

# Resolute Efforts: Patients' Reasons for Completing Antiviral Treatment for Hepatitis C

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and others

# Hepatitis C Research Projects

exploring patients' experiences

1. Patients' views of hepatitis C treatment completion or withdrawal (Clark)
2. Patients' experiences of antiviral treatment for hepatitis c in the VHA (Clark)
3. Veterans' adherence to direct-acting antiviral treatments for hepatitis C (Clark)
4. Understanding the roles of informal caregivers of veterans with hepatitis C (McInnes)
5. Development of a shared decision making aid for hepatitis C treatment (Kanwal)

# Hepatitis C

- New disease
  - Non-A/non-B identified 1974
- Bad disease
  - Slowly progressive liver damage
  - Cirrhosis, hepatocellular cancer
  - 5 to 20% chance, 20 years after infection
- Infectious
  - Transfusions with tainted blood: prior to 1985
  - Shared instruments of illicit drug use

- Prevalent
  - Most common blood borne infection
  - 120 – 170 million cases worldwide
  - 3% of US population
  - 5 to 10% of population served by VHA
- Largely asymptomatic
- Curable, but difficult to cure
  - GT 1/3: < 40%
  - GT 2:  $\approx$  80%
  - But GT 1 is 67% of cases
- About 22% of VHA patients have undergone treatment

# Treatment is evolving

- 2002: Pegylated Interferon + Ribavirin
- 2011: Pegylated Interferon + Ribavirin + Protease Inhibitor: Boceprevir or Telaprevir
- On the horizon: new protease inhibitors, Interferon-free treatment

# Treatment is very unpleasant

- Toxicities
- Side effects

Table 1: Adverse Events Reported in > 2% of Subjects in Clinical Trials

	Boceprevir		Telaprevir	
	Boceprevir	PEG/RBV	Telaprevir	PEG/RBV
Subjects with ≥ 1 adverse events	99	97	99	96
Total severe adverse events	11	8	6	2
Adverse events grade 3/severe	--	--	23	13
Adverse events requiring discontinuation	13	12	17	4
Patient discontinued due to adverse events	9	17		
Dose modifications due to adverse events	39	24	--	--
Fatigue	57	57	--	--
Rash	--	--	56	32
Pruritis (itch)	--	--	47	28
Anemia	49	27	36	17
Nausea	45	40	39	28
Vomiting	--	--	13	8
Headache	44	43	--	--
Dysgeusia (distorted sense of taste)	37	15	10	3
Chills	33	28	--	--
Diarrhea	23	18	26	17
Dizziness	--	--	14	8
Hemorrhoids	--	--	12	2
Ano-rectal discomfort	--	--	11	3
Anxiety	19	15		
Depression	29	26	16	10
Insomnia	48	41		
Neutropenia	23	18	--	--
Thrombocytopenia	4	0	3	1
Lymphopenia	--	--	15	6

Data summarized and reported in National Drug Monographs for Boceprevir and Telaprevir, VA Pharmacy Benefits Management Services, June 2011

- Adherence is often less than optimal
- Non-completion is a frequent outcome
- Reasons for stopping
  - Physician-initiated
    - no EVR, it's not working
    - too toxic, it may hurt, even kill you
  - Patient-initiated
    - We're beginning to find out, by asking them



Completion and Drop-out Rates in VHA, all patients with GT1 2002-2007

	n	%
Withdrew after indication of lack of viral response		
after lack of EVR at 12-14 weeks	783	16.6
after non-reponse at 22-26 weeks	1038	
Drop-out		
prior to possible EVR assessment (< 12 weeks)	1184	10.8
in weeks 12-24, despite EVR	317	5.1
in weeks 24-38.4, despite documented viral response	239	
at weeks 22-26		
in weeks 12-24, unknown EVR at 12-14 weeks	1023	15.0
in weeks 24-38.4, unknown viral response at weeks	619	
12-26		
Completed treatment ( $\geq$ 38.4 weeks: 80% of 48 weeks)	5767	52.6
	Total	10970

- Qualitative research
- Ask patients about their experiences with treatment
- Collect their narratives
- Compare the experiences of those who complete with those who withdraw

## Qualitative Interview: Patients Retrospective Accounts

Perhaps a good way to begin is start at the beginning. How did your experience with hepatitis C begin?

1. Finding Out
2. How do you think you got it?
3. Deciding to Pursue Treatment
4. What was your life like while you were taking interferon and ribavirin treatment?
5. How would you describe your relationships with the doctors, nurses, and others involved in caring for your hepatitis C, as you got through the course of treatment?
6. How did you find taking the medications?
7. Were there times when you felt you wanted to stop treatment?
8. What else was going on in your life while you were taking the Interferon and Ribavirin?

