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The lived experience of interferon-free treatments for hepatitis C: a thematic analysis

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Abstract

BACKGROUND: International discourse concerning the evolution in hepatitis C virus (HCV) therapy has tended to focus on improving outcomes, shortened treatment length and reduced side-effects of interferon-free regimens. How these treatments are being understood and experienced by the people receiving them has so far been overlooked. This study therefore aimed to explore the lived experience of individuals taking interferon-free HCV therapies.

METHODS: Data were generated through 16 semi-structured interviews with a purposive sample of eight participants, recruited from a university hospital in Scotland. The interviews took place between June 2015 and March 2016, before and after a period of interferon-free HCV treatment. The data was interrogated using a thematic analysis, underpinned by social phenomenological theory.

RESULTS: Three overriding themes were identified. 'Expectations and realisations' characterised the influence that interferon continued to cast over interferon-free treatment, contrasting the practicalities of taking interferon-free therapy with preconceived notions. 'An honour and a pleasure' portrayed a positive experience of an undemanding therapy, yet amongst those with a

history of drug use, was also positioned as a privilege, associated with feelings of luck and guilt. ‘Treatment needs’ illustrated the strategies participants used to search for treatment efficacy, and the value those with a significant history of drug use placed on support. One nonconforming case is then discussed to enhance rigour and trustworthiness.

CONCLUSION: This is the first qualitative exploration of the experience of interferon-free HCV treatment reported globally. The results from this study suggest a cultural lag exists between the pharmacological developments which have been witnessed, and societal understandings of them. This has implications for the way services meet the needs of, and offer therapy to, HCV positive individuals.

Background

Recent years have witnessed a rapid evolution in the treatment options available for people living with the hepatitis C virus (HCV) (Chung & Baumert, 2014; Pawlotsky *et al*, 2015). The summer of 2011 signalled the beginning of a new era in the fight against the disease, with the first direct-acting antivirals (DAAs) entering clinical practice in many high-income nations (Chung & Baumert, 2014). Although these drugs were initially added into the existing treatment regimen of pegylated interferon-α and ribavirin, swift pharmacological developments resulted in the advent of second generation DAAs which no longer required the notoriously unpleasant interferon-α backbone (Pawlotsky *et al*, 2015). These advances shortened the length of treatment to twelve weeks or less; reported a considerable reduction in side-effects; and improved sustained virological response (SVR) rates to over 90% (Asselah *et al*, 2016).

Globally, multiple barriers to accessing these medications at the patient-, provider- and governmental-level have led to only a minority of infected patients receiving them. Patient-level barriers include such issues as a lack of symptoms and social stigmatisation. Provider-level barriers encompass factors such as physicians' undue emphasis on purported contraindications to therapy (McGowan *et al*, 2013), such as exclusion criteria which penalise current injecting drug users. However, the barriers found at the governmental-level, largely concerning the high costs of these medications, are often cited as the most significant global barrier to patients receiving the best and most effective treatments available (Fung, 2015; Reau & Jensen, 2014). In Scotland, the high

medication costs have led to restricted approval of a number of interferon-free regimens, allowing access for individuals with HCV genotype 1, but denying access to individuals with other HCV genotypes unless deemed ineligible for interferon-based therapy (Healthcare Improvement Scotland and NHS National Services Scotland, 2015). However, access to treatment is only one facet of achieving successful outcomes. Gaining insights into how HCV treatment is experienced and understood is also crucial when considering how treatments can be successfully delivered and monitored in clinical practice.

Qualitative investigation into the experience of taking interferon-based treatments has provided valuable insight into this arduous and demanding course of therapy for many years. The findings from this body of work have demonstrated the severity and persistence of a range of both physical and psychological side-effects, including chronic fatigue, flu-like symptoms, myalgia, insomnia, alopecia, weight loss, mood swings, anxiety, and depression (Fraenkel *et al*, 2006; Hopwood & Treloar, 2005; Kinder, 2009; Sheppard & Hubbert, 2006; Taylor-Young & Hildebrandt, 2009; Zickmund *et al*, 2006). Further, these studies have explored how this litany of treatment-related ailments has broader social implications. They describe how interferon-based therapy can affect an individual's self-identity and their perception by others (Janke *et al*, 2008; Sheppard & Hubbert, 2006), can strain relationships with family and friends (Sgorbini, O'Brien & Jackson, 2009), and contribute to social isolation (Fraenkel *et al*, 2006; Janke *et al*, 2008; Taylor-Young & Hildebrandt, 2009). Accounts of interferon-based regimens are frequently framed as "horror

stories" within the literature, emphasising the gruelling nature of treatment and the fear and anxiety it can produce (Kinder, 2009).

