

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

Author name and affiliations: Magdalena Harris

London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H9SH, UK.

Corresponding author: Magdalena Harris, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H9SH, UK.

magdalena.harris@lshtm.ac.uk , +44 75196 19865.

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

ABSTRACT

Background: Direct-acting antivirals (DAAs) have transformed the hepatitis C (HCV) treatment landscape. These highly effective drugs are, however, not available to all. In a context of DAA rationing, clinicians are advised to "manage patient expectations" about the benefits of a HCV cure. This directive particularly pertains to people with minimal liver damage and those who have ceased injecting: populations negated in contemporary prioritisation debates.

Methods: This paper engages with the assumptions underpinning HCV treatment prioritisation discourses to explore the concept of treatment ‘benefit’ from patient perspectives. Data are from a qualitative longitudinal study exploring treatment transitions and decision-making from 2012-2015. Participants comprised 28 people living with HCV, ten treatment providers and eight stakeholders, based in London, United Kingdom (UK). One hundred hours of clinic observations were conducted at two HCV treatment hospitals. Thematic analyses pertaining to treatment expectation and outcome inform this paper.

Findings: Twenty-two participants commenced treatment. The majority who were unable to access DAAs chose to commence interferon-based treatment immediately rather than wait. Participants accounted for treatment urgency in relation to three interrelated narratives of hope and expectation. HCV treatment promised: social reconnection; social redemption and a return to ‘normality’. For many with successful treatment outcomes, these benefits appeared to be realised.

Conclusion: The DAA era heralds a discursive shift: from ‘managing [interferon] risk and difficulty’ to ‘managing [DAA] expense and expectation’. Calls to ‘manage patient expectations’ about the benefits of HCV cure are predicated on clinical benefits only, negating the social impacts of living with HCV. The public health priorities commonly articulated in treatment prioritisation debates are not consistent with those of people managing illness in their daily lives. During this ‘treatment revolution’ there is a need to be cognisant of the multiple publics living with the virus and the treatment needs of those who do not fit population-health scenarios.

Keywords: hepatitis C; treatment benefit; prioritisation; rationing; patient expectations; qualitative research.

INTRODUCTION

The hepatitis C virus (HCV) treatment landscape has been transformed by the recent development and licencing of direct-acting antiviral (DAA) treatments. Highly effective, tolerable, and simple to deliver, DAAs have been heralded as a therapeutic revolution, portending the global “end of HCV” (Sussman, Remien, & Kanwal, 2014), and enabling “eradication in the United Kingdom by 2030” (Williams et al., 2014). Given that 130-150 million people live with chronic HCV globally, with 217,000 situated in the United Kingdom (UK), eradication is not a modest aspiration. Particularly as these revolutionary drugs are not available for all. Pharmaceutical pricing is a primary barrier to widespread access, with list prices for DAA regimes in the region of £39,000 per 12-week course in the UK and \$83,000 in the United States (US). In the US and Canada, DAA treatment eligibility is commonly restricted to people with advanced liver fibrosis (Burua, 2015; Marshall et al., 2016). In the UK, DAA access is limited to 10,000 people per year, with the National Health Service taking an unprecedented step in restricting treatments recommended as ‘cost-effective’ by their national guidance body (National Institute of Health and Care Excellence, 2015). Only a few countries (such as Australia and France) publicly subsidise these treatments for all, without disease stage restriction. Consequently, widespread enthusiasm for the DAA “pharmacological revolution” is tempered with debate about fiscal management and rationing modalities (Doyle et al., 2015; Hickman et al., 2016; Martin et al., 2016).

Pharmaceutical rationing acts to shape in the present the future health and wellbeing of specific populations (Novas, 2006). Who these populations are and how their futures are constructed depends on the vision embraced (Hedgecoe & Martin, 2003). Two visions, or HCV treatment prioritisation scenarios, dominate the literature, each targeting specific populations. The first: scale up and prioritise DAA treatment for people with advanced liver disease (measured by fibrosis stage), thus curtailing severe liver morbidity (SLM). The second: scale up and prioritise DAA treatment for

people who inject drugs (PWID), thus reducing incident infections and population prevalence (Innes, Goldberg et al., 2014; Martin et al., 2016). The two visions are not mutually exclusive and are often conceptualised as a step-wise process, with health systems ideally encompassing both aims (Doyle et al., 2015: 1068).

Of interest are the evidence and assumptions drawn on and created by these visions and the populations obscured or negated in this process. Discourses of mathematical modelling, including in relation to HCV treatment affordability, cost-effectiveness, and benefit, play a central role in determining prioritisation debate. For example, Innes, Goldberg and colleagues (2014) model the scenarios outlined above (reducing SLM vs incident infections) asking of their audience “which public health outcomes do we value the most?”. They recommend that people with mild fibrosis who never, or no longer, inject drugs, are directed *away* from DAA access, as HCV cure among this group does not contribute to the aforementioned public health outcomes (cf., Martin et al., 2016). Given patient expectation and the promise of highly effective and tolerable DAAs, how might this de-prioritisation directive play out in practice?

