UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JEFFREY FOWLER, PAUL WHOOTEN, MICHAEL TURNER, and MICHAEL FITZPATRICK, on behalf of themselves and all others similarly situated,

Plaintiffs,

v.

THOMAS TURCO, Commissioner of Massachusetts Department of Correction, in his official capacity, and MASSACHUSETTS PARTNERSHIP FOR CORRECTIONAL HEALTHCARE, INC.,

Defendants.

C.A. NO. 1:15CV12298

MEMORANDUM IN SUPPORT OF PLAINTIFFS' MOTION FOR CLASS CERTIFICATION

INTRODUCTION

Plaintiffs Jeffrey Fowler, Paul Whooten, Michael Turner, and Michael Fitzpatrick seek certification of a class of all people who are or will be prisoners in the custody of the Massachusetts Department of Correction (□DOC□), and who have or will have Hepatitis C while in custody and have not yet been cured. Through their policies and practices, the DOC and its medical contractor, Massachusetts Partnership for Correctional HealthCare, Inc., (□MPCH□), are depriving prisoners with Hepatitis C of a cure for this virus that kills more people annually in the United States than the next sixty infectious diseases combined. Liver disease and its complications, up to and including death, can be avoided with timely treatment. The cost of surveilling for and treating complications from liver disease can also be avoided. Treatment with the current generation of Hepatitis C medications is simpler, shorter, and generates fewer side

effects than ever before, with near perfect cure rates. Nevertheless, Defendants deny and delay treatment, putting these prisoners at substantial risk of harm.

The acts and omissions of Defendants with respect to Hepatitis C violate the Plaintiffs' and putative class members' rights under the Eighth Amendment to the United States Constitution. To remedy this violation, Plaintiffs seek a declaration that Defendants' policies and practices with regard to Hepatitis C are unlawful, and a permanent injunction requiring Defendants to implement and adhere to a timely and effective treatment protocol for Hepatitis C. As the central issue presented by Plaintiffs is common to all putative class members, who number over 1,500, and cannot practicably be addressed through piecemeal litigation, this Court should certify a class pursuant to Federal Rule of Civil Procedure 23(a) and 23(b)(2), of all current and future DOC prisoners who have or will have Hepatitis C and have not yet been cured.

BACKGROUND

I. Hepatitis C in the Community.

Hepatitis C is a blood borne disease caused by a virus that brings about inflammation that damages the liver. It is a leading cause of liver disease and liver transplants. Hepatitis C is responsible for more deaths in the United States than the next sixty most common infectious diseases ***combined***.[1] In Massachusetts, Hepatitis C was once most prevalent among baby boomers. In recent years, however, a second peak has emerged with young adults.[2] This new

[1] Centers for Disease Control and Prevention, *Hepatitis C Kills More Americans Than Any Other Infectious Disease*, *available at* http://www.cdc.gov/media/releases/2016/p0504-hepc-mortality.html (last visited May 14, 2016).
[2] Bureau of Infectious Disease, Mass. Dep't of Public Health, *Hepatitis C Virus Infection 2015 Surveillance Report*, *available at* http://www.mass.gov/eohhs/docs/dph/cdc/reporting/surveillance-report-hepatitis-c.pdf (last visited May 14, 2016) at p. 13 (displaying age breakdown of new Hepatitis C cases in 2014, compared to 2007).

spike has been fueled in large part by the state's opioid crisis, since the virus is most commonly spread by intravenous drug use.[3]

Treatment for Hepatitis C has evolved over time. For years, the standard treatment was a combination of two drugs: Pegylated Interferon and Ribavirin. This combination therapy took 48 weeks to administer, it had the potential for serious side effects (including thrombocytopenia and depression), and it was not guaranteed to work, particularly for patients with Genotype 1, the most common genotype of Hepatitis C in the United States. *See* Ex. 1 (*MPCH Clinical Guidelines: Evaluation and Treatment of Hepatitis C and Cirrhosis* (July 1, 2013)) at 6 (combination therapy had 40-45% response rate for Genotype 1).

In 2011, the FDA approved two new protease inhibitors which, when either one was taken alongside combination therapy, produced better results – an up to 80% cure rate for Genotype 1. *Id.* This "triple therapy" became the new standard of care. Moreover, triple therapy even cured many of the patients who had previously tried combination therapy and were unsuccessful. Until the advent of triple therapy, these nonresponders or relapsers had no further treatment options.[4]

In November and December 2013, the FDA approved two new direct-acting antiviral medications, Sovaldi and Olysio.[5] Either medication could be taken with combination therapy, and they could also be used together without combination therapy. The direct-acting antivirals

[3] Bureau of Infectious Disease, Mass. Dep't of Public Health, *Shifting Epidemics: HIV and Hepatitis C Infection among Injection Drug Users in Massachusetts*, *available at* http://www.mass.gov/eohhs/docs/dph/aids/shifting-epidemics-report.pdf (last visited May 14, 2016) at p. 1.

[4] *See, e.g.*, Gara, Naveen and Marc Ghany, "The New Standard of HCV Therapy: Retreatment in Experienced Patients," *Clinical Liver Disease*, Vol. 1, No. 1 (AASLD February 2012), *available at* http://onlinelibrary.wiley.com/store/10.1002/cld.4/asset/4_ftp.pdf;jsessionid=C23561D420F9C28CAA3445886B6B9DA8.f03t04?v=1&t=io9db8xl&s=8d6299e4b407cbfea6f210f31e5ab13e886a8167) (last visited May 15, 2016), at 16-19.

[5] *See* U.S. Food and Drug Administration, "FDA approves Sovaldi for chronic Hepatitis C," *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm377888.htm (last visited May 15, 2016).

improved outcomes considerably.[6] On October 10, 2014, the FDA approved Harvoni, a one-pill regimen that combined Sovaldi with another medication to create an Interferon-free regimen, one with a cure rate well over ninety percent.[7] On December 19, 2014, the FDA approved Viekira Pak, a multiple-pill regimen that was also Interferon-free and highly effective.[8]

These Interferon-free regimens[9] marked a major advance in Hepatitis C treatment. They have an outstanding cure rate for every genotype, especially Genotype 1. They work on patients who had failed previous treatments. *See* Ex. 2 (AASLD and IDSA, "Retreatment of persons in whom prior therapy has failed," in *HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C* (last modified April 25, 2016)). They pose far less risk of significant side effects, and the standard duration of treatment has dropped from 48 weeks under combination or triple therapy, to twelve weeks with the new regimens. *Id.*

With this significant advance came significant changes in the standard of care for Hepatitis C. Previously, both patient and provider weighed the possible benefits of treatment against potential drawbacks, including the possibility of treatment failure or relapse, and the potential for bad side effects. It was standard practice for providers to try to assess patients' fibrosis level – the amount of scarring in their liver – before deciding whether to recommend treatment. The assessment was typically made by liver biopsy, and the results of that biopsy, along with the patient's other symptoms or complicating conditions, would inform the decision

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[6] Centers for Disease Control and Prevention, "What is the treatment for chronic Hepatitis C?" *HCV FAQs for Health Professionals*, *available at* http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#d3 (last visited May 15, 2016) (80-95% cure rate).

[7] U.S. Food & Drug Administration, *FDA approves first combination pill to treat hepatitis C, available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm418365.htm (last visited May 15, 2016).

[8] U.S. Food & Drug Administration, *FDA approves Viekira Pak to treat hepatitis C*, *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427530.htm (last visited May 15, 2016).

[9] They now also include Zepatier, a drug approved by the FDA in early 2016. U.S. Food & Drug Administration, *FDA approves Zepatier for treatment of chronic Hepatitis C genotypes 1 and 4*, *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm483828.htm (last visited May 15, 2016).

of whether to undergo treatment. That decision was also informed by the possibility of new medications emerging medications that would offer improved cure rates and fewer burdens.

Those new medications are here, with near-perfect cure rates, minimal side effects, and shorter treatment durations. The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) have issued guidelines for the treatment of Hepatitis C, modifying those guidelines in real time as new information becomes available. *See* www.hcvguidelines.org. The guidelines now call for the treatment of everyone with chronic Hepatitis C. *See* Ex. 3 (AASLD and IDSA, When and in whom to initiate HCV therapy, in *HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C* (last updated February 24, 2016)) (Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy).[10]

II. Hepatitis C Treatment in the DOC

Hepatitis C is highly prevalent in prisons. As combination therapy emerged in the early 2000s, the Massachusetts Department of Correction convened a task force to address diagnosis, evaluation and treatment of Hepatitis C within the state prison system. Ultimately, the DOC and

[10] The guidelines initially distinguished between patients based on their severity of disease, but the expert panel removed that provision, writing:

> When the US Food and Drug Administration (FDA) approved the first IFN-sparing treatment for HCV infection, many patients who had previously been warehoused sought treatment, and the infrastructure (experienced practitioners, budgeted health-care dollars, etc.) did not yet exist to treat all patients immediately. Thus, the panel offered guidance for prioritizing treatment first to those with the greatest need. Since that time, there have been opportunities to treat many of the highest-risk patients and to accumulate real-world experience of the tolerability and safety of newer HCV medications. More importantly, from a medical standpoint, data continue to accumulate that demonstrate the many benefits, within the liver and extrahepatic, that accompany HCV eradication. Therefore, the panel continues to recommend treatment for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy.

Id.

its then-medical contractor implemented a protocol in which treatment was rationed. Ex. 4 (Carpenter, Kathyrn and Danielle Sorenson, *The Management of Hepatitis C Treatment in Massachusetts State Correctional Facilities* (Worcester Polytechnic Institute April 26, 2007)) at 11-12. Prisoners with Hepatitis C were deemed eligible for treatment based on their liver fibrosis stage, and other complications of the illness or other co-morbidities (such as HIV). *Id.* A prisoner deemed eligible for treatment was then placed on a wait list. The DOC and its contractor then treated prisoners with combination therapy, in batches of ten. *Id.*

The DOC set a maximum number of treatment slots, *id.*, and closely monitored spending on Hepatitis C treatment, with combination therapy having a stand-alone line item in monthly pharmacy spending reports. *See* Ex. 5 (DOC pharmacy summary reports for FY09 – FY15). At its most recent high point there were 95 or 96 treatment slots, *see* Ex. 4 at 11, Ex. 6 (2010 DOC contract amendment) at Attachment C, though on average only 81 patients were being treated at any given time. Ex. 5 at p. 1 (FY09 average of 81 "Inmates on Rebetron/Pegintron"). The number of prisoners receiving combination therapy subsequently declined steadily, over a period of years. Ex. 5 (FY10 – FY14 pharmacy reports); Ex. 6 at Attachment C (reducing "treatment cap" to 70). By Fiscal Year 2014, the average number of prisoners being treated in a given month was sixteen, out of a prison population of over 10,000. Ex. 5 at 6.

Well before triple therapy supplanted combination therapy as the new standard of care, the Hepatitis C task force was reconvened. Ex. 7 (February 11, 2009 email from Patti Onorato). The imminent arrival of triple therapy, and of the direct-acting antivirals beyond that, were known and contemplated well before their FDA approval. *See* Ex. 8 (March 3, 2011 DOC Pharmacy & Therapeutics Committee minutes) at 5 (presentation made regarding medications "in late-phase development for use in Hepatitis C"). The then-medical contractor for DOC had

proposed a significant increase in commitment to treatment, Ex. 9 (excerpt from MGT of America, Inc., *Analysis of Health Care Costs in the DOC* (December 2011)) at 80, but when triple therapy arrived it was not made available in the DOC. *See* Ex. 10 (April 13, 2012 letter from Joel Thompson to Gov. Deval Patrick *et al.*); Ex. 11 (July 2, 2012 letter from Lawrence Weiner to Joel Thompson). It was not introduced into the DOC until 2013, *see* Ex. 12 (excerpt of June 2013 nonformulary medication report, reflecting orders for Boceprevir), by which time the DOC was treating fewer and fewer prisoners, and the direct-acting antivirals were approved by the FDA shortly thereafter, rendering triple therapy obsolete. *See* Ex. 5 at 5-6 (declining number of inmates on Hepatitis C medications through FY13 and FY14).

Treatment has remained out of reach for almost all DOC prisoners with Hepatitis C. The Pharmacy & Therapeutics Committee acknowledged the arrival of new medications, but for months it postponed any rollout. *Compare* Ex. 13 (April 2014 P&T minutes: "guidelines are under development) *with* Ex. 14 (August 2014: "3 patients have been evaluated and cleared to start [Sovaldi] therapy in August") *and* Ex. 15 (October 2014: five patients evaluated and cleared to begin "once operational processes are put into place"). It was October 2014 when the first DOC prisoner received one of the new medicines, Sovaldi, which he took with the old combination therapy. Ex. 16 (December 2014 P&T Committee minutes) at 2. As of February 2015, only three prisoners were receiving Hepatitis C treatment. Ex. 5 at 7.

The available treatment for Hepatitis C has become almost 100% effective, requires no Interferon, can be taken orally for a much shorter duration, and involves no major side effects, but Defendants are delaying and denying treatment for virtually everyone. This practice contrasts sharply with the AASLD/IDSA guidelines, which call for the treatment of virtually everyone with Hepatitis C.

III. Emilian Paszko.

Originally a Plaintiff in this action, Emilian Paszko died of complications from Hepatitis C on December 14, 2015. In late 2013, as Sovaldi and Olysio were obtaining FDA approval, Mr. Paszko was suffering from decompensated cirrhosis, portal hypertension, esophageal varices, and ascites. *See* Ex. 17 (selected medical records of Emilian Paszko). In the two years that followed, Mr. Paszko required multiple hospitalizations. The gastroenterologists who treated him discussed Hepatitis C treatment. As early as April 2014, a specialist noted that "at this time he is not a good candidate for the antiviral therapy *that is currently available*." *Id.* at 6 (emphasis added). In June, another hospital provider stated that "given his advanced liver disease, he is a good candidate at this time for direct-acting antivirals." *Id.* at 8. In November of 2014, after the arrival of Harvoni, the gastroenterology service noted that "the newest therapies are not approved in the DOC system at this point in time; although, the patient would certainly be a candidate for consideration of therapy once these are approved." *Id.* at 12. In the ensuing months, Mr. Paszko saw the gastroenterology service several more times and was hospitalized again, but there was no movement toward Hepatitis C treatment. *Id.* at 14-47. Finally, at an August 3, 2015 video appointment, a gastroenterologist concluded that Mr. Paszko was too sick for treatment and that a liver transplant was the primary treatment. *Id.* at 49.

Mr. Paszko was exceedingly well known to Defendants and to the specialists at Lemuel Shattuck Hospital who treated him. He should have been evaluated for Hepatitis C treatment as soon as the direct-acting antivirals became available; his specialist providers confirmed that he was a good candidate for such treatment. Instead, Defendants allowed 20 months to pass before having him evaluated for treatment, at which point it was thought to be too late.

IV. Jeffrey Fowler.

Plaintiff Jeffrey Fowler has had Hepatitis C, genotype 1a, for over 25 years. Ex. 18 (Fowler Affidavit) at ¶ 1. A nonresponder to combination therapy, Mr. Fowler was approved by MPCH for triple therapy in 2014. Unfortunately, he was a nonresponder to triple therapy also, and he suffered from serious side effects during the treatment. *Id.* ¶¶ 3-8. Mr. Fowler believed and was told that given his history and the previously approved attempts to treat him, he would be a high priority for treatment with one of the Interferon-free regimens. *Id.* ¶ 9. For almost two years, however, he has been waiting, with MPCH refusing to consider him for treatment based in part on a prior liver biopsy □a biopsy that preceded his triple therapy treatment. *Id.* ¶ 10. Mr. Fowler now has abdominal pain, and lab tests suggesting that his condition has become markedly worse; he was told that he is now recommended for treatment. But Mr. Fowler has no idea whether MPCH has or will approve treatment, or when. *Id.* at ¶ 14.

V. Paul Whooten.

Plaintiff Paul Whooten has Hepatitis C and failed combination therapy treatment in the 2000s. Ex. 19 (Whooten Affidavit) at ¶¶ 2-4. He has sought to be treated again since entering DOC custody in 2011. He has been deemed ineligible for treatment first because of his pretrial status, then because he had spent less than a year as a sentenced prisoner in DOC (despite the fact that he had spent the previous two years in DOC custody as a pretrial detainee). *Id.* at ¶¶ 5-7. Mr. Whooten has now been a sentenced prisoner for more than a year, but he has not been considered for treatment nor even had a gastroenterology consult. *Id.* ¶ 8.

VI. Michael Turner.

Plaintiff Michael Turner has Hepatitis C, is in DOC custody, and will remain so until he is released in 2021 or 2022, unless he is paroled before then. Ex. 20 at ¶¶ 1-2. Mr. Turner was

treated with combination therapy while in the DOC, in 2012, but the treatment was stopped as it was not working and was causing serious side effects. *Id.* ¶ 5. Mr. Turner sought retreatment and spoke with MPCH providers about seeking triple therapy or waiting for Interferon-free regimens to arrive. He agreed to wait. *Id.* at ¶ 6.

Accordingly, in November of 2014 (after FDA approval of Harvoni) Mr. Turner sought treatment. At that point, MPCH deemed him ineligible for treatment, suggesting that his liver function was normal, notwithstanding his previous evaluation and treatment approval years before. *Id.* at ¶ 7. Mr. Turner continued to be found ineligible until September 2015, when he saw a gastroenterologist. *Id.* at ¶ 9. That specialist told Mr. Turner that he was approved for treatment and would start medications in the following week. *Id.* Nevertheless, Mr. Turner has not begun Hepatitis C treatment; MPCH has told him that he is on a waiting list and is a "lower priority" patient. *Id.* at ¶ 10. Blood tests taken in January 2016 suggest that Mr. Turner now has stage F4 liver fibrosis. *Id.* at ¶ 11.

VII. <u>Michael Fitzpatrick.</u>

Plaintiff Michael Fitzpatrick is a DOC prisoner who is due to be released in September of this year. Ex. 21 at ¶ 1. He has Hepatitis C, genotype 1a, which has brought about cirrhosis of the liver, GAVE disease, and esophageal varices. *Id.* at ¶ 3. As early as April 2012, testing indicated cirrhosis, and a specialist recommended putting Mr. Fitzpatrick "at the top of the list" for treatment. *Id.* at ¶ 5. A year later, Mr. Fitzpatrick was started on triple therapy, but he suffered from severe side effects that forced MPCH to discontinue treatment in July 2013. *Id.* at ¶¶ 6-7.

Unsurprisingly, as early as April 2014 a specialist recommended retreatment with direct-acting antivirals. The gastroenterologist recommended treatment with Sovaldi and Olysio (the

only available Interferon-free regimen at that time, as Harvoni was not yet available). *Id.* at ¶ 8. Mr. Turner was not treated then. He was hospitalized on several occasions, where doctors found evidence of portal hypertension, splenomegaly, esophageal varices, and GAVE disease. Mr. Fitzpatrick frequently found himself coughing up blood and/or with blood in his stool. *Id.* at ¶¶ 9-10, 12-14.

MPCH declared Mr. Fitzpatrick ineligible for treatment in April 2015, for twelve months, because he had been issued a disciplinary report for possession of homebrew. *Id.* at ¶ 11. Notwithstanding the fact that he was previously recognized as a high-priority patient, and that he has suffered from serious complications of his Hepatitis C, he still awaits treatment. *Id.* at ¶ 15. Although MPCH's period of ineligibility should have lifted, he apparently falls within MPCH's exclusion of treatment for prisoners too close to their release date. *See* Ex. 1 at 4-5.

PROPOSED CLASS DEFINITION

All people who are or will be prisoners in the custody of the Massachusetts Department of Correction ("DOC"), who have or will have Hepatitis C and have not yet been cured.

ARGUMENT

Federal Rule of Civil Procedure 23(a) contains four "prerequisites" for class certification. If those prerequisites are met, and if the case also falls within one of the "types" of class actions described in Rule 23(b), then the plaintiffs "are entitl[ed]" to pursue [their] claim as a class action." *Shady Grove Orthopedic Assocs., P.A. v. Allstate Ins. Co.,* 559 U.S. 393, 398 (2010). In the present case, those conditions are satisfied.

I. <u>The Proposed Class Satisfies the Four Prerequisites of Fed. R. Civ. P. 23(a).</u>

The four prerequisites required under Fed. R. Civ. P. 23(a) are known as numerosity, commonality, typicality, and adequacy. First, the class must be "so numerous that joinder of all

members is impracticable. Fed. R. Civ. P. 23(a)(1). Second, there must be questions of law or fact common to the class. Fed. R. Civ. P. 23(a)(2). Third, the claims of the representative plaintiffs must be typical of the claims or defenses of the class. Fed. R. Civ. P. 23(a)(3). Finally, the representative plaintiffs must fairly and adequately protect the interests of the class. Fed. R. Civ. P. 23(a)(4).

A. Numerosity.

The proposed class is so numerous that joinder of all members is impracticable. *See* Fed. R. Civ. P. 23(a)(1). According to information obtained via a public records request, as of January 2015, there were 1,560 prisoners in its custody known to have Hepatitis C, out of 10,379 total prisoners. Exhibit 22 (March 5, 2015 P&T Committee minutes) at 2, 1. A high enough number is itself sufficient to render joinder impracticable, and in the First Circuit, the number is generally forty. *Reid v. Donelan, 297 F. R. D. 185* (D. Mass 2014); *George v. Nat'l Water Main Cleaning Co.*, 286 F.R.D. 168, 173 (D. Mass. 2012). *See also Scott v. Clarke*, 61 F.Supp.3d 569, 584 (W.D.Va. 2014) (certifying class s of 1,200 prisoners claiming inadequate medical care). The acknowledged number of DOC prisoners with Hepatitis C more than suffices to establish numerosity.[11]

[11] Sheer numbers aside, the turnover in the DOC prison population also satisfies Rule 23(a)(1). Courts consider the transient membership in the proposed class to determine the difficulty or inconvenience of joining all members of the class. *George*, 286 F.R.D. at 173 (quoting *Advertising Specialty Nat'l Ass'n v. Fed. Trade Comm'n*, 238 F.R.D. 108, 119 (1st Cir. 1956)). Here, the transient nature of the DOC population makes joinder impracticable: [u]nforeseen members will join the class at indeterminate points in the future, making joinder impossible. *Reid*, 297 F.R.D. at 189. Cases involving transient commitment or incarcerated populations are particularly well-suited to class certification because the inmate population is constantly revolving. *Green v. Johnson*, 513 F.Supp. 965, 975 (D.Mass. 1981). *See also J.D. v. Nagin*, 255 F.R.D. 406, 414 (E.D.La. 2009) ([t]he mere fact that the population of the [detention center] is constantly revolving during the pendency of litigation renders any joinder impracticable); *Gordon v. Johnson*, 300 F.R.D. 31, 36 (D.Mass. 2014); *Hawker v. Consovoy*, 198 F.R.D. 619, 625 (D.N.J. 2001); *Williams v. Conway*, No. 9:15-cv-427, 2016 WL 65064, at *3 (N.D.N.Y. Jan. 4, 2016) (the class action device is particularly well-suited in actions brought by prisoners due to the fluid composition of the prison population [and] generally tend[s] to be the norm in actions such as this (internal quotation marks and citation omitted)) (quoting *Clarkson v. Coughlin*, 783 F. Supp. 789, 797 (S.D.N.Y. 1992)); *Scott*, 61 F.Supp.3d at 584.

B. Commonality.

There are clearly "questions of law or fact common to the class." Fed. R. Civ. P. 23(a)(2). Commonality exists when plaintiffs "demonstrate that the class claims "depend upon a common contention" and that determining the truth or falsity of that contention "will resolve an issue that is central to the validity of each one of the claims in one stroke." *Connor B., ex rel. Vigurs v. Patrick*, 278 F.R.D. 30, 32 (D. Mass. 2011) (quoting *Wal-Mart Stores, Inc. v. Dukes*, 131 S.Ct. 2541, 2551 (2011)). "Even a single common question" is sufficient to satisfy Rule 23(a)(2). *Wal-Mart*, 131 S.Ct. at 2556 (internal quotations and citations omitted).

This case presents common questions central to the validity of the putative class" claims, which include, but are not limited to:

a. whether treatment for Hepatitis C is a serious medical need;

b. whether Defendants have knowingly failed to provide the necessary staging "the testing needed to determine the severity of the disease "of Hepatitis C-positive prisoners;

c. whether Defendants have knowingly failed to provide the most effective and appropriate treatment for Hepatitis C;

d. whether Defendants have knowingly employed policies and practices that unjustifiably delay or deny treatment for Hepatitis C;

e. whether Defendants" failures have placed Hepatitis C-positive prisoners at risk of suffering a deterioration in health, new ailments, worsening of existing ailments, and the prospect of premature or unnecessary disability or death; and

f. whether Defendants' policies and practices reflect deliberate indifference to the serious medical needs of the class members, in violation of their right to be free from cruel and unusual punishment.

The central issues presented by this case are "capable of class-wide resolution" in "one stroke." *Wal-Mart*, 131 S.Ct. at 2551. The proposed class thus "ha[s] common interest in the disposition of the disputed questions of law," *Banner v. Smolenski*, 315 F.Supp. 1076, 1080 (D. Mass. 1970), and this class action will generate common answers. *See Wal-mart*, 131 S.Ct. at 2551 (citations omitted). Additionally, the central legal issues arise from facts common to all class members. Every class member has been subjected to or is at imminent risk of suffering the same rights violations by the Defendants, as a result of the same policies and practices.

Any factual differences that may exist among class members in terms of their individual medical condition cannot defeat this commonality. The key questions do not revolve around each prisoner's particular plight, but the Defendants' systemic deficiencies in treating Hepatitis C. "Plaintiffs have alleged specific and overarching systemic deficiencies" on the part of the DOC and its medical contractor; "[t]hese systemic shortcomings provide the 'glue' that unites Plaintiffs' claims." *Connor B.*, 278 F.R.D. at 34. Courts elsewhere have similarly found the commonality requirement satisfied in claims regarding inadequate prison health care. *See, e.g., Scott*, 61 F.Supp.3d at 584-87 (whether defendants' policies and practices place current and future prisoners at substantial risk of serious harm, to which defendants are deliberately indifferent, implicates common questions of fact and law), 587-88 (citing other post-*Wal-Mart* decisions finding commonality in prisoner class actions challenging unconstitutional conditions of confinement); *Parsons v. Ryan*, 754 F.3d 657, 675-85 (9th Cir. 2014). Plaintiffs, therefore, satisfy the commonality requirement.

C. Typicality.

Plaintiffs' claims are typical of those of the proposed class. *See* Fed. R. Civ. P. 23(a)(3). Although the "claims of the entire class need not be identical," the class representatives "must generally 'possess the same interests and suffer the same injury' as the unnamed class members." *Gen. Tel. Co. of Sw. v. Falcon,* 457 U.S. 147, at 156 (1982) (citations omitted). Representative plaintiffs can show typicality by "demonstrating that [their] injuries arise from the same course of conduct as the rest of the class, and that [their] claims are based on the same legal theory as those of the class." *Glass Dimensions, Inc. v. State St. Bank & Trust Co.*, 285 F.R.D. 169, 178 (D. Mass. 2012). "Typicality 'is designed to align the interests of the class and the class representatives so that the latter will work to benefit the entire class through the pursuit of their own goals.'" *Glass Dimensions,* 285 F.R.D. at 178 (citation omitted).

Plaintiffs and members of the proposed class are, or will be, subjected to the same challenged policies, practices, and harms by the Defendants. Like all other members of the class, Plaintiffs have Hepatitis C. They have not been treated with the available medication that is nearly one hundred percent curative, with minimal side effects. They are being subjected to the same policies and practices surrounding Hepatitis C treatment, policies and practices that place them at risk of serious harm from untreated Hepatitis C, including cirrhosis, liver cancer, and other complications from end stage liver disease.[12]

In addition, as specified in the Complaint, Plaintiffs seek declaratory and injunctive relief based on the same legal theories that would provide relief to the rest of the proposed class.

[12] It does not matter that they may have suffered different complications or symptoms, or that they are at different stages of their disease progression. The fact that Plaintiffs' harm "may differ in some respects from those suffered by unnamed Plaintiffs does not undermine typicality." *Connor B. ex rel. Vigurs v. Patrick*, 272 F.R.D. 288, 296-97 (D. Mass. 2011) (citations omitted). Indeed, as with commonality, it is "[b]ecause Plaintiffs have identified specific systemic failures that expose the entire Plaintiff class" to rights violations and an unreasonable risk of additional harms that "the typicality requirement is satisfied." *Connor B.*, 272 F.R.D. at 297; *Williams*, 2016 WL 65064, at *5. Other courts have found likewise in cases challenging the adequacy of prison health care. *See Parsons*, 754 F.3d at 685-86; *Scott*, 61 F.Supp.3d at 589-90.

Accordingly, "no possibility exists that an individual claim or factual difference will "consume the merits "of this class action." *Reid v. Donelan*, 297 F.R.D. 185, 191 (D. Mass. 2014). Plaintiffs, therefore, satisfy the typicality requirement.

D. Adequacy.

Finally, Plaintiffs will "fairly and adequately protect the interests of the class." Fed. R. Civ. P. 23(a)(4). To satisfy this requirement, Plaintiffs must "first show that the interests of the representative party will not conflict with the interests of any of the class members, and second, that counsel chosen by the representative party is qualified, experienced, and able to vigorously conduct the proposed litigation." *Reid*, 297 F.R.D. at 191 (quoting *Andrews v. Bechtel Power Corp.*, 780 F.2d 124, 130 (1st Cir. 1985)). With respect to class counsel, courts must consider "(i) the work counsel has done in identifying or investigating potential claims in the action; (ii) counsel's experience in handling class actions, other complex litigation, and the types of claims asserted in the action; (iii) counsel's knowledge of the applicable law; and (iv) the resources that counsel will commit to representing the class." Fed. R. Civ. P. 23(g). Courts can also consider "any other matter pertinent to counsel's ability to fairly and adequately represent the interests of the class." *Id.*

Plaintiffs' interests are consistent with, and are "not antagonistic to or in conflict with" the interests of the proposed class as a whole. *Connor B.*, 272 F.R.D. at 297. The requested declaratory and injunctive relief will apply equally to and benefit all class members. Plaintiffs are not seeking damages or any other limited resource that could yield conflicts. Because "every member is seeking the same remedy" based on an identical theory" Plaintiffs' interests are coextensive with the class." *Reid*, 297 F.R.D. at 191.

Moreover, Plaintiffs have retained experienced and competent counsel who will fairly and adequately protect the interests of the proposed class. Plaintiffs are represented by Prisoners' Legal Services ("PLS") and the law firm Shapiro, Weissberg & Garin ("SWG"), on behalf of the National Lawyers Guild.

PLS is a not-for-profit legal services corporation established in 1972 to promote the safe, humane and lawful treatment of Massachusetts prisoners. It has litigated numerous complex civil rights class actions, and civil rights actions addressing prison health care, and is experienced in the protection of the statutory and constitutional rights of prisoners. *See, e.g., Souza v. Sheriff of Bristol County*, 455 Mass. 573 (2010); *Haverty v. Comm'r of Correction*, 440 Mass. 1 (2003); *Nunes v. Mass. Dep't of Correction*, 766 F.3d 136 (1st Cir. 2014). SWG has substantial experience litigating class actions and civil rights actions, including prison cases. *See, e.g., Ponte v. Real*, 471 U.S. 491 (1985); *Furtado v. Bishop*, 604 F.2d 80 (1st Cir. 1979); *Bl(a)ck Tea Society v. City of Boston*, 378 F.3d 8 (1st Cir. 2004); *Jews for Jesus, Inc. v. Mass. Bay Transportation Authority*, 783 F.Supp. 1500 (D. Mass. 1991); *Bentley v. Essex County*, Essex Superior Court, Civ. No. 2011-1907.

Plaintiffs' counsel have already invested substantial time and resources in this case. Before filing suit, Plaintiffs' counsel communicated with, visited, reviewed records for, and advocated for multiple DOC prisoners with Hepatitis C; investigated the Defendants' policies and practices around Hepatitis C treatment; and researched potential claims. For over a decade, PLS has advocated for prisoners about Hepatitis C specifically, and it has investigated the DOC's practices in treating this disease. *See, e.g.,* Ex. 10. These efforts and others, together with the willingness of Plaintiffs' counsel to fund all costs of this litigation through trial,

ensure that members of the proposed class will be adequately represented. *Connor B.*, 272 F.R.D. at 297.

II. The Proposed Class Meets the Requirements of Fed. R. Civ. P. 23(b).

Plaintiffs also meet at least one of the requirements of Fed. R. Civ. P. 23(b). Specifically, Plaintiffs meet the requirements of Rule 23(b)(2), which permits class certification when the adverse party "has acted or refused to act on grounds that apply generally to the class, so that the final injunctive relief or corresponding declaratory relief is appropriate respecting the class as a whole."

"The key to the (b)(2) class is the indivisible nature of the injunctive or declaratory remedy warranted – the notion that the conduct is such that it can be enjoined or declared unlawful as to all of the class members or as to none of them." *Wal-Mart*, 131 S.Ct. at 2557 (internal quotations omitted); *see also Yaffe v. Powers*, 454 F.2d 1362, 1366 (1st Cir. 1972). This feature of Rule 23(b)(2) certification makes it "uniquely suited to civil rights actions," *Connor B.*, 272 F.R.D. at 297 (quoting *Yaffe*, 454 F.2d at 1366). "[C]lass actions certified pursuant to Rule 23(b)(2) are particularly important in cases involving civil rights actions, specifically those related to hospital or prison reform," as class certification in such cases is "crucial to ensure that the granted relief benefits all members of the class." *Rolland v. Patrick*, 2008 WL 4104488, at *6 (D. Mass. Aug. 19, 2008) (citations omitted). Courts routinely certify Rule 23(b)(2) class actions within these contexts, including claims for inadequate prison health care. *See Smith v. Ashe*, 106 F.R.D. 353, 354-55 (D. Mass. 1985) (certifying a 23(b)(2) class challenging conditions of confinement and medical treatment for prisoners segregated from general population); *Parsons*, 754 F.3d at 686-87 (certifying 23(b)(2) class challenging adequacy of all health care in state prison system); *Scott*, 61 F.Supp.3d 569 (certifying 23(b)(2) class

challenging adequacy of all health care in women's prison); *id.* at 583 (citing other similar cases).

Rule 23(b)(2) certification is appropriate in this matter. Defendants have acted on grounds that generally apply to the entire class. The unlawful policies and practices of the Defendants, as well as the constitutional rights violations suffered by Plaintiffs as a result of Defendants' policies and practices, are substantially similar, if not identical, among members of the class. Furthermore, Plaintiffs seek declaratory and injunctive relief that "would benefit the entire class." *Connor B.*, 272 F.R.D. at 297; *see Gordon*, 300 F.R.D. at 38.

Additionally, cases brought by prisoners, like Plaintiffs, are well-suited to class action treatment, "due to the "fluid composition" of the prison population." *Clarkson v. Coughlin*, 783 F. Supp. 789, 797 (S.D.N.Y. 1992) (quoting *Dean v. Coughlin,* 107 F.R.D. 331, 332 (S.D.N.Y. 1985)). Prisoners are released or transferred and new prisoners arrive every day, while the underlying claims tend to remain. *Dean*, 107 F.R.D. at 323-33; *see also Henderson v. Thomas*, 289 F.R.D. 506 (M.D. Ala. 2012) (certifying class of HIV-positive prisoners who alleged discrimination based on disability); *Hernandez v. County of Monterey*, 305 F.R.D. 132 (N.D. Cal. 2015) (certifying class of jail inmates who challenged health care and disability policies and practices).

Here, there is a danger of mootness based on the nature of the prison population and the risk that the Defendants may provide treatment to the named Plaintiffs in order to seek to resolve their individual issues, which will fail to resolve the systemic problems alleged. Similarly, there is a risk that a declaration of the rights of each named Plaintiff would not resolve the problems of the other class members because requiring the Defendants to fulfill their statutory and

constitutional obligations as to several individuals will not provide a resolution for the alleged systemic problems. Accordingly, Rule 23(b)(2) certification is proper.

III. In the Alternative, the Court Should Order Class Discovery.

If, despite the above showing regarding the appropriateness of class certification, the Court finds that the present record is not adequate to determine whether a class should be certified, Plaintiffs respectfully request that the Court order class discovery. *See Yaffe*, 454 F.2d at 1367. Defendants are in possession of extensive information about members of the proposed class, limited discovery of which would further demonstrate that class certification is proper.

CONCLUSION

The proposed class satisfies the prerequisites of Fed. R. Civ. P. 23(a) and (b). Plaintiffs respectfully request that this Court certify the proposed class of DOC prisoners with Hepatitis C and appoint the undersigned counsel as class counsel under Fed. R. Civ. P. 23(g). If the Court does not now certify a class, Plaintiffs request that it order class discovery.

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non-registered participants on May 16, 2016.

/s/ Joel H. Thompson
Joel H. Thompson

Date of MPCH Approval:	7/1/13	
Date of DOC Acknowledgment	7/1/13	
Effective Date:	7/1/13	
Title & Date of Replaced Guideline:	N/A	

MPCH Clinical Guidelines

Evaluation and Treatment of Hepatitis C and Cirrhosis

1. Introduction & Purpose

The Massachusetts Partnership for Health (MPCH) has adapted this guideline from the Federal Bureau of Prisons. The clinical practice guideline for **Evaluation and Treatment of Hepatitis C and Cirrhosis** provides recommendations for the medical management of Massachusetts Department of Correction inmates with Hepatitis C.

2. Transmission of Hepatitis C Virus

Hepatitis C virus (HCV) is a single-stranded, enveloped, RNA virus with multiple genotypes and subtypes. Genotype **1** is predominant in the United States. HCV is transmitted primarily by direct percutaneous exposures to infectious blood. Modes of transmission are summarized below in *Table I.*

Table 1. Modes of Transmission of Hepatitis C Virus

Percutaneous exposure to infectious blood (primary mode):

- Injection drug use
- Transmission of contaminated blood products (prior to July 1992)
- Tattooing with shared sharps in jails or prisons (potential mode)

Other modes of transmission (inefficient):

- Sexual contact (increased risk for inmates with history of STD or multiple sexual partners)
- Fighting, biting
- Congenital transmission (risk of 5-6%)

Ways HCV is NOT transmitted:

- Breast feeding
- Kissing, sneezing, hugging, coughing
- Food or water
- Casual contact, including sharing eating utensils or drinking glasses

NOTE: Most inmates diagnosed with HCV infection have behavioral risk factors fin. acquiring HCV and were infected prior to incarceration. Low levels of HCV transmission between inmates have been documented via seroincidence studies and contact investigations. However, large HCV outbreaks have not been reported in the correctional setting.

3. Acute Hepatitis C Infection

Diagnosis of Acute HCV Infection

Acute HCV infection is diagnosed when there is circumstantial evidence of new infection (such as recent exposure to a known HCV-infected inmate) or the presence of clinical features of acute Hepatitis (jaundice, nausea, anorexia, and malaise), and where the other causes of Hepatitis have been excluded. Acute Hepatitis C rarely causes fulminant hepatic failure.

The mean incubation period, from transmission of HCV infection to the onset of symptoms, is 6-7 weeks (range: 2-26 weeks); however, only 20-30% of newly infected persons are actually symptomatic. Serum ALT levels increase 4-12 weeks after acute HCV infection. HCV RNA is detectable in serum within days to 8 weeks following infection. Antibodies to HCV (anti-HCV) are detectable 3 months after infection in 90% of inmates. A subset of those with acute HCV infection spontaneously clear the virus. Laboratory criteria for diagnosis of acute Hepatitis C are summarized below in *Table 2.*

Table 2. Laboratory Criteria for• Diagnosis ofAcute Hepatitis C

Confirmation of acute Hepatitis C is confirmed by all of the following:

1. Marked elevation in ALT (>7 times the upper limit of normal, with or without symptoms of acute Hepatitis); and
2. Negative tests for acute Hepatitis A (IgM anti-HAV) and acute Hepatitis B (1gM anti-HBc); and
3. A positive anti-HCV screening immunoassay (enzyme immunoassay, EIA, or chemoluminescence immunoassay, CIA) that is confirmed with one of the following:
   - An immunoassay with a signal to cut-off ratio predictive of a true positive for that assay; or
   - An HCV RNA assay. (HCV RNA may be detected 1-3 weeks after exposure. However, viremia may be transient post-exposure, i.e., a negative HCV RNA does not rule out acute HCV infection.)

Treatment of Acute HCV Infection

Inmates diagnosed with acute Hepatitis C should be considered for antiviral therapy, in consultation with a physician who has expertise in managing Hepatitis C. Treatment can be delayed for 8 to 12 weeks after acute onset of Hepatitis to allow for spontaneous resolution of the infection. The optimal duration of a treatment regimen for acute infection is unknown. It is reasonable to treat for at least **12** weeks; however, up to a total of 24 weeks may be considered. At treatment weeks **4** and 12, an HCV RNA assay should be obtained to assess the response to treatment. The components of treatment of Acute HCV infection are presented in *Appendix I.*

4. Chronic Hepatitis C Infection

Natural History of Chronic HCV Infection

Most persons infected with HCV develop chronic infection; however, a small subset of newly infected persons are able to clear the virus spontaneously. Chronic HCV infection frequently results in high levels of HCV RNA in the blood, ranging from 10^5 to 10^7 international units (1U)/mL, despite the presence of HCV antibodies. The majority of persons with chronic HCV infection are asymptomatic. Chronic HCV infection has an unpredictable course, frequently characterized by fluctuations in ALT levels that may or may not be associated with significant liver disease. Approximately one-third of persons with chronic HCV infection have no laboratory or biopsy evidence of liver disease.

A small, but significant subset of persons with chronic HOT infection develop progressive fibrosis of the liver that leads to cirrhosis. Transfusion-acquired HCV, high levels of alcohol consumption, older age at the time of infection, HIV infection, chronic HBV infection, and male gender are associated with an increased risk of disease progression. However, neither the degree of viremia ("viral load") nor the HCV genotype affect the progression of liver disease. Other factors that

appear to increase the risk of cirrhosis, and decrease the response to antiviral therapy, include: hepatic steatosis, marked necroinflammation on biopsy, and certain host immunologic characteristics. Once cirrhosis develops in persons with chronic HCV infection, the risk of hepatocellular carcinoma (FICC) is about 1-4% per year. HCV accounts for one-third of the cases of HCC in the U.S. each year.

Stepwise Approach for Detecting, Evaluating, and Treating Chronic Hepatitis C

Current antiviral treatment for Hepatitis C has some limitations in terms of both efficacy and toxicity. With this in mind, MPCH has adopted a stepwise, systematic approach to Hepatitis C detection, evaluation, and treatment. *Table* 3 lists the ten steps in this process.

Table 3. Steps for Detecting, Evaluating, and Treating Chronic Hepatitis C

Step 1.	Appropriately screen inmates for Hepatitis C.
Step 2.	Provide initial medical follow-up for anti-HCV positive inmates.
Step 3a.	Determine if Hepatitis C treatment is *not* recommended.
Step 3b.	Monitor HCV-infected inmates who are *not* on treatment.
	For inmates who may be eligible for Hepatitis C treatment, proceed as follows:
Step 4.	Obtain HCV RNA assay and HCV genotype.
Step 5.	Assess liver fibrosis and need for a liver biopsy.
Step 6.	Determine if treatment should be initiated.
Step 7.	Conduct a pre-treatment evaluation.
Step 8.	Determine appropriate treatment and obtain informed consent.
Step 9a.	Manage side effects.
Step 9b.	Monitor treatment response.
Step 10.	Assess for sustained viral load (SVR).

Following is a discussion of steps 1 through 10 for detecting, evaluating and treating chronic HCV. The components of the steps are presented in *Appendix 2.*

Step 1. Appropriately screen inmates for Hepatitis C.

Inmate Education

Appropriately trained personnel should provide newly incarcerated inmates with educational information on the transmission, natural history, and medical management of HCV infection, in accordance with MPCH policy. Available educational tools are referenced in *Appendix* 7.

Screening Criteria

For sentenced inmates with Hepatitis C risk factors, screening is recommended at the initial health assessment. In addition, all inmates with certain clinical conditions should be screened for Hepatitis C, regardless of sentencing status. *Appendix 2, Step 1* lists the risk factors and clinical indications that should trigger screening for Hepatitis C viral infection. Unless clinically indicated, screening should ordinarily not be pursued for asymptomatic, highly mobile, non-sentenced inmates. However, non-sentenced inmates who have a history of injection dnig use or other high-risk behaviors for HCV should be provided with counseling. Education should cover the risks for HCV infection, as well as behaviors that would reduce transmission of HCV infection during incarceration and upon release.

Screening Method

The preferred screening test for HCV infection is an immunoassay (e.g., EIA or CIA) that measures antibodies to HCV antigens.

Refusal of Testing

Sentenced inmates who have HCV risk factors — and refuse testing at the baseline visit — should be counseled about HCV testing during periodic preventive health visits.

Step 2. Provide initial medical follow-up for anti-HCV positive inmates.

Baseline Evaluation

A baseline clinician evaluation should be conducted for all inmates who are anti-HCV positive. At minimum, this evaluation should include the following:

Targeted history and physical examination: Evaluate for signs and symptoms of liver disease, quantify prior alcohol consumption, and determine risk behaviors for acquiring HCV infection. Attempt to estimate and document the earliest possible date of infection, including when risk factors for exposures started and stopped, e.g., the time period in which the inmate engaged in injection drug use, Evaluate for other possible causes of liver disease, especially alcoholism, nonalcoholic steatohepatitis (NASH), iron overload, and autoimmune Hepatitis. Inquire about prior treatment for HCV infection, specific medications used, dosages and duration of treatment, and outcomes, if known.

Laboratory tests: Recommended baseline laboratory tests are listed in *Appendix 3.* However, until it is determined that an inmate is a potential candidate for treatment (see Steps 3a and 3b, below), do not obtain an HCV RNA, an HCV genotype, or a liver biopsy.

Inmate Education

Inmates diagnosed with chronic HCV infection should be counseled by a health care provider regarding the natural history of the infection, potential treatment options, and specific measures to prevent transmitting HCV infection to others (both during incarceration and upon release). Sources for Hepatitis C educational materials are listed in *Appendix 7.*

Preventive Health Measures

All inmates who are anti-HCV positive should be evaluated to assess the need for the preventive health interventions outlined in *Appendix 2, Step 2.*

Step 3a. Determine if Hepatitis C treatment is *not recommended.*

Next, determine if treatment for Hepatitis C is not recommended based on the following criteria:

I. Pegylated interferon is contraindicated. Inmates with chronic HCV infection who are being considered for antiviral therapy should first be assessed for contraindications to interferon, as listed in *Appendix 2, Step 3a.* Inmates with contraindications to interferon cannot be treated for Hepatitis C.

2. Ribavirin is contraindicated. Inmates with chronic HCV infection who are being considered for antiviral therapy should be assessed for contraindications to ribavirin, as listed in *Appendix 2, Step 3a.* Inmates with contraindications to ribavirin may not be treated for Hepatitis C.

3. Inmate will be incarcerated for an insufficient period of time to complete treatment. Inmates who are candidates for Hepatitis C treatment but whose anticipated length of stay will not allow sufficient time to complete therapy, should ordinarily not be started on antiviral therapy. This includes pre-trial and non-sentenced inmates, or inmates whose anticipated release date will not allow sufficient time to complete treatment.

The potential for interruption of antiviral therapy for Hepatitis C places an inmate at risk for a number of adverse
outcomes, including treatment failure if the course of treatment is not completed and adverse effects from medications if the inmate does not receive the required laboratory and clinical monitoring upon release or transfer.

MPCH anticipates the course of therapy to be 3.5 years for Genotype 1, 4, 5, 6. For Genotype 2 and 3, the anticipated course of therapy is 2.5 years.

Observation	Minimum of 12 Months	PCP to identify the inmate's social, medical and mental health concerns/issues, develop necessary treatment plans, and monitor compliance.
Evaluation	Up To 12 Months	Initial specialty consult and labs to begin work-up. In-hospital liver biopsy procedure (if indicated). Follow-up specialty consultation to review results and outline treatment plan and dosage recommendations.
Treatment	Up To 12 Months	Up to 48 weeks of prescribed therapy.
Follow-Up	6 Months	Obtain SVR blood test which determines the "virologic cure" of the treatment 24 weeks after end of therapy, and provide appropriate follow-up (current practice).

NOTE: Inmates entering custody who are currently being treatedfbr Hepatitis C should be maintained on antiviral therapy (unless medically contraindicated). The process is outlined in Hepatitis C Medication Therapy Intake Worksheet (Form 8102).

In the event that an inmate is scheduled for release, a referral should be directed to MPCH Chief Coordinator of Reentry and Aftercare Services 90 days prior to release. A Discharge Planner will meet with the inmate, review the chart, and consult with HSU staff as needed. The Discharge Planner will then work with community health agencies, as well as obtain necessary releases and appropriate referrals will be made to provide continuity of care.

4. The inmate has an unstable medical or mental health condition which precludes Hepatitis C treatment, e.g., refractory HIV-infection with AIDS, uncontrolled diabetes mellitus, life-threatening COPD or CHF, or uncontrolled depression,
5. The inmate refuses treatment. Inmates should initially be provided with counseling about Hepatitis C treatment. If an inmate then refuses the possibility of treatment, the refusal should be documented in the medical record.