To date, there has been no similar exploration into the experience of taking interferon-*free* therapies. The prevailing discourse surrounding these new treatments emphasises their ease and tolerability (Coppola *et al*, 2015; Lam *et al*, 2015). However, this understanding is largely based on the results of quantitative health-related quality of life measures (Whiteley *et al*, 2015; Younossi *et al*, 2015a), which provide little context as to how an 'easier' treatment is actually experienced, and what it means for the individuals taking the medications. The aim of this study therefore, is to explore the lived experience of individuals taking interferon-free HCV therapies.

Methods

Theoretical Framework

The study is underpinned by a social phenomenological framework. This sociological approach to phenomenology was first espoused by Alfred Schütz (1967), and emphasises the profound influence of the social world in establishing the meaning of a phenomenon. This approach to research rotates phenomenology outwards, exploring how the understanding of a phenomenon is founded in the inter-subjective social world, and challenges the eidetic phenomenological assumption that intentional consciousness is the driving force in constituting an object's meaning (Ajiboye, 2012). Social phenomenology seeks to explore the commonalities that are found in the

subjective life-worlds of more than one actor, providing a more objective description and understanding of a subjective experience (Shaw & Connelly, 2012).

Participants

This theoretical framework necessitated a qualitative study design, comprising in-depth, face-to-face, semi-structured interviews with eight participants, both before and after their period of treatment. Participants were purposefully sampled from an infectious diseases outpatient clinic based at a university hospital in Scotland. Inclusion criteria consisted of being aged 16 years or over, diagnosed with HCV for more than six months, and able to converse in English. A maximum variation sampling strategy was employed which aimed to select a heterogeneous sample of participants, who differed in their experience of previous HCV treatment, their mode of HCV acquisition and their date of diagnosis. This sampling strategy assumes that common patterns that emerge from great variation are of particular interest and value in capturing the shared dimensions of a phenomenon (Patton, 2015). Diversity within the sample also allows for the comparative potential of the data to be capitalised upon (Mason, 2002).

Individuals who fulfilled the inclusion criteria were approached by their regular HCV nurse or doctor during routine clinic appointments, and consent obtained for their details to be passed to the researcher (DW) if interest was shown in participating. Records were not kept of how many individuals were approached

but declined to participate at this stage. Interested parties were then telephoned by the researcher, and a meeting arranged where the purpose of the study was explained, any questions answered, and written consent obtained to participate in one semi-structured pre-treatment interview, and to allow the researcher to contact them again with a view to conducting a further interview once their treatment was complete.

Whilst all participants received interferon-free treatment, they did not all receive the same drug regimen. During the study, national guidelines and local recommendations for HCV treatment with DAAs were repeatedly revised, resulting in changes to first-line therapy. In addition, variations in regimen occurred in line with factors such as degree of liver disease and HCV genotype. Also, one participant undertook an unlicensed interferon-free regimen as part of a separate randomised controlled trial. These factors resulted in the use of four different treatment regimens amongst the eight participants (table 1). In order to protect participant anonymity, the details of which regimen each individual received have not been specified. However, whether these regimens were single- or multi-tablet has been noted alongside participant quotes within the results.

Interviews

All interviews were conducted between June 2015 and March 2016 within a suitable room at the hospital outpatient clinic, and lasted a mean duration of 40 minutes. Topic guides were used, however the semi-structured approach

allowed participants the freedom to talk about their personal experiences as they wished. The pre-treatment interviews covered HCV treatment knowledge and perceptions, previous experiences of HCV therapy, and thoughts and feelings about their proposed course of medication. The questions posed to the participants were designed to be brief, simple and open-ended (e.g. “can you tell me what you know about hep C treatment?”) with their answers probed for further detail where appropriate. Follow-up interviews focused on the participants’ experiences of treatment and their views on the treatment service. In addition, during the post-treatment interviews, transcript excerpts from the participant’s pre-treatment interview were used to revisit their specific expectations and thoughts about treatment from a different standpoint. All interviews were conducted by DW, a registered nurse with ten years’ experience and who had worked as an HCV nurse specialist between 2009-2013. No access to paper or electronic patient case notes was permitted during the study. The interviews were recorded using an encrypted digital audio-recorder, and field notes were made upon completion and added to a research diary. Audio-files of the interviews were transcribed verbatim by DW, during which any patient identifiable information was obscured from the narrative.

