The pill rather than 'treatment' cures the patient
- 'Good care' = efficacy of the pharmaceutical rather than the therapeutic relationship (provider largely absent)

Directly Observed Treatment: an 'intensive model of care' in DAA era.

Prevail study (Litwin et al., 2017) – PWID randomised to individual (self-administered), DOT (with OST), Group treatment.
Outcomes: adherence, treatment completion, SVR12. (adherence higher for DOT, high completion and SVR all groups)

Implications for the DAA era?

You get a free therapist for an hour a week, it's great. I think there are all sorts of complex issues, it's certainly as we go forward, it will not be as simple as just handing out the pills, there's more to this, you know, human beings are not simple machines that you slot pills in and they get better or they behave by an algorithm. (London Hepatologist 2)

He's become so much more positive, he really feels like he's achieving something because he's on treatment, he's cut down on his alcohol. He's not using, he's was using a lot of cocaine at the weekends, he's not doing any of that … he feels really good about himself …. We were talking about as to whether it is the fact that he's getting a lot of [support] …. you really do end up building a very close rapport with patients …. sometimes I phone patients between appointments to see how they are and they're like really kind of, like oh I can't believe you're phoning me … generally speaking we seem to have found that it does have a very positive impact on people moving forward with their lives. (London CNS 1)

Summary / Discussion

- The promise & prioritisation of DAAs focus on clinical & public health outcomes.
- Evidence for interferon-era non-clinical 'transformative' treatment benefits.
- Interferon difficulty & candidacy criteria may inform some of these benefits – both are subject to change.
- Intensive therapeutic encounters, associated with supporting people through interferon treatment, have transformative potential.
- The simplicity, safety & need for DAA scale-up = increased pharmaceuticalisation of HCV treatment provision.
- What treatment outcomes are measured, valued and inform prioritisation? Do these accord with 'patient-important' benefits?
- How to sustain transformative non-clinical treatment outcomes in the DAA era?

Papers

Harris, M. & Rhodes, T. (forthcoming). **From the social relations of care to the pharmaceuticalisation of treatment: Transitions in treating hepatitis C.** *Health*

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Article in Press

Managing expense and expectation in a treatment revolution: Problematizing prioritisation through an exploration of hepatitis C treatment 'benefit'

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