If any one of the above criteria are present, Hepatitis C treatment should not be pursued. Document in the medical record the reason Hepatitis C treatment is not currently recommended. No further Hepatitis C testing is indicated at this time, including HCV RNA testing, HCV genotyping, or liver biopsy. However, continue to monitor the inmate, as discussed in Step 3b.

Step 3b. Monitor HCV-infected inmates who are not on treatment.

HCV-infected inmates for whom treatment is not recommended should continue to be followed in chronic care clinic, and evaluated periodically to determine if Hepatitis C treatment should be reconsidered. Monitoring recommendations are outlined in *Appendix 2, Step 3b.*

For inmates who may be eligible for Hepatitis C treatment, proceed as follows:

Step 4. Obtain HCV RNA assay and HCV genotype.

HCV RNA

The detection of anti-HCV by immunoassay in a person who has risk factors for acquiring HCV infection strongly suggests prior infection. However, before initiating antiviral therapy, an HCV RNA level (viral load) is required in order to confirm chronic infection and guide therapy. If the HCV RNA level is undetectable, the individual can be considered uninfected. Possible explanations include either host clearance of viremia or a "false-positive" immunoassay result.

NOTES:

1. *Strict adherence to current reference laboratory test processing guidelines for HCV RNA test samples is essential; viral RNA is unstable, and false negative tests may result from inadequate or inappropriate processing.*
2. *For monitoring purposes, it is important to use the same laboratory test before and during therapy.*
3. *When treating with an HCV PI-based regimen, the HCV RNA test should have a lower limit of quantitation of at least 43 IU/m1 and a lower limit of detection of at least 10 Whirl. If the HCV RNA result is below the lower limit of detection, the report should indicate further if the HCV RNA is detectable or undetectable.*
4. *The RIBA supplemental test is no longer recommended for diagnosing chronic HCV infection.*

HCV Genotype

An HCV genotype must be obtained prior to treatment initiation. The HCV genotype significantly influences the evaluation strategy, inmate counseling messages, the decision to treat, the specific medications and regimens, and the duration of therapy. Treatment response varies markedly by HCV genotype and medication regimen. Those with genotypes 2 or 3 have a 70-80% sustained viral response rate to pegylated interferon/ribavirin therapy, compared to a 4045% response rate for genotype 1. The addition of an HCV Protease Inhibitor to pegylated interferon and ribavirin increases the sustained viral response rate in genotype 1 to 60-80%. Repeat genotype testing is not indicated, except in the rare instance when re-infection is suspected.

Upon receipt of laboratory results, submit an HCV Specialty Referral to MPCH Referral Management.

Step 5. Assess liver fibrosis and need for a liver biopsy.

In inmates with chronic Hepatitis C, liver biopsy has been the primary means for determining the stage of the liver disease and the need for treatment. In general, inmates treated for HCV should have "more than portal fibrosis." General criteria for liver biopsy are outlined in *Appendix 2, Step 5.* Those with genotype 1 will ordinarily require a biopsy. Inmates with genotype 2 or 3 usually do not need a biopsy unless they are HIV-infected or another source of liver disease is suspected.

Calculation of APRI

Recent data indicate that the degree of liver fibrosis is correlated with the AST/Platelet Ratio Index (APRI), a simple ratio of two common lab values. Higher APRI values have been associated with higher stages of liver fibrosis on biopsy. Therefore, MPCH should utilize APRI values when prioritizing referral of inmates with genotype I, 4, 5, orb for liver biopsies. Inmates who have an APRI of <0.5 are lower priority for biopsy; inmates who have an APRI of >0.5 are higher priority for biopsy - with the higher the APRI, the higher the priority for biopsy. The APRI calculation is provided below in *Table 4.*

Table 4. AST/Platelet Ratio Index (APRI) Calculation

Formula:	{AST / lab upper limit of normal (ULN)* for AST x 100) / (platelet count / 1000)
Example:	AST = 80, AST laboratory ULN = **40,** Platelet count = 100,000 (80 / 40 x 100) / (100,000 / 1000) = 2.0 APRI

** Use "upper limit of normal (U1,1')" value that is used by the laboratory that ran the AST test.*

Interpretation of Liver Biopsy Results

Histologically, fibrosis progresses along a continuum, with portal fibrosis representing an earlier stage of fibrosis and cirrhosis representing a late (or advanced) stage of fibrosis. The intermediate stages of fibrosis - periportal fibrosis and bridging fibrosis - as determined histologically are generally recognized as the most appropriate stage for initiating treatment. These intermediate stages of fibrosis correlate with the IASL, Ludwig and Metavir Stages "2" and "3," and the Ishak stages "3" and "4." Regardless of genotype, treatment should be considered with liver biopsy results as follows: IASL, Batts & Ludwig, or Metavir > Stage 2; or Ishak > Stage 3.

The primary scoring systems for staging hepatic fibrosis on liver biopsy are compared in *Table 5.*

Table 5. Scoring Systems for Hepatic Fibrosis (IASL Ishak, Metavir, and Batts & Ludwig)

Score	IASL	Batts & Ludwig	Metavir	Ishak
0	No fibrosis	No fibrosis	No fibrosis	No fibrosis
I	Mild fibrosis	Fibrous portal expansion	Periportal fibrotic expansion	Fibrosis expansion of some portal areas, with or without short fibrous septa
2	**Moderate fibrosis**	**Rare bridges or septae**	**Periportal septae (>1**	Fibrous expansion of most portal areas, with or without short fibrous septa
3	**Severe fibrosis**	**Numerous bridges or septae**	**Portal-central septae .**	**Fibrous expansion of most portal areas, with occasional portal-portal bridging**
4	**Cirrhosis**	**Cirrhosis**	**Cirrhosis**	**Fibrous expansion of most portal areas, with marked bridging (portal-portal and portal-central)**
5				**Marked bridging (portal-portal, and portal-central) with occasional nodules (incomplete cirrhosis) .:**
6				**Cirrhosis, probable or definite**

*Note: The shaded area with the **bolded** text indicate a significant liver biopsy result with a degree of fibrosis for which antiviral therapy should be considered*

Reference: Ghany, et al. AASLD practice guidelines. Diagnosis, management and treatment of Hepatitis C; an update. *Hepatology,* 2009; 49:1356-1358.

Step 6. Determine if treatment should be initiated.

Current HCV treatment options have some limitations in terms of both efficacy and toxicity. Each inmate with chronic Hepatitis C should be evaluated carefully to assess the relative risks and benefits of the following: beginning therapy immediately, delaying therapy, or deferring treatment indefinitely. Prior to initiating treatment, inmates should be counseled about the potential benefits of treatment — the likelihood of achieving a sustained viral response (SVR) — as well as the potential side effects. The rationale for treatment decisions should be documented in the medical record.

Indications for Antiviral Therapy

Antiviral therapy is generally indicated for inmates with chronic Hepatitis C if they have no contraindications to treatment and present with at least one of the following:

- Genotype 1 and liver biopsy result with evidence of progressive fibrosis (either IASL, Batts & Ludwig, or Metavir > Stage 2; or Ishak > Stage 3)
- Genotype 2 or 3 (with no biopsy performed)

Genotypes 4, 5, or 6, or untypeable: The best approach to management of these cases is not clearly defined by the medical literature. Until further data become available, the indication (but not necessarily the regimen) for treatment of genotypes 4, 5, or 6, or untypeable HCV should be the same as for genotype I as noted above.

Various co-infections or co-morbidities, such as cirrhosis and renal disease, may affect treatment decisions and are discussed later in the document.

Special Considerations Related to Initiating Antiviral Therapy

The following co-morbidities, while not absolute contraindications, should be carefully assessed when considering whether or not to initiate antiviral treatment.

Mental illness: Interferon can cause or exacerbate depression, and causes mood changes in virtually all inmates. Therefore, inmates who have a history of major depression should be screened by a psychologist or a psychiatrist, and receive counseling on the risk of relapse of their depression posed by interferon treatment. For these inmates, careful consideration should be given to prophylactic treatment of depression. Utilize an SSRI (or the antidepressant that was most successful in treating the inmate's prior episodes of depression) for a period of three-to-six months prior to initiating interferon therapy. Similarly, other major psychiatric illnesses such as bipolar disorder, schizophrenia, and schizoaffective disorder should be well-controlled with stable doses of medication for at least six months prior to initiating interferon. Inmates with severe axis H diagnoses should be assessed by a mental health professional for their ability to comply with the frequent clinical and laboratory monitoring that is required for the safe administration of pegylated interferon and ribavirin.

Alcohol: HCV-infected inmates with significant alcohol abuse histories should receive specific counseling messages. Heavy and prolonged alcohol use is an independent risk factor for the development of cirrhosis, and alcohol accelerates the progression of HCV-related fibrosis. Hepatitis C treatment without abstinence from alcohol is unlikely to be of benefit. The treatment response to peginterferon plus ribavirin is significantly reduced in individuals who drink more than 30 grams of alcohol per day, and perhaps with lower levels of consumption, as well. An inmate's unwillingness to abstain from alcohol intake while incarcerated is a potential indicator of alcoholism and should be evaluated. Effective treatment for alcoholism should be offered in prison to as many HCV-infected inmates as possible, whether or not they have been administered Hepatitis C treatment or have responded to such treatment.

Substance abuse: Inmates who are significant abusers of substances other than alcohol may have a number of medical issues that can affect or be affected by Hepatitis C treatment. Injection drug users are at risk for HIV, HBV, endocarditis, and possible re-infection with HCV. Amphetamine and cocaine abuse may result in cardiovascular complications. Ongoing substance use in the controlled environment of prison or jail is, at best, an indicator that **the** inmate is not taking adequate responsibility for his or her overall health. Treatment decisions must be individualized where these issues are present,

Inmate Counseling

In weighing treatment options, the following factors should be considered and discussed with the inmate:

- For those with chronic Hepatitis C infection, the risk of developing cirrhosis ranges from 5% to 25%, and usually occurs over a period of 25-30 years after initial infection.

  It is difficult to predict which HCV-infected persons will develop cirrhosis or who will respond to treatment.

- The rate of sustained viral response (SVR) varies significantly by genotype and the medication used. Dual therapy (DT) with pegylated interferon and ribavirin achieves an SVR of 70-80% for genotypes 2 and 3, compared to only 40-45% for genotype **1.** However, triple therapy for genotype 1 that uses one of the newly approved HCV Protease Inhibitors (P1) — either boceprevir or telaprevir—in addition to pegylated interferon and ribavirin achieves SVR rates of 60-80%.
- Although current antiviral therapy is usually well-tolerated, there are many — and sometimes serious — side effects to antiviral therapy.

- Close adherence to the drug regimen is essential to increasing the likelihood of "cure," as well as decreasing the risk of virologic resistance in the case of triple therapy.

- Future Hepatitis C treatments may be more effective and better tolerated than those currently available. At this time, triple therapy is considered optimal for the treatment of HCV genotype I. However, this treatment can be complex and is associated with a higher rate of side effects than treatment with pegylated interferon and ribavirin alone; newer therapies that are projected to become available within a few years could simplify the regimen and decrease the risk of virologic resistance. For these reasons, the decision to treat HCV genotype 1 infection with stage 2 fibrosis should be made on a case-by-case basis after discussion with each inmate.

  Inmates must be willing to be treated and willing to conform to the treatment requirements, including abstinence from alcohol, illicit drugs, and tattooing.

  Treatment during pregnancy is generally contraindicated. Because treatment with ribavirin is known to be teratogenic, pregnancy must be avoided during treatment and for the six months after treatment is completed — in both female inmates and the female partners of male inmates.

Step 7. Conduct a pre-treatment evaluation.

Inmates should be evaluated by a provider and screened for other medical conditions that may complicate antiviral therapy. Lab work and tests should be obtained in accordance with the time frames enumerated in the HCV Referral Form.

Laboratory tests: See *Appendix* 3 for list of recommended baseline laboratory tests.

Baseline assessment of visual acuity, including fundoscopy for inmates with diabetes or other ophthalmologic disorders.

Pregnancy test for all female inmates: Ribavirin may cause fetal abnormalities. All female inmates of childbearing potential must have a pregnancy test immediately prior to initiating therapy and monthly thereafter up to at least 6 months post-treatment.

Cardiac risk assessment: A basic cardiac risk assessment, performed by a clinician prior to treatment initiation, is critical because the hemolysis associated with ribavirin may precipitate angina pectoris. An electrocardiogram should be obtained in inmates with preexisting cardiac disease. Symptomatic inmates should be carefully evaluated for cardiac disease prior to initiating treatment, as recommended by specialist.

Other inmate-specific diagnostic tests as medically indicated.

Mental health evaluation: Before prescribing medication therapy, a psychiatrist or psychologist should perform a mental health evaluation: to determine if mental health treatment is warranted prior to antiviral therapy and whether ongoing mental health assessments are needed during treatment.

- The evaluation should include an assessment of axis I and axis II diagnoses, including a comprehensive alcohol and substance abuse history and a suicide risk assessment. Interferon therapy has been associated with changes in mood and affect in most individuals. In a small percentage of inmates undergoing interferon therapy, significant depression, suicide attempts, and completed suicides have resulted. An inmate's history of depression or suicide attempts should prompt heightened vigilance on the part of the treating providers; however, since the absence of such a history does not appear to lessen the risk of these side effects from interferon, all inmates should be carefully monitored for changes in mood.

- Other mental illnesses or conditions, if not treated or not in remission, may adversely affect the inmate's ability to successfully complete a course of antiviral treatment, due to issues of compliance or to an inability to tolerate even mild side effects.

Evaluation of inmates with compensated cirrhosis: Prior to treatment initiation, inmates with suspected or biopsy-confirmed, compensated cirrhosis should have a liver-spleen ultrasound or abdominal CT scan, and measurements of alpha-fetoprotein. If the ultrasound result points to the possibility of portal hypertension (marked splenomegaly, ascites, retrograde flow through the portal vein), then an upper endoscopy screening for esophageal varices should be performed. CT often reveals esophageal varices, which must then be endoscopically visualized to determine size and extent. If hepatocellular carcinoma (HCC) or decompensated cirrhosis is diagnosed, antiviral therapy is contraindicated. (See compensated cirrhosis and decompensated cirrhosis in Definitions section.)

Step 8. Determine appropriate treatment and obtain informed consent.

Treatment of chronic HCV is complex and may require expert consultation. If consultants from the local community are utilized, it is important to familiarize them with the MPCH's approach to this condition.

Triple Therapy

Triple therapy with an HCV Protease Inhibitor (PI) such as boceprevir (VictrelisTM) or telaprevir (IncivekTm), in combination with pegylated interferon and ribavirin, is the preferred treatment for genotype 1 only. It is not indicated for the treatment of any other HCV genotype. HCV PIs are either contraindicated or not recommended in a number of other situations, as described below. In such cases, dual therapy for genotype 1 should be considered, unless it is contraindicated.

Indications for Triple Therapy

HCV genotype only ***aml*** liver biopsy evidence of progressive fibrosis, Le., stage 2 (Batts and Ludwicr, periportal) or higher, including compensated cirrhosis.

Treatment-naive as well as relapsers or partial responders to prior therapy with pegylated interferon and ribavirin, may be considered.

Contraindications and Exclusions for HCV PIs for Genotype 1

Contraindications to pegylated interferon and ribavirin, including decompensated cirrhosis and pregnancy (HCV PIs should never be used as monotherapy).

- Co-infection with HBV or IJW
- Solid organ transplant
- Medications that are inducers of or metabolized by CYP3A. Examples of medications that are either contraindicated, not recommended, or require dosage adjustment or close monitoring when used in combination with HCV PIs include: Certain antiarrhythmics (amiodaronc, bepredil, digoxin, flecainide, lidocaine, propafenone, quinidine), macrolide antibiotics (clarithromycin, erythromycin, telithromycin), anticonvulsants (carbamazepine, phenobarbital, phenytoin), antidepressants (desipramine, trazadone), antifiingal (itraconazole, ketoconazole, posaconazole, voriconazole), calcium channel blockers (dihydropyridine and non-dihydropyridine), ergots (ergotamine, dihydroergotamine, ergonovine, methylergonovine), immunosuppressants (cyclosporine, simlimus, tacrolimus, and some inhaled or systemic steroids), PDE5 inhibitors (sildenafil, tadalafil, vardenafil), HIV protease inhibitors, sedative/hypnotics (alprazolam, midazolam, triazolam), statins (atorvastatin, lovastatin, simvastatin), alfuzosin, bosentan, colchieine, drospirenone, pimozide, rifabutin/rifampin, salmeterol, St. John's wort, warfarin.

  NOTE: Inmates on medications that are either contraMdicated or not recommended should be assessed to determine the medical necessity of the medications they are taking, and should be considered for alternative medications in the same or a different class, as clinically appropriate.

- Inability to adhere to a complex medication regimen, as demonstrated by past history of non-adherence to treatment plans or call outs, or unwillingness to consent to treatment
- Hypersensitivity to the specific HCV PI being considered, or any of its components.

- Prior treatment failure with either a boceprevir- or telaprevir-based regimen.

Selecting the Most Appropriate WV PI for Genotype 1

Boceprevir (BCV) is the MPCH formulary agent. Telaprevir (TLV) may be considered where boceprevir is contraindicated and will be subject to non-formulary review.

Dosing of HCV Pis for Genotype 1

Boceprevir is 800 mg (four 200 mg capsules) by mouth every 8 hours (+1- 1 hour) with a snack. Telaprevir is 750 mg (two 375 mg tablets) by mouth every 8 hours (+1- 1 hour) with a 20-gram fat snack. Refer to *Appendix 2, Step 8* and *Appendix* 6 for more information on dosing of HCV Pis.

Dosing of pegylated interferon and ribavirin is the same when used as dual therapy or as triple therapy in combination with an HCV PI. Detailed drug dosages and potential side effects of pegylated interferon and ribavirin are outlined in *Appendix 2, Step 8,* and *Appendix* 5. See *Appendix 3,* Hepatitis C Treatment Monitoring Schedule for information on monitoring parameters.

Notes on dosing of HCV PIs for genotype 1:

I. HCV PIs should be prescribed and taken every 8 hours, not TID.

2. *Boceprevir or telaprevir should always be prescribed at full doses or not at all. The doses should not be increased or decreased for any reason. They should be prescribed as noted above, or either discontinued or not prescribed at all, as determined by the clinical situation.*
3. *Each dose must be taken with food. For boceprevir, a light snack is sufficient. Telaprevir must be taken with a snack that has at least 20 grams offat.*
4. *These medications must be prescribed and taken eve))' 8 hours, +/- one hour. Adherence to this regimen is necessary to achieve safe and effective outcomes. However, the inmate should be counseled on management of missed doses. For either HCV PI, ifa dose is missed, the next dose should NOT be doubled. If a boceprevir dose is missed, the missed dose may be taken with food so long as it is remembered more than 2 hours before the next dose; it should be skipped if there are 2 hours or less before the next dose. If a telaprevir dose is missed, the missed dose may he taken with a 20-gram fat snack if it is remembered more than 4 hours before the next dose, but should be skipped if there are 4 hours or less before the next dose.*

Dual Therapy

Dual therapy with once-weekly pegylated interferon (pegylated interferon, alpha 2B is the formulary) injections and twice-daily oral ribavirin is the standard treatment for all HCV genotypes except genotype 1. Dual therapy may also be appropriate for treatment of genotype I when there are contraindications or exclusions to using HCV PIs, e.g., co-infection with HBV or HIV, or use of certain medications. (Refer to the section on Triple Therapy above, under Step 8 in Section 4.)

Standard dosing is detailed in *Appendix 2, Step 8.* See *Appendix 5,* Interferon/Ribavirin Drug Information for more detailed information on dosing in certain clinical circumstances, contraindications, and side effects. See *Appendix* 3, Hepatitis C Treatment Monitoring Schedule for information on monitoring parameters.

Pretreatment Consent

The medications used to treat HCV have significant potential side effects; these side effects for dual and triple therapy are outlined in *Appendix* 5 and *Appendix 6,* and should be discussed with the inmate prior to treatment initiation. Issues unique to the HCV Pis (compared to dual therapy) should also be discussed, including: the potential for development of resistance in the event of treatment failure, and the likelihood of new medications in the near future that might entail an all-oral regimen or have fewer side effects. In cases of mono-infection with HCV genotype 1 and a lower stage of fibrosis (e.g., stage 2, predominantly periportal fibrosis), the option of postponing treatment should be presented to the inmate and discussed. The MPCH Consent to Hepatitis C Treatment Form must be reviewed with and signed by the inmate and the primary care provider, prior to starting treatment.

Step 9a. Manage side effects.

Recommended baseline, pre-treatment and ongoing clinical evaluations and laboratory studies are summarized in *Appendix 3,* Hepatitis C Treatment Monitoring Schedule. At a minimum, inmates receiving antiviral treatment should be clinically evaluated at weeks 1, 2, and 4, and then monthly thereafter. At each visit, inmates should be assessed for medication adherence, side effects and potential complications. Those with compensated cirrhosis (see compensated cirrhosis in Definitions section), HIV infection, or other co-morbid conditions will require more frequent monitoring, as will those who develop significant side effects or complications during therapy. While inmates are taking interferon, psychiatry and psychology consultations should be provided, as clinically indicated.

Throughout the inmate's treatment for Hepatitis C, the clinician's evaluations should be directed at inquiring about the common side effects of interferon and ribavirin in order to make decisions about dose adjustments; investigate new symptoms such as chest pain, dyspnea, or visual changes; or reassure the inmate that he or she is experiencing "normal" side effects of treatment.

Assessment and management of the more frequently occurring side effects from HCV treatment are discussed below:

- **Flu-like symptoms**: Muscle aches, headaches, and low-grade fevers are experienced by over 80% of inmates taking interferon. Inmates should be counseled to expect these symptoms, usually about 48 hours after the weekly injection, and resolving 24-48 hours before the next injection. These symptoms usually appear after the third or fourth dose of pegylated interferon, and tend to subside after about 3 months of treatment. Acetaminophen, up to 2 grams per day, and increased fluid intake may be recommended to manage these symptoms. Flu-like symptoms can be treated prophylactically by administering I gram of acetaminophen 30 minutes prior to peginterferon injection. *Nonsteroidal anti-inflammatory agents (NSA1Ds) ordinarily should not be prescribed because of hepatotoxicity and the underlying liver disease.*
- **Mood changes**: Virtually all inmates on interferon will experience at least some irritability. This should be discussed at each visit to determine if other symptoms of depression are developing. A low threshold for initiating an SSRI should be maintained while inmates are taking interferon.
- **Rashes**: A variety of deimatologic conditions are associated with both the HCV infection and the medications used to treat the HCV infection, including interferon/ribavirin and the HCV Pis. New rashes during treatment are usually mild and self-limited, or respond to topical low-potency corticosteroids.

  There is an increased incidence of rash with those inmates on triple therapy that includes telaprevir. Incidence of rash occurs in approximately 50% of inmates using telaprevir in triple therapy, as opposed to approximately 30% in dual therapy. The rash usually develops in the first 4 weeks of triple therapy, but may occur any time during treatment. In general, the rash improves after the discontinuation of the medication, but may take weeks to fully clear. The rash may occur with or without pruritus and may range from mild to moderate to severe; however, severe or serious rashes are rare. Mild to moderate rash is defined as involving less than 50% of the body surface area. Severe rash is generalized, covers 50% or greater of the body surface, or includes the presence of vesicles, bullae, or ulcerations. Management of mild to moderate rash includes monitoring for progression/systemic symptoms and maintaining general skin care practices; oral antihistamines and/or topical steroids may be considered. Systemic corticosteroids are NOT recommended. *Do not reduce the dose of HCV PI.* Discontinue telaprevir if the rash progresses or becomes severe, or if systemic symptoms emerge. In this setting, pegylated interferon/ribavirin may be continued following discontinuation of telaprevir, but should be discontinued if the rash shows no improvement in 7 days. Consider oral antihistamines and/or topical steroids. *Do not restart treatment.*

- **Chest pain**: New onset of chest pain during HCV treatment should be presumed to be angina pectoris until proven otherwise. The development of anemia during treatment can precipitate angina in individuals with occult coronary artery stenosis.
- **Visual disturbances**: Ischemic retinopathy and retinal or vitreous hemorrhages can occur during interferon therapy, though rarely. The risk may be greater in diabetic inmates. These inmates should be counseled to

immediately report any changes in vision. A baseline retinal examination prior to treatment is recommended for diabetics and those with preexisting ophthalmologic disorders, with fimdoscopie examinations performed periodically and as clinically indicated during treatment.

- **Hair loss:** Alopecia areata occurs in approximately 20% of inmates on HCV treatment. Inmates should be advised of this possibility, but also informed that this is self-limited after completion of treatment.
- **Thyroid dysfunction**: Approximately 4% of persons treated with interferon develop thyroid dysfunctions that may result in irreversible thyroid dysfunction — even with cessation of drug therapy, The occurrence of hypothyroidism usually can be managed with hormone replacement therapy while continuing interferon, on a case-by-case basis. Occurrence of hyperthyroidism usually necessitates discontinuation of interferon. If interferon must be discontinued due to thyroid dysfunction, the entire HCV treatment regimen must be discontinued as well.
- **Anemia:** A common complication of antiviral therapy is anemia. Ribavirin causes a dose-related hemolysis; whereas, interferon can suppress red blood cell production. The rates of anemia nearly double when one of the HCV PIs is added to pegylated interferon and ribavirin. Inmates who develop refractory anemia, progressive anemia beyond 8 weeks of treatment, or develop anemia late in the course of therapy should have a thorough evaluation for other treatable causes of anemia, such as iron deficiency anemia, gastrointestinal blood loss, and excessive menstrual blood loss. Specific strategies for managing drug-induced anemia are dependent on the degree of anemia, the presence of complicating co-morbidities such as heart disease, and the inmate-inmate's virologic response to antiviral therapy. Guidance regarding drug dosage adjustments, and criteria for the use of recombinant erythropoietin, are outlined in *Appendix 2, Step 9b.* If ribavirin must be discontinued due to anemia, the entire HCV treatment regimen must be discontinued as well.

  Neutropenia: Interferon-induced bone marrow suppression may cause neutropenia. The majority of the inmates who develop neutropenia while on interferon have few serious side effects. Inmates with cirrhosis are at higher risk of neutropenic complications, such as sepsis, and should be followed closely. Specific strategies for neutropenia management are dependent on the degree of neutropenia, the extent of liver disease, the presence of co-morbidities that predispose to infection, and the inmate-inmate's virologic response to antiviral therapy. Guidance regarding interferon dosage adjustments and criteria for the use of granulocyte colony stimulating factor are outlined in *Appendix 2, Step 9. If* pegylated interferon is discontinued due to neutropenia, the entire HCV treatment regimen must be discontinued as well.

  Thrombocytopenia: Thrombocytopenia from bone marrow suppression is a potentially serious complication of interferon therapy, particularly in inmates with cirrhosis who may have low platelet counts from the liver disease itself. Inmates with thrombocytopenia should be monitored closely while on antiviral therapy. Interferon should be dose-adjusted or discontinued, based on the degree of thrombocytopenia, as outlined in *Appendix 2, Step 9b.* If pegylated interferon is discontinued due to thrombocytopenia, the entire HCV treatment regimen must be discontinued as well.
- **Dysgeusia:** An altered sense of taste occurs more commonly in inmates treated for HCV infection, especially with the use of HCV PIs. There are no specific recommendations for the treatment of this side effect.
- **Anorectal symptoms**: Diarrhea, anorectal discomfort, hemorrhoids, itching, and burning occur more commonly with telaprevir. General measures for itching such as topical steroids or anesthetics and/or antihistamines at bedtime, and standard anti-diarrheal measures such as fiber or loperamide, may be helpful in controlling these side effects.

Step 9b. Monitor treatment response.

Assessment of the inmate's response to therapy is based on HCV RNA test results at certain intervals in the treatment process, as shown in *Table 6.* For all inmates, on-treatment HCV RNA levels should be obtained at the end of treatment weeks 4, 12, and 24, and again when the medication treatment is complete. For boceprevir-based regimens, an HCV RNA level also should be obtained at the end of treatment week 8.

Table 6. HCV Treatment Response Categories

Testing Interval	If HCV RNA test shows ...	The test result is considered ...
End of week 4*	Undetectable HCV RNA	RVR — Rapid viral response
End of weeks 4 and 12	Undetectable HCV RNA	eRVR — Extended rapid viral response
End of week 12*	> 2 $\log_{io}$ reduction in HCV RNA	EVR— Early viral response (EVR is also used to describe undetectable HCV RNA at TW 8 with BCV-based regimen)
End of week 12	< 2 $\log_{io}$ reduction in HCV RNA	Null responder
End of week 24	> 2 $\log_{io}$ reduction in HCV RNA, but still detectable	Partial responder
End of recommended treatment period	Undetectable HCV RNA	ETR — end of treatment (at treatment completion)
24 weeks after ETR**	Undetectable HCV RNA	SVR — Sustained viral response (potential cure)
24 weeks after ETR	HCV RNA detectable	Relapser

** A viral response at week 4 and week 12 is closely correlated with treatment success. "*
For more information on assessing inmates for SVR, see Step 10 below.

The duration of **triple therapy** is determined by four variables:

1. The history of and response to prior HCV treatment with pegylated interferon and ribavirin,
2. The degree of liver fibrosis, specifically the presence or absence of cirrhosis,
3. Which of the two HCV Pis is used, and
4. The on-treatment response to triple therapy.

Step 8 of *Appendix 2,* summarizes the total weeks of therapy based on these variables.

NOTES:

I. Pegylated interferon and ribavirin are prescribed for the entire duration of therapy. The HCV Pis are prescribed for a shorter duration of time during the pegylated interferon and ribavirin treatment period.

2. The term treatment week (TW) refers to the number of weeks on treatment, starting with the first day of treatment with any of the medications.

3. HCV RNA tests should be obtained at the end of TWs 4, 12, 24, and at the end of treatment, for a telaprevir-based regimen. An additional HCV RNA test should be obtained at the end of DV 8 for a boceprevir-based regimen.

The medication regimens for triple therapy are relatively complicated. Refer to the table in Step 8 of *Appendix 2,* and the flowcharts in *Appendix 4.*

Boceprevir-Based Regimens

All boccprevir-based treatment regimens start with 4 weeks of dual therapy of pegylated interferon and ribavirin, and no boceprevir. This comprises TWs I through 4. At the beginning of TW 5, triple therapy starts with boceprevir being added to the pegylated interferon and ribavirin. However, if at TW 4 an RVR (HCV RNA) is undetectable the BCV is not added. The inmate continues 44 weeks more of dual therapy.

Four different treatment durations are possible — 28 weeks, 36 weeks, and two different 48-week regimens — as described below:

28 weeks: 4 weeks of pegylated interferon and ribavirin followed by 24 weeks of boceprevir, pegylated interferon, and ribavirin

- **36 weeks:** 4 weeks of pegylated interferon and ribavirin followed, by 32 weeks of boceprevir, pegylated interferon, and ribavirin

  48 weeks (4+32+12): 4 weeks of pegylated interferon and ribavirin followed by 32 weeks of boceprevir, pegylated interferon, and ribavirin, followed by 12 more weeks of pegylated interferon and ribavirin. This regimen is the same as the 36-week regimen with an additional 12 weeks of pegylated interferon and ribavirin added at the end. Another way to understand this regimen is that pegylated interferon and ribavirin are prescribed for a fill 48 weeks from start to finish—with boceprevir added for 32 weeks in the middle, starting after TW 4 and continuing through TW 36.

- **48 weeks (4+44):** 4 weeks of pegylated interferon and ribavirin, followed by 44 weeks of boceprevir, pegylated interferon, and ribavirin. This is only indicated for inmates with compensated cirrhosis.

Which of these four regimens of boceprevir-based therapy to use for a given inmate is determined by the inmate's prior treatment history (with pegylated interferon and ribavirin) and outcome, degree of fibrosis on liver biopsy (no cirrhosis vs. compensated cirrhosis), and on-treatment response to therapy, as described below:

Treatment-naïve with no cirrhosis:

- 28-week regimen if HCV RNA is undetectable at the end of TWs 8 and 24

  48-week (4+32+12) regimen if HCV RNA is detectable at 8 weeks, < 100 1U/m1 at 12 weeks and undetectable at 24 weeks

Prior relapser or partial responder with no cirrhosis:

- 36-week regimen if HCV RNA is undetectable at the end of TWs 8 and 24
- 48-week (4+32+12) regimen if HCV RNA is detectable at 8 weeks, < 10011J/m1 at 12 weeks and undetectable at 24 weeks.

Compensated cirrhosis:

- 48-week (4+44) regimen.

Indications for early discontinuation of boceprevir-based regimens due to treatment failure, as indicated by the HCV RNA response to treatment, include the following:

- HCV. RNA 7100 1U/rill at TW 12 or
- HCV ItNA detectable at TW 24 or
- HCV RNA increase of >1 $\log_{io}$ from nadir while on treatment

If any of these criteria are met, all therapy should be discontinued, including boceprevir, pegylated interferon, and ribavirin. Other criteria for early discontinuation of therapy include the severe adverse reactions described under Step 9a, Management of Side Effects.

Telanrevir-Based ReRimens

The first 12-week period of all telaprevir-based regimens includes all three medications — pegylated interferon, ribavirin, and telaprevir.

After 12 weeks, telaprevir is discontinued, while pegylated interferon and ribavirin are continued for an additional 12 weeks (24 weeks total) or an additional 36 weeks (48 weeks total), as noted below.

Indications for 24 total weeks of therapy:

- Treatment-naïve or prior relapser with an undetectable on-treatment HCV RNA at both 4 and 12 weeks

Indications for 48 total weeks of therapy:

- Treatment-naïve or prior relapse with on-treatment HCV RNA detectable, but = 1,000 IU/int at 4 and 12 weeks, and undetectable at 24 weeks
- Partial responder to dual therapy with on-treatment HCV RNA = 1,000 IU/m1 at 4 and 12 weeks, and undetectable at 24 weeks
- Compensated cirrhosis with on-treatment HCV RNA -= 1,000 IU/m1 at 4 and 12 weeks, and undetectable at 24 weeks (see compensated cirrhosis in Definitions section)

Indications for early discontinuation of telaprevir-based regimens due to treatment failure include the following:

- FICV RNA>I000 1U/m1 at TW 4 or 12 or
- HCV RNA detectable at TW 24 or
- HCV RNA increase of > l $\log_{in}$ from nadir while on treatment

If any of these criteria are met, all therapy should be discontinued, including telaprevir, pegylated interferon, and ribavirin. Other criteria for early discontinuation of therapy include the severe adverse reactions described under Step 9a, Management of Side Effects.

The recommended duration of dual therapy varies by HCV genotype and on-treatment HCV RNA response (refer to *Appendix 4* to see the following recommendations as flowcharts):

- Genotypes 1, 4, 5, and 6 are treated for 48 weeks. Genotypes 2 and 3 are treated for 24 weeks.

The optimal duration of dual therapy treatment for genotypes 4, 5, or 6, or untypeable HCV is unknown; these inmates should be treated with the 48-week course recommended for genotype 1.

Inmates who have HIV co-infection should be treated with 48 weeks of dual therapy, regardless of genotype.

Early discontinuation of dual therapy may be indicated, based on the documented response to treatment and the occurrence of side effects (see *Appendix 2, Step* 9, and *Appendix 8).*

Failure to achieve an EVR at 12 weeks is considered treatment failure (null response). ***Treatment should be discontinued.***

If an EVR at 12 weeks is achieved, but HCV RNA is still detectable, the HCV RNA test should be repeated at 24 weeks of treatment. Detectable HCV RNA at 24 weeks is considered treatment failure. ***Discontinue treatment.***

If the inmate fails to achieve an RVR at 4 weeks, but does have an EVR at 12 weeks, then 48 weeks of treatment is usually sufficient.

For inmates who achieve an RVR at 4 weeks, but experience significant side effects:

- Genotypes 1, 4, 5, and 6: 24 weeks of treatment may be sufficient. Discontinuation of therapy after at least 24 weeks of treatment can be considered on a case-by-case basis in consultation with an expert.
- Genotypes 2 and 3: 16 weeks of treatment may be sufficient. Discontinuation of therapy after 16-20 weeks of therapy can be considered on a case-by-case basis in consultation with an expert.

Step 10. Assess for sustained viral response (SVR).

An HCV RNA test should be obtained 24 weeks after the treatment is completed. A sustained viral response (SVR) is defined as undetectable HCV RNA at 24 weeks after completion of the treatment. If an SVR is achieved, the infection is considered eradicated. Inmates who achieve an SVR should have an HCV RNA test obtained one year following the end of their treatment. Those who have undetectable HCV RNA at this time can be discontinued from the chronic care clinic (unless there are other medical problems or concerns regarding the possibility of re-infection).

Considerations Regarding Retreatment

Inmates who do not achieve an SVR from antiviral therapy can be categorized as having a null response, partial response, or relapse, as defined in *Appendix 2, Step 9b.* Retreatment of such prior treatment failures should be considered on a case-by-case basis with the approval of the Statewide Medical Director, and with consideration of the following guidance:

- For treatment failures with non-pegylated interferon (with or without ribavirin), re-treatment should be considered on a case-by-case basis. HCV genotype 1 cases should be considered for triple therapy with an HCV PI-based regimen. Dual therapy with pegylated interferon and ribavirin of 48 weeks duration (in those who demonstrate an on-treatment virologic response) is used for retreatment of all other genotypes.
- Partial responders and relapsers to a regimen of pegylated interferon and ribavirin (dual therapy) can be considered for re-treatment if they have HCV genotype 1 and are appropriate candidates for treatment with an HCV PI-based regimen. All other genotypes will ordinarily not be re-treated. Although HCV PI-based regimens are approved for treatment of prior null responders to dual therapy, the response rates are relatively low. Considering the likelihood of developing viral resistance in the majority of such cases, retreatment with an HCV PI-based regimen is not currently recommended. Cases of advanced fibrosis or cirrhosis with prior null response to pegylated interferon and ribavirin should be considered for retreatment on a case-by-case basis.
- For treatment failures with an HCV PI-based regimen, re-treatment also is not indicated.

  For inmates who are eligible for re-treatment, it should only be considered for those who are the most likely to benefit from therapy and who are at significant risk of disease progression.
- Consensus interferon (interferon alfacon-1) is not recommended as an alternative re-treatment for prior treatment failures with a pegylated interferon and ribavirin regimen, due to the need for daily administration, as well as low response rates.

  Long-term antiviral maintenance therapy for prior treatment failures has been found to be ineffective and should not be prescribed.

Section 5. Complicating Medical Conditions

Compensated and Decompensated Cirrhosis

Inmates with HCV-related compensated cirrhosis can usually be treated with a standard regimen as described in this document. However, they have a higher rate of associated side effects, lower SVR rates, and should be monitored more closely.

Antiviral therapy is ordinarily contraindicated in inmates with Hepatitis C and evidence of decompensated cirrhosis, particularly if there is evidence of ascites or hepatic encephalopathy. Inmates with an isolated lab value indicating mild

impairment in hepatic synthetic function, e.g., slightly depressed albumin or elevated 1NR, should be considered for treatment on a case-by-case basis.

Renal Insufficiency

Persons with HCV infection have an increased risk of renal disease that may be associated with ciyoglobulinemia, and histologic findings that resemble idiopathic membranoproliferative glomerulonephritis (MPGN). Clinical manifestations include hetnaturia, proteinuria that is often in the nephrotic range, and a variable degree of renal insufficiency. Further diagnostic evaluation should be considered, e.g., eiyoglobulhis or renal biopsy, in consultation with a clinician experienced in the management of these conditions. Inmates with moderate-to-severe or progressive kidney disease (e.g., nephrotic syndrome, elevated plasma creatinine concentration, new hypertension, fibrosis, or tubulointerstitial disease on biopsy) should be considered for antiviral therapy for HCV infection, even in the absence of a degree of liver disease that ordinarily warrants antiviral therapy. Specific treatment regimens should be individualized in consultation with the Statewide Medical Director and available physician experts. Ribavirin should not be administered if the creatinine is >1.5 mg/dL or the estimated GFR is <50 rnL/min. Dose adjustments should be considered if the GFR is between 51-75 inUmin. Ribavirin should not be administered to inmates on dialysis. No dosage adjustments are required for the HCV PIs, boceprevir and telaprevir; however, they should not be prescribed when ribavirin is contraindicated.

Hemodialvsis

The goal of treating Hepatitis C in persons with end-stage renal disease is to reduce the progression of liver disease and/or to clear the HCV infection in inmates who may later undergo renal transplantation. Evaluation of these inmates is complicated by several factors:

- ALT levels are more likely to be normal or near-normal in hemodialysis inmates, even in the presence of significant fibrosis
- The need for a liver biopsy must be balanced against the increased risk of severe bleeding
- Hepatitis C treatment should be considered prior to referring the inmate for transplant (in consultation with a nephrologist).

These cases will be discussed and evaluated on a case-by-case in consultation with subspecialists.

HBV and HCV Co-Infections

Coexistent infection with both HBV and HCV is estimated to be present in 10-15% of individuals with chronic Hepatitis, cirrhosis, or hepatocellular carcinoma. HCV superinfection in HBsAg carriers appears to reduce HBV DNA levels in serum and liver tissues and to increase the rate of HRsAg seroconversion. Most inmates who have dual HCV and HBV infections have detectable serum HCV RNA, but undetectable or low HBV DNA levels, which indicates that HCV is the predominant cause of liver disease in these inmates. However, in about one-third of inmates, levels of HBV DNA and HCV RNA fluctuate over time. Liver disease in co-infected individuals is usually more severe than in inmates infected by HBV alone. Inmates with dual HBV and HCV infection may also have a higher rate of HCC, compared to inmates infected by either virus alone, particularly those who are anti-HCV and HBeAg positive.

Antiviral therapy for inmates with HBV and HCV co-infections should be initiated with great caution, and only in consultation with a specialist, due to the uncertainty of the risks and benefits of treatment and the lack of a recommended treatment regimen. All cases that may be candidates for treatment should be reviewed with a physician with expertise in viral Hepatitis treatment, and be approved via the MPCH Central Office non-formulary review process. Currently, HCV Pis are not approved for use with HBV and HCV co-infection cases.

HIV and HCV Co-Infections

The usual approach for screening for HCV infection should be applied to HIV-infected inmates. HIV-infected person with unexplained liver disease, a CD4 T-cell count <500 cells/mm^3, and who are anti-HCV negative should have an HCV RNA assay obtained.

Inmates co-infected with HIV and HCV have a two-fold increased risk of cirrhosis compared to those with HCV infection alone; thus they arc high priority among potential candidates for treatment. However, HCV treatment response rates are lower in HIV-infected inmates, and they have a higher risk of serious adverse effects.

Listed below are general recommendations related to the treatment of HCV/HIV co-infection. Prior to initiating treatment, consultation with an expert is recommended.

1. Co-infected inmates whose HIV infection is controlled and who have a significant liver biopsy result (either IASL, Batts & Ludwig, or Metavir > Stage 2; or Ishak > Stage 3), regardless of genotype, should be considered for HCV antiviral therapy.
2. Treatment for HIV and HCV infections should not be initiated simultaneously. If the inmate is a strong candidate for HIV treatment (AIDS or CD4+ T-cell count <350 cells/mm3), he or she should be treated first with HIV antiretroviral therapy. If not, consider initiating HCV antiviral therapy prior to initiating HIV treatment. It is generally recommended that several months elapse after initiating HIV antiretroviral therapy prior to initiating HCV treatment—so that adverse effects associated with the antiretroviral therapy can be distinguished from those associated with HCV treatment.
3. Inmates should be treated with peginterferon alfa and ribavirin at doses similar to those with HCV monoinfection.
4. Currently, HCV Pis are not approved for use with HIV and HCV co-infection cases, due to potential drug interactions and a lack of data to support the safety and efficacy when co-administered with HIV antiretroviral agents.
5. The recommended standard duration of HCV treatment is 48 weeks, regardless of genotype.
6. Drug interactions/contraindications/adverse reactions:

   Co-infection with HIV and HCV increases the risk for antiretroviral-induced hepatotoxicity. This is especially true for stavudine, nevirapine, full-dose ritonavir, and tipranavir boosted with a low dose of ritonavir. If possible, these antiretrovirals should not be used to treat HIV inmates co-infected with HCV. Regardless of which antiretroviral therapy (ART) is used, ALT and AST should be monitored monthly with any new ART, and then every 3 months. Asymptomatic ALT elevations up to 5 times the upper limit of normal can be monitored safely and do not require discontinuation of ART. Further evaluation should be undertaken for greater increases in the ALT, which may require temporary discontinuation or changing of the ART.

   Concurrent pharmacologic treatment of both HCV and HIV increases the risk for drug-drug interactions and drug toxicities. In particular, ribavirin increases the risk for pancreatitis and lactic acidosis in inmates treated with didanosine. Ribavirin also increases the risk of anemia in inmates treated with zidovudine. If possible, didanosine and zidovudine should be avoided or switched to another appropriate antiretroviral medication in 111V-infected inmates who are being considered for treatment of HCV infection with pegylated interferon and ribavirin.
7. Monitor closely those co-infected inmates for whom treatment is deferred (see *Appendix 2, Step 3b).* Calculate an APRI (see *Table* 4) every 6 months. Re-biopsy should occur at interval recommended by co-infection specialist.

Latent TB and Chronic HCV Co-Infection

Inmates with latent TB infection (LTBI) and chronic HCV infection should be considered for isoniazid treatment. They should be monitored for hepatotoxicity in accordance with the same guidelines established for latent TB inmates who do not have HCV infection. All inmates require screening for symptoms of Hepatitis while taking isoniazid. Those inmates with baseline ALT elevations also warrant periodic monitoring of their ALT levels.

Co-infected inmates can be treated concurrently for Hepatitis C and LTBI; however, it is advisable to initiate LTBI treatment first, assess if it is tolerated, and then start Hepatitis C treatment six months later. If both treatments are started at the same time, and elevations of ALT occur, it is not possible to determine which is the offending agent. isoniazid should be discontinued in inmates with marked elevations in ALT or significant signs or symptoms of Hepatitis, in accordance with MPCH Guidelines for the Management of Tuberculosis.

Section 6. Management of Cirrhosis

Transplantation Issues

Liver transplantation is the treatment of choice for inmates with hepatic failure from chronic HBV and HCV infections. However, the lack of available donor organs limits this option, not only for inmate populations, but also for the general population.

Nevertheless, inmates with hepatic failure from viral Hepatitis may be assessed for eligibility for liver transplantation on a case-by-case basis by evaluating inmate-inmate-specific factors such as the following: MELD scores that help predict inmate-inmate mortality, medical contraindications for transplantation, mental health stability, evidence of ongoing substance abuse, criminal history factors that may negate successful transplantation, and imitate-inmate motivation (as evidenced by adherence to current treatment recommendations). Inmates who are potential candidates for liver transplantation should be advised of the limited access to donor livers and, where available, be referred to local transplant centers for evaluation.

Morbidity Assessment Based on MELD Scores

The Model for End-Stage Liver Disease (MELD) predicts liver disease severity and the risk of three-month mortality using a "score" that is based on serum creatinine, serum total bilirubin, and prothrombin time (INR). In a study of inmates with end-stage liver disease, who were awaiting liver transplantation, three-month mortality was closely correlated with MELD scores:

MELD < 9 mortality = 2%
MELD = 20-29 mortality = 20%
MELD = 30-39 mortality = 53%
MELD > 40 mortality = 71%

The value of MELD as a predictor of mortality is limited by its dependency on serum creatinine, which can fluctuate with changes in fluid status. MELD is a better predictor of mortality for particular populations than for any given individual. Nevertheless, MELD provides useful information for assessing the morbidity of inmates with end-stage liver disease.

All inmates with decompensated cirrhosis should have a MELD score determined to assess their mortality risk. MELD scores should be recalculated over several weeks for inmates with shifting fluid status. The MELD score can be calculated by utilizing a calculator provided by the United Network for Organ Sharing, available at http://optn.transplant.hrsa.gov/resources/MeldPeldCalculator.asp?index=98. Data required includes: date of birth, bilirubin, creatinine, 1NR, and dialysis status. Inmates with MELD scores of 30 or greater should be considered for Medical Referral Center designation.

NOTE: The MELD score predicts mortality, independent of clinical parameters such as hepatic encephalopathy, ascites, and variceal bleeding.

Preventive Measures

The following preventive measures should be considered for inmates with cirrhosis:

- Immunize against influenza (annually), pneumococcal pneumonia, and Hepatitis A and B (unless immune).
- Provide inmate-inmate education:

  Eat a low-salt, low-fat, "heart healthy" diet.
  Completely abstain from alcohol during incarceration and after release.
  Avoid iron supplements and potentially hepatotoxic medications, such as nonsteroidal inflammatory drugs (NSAIDS).