Analysis

Six phases of thematic analysis guided the analytical process (Braun & Clarke, 2006). Each transcript was initially read and reread in full by two researchers (DW and AW) in order to ensure subsequent coding and identification of themes remained firmly rooted in the narratives. Coding was then conducted by DW

using NVivo v.10 software, and contained both deductive and inductive elements. A broad coding framework was initially devised, informed by categories found in previous qualitative research focused on interferon-based therapy, such as 'side-effects' and 'support' (Whiteley *et al*, 2015). It was considered reasonable to assume that wide-ranging categories such as these may be a feature of any treatment experience, transcending the specifics of the medications involved. More detailed inductive codes were then added to this basic structure, formed from initial impressions of the corpus of data following further readings of the transcripts. This approach served to assist with the early analysis of the data, however codes were also developed as novel and unexpected insights were met. The pre- and post-treatment interviews were compared and contrasted, with both sets of data contributing to the generation of codes. As analysis progressed, the deductive categories were dismissed, and the inductive codes combined, reviewed and revised. This process drew groups of codes together to form a number of sub-themes. Whilst depicted as a linear progression, the interviewing, transcribing and coding process occurred in parallel, with each activity informing the others. This iterative process aided the identification of data saturation; no new codes were created during the coding of the final two transcripts as the narratives aligned with sub-themes already developed. The sub-themes were then combined into candidate themes which were examined in relation to the corpus of data, field notes, and the research diary. During this process, all four authors met regularly to review, challenge and interrogate the evolving analysis.

The trustworthiness and rigor of this endeavour were enhanced in a number of ways. Regular meetings between all authors helped to contest and question any preconceptions or assumptions DW may have brought to the study due to his work history, consistent with the concept of bracketing. Within social phenomenological research, the focus of study is the inter-subjective consciousness of which we, as researchers, are a part. In order to study this inter-subjective consciousness, the concept of bracketing demands that we suspend belief in the existence of the world as we know it, and allow doubt that the world could be anything other than it appears (Ritzer & Ryan, 2011; Schütz, 1967). Meeting the participants on more than one occasion allowed initial interpretations to be revisited and verified, and ideas expressed pre-treatment to be reconsidered by both the participant and the interviewer. Immersion in the full dataset by two of the authors ensured the findings remained data-driven and rooted in the narratives, rather than becoming too removed from the participants' voice. Where available, nonconforming cases were included in the analysis, to take into account an alternative and legitimate perspective on treatment.

Ethical approval

The study was reviewed and approved by the South East Scotland NHS Research Ethics Committee 01 (15/SS/0010) and by Edinburgh Napier University Research Ethics Committee. All participants were offered a £15 supermarket gift voucher for each interview they completed in line with national guidelines.

Results

The characteristics of the sample are shown in table 2. Each individual participated in two interviews, pre- and post-treatment, with no participant drop out during the study. The themes which resulted from the analysis: expectations and realisations; an honour and a pleasure; and treatment needs, will now be examined.

Theme: expectations and realisations

The participants' initial impressions of HCV treatment were unvaryingly negative, and bound to the interferon era. They recounted a demanding and arduous course of therapy, gathered from various 'horror stories', or through witnessing others taking interferon-based treatment first-hand:

> *I talked to people an' all, all I got to hear was – this interferon is killing me, this interferon is killing me, I don't know if I can keep on doing this.*
>
> (Gary, multi-tablet regimen)

Despite each participant receiving an interferon-free regimen, and being prepared and counselled for such by their healthcare team, the discourse surrounding treatment expectations was entangled with societal understandings of interferon-*based* therapy. The influence of the drug that defined and characterised HCV treatment for over 20 years was prominent within the

narratives. ‘Normal’ life would be forfeit for the duration of their interferon-free therapy, and the potential cure would come at a short-term cost:

> *…I mean, if I spent three months of feeling a bit groggy, tired and miserable and I come out in the end, with err, you know, with err, good err, blood, err then it’s, you know, it’s worth that sacrifice…*

(John, multi-tablet regimen)

Common side-effects of interferon were referenced explicitly as expectations for interferon-*free* treatments, with discussion of practical preparations to forestall the impact of these perceived inevitabilities commonplace. For Stewart, the strength of his beliefs around the detrimental effect of treatment on his wellbeing was demonstrated in the meticulous planning that accompanied his first dose of the drugs:

> *First tablet, went home, sick bowel, towel, duvet, tissues, waiting for it to come on (…) I prepared ready to be sick, I’d, I’d sent my partner away in case I was, really ill, know, kind a’, I don’t want a’ be sick or, or screaming at people. I thought I was gonna be agitated, angry...*

(Stewart, single-tablet regimen)

Interferon was styled as a powerful and toxic drug within the narratives, and this perception of pharmacological strength was maintained when discussion turned towards DAAs. The perceived strength of these drugs equated with the expectation of physiological collateral damage. The idea of 'no pain no gain' prevailed. An unpleasant, demanding and strenuous period of treatment must surely result from drugs formidable enough to eradicate HCV.