The authors advise that clinicians practice patient ‘expectation management’, as: “more realistic expectations may lead to patients making more conservative treatment choices if the *benefits on offer* are accepted to be modest” (Innes, Goldberg, Dillon et al., 2014, emphasis added). Here, a specific clinical and epidemiological conceptualisation of treatment ‘benefit’ is drawn on: the attainment of additional life years and healthy life years. A simulation model calculating these outcomes finds that the benefits of a SVR (sustained virological response or HCV ‘cure’) for older individuals (~60 years) are minimal with only a <3% chance of additional life years and healthy life years, whereas the benefits of an SVR for younger individuals (~30 years) with cirrhosis are high, at >55% (Innes, Goldberg, Dusheiko et al., 2014). Notably, the model is described as measuring “patient important benefits”, illustrating a slippage between and conflation of specific clinical benefits with

broader social and experiential benefits. A similar conflation occurs in a *BMJ* article, which states: “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.” (Koretz et al. 2015, emphasis added). Here, the case for restricted DAA treatment access is predicated on two interrelated assumptions: HCV is asymptomatic and the ‘benefits’ of an SVR are only measurable in clinical or population health terms.

Traditionally, PWID have been a focus of treatment access dispute. Concerns about PWID suitability for interferon-based regimes have been framed in terms of toxicity, multi-morbidities, adherence and re-infection, at times masking deeper concerns about the ‘worthiness’ of PWID for treatment (Rhodes et al., 2013). A growing body of literature both exposes and refutes these concerns, demonstrating: adherence and successful outcomes; low re-infection occurrence; and the citizenship work undertaken by PWID attempting treatment access (Grebely et al., 2011; Rhodes et al., 2013). Most influential in rehabilitating the image of PWID as a priority treatment population, has been the modelling work on which the vision of viral elimination is based (Martin et al., 2013). Here treatment is operationalised as a prevention strategy promising significant reductions in incident infections and population prevalence. The advent of DAA therapies, with their reduced risk profile, enhances this public health potential.

We can see, therefore, the emergence of discursive shift in the HCV treatment landscape, one informed by and impacting on questions of treatment prioritisation. This shift, from ‘*managing risk and difficulty*’ (‘difficult patients’, toxic regimes, uncertain efficacy, complex monitoring) to ‘*managing expense and expectation*’ (expectant patients, efficacious regimes, cost and capacity restrictions) is nested within a broader aspirational discourse of biomedical innovation and promise. The visions associated with this promise are framed in population-health terms, with a specific focus

on those who are very ill and on those who are engaging in risk practices. This paper engages with the assumptions underpinning these visions to explore the concept of ‘patient important benefit’, with a focus on the populations often obscured or negated in DAA treatment prioritisation debates. Data are generated from interviews with a range of people seeking HCV treatment, to explore participants’ narratives of HCV treatment expectation and map their anticipatory accounts to those of post treatment ‘benefit’. Many – no longer injecting, with minimal to moderate fibrosis (Metavir stage <F3) – fall outside current treatment prioritisation scenarios and into the category of patients requiring ‘expectation management’.

METHODS

This paper draws on longitudinal qualitative data generated for a study exploring HCV treatment transitions, decision-making, support needs and service delivery from 2012 to 2015. The study received ethical approval from National Research Ethics Service London-Chelsea (12/LO/0652) and London School of Hygiene and Tropical Medicine Research Ethics Committee (6115). Participants provided signed consent prior to data collection, received a £20 reimbursement for each interview and are assigned pseudonyms.

Sites & participants

Sites comprised two large HCV treatment hospitals and two linked drug treatment services in London. People living with HCV were recruited through site providers, and were required to have received a HCV specialist referral and to be available for interview before treatment commencement. Sampling was purposive and theoretical: aimed at maximising variation in age, ethnicity and eligibility for different treatment options (determined by HCV genotype, previous treatment experience and extent of liver damage) and, as time progressed, informed by early analytic questions and gaps. Participants were not purposively sampled for injecting history, but diversity in this category was also realised. Participants with HCV comprised 23 men and five women, from 27 to 63 years old (average 46). The

majority (n=18) identified as White British. Twelve reported former drug injecting, five current injecting (within last 6 months) and eleven reported never injecting. In addition, 10 providers were interviewed. They were eligible if they worked at one of the sites and were directly involved in HCV treatment provision. Providers comprised four consultant hepatologists and six clinical nurse specialists, recruited through researcher contact. This paper draws on analyses from the interviews with people living with HCV.

Data generation and analysis

The primary data generation methods were in-depth interviews with patients and providers and ethnographic observations in nurse-led HCV clinics. Observations explored the dynamics of patient-provider communication, information provision and treatment processes in situ, enabling triangulation through observing events also accounted in interviews. The initial interview guide was informed by the relevant literature and previous studies (cf. Harris et al., 2013) and modified for each interview cycle. Interviews were conducted by one researcher (MH) and took place between October 2012 and November 2015. Participants with HCV were interviewed in person up to five times each, at approximately three month intervals up until 18 months' post-treatment, dependent on treatment duration, outcome, and participant availability. Providers were interviewed once; resulting in a corpus of 84 interviews. Interviews were in-depth, of 90 to 120 minutes' duration, and audio-recorded with participant consent. Participants were invited at baseline to narrate their journey from HCV diagnosis (or acquisition) to the present date, with questions asked regarding medical experiences, treatment anticipations/decisions and day-to-day HCV impact. Follow up interviews addressed treatment perceptions/experiences; barriers and enablers to treatment commencement and completion and perceptions of the shifting treatment landscape. Providers were invited to talk about their perceptions of the changing treatment landscape; treatment decision making and prioritisation views and experiences.