- **Perform a baseline upper endoscopy (EGD)** to screen for esophageal varices. Once esophageal varices have developed, the annual rate of hemorrhage is 5-15%. The frequency of follow-up EGD is determined by the presence of risk factors for progression or bleeding of the varices, including decompensated cirrhosis, red wale marks on the variceal surface, and size of varices > 5 mm. Annual EGD is recommended for inmates with decompensated cirrhosis, whether or not varices are present, and for those with a history of variceal hemorrhage. Biennial EGD is recommended for inmates who have small varices that have not bled and who are not being treated with nonselective beta-blockers. EGD is recommended every 3 years for compensated cirrhosis with no varices. In general, routine follow-up EGD is not required for varices that have not bled if nonselective beta-blocker therapy is prescribed.
- **Nonselective beta-blocker therapy, such as propranolol or nadolol, is indicated** for prevention of variceal hemorrhage in inmates with varices of any size that have not bled, with either decompensated cirrhosis or red wale marks on the varices, and for all inmates with a history of variceal hemorrhage. Nonselective beta-blockers may be appropriate for inmates who have varices that have not bled, but who have no other risk factors for hemorrhage. This treatment is not indicated for inmates with cirrhosis who have no esophageal varices. The dose of beta-blocker should be titrated weekly to reduce the resting heart rate by 25% — without reducing the pulse to less than 55 beats/minute or the systolic blood pressure to lower than 90 mm Hg. The usual starting dose for oral propranolol is 20 mg twice each day, and for nadolol, 40 mg once daily. Once started, therapy should be continued indefinitely unless contraindicated. Nonselective beta-blocker therapy is relatively contraindicated in certain medical conditions such as asthma, peripheral vascular disease, and insulin-requiring diabetics with frequent hypoglycemic episodes.

– **Provide primary and secondary prophylaxis for spontaneous bacterial peritonitis (SBP**) with an antibiotic such as ciprofloxacin, or trimethoprim-sulfamethoxazole (TMP-SMX). Primary prophylaxis generally involves limited treatment periods in high risk inmates, such as those with upper gastrointestinal hemorrhage. Secondary prophylaxis is indicated in inmates with a history of one or more prior episodes of SBP. Oral medication options include: ciprofloxacin, 750 mg weekly; or TMP-SMX DS, one tablet daily.

– **Provide prophylaxis against hepatic encephalopathy, and be alert for the common factors which cause exacerbations of encephalopathy**. Lactulose is the mainstay of both treatment and prophylaxis for hepatic encephalopathy. Lactulose lowers the gut pH and converts NH_3 (ammonia) to NH4, which is non-absorbable and thus excreted in the stool. Certain antibiotics such as neomycin and rifaximin are also sometimes prescribed to alter the gut flora and thereby decrease ammonia production. However, good, controlled studies are lacking that clearly support the use of antibiotics over lactulose; moreover, long-term use of antibiotics has the potential for bacterial overgrowth syndromes. Neomycin also has potential nephrotoxicity and ototoxicity.

  The dose of lactulose (10 grams/15mL) is inmate-inmate-specific, typically starting at 15-30 nft. once or twice daily until the inmate-inmate is having two or three soft stools per day. If this dose does not adequately address the cognitive impairments, the dose may need to be increased, causing more frequent, semi-liquid stools.

  Lactulose enemas are the treatment of choice for somnolent inmates with encephalopathy who are unresponsive to verbal and/or painful stimuli. One liter of 20% lactulose is infused per rectum every hour until the inmate-inmate becomes arousable. Inmates with abnormal vital signs, low pulse oximetty, or periods of apnea should be hospitalized or placed on an ininmate-inmate unit at an IVIRC for this treatment.

  Common factors which exacerbate hepatic encephalopathy are:

  – Excess dietary protein intake
  – GI bleeding

    Infections (increased temperature results in dehydration)
  – Sedative/hypnotic and opiate use (even at "typical" doses)

    Overzealous diuresis with loop diuretics. (Decreased potassium and decreased plasma volume result in increased ammonia levels. Titrate diuretics incrementally, and correct hypokalemia when detected.)

  Screen for hepatoceilular carcinoma (HCC). Inmates with chronic HCV infection and cirrhosis are at increased risk for HCC. Although the optimal screening strategy is uncertain, a liver ultrasound should be considered every six months as the safest and most cost-effective approach. Screening should be conducted regardless of whether

or not the inmate has been treated for Hepatitis C. Serum alpha-ktoprotein screening is of limited use, since it is not usually elevated to a significant level until the tumor is at least 2 cm — which is easily detectable on ultrasound in virtually all inmates. CT scanning should ordinarily not be used in lieu of ultrasound for HCC screening, due to the high radiation exposure that would be anticipated over ten or more years of biannual scans.

HCC screening should begin when the inmate is found to have cirrhosis—whether by history, by liver biopsy, by presentation of decompensation such as bleeding esophageal varices or hepatic encephalopathy, or based on a pattern of clinical or laboratory findings. Ultrasound screening should be conducted on any HCV-infected inmate with the typical laboratory findings of cirrhosis, which include an inverted AST/ALT ratio, an albumin < 3.4, and a platelet count < 120-140K. An AST to platelet ratio index (APRI) significantly greater than 1.5 is also strongly suggestive of cirrhosis, and may be used as an independent marker to start screening for HCC (see *Table 4* for calculation).

Managing Complications and Co-Morbidities

Ascites: Of the major manifestations of decompensated cirrhosis, the most common is ascites. A diagnostic paracentesis by qualified personnel should be performed in newly presenting cases of ascites, and should include assessment of ascitic fluid cell count with differential, ascitic fluid total protein, and serum-ascites albumin gradient. A serum-ascites albumin gradient = 1.1 g/d1., is indicative of portal hypertension as the cause. Ascitic fluid cultures should be collected in blood culture bottles if infection is suspected, e.g., fever, abdominal pain, etc. Eighty-five percent of cases of ascites are caused by cirrhosis.

The primary treatment includes dietary sodium restriction of 2 gm/day, and a combination of oral diuretics using spironolactone and furosemide (starting at 100 mg and 40 mg, respectively) once daily in the morning. Monotherapy with spironolactone achieves less dramatic diuresis and is associated with a higher rate of hyperkalemia, but may be effective in the presence of smaller amounts of ascites or edema. If the desired weight and fluid loss is not achieved, these doses may be increased every 3 to 5 days (maintaining the same ratio) up to a maximum of 400 mg/day of spironolactone and 160 mg/day of furosemide. With this regimen, 90% of inmates with ascites can achieve the goals of treatment, which include a 24-hour urinary excretion of sodium > 78 mmol/day, and diuresis of ascites and edema with a maximum rate of weight loss of 0.5 Kg/day. A greater rate of weight loss is appropriate for inmates with greater amounts of edema. A spot urinary sodium/potassium ratio > l correlates fairly well with a 24-hour urine sodium excretion > 78 mmollday and is easier to obtain.

Failure to achieve treatment goals should prompt an assessment of adherence to sodium restriction and diuretic therapy, the use of nonsteroidal anti-inflammatories, which interfere with diuresis, and consideration of other causes of ascites. Amiloride may be used in place of spironolactone for inmates with painful gynecomastia. Although eplerenone, a selective tnineralocorticoid antagonist, has a much lower incidence of gynecomastia, its role in the treatment of ascites has not been well studied. Fluid restriction is indicated for serum sodium < 120-125 mFq/L. Diuretics should be discontinued if serum creatinine rises to > 2 ing/dL, serum sodium drops to < 120 mEq/L despite fluid restriction, or encephalopathy develops. Abstaining from alcohol and treatment for chronic Hepatitis B virus infection may improve the symptoms of decompensated cirrhosis from these causes. Treatment of ascites that is refractory to these interventions may include serial paracenteses, transjugular intrahepatic portasystemic shunt (TIPS), which usually is performed by an interventional radiologist, and/or liver transplantation. TIPS is effective in reducing ascites and rates of rebleeding from esophageal varices, but may be associated with more frequent or severe episodes of encephalopathy and does not improve mortality rates. Contraindications to TIPS include: primary prevention of variceal bleeding, congestive heart failure, moderate to severe pulmonary hypertension, uncontrolled infection or sepsis, bifiary obstruction, multiple hepatic cysts, hepatocellular carcinoma, hepatic vein obstruction or portal vein thrombosis, severe coagulopathy with 1NR > 5, or platelet count < 20,000/cm^3.

Pruritus: Pruritus in cirrhosis is thought to be due to increased bile acids from cholestasis, as well as possibly an increased production of endogenous opioids. Cholestatic pruritis may be caused by enhanced concentrations of bile salts in the systemic circulation and peripheral tissues, which is seen in inmates with primary biliary cirrhosis and chronic renal failure. Intestinal anion exchange resins such as cholestyramine, colestipol, and colesevelam bind many hydrophobic bile acids in the intestine and inhibit enterohepatic reuptake of intestinal bile salts; they are effective in decreasing disease-related, enhanced concentrations that can cause cholestatie pruritis. Sertraline, at 75-100 mg daily, has been found to be effective in inmates suffering from various forms of cholestasis. Naltrexone, an opioid antagonist, at 12.5-50 mg per day, may also

be effective. Exogenously administered narcotics can contribute to pruritus, so the inmate-inmate's need for these medications should be carefully evaluated in the context of the management of pruritus.

Depression: Inmates with cirrhosis often have comorbid depression, especially when they have decompensated cirrhosis and are struggling with ascites, wasting, and encephalopathy. Although any of the SSRIs may be effective, most require approximately 50% dose reduction to accommodate delayed hepatic metabolism. Avoid SSRIs with a long half-life, e.g., fluoxetine. Sedating antidepressants such as mirtazapine, doxepin, trazodone, and amitriptyline should be either avoided or prescribed in very low doses, due to their potential for adding to the cognitive impairments of hepatic encephalopathy.

7. Infection Control

Infection control issues including inmate-inmate education, reporting, containment, contact investigation and post-exposure management are detailed in the MPCH Infection Control Manual, available at all inmate-inmate locations.

8. Definitions & Abbreviations

APRI (AST Platelet Ratio Index) is a score based upon commonly available lab values that is sometimes used to assess the degree of liver fibrosis (see Table 4 for calculation).

Absolute contraindication is a condition or factor that by itself precludes a specific intervention.

Anti-HCV is the antibody to HCV core and nonstructural proteins, detectable from several weeks to months after clinical Hepatitis.

Anti-HCV screening assay is an immunoassay such as an enzyme immunoassay (EIA) or a chemiluminescence immunoassay (CIA); it is used to screen for HCV infection by measuring antibodies to HCV antigens.

Compensated cirrhosis is defined as: bilirubin <1.5 mg/dL; international nonnalized ratio (INR) <1.5; albumin >3.4 g/dL; and platelet count >75,000/mm3; as well as no evidence of: ascites by liver ultrasound, esophageal varices by upper endoscopy, or hepatic encephalopathy.

Decompensated cirrhosis is defined as: evidence of significant liver disease (such as ascites, encephalopathy, marked thrombocytopenia, and bleeding esophageal varices), as well as loss of liver synthetic function (e.g., albumin <3.4 g/dL, and international normalized ratio (INR) >1.5).

Early viral response (EVR) during treatment of chronic Hepatitis C is a minimum two log (2 log10) decrease in the level of HCV RNA (compared to pretreatment levels) after the first 12 weeks of treatment, as measured by an HCV RNA assay. This term has also been used to describe an undetectable HCV RNA level after 8 weeks of treatment with a boceprevir-based regimen.

End of treatment response (ETR) after antiviral treatment of chronic Hepatitis C is the absence of detectable HCV RNA immediately after the completion of a course of treatment (usually 24 weeks for genotypes 2 and 3, and 48 weeks for genotype **1).** Extended Rapid Viral Response (eRVR) to treatment for chronic Hepatitis C is defined as undetectable HCV RNA after both 4 and 12 weeks of treatment.

Hepatic steatosis, also known as "fatty liver," is the collection of excessive amounts of triglycerides and other fats inside liver cells.

Hepatitis C is an acute or chronic viral Hepatitis caused by an RNA virus that is transmitted primarily by percutaneous contact with blood.

HCV is Hepatitis C virus, an enveloped, single-stranded RNA virus.

Model for End-stage Liver Disease (MELD) is a validated, disease severity index that uses age, creatinine, bilirubin, and prothrombin time to predict mortality. Null Response to treatment for chronic Hepatitis C is defined as less than a 2 log10 decrease in HCV RNA after 12 weeks of treatment. Partial Response to treatment for chronic Hepatitis C is defined as greater than or equal to a 2 log10 decrease in HCV RNA, but where HCV RNA is still detectable after 24 weeks of treatment.

Rapid viral response (RVR) during treatment of chronic Hepatitis C is defined as undetectable HCV RNA after the first 4 weeks of treatment. Relapse associated with the treatment for chronic Hepatitis C is defined as undetectable viremia at the end of treatment, but then subsequent detection of HCV RNA virus after treatment is stopped.

Relative contraindication is a condition or factor that may preclude a specific intervention when considered in conjunction with other criteria.

RIBA (anti-HCV) is the recombinant immunoblot assay that measures antibodies to HCV antigens through immunoblot technology. RIBA is no longer routinely used to confirm HCV infection.

Standard precautions are protective measures to be used for all inmate/inmate contacts in situations where infections can be transmitted by contaminated blood and body fluids. Precautions include: (1) the wearing of gloves and other personal protective equipment that provide an impervious barrier when soiling is likely; (2) procedures for protective handling of contaminated materials and equipment (e.g., using puncture-resistant devices and leak-proof protection); and (3) routine cleaning of all contaminated surfaces and equipment.

Steatosis (see Hepatic steatosis above)

Sustained viral response (SVR) after antiviral treatment of chronic Hepatitis C is the absence of detectable HCV RNA in the serum 24 weeks after the treatment is completed; it is measured by an HCV RNA assay.

9. References

United States. US Department of Justice. Federal Bureau of Prisons. Evaluation and Treatment of Hepatitis C and Cirrhosis. Federal Bureau of Prisons, Mar. 2012. Web. Aug. 2012. <http://xww.bop.govinews/medresources.jsp>.

Health care delivery within each facility is a mutual concern of the Department of Correction and clinical provider•. Matters of clinical judgment are the sole province of the licensed health care professionals; however, all health care providers shall ensure that the delivery of health care is in accordance with the security requirements of the facility as determined by the superintendent. In doing so, variations in the implementation of these protocols may be required.

Appendix I. Treatment of Acute Hepatitis C Infection

In the patient with recent onset of high risk, the Research Assistant (RA) should be contacted by calling: or e-mailing . The RA will see the patient and draw additional laboratories as needed. If she cannot see the patient in a timely manner, the RA will contact the facility to give expert guidance regarding further laboratory assessment. Other causes of acute Hepatitis can include acute Hepatitis A and B infection.

Patients with acute Hepatitis infection need careful follow-up to determine if they are well enough to drink and cat. Also LFTs and 1NR need to be drawn if the ALT is five times normal. The ID consultant should also be contacted if the INR is abnormal.

Patients with suspected acute Hepatitis C should be seen in Dr. McGovern's Hepatitis Clinic by the 12^{1h} week after identification. At this visit, all laboratories, including the 10^{th} week HCV RNA level will be reviewed to determine if the patient may have had spontaneous resolution of infection or if the patient needs treatment for persistent infection. When treatment is offered early, the chance of cure is greater than 90%t. Furthermore, the length of therapy can often be shortened.

The RA will complete off-site consult form for this appointment and will draw, or order, the following laboratories:

Initial Visit
Consent
Research laboratory tests
HCV RNA
LFTs
Initiate off-site consent for co-infection visit for week 12

Week 4
HCV RNA
LFTs

Week 10
HCV RNA
LFTs

Week 12
Co-Infection Clinic visit to review all laboratory results and discuss treatment plan. Any other needed laboratories will be drawn at LSH at this time.

Week 16
Start therapy, if necessary.

Appendix 2. Stepwise Approach for Detecting, Evaluating, and Treating Chronic Hepatitis C

Outlined below are MPCH's steps for detecting, evaluating, and treating Hepatitis C. Refer to the text in Section 4 for further information about each step.

Inmate Name:
Inmate No.:
DOB:
Institution/Unit:

Step I. Appropriately screen for Hepatitis C.

- ❑ **Assess for presence of Hepatitis C risk factors:**
  - Presence of certain clinical conditions (regardless of sentencing status):
    - ❑ Chronic hemodialysis (screen ALT monthly and anti-HCV semi-annually)
    - ❑ Elevated ALT levels of unknown etiology
    - ❑ Evidence of extrahepatic manifestations of HCV (mixed cryoglobulinemia, mebranoproliferative glomerulonephritis, or porphyria cutanea tarda)

  Presence of. Hepatitis C risk factors (sentenced inmates only):

  - ❑ Ever injected illegal drugs or shared equipment
  - ❑ Received tattoos or body piercings while in jail or prison
  - ❑ H1V-infected or chronic HBV infection
  - ❑ Received a blood transfusion or organ transplant before 1992, or received clotting factor transfusion prior to 1987
  - ❑ History of percutaneous exposure to blood
  - ❑ Ever received hemodialysis
- ❑ Screen for anti-HCV (EIA or CIA) if risk factors are present or if inmate requests a test.

Step 2. Provide initial medical follow-up for anti-HCV positive inmates.

- ❑ **Take a medical history and perform a physical examination.**
- ❑ **Try to establish duration of HCV infection by history, e.g., time period of injection drug use.**
- ❑ **Obtain baseline labs (see *Appendix 3).***
- ❑ **Evaluate inmate for other potential causes of liver disease.**
- ❑ **initiate inmate counseling (see inmate education resources, *Appendix 7).***
- ❑ **Initiate preventive health measures listed below:**
  - Hepatitis B vaccine: Indicated for inmates with chronic HCV infection. For foreign-born inmates, consider prescreening for Hepatitis B immunity prior to vaccination. Inmates with evidence of liver disease should be priority candidates for Hepatitis B vaccination.
  - Hepatitis A vaccine: Indicated for inmates with chronic HCV infection who have other evidence of liver disease. For foreign-born inmates, consider prescreening for Hepatitis A immunity prior to vaccination.
  - Pneumococcal vaccine: Offer to all HCV-infected inmates with cirrhosis.

    Influenza vaccine: Offer to all HCV-infected inmates annually. Inmates with cirrhosis are high priority for influenza vaccine.
  - Hepatocellular carcinoma (HCC) screening: Data supporting specific parameters for HCC screening are lacking. For inmates with both cirrhosis and chronic HCV infection, some experts recommend screening by liver ultrasound every six months
  - Esophageal varices screening: Consider an upper endoscopy for any inmate with known cirrhosis, and for those

with suspected cirrhosis who are not candidates for liver biopsy.

Step 3a. Determine if Hepatitis C treatment is *not recommended.*

Hepatitis C treatment is not recommended if any of the following conditions are present:

1. **Contraindications to peginterferon:**

- ☐ Severe uncontrolled psychiatric disease, particularly depression with current suicidal risk.
- ☐ History of solid organ transplant (renal, heart, or lung)
- ☐ Certain autoimmune disorders, e.g., autoimmune Hepatitis
- ☐ Uncontrolled endocrine disorders, e.g., diabetes, thyroid disease
- ☐ Serious concurrent medical diseases, such as severe: hypertension, heart failure, coronary heart disease, COPD
- ☐ Decompensated cirrhosis (see Complicating Medical Conditions)
- ☐ Platelet count <75,000/mm3 or ANC <1,500 cells/min3
- ☐ Documented nonadherence to prior therapy, or failure to complete pretreatment evaluation process
- ☐ Ongoing injection drug use or alcohol use
- ☐ Hypersensitivity to interferon

2. **Contraindications to ribavirin:**

- ☐ Thalassemias (sickle cell anemia) or other hemoglobinopathy.
- ☐ Significant cardiac disease (arrhythmias, angina, CABG, MI) in the past 12 months.
- ☐ Pregnancy or unwillingness to use contraception in both female inmates and female partners of male inmates.Uncontrolled endocrine disorders, e.g., diabetes, thyroid disease
- ☐ Renal dialysis or creatinine clearance < 50 mL/min
- ☐ Hypersensitivity to ribavirin

3. **Inmate will be incarcerated for an insufficient period of time to complete treatment.**
4. **Inmate has an unstable medical or mental health condition which precludes antiviral therapy. (Evidence of non-compliance with medical, social, mental health treatment plan(s) within the past twelve months.)**
5. **Inmate refuses treatment.**
6. **Refusal to participate in substance abuse treatment.**
7. **Pregnancy,**

STOP If any one of the above conditions are present, then STOP further treatment-related work-up. No further HCV testing — i.e., HCV RNA, genotype, liver biopsy — is indicated at this time. If conditions change, reconsider for Hepatitis C treatment.

Step 3b. Monitor HCV-infected inmates who are *not on treatment.*

- ☐ Have a plan for each inmate: Outline the plan clearly on the Problem List.
- ☐ Get baseline laboratory evaluations: Obtain baseline labs as specified in *Appendix 3.*
- ☐ Follow-up labs:
  - Every 6 months: ALT, AST, bilirubin, albumin, and INR
  - Every year: CBC (with differential & platelets). Calculate APRI (see *Table 4* for formula).
  - Other labs as clinically indicated, e.g., Al C (diabetics); TSH and free T4 (if hyperthyroid).
- ☐ Repeat liver biopsies: The determination regarding the timing of re-biopsy (for those inmates whose treatment is deferred) should be based on subsequent increases in the AST/Platelet Ratio Index (APRI) and/or evidence of steatosis or inflammation. Those who develop clinical evidence of liver disease should be priority candidates for re-

biopsy. If the APRI < 0.5, there is a lower risk of disease progression; if the APRI > 0.5, there is a higher risk.

Note: The following tests are generally NOT indicated for inmates not on treatment.

- *HCV RNA and HCV genotype: These tests are not needed unless treatment is indicated. Do not periodically check HCV RNA values for inmates who are not currently candidates for treatment. There is no correlation between HCV RNA levels and the risk or rate of disease progression.*
- *Alpha fetoprotein: Unless cirrhosis is known or strongly suspected, alpha fetoprotein is unnedessary because the risk for hepatocellular carcinoma in HCV infection does not begin until the development of cirrhosis.*
- *Liver ultrasound or CT examination: Similarly, do not perform periodic liver ultrasound or CT examinations unless cirrhosis is present or there is another definitive indication.*
- *Serium ammonia levels: In an inmate with known liver disease, the serum ammonia level has no prognostic value; nor can it be used for monitoring the effectiveness of medications such as lactulose. Serum ammonia levels are only useful in a delirious inmate whose diagnosis is uncertain.*

For inmates who may be eligible for Hepatitis C treatment, proceed as follows.

Step 4. Obtain HCV RNA assay and HCV genotype.

☐ Before initiating antiviral therapy, an HCV RNA (viral load) is required in order to continn chronic infection and guide therapy. If the HCV RNA level is undetectable, the individual can be considered uninfected.

☐ The HCV genotype should be ordered in conjunction with the initial HCV RNA test. In general, the test for genotype Is not repeated – unless re-infection is suspected.

Step 5. Assess liver fibrosis and need for a liver biopsy.

☐ Determine if a liver biopsy is indicated based upon the criteria below:

☐ HIV infection: High priority for liver biopsy, regardless of genotype.

☐ Other liver disease suspected: High priority for liver biopsy, regardless of genotype, e.g., homozygous hemochromatosis

☐ Genotypes 1, 4, 5, 6: Biopsy is generally recommended. Prioritize referral of inmates for biopsy based on the AST/Platelet Ratio Index (APRI). If APRI < 0.5, lower risk of progression; if APRI > 0.5, higher risk.

☐ Genotypes 2, 3: Biopsy is not needed prior to treatment (except if HIV-infected or other type of liver disease is known or suspected).

☐ Compensated cirrhosis: Decide about liver biopsy on a case-by-case basis, in consultation with a Hepatitis C expert. Either perform a liver biopsy as soon as possible, or treat empirically without biopsy confirmation.

☐ Decompensated cirrhosis: Liver biopsy and treatment are generally not indicated (see section 5, Complicating Medical Conditions, in the text.)

Step 6. Determine if treatment should be initiated.

☐ Identify if any of the following indications for antiviral therapy are present:

☐ Genotype 2 or 3 with no biopsy performed.

☐ Liver biopsy reveals chronic Hepatitis with significant fibrosis: (IASL, Batts&Ludwig, or Metavir > 2, or Ishak ? 3) — regardless of genotype (see *Table 5).*

☐ Compensated liver disease (bilirubin <1.5 mg/dL; INR <1.5; albumin >3.4 g/dL; and platelets >75,000/nun3; as well as no evidence of: ascites, esophageal varices, or hepatic encephalopathy.

- ❑ **Review special considerations related to treatment initiation** (i.e., mental illness, substance abuse, adherence concerns). See section on Special Considerations under Step 6 in text.
- ❑ **Counsel inmate regarding the pros and cons of initiating Hepatitis C treatment.** See section on Inmate Counseling under Step 6 in text.
- ❑ **Determine if inmate is willing to be treated and to adhere to treatment requirements.**
- ❑ **Document rationale for decisions about treatment in the medical record.**

Step 7. Conduct a pre-treatment evaluation.

Assure that **all** recommended pre-treatment evaluations have been completed within the time frames enumerated in the "Treatment Approval Form".

- ❑ **Laboratory tests:** See *Appendix* 3 for list of recommended pre-treatment tests and evaluations.
    - ❑ Interferon — The inmate should have the following acceptable labs for treatment initiation: absolute neutrophil count >1500/cells/mm3; platelets >75,000/mm3. When starting treatment with platelet counts between 75-90,000, consult first with a physician with expertise in treatment of Hepatitis C.
    - ❑ Ribavirin — The inmate should have the following acceptable for treatment initiation: Hemoglobin >13 g/dL (men) or >12 g/dL (women); creatinine <1.5 mg/dL (or creatinine clearance >50 mL/min). Some experts recommend that an acceptable starting hemoglobin is >12 g/dL (men) or > **l 1** g/d1_, (women).
- ❑ **Pregnancy test:** Because ribavirin may cause fetal abnormalities, all female inmates of childbearing potential must have a pregnancy test immediately prior to initiating therapy, and monthly thereafter. Continue with monthly tests until 6 months after treatment is completed.
- ❑ **Cardiac risk assessment:** Prior to therapy, a cardiac risk assessment is critically important because hemolysis associated with ribavirin may precipitate angina pectoris. Also, obtain an ECG for inmates with preexisting cardiac disease.
- ❑ **Mental health evaluation** is critically important prior to initiating treatment due to the severe psychotropic effects of interferon.
- ❑ **Compensated cirrhosis:** Obtain liver-spleen ultrasound (preferred) or abdominal CT-scan, and measurements of alpha fetoprotein, prior to treatment initiation. A screening upper endoscopy is indicated if the ultrasound suggests portal hypertension.

Step 8. Determine appropriate treatment and obtain informed consent.

☐ Dual therapy (pegylated interferon plus ribavirin). Standard dosing is outlined in *Appendix* 5. Also, see *Appendix* 5 for information on dosing with renal failure and HIV/HCV co-infection.

☐ Triple therapy (pegylated interferon plus ribavirin plus HCV protease inhibitor).

Dosing and Treatment Duration in Triple Therapy

Prior Treatment History or Degree of Fibrosis	Boceprevir-Based Regimen				Telaprevir-Based Regimen	
	Total Weeks of Therapy				Total Weeks of Therapy	
	28	36	48/	48[2]	**24**	**48**
Treatment Naive, No Cirrhosis	RNA (-) at TW8 and TW24		RNA < 100 IU/m1 but (+) at TW8 and (-) at TW24		**RNA (-) at TW4 and TW . 12 .**	**RNA < 1000 IU/tni but (+). at TW4 and/or TW12 and.(-) at**
Relapser with Dual Therapy, No Cirrhosis		RNA (-) at TW8 and TW24	RNA < 100 1U/mi but (+) at TW8 and (-) at TW24		**RNA (-) at TW4 and TW 12 •**	**RNA 5 1000 IU/nil but (+) at TW4 and/or TW12 and (-) at**
Partial Responder with Dual Therapy, No Cirrhosis		RNA (-) at TW8 and TW24	RNA < 100 1U/nil but (+) at TW8 and (-) at TW24			**RNA < 1000 - Mimi at TW4 and. TW12 and (-) at TW24**
Compensated Cirrhosis				RNA < 100 Mind at TW8 and (-) at TW24		**RNA < 1000 IU/mi. at TW4 . and TW12 .. and (-) at... TW24**

☐ Obtain informed consent after reviewing potential side effects.

9a. Manage side effects.

☐ Monitor side effects of treatment. See *Appendix 3* for treatment monitoring schedule for recommended baseline, pre-treatment, and on-going clinical evaluations and laboratory studies. See Guidelines for Adjusting Therapy for CBC Changes in Step 9 below.

☐ Common toxicities to assess at each clinician visit include:

- ☐ Flu-like symptoms
- ☐ Mood changes
- ☐ Rashes
- ☐ Chest pain
- ☐ Dyspnea / cough
- ☐ Thrombocytopenia
- ☐ Anemia
- ☐ Neutropenia

Step 9b. Monitor treatment response.

Monitor for treatment response based on the following virologic end-points:

Chronic Hepatitis C Treatment Response Categories		
Response	Timeframe	Result*
RVR (Rapid Viral Response)	After 4 weeks of treatment	HCV RNA undetectable
eRVR (Extended Rapid Viral Response)	After 4 and 12 weeks of treatment	HCV RNA undetectable
EVR (Early Viral Response***)	After 12 weeks of treatment	> 2 $\log_{to}$ HCV RNA decrease**
Null Responder	After 12 weeks of treatment	< 2 $\log_{io}$ HCV RNA decrease
Partial Responder	After 24 weeks of treatment	> 2 $\log_{in}$ HCV RNA decrease but still detectable
ETR (End of Treatment Response)	At end of treatment	HCV RNA undetectable
SVR (Sustained Viral Response)	24 weeks after treatment completed	HCV RNA undetectable
Relapse	Undetectable HCV RNA at the end of treatment, but detectable sometime after treatment is stopped.	

*Throughout the course of treatment, use tie same lab for HCV RNA assays so that results are comparable.

** 2 $\log_{ic}$ decrease = by factor of 10^2; e.g., if baseline HCV RNA = 720,000 then a 2 $\log t_o$ decrease is 7,200.

*** EVR is also a term for undetectable HCV RNA level after 8 weeks of treatment with a boceprevir-based regimen.

Determine the appropriate duration of therapy: Treatment duration is based on genotype, virologic response, and the occurrence of major side effects. See also the discussion under Monitor Treatment Response in Step 9b, in Section 4 of the text, and the flowcharts for triple therapy and dual therapy *(Appendix 4).*

Duration of triple therapy is described in Step 8.

Genotype 1, 4, 5, 6: Standard duration with dual therapy = 48 weeks

- If no EVR, discontinue treatment = treatment failure.
- If EVR, but HCV RNA is still detectable at 12 weeks, repeat HCV RNA test at 24 weeks. If HCV RNA is still detectable at 24 weeks, discontinue treatment = treatment failure.
- If significant side effects occur and RVR was achieved, can consider shortening treatment to at least 24 weeks (in consultation with specialist).

Genotype 2, 3: Standard duration with dual therapy = 24 weeks

- If no EVR, discontinue treatment = treatment failure.
- If significant side effects occur and RVR was achieved, can consider shortening treatment to at least 16 - 20 weeks (in consultation with specialist).

Step 9. Manage side effects and monitor treatment response.

Guidelines for adjusting therapy for CBC changes:

Hemoglobin (Hgb)

Value	Peginterferon / Ribavirin Adjustment and Supportive Treatment	
10 — 11 g/dL	☐ Peginterferon -- No change. ☐ Ribavirin → - If no or minimal symptoms, then no dose modification. - If symptomatic, decrease ribavirin by 20 mg/day.	***Candidate for Erythropietin:*** Rule out other causes of anemia. If anemia persists at 2 weeks after reducing ribavirin — and there is no hypertension — then consider erythropoietin, especially if the patient demonstrates a virologic response. Erythropoietin should be considered primarily for patients who are cirrhotic, post-transplant, or HIV/HCV co-infected. ***Dosage:*** Epoeitin alfa 40,000 units subcutaneously weekly. ***Goal:*** Hemoglobin 12 g/dL. ***Note:*** If hemoglobin is < 12 g/dL for over 4 weeks at the reduced/adjusted dose, then discontinue ribavirin.
8.5 — 10 g/dL	☐ Peginterferon --) Reduce 50% (see note below). ☐ Ribavirin --> Reduce to 600 mg daily (200 mg in a.m. and 400 mg in p.m.)	
< 8.5 g/dL	Typically, the entire HCV treatment regimen must be discontinued. Contact GI specialist to discuss the discontinuation of therapy.	

Absolute Neutrophil Count (ANC)

Value	Peginterferon / Ribavirin Adjustment and Supportive Treatment	
< 750	LI Peginterferon —> Reduce 50% (see note below). U Ribavirin —, No change.	***Granulocyte Colony Stimulating Factor (G-CSF):*** *lithe patient is responding to treatment and neutropenia persists despite reduced peghneiferon dose, consider G-CSF (in consultation with specialist) for patients who are cirrhotic, post-transplant or HIV/ HCV co-infected.* ***Dosage:*** *Filgrastim 300 microgram subcutaneous daily.* ***Goal:*** *ANC > 1500*
< 500	Typically, the entire HCV treatment regimen must be discontinued. Contact GI specialist to discuss the discontinuation of therapy.	

Platelets

Value	Peginterferon / Ribavirin Adjustment and Supportive Treatment
< 50,000	Typically, the entire HCV treatment regimen must be discontinued. Contact GI specialist to discuss the discontinuation of therapy.
< 30,000	Typically, the entire HCV treatment regimen must be discontinued. Contact GI specialist to discuss the discontinuation of therapy.

Note: White the manufacturer of peginterferon recommends reducing dose to 50%, recent data suggest that lowering the dose to this extent may significantly reduce the likelihood of achieving an SVR. Some experts recommend a 25% dose reduction with close monitoring of hematologic parameters.

Step 10. Assess for sustained viral response (SVR).

An SVR is defined as undetectable HCV RNA at 24 weeks after treatment is completed. If HCV RNA is undetectable at the end of treatment, obtain an HCV RNA test 6 months later to assess for an SVR. Obtain a final HCV RNA test 12 months post-treatment. See Step 10 discussion in the text.

Appendix 3. Hepatitis C Treatment Monitoring Schedule

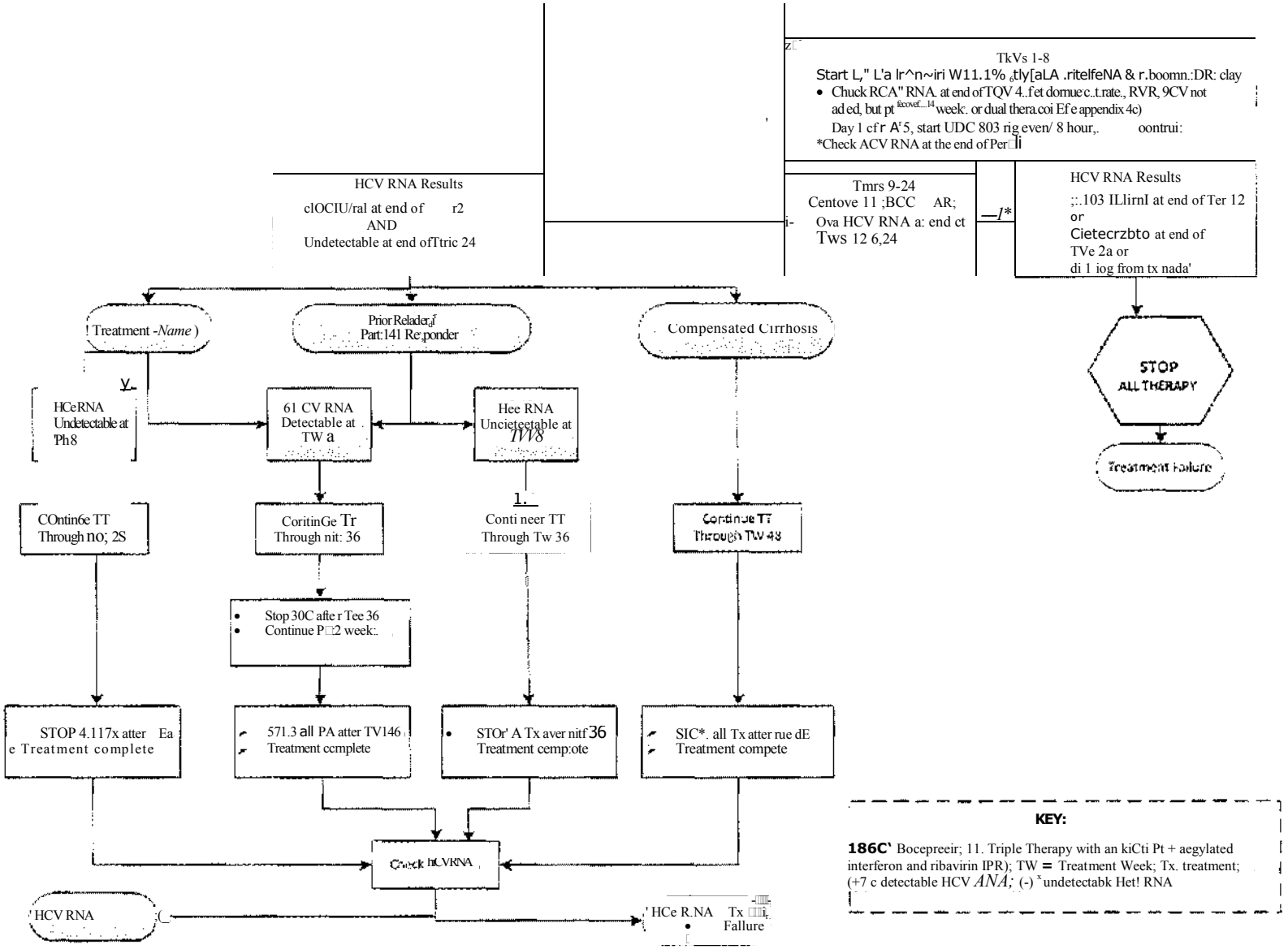
Evaluation	Baseline (Anti-HCV Positive)	Pre-Tx	Ongoing Monitoring (By Week of Treatment)															24 Weeks Post-Tx	12 Months Post-Tx
			1	2	3	4	8	12	16	20	24	28	32	36	40	44	48		
Clinician evaluation	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
HIV, HBsAg, HBsAb, Anti-HAV(IgG)	X																		
CBC, Diffl Platelets	X	X		X		X	Every 4-8 weeks during treatment												
ALT, Creatinine	X	X		X		X	Every 4-8 weeks during treatment.												
AST, Bilirubin, Alkaline, Phosphata.sc, Albumin, INR	X	X	Periodically and if signs and symptoms of liver disease.																
Uric acid (Telaprevir only)		X		X		X	X	X	As clinically indicated.										
Ferritin, iron saturation, ANA*	X																		
HCV RNA**		X				X	**	X			***	At end of treatment.						X	X
HCV genotype		X																	
Liver biopsy		If indicated.																	
Mental health evaluation		X	If indicated.																
Depression		X	Assess for signs and symptoms of depression at each clinician visit.																
Urine toxicology		X	If indicated.																
Visual acuity		X																	
Funduscopic exam of other ophthalmologic diagnosis or diabetes)		X	Periodically and as clinically indicated.																
TSH. free T4		X						X			X			X			X		
Triglycerides		X						X			X			X			X		
ECG (pre-existing CHD)		If indicated.	If indicated.																
Urine pregnancy test (if childbearing potential)		X				X	X	X	X	X	X	X	X	X	X	X	X	Monthly for six months.	

* Conduct further diagnostic evaluations as clinically warranted to identify other potential causes of the patient's liver disease such as hemochromatosis. Wilson's disease, or autoirnrnune hepatitis (e.g., serum iron, serum copper, ESR). If any of these conditions are diagnosed or arc strongly suspected, a liver biopsy should be performed prior to treatment regardless of genotype.

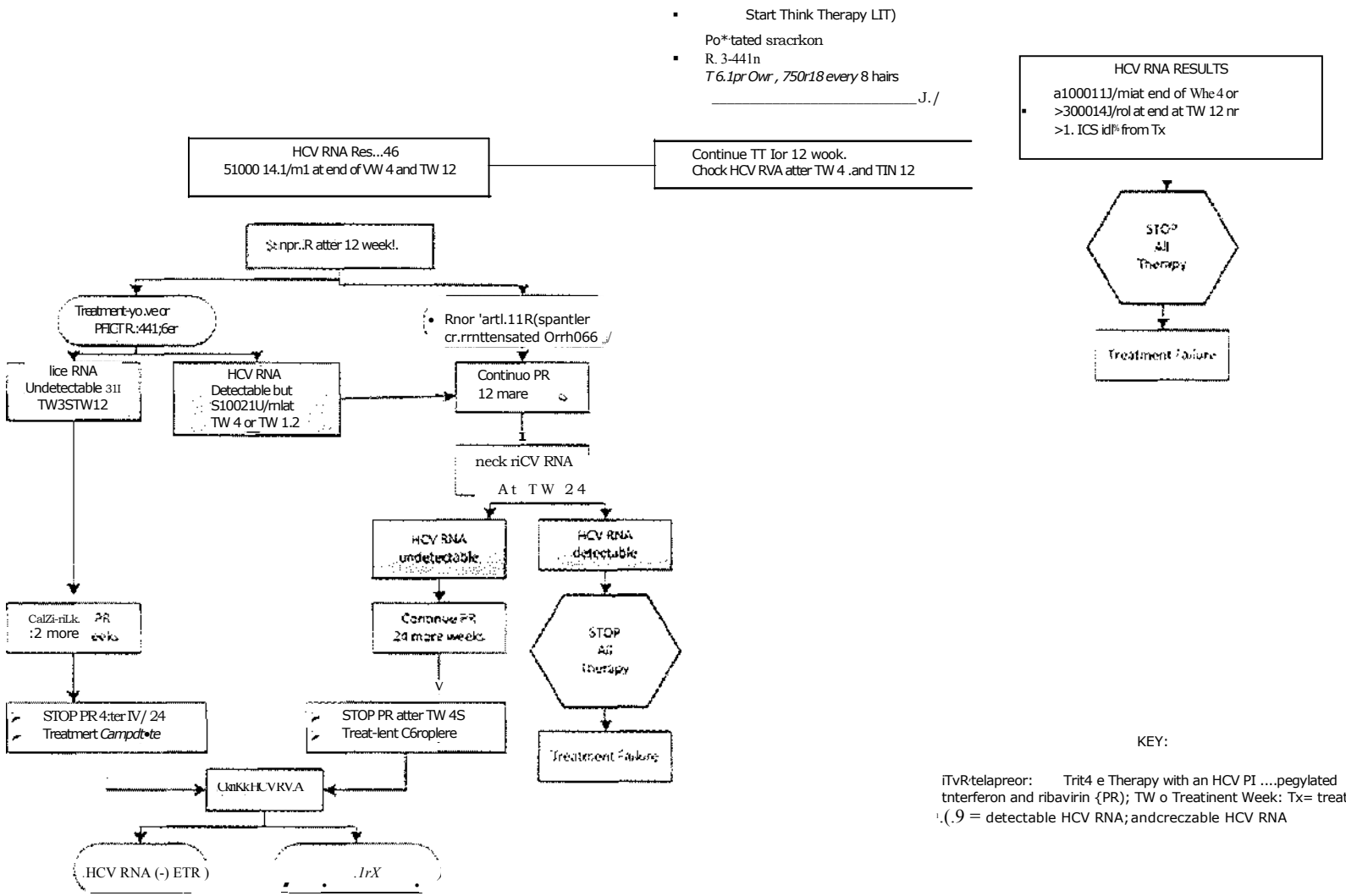
** More HCV RNA tests may be warranted during course of treatment depending upon results of previous HCV RNA assays (see Appendices 4a, 4b, 4c, and 4d). If treating with boceprevir, an HCV RNA test should also be obtained at the end of treatment week 8.

*** An HCV RNA is obtained in all patients who are still on therapy at the end of 24 weeks. For some, this will be at the end of their treatment, e.g.. HCV genotypes

Appendix 4a. Timeline for HCV Treatment Decisions (Based on Viral Response): Genotype 1 on Triple Therapy with Boceprevir



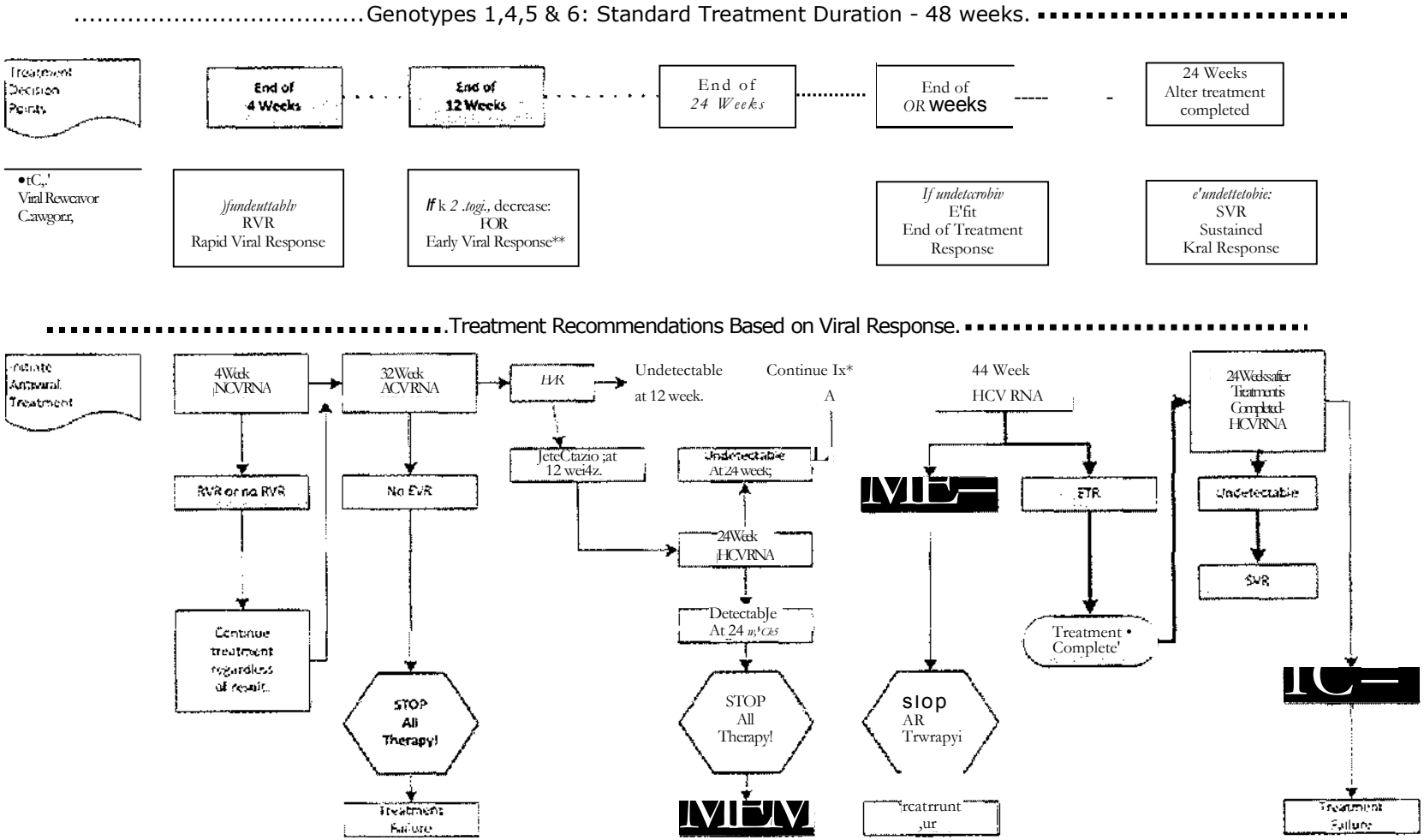
Appendix 4b. Timeline for HCV Treatment Decisions (Based on Viral Response): Genotype 1 on Triple Therapy with Telaprevir



KEY:

iTvR:telapreor: Trit4 e Therapy with an HCV PI ....pegylated tnterferon and ribavirin {PR); TW o Treatinent Week: Tx= treatment; .(.9 = detectable HCV RNA; andcreczable HCV RNA

Appendix 4c. Timeline for HCV Treatment Decisions Based on Viral Response: Genotypes 1, 4, 5, and 6 on Dual Therapy



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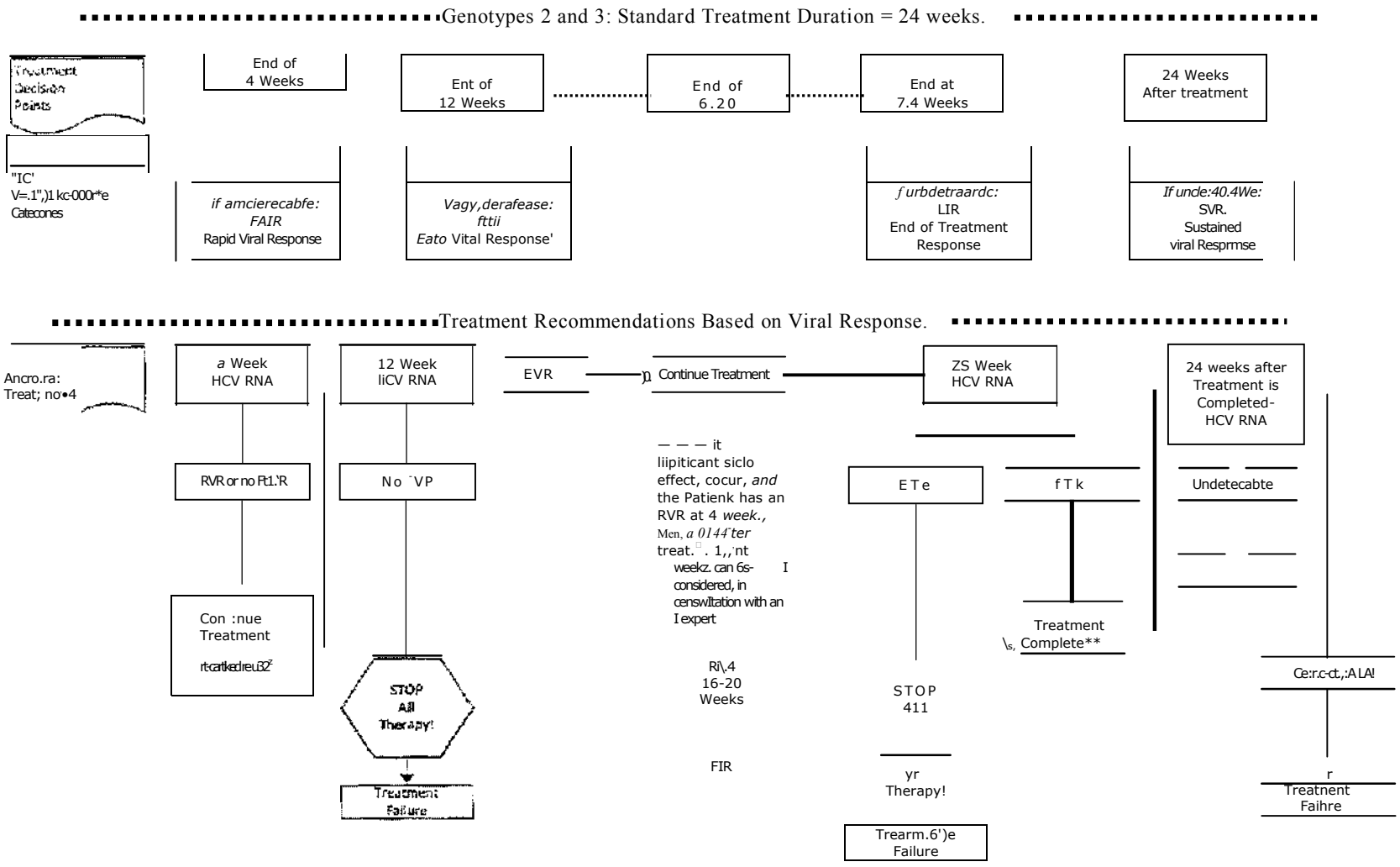
Appendix 4d. Timeline for HCV Treatment Decisions Based on Viral Response: Genotypes 2 and 3 on Dual Therapy



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Appendix 5. Interferon I Ribavirin Drug Information

Peginterferon

Descriptions:

A long-acting, synthetic interferon that is indicated for use alone or in combination with ribavirin for the treatment of chronic Hepatitis C, or with ribavirin and an HCV protease inhibitor for treatment of chronic HCV genotype I.