For the majority of participants, the realisation of their worst fears and expectations did not materialise during their period of therapy, however a discourse surrounding treatment side-effects did become evident. Examination of these narratives revealed a generally mild and manageable experience, significantly removed from the imagined horrors of therapy which had been so vividly constructed. Side-effects were rarely stressed or emphasised, more commonly mentioned in passing or casually alluded to as minor inconveniences. Descriptions of specific physical ailments were embedded within concurrent narratives of feeling well, and having little to complain about:

> *…because physically I was fine, I cannae say there was anything really bad, the first two weeks, the headaches an' I got quite a lot a' bleeding noses, but then I jus' started sort a' taking painkillers for the headaches, then…when I came [to the clinic], I had quite a bit a' constipation, so they gave me something for that, but that was it, nothing else.*
>
> (Danielle, single-tablet regimen)

In addition to physical side-effects, a number of participants also related accounts of low mood and transient depression during treatment, however potential explanations for these ailments encompassed more than the pharmacology of the drugs. The physical act of taking HCV therapy brought the disease to the forefront of participants' minds, and meant confronting a reality many had previously been able to put to one side:

> *…it's got a lot to do wi' the mental side of it like, y'know, because you're really wanting this treatment a' work an you're conscious of it, you're conscious of always being on this treatment, so likes, when I wasn't I, I'd forget about it for months, I forgot all about I had hep C. Y'know what I mean?*
>
> (Steve, multi-tablet regimen)

Emotional strain during the treatment process grew from the importance participants placed on being cured of HCV. However, the impact on mental health from interferon-free treatment was considered and framed in respect to the imagined greater influence that interferon-based therapy would have, and as such its significance was diminished and symptoms became manageable. For example, the account above appeared towards the end of Steve's narrative, almost as an afterthought or addendum. Earlier in his interview Steve had described his treatment as *"nowhere near as bad on your mental health as [interferon]"* and how he *"thought the medication was fantastic*".

Despite an impression of the side-effects of interferon-free therapy being comparatively innocuous, every participant drew attention to other difficulties which they had encountered during treatment. The physical size of the tablets and the difficulty in swallowing them were emphasised, and for those on multi-tablet regimens, a sense of being misled as to the simplicity of treatment became noticeable:

> *The, the biggest thing that I think, was the fact when the new treatment came out it was, it sounded more like it was jus' like more or less a single or two single type a' tablets (…) even though the course was of three, four, five – ten different tablets that I was taking during the day anyway, so, that was the only thing that I was slightly sceptical in the way that that came across…*
>
> (Gary, multi-tablet regimen)

The accounts of participants on multi-tablet regimens underscored how the therapy was not taken in isolation, but incorporated into a life which was often already crowded with complex polypharmacy. Opioid substitution therapy, anxiolytics, anti-psychotics and anti-retrovirals were just some of the medications participants reported as part of their daily routine. Pill burden remained a significant feature of their course of treatment.

Theme: an honour and a pleasure

The majority of participants related a largely positive and favourable account of their treatment, constructing their experience of interferon-free therapy as physically undemanding and relatively straightforward. The short length of treatment and reduction in side-effects in relation to socially informed understandings of interferon-based therapy were framed as the most significant benefits of interferon-free regimens. Participants who had previous first-hand encounters of interferon-based treatment were able to make contrasts with those eventful and side-effect laden experiences:

> *…it was all easy, compared to the last time, 'cause I…'cause I done the treatment, the interferon one, an' compared to that, this was a breeze [laughs], this was like, jus' like taking y'know, Lemsip or something…*

(Keith, single-tablet regimen)

Whilst the participants' narratives were largely positive in tone, a perception from some that they had been fortunate or lucky to access these treatments underpinned the discourse. Those with histories of drug use described feeling guilty at what they perceived as good fortune of being in the right place at the right time, underlining an understanding that interferon-free therapy was not available to everyone, but a privilege and an honour. For John, the guilt he experienced was rooted in his perception that some degree of atonement should be necessary to cure a disease which he felt he had brought upon himself. The ease and simplicity of his treatment experience jarred with his

belief that a penance should be paid for the removal of HCV from his life, and that he had got away lightly compared to others he knew. John felt he had escaped HCV with impunity, and this unsettled him:

> *I'll tell you why I felt guilty about it – I've got a really close friend who's got like this medical situation, an' he copes with it brilliantly, an' he, erm, he hadn't caused it himself or anything, he was jus', y'know, erm, suffering from this condition an' he has to struggle along an' get on with it, y'know, an' I've jus' been more or less given a solution to my problem an' have kind of got away with it scot-free.*
>
> (John, multi-tablet regimen)