Audio-recordings were transcribed verbatim and entered into NVivo10. Observational notes and interview transcripts were coded as collected to inform subsequent data collection and analysis. Thematic coding was conducted by one researcher (MH) and comprised five stages: 1) data familiarisation, generating analytic memos, case summaries and follow-up questions; 2) first level “top down” (Saldana, 2015) coding of interview and observation data into low inference descriptive categories; 3) line-by-line open coding within each category concentrating on the generation of data driven and in vivo codes; 4) focused coding within each category reducing and refining open codes; 5) Cross-sectional mapping of developed codes within and across overarching themes, and longitudinally by case with particular analytic focus on changes over time.

This aim of this paper is to present analyses pertaining to participant treatment decision making, expectations and outcomes in a period of HCV biomedical transition and, through doing so, to explore the relevance and fit of contemporary public health discourses regarding ‘patient important benefits’ and HCV treatment prioritisation for this population.

FINDINGS

Treatment decision-making

The nurse turns her chair to face Connor and says there are two options – the protease inhibitors with interferon, but also clinical trials coming up of the new interferon free drugs ... For him “to think about” – there will be no injection and up to 4 pills a day. He says “I just want to get started as quick as I can” ... The one reason he doesn’t want to enter the trial is the possible delay in starting treatment. (Observation notes, Dec 2012)

Throughout the study period the promise of more effective and tolerable DAA HCV treatments was on the horizon. The standard of care in the participating hospitals at study commencement was triple therapy (interferon, ribavirin, protease inhibitor) for people with HCV genotype one, and

interferon and ribavirin for those with genotypes two and three. The first-generation protease inhibitors (PIs) Telaprevir and Boceprevir, were a new treatment addition – approved for UK use in 2012. Although these PIs improved treatment efficacy, they added to the side effect and monitoring burden. Observations of the clinical encounter illustrated that that the option of treatment deferral was generally provided to patients – albeit with an uncertain timescale for DAA availability. Those who met the criteria for DAA clinical trials or compassionate access were provided with this option. Of the participants’ ineligible for a trial or compassionate access, only one chose to wait for an all-oral DAA regime, due to the potential exacerbation of his mental health condition by interferon.

Twenty-two of the 28 patient participants commenced treatment during the study duration. Ten participants (genotype one) commenced a 24-48 week regime comprising interferon, ribavirin and a protease inhibitor. Six participants (genotype three) commenced a 24 week course of interferon and ribavirin. Two participants entered clinical trials and four qualified for compassionate access to DAA treatment. For eight participants, these initial treatment rounds were unsuccessful. Sixteen of the 22 participants (72%) had a successful treatment outcome, with three experiencing post-treatment relapse, and three discontinuing due to non-response, imprisonment or poor adherence. Six participants (all drug treatment service clients) did not commence treatment during the study period, although all but one expressed a desire to start immediately.

Treatment urgency

Of note, was not only the decision by most participants to commence interferon-based therapy, but the urgency with which this decision was framed. Several participants, with mild to moderate liver fibrosis, could have safely deferred treatment. Indeed, in the clinical encounter, there was much to put patients off choosing the currently available regimens:

The nurse tells him about side effects: flu-like symptoms and mood changes, including getting tearful and depressed. He might experience difficulty concentrating and/or sleeping,

dry skin, dry eyes, persistent thirst and skin rashes. Skin rashes are concerning if they spread very quickly, particularly if accompanied by a temperature or blistering of the mucous membranes. Regular blood tests will enable monitoring of complications such as anaemia and thyroid changes. As “in a very small amount of people there can be permanent thyroid damage”. Then: “I have saved the best for last – anal pain! The treatment is excreted through your poo so that can be sore and itchy”. (Observational notes, Nov 2013)

Given this litany of misery it is surprising anyone chose treatment at all. However, most were undeterred. Ryan opted for 48 weeks of triple therapy with Teleprevir rather than waiting for the possibility of an easier regime: “I’d get rid of it straightaway ... I’d seen what it said about the side-effects and I thought, I don’t care ... I just said, get me on it. Now!” Aisha refused a clinical trial in case it prolonged her start date: “I have to get the treatment, I got the disease so I have to take the treatment I just want to start now”. Omar framed treatment as an unquestioned imperative: “if you find out you have anything wrong in your body, you must be starting treatment”. For Moira, HCV was conceptualised as a colonising ‘other’ which required immediate removal: “Can I start treatment ... I want to not let this virus thrive in me anymore, I want to do it now.”

For many, the post-diagnosis period was a time of limbo – of stasis: “I don’t want my life on hold for any longer” (Bella). Here, treatment held the promise of progress, of new possibilities. While acknowledged as unpleasant, it was necessary to action immediately: “I just want to get it done ... I just want to get it out of the way, I don’t want to be pending or wait a few years.” (Taj). Waiting was ‘messaging about’, it contravened a sense of the active, purposeful self:

I’m looking forward to getting started and getting it over with, I mean that’s me, if I’m going to do something I want to get it done ... I don’t want to fanny about, mess about, I’d rather get it done and then it’s done, straight down the line. (Bella)

With reference to the clinical literature, this treatment urgency is understandable and actionable for people with advanced liver fibrosis. It aligns with the premise that “the avoidance of end stage liver

disease is a primary patient concern” (Innes, Goldberg, Dillon, et al., 2014). How then – for participants with a variety of disease stages – were the benefits of treatment conceptualised? What factors informed this urgency?