If patient stopped treatment before planned 24 or 48 weeks:

9. What went into your decision to stop?

# Interviews with Patients

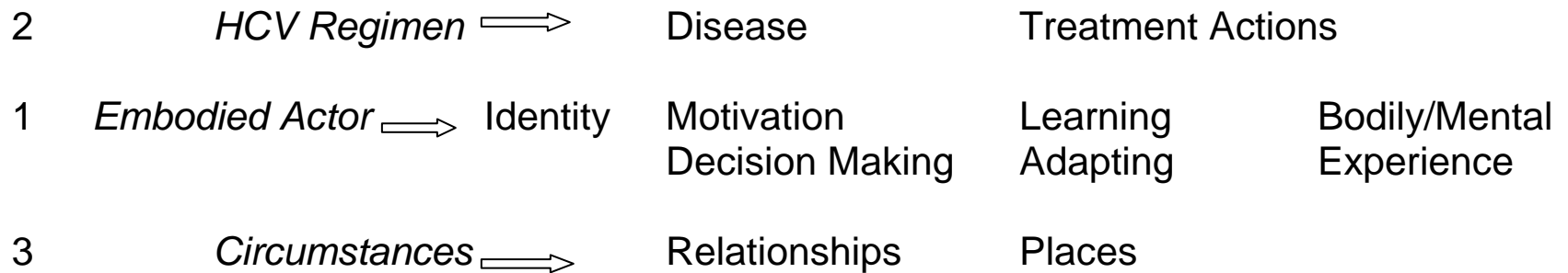
- Retrospective interviews
  - ended treatment  $\leq$  12 months previously
  - 5 completers
  - 10 non-completers
- Prospective interviews
  - 12 patients about to start treatment
  - Pretreatment
  - Follow up at 4, 20, 40 weeks, or after stopping

# The “Big Study” Sample

	Retrospective	Prospective	
		GT1	GT2/3
Completed treatment	23	16	5
Did not complete treatment	<u>37</u>	<u>15</u>	<u>3</u>
Lack of EVR	6	1	2
Provider ended	15	9	0
Patient ended	16	5	1
Died during treatment	--	1	0
Total	60	32	8

6 additional prospective patients completed baseline interviews but did not start treatment

# Framework for Rendering Patients' Accounts of Antiviral Treatment



<b>HCV Regimen:</b>		<b>Disease</b>			<b>Treatment Actions</b>	
		Disease experience how contracted how diagnosed disease outcome Disease object clinical information knowledge of HCV, treatment HIV/HCV Personal significance of disease response to diagnosis contagiousness stigma acceptance	Monitoring surveillance treatment follow up Preparing treatment preparation Acting treatment history protocol medication practices managing treatment logistics managing side effects complementary modalities (therapies, strategies)	Ending Treatment termination of completed course termination of noncompleted course		
<b>Embodied Actor:</b>	<b>Identity</b>	<b>Motivation/Decision Making</b>	<b>Learning/Adapting</b>	<b>Bodily/Mental Experience</b>		
	Identity Religion/spirituality Embodied HCV risk risky behavior sobriety Veteran	Rationale for treatment decision to start decision to stop treatment outcome future return to treatment retrospective feelings/thoughts about treatment Motivation	learning about HCV and treatment coping: cognitive, affective	<i>Prior</i> health constitutional resources other health conditions Disease symptoms Side effects flu-like symptoms anemia/fatigue skin/hair depressive affect side effects (unspecified) other side effects		

Circumstances:	Relationships	Places
	<p>Clinical</p> <ul style="list-style-type: none"> <li>HCV clinic doctor</li> <li>HCV clinic nurse</li> <li>HCV clinic NP/PA</li> <li>HCV other provider</li> <li>Non-HCV clinician</li> </ul> <p>Personal –close/primary</p> <ul style="list-style-type: none"> <li>family</li> <li>intimacy</li> <li>friends</li> </ul>	<p>Personal-distal/secondary</p> <ul style="list-style-type: none"> <li>HCV patients</li> <li>icon</li> <li>other relations</li> </ul> <p>Interpersonal dynamics</p> <ul style="list-style-type: none"> <li>disclosure of HCV, treatment</li> <li>impact of HCV treatment</li> <li>social withdrawal</li> </ul> <p>Social support</p>

VA

- VA
- VA HCV clinic
- VA pharmacy

Residence

Rehab program

Criminal justice

Work



# Patients' stories explain their actions

- Tell me what it's been like for you... since it all started
- Events leading to treatment
  - Contracted HCV
  - Got a diagnosis
  - Decided to start
- Getting through treatment
  - Early indication that it's working, or not
  - Side effects are tolerable, or not
  - Circumstances are conducive, or not



treatments [P: uh-hmm], and maybe, you know, the best way to begin is, tell me how Hepatitis, the whole experience began for you? Like when did you find out you had Hep C?