Formulations:

Peginterferon alfa-2b (Peg-Intron®)

Standard Dosing:

Peg-Intron® is administered subcutaneously, once weekly. The dosing below is based on recommended dose of 1.5 micrograms (meg) per kilogram per week (regardless of HCV genotype). It comes in four different vial strengths; utilize the appropriate vial strength related to the inmate's weight.

Body Weight (Pounds)	Vial Strength (mcg/0.5mL)	Dose to Administer (1.5 mcgikg/wk)	Volume to Administer (mi.)
< 88	50	50	0.5
88 — 111	80	64	0.4
112 — 133	80	80	0.5
134— 144	120	96	0.4
145 — 166	120	96	0.4
167 — 177	120	120	0.5
178— 187	120	120	0.5
188 — 231	150	150	0.5
> 231	150	150	0.5

Ribavirin

In Genotypes 1, 4, 5, and 6 ribavirin dosing is weight-based:

Body Weight (Pounds)	Every AM	Every PM
<88	400	400
88 — 111	400	400
112 — 133	400	400
134— t44	400	400
145— 166	400	600
167 — 177	400	600
178 — 187	600	600
188-231	600	600
>231	600	600

In Genotypes 2 and 3 a total daily dose of 800 mg is administered as 400mg orally twice daily (regardless of weight).

Dosing In Certain Clinical Circumstances:

Renal Dysfunction

- ✓ Peg-Wrongs: In inmates with moderate renal function (CrCl of 30-50 mL/min), the Peg-Intron dose should be reduced by 25%. If severe renal function impairment (CrCl 10-29 mL/min), including hemodialysis, reduce dose by 50%. If renal function decreases during treatment, discontinue treatment.
- ✓ Ribavirin is not indicated in inmates with a CrCl <50 milmin.

Hemodialysis

- ✓ Peg-IntronO: Reduce dose br 50%.
- ✓ Ribavirin is not indicated.

HIV/HCV Co-infection

- ✓ Treat for 48 weeks, regardless of genotype. See Section 4.

Contraindications:

- ✓ Severe uncontrolled psychiatric disease, particularly depression with current suicidal risk.
- ✓ History of solid organ transplant (renal, heart, or lung)
- ✓ Certain autoimmune disorders, e.g., autoimmune Hepatitis
- ✓ Uncontrolled endocrine disorders, e.g., diabetes, thyroid
- V Thalassemia or other hemoglobinopathy
- ✓ Significant cardiac disease (arrhythmias, angina, CABG, MI) in the past 12 months
- ✓ Pregnancy or unwillingness to use contraception in both female inmates and in female partners of male inmates.

Peginterferon	Ribavirin
disease V Serious concurrent medical diseases such as: severe hypertension, heart failure, CHD, COPD, decompensated cirrhosis (see definition) V Platelet count <75,000/rnin3 or ANC <1,500 cells/1111113 V Documented nonadherence to prior therapy, or failure to complete pretreatment evaluation process V Ongoing injection drug use or alcohol use V Hypersensitivity to interferon	V Renal dialysisSerum creatinine =1.5 IngidL or creatinine clearance —50 mLimin V Hemoglobin <12 g/dL in men or <II g/dL in women V Hypersensitivity to ribavirin
Major Side Effects:	
May cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.	Has a primary clinical toxicity of hemolytic anemia. Since ribavirin-associated anemia has been known to lead to myocardial infarction, it is contraindicated in imnates with significant or unstable cardiac disease. Significant teratogenic effects have been noted in all animal species exposed to ribavirin. Pregnancy should be prevented during therapy, and for the six months after the completion of therapy, in both female inmates and female partners of male inmates.
Side Effects:	
✓ Autoimmune disorders: Can result in development or exacerbation of disorders ✓ Bone marrow suppression: Can cause severe cytopenias (see Appendix 2, Step 9a) ✓ Cardiovascular disorders: Hypertension, arrhythmias, and myocardial infarction ✓ Cerebrovascular disorders: Ischemic and hemorrhagic cerebrovascular events ✓ Colitis: Ulcerative and hemorrhagic/ischemic colitis, sometimes fatal ✓ Dermatologic effects: Alopecia, pruritis, and local injection site reaction ✓ Endocrine disorders: Hypo- or hyperthyroidism, hypo- or hyperglycemia & diabetes ✓ Flu-like symptoms: Fever, myalgia, fatigue, headache ✓ Gastrointestinal effects: Nausea, vomiting, diarrhea, and anorexia ✓ Hypersensitivity (anaphylaxis and angioedema): Severe and acute ✓ Infections (bacterial, fungal, and viral): Can be severe and sometimes fatal ✓ Hepatic failure and Hepatitis exacerbations with hepatic decompensation and death ✓ Neuropsychiatric symptoms: Life threatening or fatal neuropsychiatric reactions ✓ Ophthalmologic disorders: Loss of vision, retinopathy including macular edema ✓ Pancreatitis: Sometimes fatal ✓ Pulmonary disorders: Dyspnea, pulmonary infiltrates, pneumonia, and sarcoidosis ✓ Renal failure ✓ Seizures ✓ Triglyceride elevations	Black Box Warnings: ✓ Hemolytic Anemia Warning (primarily in the first two weeks of therapy) ✓ Pregnancy Warning (negative pregnancy test is required pre-therapy) ✓ Respiratory Warning for inmates requiring assisted Additional Side Effects: ✓ Cardiovascular effects: Fatal and non-fatal myocardial infarction ✓ Dermatologic effects: Alopecia, pruritis, and rashes ✓ Flu-like symptoms: Myalgia, fatigue, and headache ✓ Gastrointestinal effects: Nausea, anorexia, and vomiting ✓ Hetnatologic: Neutropenia and thrombocytopenia (see Appendix 2, Step 9a) ✓ Hepatic decompensation and death ✓ Hypersensitivity—acute: Anaphylaxis, angioedema, and bronchoconstriction ✓ Pulmonary symptoms: Dyspnea, pneumonia, and pulmonary infiltrates ✓ Teratogen (significant), carthogenesis, and mutagenesis

Appendix 6. Boceprevir / Telaprevir Drug Information

Boceprevir	Telaprevir
Descriptions:	
An oral medicine that acts directly on the Hepatitis C virus protease, an enzyme essential for viral replication. Boceprevir should always be taken in combination with peginterferon alfa and ribavirin. Boceprevir should not be used alone as monotherapy for Hepatitis C.	An oral medicine that acts directly on the Hepatitis C virus protease, an enzyme essential for viral replication. Telaprevir should always be taken in combination with peginterferon alfa and ribavirin. Telaprevir should not be used alone as monotherapy for Hepatitis C.
Formulations:	
Boceprevir (VictrelisTM) is manufactured as 200 mg oral capsules that are packaged in daily dosage bottles of 12 capsules each. The dose for boceprevir is 800 mg (four 200 mg capsules) three times daily (every 7-9 hours), taken with food (a meal or light snack).	Telaprevir (IncivekTM) is manufactured as 375 mg tablets that are packaged into cartons containing a four-week supply: 4 weekly blister cards, with each card consisting of 7 daily blister strips of 6 tablets each. The dose for telaprevir is 750 mg (two 375 mg tablets) three times daily (every 7-9 hours), with each dose taken 30 minutes after eating a meal or snack that contains at least 20 grams of fat.
Standard Dosing:	
Boceprevir has been approved for administration according to a specific response-guided therapy algorithm (see *Appendix 4).* Therapy is initiated with peginterferon and ribavirin for the first 4 weeks of treatment (peginterferon/ribavirin "lead in" period) prior to adding boceprevir. Weeks 1-4: - Peginterferon (Peglntron 1.5 meg/kg/week) and - Ribavirin (in 2 divided doses) with food Refer to *Appendix* 5 for appropriate dosing of peginterferon and ribavirin. Beginning at Week 5: - Boceprevir 800 mg orally (4 x 200 mg capsules) every 8 hrs (+1-1 hour) with food plus peginterferon and ribavirin. Total treatment duration is guided by on-treatment HCV RNA response and inmate characteristics, as described in boceprevir treatment algorithm (see *Appendix 4).*	Telaprevir is dosed 750 mg orally (2 x 375 mg tablets) every 8 hours (+/— lhr) with food (containing a minimum of 20g of fat) for 12 weeks, plus: - Peginterferon (Peglntron 1.5 mcg/kg/week) and - Ribavirin (in 2 divided doses) with food Refer to *Appendix 5* for appropriate dosing of peginterferon and ribavirin. Total treatment duration is guided by on-treatment HCV RNA response and inmate characteristics, as described in telaprevir treatment algorithm (see *Appendix 4).*
Dosing and Treatment Duration in Triple Therapy:	
The first 8 weeks of treatment are the same for all boceprevir-based regimens, as follows: Start therapy with a 4-week lead-in period of dual therapy, using standard doses of pegylated interferon and ribavirin. Boceprevir is added to the regimen after 4 full weeks of dual therapy, and pegylated interferon and ribavirin are continued. In other words, treatment week 5 is the first week of triple therapy. Boveprevir dose is 800 mg (four 200 mg capsules) by moot every 8 hours (+/- 1 hour) with food/light snack.	The telaprevir-based regimen starts with all three medications, all of which are continued for12 weeks. After 12 weeks, telaprevir is discontinued while pegylated interferon and ribavirin are continued for an additional 12 weeks (24 weeks total) or an additional 36 weeks (48 weeks total). Telaprevir dose is 750 mg (two 375 mg tablets) by niout every 8 hours (+/- 1 hour) with a 20-gram fat snack. HCV RNA levels are obtained at the end of treatment weeks 4, 12, 24 and at the end of treatment. (-) means undetectable HCV

Boceprevir	Telaprevir•
HCV RNA levels are obtained at the end of treatment weeks 4, 8, 12, 24 and at the end of treatment. (-) means undetectable HCV RNA levels; (+) means detectable, but < 100 IU/ml. Four different treatment durations are possible, as described in Appendix 2, Step 8. Discontinue all HCV medications if any of the following occur: RNA > 100 whim at treatment week 12, RNA detectable at treatment week 24, while on treatment, HCV RNA increases by 1 log_{io} above treatment nadir.	RNA levels; (+) means detectable, but < 1000 IU/ml. Discontinue all HCV medications if any of the following occur: RNA > 1000 1U/m1 at treatment week 4 or 12, RNA detectable at treatment week 24, while on treatment, HCV RNA increases by 1 log_{io} above treatment nadir.
Dosing In Certain Clinical Circumstances: ''	
Renal Impairment No dosage adjustment of boceprevir or telaprevir is necessary for inmates with □ mild, moderate, or severe renal impairment; telaprevir was not studied in inmates with end-stage renal disease or on hemodialysis. **HBV/HCV Co-Infection** No safety or efficacy data are available in this population. Treatment with telaprevir or boceprevir for Hepatitis C is not indicated and has not been approved for inmates co-infected with HBV.	
Contraindications* -..	
✓ All contraindications to peginterferon alfa and ribavirin, since boceprevir must be administered with peginterferon alfa and ribavirin ✓ Pregnant women and men whose female partners are pregnant, because ribavirin may cause birth defects and fetal death ✓ Decompensated cirrhosis ✓ Co-infection with HBV or HIV ✓ Solid organ transplant recipient ✓ Co-administration with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events, e.g., AlfUzosin, Ergot derivatives (dihydroergotamine, ergonovine, ergotamine, methylergonovine), cisapride, some statins (simvastatin, lovastatin), drosperinone, PDE5 enzyme Inhibitors (sildenafil, tadalafil), pimozide, triazolam , and orally administered midazolam ✓ Co-administration with drugs that strongly induce CYP3A, which may lead to lower exposure and loss of efficacy of boceprevir, e.g,. certain anticonvulsants (carbamazepine, phenobarbital, phenytoin), rifampin, and St. John's wort	✓ All contraindications to peginterferon alfa and ribavirin, since telaprevir must be administered with peginterferon alfa and ribavirin ✓ Pregnant women and men whose female partners are pregnant, because ribavirin may cause birth defects and fetal death ✓ Decompensated cirrhosis ✓ Co-infection with HBV or HIV ✓ Solid organ transplant recipient ✓ Co-administration with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events, e.g., Alfuzosin, Ergot derivatives (dihydroergotainine, ergonovine, ergotamine, methylergonovine), cisapride, some statins (atorvastatin, simvastatin, lovastatin), PDE5 enzyme inhibitors (sildenafil, tadalafil), pimozide, triazolam , and orally administered midazolam ✓ Co-administration with drugs that strongly induce CYP3A, which may lead to lower exposure and loss of efficacy of teleprevir, e.g,. rifampin and St. John's wort
Use With Caution:	
The following medications may pose risk for potential interaction with boceprevir that may require close monitoring, alteration of drug dosage, or timing of administration: ✓ Analgesics (buprenorphine, methadone) ✓ Antiarrhythmis (amiodarone, bepridil, digoxin, flecainide, lidocaine, propafenone, quinidine) ✓ Antibacterials (clarithromycin, erythromycin, rifabutin, telithromycin) ✓ Antidepressants (desipramine, escitalopram, trazodone)	The following medications may pose risk for potential interaction with telaprevir that may require close monitoring, alteration of drug dosage, or timing of administration: ✓ Analgesics (buprenorphine, methadone) ✓ Antiarrhythmics (amiodarone, bepridil, digoxin, flecainide, lidocaine, propafenone, quinidine) ✓ Antibacterials (clarithromycin, erythromycin, rifabutin, telithromycin) ✓ Anticonvulsants (carbamazepine, phenobarbital, phenytoin)

Boceprevir	Telaprevir
✓ Antifimpls (itraconazole, ketoconazole, posaconazole, voriconazole) ✓ Antipsychotics (clozapine) ✓ Anxiolytics/hypnotics/sedatives (alprazolam, parenteral midazolam, zolpidem) ✓ Bronchodilators (salmeterol) ✓ Calcium channel blockers (amlodipine, diltiazem, felodipine, nicardipine, nifedipine, nisoldipine, verapamil) ✓ Contraceptives/hormonal replacement (ethinyl estradiol, norethindrone) ✓ Erectile dysfunction agents (sildenafil, tadalafil, vardenafil) ✓ Gastrointestinal agents (cimetidine, ranitidine) ✓ HIV dnigs (maraviroc, delavirdine, efavirenz, etravirine, nevirapine, zidovudine, atazanavir, daninavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir) ✓ Immunosuppressants (cyclosporine, sirolimus, tacrolimus) ✓ Lipid-lowering agents (atorvastatin) ✓ Steroids (budesonide, dexamethasone, fluticasone, methylprednisolone, prednisone) ✓ Other drugs (bosentan, colchicine, warfarin)	✓ Antidepressants (desipramine, escitalopram, trazodone) ✓ Antifbngals (itraconazole, ketoconazole, posaconazole, voriconazole) ✓ Antipsychotics (clozapine) ✓ Anxiolytics/hypnotics/sedatives (alprazolam, parenteral midazolam, zolpidem) ✓ Bronchodilators (salmeterol) ✓ Calcium channel blockers (amlodipine, diltiazem, felodipine, nicardipine, nifedipine, nisoldipine, verapamil) ✓ Contraceptives/hormonal replacement (drospirenone, ethinyl estradiol, norethindrone) ✓ Erectile dysfunction agents (sildenafil, tadalafil, vardenafil) ✓ Gastrointestinal agents (cimetidine, ranitidine) ✓ HIV drugs (maraviroc, delavirdine, efavirenz, etravirine, nevirapine, tenofovir, zidovudine, atazanavir, dar□ navir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir) ✓ Immunosuppressants (cyclosporine, sirolimus, tacrolimus) ✓ Steroids (budesonide, dexamethasone, fluticasone, methylprednisolone, prednisone) ✓ Other drugs (bosentan, colchieine, warfarin)
Side Effects:	
✓ Dermatologic effects: Pruritis ✓ Flu-like symptoms: Myalgia, fatigue, and headache ✓ Gastrointenstinal effects: Dysgeusia, nausea, anorexia, and vomiting ✓ Hematologic: • Anemia: The addition of boceprevir to peginterferon alfa and ribavirin (PEG/riba) is associated with an additional decrease in hemoglobin concentrations. • Neutropenia: The addition of boceprevir to PEG/riba is associated with an additional decrease in neutrophil counts. Decreases in neutrophil counts may require dose reduction or discontinuation of PEG/riba. No dose adjustment should be made to boceprevir. If PEG/riba is discontinued, boceprevir should be discontinued and not restarted (see Appendix 2, Step 9).	✓ Hematologic effects: Anemia; the addition of telaprevir to peginterferon alfa and ribavirin is associated with an additional decrease in hemoglobin concentrations (see Appendix 2, Step 9). ✓ Dermatologic effects: Rash with or without pn□ ritis ✓ Flu-like symptoms: Myalgia, fatigue, headache ✓ Gastrointestinal effects: Dysgeusia, nausea, vomiting, diarrhea, and auorectal discomfort, anal pn□ ritis, hemorrhoids

Appendix 7. Resources

Health Care Professionals

American Association for the Study of Liver Diseases
http://www.aasld.org/Pages/Defaultaspx

Centers for Disease Control and Prevention National Center for Infectious Diseases — Hepatitis Branch
http://www.cdc.govincidod/diseases/Hepatitis/

MELD Score Calculator
littp://optn.transplant.hrsa.goviresources/IvIeldPeldCalculator.asp?index=98

National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases http://www.niddk.nih.gov

National Clinicians' Post-Exposure Prophylaxis PEPline: (888) 448-4911 http://www.nccc.ucstedu/

U.S. Department of Veterans Affairs National Hepatitis C Program
http://www.Hepatitis.va.gov/

inmates

American Liver Foundation (ALF) \\ ww. liverfoundation.org

Centers for Disease Control and Prevention (CDC)
www.cde.gov/idtt/Hepatitis/index.htm

Hepatitis Foundation International (RFD wmv.hepfi.org

The National Digestive Diseases Information Clearinghouse (NDDIC)
http://wmv.digestive.niddk.nih.goviddiseases/pubs/hepcez/index.htm

U.S. Department of Veterans Affairs National Hepatitis C Program — For Veterans and the Public
www.Hepatitis.va.gov/inmate/index.asp

Published on *Recommendations for Testing, Managing, and Treating Hepatitis C* (http://www.hcvguidelines.org)

RETREATMENT OF PERSONS IN WHOM PRIOR THERAPY HAS FAILED

Expansions and notes for abbreviations used in this section can be found in Methods Table 3.

A summary of recommendations for retreatment is found in the BOX.

This section provides guidance on the retreatment of a person with chronic HCV infection in whom prior therapy has failed.

The level of the evidence available to inform the best regimen for each patient and the strength of the recommendation vary, and are rated accordingly (see Methods Table 2). In addition, specific recommendations are given when treatment differs for a particular group (eg, those infected with various genotypes). **Recommended** regimens are those that are favored for most patients in that subgroup, based on optimal efficacy, favorable tolerability and toxicity profiles, duration, and pill burden. **Alternative** regimens are those that are effective but have, relative to Recommended regimens, potential disadvantages, limitations for use in certain patient populations, or less supporting data than Recommended regimens. In certain situations, an Alternative regimen may be an optimal regimen for a specific patient. **Not Recommended** regimens are clearly inferior compared to Recommended or Alternative regimens due to factors such as lower efficacy, unfavorable tolerability and toxicity, longer duration, and/or higher pill burden. Unless otherwise indicated, such regimens should not be administered to patients with HCV infection. Specific considerations of persons with HIV/HCV coinfection, decompensated cirrhosis (moderate or severe hepatic impairment; Child Turcotte Pugh [CTP] class B or C), HCV infection post-liver transplant, and those with severe renal impairment or end-stage renal disease are addressed in other sections of the Guidance.

Recommended and Alternative regimens are listed in order of level of evidence. When several regimens are offered at the same level of evidence, they are listed in alphabetic order. Choice of regimen should be determined based on patient-specific data, including drug interactions. As always, patients receiving antiviral therapy require careful pretreatment assessment for comorbidities that may influence treatment response. All patients should have careful monitoring during treatment, particularly for anemia if RBV is included in the regimen. (See Monitoring Section)

I. Genotype 1

Five highly potent oral DAA combination regimens are recommended for patients with HCV genotype 1 infection, although there are differences in the Recommended regimens based on the viral subtype and the presence or absence of baseline NS5A resistance-associated variants (RAVs), and the presence or absence of cirrhosis. With certain regimens, patients infected with genotype 1a may have higher rates of virologic failure than those infected with genotype 1b. HCV genotype 1 infection that cannot be subtyped should be treated as genotype 1a infection.

Approximately 10%-15% of HCV genotype 1-infected patients without prior exposure to NS5A inhibitors will have detectable HCV NS5A RAVs at the population level prior to treatment. While the clinical impact of NS5A RAVs remains to be fully elucidated, in patients with genotype 1a infection the presence of baseline NS5A RAVs that cause a large reduction in the activity of NS5A inhibitors (>5 fold) adversely impact response to NS5A-containing regimens. (Zeuzem, 2015b); (Jacobson, 2015b) These RAVs include variants at positions M28, Q30, L31, and Y93 in genotype 1a and are found by population sequencing in roughly 5%-10% of patients. Given that baseline NS5A RAVs are one of the strongest pre-treatment predictors of treatment outcome with certain regimens in patients with genotype 1a infection, testing for these RAVs prior to deciding on a therapeutic course is recommended in select situations. (Zeuzem, 2015c)

The introduction of DAAs into HCV treatment regimens increased the risk of drug interactions with concomitant medications and now with combinations of DAAs, attention to drug interactions is all the more important (see Drug Interactions Table). The product prescribing information and other resources (eg, http://www.hep-druginteractions.org) should be referenced regularly to ensure safety when prescribing DAA regimens. Important interactions with commonly used medications (eg, antacids, lipid lowering drugs, anti-epileptics, antiretrovirals, etc) exist for all of the regimens discussed below.

Genotype 1a PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed, and in whom no baseline NS5A RAVs[§] for elbasvir are detected.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dasabuvir (250 mg) and weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**

Rating: Class I, Level A

- **Daily simeprevir (150 mg) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

§ Includes G1a polymorphisms at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Genotype 1a PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis‡ - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed, and in whom no baseline NS5A RAVs§ for elbasvir are detected.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 24 weeks is a Recommended regimen for patients with HCV genotype 1a infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) plus weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 1a infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

‡ For decompensated cirrhosis, please refer to the appropriate section.
§ Includes G1a polymorphisms at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.

Genotype 1a PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis - Alternative

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based RBV for 16 weeks is an Alternative regimen for patients with HCV genotype 1a infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed, and who have baseline NS5A RAVs[§] for elbasvir.**
  Rating: Class I, Level B

[§] Includes G1a polymorphisms at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.

Genotype 1a PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis[‡] - Alternative

Alternative regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) and weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 1a infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.[†]**
  Rating: Class I, Level A

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based RBV for 16 weeks is an Alternative regimen for patients with HCV genotype 1a infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed, and who have baseline NS5A RAVs[§] for elbasvir.**
  Rating: Class I, Level B

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with or without weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 1a infection, who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

- **Daily simeprevir (150 mg) plus sofosbuvir (400 mg) with or without weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 1a infection with compensated cirrhosis who are negative for the Q80K variant by commercially available resistance assay, in whom prior PEG-IFN/RBV treatment has failed. Other Recommended or Alternative regimens should be used for patients with compensated cirrhosis and HCV genotype 1a infection in whom the Q80K variant is present.**
  Rating: Class IIa, Level B

[‡] For decompensated cirrhosis, please refer to the appropriate section.
[†]Please see statement on FDA warning regarding the use of PrOD or PrO in patients with cirrhosis.
[§] Includes G1a polymorphisms at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Genotype 1b PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis -

Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily simeprevir (150 mg) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Genotype 1b PEG-IFN/RBV Treatment-experienced with Compensated Cirrhosis‡ - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) plus weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 24 weeks is a Recommended regimen for patients with HCV genotype 1b infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1b infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**[†]
  Rating: Class I, Level A

[‡] For decompensated cirrhosis, please refer to the appropriate section.
[†] Please see statement on FDA warning regarding the use of PrOD or PrO in patients with cirrhosis.

Genotype 1b PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis[‡] - Alternative
Alternative regimens are listed in groups by level of evidence, then alphabetically.

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with or without weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 1b infection, who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

- **Daily simeprevir (150 mg) plus sofosbuvir (400 mg) with or without weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 1b infection who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

[‡] For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Elbasvir/grazoprevir

The fixed-dose, once-daily combination of elbasvir (50 mg) and grazoprevir (100 mg) (hereafter, elbasvir/grazoprevir) was evaluated in patients who had previously failed PEG-IFN/RBV in C-EDGE TE. In this phase III trial, patients were randomized to receive elbasvir/grazoprevir for 12 or 16 weeks with or without RBV. Genotype 1 patients treated for 12 weeks without RBV had an overall high SVR rate of 93.8% (90/96) which was similar to response rates in patients treated for 12 weeks with RBV (94.4%, 84/89). Response rates were similar in the 16-week arms without RBV (94.8%, 91/96) and with RBV (96.9%, 93/96). A subset analysis of patients with compensated cirrhosis revealed similar response rates to the noncirrhotic population when treated with elbasvir/grazoprevir without RBV for 12 weeks: SVR in cirrhosis 95% (19/20) vs no cirrhosis 94.9% (37/39).

The presence of certain baseline NS5A RAVs appears to be the single best predictor of relapse with the 12-week elbasvir/grazoprevir regimen. In genotype 1a patients treated with elbasvir/grazoprevir, decreased efficacy was seen among those with baseline NS5A resistance-associated varients (RAVs) when assessed by population sequencing (limit of detection 25%). These resistance-associated variants included mutations at positions M28, Q30, L31, H58, and Y93. Among 21 genotype 1a patients with baseline high fold-change NS5A RAVs (>5 fold), 11 patients achieved SVR (52.4%) due to higher relapse. (Kwo, 2015b) A subsequent integrated analysis of phase II and III trials confirmed a lower SVR in treatment-experienced genotype 1a patients with these specific baseline NS5A RAVs (90%, 167/185) vs patients without baseline RAVs (99%, 390/393). (Zeuzem, 2015b) In patients treated with 12 weeks of elbasvir/grazoprevir without ribavirin, 64% (9/14) of patients with baseline EBR NS5A RAVs achieved SVR, compared to 96% (52/54) of those without baseline RAVs. Extension of therapy to 16 weeks or 18 weeks with the addition of weight-based RBV increased response rates to 100% regardless of presence of baseline NS5A RAVs, suggesting this approach can overcome the negative impact of NS5A RAVs seen in the 12-week arms. (Jacobsen, 2015b) Based on the known inferior response in patients with specific NS5A RAVs, NS5A resistance testing is recommended in genotype 1a patients who are being considered for therapy with elbasvir/grazoprevir. If these RAVs are present, treatment extension to 16 weeks with the addition of weight-based RBV (1000 mg [<75 kg] to 1200 mg [≥75 kg]) is recommended to decrease the risk of relapse.

Lack of RAV testing results or lack of access to RAV testing should not be used as a means to limit access to HCV therapy.

Ledipasvir/sofosbuvir

The fixed-dose combination of ledipasvir (90 mg) and sofosbuvir (400 mg) (hereafter, ledipasvir/sofosbuvir) has been evaluated in patients with and without cirrhosis in whom prior treatment with PEG-IFN/RBV, with or without HCV protease inhibitors (telaprevir or boceprevir), failed. In the ION-2 study, patients who had not responded to prior PEG-IFN/RBV were treated with ledipasvir/sofosbuvir. This regimen was given for 12 weeks or 24 weeks, with or without RBV. In the population without cirrhosis, the overall response rate was 98% (95% confidence interval [CI], 96%-99%). Specifically, in patients without cirrhosis who did not respond to PEG-IFN/RBV, 33 of 35 (94%) achieved an SVR after treatment with ledipasvir/sofosbuvir for 12 weeks, and 38 of 38 (100%) patients achieved SVR after treatment with ledipasvir/sofosbuvir and RBV for 12 weeks. (Afdhal, 2014b) This regimen was well tolerated in all groups, with no serious adverse events reported in the 12-week regimen with or without RBV. In the population with cirrhosis, patients treated for 24 weeks had higher SVR rates than those treated for 12 weeks, supporting the recommendation that HCV treatment-experienced patients with cirrhosis receive 24 weeks of treatment without RBV.

In SIRIUS, a double-blind placebo-controlled French study, patients with cirrhosis who did not respond to PEG-IFN/RBV plus telaprevir or boceprevir, were randomized to receive placebo for 12 weeks followed by ledipasvir/sofosbuvir plus RBV for 12 weeks or ledipasvir/sofosbuvir plus placebo for 24 weeks. The SVR rate was similar in each group, 74 of 77 (96%) in the group that received ledipasvir/sofosbuvir plus RBV for 12 weeks (3 patients with relapse) and 75 of 77 (97%) in the group that received ledipasvir/sofosbuvir for 24 weeks (2 patients with relapse). This observation was further supported by a meta-analysis of treatment-naïve and -experienced patients with cirrhosis who were treated with ledipasvir/sofosbuvir in phase II and III studies (including the SIRIUS study). In this analysis, ledipasvir/sofosbuvir for 12 weeks was inferior to ledipasvir/sofosbuvir for 24 weeks and ledipasvir/sofosbuvir plus RBV for 12 weeks; no difference in SVR was detected between the latter two groups. Safety and tolerability were similar in

each group, and with the exception of anemia, reported adverse events did not differ substantially between patients treated with or without RBV. (Bourliere, 2015); (Reddy, 2015)

Baseline NS5A RAVs adversely impact responses to LDV/SOF therapy; though the magnitude of this impact varies based on a number of factors including virus (genotype subtype, specific RAV), regimen (companion drugs, use of RBV) and patient factors (treatment experience, presence of cirrhosis). In an analysis of over 350 HCV genotype 1 treatment-experienced patients with cirrhosis the presence of baseline LDV RAVs (defined as RAVs resulting in a >2.5 fold-shift in LDV EC_{50}) detected at a 1% level resulted in lower SVR12 rates compared to those without baseline RAVs. (Zeuzem, 2015b) The SVR12 rates were 89% (RAVs) versus 96% (no RAVs) when ledipasvir/sofosbuvir plus RBV for 12 weeks was used and 87% versus 100%, respectively, with ledipasvir/sofosbuvir for 24 weeks. The impact is likely to be larger in a genotype 1a only population. *Given the vulnerable nature of this population, baseline NS5A resistance testing should be considered in genotype 1a treatment-experienced patients with cirrhosis prior to use of ledipasvir/sofosbuvir. If ledipasvir associated RAVs are detected consideration should be given to adding RBV to the regimen and extending therapy to 24 weeks.* This is based on a 100% SVR12 rate in 14 patients with cirrhosis and baseline LDV RAVs treated with 24 weeks of ledipasvir/sofosbuvir plus RBV. (Sarrazin, 2015)

Paritaprevir/ritonavir/ombitasvir + dasabuvir

In SAPPHIRE-2, the daily fixed-dose combination of paritaprevir (150 mg), ritonavir (100 mg), and ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) (PrOD) with weight-based RBV (1000 mg [<75 kg] to 1200 mg [≥75 kg]) was investigated for treatment of patients with HCV genotype 1 infection, in whom previous PEG-IFN/RBV therapy failed. (Zeuzem, 2014) In this phase III trial, patients who did not have cirrhosis and who were treated for a total of 12 weeks had a high overall rate of response with 286 of 297 (96.3%). Response rates did not differ substantially when stratified by subtype (genotype 1a, 96.0% [166/173]; genotype 1b, 96.7% [119/123]) or kinetics of prior response to PEG-IFN/RBV (relapse, 95.3% [82/86]; partial response, 100% [65/65]; null response, 95.2% [139/146]). In the PEARL-II study, 179 patients without cirrhosis and HCV genotype 1b infection, in whom previous therapy with PEG-IFN/RBV failed, were treated with PrOD with or without weight-based RBV for 12 weeks. (Andreone, 2014) SVR rates were high in both arms: 100% (91/91) in the RBV-free arm and 96.6% (85/88) in the RBV-containing arm, supporting the recommendation that this regimen may be used without RBV for patients with HCV genotype 1b infection.

In the TURQUOISE-II study, patients with CTP class A cirrhosis were treated with PrOD and RBV for 12 weeks or 24 weeks. (Poordad, 2014) Of the 380 patients enrolled in this study, 220 had received prior PEG-IFN/RBV therapy that failed. Among the treatment-experienced patients, SVR12 was achieved in 90.2% (110/122) of patients in the 12-week arm and 96.9% (95/98) of patients in the 24-week arm. In multivariate logistic regression analysis, both prior null response to PEG-IFN/RBV therapy and genotype 1a subtype were associated with lower likelihood of SVR in patients who received 12 weeks of therapy. Therefore, patients with HCV genotype 1a infection and cirrhosis should be treated for 24 weeks. Hemoglobin decline to less than 10 g/dL occurred in 7.2% of the 12-week arm and 11.0% of the 24-week arm; however, treatment discontinuation for adverse events was rare overall (2.1%). To address the need for RBV with this regimen in patients with HCV genotype 1b and cirrhosis, the TURQUOISE-III study evaluated the safety and efficacy of PrOD without RBV for 12 weeks in patients with HCV genotype 1b infection and compensated cirrhosis. Sixty patients (62% men, 55% treatment-experienced, 83% with the IL28B non-CC genotype, 22% with platelet counts <90 x 10^9/L, and 17% with albumin levels <3.5 g/dL) were enrolled. All patients completed treatment, and all patients achieved an SVR12. On the basis of this

study, treating patients with HCV genotype 1b with PrOD without RBV is recommended, regardless of prior treatment experience or presence of cirrhosis. (Feld, 2015)

In October 2015, the FDA released a warning regarding the use of the PrOD or PrO (without dasabuvir) in patients with cirrhosis. (This statement is based on our review of the limited data available from the FDA and will be updated if and when more data become available.) PrOD and PrO are contraindicated in patients with Child Turcotte Pugh (CTP) class B or C hepatic impairment (decompensated liver disease). The manufacturer's pharmacovigilance program reported rapid onset of liver injury and in some cases hepatic decompensation in patients with cirrhosis, including CTP class A compensated cirrhosis and decompensated cirrhosis, who were receiving PrOD or PrO. The liver injury and decompensating events occurred largely during the first 4 weeks of therapy and primarily involved a rapid increase in total and direct bilirubin, often associated with a concomitant increase in liver enzyme levels. In most cases, early recognition and prompt discontinuation of PrOD or PrO resulted in resolution of injury, although some patients, including at least 2 patients with CTP class A compensated cirrhosis, died or required liver transplantation. Although cirrhosis carries a 2% to 4% annual risk of hepatic decompensation, the rapid onset of hepatic decompensation and in many cases its resolution with discontinuation of treatment with PrOD or PrO is suggestive of drug-induced liver injury. Although PrOD and PrO are contraindicated in patients with CTP class B or C cirrhosis and decompensated liver disease, predictors of these events in patients with CTP class A cirrhosis are currently unclear.

For patients with CTP class A cirrhosis, the unlikely but real possibility of drug-induced liver injury should be discussed with the patient. If the decision is made to initiate treatment with PrOD or PrO, close monitoring of total and direct bilirubin and transaminase levels every 1 week or 2 weeks for the first 4 weeks is recommended to ensure early detection of drug-induced liver injury. Also, educating patients about the importance of reporting systemic symptoms such as jaundice, weakness, and fatigue is strongly recommended. The regimen should be discontinued immediately if drug-induced liver injury is suspected. If a patient is already taking PrOD or PrO and is tolerating the regimen, laboratory monitoring as above without discontinuation is recommended unless there are signs or symptoms of liver injury. If heightened monitoring cannot be provided in the first 4 weeks of therapy with PrOD or PrO in patients with cirrhosis, the use of these regimens is not recommended.

Simeprevir + sofosbuvir

In the phase IIa COSMOS study, 167 participants received simeprevir (150 mg once daily) plus sofosbuvir (400 mg once daily) with or without weight-based RBV for 12 weeks or 24 weeks. Overall SVR12 was 92% (90% among 80 patients with prior PEG-IFN/RBV nonresponse and limited (Metavir F0-F2) fibrosis, and 94% among 87 patients with Metavir F3-F4 fibrosis), and the regimens were well tolerated confirming high efficacy and safety. (Lawitz, 2014b) The OPTIMIST-1 and -2 phase III studies subsequently evaluated the combination of sofosbuvir plus simeprevir for 12 weeks in patients with HCV genotype 1 infection who were HCV treatment-naïve and -experienced and without or with cirrhosis, respectively. (Lawitz, 2015); (Kwo, 2015) In OPTIMIST-1, patients with HCV genotype 1 infection and no evidence of cirrhosis were randomized to 8 weeks or 12 weeks of treatment. Superiority in SVR12 was assessed for simeprevir plus sofosbuvir at 12 and 8 weeks versus a composite historical control SVR rate. The SVR12 in the 12-week arm was 97%, meeting superiority versus the historical control (87%); however, the 8-week arm only achieved an SVR12 of 83%, which did not meet superiority versus the historical control. Among those treated for 12 weeks, the SVR rate in PEG-IFN plus RBV treatment-experienced patients was 95% (38/40) and the SVR rate in patients with genotype 1a infection with the baseline Q80K polymorphism (96%; 44/46) was similar to that observed in patients without the Q80K variant (97%; 69/70). In contrast,

in the OPTIMIST-2 study (a single-arm study), 79% (42 of 53) of treatment-experienced patients with HCV genotype 1 infection and cirrhosis who were treated with 12 weeks of simeprevir and sofosbuvir achieved SVR. Overall, in this population of patients with cirrhosis, the SVR rate was lower in patients with HCV genotype 1a with the Q80K variant (74%; 25 of 34) than in patients with HCV genotype 1a without the Q80K variant (92%, 35 of 38). Taken together, these studies support the evaluation of treatment-experienced patients with cirrhosis and HCV genotype 1a for the presence of the Q80K polymorphism. If the Q80K polymorphism is detected, a different treatment regimen should be used. If Q80K polymorphisms are not detected then a 24-week regimen should be used. (Janssen Therapeutics, 2013); (Lawitz, 2014b)

Daclatasvir + sofosbuvir

The combination of daclatasvir and sofosbuvir has been studied in HCV genotype 1 treatment-experienced patients who have previously been treated with PEG-IFN/RBV in two observational early access programs in the United Kingdom and France. (Foster, 2015); (Pol, 2015); (Foster, 2015b) In the French cohort, patients were treated with daclatasvir and sofosbuvir with or without RBV for 12 weeks or 24 weeks. In patients treated with daclatasvir and sofosbuvir alone, a numerically higher rate of sustained virologic response at 4 weeks (SVR4) was seen in those treated for 24 weeks (12 weeks, 15/18 or [82.6%] vs 24 weeks, 75/78 or [96.1%]). Patients treated with daclatasvir, sofosbuvir, and RBV had high response rates in the 12-week and the 24-week treatment groups (100% and 97.1%, respectively), but only 4 patients were treated for 12 weeks. In the United Kingdom cohort, 235 HCV genotype 1-infected patients with decompensated cirrhosis (45% had prior IFN-based HCV treatment failures) were treated with 12 weeks of sofosbuvir plus ledipasvir or daclatasvir with or without RBV as part of a compassionate access program. The selection of daclatasvir or ledipasvir and the use of RBV was at the discretion of the treating physician; most patients (94.4%) had RBV in their regimen. Among patients treated with sofosbuvir plus RBV for 12 weeks, the SVR rate was 86% for those who received ledipasvir (n=164) and 82% for those who received daclatasvir (n=82). Based on these limited data, consideration should be given to the addition of RBV when treating more difficult-to-treat patients, such as those with cirrhosis.

Genotype 1 Sofosbuvir plus Ribavirin with or without PEG-IFN Treatment-experienced Patients - Recommended

- **No Cirrhosis:**
  Daily fixed-dose combination of ledipavir (90 mg)/sofosbuvir (400 mg) with weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who do not have cirrhosis, in whom a previous sofosbuvir plus RBV-containing regimen with or without PEG-IFN has failed.
  Rating: Class IIa, Level B

- **Compensated Cirrhosis:**‡
  Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with weight-based RBV for 24 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who have compensated cirrhosis, in whom a previous sofosbuvir plus RBV-containing regimen has failed.
  Rating: Class IIa, Level B

‡ For decompensated cirrhosis, please refer to the appropriate section.

To date, clinical experience and trial data on the retreatment of sofosbuvir-experienced patients are very limited. However, retreatment after a sofosbuvir-containing treatment failure with a second course of treatment using sofosbuvir plus new agents, or retreatment with the same sofosbuvir-based regimen for a longer duration, have been reported.

Retreatment with ledipasvir/sofosbuvir in subjects with HCV genotype 1 infection, with or without cirrhosis, in whom a sofosbuvir-containing regimen failed has been evaluated in two small pilot studies utilizing ledipasvir/sofosbuvir for 12 weeks. With prior failures of 24 weeks of sofosbuvir plus RBV, high SVR rates were noted when patients were retreated with ledipasvir/sofosbuvir for 12 weeks. (Osinusi, 2014a) Ledipasvir/sofosbuvir plus RBV has also been evaluated in subjects in whom prior treatment with sofosbuvir plus PEG-IFN/RBV or sofosbuvir and RBV failed. In this study of 51 patients, retreatment with ledipasvir/sofosbuvir plus RBV for 12 weeks led to SVR12 in 100% of 50 patients with HCV genotype 1 infection; 1 virologic failure was observed in a patient determined to have HCV genotype 3 infection prior to retreatment. (Wyles, 2015b) There are exceedingly limited data on the retreatment of such patients with cirrhosis. However, a post-hoc analysis of 352 previously treated patients with cirrhosis (240 of whom had prior protease inhibitor-based treatment failures) who were retreated with 12 weeks or 24 weeks of ledipasvir/sofosbuvir with or without RBV found that SVR12 was achieved in 95% to 98%. (Reddy, 2015) Thus, for previously treated HCV genotype 1-infected patients with compensated cirrhosis, retreatment with 24 weeks of ledipasvir/sofosbuvir plus RBV is recommended.

There are no published data on retreatment of sofosbuvir-containing treatment failures with non-sofosbuvir based DAA regimens. In theory the lack of cross resistance between SOF and all other currently available DAAs suggests that such regimens may be efficacious in retreatment settings. However, given the lack of available data recommendations cannot be made. If use of non-sofosbuvir based DAA regimens is being considered, those patients should be treated in line with the recommendations for pegylated interferon-experienced patients according to genotype subtype and cirrhosis status.

Genotype 1 HCV nonstructural protein 3 (NS3) protease inhibitor (telaprevir, boceprevir, or simeprevir) plus PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for treatment of patients with HCV genotype 1 infection, regardless of subtype, who do not have cirrhosis, in whom prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed.**
  Rating: Class I, Level A

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who do not**

have cirrhosis, in whom prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed.
Rating: Class IIa, Level B

- **Daily fixed-dose combination elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for 12 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who do not have cirrhosis, in whom prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed. Genotype 1a patients who have baseline high fold-change NS5A RAVs[§] for elbasvir should have this treatment extended to 16 weeks.**
  Rating: Class IIa, Level B

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

[§] Includes G1a polymorphisms at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.

Genotype 1 HCV nonstructural protein 3 (NS3) protease inhibitor (telaprevir, boceprevir, or simeprevir) plus PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis[‡] - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg) plus weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who have compensated cirrhosis, in whom prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg) for 24 weeks is a Recommended regimen for retreatment of patients with HCV genotype 1 infection, regardless of subtype, who have compensated cirrhosis, in whom prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed.**
  Rating: Class I, Level A

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with or without weight-based RBV for 24 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who have compensated cirrhosis, in whom prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed.**
  Rating: Class IIa, Level B

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) plus weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 1 infection, regardless of subtype, who have compensated cirrhosis, in whom a prior treatment with an HCV protease inhibitor plus PEG-IFN/RBV has failed. Genotype 1a patients who have baseline high fold-change NS5A RAVs[§] for elbasvir should have this treatment extended to 16 weeks.**
  Rating: Class IIa, Level B

‡ For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.
§ Includes G1a polymorphisms at amino acid positions 28, 30, 31, or 93. Amino acid substitutions that confer resistance.

The safety and efficacy of ledipasvir/sofosbuvir was evaluated in subjects in whom prior treatment with an HCV protease inhibitor (telaprevir or boceprevir) plus PEG-IFN/RBV has failed. (Afdhal, 2014b) SVR12 rates with 12- and 24-week regimens were high during both treatment durations (94% and 98%, respectively). Relapse rates in the ION-2 retreatment trial were numerically higher in the 12-week arms than in the 24-week arms. The pretreatment presence of cirrhosis or nonstructural protein 5A (NS5A) resistance-associated variants (RAV) were the major reasons for the higher relapse rate in the 12-week arm. Thus, patients with cirrhosis in whom a prior regimen of PEG-IFN, RBV, and an HCV protease inhibitor has failed should receive 24 weeks of ledipasvir/sofosbuvir, and patients without cirrhosis should receive 12 weeks of ledipasvir/sofosbuvir. Based on data from the SIRIUS study, patients with cirrhosis in whom a prior protease inhibitor-containing regimen failed may also receive ledipasvir/sofosbuvir plus weight-based RBV for 12 weeks. (Bourliere, 2015)

The combination of daclatasvir and sofosbuvir was studied in 41 patients without cirrhosis in whom previous therapy with PEG-IFN, RBV, and an HCV protease inhibitor had failed. Of these patients, 21 were treated with daclatasvir and sofosbuvir for 24 weeks and 20 were treated with daclatasvir and sofosbuvir plus RBV for 24 weeks. Both groups had high cure rates and no additional benefit was seen with the inclusion of RBV (98% SVR12 overall). (Sulkowski, 2014b) Although data are limited, the addition of RBV can be considered in difficult-to-treat situations, such as in patients with cirrhosis. (Pol, 2015)

Grazoprevir is a next-generation protease inhibitor that retains activity in vitro against many common protease inhibitor resistant variants. (Summa, 2012); (Howe, 2014) The combination of grazoprevir (100 mg) plus elbasvir (50 mg) with expanded weight-based RBV (800-1400 mg) was evaluated in an open-label phase II study of 79 patients who had failed prior interferon-based HCV therapy including a protease inhibitor. (Forns, 2015a) The majority of enrolled subjects had failed prior PEG-IFN/RBV plus either boceprevir (35%, n=28) or telaprevir (54%, n=43); importantly 83% experienced virologic failure with their prior PI-containing regimen and 44% had detectable NS3 RAVs to early generation PIs at study entry. Sustained virologic response 12 weeks after completion of therapy was attained in 96% of patients including in 93% (28/30) of genotype 1a patient and 94% (32/34) of those with cirrhosis. Baseline NS3 RAVs did not appear to have a large impact on responses with a SVR12 rate of 91% (31/34). Presence of NS5A or dual NS3/NS5A variants was associated with lower SVR12 rates of 75% and 66%, respectively, but with only 3 failures in the entire study firm conclusions cannot be drawn. Consistent with the recommendations for other populations, extension of therapy to 16 weeks with RBV is recommended in patients with baseline NS5A RAVs resulting in a >5-fold shift in elbasvir potency.