In addition to feeling fortunate in comparison to other people, participants' awareness of the cost of the drugs contributed to their sense of honour in receiving these therapies. Whilst feelings of shock at the expense of the medications were voiced, these views contributed to a sense of privilege in gaining access to medications which were not universally available. The price-tags of these medications were not only discussed in relation to other treatments for HCV, but also in the context of distributive justice within other diseases:

> *It makes me feel…bloody privileged, 'cause, y'know what I mean, 'cause…no' many people are getting that, I mean there's people oot*

there that've got cancers an' stuff an' they're getting knocked back for treatments that cost that much.

(Keith, single-tablet regimen)

A few participants mentioned the media as the source of their information on medication costs. However, a number of others implied that this knowledge was explicit in the discourse of the treating healthcare team, with participants trained in the price of their cure from an early stage:

I knew that fae, the first week, how much these, all these cost an' all that, I mean coming here you get taught, you get told what they're trying a' do here, an' you find out how expensive they all are…

(Stewart, single-tablet regimen)

The narratives of some participants suggested the guilt and privilege felt at being able to access such expensive therapies had implications which extended beyond HCV therapy. The experience of being prescribed these drugs strengthened, or built a resolve, that the investment made in them, both financially and personally, would reap long-term rewards:

I feel sort a', it makes me, it'll make me think twice about going back taking drugs or alcohol or getting, going back on that kind a' thing when you, you've been privileged enough for people a' fight to get you better.

(Keith, single-tablet regimen)

Theme: treatment needs

The belief that HCV treatment should be an onerous undertaking, rather than a straightforward and undemanding process, constructed a compelling discourse relating how participants subsequently searched for signs and indicators that their treatment was working. A need to substantiate the efficacy of the drugs permeated the participants' narratives, shaping a perception that side-effects were almost desirable and advantageous:

> *…when I came after four week I ask [the HCV nurse], she said do you feel anything? Are you tired or this? An' I say no, I say actually sometime I think I'm on a placebo, because there is no any effect at all.*

(Peter, single-tablet regimen)

The hunt for side-effects increased the likelihood that any irregularities may be attributed to treatment, and relatively minor events such as single bouts of diarrhoea, or episodes of absent-mindedness were automatically ascribed to the medications. The identification of possible side-effects was not the only method by which markers of efficacy were sought however. The importance to participants of hearing how they were progressing through treatment from healthcare professionals also became a recurring refrain within the narratives.

The significance of receiving results from routine blood tests detailing the downward trajectory of the HCV viral load was repeatedly emphasised, situating them as beacons of reassurance, hope and motivation:

> *…I started off really high, I was [x] million, which is very very high, an' I went down to [states much lower figure] within three weeks – that's impossible! Err, so, it's when you find out how quickly the treatment is working, err, in the first three week period an' you're thinking – that's only three weeks, so it gives you that massive hope, y'know…*
>
> (Steve, multi-tablet regimen)

In addition, a couple of participants described a further instinctive approach to evaluating the effectiveness of treatment; they simply felt better whilst taking it. Primarily describing a feeling of reduced fatigue, this discourse was present in the narratives of those participants taking interferon- *and* ribavirin-free regimens:

> *…maybe the hepatitis made me slow down but I didn't realise, an' I thought it was jus' age! An' then I thought, I supposed to be feeling less energetic [on treatment], but, I want to do things all the time (….), it was fantastic, because I was feeling better after the four weeks, I say I feel more energy…*
>
> (Peter, single-tablet regimen)

Support was framed in broad terms within the discourse, not solely focused on the practicalities of HCV treatment, but viewed more holistically, as caring for the complete individual. Whilst support was acknowledged by all participants, a sharp contrast became evident in the perceived value and need for that support between participants who recounted extensive and graphic histories of drug use, and those who did not. For those who did not, the support received, although highly regarded, was ultimately deemed unnecessary on retrospective reflection:

> *No, no, not at all, no, no. No. Not with [this drug], nothing at all, I never felt I needed any support with [this drug], not at all, not at all.*
>
> (Happy, single-tablet regimen)

By contrast, the discourse from those with a history of drug use and drug dependence treatment emphasised the significance of support, highlighting its value to both practical and emotional aspects of therapy:

> *…it is quite hard to jus' keep it, doing it yourself (…) it's really quite difficult, erm, you may think oh it's easy jus' take it err next, nine in the morning, nine at night, but likes, when you're not working an' you're likes, err, like I said, really heavily medicated, it doesn't work out like that…*