011  
012 P: Uh, I believe it was, uh, '95 [I: Yeah?] and um... I was in a drug and alcohol program up in Maine that wasn't um... it was a private program, and um, they used Togas and they had, they had tested me and uh, had told me and, at the time it was no big deal, you know I didn't really, uh... know all that. I mean I knew what it was but basically didn't know, um, you know what it did to your body as far as how long or, or, you know the damage it did, and, um. I'd go back a little ways, you know, I used to shoot dope and um... uh, a few of the people that, you know, I used to hang out with had gotten um... had gotten the HIV virus,, you know, on top of the Hep and, you know for a couple of years I, you know, I thought that... I'd gotten it too and um, you know, thank God I didn't. I mean I, I was happy just finding out I just had the Hep, you know? [I: Yeah] And uh, you know, I haven't shot any drugs since uh, early '80's. [And uh... when I finally got tested again it was, you know, it was no big deal, and you know, they explained to me, basically what it was, not what I could do about it except not drink and, you know I don't, I don't believe, there wasn't any treatment at that time. And uhm, I suffered from, I still suffer from major depression but, you know, thank God you know it's in check right now. It's the first time in years that, you know, I could actually say that I, you know, that I feel human. [I: Hmm] And uh... uh prior to, uh... I still, you know, I drank and I did you know, other drugs you know, over the years. I had, had gotten three and a half years clean until I, you know, blew one of my knees out again and they put me back on painkillers and you know, it just snowballs after that and uh... I had a, I had a very good doctor down in um, Pennsylvania that I was seeing but she wouldn't, because of the depression she wouldn't, and I, at the time I didn't want to take it either because I had friends who'd taken, you know, the interferon and uh, you know, they had told me, you know how horrible it was and it only worked, you know, like a third of the people that, that uh went through the treatment. And um, (long pause) so again I, I mean I put it off for years and, you know, um and I was okay with

ID: Sobriety~ Dz: Knowledge~  
Dz: How Diagnosed~

Tx: Surveillance~ Dz: HCV/HIV~

Rel: Non-HCV Clinic Provider~

BM: Other Health Conditions~

ID: Risky Behavior~

MDM: Decision to Start~ BM: Oth  
Dz: Kno  
Rel: HC  
Rel: Nor

# The central narrative evolves

- Guiding interest at the outset: why do patients withdraw or otherwise “fail” to complete treatment?
- Patients often told a different story: resolute efforts to complete treatment

- Patients with HCV
  - assume complex responsibilities
  - for completing complicated, debilitating regimens
  - offering uncertain benefits
- Responsible actions are not well characterized
- Approach in lit: patients pursue unless they fail to tolerate the side effects
- “tolerate side effects” has not be explicated
- Why do patients pursue treatment given the burden and the low probability of benefit?
  - Jenner and Scott, Soc of Hlth & Illness 2008

# 4 reasons for pursuing treatment

- Pilot study: 21 patients

17 completed; 4 ended prematurely

## 1. CURE: 7

sought to cure the disease, according to a medical rationale

## 2. BUY TIME: 14

highlighted inexorable progression; sought not “cure,” but to avoid coming to a “bad end”

for 9 the end was coming soon

- **MEET CHALLENGE: 15**

side effects as personal challenges to be overcome without complaint, with notable pride

- **REDEMPTION: 9**

defined treatment as part of recovery from a once dissolute life with substance abuse, demonstrating new personal worth

## **Cure:** *I was holding out hope that I would get rid of it*

- doctor said he did not have to undertake the treatment, but “we could try and cure it all completely”
- “if you complete the treatment, there is a good chance that it will show up as not non-existent, but non-traceable”
- “it showed right on board where she showed it to me. And I saw the progression of it. I saw it from my own eyes. That’s one of the things that made me hang in there... Yeah, I saw it making progress

**Avoid a bad end:** *You can maybe [get] 25 more years if you take care of it. If I didn't then it would get bad.*

- alternative to treatment was “developing liver cancer and that is no way to go”
- Yeah it occurs to you. Because when you're sick there's a way of stopping it. Then again there was a guy who was sick from it, and they took him off of it. And he died six months later of liver cancer or a year later of liver cancer. So that's something you look at too.
- : “...the doctor told me, ‘You could live 25 more years and enjoy your grandchildren.’ I'll never forget his words. That's why I took care of it. Okay?”



## **Persevere through personal trial by force of will: *My will is stronger than the crappiness***

- Considered skipping meds for a day? Yes, “everyday”
  - “I don’t want to do this but I have to. ...if I want to try to get healthy, I have to do this. You do what you got to do. If I want to do something, I do it.”
- No. There were times when I really got sick. And you think about it a little bit but not serious. But you think, ‘Come on. Hang tough. You were an Army guy. Gee whiz! Don’t be such a sissy.’