Genotype 1 Simeprevir plus Sofosbuvir Treatment-experienced Patients - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Deferral of treatment is recommended, pending availability of data, for patients with HCV genotype 1 infection, regardless of subtype, in whom prior treatment with the HCV protease inhibitor simeprevir plus sofosbuvir has failed (no prior NS5A treatment), who do not have cirrhosis, and do not have reasons for urgent retreatment.**
  Rating: Class IIb, Level C

- **Testing for resistance-associated variants that confer decreased susceptibility to NS3 protease inhibitors and to NS5A inhibitors is recommended for patients with HCV genotype 1 infection, regardless of subtype, in whom prior treatment with the HCV protease inhibitor simeprevir plus sofosbuvir has failed (no prior NS5A treatment), who have compensated cirrhosis,‡ or have reasons for urgent retreatment. The specific drugs used in the retreatment regimen should be tailored to the results of this testing as described below.**

- **When using nucleotide-based (eg, sofosbuvir) dual DAA therapy a treatment duration of 24 weeks is recommended, and weight-based RBV, unless contraindicated, should be added.**

- **If available, nucleotide-based (eg, sofosbuvir) triple or quadruple DAA regimens may be considered. In these settings treatment duration ranges from 12 weeks to 24 weeks (see text), and weight-based ribavirin, unless contraindicated, are recommended.**

Rating: Class II, Level C

‡ For decompensated cirrhosis, please refer to the appropriate section.

Recommended for Genotype 1 HCV NS5A inhibitor Treatment-experienced Patients

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Deferral of treatment is recommended, pending availability of data for patients with HCV genotype 1, regardless of subtype, in whom previous treatment with any HCV nonstructural protein 5A (NS5A) inhibitors has failed, who do not have cirrhosis, and do not have reasons for urgent retreatment.**
  Rating: Class IIb, Level C

- **Testing for resistance-associated variants that confer decreased susceptibility to NS3 protease inhibitors and to NS5A inhibitors is recommended for patients with HCV genotype 1, regardless of subtype, in whom previous treatment with any HCV nonstructural protein 5A (NS5A) inhibitors has failed, and who have compensated cirrhosis,‡ or have reasons for urgent retreatment. The specific drugs used in the retreatment regimen should be tailored to the results of this testing as described below.**

- **When using nucleotide-based (eg, sofosbuvir) dual DAA therapy a treatment duration of 24 weeks is recommended, and weight-based RBV, unless contraindicated, should be added.**

- **If available, nucleotide-based (eg, sofosbuvir) triple or quadruple DAA regimens may be**

considered. In these settings treatment duration ranges from 12 weeks to 24 weeks (see text), and weight-based ribavirin, unless contraindicated, are recommended.

Rating: Class IIb, Level C

‡ For decompensated cirrhosis, please refer to the appropriate section.

Simeprevir + sofosbuvir failures

Data suggest that approximately 5% to 10% of patients without cirrhosis and with HCV genotype 1 infection treated for 12 weeks with simeprevir plus sofosbuvir will experience treatment failure, typically due to viral relapse. (Kwo, 2015b) Failure rates in patients with cirrhosis treated for 24 weeks with this regimen are limited; however, treatment failure appears to be more common in persons infected with HCV genotype 1a and those with cirrhosis. Data from the OPTIMIST-1 and -2 studies indicate that treatment failure following a regimen of simeprevir plus sofosbuvir is associated with resistance to simeprevir and cross-resistance to other HCV NS3 protease inhibitors such as paritaprevir, telaprevir, and boceprevir; grazoprevir cross-resistance may also occur in the setting of D168 or A156 variants. (Kwo, 2015b); (Lawitz, 2015d) On the other hand, only a single patient developed the signature sofosbuvir RAV S282T in the OPTIMIST trials supporting the rare occurrence of this variant in clinical practice.

Data on retreatment of simeprevir plus sofosbuvir failures is extremely limited. Interim data from a cohort of 31 patients who had failed simeprevir plus sofosbuvir therapy indicated reasonable response rates to 12-24 weeks of ledipasvir/sofosbuvir therapy with or without RBV. (Gonzales, 2015) In the subset of pateints with SVR12 data available, 85% SVR12 was achieved in non-cirrhotic patients and 91% in cirrhotic patients. Given the lack of a standardized treatment approach and heterogeneous nature of the population, conclusions on the optimal retreatment regimen cannot be drawn.

Ledipasvir/sofosbuvir failures

Data on the retreatment of patients for whom prior treatment with ledipasvir/sofosbuvir has failed are very limited. In a pilot study, 41 patients with and without cirrhosis who did not achieve an SVR with 8 weeks or 12 weeks of ledipasvir/sofosbuvir were retreated with 24 weeks of ledipasvir/sofosbuvir. (Lawitz, 2015b) SVR12 rates varied according to the presence or absence of NS5A inhibitor RAVs. Among 11 patients for whom NS5A inhibitor RAVs were not detected, SVR occurred in 11 of 11 (100%); in contrast, among 30 patients for whom NS5A inhibitor RAVs were detected, SVR occurred in 18 of 30 (60%). Importantly, NS5B inhibitor RAVs (eg, S282T) known to confer decreased activity of sofosbuvir were observed in 3 of 12 (25%) patients for whom the retreatment regimen was not successful. (Lawitz, 2015b) Similarly, in the OPTIMIST-2 study in which patients with cirrhosis were treated with simeprevir and sofosbuvir, the presence of NS3 RAVs, namely the Q80K polymorphism, led to a decreased SVR rate in patients with HCV genotype 1a infection. SVR occurred in 25 of 34 (74%) patients with HCV genotype 1a and the Q80K RAV and in 35 of 38 (92%) patients with HCV genotype 1a without the Q80K RAV. (Lawitz, 2015) Based on these data, retreatment for patients for whom an NS5A inhibitor-containing regimen has failed should be considered in the context of retreatment urgency and the presence or absence of RAVs to inhibitors of NS3 and NS5A. Further, based on limited data, RBV is recommended as part of all retreatment regimens for patients in whom prior treatment with NS5A inhibitors has failed. Although no data exist, consideration may also be given to the addition of PEG-IFN to the retreatment regimen in patients who are eligible for this agent; PEG-IFN will have antiviral activity regardless of the

RAVs present.

Retreatment approach and potential regimens (including other NS5A regimen containing failures)

For patients with cirrhosis or other patients who require retreatment urgently, testing for RAVs that confer decreased susceptibility to NS3 protease inhibitors (eg, Q80K) and to NS5A inhibitors should be performed using commercially available assays prior to selecting the next HCV treatment regimen. For patients with no NS5A inhibitor RAVs detected, retreatment with ledipasvir/sofosbuvir and RBV for 24 weeks is recommended. For patients who have NS5A inhibitor RAVs detected and who do not have NS3 inhibitor RAVs detected, treatment with simeprevir, sofosbuvir, and RBV for 24 weeks is recommended. For patients who have both NS3 and NS5A inhibitor RAVs detected, limited data suggest a retreatment approach based on sofosbuvir combined with either elbasvir/grazoprevir or PrOD may be efficacious. (Lawitz, 2015e); (Poordad, 2015a) In a retreatment arm of the C-SWIFT study, 23 patients who had failed shorter courses of elbasvir/grazoprevir plus sofosbuvir were retreated with 12 weeks of this combination plus weight-based RBV. In a per protocol analysis a 100% SVR12 rate was achieved (23/23), including SVR in 9/9 patients with dual NS3 and NS5A RAVs. (Lawitz, 2015e) A second phase II study of 22 patients, including 14 PrOD failures, evaluated retreatment with 12-24 weeks of PrOD plus sofosbuvir. Treatment duration and RBV usage were determined by cirrhosis status, HCV RNA response on therapy, and genotype subtype. SVR12 data was available on 15 patients with 14/15 (93%) attaining SVR12. Based on these limited data, patients with dual NS3 and NS5A class RAVs may be retreated with elbasvir/grazoprevir plus sofosbuvir with weight-based RBV for 12 weeks or PrOD plus sofosbuvir for 12 weeks in genotype 1b and 24 weeks with weight-based RBV in those with genotype 1a. If these regimens are unavailable, retreatment should be conducted in a clinical trial setting, as an appropriate treatment regimen cannot be recommended at this time.

The following regimens are Not Recommended for patients with HCV genotype 1 infection in whom prior treatment that included an HCV protease inhibitor has failed.

- **Any regimen containing PEG-IFN, including:**
  - **Simeprevir, PEG-IFN, and RBV**
  - **Sofosbuvir, PEG-IFN, and RBV**
  - **Telaprevir or boceprevir, PEG-IFN, and RBV**
  - **PEG-IFN/RBV alone**

Rating: Class IIb, Level A

- **Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral**

  Rating: Class III, Level A

- **Any IFN-free regimen containing the HCV protease inhibitors:**
  - **Simeprevir**
  - **Paritaprevir**

Rating: Class IIb, Level A

In the phase IIb ASPIRE trial, simeprevir was combined with PEG-IFN/RBV to treat patients in whom previous PEG-IFN/RBV failed. (Zeuzem, 2014c); (Janssen Therapeutics, 2013); (www.fda.gov; package insert) The SVR24 rate after 48 total weeks of therapy in the simeprevir 150 mg per day arm was 65% in

patients with a previous partial response (n=23) and 53% in patients with a prior null response (n=17). Based on a relatively poor response to treatment, a need for prolonged therapy, and poor tolerability, this treatment is no longer recommended.

Sofosbuvir combined with PEG-IFN/RBV has high efficacy in treatment-naïve patients but has not been studied prospectively in the treatment-experienced population. Based on limited prospective data and poor tolerability to PEG-IFN-based regimens, this treatment is no longer recommended.

Triple-therapy with boceprevir plus PEG-IFN/RBV for 48 weeks may result in SVR for up to 52% of patients who had a partial response to previous PEG-IFN/RBV treatment (RESPOND 2), (Bacon, 2011) and up to 38% of patients with a prior null response. (PROVIDE); (Sterling, 2015) Similarly, telaprevir plus PEG-IFN/RBV resulted in an SVR24 rate of 54% to 59% among patients who had a partial response to previous treatment and an SVR24 rate of 29% to 33% among those who had a prior null response. (REALIZE); (Zeuzem, 2011) Because of relatively poor efficacy, need for prolonged therapy (48 weeks), and poor tolerability, these regimens are no longer recommended.

Monotherapy with PEG-IFN, RBV, or any of the available DAAs is ineffective; further, DAA monotherapy leads to rapid selection of resistant variants.

II. Genotype 2

Genotype 2 PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily sofosbuvir (400 mg) and weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 2 infection, who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class I, Level A

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 2 infection, who do not have cirrhosis, in whom prior PEG-IFN/RBV treatment has failed, and who are RBV ineligible.**
  Rating: Class IIa, Level B

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Genotype 2 PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis‡ - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 16 weeks to 24 weeks is a Recommended regimen for patients with HCV genotype 2 infection, who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed, and who are RBV ineligible.**
  Rating: Class IIa, Level B

- **Daily sofosbuvir (400 mg) and weight-based RBV for 16 weeks to 24 weeks is a Recommended regimen for patients with HCV genotype 2 infection, who have compensated cirrhosis, in whom prior PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

‡ For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

High SVR12 rates were demonstrated in patients with HCV genotype 2 infection in whom prior treatment with PEG-IFN/RBV had failed who were retreated with 12 weeks of sofosbuvir plus RBV. Limited data are available for treatment-experienced patients with HCV genotype 2 infection and cirrhosis; however, in the FUSION study, numerically higher SVR12 rates were seen with extension of therapy from 12 weeks (60%) to 16 weeks (78%). (Lawitz, 2014b) In contrast, the VALENCE trial found high SVR12 rates among HCV genotype 2-infected persons with cirrhosis after only 12 weeks of sofosbuvir plus RBV (88%). (Zeuzem, 2013b) Further, in the BOSON study, 48 patients with HCV genotype 2 infection who did not respond to prior treatment with PEG-IFN plus RBV were treated with sofosbuvir plus RBV for 16 weeks (n=15) or 24 weeks (n=17) or in combination with PEG-IFN for 12 weeks (n=16). (Foster, 2015) SVR was achieved in 13 of 15 (87%) and 17 of 17 (100%) patients treated with sofosbuvir plus RBV for 16 weeks and 24 weeks, respectively. Among those who received sofosbuvir, PEG-IFN, and RBV for 12 weeks, SVR occurred in 15 of 16 (94%). Thus, definitive recommendations on the appropriate duration of sofosbuvir and RBV for treatment-experienced, HCV genotype 2-infected persons with cirrhosis cannot be made at this time. The decision to extend therapy with sofosbuvir plus RBV to 16 weeks or 24 weeks or to add PEG-IFN for 12 weeks should be made on an individual patient basis.

The once-daily combination of daclatasvir (60 mg) plus sofosbuvir (400 mg) for 12 to 24 weeks has been shown to have efficacy in HCV genotype 2 infection, however available data in patients previously treated with PEG-IFN/RBV is very limited. (Wyles, 2015a); Sulkowski, 2014a) For patients who require treatment and are ineligible to receive RBV, treatment with dacalatasvir/sofosbuvir for 12 weeks is recommended with consideration of extension of therapy to 24 weeks in more difficult patients to treat such as those with cirrhosis.

Genotype 2 PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis‡ - Alternative

Alternative regimens are listed in groups by level of evidence, then alphabetically.

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an**

Alternative regimen for patients who have HCV genotype 2 infection, who have compensated cirrhosis, in whom previous treatment with PEG-IFN/RBV has failed, and who are IFN eligible.
Rating: Class IIa, Level B

‡ For decompensated cirrhosis, please refer to the appropriate section.

In recognition of the potential limitations of sofosbuvir plus RBV in harder-to-treat, HCV genotype 2-infected patients in whom a prior treatment had failed, particularly those with cirrhosis, treatment that included PEG-IFN has been studied. The LONESTAR-2 trial (an open-label, single-site, single-arm, phase II trial) evaluated PEG-IFN (180 µg weekly), sofosbuvir (400 mg daily), and weight-based RBV (daily in 2 divided doses for 12 weeks) in treatment-experienced patients with HCV genotype 2 or 3. (Lawitz, 2014a) Cirrhosis was present at baseline in 61% of patients. SVR12 was achieved in 22 of 23 (96%) persons with HCV genotype 2 infection. For patients with and without cirrhosis, SVR occurred in 13 of 14 patients (93%) and 9 of 9 patients (100%), respectively. Despite the limitations of the data from this small study and accounting for the potential challenges inherent with IFN-based therapy, sofosbuvir plus PEG-IFN/RBV for 12 weeks is an Alternative regimen for HCV genotype 2-infected patients with cirrhosis.

Genotype 2 Sofosbuvir plus Ribavirin Treatment-experienced Patients - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with or without weight-based RBV for 24 weeks is a Recommended regimen for patients with HCV genotype 2 infection, regardless of cirrhosis status,‡ in whom previous treatment with sofosbuvir and RBV has failed, and who are ineligible to receive PEG-IFN and/or RBV.**
  Rating: Class IIa, Level C

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is a Recommended regimen for patients who have HCV genotype 2 infection, regardless of cirrhosis status,‡ in whom previous treatment with sofosbuvir and RBV has failed, and who are IFN eligible.**
  Rating: Class IIa, Level C

‡ For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

To date, there are little data available to guide therapy in patients with HCV genotype 2 infection in whom prior treatment with sofosbuvir and RBV has failed. In the BOSON study, patients who had prior treatment with PEG-IFN/RBV had high response rates (SVR12 in 15 of 16 patients) when retreated with

sofosbuvir, PEG-IFN, and RBV for 12 weeks. Although patients who were previously treated with sofosbuvir plus RBV were not specifically studied, retreatment with the addition of PEG-IFN will likely improve response rates and may be considered in an IFN-eligible patient in need of more-immediate therapy. (Foster, 2015)

The combination of daclatasvir and sofosbuvir is effective in patients with HCV genotype 2 infection, but there are limited data about this therapy in treatment-experienced patients with HCV genotype 2 infection. (Sulkowski, 2014b); (Wyles, 2015) For patients in whom prior treatment with sofosbuvir and RBV failed who are IFN ineligible, the decision to treat with daclatasvir and sofosbuvir should be made on an individual patient basis with consideration of extension of therapy to 24 weeks with the addition of RBV, especially in difficult-to-treat patients such as those with cirrhosis.

The following regimens are Not Recommended for patients with HCV genotype 2 infection in whom prior HCV therapy with PEG-IFN/RBV has failed.

- **PEG-IFN/RBV with or without telaprevir or boceprevir**
  Rating: Class IIb, Level A
- **Ledipasvir/sofosbuvir**
  Rating: Class III, Level A
- **Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral**
  Rating: Class III, Level A

No HCV protease inhibitors have been approved by the US Food and Drug Administration (FDA) or are indicated for the treatment of HCV genotype 2 infection. However, there is in vitro and in vivo evidence that simeprevir has activity against HCV genotype 2. Although PEG-IFN plus RBV has been the mainstay of treatment for HCV genotype 2, it requires a longer duration of therapy, is less efficacious, and has more adverse effects than the recommended regimens.

III. Genotype 3

Genotype 3 PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 3 infection, who do not have cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed.**
  Rating: Class I, Level A

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is a Recommended regimen for patients with HCV genotype 3 infection, who do not have cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed, and who are IFN eligible.**
  Rating: Class I, Level A

* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Genotype 3 PEG-IFN/RBV Treatment-experienced Patients with Compensated Cirrhosis‡ - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is a Recommended regimen for patients with HCV genotype 3 infection, who have compensated cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed, and who are eligible to receive PEG-IFN.**
  Rating: Class I, Level A

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with weight-based RBV for 24 weeks is a Recommended regimen for patients with HCV genotype 3 infection, who have compensated cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed, and who are IFN ineligible.**
  Rating: Class IIa, Level B

‡ For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

In the LONESTAR-2 study, adding 12 weeks of PEG-IFN to the sofosbuvir and RBV regimen resulted in a numerically higher response rate among persons with HCV genotype 3 infection than that achieved with sofosbuvir and RBV alone for 24 weeks. (Lawitz, 2014a) Of HCV genotype 3-infected patients with and without cirrhosis, 10 of 12 (83%) achieved an SVR. These preliminary findings were confirmed in the BOSON study in which patients with HCV genotype 3 infection were randomly assigned to receive treatment with one of three regimens: sofosbuvir and RBV for 16 weeks; sofosbuvir and RBV for 24 weeks; or PEG-IFN (alfa-2a 180 mcg SC weekly), sofosbuvir, and RBV for 12 weeks. Among patients with HCV genotype 3 infection, SVR12 was achieved in 168 of 181 patients (92.8%) treated with 12 weeks of PEG-IFN, sofosbuvir, and RBV and 153 of 182 patients (84.1%) treated with 24 weeks of sofosbuvir and RBV; only 128 of 181 patients (70.7%) treated with 16 weeks of sofosbuvir and RBV achieved an SVR12. (Foster, 2015) Treatment with PEG-IFN, sofosbuvir, and RBV for 12 weeks led to a higher SVR rate than sofosbuvir and RBV in treatment-experienced patients with HCV genotype 3 infection with (85.7% and 76.5%, respectively) and without cirrhosis (94.2% and 81.5%, respectively). No difference was observed with respect to safety and tolerability of the studied regimens. Accordingly, data from these randomized controlled trials strongly support the addition of PEG-IFN to sofosbuvir and RBV in all treatment-experienced patients with HCV genotype 3 infection, including those without cirrhosis when compared with sofosbuvir and RBV alone.

Data are limited for treatment-experienced HCV genotype 3-infected patients with cirrhosis, especially those who are ineligible for IFN. In the ALLY-3 study, a suboptimal response to 12 weeks of daclatasvir

plus sofosbuvir (SVR12 69% [9/13]) was seen. (Nelson, 2015) In contrast, treatment-experienced patients without cirrhosis did well in the ALLY-3 study with an SVR12 rate of 94% (32/34). In a follow-up study (ALLY-3+), 36 genotype 3 cirrhotic patients were randomized to daclatasvir plus sofosbuvir with RBV for 12 or 16 weeks. An on-treatment analysis showed similar SVR12 rates of 88% (15/17) and 89% (16/18), respectively, in the 12-week and 16-week treatment arms. (Leroy, 2016) These data suggest at a minimum RBV should be included, if possible, for all cirrhotic patients treated with this regimen. Given the vulnerable nature of this population, treatment with daclatasvir and sofosbuvir plus RBV for 24 weeks is recommended pending additional data; however, omission of RBV can be considered for patients in whom RBV-containing therapy is contraindicated.

Baseline NS5A polymorphisms in genotype 3 also impact DAA treatment response with the Y93H variant being most problematic. In the ALLY-3 study the Y93H was detected in 13 (9%) of patients with an SVR12 of 54% (7/13); including a 67% SVR12 in patients without cirrhosis. Given that cirrhotic patients are already recommended to have RBV added and extend therapy, baseline testing for NS5A RAVs in GT 3 would only impact treatment approaches for patients without cirrhosis. Pending additional data, baseline NS5A RAV testing should be considered in all treatment-experienced genotype 3 patients without cirrhosis. If the Y93H variant is identified, weight-based RBV should be added to the treatment course.

Genotype 3 Sofosbuvir and RBV Treatment-experienced Patients - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with weight-based RBV for 24 weeks is a Recommended regimen for patients with HCV genotype 3 infection, regardless of cirrhosis status,‡ in whom prior treatment with sofosbuvir and RBV has failed, and who are IFN ineligible.**
  Rating: Class IIa, Level C

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is a Recommended regimen for patients with HCV genotype 3 infection, regardless of cirrhosis status,‡ in whom prior treatment with sofosbuvir and RBV has failed, and who are IFN eligible.**
  Rating: Class IIa, Level C

‡ For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

In the ALLY-3 study, 7 patients previously treated with sofosbuvir-containing regimens were retreated with daclatasvir and sofosbuvir for 12 weeks. Of these patients, 5 (71%) achieved an SVR12. (Nelson, 2015) Based on these limited data, 12 weeks of daclatasvir and sofosbuvir may be insufficient, and extending the duration to 24 weeks of therapy and adding weight-based RBV is recommended.

The following regimens are Not Recommended for patients with HCV genotype 3 infection, in whom prior treatment with PEG-IFN/RBV has failed.

- **PEG-IFN/RBV for 24 weeks to 48 weeks**
  Rating: Class IIb, Level A
- **Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral**
  Rating: Class III, Level A
- **Telaprevir-, boceprevir-, or simeprevir-based regimens**
  Rating: Class III, Level A

No HCV protease inhibitors have been approved or are indicated for the treatment of HCV genotype 3 infection. Although PEG-IFN plus RBV has been the mainstay of treatment of HCV genotype 3 infection, it is less efficacious and has more adverse effects than the Recommended regimens.

IV. Genotype 4

Genotype 4 PEG-IFN/RBV Treatment-experienced Patients without Cirrhosis - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) (PrO) and weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 4 infection, who do not have cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed.**
  Rating: Class I, Level A

- **Daily fixed-dose combinatoin of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for patients who have HCV genotype 4 infection, who do not have cirrhosis, who experienced virologic relapse after prior PEG-IFN/RBV therapy. Genotype 4 patients with prior on-treatment virologic failure (failure to suppress or breakthrough) while on PEG-IFN/RBV should be treated with 16 weeks and have weight-based RBV added to the treatment regimen.**
  Rating: Class IIa, Level B

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 4 infection, who do not have cirrhosis, in whom prior treatment with PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

Genotype 4 PEG-IFN/RBV Treatment-experienced Patients with Compensated cirrhosis‡ - Recommended

Recommended regimens are listed in groups by level of evidence, then alphabetically.

- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) (PrO) and weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 4 infection who have compensated cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed.**[†]
  Rating: Class I, Level A

- **Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for patients who have HCV genotype 4 infection, who have compensated cirrhosis, and who experienced virologic relapse after prior PEG-IFN/RBV therapy. Genotype 4 patients with prior on-treatment virologic failure (failure to suppress or breakthrough) while on PEG-IFN/RBV should be treated with 16 weeks and have weight-based RBV added to the treatment regimen.**
  Rating: Class IIa, Level B

- **Daily ledipasvir (90 mg)/sofosbuvir (400 mg) and weight-based RBV for 12 weeks is a Recommended regimen for patients with HCV genotype 4 infection, in whom prior treatment with PEG-IFN/RBV has failed, and who are eligible for RBV.**
  Rating: Class IIa, Level B

- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 24 weeks is a Recommended regimen for patients with HCV genotype 4 infection, in whom prior treatment with PEG-IFN/RBV treatment has failed.**
  Rating: Class IIa, Level B

[‡] For decompensated cirrhosis, please refer to the appropriate section.
[†]Please see statement on FDA warning regarding the use of PrOD or PrO in patients with cirrhosis.

Genotype 4 Treatment-experienced Patients with or without cirrhosis - Alternative

Alternative regimens are listed in groups by level of evidence, then alphabetically.

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an Alternative regimen for patients with HCV genotype 4 infection, who do not have cirrhosis, in whom prior treatment has failed, and who are eligible for PEG-IFN.**
  Rating: Class IIa, Level B

- **Daily sofosbuvir (400 mg) and weight-based RBV for 24 weeks is an Alternative regimen for patients with HCV genotype 4 infection, in whom prior treatment has failed, and who are IFN ineligible.**
  Rating: Class IIa, Level B

PEARL-I was an open-label phase IIb study that included a cohort of 49 treatment-experienced patients with HCV genotype 4 infection without cirrhosis who received 12 weeks of paritaprevir, ritonavir, and ombitasvir (PrO) with or without weight-based RBV. In intention-to-treat analysis, SVR12 was achieved in

41 of 41 (100%) patients. This regimen was well tolerated with no serious adverse events reported. (Hezode, 2015) The AGATE-I trial, in its first phase, randomized 120 treatment-naïve and -experienced patients with genotype 4 HCV and compensated cirrhosis to receive 12 weeks or 16 weeks of paritaprevir/ritonavir/ombitasvir (PrO) plus weight-based ribavirin. The SVR12 rates in the 12-week and 16-week arms were 96% and 100%, respectively. The regimens were well tolerated (Asselah, 2015a). Similarly, the ongoing AGATE-II trial offered 100 treatment-naïve and -experienced noncirrhotic patients with genotype 4 PrO plus weight-based RBV for 12 weeks. The SVR12 was 94%. Additionally, AGATE-II randomized 60 treatment-naïve and -experienced genotype 4-infected patients with compensated cirrhosis to receive either 12 or 24 weeks of PrO plus weight-based RBV. The SVR12 rate from the 12-week arm, reported recently, was 97%. These data continue to support the use of PrO plus RBV for 12 weeks in treatment-experienced genotype 4 patients, including those with cirrhosis. (Esmat, 2015)

Sofosbuvir-based regimens have also shown efficacy in patients infected with HCV genotype 4. Sofosbuvir administered with PEG-IFN/RBV for 12 weeks was investigated in the phase III NEUTRINO trial. (Lawitz, 2013a) Of the 28 treatment-naïve patients with HCV genotype 4 infection, 27 (96%) achieved SVR12. In a pilot study of treatment-experienced patients of Egyptian ancestry with HCV genotype 4 infection, patients were randomly assigned to receive sofosbuvir and RBV for 12 weeks or 24 weeks. SVR12 rate was numerically higher in the 24-week arm (89% [24/27] in the 24-week arm vs 70% [19/27] in the 12-week arm), supporting the recommendation for longer treatment duration with a sofosbuvir and RBV regimen. (Esmat, 2014) In the SYNERGY trial, 20 patients with HCV genotype 4 infection were treated with ledipasvir/sofosbuvir for 12 weeks. Of these patients, 40% were treatment-experienced and 40% had advanced fibrosis. Preliminary data demonstrate efficacy, with 95% achieving SVR12 based on an intention-to-treat analysis. (Kapoor, 2014)

An integrated analysis of all phase 2/3 elbasvir/grazoprevir studies demonstrated efficacy of this regimen for both treatment-naïve (n=66) and -experienced (n=37) patients with genotype 4 HCV infection. (Asselah, 2015b) The overall SVR12 rate among treatment-experienced genotype 4 infected patients was 87% (32/37) with numerical response differences based on prior interferon treatment response (relapse vs. on-treatment viral failure) and elbasvir/grazoprevir duration (12 vs 16 weeks) and/or RBV usage (no RBV vs RBV). Numbers within any specific subgroup are too small to make definitive recommendation; however, trends emerged which were used to guide the current recommendations pending additional data. No treatment failures were seen in patients who relapsed after prior PEG-IFN/RBV therapy, regardless of elbasvir/grazoprevir treatment duration or RBV usage. In contrast, response rates were numerically lower in patients with prior on-treatment virologic failure in the non-RBV-containing arms (12 weeks: 78%, 16 weeks: 60%) compared to RBV-containing treatment (12 weeks + RBV: 91%, 16 weeks + RBV: 100%). Given the lack of sufficient numbers to differentiate response between 12 weeks with RBV and 16 weeks with RBV, the use of 16 weeks plus RBV in genotype 4-infected patients with prior on-treatment virologic failure represents the most conservative approach.

The following regimens are Not Recommended for patients with HCV genotype 4 infection, in whom prior treatment with PEG-IFN/RBV has failed.

- **PEG-IFN/RBV with or without telaprevir or boceprevir**
  Rating: Class IIb, Level A
- **Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral**
  Rating: Class III, Level A

PEG-IFN/RBV for 48 weeks was previously recommended for patients with HCV genotype 4 infection. (AASLD-IDSA, 2015) Adding sofosbuvir (400 mg daily) to PEG-IFN/RBV increases SVR rates and markedly shortens therapy with no apparent additional adverse effects. The addition of simeprevir to PEG-IFN/RBV increases response rates but has inferior SVR rates compared with SVR rates of other available regimens and requires a longer duration of PEG-IFN/RBV therapy, which increases the risk of adverse events. Therefore, this treatment is no longer recommended. (Moreno, 2013b)

Because of their limited activity against HCV genotype 4 in vitro and in vivo, neither boceprevir nor telaprevir should not be used to treat patients with HCV genotype 4 infection.

V. Genotype 5 and 6

Few data are available to help guide decision making for patients infected with HCV genotype 5 or 6. Thus, for those patients for whom immediate treatment is required, the following recommendations have been drawn from available data.

Genotype 5 or 6 PEG-IFN/RBV Treatment-experienced Patients with or without Cirrhosis - Recommended

- **Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is a Recommended regimen for patients with HCV genotype 5 or 6 infection regardless of cirrhosis status, in whom prior treatment with PEG-IFN/RBV has failed.**
  Rating: Class IIa, Level C

Genotype 5 or 6 PEG-IFN/RBV Treatment-experienced Patients with or without Cirrhosis‡ - Alternative

- **Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an Alternative regimen for patients with HCV genotype 5 or 6 infection regardless of cirrhosis status, in whom prior treatment with PEG-IFN/RBV has failed, and are IFN eligible.**
  Rating: Class IIa, Level C

‡ For decompensated cirrhosis, please refer to the appropriate section.

In the phase III NEUTRINO trial, (Lawitz, 2013a) treatment-naïve patients with HCV genotypes 1 (n=291), 4 (n=28), 5 (n=1), and 6 (n=6) were treated with sofosbuvir (400 mg daily) plus PEG-IFN (2a 180 µg weekly) and weight-based RBV (1000 mg [<75 kg] to 1200 mg [≥75 kg]) for 12 weeks. All six patients with HCV genotype 6 and the one patient with HCV genotype 5 achieved SVR12. The adverse event profile in these patients and in the larger study population was similar to that seen with PEG-IFN/RBV

therapy.

Ledipasvir has in vitro activity against most HCV genotype 6 subtypes (exception 6e). (Wong, 2013); (Kohler, 2014) A small, two-center, open-label study (NCT01826981) investigated the safety and in vivo efficacy of ledipasvir/sofosbuvir for 12 weeks in treatment-naïve and -experienced patients with HCV genotype 6 infection. Twenty-five patients (92% treatment-naïve) who were primarily of Asian descent (88%) were infected with different subtypes of HCV genotype 6 (32%, 6a; 24%, 6e; 12%, 6l; 8%, 6m; 12%, 6p; 8%, 6q; 4%, 6r). Two patients (8%) had cirrhosis. The SVR12 rate was 96% (24/25). The 1 patient who experienced relapse had discontinued therapy at week 8 because of drug use. No patient discontinued treatment owing to adverse events.

The following regimens are Not Recommended for patients with HCV genotype 5 or 6 infection in whom prior treatment has failed.

- **Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral**
  Rating: Class III, Level A
- **Telaprevir- or boceprevir-based regimens**
  Rating: Class III, Level A

Because of their limited activity against HCV genotypes 5 and 6 in vitro and in vivo, neither boceprevir nor telaprevir should not be used as therapy for patients with HCV genotype 5 or 6 infection.

Mixed genotypes

Rarely, genotyping assays may indicate the presence of a mixed infection (eg, genotypes 1a and 2). Treatment data for mixed genotypes with DAAs are sparse, and awaiting the availability of a pangenotypic regimen may be considered. Until then, when treatment is necessary, the choice of antiviral combination and duration of treatment should maximize efficacy against each genotype represented in the assay. When the correct combination or duration is unclear, expert consultation should be sought.

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WHEN AND IN WHOM TO INITIATE HCV THERAPY

Successful hepatitis C treatment results in sustained virologic response (SVR), which is tantamount to virologic cure, and as such, is expected to benefit nearly all chronically infected persons. When the US Food and Drug Administration (FDA) approved the first IFN-sparing treatment for HCV infection, many patients who had previously been "warehoused" sought treatment, and the infrastructure (experienced practitioners, budgeted health-care dollars, etc) did not yet exist to treat all patients immediately. Thus, the panel offered guidance for prioritizing treatment first to those with the greatest need. Since that time, there have been opportunities to treat many of the highest-risk patients and to accumulate real-world experience of the tolerability and safety of newer HCV medications. More importantly, from a medical standpoint, data continue to accumulate that demonstrate the many benefits, within the liver and extrahepatic, that accompany HCV eradication. Therefore, the panel continues to recommend treatment for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Accordingly, prioritization tables are now less useful and have been removed from this section.

Despite the strong recommendation for treatment for nearly all HCV-infected patients, pretreatment assessment of a patient's understanding of treatment goals and provision of education on adherence and follow-up are essential. A well-established therapeutic relationship between practitioner and patient remains crucial for optimal outcomes with new direct-acting antiviral (DAA) therapies. Additionally, in certain settings there remain factors that impact access to medications and the ability to deliver them to patients. In these settings, practitioners may still need to decide which patients should be treated first. The descriptions below of unique populations may help physicians make more informed treatment decisions for these groups. (See **Unique Patient Populations: Patients with HIV/HCV Coinfection**, **Unique Patient Populations: Patients with Decompensated Cirrhosis**, **Unique Patient Populations: Patients who Develop Recurrent HCV Infection Post-liver Transplantation**, and **Unique Patient Populations: Patients with Renal Impairment**).

Expansions and notes for abbreviations used in this section can be found in Methods Table 3.

A summary of recommendations for When and in Whom to Initiate HCV Therapy is found in the BOX.

Goal of Treatment

- **The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.**
  Rating: Class I, Level A

Recommendations for When and in Whom to Initiate Treatment

- **Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.**
  Rating: Class I, Level A

Clinical Benefit of Cure

The proximate goal of HCV therapy is SVR (virologic cure), defined as the continued absence of detectable HCV RNA at least 12 weeks after completion of therapy. SVR is a marker for cure of HCV infection and has been shown to be durable, in large prospective studies, in more than 99% of patients followed up for 5 years or more. (Swain, 2010); (Manns, 2013) Patients in whom an SVR is achieved have HCV antibodies but no longer have detectable HCV RNA in serum, liver tissue, or mononuclear cells, and achieve substantial improvement in liver histology. (Marcellin, 1997); (Coppola, 2013); (Garcia-Bengoechea, 1999) Assessment of viral response, including documentation of SVR, requires use of an FDA-approved quantitative or qualitative nucleic acid test (NAT) with a detection level of 25 IU/mL or lower.

Patients who are cured of their HCV infection experience numerous health benefits, including a decrease in liver inflammation as reflected by improved aminotransferase (ie, alanine aminotransferase [ALT], aspartate aminotransferase [AST]) levels and a reduction in the rate of progression of liver fibrosis. (Poynard, 2002b) Of 3010 treatment-naive HCV-infected patients with pretreatment and posttreatment biopsies from 4 randomized trials of 10 different IFN-based regimens (biopsies separated by a mean of 20 months), 39% to 73% of patients who achieved an SVR had improvement in liver fibrosis and necrosis (Poynard, 2002b), and cirrhosis resolved in half of the cases. Portal hypertension, splenomegaly, and other clinical manifestations of advanced liver disease also improved. Among HCV-infected persons, SVR is associated with a more than 70% reduction in the risk of liver cancer (hepatocellular carcinoma [HCC]) and a 90% reduction in the risk of liver-related mortality and liver transplantation. (Morgan, 2013); (van der Meer, 2012); (Veldt, 2007)

Cure of HCV infection also reduces symptoms and mortality from severe extrahepatic manifestations, including cryoglobulinemic vasculitis, a condition affecting 10% to 15% of HCV-infected patients. (Fabrizi, 2013); (Landau, 2010); (Sise, 2015) HCV-infected persons with non-Hodgkin lymphoma and other lymphoproliferative disorders achieve complete or partial remission in up to 75% of cases following successful therapy for HCV infection. (Gisbert, 2005); (Takahashi, 2012); (Svoboda, 2005); (Mazzaro,

2002); (Hermine, 2002) These reductions in disease severity contribute to dramatic reductions in all-cause mortality. (van der Meer, 2012); (Backus, 2011) Lastly, patients who achieve SVR have substantially improved qualities of life, which include physical, emotional, and social health. (Boscarino, 2015); (Neary, 1999); (Younossi, 2013) Because of the many benefits associated with successful HCV treatment, clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving an SVR, preferably early in the course of chronic HCV infection before the development of severe liver disease and other complications.

Benefits of Treatment at Earlier Fibrosis Stages (Metavir Stage Below F2)

Initiating therapy in patients with lower-stage fibrosis augments the benefits of SVR. In a long-term follow-up study, 820 patients with Metavir stage F0 or F1 fibrosis confirmed by biopsy were followed up for up to 20 years. (Jezequel, 2015) The 15-year survival rate was statistically significantly better for those who experienced an SVR than for those whose treatment had failed or for those who remained untreated (93%, 82%, and 88%, respectively; P =.003). The study results argue for consideration of earlier initiation of treatment. Several modeling studies also suggest a greater mortality benefit if treatment is initiated at fibrosis stages prior to F3. (Øvrehus, 2015); (Zahnd, 2015); (McCombs, 2015)

Treatment delay may decrease the benefit of SVR. In a report of long-term follow-up in France, 820 patients with biopsy-confirmed Metavir stage F0 or F1 fibrosis were followed up for as long as 20 years. (Jezequel, 2015) The authors noted rapid progression of fibrosis in 15% of patients during follow-up, and in patients treated successfully, long-term survival was better. Specifically, at 15 years, survival rate was 92% for those with an SVR versus 82% for treatment failures and 88% for those not treated. In a Danish regional registry study, investigators modeled treatment approaches with the aim of evaluating the benefit to the region in terms of reductions in morbidity and mortality and HCV prevalence. (Øvrehus, 2015) Although they note that in their situation of low HCV prevalence (0.4%), with approximately 50% undiagnosed, a policy that restricts treatment to those with Metavir fibrosis stage F3 or higher would decrease mortality from HCC and cirrhosis, the number needed to treat to halve the prevalence of the disease is lower if all eligible patients receive treatment at diagnosis. A modeling study based on the Swiss HIV Cohort Study also demonstrated that waiting to treat HCV infection at Metavir fibrosis stages F3 and F4 resulted in 2- and 5-times higher rates of liver-related mortality, respectively, compared with treating at Metavir stage F2. (Zahnd, 2015)

A US Veterans Administration dataset analysis that used very limited end points of virologic response dating from the IFN-treatment era suggested that early (at a Fibrosis-4 [FIB-4] score of <3.25) initiation of therapy increased the benefit attained with respect to likelihood of treatment success and mortality reduction and ultimately decreased the number of patients needed to treat to preserve 1 life by almost 50%. (McCombs, 2015)

Considerations in Specific Populations

Despite the recommendation for treatment of nearly all patients with HCV infection, it remains important for clinicians to understand patient- and disease-related factors that place individuals at risk for HCV-related complications (liver and extrahepatic) as well as for HCV transmission. Although these groups are no longer singled out for high prioritization for treatment, it is nonetheless important that practitioners recognize the unique dimensions of HCV disease and its natural history in these populations. The discussions offered below may assist clinicians in making compelling cases for insurance coverage of treatment when necessary.

Persons With Advanced Liver Disease

For persons with advanced liver disease (Metavir stage F3 or F4), the risk of developing complications of liver disease such as hepatic decompensation (Child Turcotte Pugh [CTP] Class B or C [**Methods Table 3**]) or HCC is substantial and may occur in a relatively short timeframe. A large prospective study of patients with cirrhosis resulting from HCV infection examined the risk of decompensation, including HCC, ascites, jaundice, bleeding, and encephalopathy, and found that the overall annual incidence rate was 3.9%. (Sangiovanni, 2006) The National Institutes of Health (NIH)-sponsored HALT–C study included a group of 220 patients with cirrhosis resulting from HCV infection who were observed for approximately 8 years. A primary outcome of death, hepatic decompensation, HCC, or increase in CTP score of 2 or higher occurred at a rate of 7.5% per year. (Everson, 2006); (Di Bisceglie, 2008) Patients with a CTP score of 7 or higher experienced a death rate of 10% per year.

Numerous studies have demonstrated that hepatitis C therapy and the achievement of an SVR in this population results in dramatic decreases in hepatic decompensation events, HCC, and liver-related mortality. (Morgan, 2013); (van der Meer, 2012); (Backus, 2011); (Dienstag, 2011); (Berenguer, 2009); (Mira, 2013) In the HALT-C study, patients with advanced fibrosis secondary to HCV infection who achieved an SVR, compared with patients with similarly advanced liver fibrosis who did not achieve an SVR, had a decreased need for liver transplantation (hazard ratio [HR], 0.17; 95% confidence interval [CI], 0.06–0.46), decreased development of liver-related morbidity and mortality (HR, 0.15; 95% CI, 0.06–0.38) and decreased HCC (HR, 0.19; 95% CI, 0.04–0.80). (Dienstag, 2011) Importantly, persons with advanced liver disease also require long-term follow-up and HCC surveillance regardless of treatment outcome (see **Monitoring Patients who are Starting Hepatitis C Treatment, are on Treatment, or have Completed Therapy**).

Given the clinical complexity and the need for close monitoring, patients with advanced liver disease that has already decompensated (CTP Class B or C [**Methods Table 3**]) should be treated by physicians with experience in treating HCV in conjunction with a liver transplantation center if possible (see Unique Patient Populations: Patients with Decompensated Cirrhosis).

Persons Who Have Undergone Liver Transplantation

In HCV-infected individuals, HCV infection of the liver allograft occurs universally in those with viremia at the time of transplantation. Histologic features of hepatitis develop in about 75% of recipients in the first 6 months following liver transplantation. (Neumann, 2004) By the fifth postoperative year, up to 30% of untreated patients have progressed to cirrhosis. (Neumann, 2004); (Charlton, 1998) A small proportion of patients (4%-7%) develop an accelerated course of liver injury (cholestatic hepatitis C, associated with very high levels of viremia) with subsequent rapid allograft failure. Recurrence of HCV infection posttransplantation is associated with decreased graft survival for recipients with HCV infection compared to recipients who undergo liver transplantation for other indications. (Forman, 2002)

Effective HCV therapy pretransplantation resulting in an SVR (virologic cure) prevents HCV recurrence posttransplantation. (Everson, 2003) In addition, complete HCV viral suppression prior to transplantation prevents recurrent HCV infection of the graft in the majority of cases. (Forns, 2004); (Everson, 2005) Preliminary data from a study of patients with complications of cirrhosis secondary to HCV infection, who were wait-listed for liver transplantation, that included patients with MELD scores up to 14 and CTP scores up to 8 found that treatment with sofosbuvir and weight-based RBV for up to 48 weeks was well tolerated and was associated with an overall posttransplant SVR rate of 70%. (Curry, 2015)

Posttransplant SVR was nearly universal among patients who had undetectable HCV RNA for 28 days or longer prior to transplantation.

Treatment of established HCV infection posttransplantation also yields substantial improvements in patient and in graft survival. (Berenguer, 2008); (Picciotto, 2007) The availability of effective IFN-free HCV treatments has addressed the major hurdles to treating HCV recurrence posttransplantation: poor tolerability and efficacy. In a multicenter, open-label study that evaluated the ability of sofosbuvir plus RBV to induce virologic suppression in 40 patients post–liver transplant with compensated recurrence of HCV infection, daily sofosbuvir and RBV for 24 weeks achieved an SVR at 12 weeks (SVR12) in 70%. (Charlton, 2015) No deaths, graft losses, or episodes of rejection occurred. Six patients had serious adverse events, all of which were considered unrelated to study treatment. There were no drug interactions reported between sofosbuvir and any of the concomitant immunosuppressive agents. In contrast, treatment with sofosbuvir plus RBV with or without PEG-IFN in 64 patients with severe, decompensated cirrhosis resulting from recurrence of HCV infection following liver transplantation was associated with an overall SVR12 rate of 59% and a mortality rate of 13%. (Forns, 2015) On an intent-to-treat basis, treatment was associated with clinical improvement in 57% and stable disease in 22% of patients. Given the clinical complexity including drug interactions and the need for close monitoring, patients with liver transplant should be treated by physicians with experience in treating this population (see Unique Patient Populations: Patients who Develop Recurrent HCV Infection Post-Liver Transplantation).

Persons at Greater Risk for Rapidly Progressive Fibrosis and Cirrhosis

Fibrosis progression is variable across different patient populations as well as within the same individual over time. Many of the components that determine fibrosis progression and development of cirrhosis in an individual are unknown. However, certain factors, such as coinfection with HIV or hepatitis B virus (HBV) and prevalent coexistent liver diseases (eg, nonalcoholic steatohepatitis [NASH]), are well-recognized contributors to accelerated fibrosis progression.

HIV coinfection. HIV coinfection accelerates fibrosis progression among HCV-infected persons, (Benhamou, 1999); (Macias, 2009); (Konerman, 2014) although control of HIV replication and restoration of CD4+ cell counts may mitigate this to some extent. (Benhamou, 2001); (Bräu, 2006) However, antiretroviral therapy is not a substitute for HCV treatment. In the largest paired-biopsy study, 282 HIV/HCV-coinfected patients with 435 paired biopsies were prospectively evaluated; (Konerman, 2014) one-third of patients showed fibrosis progression of at least one Metavir stage at a median of 2.5 years. Importantly, 45% of patients with no fibrosis on initial biopsy had progression. Finally, a more rapid progression to death following decompensation combined with a lack of widespread access to liver transplantation and poor outcomes following transplantation highlight the need for treatment in this population regardless of current fibrosis stage (see Unique Patient Populations: Patients with HIV/HCV Coinfection). (Pineda, 2005); (Merchante, 2006); (Terrault, 2012)

HBV coinfection and other coexistent liver diseases. The prevalence of HBV/HCV coinfection is estimated at 1.4% in the United States and 5% to 10% globally. (Tyson, 2013); (Chu, 2008) Persons with HBV/HCV coinfection and detectable viremia of both viruses are at increased risk for disease progression, decompensated liver disease, and the development of HCC.

HBV/HCV coinfected individuals are susceptible to a process called viral interference wherein one virus may interfere with the replication of the other virus. Thus, when treating one or both viruses with

antiviral drugs, periodic retesting of HBV DNA and HCV RNA levels during and after therapy is prudent, particularly if only one of the viruses is being treated at a time. Treatment of HCV infection in such cases utilizes the same genotype-specific regimens as are recommended for HCV monoinfection **(see Initial Treatment of HCV Infection)**. HBV infections in such cases should be treated as recommended for HBV monoinfection. (Lok, 2009)

Persons with other chronic liver diseases who have coincident chronic HCV infection should be considered for hepatitis C therapy, given the potential for rapid progression of liver disease. An IFN-free regimen is generally preferred for immune-mediated liver diseases such as autoimmune hepatitis, because of the potential for IFN-related exacerbation.