(Steve, multi-tablet regimen)

Interviewer: *Was [the support received from the HCV treatment centre] important to you?*

Keith: *Aye, it was good to come here.*

Interviewer: *Why?*

Keith: *The mental, the friendship, the feeling a' care, people caring about you, d'you get what I mean? If you do that in the community you're jus' going in a' see somebody, you're getting your tablets an' you're fucking off for three months, it's no' gonna be the same. You're no' gonna have that…*

(Keith, single-tablet regimen)

For these individuals, support was portrayed as an expected, integral and essential component of the HCV treatment package, irrespective of the HCV drug combination or ease of therapy. This is well illustrated by Danielle, who felt short-changed and cheated by her interferon-free course of therapy compared to other people she knew prescribed interferon-based regimens:

…oh, I don't know how a' explain this one really. I think people are all getting treated differently, right, when you're on triple therapy , right, you're getting all the support, all *the support, money-wise, mentally, the doctors, all the rest a' it, this therapy you dunnae get nothing.*

(Danielle, single-tablet regimen)

Of note, peer support was repeatedly mentioned as being of particular worth to this sub-group of participants. They spoke of the immense value it had contributed to their experience, and positioned repaying that support, and using their own experience to benefit others, as a natural and obvious next step. For Gary, this step had already been taken as he described placing himself at the centre of a local support network:

…speaking out aloud at the group an' being one of the fore [pauses] I was gonna say forefathers there! Because we've jus' kinda taken it from nowhere an' we've put ourselves up for being this support, support group, now we're looking at the angles where we can, can take things…

(Gary, multi-tablet regimen)

A nonconforming account

Gary's experience of treatment grated with the predominant discourse emerging from the other participants. Whilst the expectation of a demanding course of therapy was widely held, Gary was alone in having his worst expectations confirmed:

> *…I started getting quite violently ill, sick, migraines, constant headaches were coming along, I spent about two weeks, literally, feeling like vomiting, couldn't move off the sofa, lying in the same clothes, never had any energy, very lackadaisical, very very aggravated, I got myself so agitated, they ended up putting me on erm…[an antipsychotic], 'cause a' my, I was so, getting so stressed…*
>
> (Gary, multi-tablet regimen)

Whilst Gary was not alone in experiencing side-effects, his account was unusual in the prominence he gave them. He characterised his experience of treatment as one of illness and disorder, in contrast to other participants whose narratives mainly emphasised wellness and vitality punctuated by occasional complaints. It is possible that these medications may have severe adverse side -effects for a minority of people taking them. However, Gary's narrative displayed a depth and intensity of expectation which was noticeable among the collected testimonies, and positioned his temporary illness as an absolute necessity in order for his therapy to be effective:

…I, I, I kinda got to that stage where I knew, for treatment to be successful, there's gonna be, there's gonna *be elements a' illness in there, it's gonna do things to your body, so – aye, I kinda jus' kept my mind in that…*

(Gary, multi-tablet regimen)

…jus' because I knew, listen, this is part of it, an' I kinda structured my mind so I know I've gotta get ill to get better type a' thing.

(Gary, 38, multi-tablet regimen)

Whilst initially appearing divergent from the prevailing discourse, Gary's narrative strengthens and augments many key aspects of the themes found within the collected data, emphasising the importance of considering the themes collectively, rather than in isolation. Although he did not describe the primarily positive experience of treatment constructed by the other participants, he acknowledged the luck he felt in receiving it, and assembled an account which reinforced the discourse concerning treatment needs and the hunt for efficacy. Whilst it is possible that Gary experienced an atypical physiological reaction to the medication he was given, the side-effects he experienced may also have been borne of a belief that HCV therapy needed to be powerful, and the more toxicity he experienced, the greater the chance of the treatment working. His testimony suggests that despite his difficulties, he believed the treatment he was taking was having a curative effect:

I never ever thought to myself I'm gonna stop this treatment, but there was, that niggling in the back of my head saying – can you carry on? I thought, no, I've come this far, I'm, I'm not gonna back out an' stop my treatment, no matter how hard-core it is…

(Gary, 38, multi-tablet regimen)

Discussion

Quantitative reports of health-related quality of life during interferon-free HCV treatments have noted improvements in both mental and physical health domains compared to interferon-based regimens (Younossi *et al*, 2015a; Younossi *et al*, 2015b; Younossi *et al*, 2015c). To date however, qualitative interpretations of the lived experience of these treatments have remained absent, preventing any contextual insights into the meaning of these numeric reports of 'easier' therapies.