Treatment hopes and expectation

Participants accounted for HCV treatment urgency in relation to three interrelated narratives of hope and expectation. Treatment promised: *social reconnection*; *social redemption* from the drug using past; and a *return to ‘normality’*.

Social reconnection

Ivor’s account references all three expectations – reconnection, redemption and a return to normality. For Ivor, ‘normality’ is framed as a life without drugs and without HCV. Having ceased injecting and recently weaned himself off methadone, HCV was all that stood in the way of getting “back to normal”. By facilitating a return to normality, treatment also held the promise of reconnection:

I have a son from my country and I want back for my son. I want back to normal without anything, without drugs, without the hepatitis ... I’m not close with his mother. I tell her what I’m having, HCV. It’s not nice. Because she tells me “oh no, you don’t see your son, because it’s infection” (Ivor).

Like Ivor, Ryan spoke of social dislocation due to transmission fears. Although aware that HCV is rarely transmitted heterosexually, Ryan ceased all sexual relationships after diagnosis – an action which, for him, meant the end to life as he knew it:

I found out I got hep C ... that’s it, my life’s over, that means women are gone ... I’m scared of giving it to them and I think to myself, if I can get rid of it I don’t have to worry ... It was the biggest [treatment incentive] for me. Definitely, quite far and away the biggest one (Ryan).

Ryan characterised the two years between diagnosis and treatment commencement as stasis. For this time his life “completely stopped”. Treatment was viewed with hope – it held the promise of movement, of reconnection and continuance.

Garry and Connor spoke of similar hopes and constraints. Both men described diagnosis as constituting a biographical disruption, in large part driven by transmission fears and stigma:

I knew what would happen when I told her [wife] ... "we all sit at this side of the table and you can sit on the settee over there. Don't play with the kids too rough". "Don't cuddle up at night" ... "I'm not touching you, no, we ain't going there". (Garry)

Connor's sense of self as infectious also impacted on his family interactions:

I was a bit reluctant with [grandchildren]. Well because of the disease ... I like to play with them and have a rough and tumble. I haven't been so close to them since I've had it ... it's sad, especially when they jump and try and give me a cuddle.

Perceptions of infectivity can be intractable – as Garry later stated, the provision of transmission information would not be enough to allay his wife's concerns. Treatment was the only option.

Relationships with others were central to treatment urgency accounts. In each of her four interviews Bella emphasised the importance of family and the role they played in her treatment decision-making:

Devastated for my children ... devastation, not for dying because I don't think there's anything to be scared of, but it's leaving my children, that was it for me.

HCV evoked mortality concerns for some, particularly for those who were living with cirrhosis. Yet death itself was not conceptualised as the primary fear – but the leaving of loved ones behind:

What's going to happen if I die tomorrow? What's going to happen to [partner] ... I've got to put it back together, that's who I worry about is my partner. (Bobby)

For these participants' treatment holds the hope of 'putting it back together' – of mending fractured relationships and continuing those already strong.

Redemption and return

HCV has a strong connection with injecting drug use in both the academic literature and the public imagination. This linkage, if not conflation, acts in specific ways to constitute the meanings and responsibilities associated with the virus (Fraser & Seear, 2011). As Bella articulated:

[With cancer] you wouldn't be isolated would you? You'd just be an unlucky cancer victim.

This way you've brought it on yourself through sex and drugs.

The responsibilising of HCV transmission and associated binary demarcation of people with HCV into 'innocent' or 'guilty' 'victims' is reflected in participant narratives of redemption – whereby HCV treatment offers a symbolic break with the past, either solidifying or providing the foundation for drug use cessation:

I've got to stay on it [treatment] and I've got to persevere with whatever I've got coming ... I

don't really want to stop because I want to sort myself out and I want to come off the

Methadone as well. I want to come off all drugs. (Bobby)

Here, HCV treatment is part of a broader project of 'sorting out' the self. Perseverance in the face of adverse and ongoing side effects demonstrates, to the self and others, the ability to tackle other prolonged rigors (such as methadone withdrawal) and, in doing so, facilitate a new redeemed and responsible self.

Liam and Declan also framed HCV treatment as enabling change and solidifying life transformation:

You can be 110% sure that I will carry on with the treatment because I want rid of this

affliction, be it self-afflicted ... I thought new treatment, new start. (Liam)

If I can get rid of the hep C then I know I'm on the way back ... I know I can come off the

methadone, it's just this. (Declan)

Treatment simultaneously offers a 'new start' and a 'return' – a return to 'normality' and the social body. Although Declan evokes return: "I'm on the way back", his narrative also evidences a tension between 'return' and the unfamiliarity of this desired 'normal' state: "I've never had a normal life in 42 years and this is my time to get me normal life back together."

HCV fractures 'normality' not only due to its symbolic association with drug injecting and the impact of contagion fears on social relationships, but also because of its embodied, physical effects.

Ubiquitously described in the literature as 'asymptomatic' (e.g. Doyle et al., 2015), these physical effects rarely receive validation or acknowledgement:

I find it annoying ... people don't actually realise how much it really does affect you. The worst thing is no energy ... it knocks it out of you and you just don't feel like doing anything and it just kills it all, ever so slowly and then you realise it. (Harry)

Bobby spoke of how HCV had rendered his body foreign to him. Treatment not only offered the hope of sustained life with his partner, but of inhabiting his body as he used to: "I might have a few years left still and I want to feel good ... I'm in bad shape ... I mean I used to be a fighter."