Persons With Extrahepatic Manifestations of Chronic HCV Infection

Severe renal impairment. Chronic hepatitis C is associated with a syndrome of cryoglobulinemia and an immune complex and lymphoproliferative disorder that produces arthralgias, fatigue, palpable purpura, renal disease (eg, membranoproliferative glomerulonephritis), neurologic disease (eg, peripheral neuropathy, central nervous system vasculitis), and reduced complement levels. (Agnello, 1992) Because patients with chronic hepatitis C frequently have laboratory evidence of cryoglobulins (more than 50% in some series), antiviral treatment is imperative for those with the syndrome of cryoglobulinemia and symptoms or objective evidence of end-organ manifestations. IFN-based regimens can produce clinical remission; however, the adverse effects of IFN may mimic manifestations of cryoglobulinemia. (Saadoun, 2014) Although clinical data are not yet available, the use of IFN-free DAA regimens is an attractive option for these patients. Organ-threatening disease (eg, severe neuropathy, renal failure, digital ischemia), in addition to antiviral HCV therapy, should be treated more acutely with immunosuppressive agents or plasmapheresis to clear immune complexes.

Glomerular disease results from deposition of HCV-related immune complexes in the glomeruli. (Johnson, 1993) Successful treatment of HCV using IFN-based regimens can reverse proteinuria and nephrotic syndrome but usually does not fully ameliorate azotemia. (Johnson, 1994) No clinical trial data are yet available on IFN-free regimens, but the high rates of SVR (virologic cure) with antiviral therapy support their use in management of hepatitis C–related renal disease and cryoglobulinemia.

Nonhepatic Manifestations of Chronic HCV Infection

The relationship between chronic hepatitis C and diabetes (most notably type 2 diabetes and insulin resistance) is complex and incompletely understood. The prevalence and incidence of diabetes is increased in the context of hepatitis C. (White, 2008) In the United States, type 2 diabetes occurs more frequently in HCV-infected patients, with a more than 3-fold greater risk in persons older than 40 years. (Mehta, 2000) The positive correlation between quantity of plasma HCV RNA and established markers of insulin resistance confirms this relationship. (Yoneda, 2007) Insulin resistance and type 2 diabetes are independent predictors of a more rapid progression of liver fibrosis and an impaired response to IFN-based therapy. (Petta, 2008) Patients with type 2 diabetes and insulin resistance are also at increased risk for HCC. (Hung, 2010)

Successful antiviral treatment has been associated with improved markers of insulin resistance and greatly reduced incidence of new onset of type 2 diabetes and insulin resistance in HCV-infected patients. (Arase, 2009) Most recently, antiviral therapy for HCV infection has been shown to improve clinical outcomes related to diabetes. In a large prospective cohort from Taiwan, the incidence rates of end-stage renal disease, ischemic stroke, and acute coronary syndrome were greatly reduced in HCV-

infected patients with diabetes who received antiviral therapy compared with untreated, matched controls. (Hsu, 2014) Therefore, antiviral therapy may prevent progression to diabetes in patients with prediabetes who have hepatitis C and may reduce renal and cardiovascular complications in patients with established diabetes who have hepatitis C.

In patients with chronic hepatitis C, fatigue is the most frequently reported symptom and has a major effect on quality of life and activity level evidenced by numerous measures of impaired quality of life. (Foster, 1998) The presence and severity of fatigue appears to correlate poorly with disease activity, although it may be more common and severe in HCV-infected individuals with cirrhosis. (Poynard, 2002a) Despite difficulties in separating fatigue symptoms associated with hepatitis C from those associated with other concurrent conditions (eg, anemia, depression), numerous studies have reported a reduction in fatigue after cure of HCV infection. (Bonkovsky, 2007) In the Virahep-C study, 401 patients with HCV infection were evaluated for fatigue prior to and after treatment, using validated scales to assess the presence and severity of fatigue. (Sarkar, 2012) At baseline, 52% of patients reported having fatigue, which was more frequent and severe in patients with cirrhosis than in those without cirrhosis. Achieving an SVR was associated with a substantial decrease in frequency and severity of fatigue. A recent analysis of 413 patients from the NEUTRINO and FUSION trials who were treated with a sofosbuvir-containing regimen and who achieved an SVR12 demonstrated improvement in patient fatigue (present in 12%) from the pretreatment level. (Younossi, 2014) After achieving an SVR12, participants had marked improvements in fatigue over their pretreatment scores measured by 3 separate validated questionnaires. Additional studies support and extend these findings beyond fatigue, with improvements in overall health-related quality of life and work productivity observed following successful HCV therapy.(Gerber, 2015); (Younossi, 2015b); (Younossi, 2015c); (Younossi, 2015d)

The reported prevalence of HCV infection in patients with porphyria cutanea tarda approximates 50% and occurs disproportionately in those with cirrhosis. (Gisbert, 2003) The treatment of choice for active porphyria cutanea tarda is iron reduction by phlebotomy and maintenance of a mildly iron-reduced state without anemia. However, although improvement of porphyria cutanea tarda during HCV treatment with IFN has frequently been described (Takikawa, 1995), there are currently insufficient data to determine whether treating HCV infection with DAAs and achievement of SVR improve porphyria cutanea tarda.

Lichen planus is characterized by pruritic papules involving mucous membranes, hair, and nails. Antibodies to HCV are present in 10% to 40% of patients with lichen planus, but a causal link with chronic infection is not established. Resolution of lichen planus has been reported with IFN-based regimens, but there have also been reports of exacerbation of lichen planus with these treatments. Although it is unknown whether DAAs will have more success against lichen planus, treatment with IFN-free regimens would appear to be a more advisable approach to addressing this disorder. (Gumber, 1995)

Benefit of Treatment to Reduce Transmission

Persons who have successfully achieved an SVR (virologic cure) no longer transmit the virus to others. As such, successful treatment of HCV infection benefits public health. Several health models have shown that even modest increases in successful treatment of HCV infection among persons who inject drugs can decrease prevalence and incidence. (Martin, 2013a); (Durier, 2012); (Martin, 2013b); (Hellard, 2012) Models developed to estimate the impact of HCV testing and treatment on the burden of hepatitis C at a country level reveal that large decreases in HCV prevalence and incidence are possible as more persons are successfully treated. (Wedemeyer, 2014) There are also benefits to eradicating HCV infection between couples and among families, and thus eliminating the perception that an individual might be

contagious. In addition, mother-to-child transmission of HCV does not occur if the woman is not viremic, providing an additional benefit of curing a woman before she becomes pregnant. (Thomas, 1998) However, the safety and efficacy of treating women who are already pregnant to prevent transmission to the fetus have not yet been established, and thus treatment is not recommended for pregnant women.

The Society for Healthcare Epidemiology of America (SHEA) advises that health-care workers who have substantial HCV viral replication (≥104 genome equivalents/mL) be restricted from performing procedures that are prone to exposure (Henderson, 2010) and that all health-care workers with confirmed chronic HCV infection should be treated. For reasons already stated above, the achievement of an SVR in such individuals will not only eliminate the risk of HCV transmission to patients but also decrease circumstantial loss of experienced clinicians. Given concerns about underreporting of infection and transmission (Henderson, 2010), the availability of effective, all-oral regimens should lead to greater willingness on the part of exposure-prone clinicians to be tested and treated.

Successful treatment of HCV-infected persons at greatest risk for transmission represents a formidable tool to help stop HCV transmission in those who continue to engage in high-risk behaviors. To guide implementation of hepatitis C treatment as a prevention strategy, studies are needed to define the best candidates for treatment to stop transmission, the additional interventions needed to maximize the benefits of HCV treatment (eg, preventing reinfection), and the cost-effectiveness of the strategies when used in target populations.

Persons who inject drugs. Injection drug use (IDU) is the most common risk factor for HCV infection in the United States and Europe, with an HCV seroprevalence of 10% to 70%; (Amon, 2008); (Nelson, 2011) IDU also accounts for the majority of new HCV infections (approximately 70%) and is the key driving force in the perpetuation of the epidemic. Given these facts and the absence of an effective vaccine against HCV, testing and linkage to care combined with treatment of HCV infection with potent IFN-free regimens has the potential to dramatically decrease HCV incidence and prevalence. (Martin, 2013b) However, treatment-based strategies to prevent HCV transmission have yet to be studied, including how to integrate hepatitis C treatment with other risk-reduction strategies (eg, opiate substitution therapy, needle and syringe exchange programs). (Martin, 2013a)

In studies of IFN-containing treatments in persons who inject drugs, adherence and efficacy rates are comparable to those of patients who do not use injection drugs. A recent meta-analysis of treatment with PEG-IFN with or without RBV in active or recent injection drug users showed SVR rates of 37% and 67% for HCV genotype 1 or 4 and 2 or 3, respectively. (Aspinall, 2013) As shorter, better-tolerated, and more efficacious IFN-free therapies are introduced, these SVR rates are expected to improve. Importantly, the rate of reinfection in this population is lower (2.4/100 person-years of observation) than that of incident infection in the general population of injection drug users (6.1-27.2/100 person-years), although reinfection increases with active or ongoing IDU (6.44/100 person-years) and available data on follow-up duration are limited. (Aspinall, 2013); (Grady, 2013)

Ideally, treatment of HCV-infected persons who inject drugs should be delivered in a multidisciplinary care setting with services to reduce the risk of reinfection and for management of the common social and psychiatric comorbidities in this population. Regardless of the treatment setting, recent and active IDU should not be seen as an absolute contraindication to HCV therapy. There is strong evidence from various settings in which persons who inject drugs have demonstrated adherence to treatment and low rates of reinfection, countering arguments that have been commonly used to limit access to this patient population. (Aspinall, 2013); (Hellard, 2014); (Grebely, 2011) Indeed, combining HCV treatment with

needle exchange and opioid agonist therapy programs in this population with a high prevalence of HCV infection has shown great value in decreasing the burden of HCV disease. Elegant modeling studies illustrate the high return on the modest investment of addressing this often-ignored segment of the HCV-infected population. (Martin, 2013b) These conclusions were drawn before the introduction of the latest DAA regimens. Conversely, there are no data to support the utility of pretreatment screening for illicit drug or alcohol use in identifying a population more likely to successfully complete HCV therapy. These requirements should be abandoned, because they create barriers to treatment, add unnecessary cost and effort, and potentially exclude populations that are likely to obtain substantial benefit from therapy. Scale up of HCV treatment in persons who inject drugs is necessary to positively impact the HCV epidemic in the United States and globally.

HIV-infected men who have sex with men (MSM) who engage in high-risk sexual practices. Over the past decade, a dramatic increase in incident HCV infections among HIV-infected MSM who did not report IDU as a risk factor has been demonstrated in several US cities. (van de Laar, 2010) Recognition and treatment of HCV infection (including acute infection) in this population may represent an important step in preventing subsequent infections. As with persons who inject drugs, HIV/HCV-coinfected MSM who engage in ongoing high-risk sexual practices should be treated for their HCV infection in conjunction with continued education on risk-reduction strategies. In particular, safer-sex strategies should be emphasized given the high rates of reinfection after SVR, which may approach 30% over 2 years, in HIV-infected MSM with acute HCV infection. (Lambers, 2011)

Incarcerated persons. Among incarcerated individuals, the rate of HCV seroprevalence ranges from 30% to 60% (Post, 2013) and the rate of acute infection is approximately 1%. (Larney, 2013) Screening for HCV infection is relatively uncommon in state prison systems. Treatment uptake has been limited in part because of the toxic effects and long treatment duration of older IFN-based therapies as well as concerns about cost. (Spaulding, 2006) In particular, truncation of HCV treatment owing to release from prison has been cited as a major limitation to widespread, effective HCV treatment in correctional facilities. (Post, 2013); (Chew, 2009) Shorter (12- to 24-week) HCV therapies reduce duration of stay-related barriers to HCV treatment in prisons. Likewise, the improved safety of newer, all-oral regimens diminishes concerns of toxic effects. Coordinated treatment efforts within prison systems would likely rapidly decrease the prevalence of HCV infection in this at-risk population, although research is needed in this area.

Persons on hemodialysis. The prevalence rate of HCV infection is markedly elevated in persons on hemodialysis and ranged from 2.6% to 22.9% in a large multinational study. (Fissell, 2004) Studies in the United States found a similarly elevated prevalence rate of 7.8% to 8.9%. (Centers for Disease Control and Prevention, 2001); (Finelli, 2005) Importantly, the seroprevalence of HCV was found to increase with time on dialysis, suggesting that nosocomial transmission, among other risk factors, plays a role in HCV acquisition in these patients. (Fissell, 2004) Improved education and strict adherence to universal precautions can drastically reduce nosocomial HCV transmission risks for persons on hemodialysis, (Jadoul, 1998) but clearance of HCV viremia through treatment-induced SVR eliminates the potential for transmission.

HCV-infected persons on hemodialysis have a decreased quality of life and increased mortality compared with uninfected persons on hemodialysis. (Fabrizi, 2002); (Fabrizi, 2007); (Fabrizi, 2009) HCV infection in this population also has a deleterious impact on kidney transplantation outcomes with decreased patient and graft survival. (Fabrizi, 2014) The increased risk for nosocomial transmission and the substantial clinical impact of HCV infection in those on hemodialysis are compelling arguments for HCV therapy as

effective antiviral regimens that can be used in persons with advanced renal failure become available (see Unique Patient Populations: Patients with Renal Impairment).

Populations Unlikely to Benefit From HCV Treatment

Patients with a limited life expectancy that cannot be remediated by treating HCV, by transplantation, or by other directed therapy do not require treatment. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert. Chronic hepatitis C is associated with a wide range of comorbid conditions. (Butt, 2011); (Louie, 2012) Little evidence exists to support initiation of HCV treatment in patients with limited life expectancy (less than 12 months) owing to non–liver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized and palliative care strategies should take precedence. (Holmes, 2006); (Maddison, 2011)

Recommendations for Pretreatment Assessment

- **Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening). (see HCV Testing and Linkage to Care)**
  Rating: Class I, Level A

An accurate assessment of fibrosis remains vital, as degree of hepatic fibrosis is one of the most robust prognostic factors used to predict HCV disease progression and clinical outcomes. (Everhart, 2010) Individuals with severe fibrosis require surveillance monitoring for liver cancer, esophageal varices, and hepatic function. (Garcia-Tsao, 2007); (Bruix, 2011) In some instances, the recommended duration of treatment is also longer.

Although liver biopsy is the diagnostic standard, sampling error and observer variability limit test performance, particularly when inadequate sampling occurs. Up to one-third of bilobar biopsies had a difference of at least 1 stage between the lobes. (Bedossa, 2003) In addition, the test is invasive and minor complications are common, limiting patient and practitioner acceptance. Serious complications such as bleeding, although rare, are well recognized.

Noninvasive tests to stage the degree of fibrosis in patients with chronic HCV infection include models incorporating indirect serum biomarkers (routine tests), direct serum biomarkers (components of the extracellular matrix produced by activated hepatic stellate cells), and vibration-controlled transient liver elastography. No single method is recognized to have high accuracy alone and each test must be interpreted carefully. A recent publication of the Agency for Healthcare Research and Quality found evidence in support of a number of blood tests; however, at best, they are only moderately useful for identifying clinically significant fibrosis or cirrhosis. (Selph, 2014)

Vibration-controlled transient liver elastography is a noninvasive way to measure liver stiffness and correlates well with measurement of substantial fibrosis or cirrhosis in patients with chronic HCV infection. The measurement range does overlap between stages. (Ziol, 2005); (Afdhal, 2015); (Castera, 2005)

The most efficient approach to fibrosis assessment is to combine direct biomarkers and vibration-controlled transient liver elastography. (Boursier, 2012); (European Association for the Study of the Liver and Asociacion Latinoamericana para el Estudio del Higado, 2015) A biopsy should be considered for any patient who has discordant results between the 2 modalities that would affect clinical decision making. For example, one shows cirrhosis and the other does not. The need for liver biopsy with this approach is markedly reduced.

Alternatively, if direct biomarkers or vibration-controlled transient liver elastography are not available, the AST-to-platelet ratio index (APRI) or FIB-4 index score can help, (Sebastiani, 2009); (Castera, 2010); (Chou, 2013b) although neither test is sensitive enough to rule out substantial fibrosis. (Chou, 2013b) Biopsy should be considered in those in whom more accurate fibrosis staging would impact treatment decisions. Individuals with clinically evident cirrhosis do not require additional staging (biopsy or noninvasive assessment).

Recommendations for Repeat Liver Disease Assessment

- **Ongoing assessment of liver disease is recommended for persons in whom therapy is deferred.**
  Rating: Class I, Level C

When therapy is deferred, it is especially important to monitor liver disease in these patients. In line with evidence-driven recommendations for treatment of nearly all HCV-infected patients, several factors must be taken into consideration if treatment deferral is entertained or mandated by lack of medication access. As noted, strong and accumulating evidence argue against deferral because of decreased all-cause morbidity and mortality, prevention of onward transmission, and quality-of-life improvements for patients treated regardless of baseline fibrosis. Additionally, treatment of HCV infection may improve or prevent extraheptatic complications, including diabetes mellitus, cardiovascular disease, renal disease, and B-cell non-Hodgkin lymphoma, (Conjeevaram, 2011); (Hsu, 2015); (Torres, 2015) which are not tied to fibrosis stage. (Allison, 2015); (Petta, 2015) Deferral practices based on fibrosis stage alone are inadequate and shortsighted.

Fibrosis progression varies markedly between individuals based on host, environmental, and viral factors (**Table 1**). (Feld, 2006) Fibrosis may not progress linearly. Some individuals (often those aged ≥50 years) may progress slowly for many years followed by an acceleration of fibrosis progression. Others may never develop substantial liver fibrosis despite longstanding infection. The presence of existing fibrosis is a strong risk factor for future fibrosis progression. Fibrosis results from chronic hepatic necroinflammation, and thus a higher activity grade on liver biopsy and higher serum transaminase values are associated with more rapid fibrosis progression. (Ghany, 2003) However, even patients with normal ALT levels may develop substantial liver fibrosis over time. (Pradat, 2002); (Nutt, 2000) The limitations of transient elastography and liver biopsy in ascertaining the progression of fibrosis must be recognized.

Host factors associated with more rapid fibrosis progression include male sex, longer duration of infection, and older age at the time of infection. (Poynard, 2001) Many patients have concomitant nonalcoholic fatty liver disease, and the presence of hepatic steatosis with or without steatohepatitis on liver biopsy, elevated body mass index, insulin resistance, and iron overload are associated with fibrosis

progression. (Konerman, 2014); (Everhart, 2009) Chronic alcohol use is an important risk factor because alcohol consumption has been associated with more rapid fibrosis progression. (Feld, 2006) A safe amount of alcohol consumption has not been established. Cigarette smoking may also lead to more rapid fibrosis progression. For more counseling recommendations, please see Testing and Linkage to Care.

Immunosuppression leads to more rapid fibrosis progression, particularly HIV/HCV coinfection and solid organ transplantation. (Macias, 2009); (Konerman, 2014); (Berenguer, 2013) Therefore, immunocompromised patients should be treated even if they have mild liver fibrosis at presentation.

Level of HCV RNA does not correlate with stage of disease (degree of inflammation or fibrosis). Available data suggest that fibrosis progression occurs most rapidly in patients with HCV genotype 3 infection. (Kanwal, 2014); (Bochud, 2009) Aside from coinfection with HBV or HIV, no other viral factors are consistently associated with disease progression.

Although an ideal interval for assessment has not been established, annual evaluation is appropriate to discuss modifiable risk factors and to update testing for hepatic function and markers for disease progression. For all individuals with advanced fibrosis, liver cancer screening dictates a minimum of evaluation every 6 months.

When and in Whom to Initiate HCV Therapy Table 1. Factors Associated With Accelerated Fibrosis Progression

Host	Viral
Nonmodifiable	HCV genotype 3
Fibrosis stage	Coinfection with hepatitis B virus or HIV
Inflammation grade	
Older age at time of infection	
Male sex	
Organ transplant	
Modifiable	
Alcohol consumption	
Nonalcoholic fatty liver disease	
Obesity	
Insulin resistance	

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The Management of Hepatitis C Treatment in Massachusetts State Correctional Facilities

An Update and Analysis of the Current HCV Database

A Major Qualifying Project Report submitted to the faculty of
WORCESTER POLYTECHNIC INSTITUTE
in partial fulfillment of the requirements for the Degree of Bachelor of Science

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Abstract

In 2004, a database was implemented to assess the treatment of inmates infected with hepatitis C in Massachusetts state correctional facilities. The purpose of this project was to update the database and examine the current treatment system. Inmate demographics, treatment success, and viral characteristics were assessed and analyzed for potential correlations. Recommendations to improve the database included focusing on the collection of missing data, namely the inmate's history of substance abuse and health conditions and follow up viral load measures.

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What is Hepatitis C?

By definition, hepatitis is an "inflammation of the liver" (Merriam-Webster Incorporated, 2006). It is a gastroenterological disease that results in damage to the liver cells, and depending on the severity, may even destroy them. There are a number of different types of hepatitis which can be caused by a variety of factors including other illnesses or diseases, noninfectious substances such as drugs, alcohol, or toxic chemicals, and infectious agents such as viruses or parasites (Encyclopedia Britannica, Inc., 2007). In the most common cases, hepatitis is the result of a viral infection.

Hepatitis C is one of six currently identified types of viral hepatitis (A, B, C, D, E, and G). It has become a major health concern in the United States, today, is one of the leading causes of liver disease, and a major reason for liver transplants (Jetter, 2005). True to its name, hepatitis C is a blood borne disease of the liver caused by the hepatitis C virus (HCV), a single-stranded RNA virus of the family Flaviviridae. HCV can be categorized into six major genotypes and more than 50 subtypes. Genotypes range in geographic distribution and response to treatment, but show little difference in the severity of the disease or outcome. The most common genotypes in the US are 1a and 1b, which account for over 70% of the cases (National Digestive Diseases Information Clearinghouse [NDDIC], 2006).

Characteristic of a blood borne infection, HCV is carried through the blood and transmitted primarily via contact with infected blood and blood products (NDDIC, 2006). Major risk factors associated with the transmission of HCV include blood transfusions and transplants, injection or use of illegal drugs, occupational exposure (i.e. healthcare workers), high risk sexual behavior with an infected partner, and non-sterile instrument use for tattoos or body piercing (Centers for Disease Control and Prevention [CDC], 1998). HCV may not be transmitted through casual contact with an infected person and is rarely acquired through maternal-infant transmission or household contact with infected blood or fluids. At present, injection drug use is the most common form of HCV transmission in the United States (NDDIC, 2006).

Types and Symptoms

Hepatitis C is typically categorized into one of two stages: acute hepatitis C or chronic hepatitis C. Each stage refers to the current progression of the viral infection and depends upon the length of infection time and the severity of the disease. In either case, HCV poses a potential number of dangers to the liver.

Acute hepatitis C is used to describe the first six months of infection, during which the liver is first attacked by HCV, liver inflammation initiates, and liver enzyme levels begin to rise. Persons with acute infections are usually asymptomatic and unaware of the virus they are carrying. Those who do develop symptoms exhibit mild, non-specific flu-like signs such as fatigue, sore muscles, headaches, nausea, and loss of appetite, and in some cases, may also acquire jaundice (Jetter, 2005). These symptoms usually do not develop until 6-7 weeks after infection and are often mistaken for other medical conditions or disappear before raising any serious concern. According to studies and organizations such as the National Institute of Diabetes and Digestive and Kidney Diseases, between 75% and 85% of those with acute hepatitis C will eventually progress

into a more severe, long-term chronic form of hepatitis C due to a lack of treatment or failure to respond to treatment within the first six months (CDC, 1998).

Chronic hepatitis C is defined as an HCV infection that has progressed beyond six months. It the most commonly diagnosed form of hepatitis C and is a major cause of cirrhosis, liver failure, and liver cancer (Liang, Rehermann, Seef, & Hoofnagle, 2000). Depending upon the severity of the infection, chronic hepatitis C varies greatly among patients in its course and outcome. For instance, those with mild chronic hepatitis C typically have no signs or symptoms of liver disease and exhibit rather minor damage to the liver. On the other hand, those patients with severe chronic hepatitis C demonstrate high levels of HCV virus in the blood, elevated liver enzyme levels (indicating liver disease), severe physical damage to the liver, and more specific symptoms such as muscle weakness, weight loss, itching, dark urine, fluid retention, and abdominal swelling. The majority of these patients will ultimately develop cirrhosis and end-stage liver disease. For the many patients who fall in the middle of the spectrum, chronic HCV infection is characterized by mild to moderate elevations in liver enzymes and few or no symptoms. In 1-2% of patients, chronic hepatitis C can cause complications outside the liver known as extrahepatic manifestations. These may include such conditions as cyroglobulinemia, glomerulonephritis, and porphyria cutanea tarda (NDDIC, 2006).

Despite the potential dangers of HCV infection, hepatitis C lies dormant in most patients for years. Statistics have shown that as many as 70% of those infected with HCV are unaware of the virus and more than half show no signs or symptoms of HCV infection. (Jetter, 2005; Henkel, 1999) In fact, hepatitis C is frequently not recognized until infected individuals undergo blood-donor screenings that are positive for HCV or routine physical exams that show elevated liver enzyme levels (CDC, 1998).

Testing and Diagnosis

Persons suspected to have an HCV infection must undergo a number of blood tests before they can be diagnosed with hepatitis C. Blood tests range in specificity and are designed to test for indicators of an HCV infection, HCV antibodies, and the HCV virus itself.

One of the most frequent indicators of a potential HCV infection is elevated levels of liver enzymes, or more specifically, alanine aminotransferase (ALT). Most people infected with HCV exhibit elevated levels of liver enzymes, such as ALT, on a routine blood test within 50 days of exposure (Jetter, 2005). Although not all infected patients show signs of alteration in their ALT levels, persistently abnormal levels of ALT are fair indicators that an infection may be present and that further tests should be conducted. ALT tests are not designed to confirm HCV infection, but are rather a nonspecific means of initially screening for infection (Herrine, 2002).

To determine whether or not an HCV infection is actually present, individuals are screened for the presence of HCV antibodies (anti-HCV) using a series of U.S. Food and Drug Administration (FDA) approved diagnostic tests (CDC, 1998). Anti-HCV is usually present in the blood of infected individuals within one month of exposure to the virus (NDDIC, 2006). If hepatitis C is suspected based on symptoms and/or ALT levels, an enzyme immunoassay (EIA) is first conducted and then later confirmed by a supplementary recombinant immunoblot assay (RIBA), a western blot specific for anti-HCV. Two positive results indicate an HCV infection, while two negative results

indicate no infection. Indeterminate results are usually indicative of a recently infected person, a person with chronic HCV, or poor testing. Anti-HCV test results do not characterize the type of hepatitis C or distinguish between patients with an acute, chronic, or recently treated infection (CDC, 1998).

In most patients, hepatitis C viral RNA can be detected within one to two weeks of HCV infection, long before the presence of anti-HCV or elevated ALT levels (CDC, 1998). As further confirmation of an active HCV infection, qualitative and quantitative assays can be done to detect the presence or absence of HCV RNA. Qualitative assays, such as the polymerase chain reaction (PCR) and transcription-mediated amplification (TMA) are usually done to determine whether or not HCV RNA is present in the serum. Quantitative assays, on the other hand, are conducted as indirect assessments of the amount of HCV RNA present in the blood. These viral loads determined by assays such as quantitative RT-PCR and branched DNA signal amplification do not directly correlate with the severity of hepatitis C, but are a good indication of the likelihood of a response to antiviral therapy (NDDIC, 2006).

In the majority of cases, elevated ALT levels and the presence of anti-HCV in the blood serum is enough to diagnose an individual with hepatitis C. Additional testing is typically done to either confirm the diagnosis or characterize the infection in preparation for treatment. Genotyping and liver biopsies are common examples of characterization tests performed to determine the genotype of the hepatitis C virus and the severity of the infection, respectively. Tests, like these, are good indicators of how a patient will respond to different treatments and which treatment will work best (NDDIC, 2006). Some states have also found these tests, particularly the liver biopsy, to be cost effective. In 2004, the Virginia Department of Corrections offered all inmates who tested positive for HCV RNA the opportunity to get a liver biopsy. This approach allowed physicians to avoid unnecessary treatment by treating only those inmates in the advanced state of the disease. It was estimated that liver biopsies saved almost $125,000 per 100 patients (Sterling, 2003).

Treatment

Presently, there is no cure or vaccine for hepatitis C. Like most viruses that cause chronic conditions, HCV RNA mutates very rapidly inside the human body. HCV infection elicits some response from the immune system early on, but constant mutations essentially allow the virus to evade the immune system over time and inhibit the development of preventative drugs (NDDIC, 2006). Consequently, the only options available for patients today are moderately successful treatments aimed at the elimination of detectable virus in the blood serum. Success of treatment is usually measured in terms of sustained virologic response, which can be defined as "the absence of HCV RNA in the serum during therapy and six months after completion of therapy" (Herrine, 2002).

Effective treatment for hepatitis C first began over 10 years ago, when alpha interferon was approved for treatment of non-A and non-B hepatitis in 1991 (Herrine, 2002). Treatment required that the antiviral protein be injected subcutaneously at least three times a week for approximately 12 months. Initial results indicated normalized ALT levels and a loss of detectable HCV RNA in the serum of most patients by the end of the therapy. However, long term studies of treatment with alpha interferon have

demonstrated a high relapse rate among patients and sustained viral response rates of only 15%-25% (CDC, 1998).

Current treatment therapies have replaced alpha interferon with pegylated interferon (peginterferon), a more successful recombinant form of the original protein. Chemical modification of alpha interferon by the addition of polyethylene glycol has improved the uptake, distribution, and excretion of interferon, and increased active inhibition of HCV. Like alpha interferon, peginterferon must be injected subcutaneously. Chemical improvements, however, have reduced the treatment requirements from injections three times a week to only once a week for approximately 48 weeks. Studies have shown an overall increase in sustained viral response rates with peginterferon monotherapy to approximately 35% (NDDIC, 2006).

In 1998, hepatitis C treatment was further enhanced when the FDA approved the combination of interferon and ribavirin as treatment for patients with chronic hepatitis C (Herrine, 2002). Ribavirin is an antiviral agent that is usually taken orally two times a day. It has little effect on HCV by itself, but in combination with interferon, can lower relapse rates, increase sustained viral response rates to as high as 55%, and has been shown to rapidly lower ALT levels and eliminate detectable HCV RNA in up to 70% of patients (NDDIC, 2006). Combination therapy, as it is most often referred to, has become today's standard form of hepatitis C treatment. Unless specific factors prevent the use of ribavirin, combination therapy will be applied over interferon monotherapy in all present cases (Ward and Kugelmas, 2005).

Despite the advances made over the past decade, problems continue to hinder the success of hepatitis C treatment. One of the biggest problems facing patients today is cost. On average, treatment costs approximately $20,000-$30,000 per year for the medication alone (Ward and Kugelmas, 2005). Although treatment is necessary for the management of hepatitis C in most cases, the expense of therapy often prevents individuals from pursing treatment. For those who receive treatment, medication poses the potential for side effects that can result in reduced medication dosages or an overall discontinuation of treatment. Common side effects of alpha and pegylated interferon include fatigue, muscle aches, headaches, depression, mild bone marrow suppression, and other related problems. Side effects range from mild to moderate in severity and usually diminish following the first few weeks of treatment. Common side effects of ribavirin, on the other hand, include anemia, fatigue, irritability, itching, birth defects, nasal stuffiness, sinusitis, and cough. Ribavirin is not advised for women who are pregnant or likely to become pregnant or for patients with blood related problems. Less than 2% of patients exhibit side effects uncharacteristic of interferon or ribavirin (NDDIC, 2006).

Because of the problems associated with hepatitis C therapy, treatment is not recommended for all patients. In fact, treatment is only highly recommended for chronic hepatitis C patients who have persistently elevated ALT levels, detectable HCV RNA, and a liver biopsy indicating severe inflammation or damage to the liver. These patients are considered to be at a greater risk for progression, and consequently, require treatment in order to survive. All other patients, including those with persistently normal ALT levels, advanced cirrhosis, alcohol or drug abuse problems, or contraindications such as depression, hyperthyroidism, life-threatening complications, or evidence of pregnancy, are not recommended for treatment and must receive medical clearance before beginning any such therapy (CDC, 1998).

Epidemiology

In 2000, the United States Surgeon General declared hepatitis C a "silent epidemic." With approximately 2% of the U.S. adult population infected, this appropriate declaration stems from the fact that hepatitis C is the most common chronic blood borne infection in the United States (Kim, 2002). Many of these infections will go undetected for years because victims display little to no symptoms during the early onset stages of the disease (CDC, 1998). Disease progression varies amongst individuals and depends on factors such as co-infection with other diseases, age, and alcohol/substance abuse patterns. Of those infected with the virus, up to 80% will develop chronic hepatitis and as much as 20% will progress into cirrhosis of the liver (Munoz-Plaza, et al., 2005).

Since the hepatitis C virus was only identified in the early 1990's, accurate and reliable estimates of HCV infections and mortality rates in the United States are limited. Also, many patients with acute hepatitis are asymptomatic and, therefore, are never diagnosed. Additionally, some infected individuals may not have access to medical care, a factor which also contributes to the under-reporting of hepatitis C infection. These challenges make it very difficult to assess the true incidence of infection (Munoz-Plaza, et al., 2005).

As the identification and awareness of hepatitis C has led to an expanding movement of education, means of prevention, and enhanced testing efforts among injection drug users and blood donors, it is safe to predict that the incidence of HCV infection should begin to decline. In fact, the number of people with transfusion-associated HCV infection has already decreased significantly after the 1985 guidelines for selecting safer blood donors was implemented. Similarly, an effective system for screening blood for hepatitis C via HCV antibodies began in 1989, a step forward in the prevention of this epidemic. Moreover, the occurrence of safer needle-using practices among injection drug users has increased due to HIV and HCV awareness programs (Kim, 2002).

Unfortunately, the decrease in incidence of infection is not necessarily correlated with a decrease in the frequency of individuals infected with the virus. In fact, it is predicted that the prevalence of hepatitis C will increase over the years. This is due to the fact that many people who have already been infected are asymptomatic and have not yet been reported. There is often a significant lag time between the time of infection and the symptomatic manifestation of liver disease. In fact, some people will not develop symptoms for up to 20 years or more. As a result of this duration, the Center for Disease Control and Prevention predicts a four fold increase in the number of people reported to be chronically infected between 1990 and 2015 (Kim, 2002).

Similar to the underestimations of HCV infections, the mortality projections due to HCV are undoubtedly misrepresented. Most deaths caused from hepatitis C infection are due to liver failure and chronic liver disease. However, mortality statistics are based on the "underlying cause of death". Therefore, in many cases, the U.S. system of death designation will list liver failure rather than hepatitis C as cause of death, even if the liver failure was caused by hepatitis C. In an attempt to estimate the number of deaths attributed to hepatitis C, the amount of in-hospital deaths from liver disease related to HCV was reviewed from the Healthcare Utilization Project database. In 1998, approximately 4,500 people died in hospitals in the U.S. from HCV-related liver disease (CDC, 2007).

The largest range of recorded data was used in the third National Health and Nutrition Examination Survey (NHANES) to estimate the overall prevalence of HCV in the United States. In this survey, 21,000 non-institutionalized citizens were tested for HCV antibodies as well as viral HCV RNA in serum. Percentages from of this pool of data were collected and projected onto the United States population. According to the results of the NHANES, 3.9 million U.S. civilians were infected with HCV and 2.7 million of those infected suffered from chronic infection. Demographic disparities in the results indicated that infection was more prevalent in the age range of 30 to 49 years old: men were 20% more likely to be infected than women. The disease was most common in non-Hispanic blacks and least common in non-Hispanic whites. Only 1.5% of non-Hispanic whites had HCV whereas 3.2% of non-Hispanic blacks had HCV (Kim, 2002).

Studies also suggest that individuals who suffer from severe mental illness are at a substantially higher risk for contracting blood-borne diseases such as HCV. For example, a particular study which focused on the occurrence of HCV among psychiatric patients had found that up to 19.6% of the 931 patients tested positive for HCV; this incidence rate is about 11 times higher than that of the rate of the normal adult population (Rosenberg, et al., 2001). This pattern of infection among psychiatric patients is most likely due to the high occurrence of drug use among the depressed and mentally ill populations.

Because syringe sharing and injection drug use is the major cause of HCV transmission and infection, the prevalence of HCV infection is extremely high among injection drug users. Several seroprevalence studies have shown that HCV infection occurs in up to 90% of injection drug users (Patrick, Buxton, Bigham & Mathias, 2000). When users were tested in some methadone maintenance treatment centers, as much as 96% were seropositive for HCV antibody while 62% were positive for HCV RNA (McCarthy & Flynn, 2001).

HCV in Correctional Facilities

About 85% of HCV infected inmates who were entering a Massachusetts prison reported a history of hepatitis, needle-sharing and previous drug use. Research studies have found that many inmates either begin or continue to engage in injection drug use during incarceration (Munoz-Plaza, et al., 2005). Since syringes tend to be more frequently used by many inmates in prison, the risk for sharing needles and needle syringe contamination is much higher than the outside world (Muller et al., 1995). As a result, HCV infection is relatively elevated among correctional populations.

Because injection drug users represent a dominant subpopulation in correctional facilities, a large percentage of HCV infected persons will inhabit or pass through prisons. According to surveys from the Bureau of Justice Statistics, the average length of a prison stay is approximately two-three years. One of the most recent in-depth studies was performed in 1997. It was deduced that between 29% and 43% of HCV infected people in the U.S. are released from a correctional facility in a given year (Hammett, Harmon & Rhodes, 2002). Since limited factual data is available on HCV infections, an indirect method was used to produce a rough estimate of HCV infection in prison populations. The logic of this study used the CDC's estimate of 72% to 86% of injection drug users are infected with HCV. The estimate of 24% of prison inmates with history of injection drug use was multiplied by 72% and 86% to yield an approximation that 17% to

21% of prison inmates are infected with HCV (Munoz-Plaza, et al., 2005). Furthermore, in 1997, a statistical analysis of this study produced an estimation of 1.3 to 1.9 million releases from prison had HCV; this implies that 29% to 43% of people with HCV infection have passed through a correctional facility in one year (Hammett, Harmon & Rhodes, 2002).

Despite the fact that such a large proportion of Americans with hepatitis C pass through a correctional facility, there is no national data on HCV incidence among inmates. Similarly, there is scarcely any data associating risk behaviors in prison with HCV contraction. This deficit in factual and statistical information contributes to the absence of a standardized system of health care and treatment programs in correctional settings. The collection of more data in prisons nationwide would allow for the better understanding of hepatitis C prevalence as well as the effectiveness of treatment; this would also help alleviate the controversies and challenges which have stood in the way of establishing national guidelines and recommendations for the management of this epidemic. Perhaps the establishment of a central database such as those used for cancer and HIV registries would enhance the progress of HCV intervention strategies (Allen, 2003).

Because of the growing frequency of HCV infections among incarcerated populations, the National Institute of Health (NIH) and the Center for Disease Control and Prevention have recognized the importance of improving HCV interventions in correctional facilities. Specifically, the 2002 NIH consensus statement supported a more aggressive approach to treatment compared with the 1997 statement (Hammett, 2003). It has seemed to become apparent to these organizations that the period of incarceration provides a window of opportunity to diagnose, evaluate and treat those at risk for severe health problems caused by hepatitis C. At the least, the development of a systemic screening program would identify those infected and those at risk in an attempt to reduce contraction during incarceration (Allen, 2003).

The prospect for the establishment of prevention, education and treatment programs in prisons does seem ideal considering that such a large percentage of people infected with HCV are in a confined setting. As a majority of inmates are only temporarily imprisoned and serve an average sentence of two to three years, healthcare addressing HCV would not only benefit the health of the inmates but the safety and health of the friends, families and communities to which the released prisoners return. Additionally, prison administrators and authorities are legally obligated to administer a satisfactory degree of healthcare, which treatment programs could potentially provide. A lack of interventions may leave prisons susceptible to lawsuits and criticism for neglecting the welfare of their inmates as well as the communities to which a majority of them are returned. For example, lawsuits have taken place in New Jersey when prisoners became aware of HCV programs in Pennsylvania prisons which dwarfed the comparable programs available in New Jersey facilities (Hammett, 2003).

As this issue remains a fairly new one, only a handful of prison systems have incorporated an HCV intervention program into their health management systems; among them are the Federal Bureau of Prisons, and facilities in Pennsylvania, Rhode Island, Wisconsin, Massachusetts and Indiana. (Hammett, 2003).

Management Strategies for Correctional Settings

There are many components involved in the establishment of an efficient and productive HCV treatment system in correctional facilities. The level of staff involvement, medical resources, and funding allotted for the development of an HCV management program usually varies between state correctional systems. As a result, there exists a range of protocols and tactics implemented by different correctional facilities in addressing this prevalent disease. Nevertheless, HCV management systems in correctional facilities will employ comparable strategies as well as encounter similar challenges.

Prevention and Education

A major component involving the management and containment of this disease involves methods of prevention. Because there is no vaccine for HCV, preventative tactics must rely on education and risk-reduction practices. Health education can take the form of workshops, class presentations, videos, posters and brochures. Information dispersed covers risk factors for infection, methods of prevention such as clean needle use and routes of transmission. For example, a grassroots organization in Oregon conducts educational workshops for prisoners throughout the state (Munoz-Plaza, et al., 2005). Other prisons have utilized a peer education program in which professionals train inmates on how to provide counseling and education to fellow inmates. These peer educators have several advantages including the fact that they are much more accessible for private discussions than prison authorities and staff. Also, peers provide a more trustworthy, credible and comfortable source of consultation. Prisoners have admitted that they rarely listen to staff, but they will take advice from other inmates much more seriously. Furthermore, prisoners have reported that they fear appearing like a "snitch" if they are seen while engaged in a private discussion with a staff member (Munoz-Plaza, et al., 2005).

In an Australian journal article, other more extreme measures of prevention have been suggested to combat the HCV epidemic in the Australian prison system. One approach to limit HCV incidence is to provide methadone maintenance treatments for prisoners. Methadone substitution should help opiate-dependent injectors to decrease injecting usage. Another suggestion is for prison authorities to enforce lesser punishments for the use of non-injectable drugs compared with injectable drugs. This should encourage drug-dependent prisoners to try alternative drug methods which should decrease the usage of needle use amongst inmates (Dolan, 2001). Moreover, a third major strategy would be to make sterile injection resources more available, provide disinfectants to clean needles, and/or to implement sanitary needle/exchange programs. However, this remains to be a controversial topic as authorities do not want to condone drug usage (Vlahov, Astemborski, Solomon & Nelson, 1994). It is also believed that transmission of HCV in prisons is due to unsanitary tattooing practices. An approach to limit HCV infection would be to properly train selected inmates on the sterile and proper techniques of tattooing as well as provide autoclaves and single-use ampoules of ink (Dolan, 2001).

Screening

Aside from the educational and preventative measures taken by some correctional facilities, a major initial step in an HCV management program is screening individuals for infection. Recent guidelines from the Center for Disease Control indicate that all inmates should be questioned for risk factors regarding HCV infection during their entry medical evaluation. Those inmates who affirm to any of those risk factors should be tested for HCV.

Both universal and targeted screening approaches have been practiced in different prison systems. In Indiana, mandatory testing for HCV and HIV has been enforced. The Indiana Department of Health oversees the testing procedures in which each inmate must donate blood samples. The system in Wisconsin practices a targeted screening approach in which select individuals require testing if their answers to risk-based assessments imply risk. Some of the many risks listed in the survey included a history of needle sharing, being a recipient of blood clotting factor before 1987, being on long-term hemodialysis, having been infected with hepatitis B, and having evidence of liver disease (Allen, 2003).

Although a systematic approach for antiviral treatment is available, the HCV management system in Rhode Island correctional facilities has a weakness in its screening methods. They lack any form of routine screening despite the high percentage (~26%) of inmates who are infected at any given time. As screening is not mandatory or routine, inmates in Rhode Island must individually request to be tested (Hammett, 2003).

Mental Illness and Substance Abuse

The correctional population has a high percentage of inmates with psychiatric illness and/or histories of substance abuse. These two groups used to be excluded from any type of HCV treatment. However, several findings have allowed the NIH consensus statement in 2002 to lift the standard contraindication for therapy for those with substance abuse problems. Experts believe that a correctional setting can be an ideal place for treatment since sobriety is heavily enforced. As long as substance abuse counseling is readily available and inmates are monitored closely while on treatment, substance abuse is no longer an accepted contraindication for HCV treatment. Similarly, having psychiatric illness will no longer exclude a prisoner from treatment. Because interferon will chemically lower the body's amount of tryptophan, which is a precursor of serotonin, it was originally believed that treating a mentally ill patient with interferon would dangerously exacerbate his/her psychiatric state. Currently, several studies have shown no evidence supporting the assumption that treatment will cause more severe depression in those already afflicted with mental health disorders. In addition, the close clinical monitoring which can be provided in prison may provide a safer clinical setting for treatment for mentally ill inmates. However, the eligibility criteria for receiving treatment will ultimately be decided by each correctional setting (Allen, 2003).

Challenges

Healthcare administrations for correctional facilities are concerned that the high occurrence of HCV infection among incarcerated populations combined with the steep cost of HCV treatment will overwhelm already constricted healthcare budgets. Hence, the

cost of a treatment program for HCV is most likely the largest challenge facing the establishment of diagnosis and treatment programs.

However, the development of efficient systemic approaches to testing and evaluation for treatment will drastically reduce the number of inmates eligible for treatment. As previously stated, only those with advanced infection and liver disease will receive treatment. Furthermore, inmates will be excluded from treatment if their period of incarceration is not long enough to cover the full course of treatment.

Specifically, in Rhode Island correctional systems, only a very small fraction of HCV-infected inmates received treatment. Between 1997 and 2000, 349 tested positive for HCV infection. Of this number, ninety were eligible for treatment. In order to become eligible for treatment, inmates were required to meet a list of criteria. Among the requirements, inmates had to have at least fifteen months left to serve. This would ensure that enough time was available for treatment and follow-up. In addition to this, patients had to be psychiatrically cleared on a case by case basis and those who had a history of substance abuse had to either enter a substance abuse treatment or had to have been sober for at least one year. Of the inmates eligible for treatment, forty-one of them completed the full course of treatment while the remaining forty-nine were assumed to have completed half the course. At the time, the cost of one course of antiviral treatment was about $9,500; thus, the estimated total cost was $622,250. This represented about 5% of the total health care budget of the Rhode Island Department of Corrections. Overall, this expense was not overburdening to Rhode Island's healthcare budget (Hammett, 2003). Also, an advantage of antiviral treatment for HCV is that unlike treatment for HIV which involves ongoing medical attention, it is only given for one course and then it is completed, thus

Besides cost, other factors will challenge the feasibility of the integration of HCV prevention, diagnosis and management programs in correctional facilities. Some constraints include a limited working staff as well as other healthcare priorities which may compete with HCV care. Also, a devoted cooperation and communication between correctional health and public/private health-care practices needs to be established. Moreover, incarcerated populations are relatively disliked and ostracized by the general public. The combined lack of political power and influence makes it easy for government officials to overlook their needs (Hammett, Harmon & Rhodes, 2002).

The Current Evaluation and Management Practices for the Treatment of Hepatitis C in Massachusetts Correctional Facilities

The process by which Massachusetts inmates are screened and evaluated for HCV treatment involves a methodical and thorough series of steps. To start with, instructive resources such as peer education and counseling on preventative measures are available to all inmates, regardless of their HCV status. Information offered covers the symptoms of HCV, ways the disease can be contracted, treatment options, and the side effects associated with treatment. Additionally, infected inmates are informed of behaviors which could exacerbate their condition, such as alcoholic intake which will augment liver damage.

Screening for Treatment Eligibility

During their entry medical evaluation, an individual's likelihood of HCV infection is assessed through the inmates' history of several risk factors. If the individual has a history of intravenous drug use, has received a blood transfusion before July of 1992, has had multiple sexual partners and/or has had a sexual partner with HCV, then he/she is deemed at high risk for having contracted the disease. Only one affirmation to these experiences is needed to qualify for an HCV antibody test. If the individual tests positive for HCV antibodies, then liver function tests are checked periodically. During this time, hepatitis A and hepatitis B statuses are checked and the individual is immunized for hepatitis A and hepatitis B, if possible (Brewer, Marshall, Demaria, 2007).

After one year has passed since the HCV antibodies were detected, the HCV RNA viral load is measured. If the individual tests positive for HCV RNA, then he/she undergoes a series of both medical and laboratory evaluations to determine his/her eligibility for a liver biopsy. The medical evaluation ensures that the inmate has no history of renal transplantation, decompensated cirrhosis, severe depression, major medical illnesses such as diabetes or chronic obstructive pulmonary disease (COPD), intravenous drug use or alcohol use within the past twelve months, or disciplinary reports within the past year involving substance abuse. In addition, individuals should show no evidence of any autoimmune disease and, if female, should not be pregnant. Failure to meet these criteria will most likely exclude an HCV infected individual from continuing with the treatment evaluation process.

The laboratory segment of the evaluation process consists of white blood count, serum creatine, platelet, bilirubin, albumin and prothrombin level measurements. In most cases, abnormal levels for these labs will prevent an individual from proceeding onto a liver biopsy. However, abnormal lab values are not an absolute contraindication for continuing with the treatment qualification process. An antibody test for HIV is also implemented to determine if the patient should be referred to the HIV/HCV co-infection clinic.