The experience of interferon-free HCV treatment is illustrated by the three themes previously described. These themes do not exist in isolation, but interweave within and between each individual narrative, demonstrating how understandings which have been presented discretely, are necessarily intertwined. For example, the self-monitoring and importance of support described within 'treatment needs' was not only the product of participants questioning an easier than expected treatment, but was also integral *to* the

construction of that positive experience. That is not to say tensions do not exist. For example, the accounts of side-effects discussed in 'expectations and realisations' sit uneasily next to the discourse which described participants hunting for non-existent side-effects in 'treatment needs'. These two positions should be considered in counterpoise to one another, where equilibrium was maintained between the volume and intensity of side-effects experienced and the proactive search for further signs of efficacy. This illustrates the way in which apparently contradictory aspects of these themes wax and wane in relation to each other, emphasising their fundamental interdependence.

This study reveals the legacy of interferon-α currently casts a long shadow over the experience of interferon-*free* regimens, with the participant testimonies intricately tied to the historical touchstone of interferon-based treatment. For example, discussion of side-effects continued to dominate the narratives. However, whilst the burden and severity of these ailments was the historical focus of concern (Hopwood & Treloar, 2005; Kinder, 2009; Sheppard & Hubbert, 2006), it was disbelief at the relative *absence* of side-effects which now took precedence within the participants' accounts.

The understanding of HCV therapy as a rigorous and demanding undertaking, informed the notion that effective treatment must be accompanied by toxicity and short-term suffering. Insights gained from this study suggest participants actively sought out side-effects from interferon-*free* therapies as biomarkers for the effectiveness of the drugs, echoing reports from the interferon era which

found participants expecting to be unwell in order to get better (Taylor-Young & Hildebrandt, 2009). Although not widely reported, this phenomenon has been noted in other disciplines, particularly in the fields of oncology and rheumatology (Goodacre & Goodacre, 2004; Gradishar, 2015; Lorish, Richards and Brown, 1990), with periodic reports of patients requesting more aggressive and noxious therapies in the belief that these equate with improved efficacy (Gradishar, 2015; Trusson & Pilnick, 2016). This insight exposes a cultural lag between the rapid pharmacological developments which have been witnessed, and the social understanding of them, creating conflict between what patients *ought* to need, and what they actually require.

Whilst the majority of participants recounted a relatively straightforward period of therapy (the exception being Gary), the discourse of luck and guilt was solely located in the narratives of those participants with histories of drug use. This resonates with the acceptance of health inequalities, lack of entitlement, and the tolerance of rights violations which disenfranchised HCV communities have grown accustomed to over the years (Wolfe *et al*, 2015). The discourse of luck and guilt positions those participants with histories of drug use as submissive recipients of healthcare, rather than active and emboldened consumers. The absence of this narrative from the three participants who did not identify as drug users only serves to illustrate this point more effectively. However, the 'privilege' of treatment may also promote wider beneficial outcomes. Transformation narratives within the data suggest undertaking a course of interferon-free therapy may positively affect an individual's self-worth, and aid

personal rehabilitation, consistent with previous studies conducted during the interferon era (Batchelder *et al*, 2015; Clark & Gifford, 2014; Rance & Treloar, 2014).

All participants in this study successfully completed their treatment regimen, and subsequently achieved an SVR. Their treatment was delivered through a hospital-based clinic, however there is an emerging evidence base that moving therapy away from secondary care and into more diverse settings is a feasible objective (Alavi *et al*, 2013; Brew, Butt & Wright, 2013). Interferon-based treatments have been successfully delivered in opioid substitution settings and prisons, achieving comparable adherence and response rates to those reported in more conventional locations (Grebely *et al*, 2016; Litwin *et al*, 2009; Rice *et al*, 2012), but these support-intensive models of treatment delivery may be reviewed in light of fewer perceived patient requirements with 'easier' drugs. As interferon-free (and increasingly ribavirin-free) treatments proliferate, the clinical need for close haematological and side-effect monitoring of patients recedes (Lam *et al*, 2015), however the significance of knowing the treatment to be working, and the continued importance of support for individuals with significant histories of drug use and drug treatment are key findings within this analysis. Whilst the global HCV discourse tends to focus on improving SVR rates, reduced side-effect profiles and decreasing treatment times (Asselah *et* al, 2016; Chung & Baumert, 2014; Pawlotsky *et al*, 2015), understanding what motivates and reassures individuals whilst taking the drugs is essential in ensuring improved adherence and integral to interferon-free treatments

reaching their full potential. The cultural lag observed within this study suggests caution should be exercised in any reconsideration of how best to deliver interferon-free therapies to patients, as the experience of interferon-free treatment continues to demonstrate a significant and essential discourse of needs.