**Int:** Yeah. Did you ever think of quitting treatment, so you can say, “Forget it, I’m not finishing this treatment?”

**Pt:** Man. I was just too far up into it ...to even try to turn back, to even stop. And actually-- I felt like a quitter! I felt like I was quitting. I mean, I said I was off to get some enhancement, and then my motivation was that I was going to get somebody to love me, or have-- what you guys are saying, that I was going to feel better about myself. I mean, the price of feeling good was-- I don’t know what that meant, I mean feel good, and then more as a person, the hepatitis stuff works on your immune system, yadda yadda yadda, and you needed your immune system and stuff like that. So I had to better my insides to begin to feel good on the outside. So it’s something to work with. So I began to want to become a little healthier.

# **Personal Rehabilitation:**

*I needed to clean up my life*

So as far my deciding factors would be I just wanted it. I just wanted to get rid of this as possible. Plus I needed to clean up my life. This was the incentive to get away from the drinking. To get away from all of the crap that I was doing to myself. Self-destructive stuff. I said to myself “This is it. This is it. I can’t continue like this anymore.” Killing myself. Literally. Just like that. Especially like that.

# Personal Rehabilitation:

## *I needed to clean up my life*

INT: Where is that determination coming from?

PT: Where does it come from? I'm an old man, I'm a nothing. It's the only way I can put it--

INT: And you don't want to die.

PT: Yeah. I don't know. That might be a consolation [laughter]. I don't want to die with nothing. I don't want to die living like a dog. I know how to live on the top shelf, and I know how to live in the gutter. And I have a preference for the top shelf.

INT: And that's what keeps you going?

PT: It is. I don't like people looking down on me, which I know they do because of the situation I'm in. But I can change all that. I don't have to live in that situation.

# Personal Rehabilitation:

## *I needed to clean up my life*

Now when he looked at me and the first time he seen me *he thought I was just going to be one of them people that didn't care even though the medication was very expensive. But I showed him I did care for my health.*

Int: What do you mean? Do you think he was sizing you up and thinking you weren't going to care? What do you mean by that?

Pt: Okay. This is what I'm literally getting at. There's so many people that will go in there and try to get help for their HEP C and they can't finish the program. Because either it's too rough for them or "Blah, blah this and that." Or very sick. And he looked at me and told me because me and him basically sit in his office and he goes "Are you sure you want to do this? *Because we don't want to waste all this medication and stuff if it isn't going to work out for you.*" So basically I met him half way. I proved to him that I could literally do it. I've been doing this for two consecutive years. After my two consecutive years I've been done; I'm still clean, haven't smoked, haven't done nothing. So I think I would be a really good example right now to this research that you're doing.

# Summary

- Avoid bad end: 14
- Demonstrate strength: 15
- Both: 10
  
- Cure was expressed with other reasons
  
- But cure and rehabilitation expressed by 1

# Rethinking “candidacy for treatment”

- Only about 22% of VHA patients with HCV have attempted antiviral treatment
- Many are poor candidates
  - liver disease not bad enough, or too advanced
  - medical comorbidities
  - contraindications
    - substance abuse
    - readiness to pursue treatment
    - social circumstances: residence, support, work

- Determination of candidacy involves negotiation, judgment
- Patients have histories of being judged poorly by clinicians
- Patients endure pronounced stigma
- HCV is largely a guilty disease



# Selection for treatment

- Integrated care in VHA
  - Psychosocial socialization prior to initiating treatment: accomplishment of sobriety
  - Work clinicians to demonstrate readiness
- RCT of preparation for treatment program at UNC
  - Abstain, attend substance abuse program, comply with liver clinic appointments, engage in motivational interviewing
  - Judged by “blind” clinicians to be good candidates

- Pretreatment rehabilitation and socialization may build motivation
- Selection for candidacy provides a way for patients to talk about their treatment
- They may adopt, follow accepted scripts, analogous to recent studies of drug rehab
- Moral selection may exclude patients who just want to cure their HCV

# She was everything to me...

- In their narratives, it was a specific nurse (RN or NP) or PA who played a major role helping them deal with treatment
  - Physicians were assigned minor roles
- CANDOR.
  - completers: substantially greater candor
  - non-completers withheld side effects, personal concerns, and inner struggles to persevere
- COMMUNICATION
  - completers: availability and responsiveness to their concerns
  - non-completers: lapses in communication around key aspects of treatment and dissonance between their wishes and provider responses
- PREPARATION
  - completers felt well-informed about treatment process; efforts to achieve candidacy for treatment, including sobriety, were supported
  - non-completers felt pressure to undertake treatment
- EMOTIONAL SUPPORT
  - completers: highlighted emotional support, encouragement to persevere
  - non-completers: emphasized informational support
- RELATIONSHIP QUALITY
  - completers uniquely described collaborative decision-making, cooperation, and shared problem-solving.