Treatment outcomes

Participant narratives demonstrated an extraordinary investment in the promise of HCV treatment – with treatment urgency figured in terms of resurrecting social relationships, enabling drug use cessation and providing a return to 'normality'. In the light of calls for 'patient expectation management' it is pertinent to ask if these hopes were realised. Did treatment live up to its promise? Was the urgency with which participants framed their decision warranted? The longitudinal method of the research enables an exploration of these questions.

Reconnection: exceeding the social

Desires and hopes for reconnection prior to treatment commencement were primarily figured in terms of social relationships and negating transmission fears and stigma. For Garry, Bobby and Ivor, treatment was either unsuccessful or interrupted by incarceration. Their reconnection hopes and expectations remained unrealised. For those with successful outcomes, social reconnection expectations appeared fulfilled: “It’s amazing ... I’m clean. I don’t feel like a leper anymore” (Bella), “I pick them up and play with them [grandchildren] now” (Connor), “I’m fixed so I don’t have to worry about how I deal with people like I was before” (Ryan).

While pre-treatment reconnection hopes were framed in terms of the social, participant’s post-treatment accounts drew on a broader frame of reference. Connor described treatment success as providing not only a reconnection with others, but with a previously hidden side of the self:

[Before treatment] foggy, like if I watched a sad film, nothing, but if I watch it now I get the tear roll down. Never had it before. I felt it but not connecting properly I didn’t realise how ill I was. It [HCV] affected my brain, it affected my sex drive, it affected all parts of my body ... it’s all gradually reappearing, it’s like being born again ... it’s funny how you get used to something and don’t realise.

Moira also spoke of a renewed embodied connection:

My mood is different, my thinking is different, it’s hard to explain but I feel like a different person, I feel like the person I used to be some years ago ... I was overwhelmed with the symptoms but not recognising them and putting them down to different things.

Return and redemption: a reappraisal

These narratives of rebirth and renewal are both determined by and trouble the biomedical discourse of HCV as ‘asymptomatic’. It is only once the virus is cleared that its symptoms become evident. This reappraisal of what it was to be ‘normal’ was common to the majority of participants

who cleared the virus. Thus 'normality' was framed not so much as a 'return' but as a reawakening.

As Bella said:

You can see then if you look back ... you can see and pick out things ... It was the illness, but you don't know at the time. It's your normal so you don't know any different.

For Ryan, HCV treatment precipitated an unexpected, and sustained, break from his heavy drinking – the old 'normal':

I'm thinking "what is gonna be normal?" Because I'm not drinking, that's not normal for a start. And I probably won't go back to it. I don't think I'll go back to the way I was, no.

Liam's reference to 'normal' speaks to the realisation of his redemptive hopes ("new treatment, new start"). Treatment success constituted a final break with his drug using past: "I'm glowing with happiness ... I have now the normal worries of life, what people have".

Expectations: exceeded and constrained

For many, the post-treatment experience exceeded expectations. Treatment success, in and of itself, permitted a future:

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 ... I've got a future now. (Ryan)

For some, embodied inscriptions of marginality were resistant to treatment success. Connor spoke of how HCV, even in its absence, still made him "feel dirty": "It's associated with drug addicts, prostitution, *you've no getting away from it.*" Connor's overarching post-treatment narrative was of rebirth and renewal. This slightly disjunctive statement illuminates the stickiness of HCV stigma – a residual underbelly of shame in an otherwise sanguine account.

For Kaiser, HCV stigma was not only sticky but scarring. When asked if there was "any spark of light" in having cleared HCV, he replied:

No, because the scarring's already there. Mental scarring ... things that she said to me that, even though I've cleared the virus, still hurt, mentally ... *It doesn't just go away.*

This is not an account of dashed expectation. Kaiser's pessimism preceded treatment commencement – and was not alleviated by its success. In this respect 'clearing' or 'curing' HCV is not clear cut. While biological markers can indicate absence, scars – both mental and physical (those on the liver and others less tangible) might remain. As Pedro, at seven months' post treatment, illustrates:

I am tired, my mood is very low. I am sad about that. My symptoms are the same, worse than before. ... I am pleased the HCV is gone, but I am very confused ... Apparently I am not sick, but at the same time I am feeling worse than before.

Here, the post treatment period is one of heightened liminality. No longer officially ill, Pedro and Kaiser continue to live encumbered with the memory of the virus.

Discussion

At a time of HCV treatment transition, most participants chose to commence a complex and potentially debilitating interferon-based regime rather than wait for the DAAs. This is notable regarding participants with minimal fibrosis, for whom treatment deferral and 'expectation management' are increasingly proposed (Innes, Goldberg, Dillon, et al., 2014; Rice, 2015).

Commencing treatment was spoken of with urgency – as holding the promise of movement from a place of stasis and disconnection to the opening up of multiple possible futures. For some, these expectations were exceeded – with accounts of reconnection not only to the social, but to a previously unattainable self. For others, these expectations remained unrealised – either due to treatment failure, or because of the residual stickiness of HCV stigma and symptoms. Participant accounts of treatment expectations and outcomes do not accord with predominant prioritisation discourses in that they gave little weight to clinical markers, such as stage of liver disease. Notably, the healing promise of treatment was primarily existential – it could 'fix', 'sort out' and mend a

fractured self. As explored below, these accounts are produced in conjunction with experiences of specific treatment systems and cultural narratives of biomedical promise and personal redemption, yet they can also be read in terms of social suffering (Honkasalo, 2006) – a suffering rarely acknowledged in treatment prioritisation debates.