Upon satisfying the criteria for both the medical and laboratory assessments, the HCV infected person will undergo a liver biopsy. Liver biopsies provide the physician with evidence on whether or not moderate inflammation and/or fibrosis of the liver are occurring. Treatment is not recommended if the liver biopsy is fairly normal, but it is recommended when the health status of the liver is compromised.

Pre-treatment Protocol

Once HCV treatment is recommended, the Hepatitis C worksheet (Appendix A) must be filled out and sent to the Hepatitis C Program Manager in the UMass Correctional Health Program of UMass Medical School. The Hepatitis C Program Manager oversees the treatment waiting list for all HCV infected inmates in the seventeen Massachusetts correctional facilities. As of February 2007, there were sixty-eight inmates on therapy and twenty on the waitlist. The maximum number of inmates allowed on HCV therapy at one time is ninety-five. It is part of the manager's responsibility to update records as well as keep track of who is currently on therapy and which individuals are next on the waitlist. Inmates who have been approved to receive treatment but are on the waitlist are divided into 4 categories:

1. Treatment naïve
    a. Genotype 1, 2, 3 and 4
2. Dual Diagnosis (HCV/ HIV)
    a. Fulminant (go to top of list)
    b. Non-Fulminant
3. Relapsers, Treatment Failures and Non-Responders after Interferon/Ribavirin Combination Therapy
4. Date of biopsy and length of time since biopsy will be considered

The selection of patients to be treated occurs in increments of ten. Five individuals from category one, two to three from category two, and two to three patients from category three are chosen. Patients classified under the "Fulminant Dual Diagnosis" category are given top priority for treatment. They are the most critically sick, and as a result, are moved to the top of the list regardless of the date they were diagnosed. Additional factors which place a higher urgency to treat include the severity of the liver biopsy as well as the length of time a patient has been waiting on the treatment waitlist. Each patient in a group of ten will receive treatment before an additional group of ten inmates is to be selected (Brewer, Marshall, Demaria, 2007).

Prior to initiating HCV therapy, several parameters must be addressed. First of all, it must be verified that the patient will be incarcerated for greater than one year after treatment begins. A short sentence prevents patients from receiving a complete course of treatment as well as follow-up testing to monitor their HCV status and evaluate treatment effectiveness. Secondly, a full history and physical examination must be conducted and recorded on the Hepatitis C worksheet (Appendix A). Patients with certain other health conditions must undergo additional testing before they can be cleared for therapy. For example, patients with a history of coronary artery disease are required to have an EKG and possibly a stress test, while patients with diabetes should be tested for fasting glucose and hemoglobin levels.

The next step requires the patient to read, understand and sign the "Inmate Agreement" form (Appendix B). This sheet represents the patient's consent to begin treatment. By signing this form, the patient acknowledges his/her understanding of the disease process, its effects on their health, treatment options, side effects of treatment and the varying levels of success experienced by different HCV infected patients on treatment. The patients must acknowledge all of the health risks associated with therapy and must inform the medical staff of any symptoms. They must also pledge to avoid illegal drug and alcohol use, and tattoos. Infringing upon these rules will result in termination of treatment.

Another step before initiating therapy is the measurement of several baseline lab values, the most important being the HCV RNA viral load just prior to treatment. Others include ALT, white blood cell, hemoglobin, hematocrit, platelets, cholesterol, triglycerides, glucose, albumin and thyroid stimulating hormone (TSH) levels. Woman must take a pregnancy test to verify they are not pregnant while on treatment. Once treatment is initiated, patients are closely monitored by the medical staff to ensure they are comfortable on therapy and remain symptom free. As previously mentioned, common side effects of pegylated interferon and ribavirin are flu-like symptoms, nausea, abdominal discomfort, loss of appetite, edema, rash, reactions at injection site, muscle

aches, loss of hair and symptoms associated with depression (Brewer, Marshall, Demaria, 2007).

The Process of HCV Therapy

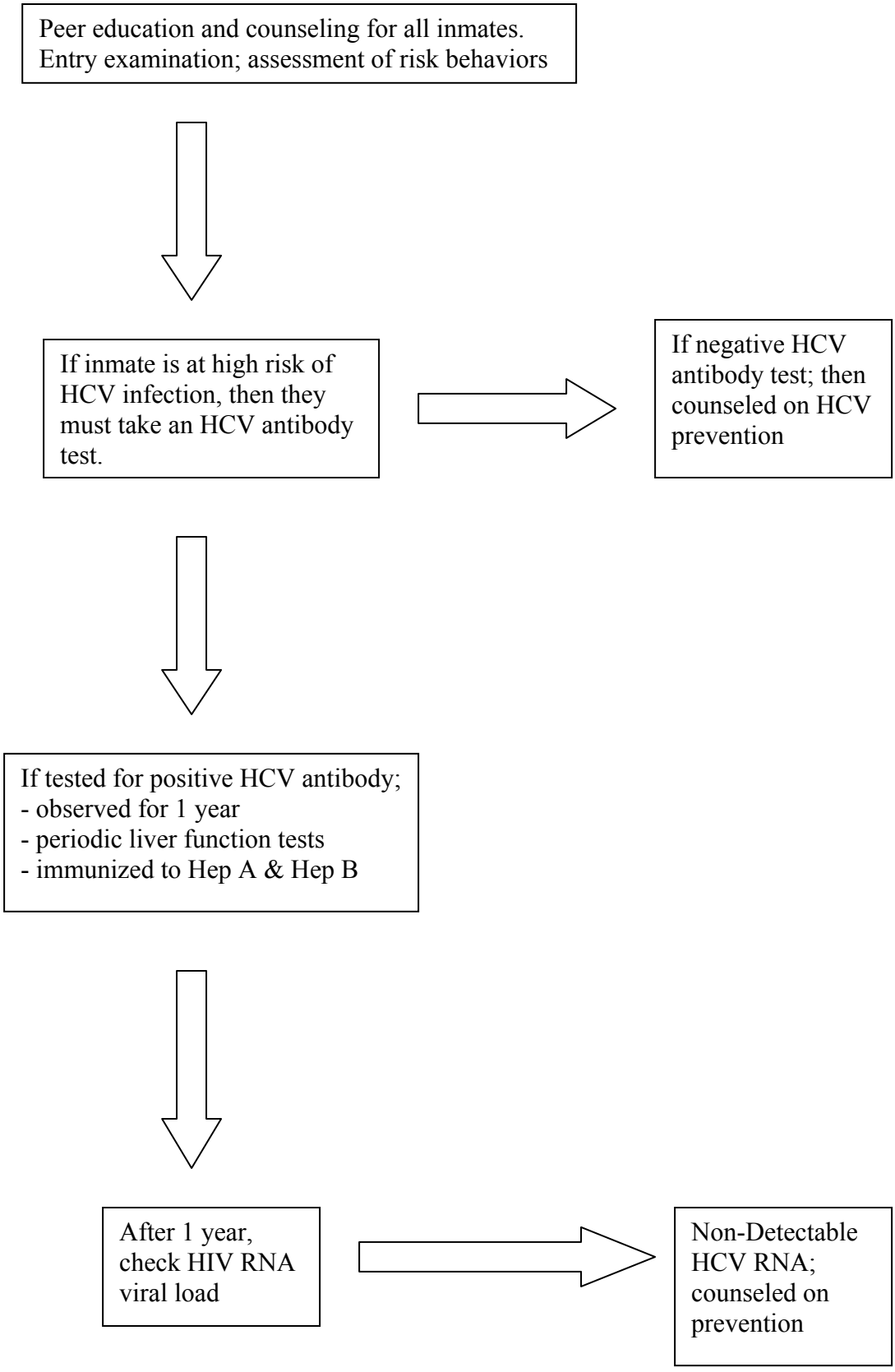
The most commonly used medications for the treatment of HCV are pegylated interferon and ribavirin. This combination therapy is recommended for all patients except for those with special circumstances, such as patients who are co-infected with HIV and HCV. After twelve weeks of HCV therapy, the HCV RNA viral load is tested. Only if there is at least a two log reduction of the HCV RNA viral load will the treatment be continued. If there is less than a two log reduction, the patient is considered unresponsive to treatment. In this case, the medication is discontinued and the patient is then closely monitored in chronic care. A full course of HCV therapy for genotypes 2 and 3 is twenty-four weeks while for other genotypes it is forty-eight weeks. The HCV-RNA viral load is again measured at the completion of treatment as well as six months after therapy ends to assess for a sustained anti-viral response.

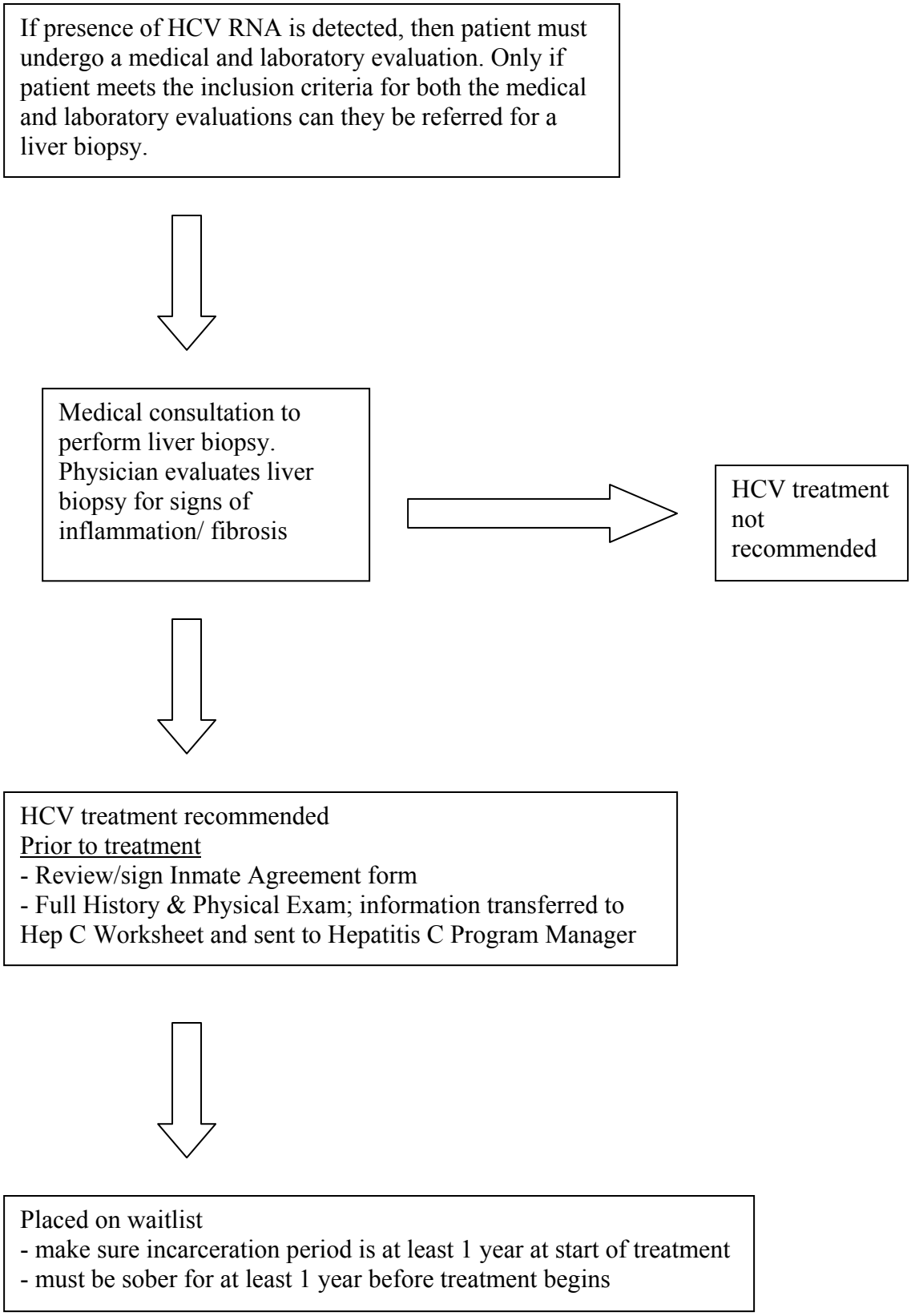
In addition to HCV RNA viral loads, complete blood counts are drawn throughout the course of treatment to examine the effects of the medications on hemoglobin, white blood count, neutrophils, platelets, hematocrit, ALT, TSH, and viral load levels. If hemoglobin levels drop, the dosage of ribavirin is decreased. If the white blood cell count, absolute neutrophils and platelets drop, then pegylated interferon is decreased. Besides blood tests, females must also take a pregnancy test every month during therapy (Brewer, Marshall, Demaria, 2007).

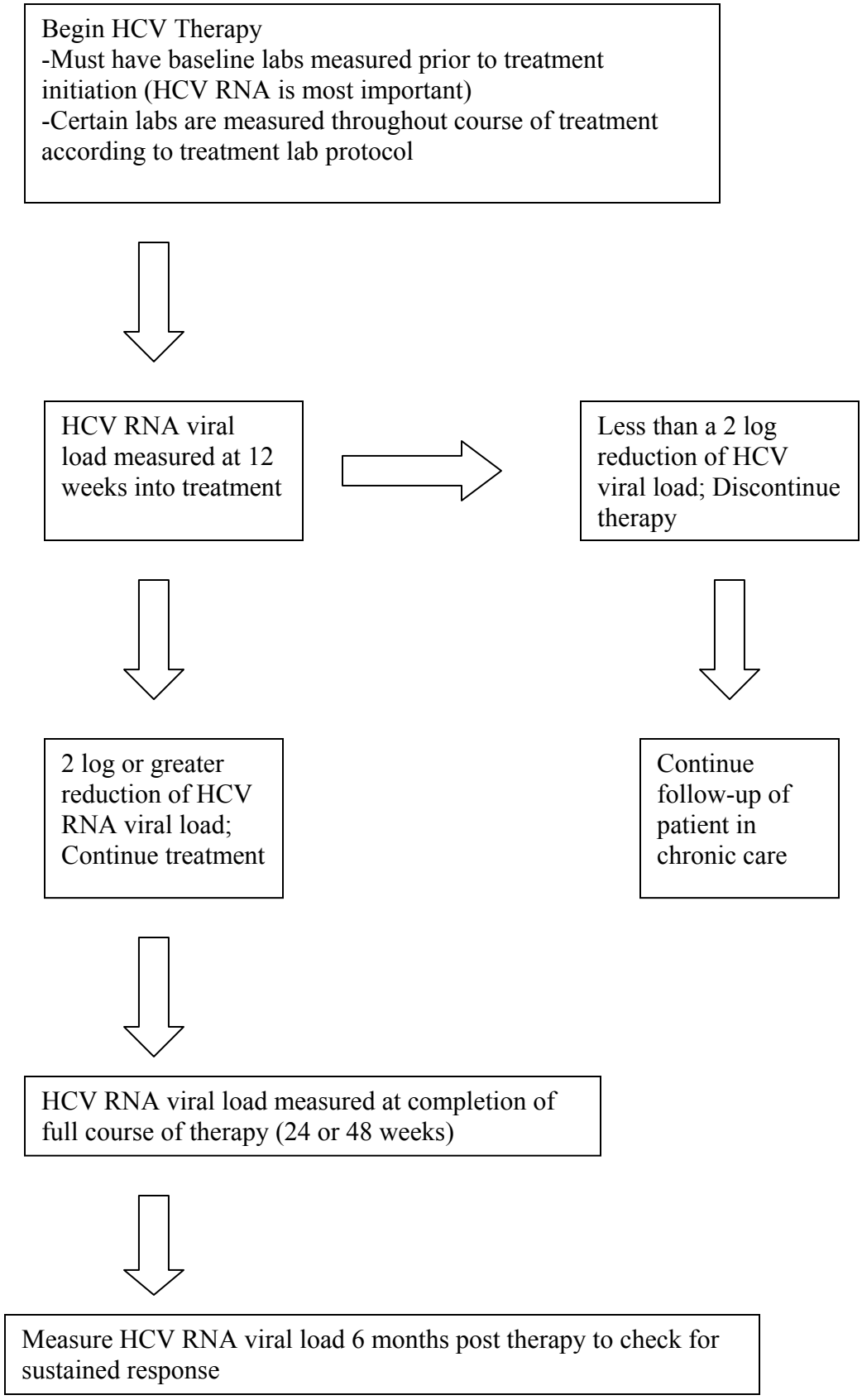
The overall evaluation process for the management and treatment of hepatitis C infected inmates in Massachusetts facilities are summarized in the flow charts found on the following pages.

Inmates Co-infected with HIV and HCV

In order to be referred to the HIV/HCV co-infection clinic, the patient must have tested positive for HIV antibodies or detectable HIV RNA as well as have a positive HCV antibody test or evidence of HCV RNA. Similar to mono-infected inmates, liver function tests along with baseline labs should be drawn including complete blood counts, CD4 counts and percentages, albumin, prothrombin, and HIV RNA levels. Evaluation by the gastroenterologist and the infectious disease specialist will determine whether or not a liver biopsy will be conducted. An additional right upper quadrant ultrasound is to be done before the biopsy. If chronic HCV infection along with HIV viremia is present, Pegasys plus/minus ribavirin will be recommended as therapy if no other contraindications exist. A closer follow-up is necessary with co-infected patients in order to monitor for the expected side effects as well as the potential for other severe symptoms to occur. For some co-infected patients on treatment, antiretroviral therapy has had to be terminated due to hepatotoxicity. Other patients must have frequent endoscopies if their cirrhosis worsens in order to verify whether or not they have esophageal varices (Brewer, Marshall, Demaria, 2007).


Peer education and counseling for all inmates.
Entry examination; assessment of risk behaviors
If inmate is at high risk of HCV infection, then they must take an HCV antibody test.
If negative HCV antibody test; then counseled on HCV prevention
If tested for positive HCV antibody;
- observed for 1 year
- periodic liver function tests
- immunized to Hep A & Hep B
After 1 year, check HIV RNA viral load
Non-Detectable HCV RNA; counseled on prevention


If presence of HCV RNA is detected, then patient must undergo a medical and laboratory evaluation. Only if patient meets the inclusion criteria for both the medical and laboratory evaluations can they be referred for a liver biopsy.
Medical consultation to perform liver biopsy. Physician evaluates liver biopsy for signs of inflammation/ fibrosis
HCV treatment not recommended
HCV treatment recommended
Prior to treatment
- Review/sign Inmate Agreement form
- Full History & Physical Exam; information transferred to Hep C Worksheet and sent to Hepatitis C Program Manager
Placed on waitlist
- make sure incarceration period is at least 1 year at start of treatment
- must be sober for at least 1 year before treatment begins


Begin HCV Therapy
-Must have baseline labs measured prior to treatment initiation (HCV RNA is most important)
-Certain labs are measured throughout course of treatment according to treatment lab protocol
HCV RNA viral load measured at 12 weeks into treatment
Less than a 2 log reduction of HCV viral load; Discontinue therapy
2 log or greater reduction of HCV RNA viral load; Continue treatment
Continue follow-up of patient in chronic care
HCV RNA viral load measured at completion of full course of therapy (24 or 48 weeks)
Measure HCV RNA viral load 6 months post therapy to check for sustained response

The HCV Database

The prospect of establishing hepatitis C management programs in correctional facilities does seem ideal considering that such a large percentage of people infected with HCV are in a confined setting. It has become apparent to several states that the period of incarceration provides a window of opportunity to screen, evaluate and treat those at risk for hepatitis C. Among the states which have implemented a hepatitis C treatment program in correctional facilities is Massachusetts. In 2004, a database was created to monitor and assess the treatment of hepatitis C infected individuals in Massachusetts correctional facilities. As of March 2005, 262 inmates treated were entered into this database. An analysis conducted for this data set revealed that the majority of inmates treated were Caucasian, male and infected with HCV genotype 1. The database also provided information regarding treatment response and success rates; almost half of the inmates treated had achieved a successful response, reaching an undetectable HCV viral load (Kelly, 2005).

The purpose of this project was to update the database with additional inmates who were treated up until February 2007. After the medical and treatment information from the forms of these inmates were transferred into the database, a demographic analysis was performed such that the characteristics (gender, race, age, facility) of inmates treated could be summarized. A demographic synopsis provided a review of who is treated with the benefit of minimizing any intentional or unintentional bias. Predispositions of the facilities to treat certain populations over others can be exposed through this analysis, providing the management incentive to review protocols.

Response to treatment was similarly assessed based on lab results entered in the database. HCV RNA viral loads and ALT levels proved to be important indicators of treatment success. Consequently, HCV RNA levels were used to examine any correlations between the success of treatment and viral genotype as well as HIV co-infection. Results have shown that inmates with genotype 1 have the least successful responses when compared with genotypes 2, 3 and 4. In addition, co-infection with HIV was found to drastically reduce the chance of successful treatment outcomes.

Other major components looked at in the database were reasons for treatment interruptions and causes of premature termination of treatment. Among others, these included severe and intolerable side effects, poor anti-virological response to the medications, and early release from prison. Although an inadequate amount of data was available to perform a quantitative analysis, a qualitative evaluation of the reasons for unsuccessful and incomplete courses of treatment may serve as a reference for improving upon the efficiency of the screening and treatment protocols. Several recommendations for improvements in the database included the collection of missing data and the development of a stricter follow-up system. Variables such as inmates' history of substance abuse and the presence of mental and physical health conditions were missing data for nearly half the inmates. Follow-up HCV RNA measurements were similarly missing for an even larger percentage of inmates. This information is vital in determining the success rate of treatment.

The value of the hepatitis C treatment database for HCV infected inmates in Massachusetts correctional facilities is in its contributions to the limited knowledge of this disease and its management. Despite the large proportion of HCV infected people who pass through a correctional facility, there is still a shortage of factual and statistical

information on HCV infection among inmates. Not having a database for tracking HCV incidence and treatment contributes to the absence of a standardized system of health care and treatment programs in correctional settings. The collection of more data in correctional facilities would allow for the better understanding of hepatitis C prevalence as well as the effectiveness of its treatment. Ideally, more facilities will follow in the footsteps of the Massachusetts treatment program and employ an efficient system of data collection and organization.

Materials and Methods

This project was conducted over a six month period, from November 2006 to April 2007. During this time, research was approved, data was collected, and the SPSS database was revised and updated. An analysis of the data was used to assess the effects of changes made to the original data collection process as well as examine the current state of hepatitis C treatment in Massachusetts state correctional facilities.

Research Preparation

Preparation for data collection and handling began as early as November 2006. Prior to the start of any clinical research project, an intensive review must be conducted by the Institutional Review Board (IRB). The IRB is a review committee typically composed of five members of various sexes, backgrounds, and professions. It was originally created in the 1970's to help protect the rights and welfare of human research subjects by ensuring that clinical studies are well designed, ethical, legal, and safe. IRBs have the authority to modify, approve, or disapprove any research study involving human subjects after an extensive review of the proposed course of action. Most research institutions, professional organizations, and scholarly journals have established IRBs (Epley, Erickson, and Selwitz, 2006; National Cancer Institute [NCI], n.d.).

For this particular project, data collection could not begin until an IRB training course had been completed by each individual researcher. The Collaborative IRB Training Initiative (CITI) is an online course in the protection of human research subjects that is required by the University of Massachusetts, Worcester. It is comprised of various training modules regarding the history of the IRB, the function of the IRB, and the conduction of research involving different human populations including vulnerable subjects such as prisoners. Completion of the course required a review of each module as well as a corresponding quiz. Individual certificates of completion were received at the conclusion of the course and sent for approval by the IRB at the University of Massachusetts, Worcester as well as the Massachusetts Department of Correctional Facilities. Complete IRB approval was achieved by December 2006.

Data Collection

Data was collected for this project over a two month period, from January 1, 2007 to March 1, 2007. Demographic, health, and treatment-related information was gathered on a total of 177 inmates including 109 inmates now off treatment and sixty-eight inmates currently on treatment. Data for each inmate was extracted directly from individual hepatitis C worksheets (Appendix A) completed and stored in the medical records file of each individual.

The current hepatitis C worksheet is a one-page record of inmate history and treatment. It contains basic information such as name, age, race, weight, and height; a brief medical history including current health or mental health conditions, a history of alcohol or drug abuse, and a history of co-infection; as well as treatment-related data such as treatment start and end date, lab figures, changes in treatment, and any necessary notes. Originally, the hepatitis C worksheet was a two-page treatment record updated regularly by nurses and doctors (Appendix C). However, when data collection began in 2004, information from these original worksheets was extracted and transferred to a more

organized data collection worksheet (Appendix D). Although this worksheet included all the information necessary to monitor the progress of the inmates and the types of inmates being treated, the extensive length of the paperwork resulted in an increasing amount of missing data. On September 27, 2004, a new one-page hepatitis C worksheet was created and later revised to the current worksheet in 2005 (Appendix A). This treatment record is typically filled out prior to the start of treatment by HIV/Hepatitis C case managers at each health service unit. Following the start of treatment, sheets are transferred and information is continually updated by the Hepatitis C Program Manager for UMass Medical School and the UMass Correctional Health Program.

In order to maintain the confidentiality of inmates during the data collection process, names were blacked out and inmates were coded with an arbitrary five digit number beginning with 55 or 88. A 55 number indicated inmates with data from the old hepatitis C worksheets, while an 88 number indicated inmates with data from the new hepatitis C worksheets. All data input over the course of this project was extracted from the new worksheets. This included updated information for inmates that had already completed or discontinued treatment in the past three years, old data from 2004 and 2005, and new data for inmates that had recently started treatment.

Differences were noted in the amount of information each worksheet contained. Worksheets completed within the past year were nearly, if not entirely, complete. Older, worksheets, however, were frequently missing large amounts of important information such as height, weight, incarceration date, current health conditions, history of alcohol or drug abuse, and reasons for any discontinuation of or interruptions in treatment. It was unclear as to whether or not this data was actually missing, unknown, or not applicable. In either case, all data considered missing was compiled into various "missing data logs" and sent to the program manager who had direct contact with inmates and case managers and could potentially retrieve necessary data.

Data Entry

All information collected during the course of this project was input into an SPSS database. SPSS for Windows is an analytical software program devised by SPSS Inc. for data collection, data access, data management and preparation, statistical data analysis, and reporting (SPSS Inc., 2007). Actual data entry was conducted in a large SPSS spreadsheet. Different rows indicated different inmates whereas different columns indicated different fields of data associated with the hepatitis C worksheet. Assigned row numbers and specific column headers were used to differentiate inmates and identify data requirements, respectively. Inmates were numerically ordered in the database according to their assigned five digit code beginning with 55 or 88. All data was entered into the appropriate rows and columns based on specific variables previously coded into the SPSS system. Number as well as word variables were used to define available and unknown data. Missing information was indicated in the database by blank fields.

Data Analysis

Between March 2007 and April 2007, a statistical analysis of the complete data set was conducted using the SPSS program. The analysis was focused primarily on characterizing the types of inmates being treated, summarizing the overall progress of hepatitis C treatment, and identifying potential trends or correlations between inmate

characteristics and the success of treatment. Only those fields of data which had limited amounts of missing information in the database were assessed.

To account for the changes that have taken place in hepatitis C treatment since 1999, data was analyzed based on one of two different categories: inmates who have received treatment since 1999 and inmates who have received treatment since August 2002. February 1999 marked the start of hepatitis C treatment for inmates in the database, whereas August 2002 marked the start of combination therapy as the standard form of treatment in Massachusetts state correctional facilities. Creation of the two categories allowed for a more accurate assessment of the types of inmates being treated and the current progress of treatment.

For inmates who had received treatment since 1999, data analyses were conducted to summarize the trends in inmate characteristics and treatment center operations that were unaltered by the 2002 changes in hepatitis C treatment. In particular, data was used to assess inmate demographics such as gender, age, and race, the frequency of genotypes among inmates, and the frequency of treatment at each treatment center. Assessments of additional information such as health conditions, mental health conditions, and prior history of substance or alcohol abuse were not made due to the large percentage of missing data in these fields.

Although the 2002 changes in standard treatment did not affect the types of inmates who had received treatment since 1999, they could have affected the overall outcome and progress of treatment. In order to accurately assess these effects, treatment related data was only analyzed for those inmates who had received treatment since August 2002. Data was used specifically to assess variations in ALT and HCV RNA levels prior to the start of treatment, the frequency of undetectable viral loads attained by the end of treatment, the frequency of genotypes among inmates and their potential correlation with treatment outcome, the frequency of HIV co-infection among inmates and its potential correlation with treatment outcome, the frequency of treatment interruption, and the frequency of treatment discontinuation as well as the reasons given for stopping treatment. Any additional assessments were deemed unnecessary or could not be made due to missing data constraints.

Results

To account for the division in statistical analyses, results have been classified under two different categories: inmate characteristics and response to treatment. Each category is based on a specific set of inmates whose data was used to assess a number of different fields. The results for each analyzed field have been individually summarized within their corresponding category and are based on statistical data tables originally output by SPSS. Summaries are characterized by verbal highlights, graphs, and tables similar to those generated by SPSS.

All results have been organized by SPSS in terms of valid and missing data. Valid is an expression used to define all known and legitimate data that has been input into the database. Missing, on the other hand, is an expression used to define all data that is either missing from the database, has been input into the database as unknown, or has been incorrectly input into the database as an undefined variable. Undefined variables and unknown data are specifically referred to as unknown, whereas data missing from the system is referred to by the term system.

Results from the actual SPSS analysis of valid and missing data are presented in three different forms: frequency, percent, and valid percent. "Frequency" refers to the actual number of inmates that fall within a given category. This result represents the total number of inmates analyzed within a given field, and thus includes all valid and missing data. "Percent" is the calculated percentage of inmates within a given category based on the total number of inmates analyzed. This, again, represents the total number of inmates analyzed and includes both valid and missing data. "Valid Percent" is the only result that does not include missing data. It is the calculated percentage of inmates within a given category based solely on the total number of inmates with valid data.

Due to the extent of missing data in the database, the total number of inmates with valid data was not equivalent to the number of inmates analyzed within each field. However, these figures were the most accurate representation of the data within the database. Consequently, valid frequencies and valid percents were used to summarize the results of each field.

Inmate Characteristics

The following results are based on all inmates who have received treatment since 1999. This year marked the start of hepatitis C therapy for inmates included in the database. As of March 1, 2007, data on a total of 510 treated inmates has been collected and input into the HCV database. This data was used to assess the overall characteristics of inmates receiving treatment including the facility at which they first began treatment as well as their gender, age, race, and HCV genotype.

Facility at Start of Treatment

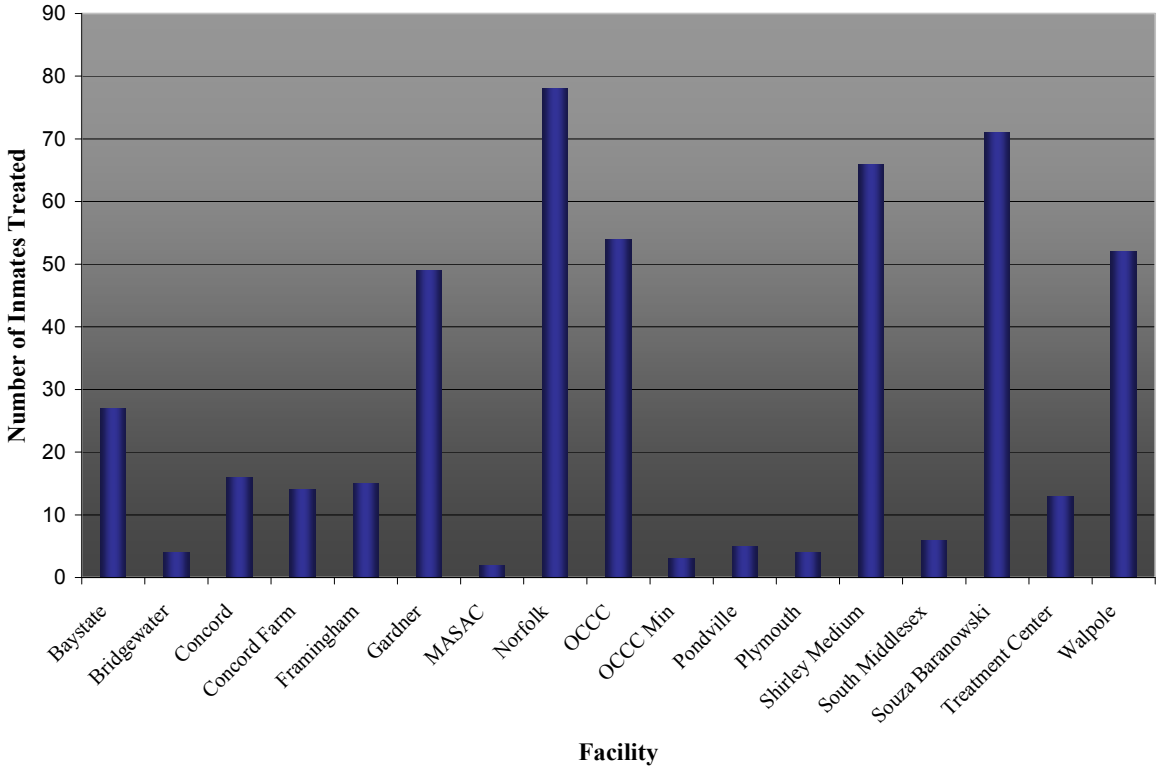
Out of 510 inmates treated, 479 (93.9%) inmates had a documented name for the correctional facility at which their treatment was initiated. A total of 17 correctional facilities were identified as having provided hepatitis C treatment since 1999. The number of inmates treated varied among the facilities, ranging from as low as 2 inmates to as high as 78 inmates. The majority were treated at Massachusetts Correctional Institution - Norfolk (78), Souza-Baranowski Correctional Center (71), and Massachusetts Correctional Institution – Shirley (66). A limited number of inmates

received treatment at the Massachusetts Alcohol and Substance Abuse Center (2), Old Colony Correctional Center Min (3), Bridgewater State Hospital (4), and Massachusetts Correctional Institution - Plymouth (4). Results for all 17 correctional facilities have been summarized in Table 1. A bar graph of the number of inmates treated at each facility at the start of treatment is shown in Figure 1.

Table 1: Frequency and Percentage of Inmates among Massachusetts State Correctional Facilities at the Start of Treatment

Facility		Number of Inmates	Percent	Valid Percent
Valid	Baystate	27	5.3	5.6
	Bridgewater	4	0.8	0.8
	Concord	16	3.1	3.3
	Concord Farm	14	2.7	2.9
	Framingham	15	2.9	3.1
	Gardner	49	9.6	10.2
	MASAC	2	0.4	0.4
	Norfolk	78	15.3	16.3
	OCCC	54	10.6	11.3
	OCCC Min	3	0.6	0.6
	Pondville	5	1	1
	Plymouth	4	0.8	0.8
	Shirley Medium	66	12.9	13.8
	South Middlesex	6	1.2	1.3
	Souza Baranowski	71	13.9	14.8
	Treatment Center	13	2.5	2.7
	Walpole	52	10.2	10.9
	Total	479	93.9	100
Missing	Unknown	6	1.2	
	System	25	4.9	
	Total	31	6.1	
Total		510	100	

Figure 1: Distribution of Inmates among Massachusetts State Correctional Facilities at the Start of Treatment



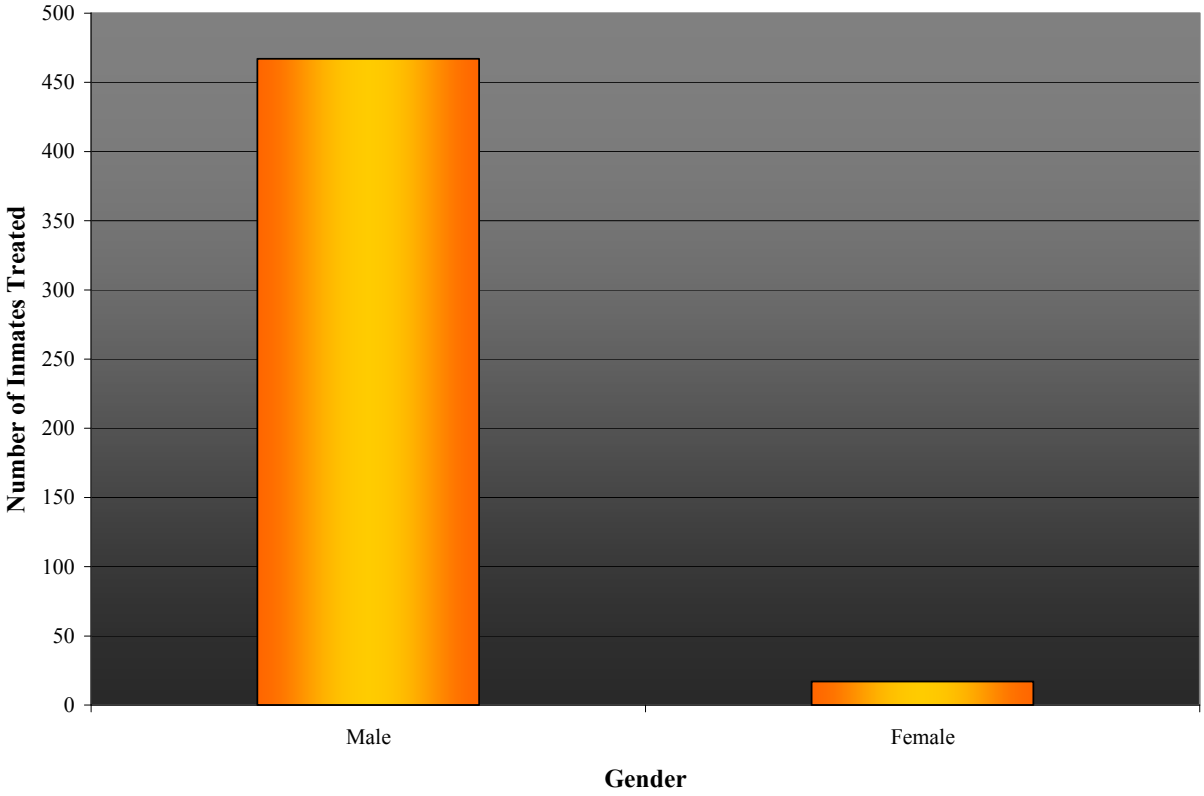
Gender

Out of 510 inmates treated, 484 (94.9%) inmates had a documented gender. 467 (96.5%) of those inmates were male, whereas only 17 (3.5%) of those inmates were female. All 17 female inmates received hepatitis C treatment at either the Massachusetts Alcohol and Substance Abuse Center (MASAC) or Massachusetts Correctional Institution – Framingham (MCI – Framingham). Statistical results for the frequency of male and female inmates treated have been summarized in Table 2 and graphed in Figure 2.

Table 2: Frequency and Percentage of Male and Female Inmates Treated

Gender		Number of Inmates	Percent	Valid Percent
Valid	Male	467	91.6	96.5
	Female	17	3.3	3.5
	Total	484	94.9	100
Missing	Unknown	1	0.2	
	System	25	4.9	
	Total	26	5.1	
Total		510	100	

Figure 2: Distribution of Male and Female Inmates Treated



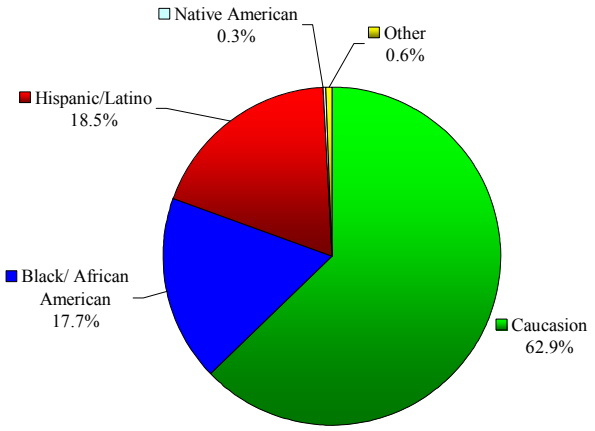
Race

The race/ethnicity of those treated for HCV in Massachusetts Correctional facilities was recorded for 356 (69.8%) of the inmates in the database. According to the known data, Caucasians were the most frequently treated race with 224 (62.9%) inmates. Hispanic/Latino and African Americans were nearly tied for the second highest race/ethnicity treated for HCV in MA facilities. There were 66 (18.5%) Hispanic/Latino inmates treated while there were 63 (17.7%) African Americans treated. One (0.3%) Native American and two (0.6%) inmates classified under "other ethnicity" were treated. Table 3 contains all of the frequencies and percentages of the inmates' ethnicities and Figure 3 displays the valid percentages of the inmates' race/ethnicities.

Table 3: Frequency and Percentage of Race/Ethnicity among Inmates Treated

Race/Ethnicity		Number of Inmates	Percent	Valid Percent
Valid	Caucasian	224	43.9	62.9
	Black/African American	63	12.4	17.7
	Hispanic/ Latino	66	12.9	18.5
	Native American	1	0.2	0.3
	Other	2	0.4	0.6
	Total	356	69.8	100
Missing	Unknown	87	17.1	
	System	67	13.1	
	Total	154	30.2	
Total		510	100	

Figure 3: Race/Ethnicity of Inmates Treated



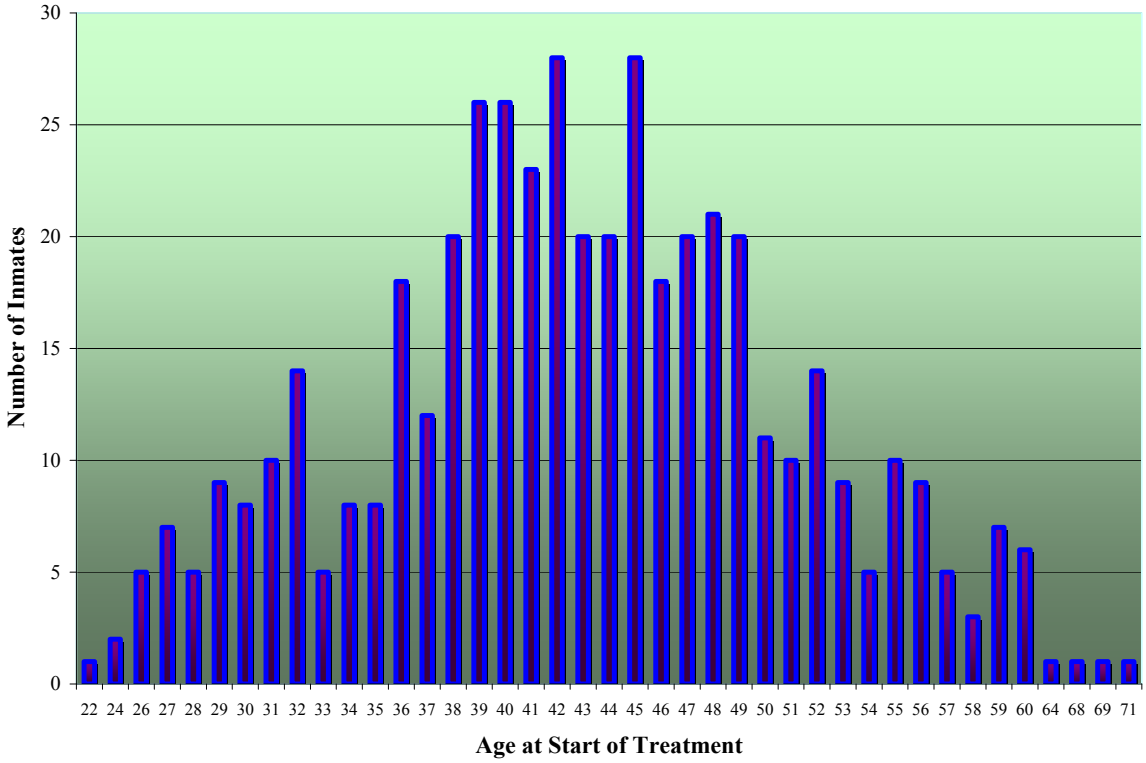
Age

A majority of the information regarding the ages of the inmates at the start of HCV therapy was entered into the database; out of the 510 inmates, 475 (93.1%) had a recorded age. The ages of those inmates who started treatment ranged from as young as 22 to as high as 71 years old. The majority of those individuals on HCV therapy began treatment when their age fell within the range of middle thirties to late forties. The two ages which had the highest number of inmates treated (28 patients), were 42 and 45 years old. The average age of inmates beginning treatment was 42.9 while the median was 43 years old. See Table 4 for the complete age data set. Figure 4 shows the number of inmates who started therapy at each specific age.

Table 4: Age of Inmates at the Start of Treatment

Age		Number of Inmates	Percent	Valid Percent
Valid	22	1	0.2	0.2
	24	2	0.4	0.4
	26	5	1	1.1
	27	7	1.4	1.5
	28	5	1	1.1
	29	9	1.8	1.9
	30	8	1.6	1.7
	31	10	2	2.1
	32	14	2.7	2.9
	33	5	1	1.1
	34	8	1.6	1.7
	35	8	1.6	1.7
	36	18	3.5	3.8
	37	12	2.4	2.5
	38	20	3.9	4.2
	39	26	5.1	5.5
	40	26	5.1	5.5
	41	23	4.5	4.8
	42	28	5.5	5.9
	43	20	3.9	4.2
	44	20	3.9	4.2
	45	28	5.5	5.9
	46	18	3.5	3.8
	47	20	3.9	4.2
	48	21	4.1	4.4
	49	20	3.9	4.2
	50	11	2.2	2.3
	51	10	2	2.1
	52	14	2.7	2.9
	53	9	1.8	1.9
	54	5	1	1.1
	55	10	2	2.1
	56	9	1.8	1.9
	57	5	1	1.1
	58	3	0.6	0.6
	59	7	1.4	1.5
	60	6	1.2	1.3
	64	1	0.2	0.2
	68	1	0.2	0.2
	69	1	0.2	0.2
	71	1	0.2	0.2
	Total	475	93.1	100
Missing	Unknown	8	1.6	
	System	27	5.3	
	Total	35	6.9	
Total		510	100	

Figure 4: Age Distribution at Start of Treatment



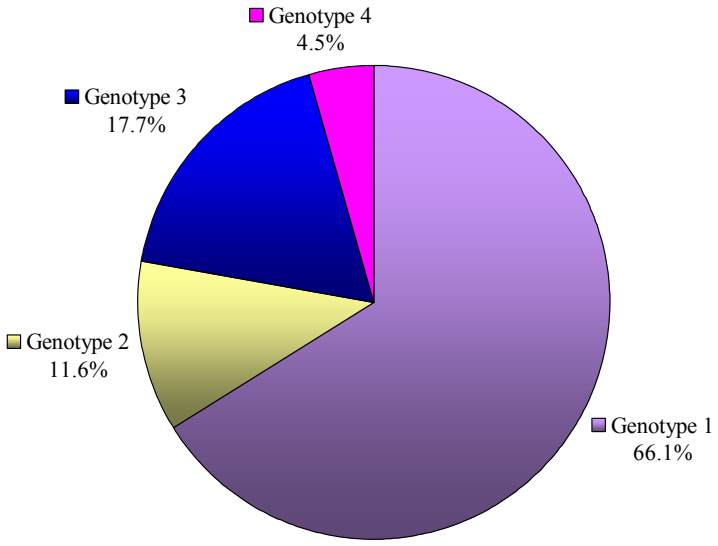
HCV Genotype

A summary of viral genotype groups was conducted from the 440 (86.3%) inmates who had a recorded HCV genotype in the database. With a frequency of 291 (66.1%), the majority of inmates were infected with HCV genotype 1. 78 (17.7%) inmates were infected with genotype 3 while 51 (11.6%) inmates were infected with genotype 2. Only 20 (4.5%) inmates had genotype 4. Table 5 lists the frequencies and percentages of the HCV genotypes. Figure 5 displays the distribution of HCV genotype groups among infected inmates who began treatment.

Table 5: Frequency and Percentage of HCV Genotypes among Inmates Treated

HCV Genotype		Number of Inmates	Percent	Valid Percent
Valid	Genotype 1	291	57.1	66.1
	Genotype 2	51	10	11.6
	Genotype 3	78	15.3	17.7
	Genotype 4	20	3.9	4.5
	Total	440	86.3	100
Missing	Unknown	39	7.7	
	System	31	6.1	
	Total	70	13.7	
Total		510	100	

Figure 5: Distribution of HCV Genotypes among Inmates Treated



Response to Treatment

The following results are based on all inmates who have received treatment since August 2002. This date marked the start of combination therapy (interferon + ribavirin) as the standard form of treatment in Massachusetts state correctional facilities. As of March 1, 2007, a total of 370 inmates have been documented in the database as having received treatment since August 2002. Data from these inmates was used to assess the overall response of inmates to treatment including variations in ALT and HCV RNA levels prior to the start of treatment, the frequency of undetectable viral loads attained by the end of treatment, the frequency of genotypes among patients and their potential correlation with treatment outcome, the frequency of HIV co-infection among patients and its potential correlation with treatment outcome, the frequency of treatment interruption, and the frequency of treatment discontinuation as well as the reasons given for stopping treatment.