How these needs are met is an important consideration. The value placed on peer support was evident within the narratives, and emphasises that participants' appreciated support which came from within their own communities and social networks. Peer support has been recognised as an important factor in the facilitation of access to HCV services for populations that may experience significant barriers to accessing care (Crawford & Bath, 2013). The ETHOS project in Australia has repeatedly demonstrated how peer support workers within opioid substitution clinics perform a valuable role in reducing barriers to HCV care and treatment, and how these workers are regarded as highly credible and trustworthy by those they support (Keats *et al*, 2015, Treloar *et al*, 2015). Peer support has been cited as one of ten priorities for expanding access to HCV treatment amongst drug users in low- and middle- income countries (Ford *et al*, 2015), and this study suggests its value also extends to other more traditional care settings in high-income nations.

The differing account provided by Gary also highlights an important consideration; these themes and findings must be considered within the context of each individual person. The nocebo phenomenon, in which placebos

produce adverse side-effects, can also offer insight into the reporting of nonspecific side-effects in patients taking active medications (Faasse & Petrie, 2013). Patient expectations and pre-treatment conditioning are often designated as key constituents of this phenomenon. However, there are numerous personal, psychological, situational and contextual factors which have also been identified as potential components, such as learning from past experiences, and pre-existing anxiety and depression (Barsky *et al*, 2002). Whilst the thrust of this analysis stems from a realisation of largely unmet pre-treatment expectations, there may be particular individuals whose specific set of circumstances and attributes allows those expectations to be realised. Gary's narrative accentuates the importance of a contextual understanding of interferon-free treatment.

This study has a number of limitations. The participants were all recruited from a hospital-based outpatient clinic, and may therefore be more engaged with healthcare and knowledgeable about HCV treatment. The sample was also drawn from one treatment site within one geographical area, however the findings are transferable to other localities which have similar methods of treatment delivery and serve similar populations of individuals with HCV. The sample size was also small, and the findings are therefore exploratory in nature. Finally, whilst the participants were prescribed different interferon-free therapies, the primary focus of analysis was not the variation between interferon-free regimens, but how HCV treatment is understood and

experienced when it no longer includes the one drug, interferon-α, which has defined and characterised it for over 20 years.

Conclusion

This is the first qualitative exploration of interferon-free HCV treatment reported globally. It reveals that the perception of interferon-free treatment remains entwined with cultural understandings of interferon-based therapies. Despite an acknowledgement that interferon-free treatment was less physically and emotionally demanding than expected, the importance of support and reassurance remained integral to the experience of therapy for those individuals with a significant history of drug use. The way in which these medications are delivered in clinical practice now, and in the immediate future, should acknowledge and take these findings into account.

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Table 1

Table 1: Details of the four different HCV treatment regimens taken by participants.

Treatment Regimen	Single- or Multi-Tablet Regimen	Number of Participants
Sofosbuvir/ledipasvir (*Harvoni®*): combination tablet taken once daily. Licensed for use within Scotland for the treatment of HCV genotype 1 and 4, and for restricted use in genotype 3 (Scottish Medicines Consortium [SMC], 2015a).	Single-Tablet	4
Ombitasvir/paritaprevir/ritonavir (*Viekirax®*) + dasabuvir (*Exviera®*) + ribavirin: a combination tablet taken once daily, in conjunction with two twice daily medications. Licensed within Scotland for the treatment of HCV genotype 1 {SMC, 2015b).	Multi-Tablet	2
Sofosbuvir (*Sovaldi®*) + daclatasvir (*Daklinza®*) + ribavirin: combination of two once daily tablets in conjunction with one twice daily medication. Licensed in Scotland for use in the treatment of patients with significant fibrosis or compensated cirrhosis in genotypes 1,3 and 4 (SMC, 2014).	Multi-Tablet	1
Glecaprevir + pibrentasvir: fixed dose combination with pangenotypic action, currently in phase III clinical trials. Not currently licensed for use in Scotland (UK Medicines Information, 2016)	Single-Tablet	1

Table 2

Table 2: Demographic information for the eight participants. All information was self-reported by the participants during their initial interviews.

Gender	Male	6
	Female	2
Ethnicity	UK	6
	Other	2
Age	0-39	1
	40-49	2
	50-59	5
Opioid substitution therapy?	Yes	3
	No	5
Mode of acquisition	Injecting drug use	5
	Other	3
Date of diagnosis	Up to 2011	4
	2011 and after	4
Degree of liver disease	Pre-cirrhotic	6
	Cirrhotic	2
Previous interferon-based HCV treatment?	Yes	2
	No	6

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