The making and managing of expectations

Accounts emphasising perseverance and/or the promise of rehabilitation are common to the qualitative HCV treatment literature (Clark & Gifford, 2015; Harris et al., 2013; Rance & Treloar, 2014; Rhodes et al., 2013) and intertwine in study participant narratives. Taking on a difficult interferon-based treatment now, as opposed to an easier DAA therapy later, accords with cultural scripts of redemption through personal trial (Clark & Gifford, 2015; Coupland & Maher, 2010) and demonstrates an active responsible citizenship (Rhodes et al., 2013). This demonstration aligns with the forms of subjectivity accepted and performed by treatment systems (Fraser & Seear, 2011) where most treating clinicians favour individuals who are perceived to be responsible and stable, particularly in terms of recovery from drug use. In order to obtain treatment, certain performances are made; those unwilling or unable to demonstrate stability and perseverance are required to wait. Treatment narratives are, therefore, local productions in context – they reflect attributes of the institutional health policies, services and cultures in which treatments are realised (Clark & Gifford, 2015).

It is for this reason, among others, that a sample was selected who were yet to commence treatment, with the longitudinal design allowing analysis of both temporal change in expectation/experience and of the circuits of exclusion and inclusion that determined treatment involvement. Given pervasive interferon treatment barriers (Harris & Rhodes, 2013; Treloar et al., 2013), it is perhaps unusual that such a high percentage commenced treatment – particularly during this time of biomedical transition. The study sampling criterion of specialist referral requires

acknowledgement here, with those reaching this stage likely to have demonstrated treatment interest and/or be less impacted by institutional barriers to treatment access. The six participants not to commence HCV treatment were all drug treatment service clients. For all but one, their desire to commence treatment was high. Structural barriers such as homelessness can be seen to preclude uptake for some (see Harris & Rhodes, 2016), yet this also reflects institutional preferences for 'stability' as outlined above.

With the move from interferon to DAA treatments, and associated discursive shift from 'managing risk and difficulty' to 'managing expense and expectation', prioritisation preferences are subject to change. Increased acceptance of PWID as a priority population has coincided with treatment deferral recommendations for people with mild disease who are not injecting. This is a notable shift, one that draws on a population health appraisal of benefit and need. The benefits posited are for health systems (treat advanced disease = reduce SLM burden) and populations (treat PWID = reduce disease prevalence) rather than assessed in individual terms. As outlined in this paper, these public health visions do not necessarily resonate with those managing HCV in their daily lives.

Rationed expectations and constructed futures

Regarding a future of managed expectations, the choices made by participants in this study are potentially prescient. For those marginalised, injecting or not, 'choice' is often circumscribed. Many had been waiting for a treatment opportunity, and the timescale for DAA access was unclear. Protease inhibitors were 'new drugs' – holding promise of a successful outcome, along with increased toxicity and risk. Moreover, expectations of access to better treatments were rationed. Accounts of rationed expectation and biotechnical embrace intertwined in participants' narratives; with analysis of the latter opening up perspectives on the former. The term 'biotechnical embrace' describes the affective response of clinicians and patients to new biotechnologies and experimental treatments (Good, 2001) and is apposite to convey participants' emotional investment in the

promise of both the old and the new to effect existential change. For many, interferon-based therapies were embraced as offering reconnection – both to the self and the social body. Hopes of reconnection, and aspirational accounts of ‘normalcy’, are premised on feelings of disconnection – of partial and precluded citizenship. A questionable citizenship status, accompanied by institutional practices of delay, can act to impede perceptions of entitlement to breakthrough drug developments.

The differential structuring of imagined futures and entitlement to biomedical advance is of concern in a context where directives for treatment prioritisation can be opaque and open to clinician interpretation. For example, the recent NICE appraisal guidelines recommend access to all-oral DAA regimens for people with HCV genotypes one and four but for access to be prioritised *for people with the highest unmet clinical need* (National Institute for Health and Care Excellence, 2015). What constitutes clinical need is not defined, however the term implies privileging clinical markers of liver disease over and above lived experience of distress. The absence of a definition can provide leeway for multi-disciplinary teams to consider treatment benefit complexities, yet this also poses problems. As a review of ‘bedside rationing practices’ found, clinicians often implicitly categorize patients, with treatment allocation decisions influenced by the patient’s age, their ability to exercise pressure and “their relative contribution to society” (Strech et al., 2008).

Expected futures and their potential attainment are in this sense produced by treatment systems, public health policies and presentations of worth, stability and entitlement. The deployment of the latter are differentially influenced by class, education, wealth and social mobilisation (Novas, 2006). The construction of HCV as stigmatised, contagious, as associated with “drug addicts, prostitution”, precludes such mobilisation, particularly among people who are either criminalised due to their drug consumption practices, or who wish to distance themselves from such associations. The collectivising moment of biosocial citizenship, as instantiated by activism, is weak in relation to HCV

(Rhodes et al., 2013). While this can help to explain rationed expectations regarding the promise of future treatment and its personal attainment, it is important not to overlook or explain away the urgency with which commencing treatment **now** was articulated.

Acknowledging social suffering

Participants' narratives evidenced an extraordinary investment in the power of the biomedical to effect existential change. While these accounts are inevitably influenced by cultural scripts of biomedicine as transformative (Good, 2001), they also express experiences of social suffering that require acknowledgement. Social suffering, as "the harms done to a person's sense of social value and moral worth", "takes place in relation to events and processes that are most meaningful for people's lives, such as being in love, acquiring a sense of well-being or the ability to work" (Honkasalo, 2006: 28). Accounts of treatment urgency were primarily framed within these terms – as countering threats to what was at stake, what mattered. For Ivor, this was being able to see his son; for Ryan and Gary, being able to commence and sustain sexual relationships; for Connor, Gary and Bella – to enjoy uninhibited play with their children and grandchildren. In these terms, the anticipated and realised benefits of treatment success were immeasurable. We need to ask therefore, if treatment benefit can be purely conceptualised in clinical terms, and – in relation to treatment prioritisation policies – is it ethical to do so?

It can be argued that the examples provided above evidence misconceptions; that this suffering could be ameliorated by information provision as much as treatment. HCV is very rarely heterosexually transmitted and not contracted through practices such as hugging and playing. This however, is not simply a matter of ignorance; of inadequate knowledge transfer. While many participants realised the risks articulated were minimal, the symbolic weight of HCV stigma constrained their actions. Normalcy talk references this symbolic weight; it evidences awareness of occupying a socially undesirable status (Nettleton, Neale, & Pickering, 2013). Prior to treatment

'normality' was aspirational rather achieved – life without, rather than with, HCV. HCV connotes abjection, due to associations with injecting drug use, but also contagion and physical debility (Harris, 2009). For the symptomatic, ubiquitous references to HCV as 'asymptomatic' in clinical practice and literature (Doyle et al., 2015) can amplify experienced disconnection and stigma (Harris, 2009). Although there is a literature referencing and quantifying HCV quality of life (Younossi et al., 2015; Whiteley et al., 2015), this concept lacks potency in expressing the social suffering experienced by many.

Conclusion

In this period of transition from *'managing risk and difficulty'* to *'managing expense and expectation'* it is crucial that the impact of HCV on the social is accorded weight in clinical literature and practice. The existential promise of treatment to alleviate social suffering can render expectations impervious to clinical management – posing problems for clinicians assigned this task. Treatment systems fashion the accounts of those engaged with them, as well as pre-selecting research accounts available to access. Changing circuits of biomedical inclusion and exclusion may mean those previously deemed 'unstable' become prioritised for treatment, producing different accounts of expectation and imagined futures. For most participants in this study, their treatment urgency was deemed not clinically necessary, and indeed – in an era of biomedical innovation – could be perceived as self-defeating. However, in a context of rationed expectation, this urgency operated to counter threats to what mattered: offering the promise of reconnection, continuance and return – both to the social body and a previously unattainable self. Until there is a fundamental change in associations of HCV with the abject it is imperative that these social benefits are acknowledged in prioritisation debates.

Acknowledgements

Thank you to all the participants who gave their time for this study. Also to Professors Lisa Maher and Charlotte Paul for valuable comment on manuscript drafts. The study was funded by The National Institute of Health Research, grant number [NIHR-PDF-2011-04-031].

References

- Barua, S., Greenwald, R., Grebely, J., Dore, G. J., Swan, T., & Taylor, L. E. (2015). Restrictions for Medicaid reimbursement of sofosbuvir for the treatment of hepatitis C virus infection in the United States. *Annals of Internal Medicine*, *163*(3), 215-223.
- Clark, J., & Gifford, A. (2015). Resolute efforts to cure hepatitis C: Understanding patients' reasons for completing antiviral treatment. *Health*, *19*(5), 473-489.
- Coupland, H., & Maher, L. (2010) Notions of injecting drug users' candidacy for hepatitis C treatment: Conflicting provider, patient and public health perspectives. *Contemporary Drug Problems*, *37*(4):549-573.
- Doyle, J., Aspinall, E., Hutchinson, S., Quinn, B., Gore, C., Wiktor, S., & Hellard, M. (2015). Global policy and access to new hepatitis C therapies for people who inject drugs. *International Journal of Drug Policy*, *26*(11), 1064-1071.
- Fraser, S., & Seear, K. (2011). *Making disease, making citizens: The politics of hepatitis C*. Surrey, Burlington: Ashgate.
- Good, M.-J. (2001). The Biotechnical Embrace. *Culture, Medicine and Psychiatry*, *25*(4), 395-410.
- Grebely, J., Matthews, G., Hellard, M., Shaw, D., Van Beek, I., Petoumenos, K., . . . Dore, G. (2011). Adherence to treatment for recently acquired hepatitis C virus (HCV) infection among injecting drug users. *Journal of Hepatology*, *55*(1), 76-85.
- Harris, M. (2009). Injecting, Infection, Illness: Abjection and Hepatitis C Stigma. *Body & Society*, *15*(4), 33-51.
- Harris, M. & Rhodes, T. (2013). Hepatitis C treatment access and uptake for people who inject drugs: A review mapping the role of social factors. *Harm Reduction Journal* **10**:7

- Harris, M., Martin, A., & Rhodes, T. (2013). Taming systems to create enabling environments for HCV treatment: Negotiating trust in the drug and alcohol setting. *Social Science & Medicine*, 83, 19-26.
- Harris, M., & Rhodes, T. (2016). Scaling up hepatitis C treatment: taking into account the needs and perspectives of people who inject drugs. In N. Martin & M. Hickman (Eds.), *EMCDDA Insights: Hepatitis C virus infection treatment among people who inject drugs* Lisbon: EMCDDA.
- Hedgecoe, A., & Martin, P. (2003). The Drugs Don't Work: Expectations and the Shaping of Pharmacogenetics. *Social Studies of Science*, 33(3), 327-364.
- Hickman, M., Martin, N. K., & Huxtable, R. (2017). Hepatitis C virus prevention and treatment prioritization—ethical, economic and evidential dimensions of early rather than delayed treatment for people who inject drugs. *Addiction*, 112(2), 201-203.
- Honkasalo, M.-L. (2006). Fragilities in life and death: Engaging in uncertainty in modern society. *Health, Risk & Society*, 8(1), 27-41.
- Innes, H., Goldberg, D., Dillon, J., & Hutchinson, S. (2014). Strategies for the treatment of Hepatitis C in an era of interferon-free therapies: what public health outcomes do we value most? *Gut*.
- Innes, H., Goldberg, D., Dusheiko, G., Hayes, P., Mills, P., Dillon, J. et al. (2014). Patient-important benefits of clearing the hepatitis C virus through treatment: A simulation model. *Journal of Hepatology*, 60(6), 1118-1126.
- Koretz, R., Lin, K., Ioannidis, J., & Lenzer, J. (2015). Is widespread screening for hepatitis C justified? *BMJ*, 350.
- Leidner A.J., Chesson H.W., Xu F., Ward J.W., Spradling P.R., Holmberg S.D. (2015). Cost-effectiveness of hepatitis C treatment for patients in early stages of liver disease. *Hepatology*, 61:1860–1869.

- Marshall, A. D., Saeed, S., Barrett, L., Cooper, C. L., Treloar, C., Bruneau, J. et al. (2016). Restrictions for reimbursement of direct-acting antiviral treatment for hepatitis C virus infection in Canada: a descriptive study. *CMAJ Open*, 4(4), E605-E614.
- Martin, N. K., Vickerman, P., Dore, G. J., Grebely, J., Miners, A., Cairns, J., ... Hickman, M. (2016). Prioritization of HCV treatment in the direct-acting antiviral era: An economic evaluation. *Journal of Hepatology*, 65(1), 17–25.
- Martin, N., Vickerman, P., Grebely, J., Hellard, M., Hutchinson, S., Lima, V., . . . Hickman, M. (2013). Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. *Hepatology*, 58(5), 1598-1609.
- National Institute for Health and Clinical Excellence. (2015). Ledipasvir–sofosbuvir for treating chronic hepatitis C. NICE technology appraisal guidance [TA363]. Retrieved 15 December 2015, from <http://www.nice.org.uk/guidance/ta363/chapter/1-guidance>
- Nettleton, S., Neale, J., & Pickering, L. (2013). 'I just want to be normal': An analysis of discourses of normality among recovering heroin users. *Health*, 17(2), 174-190.
- Novas, C. (2006). The Political Economy of Hope: Patients Organizations, Science and Biovalue. *BioSocieties*, 1(3), 289-305.
- Rance, J. & Treloar, C. (2014). 'Not just methadone Tracy': transformations in service-user identity following the introduction of hepatitis C treatment into Australian opiate substitution settings. *Addiction*, 109(3), 452-459.
- Rhodes, T., Harris, M., & Martin, A. (2013). Negotiating access to medical treatment and the making of patient citizenship: the case of hepatitis C treatment. *Sociology of Health & Illness*, 35(7), 1023-1044.
- Rice, J. (2015). Hepatitis C treatment: Back to the warehouse. *Clinical Liver Disease*, 6(2), 27-29.
- Saldana, J. (2015). *The coding manual for qualitative researchers*. Los Angeles, New Dehli, London: Sage

- Strech, D., Synofzik, M., & Marckmann, G. (2008). How physicians allocate scarce resources at the bedside: a systematic review of qualitative studies. *J Med Philos*, *33*(1), 80-99.
- Sussman, N., Remien, C., & Kanwal, F. (2014). The End of Hepatitis C. *Clinical Gastroenterology and Hepatology*, *12*(4), 533-536.
- Treloar, C., Rance, J., & Backmund, M. (2013). Understanding barriers to hepatitis C virus care and stigmatization from a social perspective. *Clinical Infectious Diseases*, *57*(Suppl. 2), S51–S55.
- Whiteley, D., Elliott, L., Cunningham-Burley, S., & Whittaker, A. (2015). Health-Related Quality of Life for individuals with hepatitis C: A narrative review. *International Journal of Drug Policy*, *26*(10), 936-949.
- Williams, R., Aspinall, R., Bellis, M., Camps-Walsh, G., Cramp, M., Dhawan, A., . . . Smith, T. (2014). Addressing liver disease in the UK. *The Lancet*, *384*(9958), 1953-1997.
- Younossi, Z. M., Stepanova, M., Marcellin, P., Afdhal, N., Kowdley, K. V., Zeuzem, S., & Hunt, S. L. (2015). Treatment with ledipasvir and sofosbuvir improves patient-reported outcomes: Results from the ION-1, -2, and -3 clinical trials. *Hepatology*, *61*(6), 1798-1808.