Baseline ALT Levels

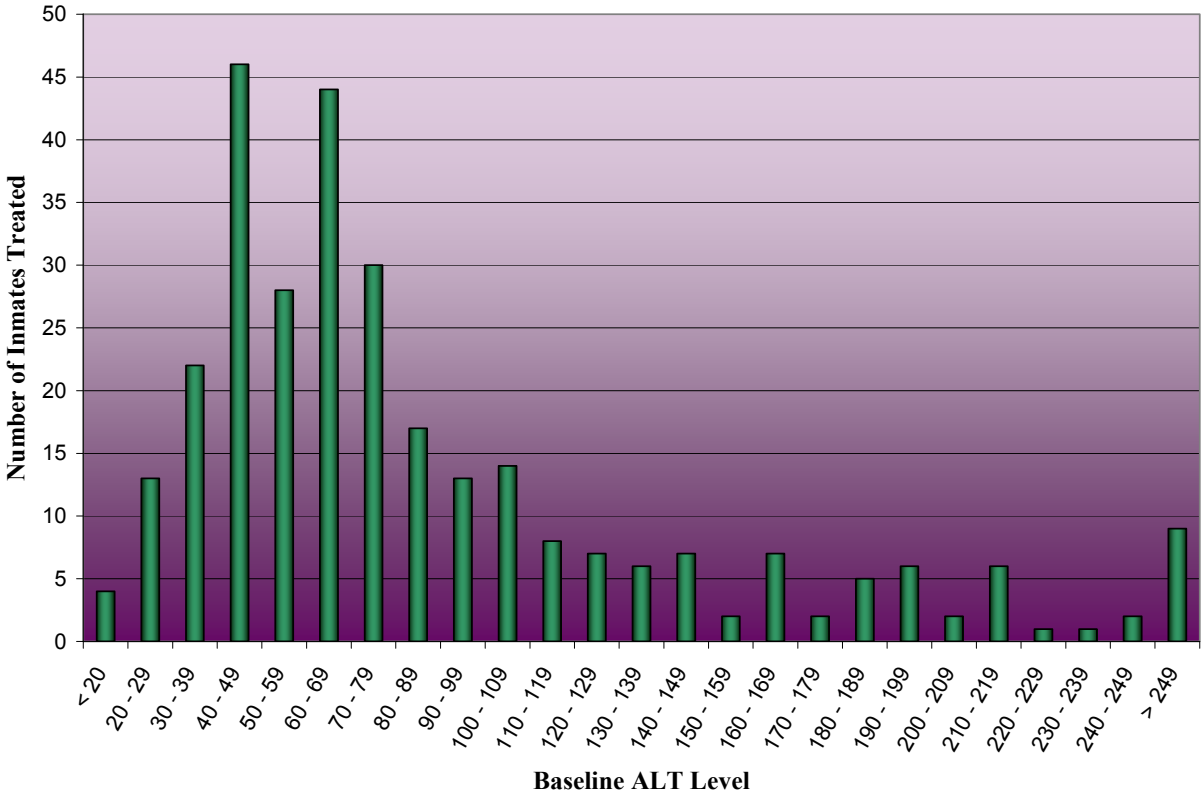
Out of 370 inmates treated, 302 (81.6%) inmates had a documented baseline value for the level of alanine aminotransferase (ALT) in the blood. These values were measured in terms of International Units per Liter (IU/L). Typically, in a normal and healthy individual, ALT levels in the blood tend to range between 0 and 40 IU/L (Franciscus and Teeter, 2006). According to the labs of inmates treated, baseline ALT levels ranged from 12 IU/L to 627 IU/L. The average ALT level was calculated around 90.26 IU/L, whereas the median ALT level was approximately 68 IU/L. The majority of inmates (60.5%) had baseline ALT levels between 30 IU/L and 79 IU/L. Due to the large

percentage of missing data, ALT levels at 12 weeks and 24 weeks into treatment could not be assessed. Refer to Table 6 for all relative data figures and percentages and Figure 6 for a bar graph of the number of inmates and their associated baseline ALT levels.

Table 6: Baseline ALT Levels among Inmates Treated

Baseline ALT Level		Number of Inmates	Percent	Valid Percent
Valid	< 20	4	1.1	1.3
	20 – 29	13	3.5	4.3
	30 - 39	22	5.9	7.3
	40 - 49	46	12.4	15.2
	50 - 59	28	7.6	9.3
	60 - 69	44	11.9	14.6
	70 - 79	30	8.1	9.9
	80 - 89	17	4.6	5.6
	90 - 99	13	3.5	4.3
	100 - 109	14	3.8	4.6
	110 - 119	8	2.2	2.6
	120 - 129	7	1.9	2.3
	130 - 139	6	1.6	2
	140 - 149	7	1.9	2.3
	150 - 159	2	0.5	0.7
	160 - 169	7	1.9	2.3
	170 - 179	2	0.5	0.7
	180 - 189	5	1.4	1.7
	190 - 199	6	1.6	2
	200 - 209	2	0.5	0.7
	210 - 219	6	1.6	2
	220 - 229	1	0.3	0.3
	230 - 239	1	0.3	0.3
	240 - 249	2	0.5	0.7
	> 249	9	2.4	3
	Total	302	81.6	100
Missing	Unknown	0	0	
	System	68	18.4	
	Total	68	18.4	
Total		370	100	

Figure 6: Distribution of ALT levels at the Start of Treatment



HCV Viral Load

Out of 370 inmates treated, 332 (89.7%) inmates had a documented baseline value for the level of HCV RNA in the blood. These values were measured in terms of International Units per milliliter (IU/mL). Baseline HCV RNA levels ranged from as low as 353 IU/mL to as high as 98,400,000 IU/mL. The average HCV RNA level was calculated around 2,363,344.53 IU/mL, whereas the median HCV RNA level was only 1,131,740 IU/mL.

Due to the large percentage of missing data, HCV RNA levels at 12 weeks, 24 weeks, and 48 weeks into treatment could not be assessed. However, results did show that inmates achieved an undetectable viral load (<615 IU/mL) as early as 12 weeks into treatment. Of the 232 inmates who had HCV RNA levels recorded beyond the baseline value, 178 (76.7%) of them achieved an undetectable viral load by the end of treatment. Not enough data was available to summarize the number of inmates who were able to attain a sustained virologic response.

Results regarding the frequency of undetectable HCV viral loads among inmates have been outlined in Table 7.

Table 7: Undetectable Viral Loads among Inmates Treated

Did Subject Have Undetectable HCV Viral Load?		Number of Inmates	Percent	Valid Percent
Valid	No	54	14.6	23.3
	Yes	178	48.1	76.7
	Total	232	62.7	100
Missing	Unknown	43	11.6	
	System	95	25.7	
	Total	138	37.3	
Total		370	100	

Correlation between HCV Genotype and Success of Treatment

Out of 370 inmates treated, 217 (58.6%) inmates had a documented HCV genotype as well as HCV RNA levels recorded beyond the baseline value. Of the 149 inmates infected with HCV genotype 1, 106 (71.1%) of them achieved an undetectable viral load (<615 IU/mL) by the end of treatment. Of the 68 inmates infected with HCV genotypes 2, 3, or 4, 62 (91.2%) of them were able to achieve a similar success in treatment with an undetectable viral load (<615 IU/mL). Statistical results regarding the correlation between HCV genotype and an inmate's ability to achieve an undetectable viral load (< 615 IU/mL) have been summarized in Table 8.

Table 8: The Effect of HCV Genotype on HCV Viral Loads

Did Subject Have Undetectable HCV Viral Load?		Genotype	
		Genotype 1	Genotype Other (2, 3, 4)
No	Number of Inmates	43	6
	Valid Percentage within Genotype	28.90%	8.80%
Yes	Number of Inmates	106	62
	Valid Percentage within Genotype	71.10%	91.20%
Total	Number of Inmates	149	68
	Valid Percentage within Genotype	100%	100%

HIV Co-infection

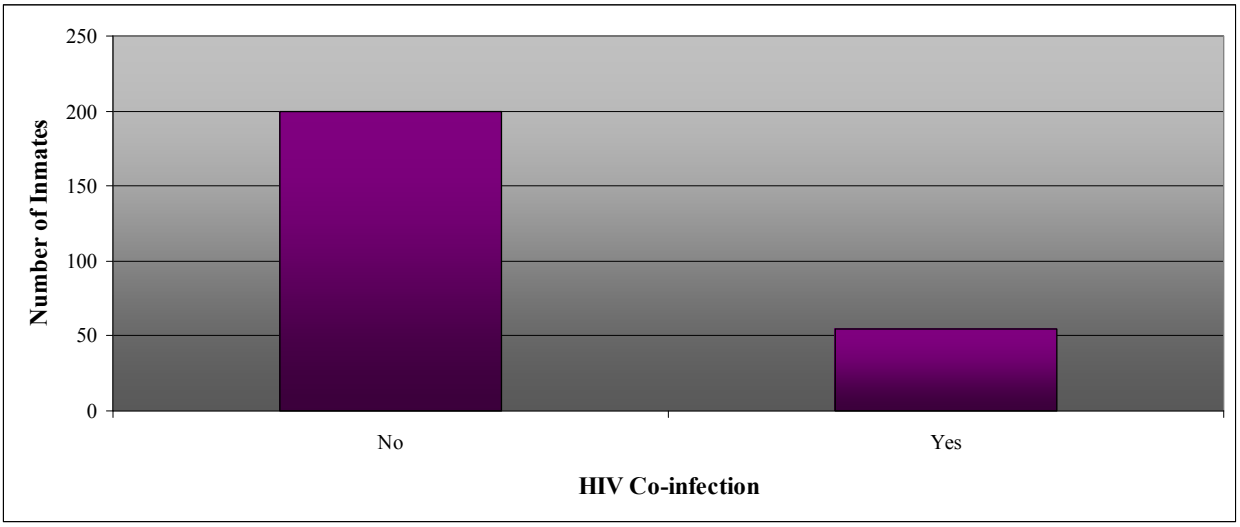
255 (68.9%) of the 370 inmates on HCV combination therapy had a documented HIV status. 200 (78.4%) were only mono-infected with HCV while 55 (21.6%) inmates

were co-infected with HIV. Table 9 lists the data involving the HIV co-infection status of inmates on HCV therapy. Figure 7 shows the frequency of patients who were either mono-infected with HCV or co-infected with HCV and HIV.

Table 9: Frequency and Percentage of Inmates Co-infected with HIV

Did Subject Have HIV Co-infection?		Number of Inmates	Percent	Valid Percent
Valid	No	200	54.1	78.4
	Yes	55	14.9	21.6
	Total	255	68.9	100
Missing	Unknown	81	21.9	
	System	34	9.2	
	Total	115	31.1	
Total		370	100	

Figure 7: Distribution of Inmates with HIV/HCV Co-infection



Correlation between HIV Co-infection and Success of Treatment

Out of the 370 inmates on combination therapy, only 165 (44.6%) inmates had a known HIV status and a recorded HCV viral load during or at the end of treatment. Despite the substantial amount of missing information, the recorded data between HIV status and treatment success was compared in an attempt to define any relationship between the two. Out of the 143 inmates who were only mono-infected with HCV, 116 (81.1%) had achieved an undetectable HCV viral load. Out of the 22 inmates who were co-infected with HIV, 12 (54.5%) had achieved an undetectable HCV viral load. Table 10 displays the cross-tabulation of data on whether or not the inmate was infected with HIV and whether or not he/she had reached undetectable HCV RNA levels.

Table 10: The Effect of HIV Co-infection on HCV Viral Loads

Did Subject Have Undetectable HCV Viral Load?		HIV Co-infection	
		No	Yes
No	Number of Inmates	27	10
	Valid Percentage within HIV Co-infection	18.90%	45.50%
Yes	Number of Inmates	116	12
	Valid Percentage within HIV Co-infection	81.10%	54.50%
Total	Number of Inmates	143	22
	Valid Percentage within HIV Co-infection	100%	100%

Treatment Interruptions

223 (60.3%) inmates had documented information on whether or not they had experienced any treatment interruptions. From this known data, 40 (17.9%) inmates did have treatment interruptions while 183 (82.1%) inmates did not. These values and percentages are organized in Table 11.

Table 11: Number of Inmates Who Experienced Treatment Interruptions

Did Subject have any Treatment Interruptions?		Number of Inmates	Percent	Valid Percent
Valid	No	183	49.5	82.1
	Yes	40	10.8	17.9
	Total	223	60.3	100
Missing	Unknown	1	0.3	
	System	146	39.5	
	Total	147	39.7	
Total		370	100	

Early Discontinuation of Treatment

From the total number of inmates on HCV combination therapy, 243 (65.7%) had recorded data on whether or not they had to stop treatment early. 137 (56.4%) inmates had prematurely terminated treatment while 106 (43.6%) inmates did not stop treatment early. Table 12 lists data regarding the amount of inmates who have discontinued treatment before they had completed a full course of therapy.

Table 12: Early Discontinuation of Treatment among Inmates

Was Treatment Stopped Early?		Number of Inmates	Percent	Valid Percent
Valid	No	106	28.6	43.6
	Yes	137	37	56.4
	Total	243	65.7	100
Missing	Unknown	6	1.6	
	System	121	32.7	
	Total	127	34.3	
Total		370	100	

Reasons for stopping treatment early was input in the database and can be classified into three main categories: poor virologic response to treatment, severe side effects and poor compliance with treatment. According to the protocol followed by MA correctional facilities, if the patient did not reach a 2 log reduction in HCV RNA viral load by the twelfth week into treatment, then that person was discontinued from therapy because he/she was not responding to the medications. Several inmates stopped treatment early for this reason.

As cautioned to the inmates before initiating therapy, HCV treatment may elicit several side effects. These side effects vary in degree and may be difficult to tolerate. Among the most common physical symptoms that were listed as reasons why treatment was stopped early are cotton wool spots, chest pain, rash, visual problems, back pain, and gastrointestinal problems including nausea, vomiting, and diarrhea. The mental health status of some inmates was also affected by the medications; other reasons for discontinuing treatment were anxiety, mood swings, agitation, and neurological symptoms including seizures and shakes. Other side effects which resulted in ending treatment early were anemia, and a decrease in hemoglobin, neutrophils and/or white blood cells. Experiencing severe side effects was the predominant category of reasons why treatment was terminated early.

Before beginning treatment, inmates were advised to avoid any high-risk behaviors as outlined in the "Inmate Treatment Agreement" form. Only a few inmates were recorded as having to end treatment early because of risky behaviors. These behaviors included getting a home-made tattoo, exhibiting maniac behavior, and having a "dirty" urine sample (testing positive for substance abuse) while on therapy. Several inmates also ended treatment early because they were released early from prison and therefore could not complete the full course of therapy.

Discussion

Over the past decade, hepatitis C has become an increasingly common occurrence in Massachusetts state correctional facilities. In a 2003 report by the Metro West Daily News, it was estimated that of the 10,000 inmates in the Massachusetts state prison system, 3,000 inmates were infected with hepatitis C, accounting for 30% of the male population and 40% of the female population (Hillman, 2003). In an effort to raise awareness of this growing epidemic and prevent the spread of hepatitis C within prisons and the society where many inmates will be released, hepatitis C treatment has become a standard in Massachusetts state correctional facilities. Since its initiation in 1999, over 500 inmates have received some form of treatment for an HCV infection.

In order to monitor the overall progress of treatment among inmates and assess the state of the treatment system in Massachusetts correctional facilities, the HCV database was created between 2004 and 2005 as a means to collect and organize information regarding the demographics, health, and treatment of inmates. In 2005, data on more than 200 inmates was collected and input into the database. By the end of this project, data on a total of 510 inmates was included in the database. This updated data was used to assess the current state of the treatment system as well as the condition of the HCV database. In terms of the treatment system, conclusions can be drawn from the results regarding the general characteristics of inmates who are receiving treatment in Massachusetts state correctional facilities and the overall response of inmates to treatment since the start of combination therapy in August 2002. Additional conclusions concerning the importance of the HCV database and ways in which it can potentially be improved can be made as well.

Characteristics

The characteristics of those inmates who were treated for hepatitis C were summarized according to five different categories. To start with, data collected on the locations of where inmates started treatment showed that a majority of HCV infected inmates were treated at Massachusetts Correctional Institution - Norfolk (78), Souza-Baranowski Correctional Center (71), and Massachusetts Correctional Institution – Shirley (66). A limited number of inmates received treatment at the Massachusetts Alcohol and Substance Abuse Center (2), Old Colony Correctional Center Min (3), Bridgewater State Hospital (4), and Massachusetts Correctional Institution - Plymouth (4). Factors which may have contributed to why certain facilities had more inmates treated than others include the populations within each facility, the percentage of inmates with long enough sentences to qualify for treatment, and the healthcare services and resources available at each facility. For example, with an average daily population of 1250 inmates, the Massachusetts Correctional Institution at Norfolk is the largest facility of its type in the Commonwealth of Massachusetts. In addition, about eighty-percent of the inmate population at the facility is serving time for violent crimes (Massachusetts Department of Correction, 2007). Based on the mere size of the facility and the percentage of inmates with long sentence times, it makes sense that Norfolk currently has the highest number of inmates who have been treated for HCV. The facility with the second highest frequency of inmates treated was Sousa Baranowski which is the state's newest correctional facility. It is a maximum security prison that offers a full range of educational, vocational, and substance abuse programming. The recent establishment of

this high security facility as well as the up-to-date healthcare program equally contributes to the high percentage of inmates receiving treatment. Massachusetts Correctional Institution-Shirley was the facility with the third highest frequency of inmates who were treated for HCV. This is likely due to the fact that MCI-Shirley Health Services Unit is fully staffed seven days a week and 24 hours a day. Healthcare includes services in the fields of medicine, dentistry, podiatry, optometry, mental health, psychiatry, psychology, and physical therapy. Inmates from all other Department of Correction facilities are transported as necessary to MCI-Shirley for these services (Massachusetts Department of Correction, 2007).

An analysis of the gender of inmates treated in Massachusetts correctional facilities showed that 96.5% of inmates treated were male while only 3.5% were female. These numbers were very consistent with the actual gender breakdown of the total inmate population in Massachusetts facilities. As of January 1, 2006, a survey from the Department of Corrections counted 8,802 males and 603 females, representing 94% and 6% of the inmate population, respectively (Massachusetts Department of Correction: Research and Planning Division, 2006). Besides the overall low percentage of female inmates in the Massachusetts facilities, it is important to note that the lower number of females receiving treatment can also be attributed to the fact that women often have shorter incarcerations, which exclude them from qualifying for the long course of HCV therapy (Carol Bova, personal communication).

According to the results regarding race/ethnicity of inmates, Caucasians were the most frequently treated race, accounting for 62.9% of all treated inmates with valid data. Hispanic/Latino and African Americans were nearly tied for the second highest race/ethnicity treated with valid percents of 18.5% and 17.7%, respectively. These values are only partially reflective of the breakdown of race amongst Massachusetts inmate populations. Between 1997 and 2006, the proportion of Caucasian inmates decreased from 48% in 1997 to 44% in 2006. The percentage of African American similarly decreased from 29% in 1997 to 27% in 2006. The percentage of Hispanic inmates was the only one to increase from 22% to 27% during this ten-year duration (Massachusetts Department of Correction: Research and Planning Division, 2006). Indeed, it is the Caucasian race that accounts for the majority of the inmate population as well as the inmates treated for HCV. However, a large disparity does exist between the high percentage of Caucasian inmates treated and the lower percentage of Caucasians within the entire inmate population. Likewise, the inmate population percentages of both Hispanics and African Americans are higher than the percentages of Hispanic and African American inmates treated for HCV. This particular data may serve as an incentive for management to reexamine treatment selection protocols. Ideally, knowing the number of inmates infected with HCV as well as the breakdown of their ethnicity would allow for a more direct display of any treatment selection bias. Unfortunately, information from the database only included information on the inmates who were selected for HCV treatment, not for all of the inmates who were infected with this virus, including those who did not apply or qualify for treatment, and the reasons for exclusion.

An analysis of the age at which inmates started treatment showed that the majority of individuals on HCV therapy began treatment in their mid thirties to late forties. The average age of inmates treated was 42.9 while the median was 43 years old. These numbers are fairly consistent with the average age of inmates among

Massachusetts correctional populations. According to the Department of Corrections survey, the median age of inmates has increased from 33 years in 1997 to 36 years in 2006. Similarly, the mean age of inmates has increased from 34 to 38 years during this ten year period. As of 2006, 39% of Massachusetts inmates are ages 40-64 while 31% are ages 30-39 (Massachusetts Department of Correction: Research and Planning Division, 2006). Because the ages of those inmates who started treatment ranged from as young as 22 to as high as 71 years old, age does not seem to influence HCV treatment eligibility.

Data collected on HCV genotype showed that the majority of inmates were infected with HCV genotype 1 (66.1%). 17.7% of Massachusetts inmates were infected with genotype 3, 11.6% of inmates was infected with genotype 2 and only 4.5% of inmates had genotype 4. At 66.1%, this high percentage of inmates infected with HCV genotype 1 directly correlates with the high prevalence of genotype 1 in the general public. It is believed that HCV genotype 1 accounts for around 70% of hepatitis C cases in the United States (NDDIC, 2006).

Treatment Outcomes

Since August 2002, combination therapy has become the standard form of treatment in Massachusetts state correctional facilities. To summarize the effects of this therapy on the outcome of treatment and to identify potential correlations between inmate characteristics and the success of treatment, various aspects of the treatment process were analyzed.

As a historical indicator of a potential HCV infection, baseline ALT levels were first analyzed to determine whether or not they accurately correlated with HCV infection among inmates. Alanine aminotransferase, or ALT, is an enzyme produced primarily by cells in the liver. In a normal, healthy individual, ALT levels in the blood tend to range between 0 and 40 IU/L; however, this range may vary depending upon the laboratory, gender, and biological make-up of an individual. When cells in the liver are damaged or die, ALT levels tend to increase in the blood. The amount of ALT does not necessarily correlate with the amount of damage to the liver, but it does signal that something may be wrong with the liver. In most individuals with hepatitis C, ALT levels are elevated at least slightly above normal. For approximately 30% of these individuals, though, ALT levels remain normal (Franciscus and Teeter, 2006).

According to the results, baseline ALT levels among inmates ranged from 12 IU/L to 627 IU/L, with the most frequent levels between 30 IU/L and 79 IU/L. The average ALT level was calculated around 90.26 IU/L; however, this value was slightly skewed as a result of the large range in ALT levels among inmates. The median value of 68 IU/L was a more accurate representation of the average baseline. Out of the 302 inmates represented in Table 6, only 43 inmates (14.2%) had baseline ALT levels in the suggested normal range of 0 IU/L to 40 IU/L. The majority of inmates (86%) had what would be considered elevated ALT levels (> 40 IU/L). Although there were a large percentage of inmates with significantly elevated ALT levels, this does not necessarily imply that ALT levels correspond with HCV infection and the potential severity of it. Many inmates may not have experienced elevated ALT levels at all, but rather, had a natural baseline ALT level outside of 40 IU/L. Studies have also shown that there is a poor correlation of ALT levels with disease progression in HCV (Carol Bova, personal

communication). The only accurate conclusion that can be drawn from these results is that ALT levels may be a fairly good indicator of an HCV infection, but they are not 100% accurate, and thus, should not be the only determinant of HCV infection. Additional tests, such as liver biopsies and HCV viral loads, should be performed to confirm whether or not liver damage is present and/or the HCV virus is present in the blood.

To evaluate the effects of treatment on baseline ALT levels, the original intent of this assessment was to look at changes in ALT levels over time. At 12 weeks and 24 weeks into treatment, reductions in ALT levels were expected to occur in direct correspondence with reductions in the level of HCV RNA in the blood. Unfortunately, there was not enough data to accurately assess ALT levels beyond the baseline measurement.

In order to determine the overall effectiveness of treatment among inmates, changes in the level of HCV RNA were assessed over time. Quantitative HCV RNA tests are used to measure the level of HCV RNA in the blood of an individual with hepatitis C. These tests do not indicate the severity of the disease or the level of damage to the liver, but they do give an exact measurement of the amount of virus in the blood. This value is most often referred to as the viral load. Prior to the start of treatment, quantitative tests are used to establish a baseline HCV RNA level (United States Department of Veterans Affairs, 2007). Values greater than 800,000 IU/mL are referred to as "high" viral loads, whereas values less than 800,000 IU/mL are referred to as "low" viral loads (Franciscus, 2006). These values are an important indication of whether or not patients will have a successful treatment as it is much more difficult to lower the level of virus in patients with "high" viral loads than patients with "low" viral loads (United States Department of Veterans Affairs, 2007).

According to the results of this study, baseline HCV RNA levels varied significantly among inmates, ranging from as low as 353 IU/mL to as high as 98,400,000 IU/mL. Because of the large range, the mean was calculated at a slightly skewed value of 2,363,344.53 IU/mL. It was more reasonable to consider the average baseline HCV RNA level around the slightly lower median value of 1,131,740 IU/mL. Of the inmates included in the aforementioned range of baseline HCV RNA levels, the majority had what would be considered "high" viral loads. Based on this data, no accurate conclusions can be drawn regarding the severity of HCV infection among inmates with higher HCV RNA levels, or whether or not there is any significance in the fact that most inmates had "high" viral loads. This data may, however, serve as an indicator for predicting which inmates have a considerably lower chance of responding well to treatment and achieving lower levels of virus within their system.

To assess the accuracy of this prediction, changes in HCV RNA levels needed to be measured over time. A patient responding well to treatment would achieve a 2-log reduction in the level of HCV RNA within 12 weeks. Unfortunately, there was not enough data to assess HCV RNA levels at 12 weeks, 24 weeks, or 48 weeks into treatment. The only factor which could accurately be assessed beyond baseline HCV RNA levels was the number of inmates who were able to successfully achieve an undetectable viral load. An undetectable viral load can be defined as the complete elimination of HCV RNA in the blood or a level of HCV RNA too low for a quantitative

assay to detect. In either case, an undetectable viral load is reported in labs as < 615 IU/mL (United States Department of Veterans Affairs, 2007).

Results showed that inmates were able to achieve undetectable viral loads (< 615 IU/mL) as early as 12 weeks into treatment. Success this early into treatment suggests that inmates either had "low" baseline viral loads or responded well to treatment as a result of health factors, viral characteristics, or overall good compliance. Of the 232 inmates with HCV RNA levels recorded beyond baseline, a total of 178 (76.7%) of them were able to achieve an undetectable viral load at least at some point during treatment. These numbers are a good indication that treatment was successful among most inmates during therapy. However, a completely successful treatment is measured in terms of a sustained virologic response. For most inmates, HCV RNA levels were not recorded beyond the end of therapy. Consequently, it could not be determined, based on the amount of available information, as to whether or not inmates who attained an undetectable viral load (< 615 IU/mL) during therapy were able to maintain the same level of virus six months later.

For those 54 (23.3%) inmates in Table 7 who were unable to achieve an undetectable viral load, a lack of success can be accounted for by a number of factors including "high" viral loads at the start of treatment, problems associated with the medication, or alternative health and viral aspects which may have hindered the inmate's response to treatment. Particular factors addressed in this project were HCV genotype, HIV co-infection, and problems associated with therapy.

An analysis was first conducted to determine whether or not HCV genotype had any effect on an inmate's ability to achieve an undetectable viral load (< 615 IU/mL). Studies have shown that variations in HCV genotype are an important indication of how a patient will respond to interferon therapy. HCV genotype 1 accounts for approximately 75% of HCV infections in the United States; however, patients infected with this genotype tend to have the most difficulty responding to interferon. Patients with genotypes 2 and 3, on the other hand, account for only 10 to 20 percent of cases in the United States and are the most likely to respond to interferon therapy (NDDIC, 2006). HCV infections caused by genotype 4 are rarely seen in the United States, but reports show that these patients have a similar difficulty in responding to interferon therapy as those infected with genotype 1 (Herrine, 2002). To account for these differences in HCV genotype and response to therapy, Massachusetts protocol requires that inmates with more problematic genotypes such as 1 and 4 receive a longer period of treatment. Whether or not this extension in treatment length actually helps inmates to achieve an undetectable viral load was the focus of the analysis.

According to the results, there were 217 inmates with a documented HCV genotype who also had recorded HCV RNA levels measured beyond the baseline value. Of the 149 inmates infected with HCV genotype 1, 106 (71.1%) were able to achieve an undetectable viral load (< 615 IU/mL) at some point during treatment. By comparison, 62 (91.2%) of the 68 inmates infected with HCV genotypes 2, 3, or 4, were able to achieve a similar HCV RNA level during treatment. Based on the shear number of inmates infected with each genotype, it is evident that the trends in HCV infection within prisons are accurately representative of the current trends in HCV infection throughout the United States. However, no definitive conclusions can be drawn as to whether or not genotype had any effect on the inmate's abilities to achieve undetectable viral loads (<

615 IU/mL). The percentages suggest that inmates with genotypes 2, 3, and 4 are more likely to achieve an undetectable viral load, but there was also a much smaller number of inmates infected with these genotypes than those infected with genotype 1. A larger set of inmates infected with genotypes 2, 3, or 4 could have caused a drastic change in the percentage that was able to achieve an undetectable viral load (< 615 IU/mL). All in all, there does not appear to be any significant correlation between HCV genotype and the success of treatment. Inmates infected with HCV genotypes 1 or 4 may not respond as well to interferon therapy, but alterations in the length of treatment seemed to help the majority of inmates achieve an undetectable viral load regardless of their genotype.

An additional factor which may account for the unsuccessful outcome of inmates in response to treatment is HIV co-infection. Like hepatitis C, HIV has been a long time problem in the prison system. In a 2003 report by the Metro West Daily News, it was estimated that of the 10,000 inmates in the Massachusetts state prison system, 300 inmates are HIV positive. Of these inmates, 70% are co-infected with HCV. This number accounts for 10% of the estimated 3,000 inmates infected with hepatitis C (Hillman, 2003). To determine whether or not this percentage was reflected in the number of inmates receiving treatment in Massachusetts state correctional facilities, the prevalence of HIV co-infection among inmates in the HCV database was assessed. Results showed that of the 255 inmates with a documented HIV status, 55 (21.6%) were HIV positive. This value represents a slightly higher percentage of inmates with an HCV/HIV co-infection than originally predicted in 2003, but this could be due to a number of factors including a lack of available data regarding HIV status, an increase in the number of inmates with an HCV/HIV co-infection in the Massachusetts prison system, or treatment preference. Under the Massachusetts protocol, inmates co-infected with HIV and HCV are moved to the top of the priority list regardless of when they were diagnosed. This preference, as well as the prevalence of HIV/HCV co-infection in Massachusetts state correctional facilities, is what is most likely reflected in the percentage of inmates who have an HIV co-infection and have received treatment since August 2002.

For most patients with an HIV co-infection, the severity of the HCV infection is amplified. Damage to the liver occurs more rapidly, HCV RNA levels in the blood are typically higher, and response to treatment is compromised. In fact, treatment for patients co-infected with HIV usually requires a much longer time period (6-12 months) and a number of extra precautions not necessarily taken in a normal therapy (CDC, 2005; CDC, 2007). For the inmates with an HIV co-infection in the HCV database, an analysis was conducted to determine whether or not HIV co-infection had any effect on an inmate's ability to achieve an undetectable viral load (< 615 IU/mL). According to the results, 165 inmates with a documented HIV status as well as HCV RNA levels recorded beyond the baseline value were taken into consideration. Of the 143 inmates infected with only HCV, 81.1% were able to achieve an undetectable viral load (< 615 IU/mL). This value is reflective of the results of the previous HCV RNA analysis and further confirms the effectiveness of combination therapy towards a successful treatment. By comparison, only 54.5% of the 22 inmates co-infected with HIV were able to achieve a similar undetectable viral load (< 615 IU/mL). These results suggest that an HIV co-infection at least slightly inhibits an inmate's ability to achieve an undetectable viral load. Out of 22 inmates, there were still a reasonable number of inmates that were able to

respond to treatment. The limited percentage is likely just a reflection of the complications caused by HIV co-infection during treatment. Further data would need to be collected in order to make any more definitive conclusions regarding the correlation between HIV co-infection and the success of treatment. However, based solely on these results, inmates with an HIV co-infection should not be excluded based on this health criterion, alone.

Besides HCV genotype and HIV co-infection, a major factor which may have contributed to the unsuccessful outcome of inmates in response to treatment is complications associated with combination therapy. In the current treatment system, complications are addressed by either a reduction in the dosage of medication or an entire discontinuation of treatment. The solution usually depends upon the nature and severity of the problem. To determine the extent to which these events have occurred since the start of combination therapy, treatment interruptions and early discontinuations in treatment were each individually assessed.

Treatment interruptions can be defined as brief periods of time in which treatment is altered in some manner. These are usually the result of side effects that require alterations in the dosage of medication or a movement between correctional facilities. Results from this study were based on the 233 inmates who had a documented indication of whether or not they had incurred an interruption during treatment. For 183 (82.1%) of these inmates, treatment was administered uninterrupted. This suggests that the majority of inmates either completed treatment successfully or discontinued treatment early as a result of a severe problem. For the remaining 40 (17.9%) inmates, at least one interruption was noted at some point during treatment. Most of these interruptions were recorded as changes in the dosage of interferon and/or ribavirin. Based on these results, it is evident that treatment interruptions were an uncommon occurrence for most inmates on combination therapy. There is no clear indication, however, as to whether or not inmates who experience interruptions in treatment still have the potential to complete treatment successfully or are more likely to cease treatment early. The only conclusion that can be drawn from this information is that for any given hepatitis C treatment, at least a few minor interruptions are to be expected. Medication dosages are not standard for every patient and may require slight variations depending upon individual responses.

Early discontinuation is normally advised for those inmates who experience more severe complications in response to therapy or have an inability to cooperate with treatment. Discontinuation of treatment is defined by a complete cessation in the administration of interferon and ribavirin. Like undetectable viral loads (< 615 IU/mL), the number of inmates who stop treatment early is a fair measure of the success of combination therapy among inmates. According to the results of this study, 243 inmates had a valid indication of whether or not their treatment was stopped early. For as many as 137 (56.4%) of these inmates, treatment was prematurely terminated. This was due primarily to complications with therapy, which appeared to be the most common reason for an inmate's inability to achieve an undetectable viral load (< 615 IU/mL). This data suggests that although combination therapy is successful among a large percentage of inmates, it is evidently just as problematic for a similar proportion of inmates. Because these results are based on a unique set of inmates with valid data, no reliable comparisons can be made between these results and those for the percentage of inmates who were able to achieve an undetectable viral load.

A qualitative assessment of the reasons for ending treatment early showed that termination for most inmates was the result of a specific, individual problem associated with therapy. Broad categories such as poor virologic response, severe side effects, and poor compliance with treatment were used to classify each specific problem and eliminate the large variation in data. The original intention of this assessment was to qualitatively as well as quantitatively analyze the frequency of each particular problem. An understanding of why most inmates are unable to achieve an undetectable viral load would not only contribute to the education of other inmates preparing for hepatitis C treatment, but it would help healthcare managers to prepare appropriately for any potential problem. Unfortunately, there was a limited amount of data from which accurate results or conclusions could be drawn.

Importance of Database

A hepatitis C treatment database is valuable tool for the collection, storage, and organization of an abundant amount of information. As a result of the data collected, demographic summaries can be periodically performed to characterize those inmates who are selected for HCV treatment. Specifically, this report has revealed a slight bias in the proportion of race/ethnicity of inmates who have been eligible for treatment. This finding was also revealed in the 2005 analysis of Massachusetts inmate demographics (Kelly, 2005). The managers of the HCV treatment program can use inmate characteristic summaries like these as a reference to minimize any intentional or unintentional bias which may be a product of the current screening/evaluation protocols and treatment qualifications.

In addition to inmate characteristics, data assessments regarding treatment response and outcomes can also provide direction for the improvement of Massachusetts correctional facility protocols for the management of hepatitis C. For example, as recently as 2005, the screening process for HCV treatment eligibility was different from the currently implemented system. At that time, elevated ALT levels (> 60 IU/L) were needed in order for an inmate to continue with the treatment evaluation process and get a liver biopsy (Kelly, 2005). However, it was later realized that many HCV infected African Americans would still have normal ALT levels (0-40 IU/L) even if they were seriously ill with HCV (Carol Bova, personal communication). As a result of this finding, alterations were made to the protocol in order to eliminate ALT eligibility requirements. Tests for HCV antibody and HCV RNA levels are now used to determine whether or not an inmate qualifies for a liver biopsy and possibly HCV therapy. This alteration will ideally minimize the exclusion of African Americans from treatment in Massachusetts correctional facilities. In this case, summaries of the demographics and outcomes of inmates revealed an issue which may have never been exposed or dealt with had their not been a system for collecting, organizing, and analyzing treatment data.

Beyond the actual process and management of the treatment system, data regarding treatment outcomes and response can serve as an important indicator of whether or not therapy is successful and whether or not this HCV treatment system is worth continuing. For instance, if only a small percentage of inmates were successfully responding to therapy, then it may be in the best interest of the Massachusetts correctional health system to invest their money and limited budget in the treatment and

care of other medical ailments. However, results from this study have shown that HCV treatment in Massachusetts correctional facilities has been very effective.

For inmates who are unable to respond successfully to treatment, data collection can only help to further improve healthcare facilities in prisons. Information regarding treatment complications such as poor response to therapy and medication side effects will keep the staff informed of common medical problems associated with HCV treatment and facilitate them in being more prepared and better equipped to help patients cope with difficult symptoms while on treatment. This information may also be used to help educate inmates on what to expect during treatment prior to the start of therapy.

Recommendations

One of the primary constraints of this project was the limited amount of available data. For all inmates, information was extracted directly from individual hepatitis C worksheets. Any areas that were left blank or had no indication of an unknown or non-applicable variable were correspondingly left blank in the database. These blank spaces were accumulatively referred to by SPSS as "missing system" data.

For most inmates, data was missing in at least one or two different fields. However, for an even larger proportion of inmates, data was missing in nearly every field. Variables such as sustained viral load measures and the inmate's history of substance abuse and health conditions were recorded for less than half the inmates included in the database. This factor not only affected the accuracy of the analyses performed for this project, but also limited the number of fields that could be assessed. In order to ensure the quality and reliability of the database as well the accuracy of statistical analyses based on information in the database, improvements must be made in the collection and recording of data.

One major problem that accounted for the majority of "missing system" data was the irregularity in data recording on the hepatitis C worksheets. Some HIV/Hepatitis C case managers indicated unknown and non-applicable fields on the worksheet with an N/A, an Ø, or a brief note. Other case managers simply left the areas blank with no indication as to whether or not information was unknown, missing, or not applicable. As a standard procedure for data collection, these blank fields were left blank in the database, but whether or not data was actually missing from these fields was unclear.

In order to avoid confusion and future issues like these, it would be ideal for all case managers to follow a standard protocol. This does not mean that data needs to be recorded in exactly the same way for every inmate, but it should be clear in every area of the hepatitis C worksheet as to whether or not data is known, unknown, missing, or not applicable. Regularity among the hepatitis C worksheets would potentially help to eliminate a large proportion of "missing system" data in the database, particularly in areas such as health conditions, mental health conditions, and history of substance abuse and alcohol abuse.

The only other major problem that accounted for "missing system" data and altered the outcome of many of the data analyses conducted for this project was the extent of missing lab results. For some inmates, lab results were extensive. Values were recorded in the hepatitis C worksheet for nearly every lab prior to the start of treatment and during treatment. For the majority of inmates, however, lab results were nearly

nonexistent. Baseline levels were recorded for the required labs, but few values were recorded beyond the start of treatment. In particular, HCV RNA levels 6 months following treatment were missing for nearly every inmate. Less than a quarter of them had any note of a sustained virologic response. The consequences of this missing data were noted primarily during this project in the inability to monitor treatment progress and success among inmates.

As a suggestion to improve the collection of lab data, specifically during and following treatment, the correctional health system may want to consider implementing a stricter data collection system. Any inmate who is receiving treatment for hepatitis C should be closely monitored both during treatment and six months following treatment. Case managers or other health care personnel within the individual facilities should help to ensure during this time that necessary labs are performed at the required times. Lab results recorded immediately following the lab will help to guarantee that data is not missing from the hepatitis C worksheet.

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Appendix A: Hepatitis C Worksheet

SITE: _____ **ID#:** _____

Hepatitis C Work Sheet (revised 3/05)

Name: _____ _____
Last First
DOB: ____/_____/_____ **AGE:** _____

Gender: Male ( ) Female ( ) **Race:** _____

Release Date: ___/___/___ Life ( )
Incarceration Date: ____/____/____
Time remaining in prison: _____ *Months*

D Report Information: _____

Ht: _____ **Wt:** _____ **WHC:** _____

HIV Positive: Yes ( ) No ( ) Unknown ( )
Antiretroviral Therapy: Yes ( ) No ( ) N/A ( )

Hep B Status: ( ) immune ( ) not immune
Hep B Labs: HBsAg ( ) pos ( ) neg
Anti-HBs ( ) pos ( ) neg
Anti-HBc ( ) pos ( ) neg

Hep A Status: ( ) immune ( ) not immune

Health Conditions (check all that apply)
Arthritis ( ) Cancer ( ) type: _____
Diabetes ( ) Hypertension( )
Asthma ( ) COPD ( )
GERD ( ) PPD + ( )
Other ( ) *Please list*: _____
_____ _____
_____ _____

Mental Health Conditions (check all that apply)
Depression ( ) PTSD ( )
Anxiety( ) Bipolar( )
Schizophrenia ( ) Personality Disorder ( )
OCD ( ) Other ( ) List: _____
_____

Current Medications (please list- include HIV meds):
_____
_____
_____.
_____

History of Substance Abuse? Yes ( ) No ( )
History of IV Drug Use? Yes ( ) No ( )
If yes, age at onset of IV drug use: _____
History of Alcohol Abuse? Yes ( ) No ( )
If yes, age of onset of heavy alcohol use: _____
> 5 drinks per day for how many years? _____

History of Prior HCV Treatment: ( ) YES ( ) No
Specify medications and date: _____
_____

HCV Genotype: _____
ABD US: ( ) Result: _____
Liver Biopsy: ( ) Grade: _____
Date: _____ Stage: _____
Steatosis: _____
Baseline HCV RNA: _____ Date: _____

DATE					
RESULT					
HCV RNA					
AFP					
ALT					
AST					
WBC					
Hgb					
HCT					
PLT					
Cholesterol					
Triglycerides					
F. Glucose					
Albumin					
INR					
CD4/CD4%					
HIV RNA					

Start Date: HCV Treatment: ____/_____/_____

HCV Medications[1] **Dose**
1. _____ _____
2. _____ _____

Stop Date: HCV Treatment: _____/____/_____
- Length of Treatment: _____ weeks
- Was Epogen used? Yes ( ) No ( )
- Was Neupogen used? Yes ( ) No ( )
- Any treatment interruptions? Yes ( ) No ( )
- Any dose reductions? Yes ( ) No ( )

If yes - reasons why: _____
- Was treatment stopped early? Yes ( ) No ( )

If yes, reason why: _____

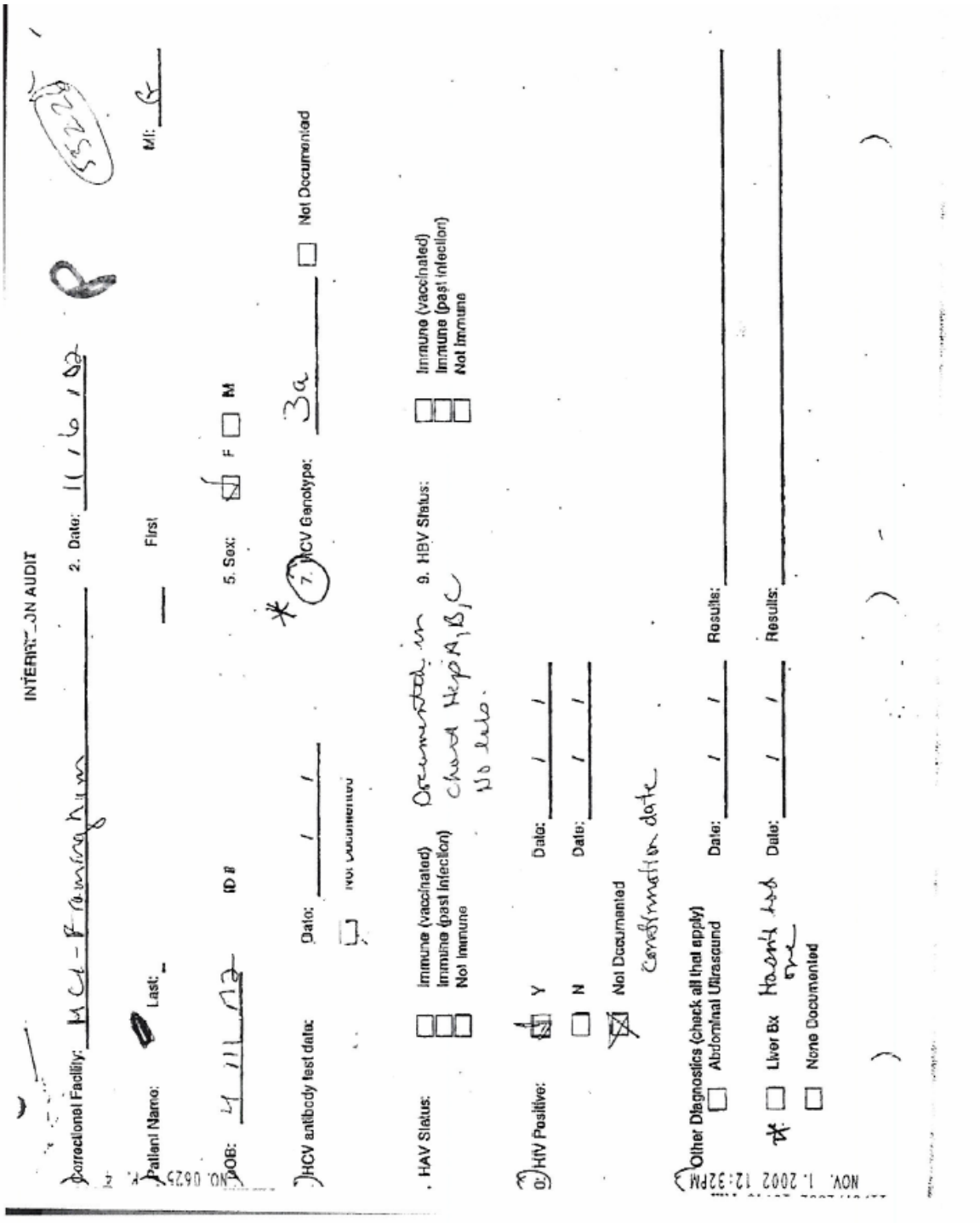
Interferon Adherence:
( ) Excellent (no missed doses)
( ) Good (only one dose per month missed < 80%)
( ) Poor (> one dose missed per month > 80% missed doses)

Ribavirin Adherence:
On average missed how many doses per month?
( ) None ( ) 7-9 missed doses
( ) 3 or fewer ( ) 10 or greater: specify_____
( ) 4-6 missed

[1] If med or dose changes – please list changes on back:

Appendix B: "Inmate Agreement" Form

Appendix C: Example of an Original Inmate Treatment Record



INTERFERON AUDIT

r each date identified, document the results of each lab test done.
VERY IMPT.
LT/AST and V.L.

	DATE		10-18-02	10-28-02	10-1-02						
	Result	10-31-02 187	SGOT	ALT 59							
nine Aminotransferase	ALT										
ha Feto Protein	AFP										
atitis C Viral Load	HCV-RNA										
V Viral Load	HIV VL	<50 <47									
V CD4 Count	CD4 ct										
V CD4 Percent	CD4 %										

TREATMENT

3.

Medication Regimen	Start Date	Stop Date	6mt post tx ALT	6mt post tx HCV VL
erferon 3 MU t.i.w.	/ /	/ /		
erferon 5 MU t.i.w.	/ /	/ /		
avirin 1,200 mg/day	/ /	/ /		
avirin 1,000 mg/day	/ /	/ /		
ylated Interferon-a2b (PEG-Intron)	12 / 17 / 02	1 / 30 / 03		
er:	/ /	/ /		

. INFO WOULD BE: Clinic notes + psyche comments, etc. (wrap up time)
DITIONAL COMMENTS: will be here until August 1 + see top sheets.

Appendix D: Copy of First Data Collection Form

DOC/HCV Data Collection Form

ID Number _____

Facility (at start of RX)
( ) Baystate (1)
( ) Bridgewater (2)
( ) Boston Pre Rel (3)
( ) Concord (4)
( ) Concord Farm (5)
( ) Framingham (6)
( ) Gardner (7)
( ) MASAC (8)
( ) Norfolk (9)
( ) OCCC (10)
( ) OCCC Min (11)
( ) Pondville (12)
( ) Plymouth (13)
( ) Shirley Med (14)
( ) S. Middlesex (15)
( ) Souza Baran. (16)
( ) Treatment Cent (17)
( ) Walpole (18)

Time remaining in prison: _____ (months)

HCV Treatment Start Date ____ ____ ____

Age _____ (years)

Height: _____ (inches)

Weight: _____ (lbs)

BMI[1]: _____

Gender
( ) Male (1)
( ) Female (2)
( ) Transgender (3)

[1] Short cut to calculate BMI - Step 1: Multiply weight (in pounds) by 703, Step 2: Multiply height (in inches) by height (in inches), Step 3: Divide the answer for step 1 by the answer in step 2, Step 4: round off to nearest number

Race/Ethnicity
( ) Caucasian (1)
( ) Black/African American (2)
( ) Hispanic/Latino (3)
( ) Native American (4)
( ) Asian (5)
( ) Other: _____ (6)

HCV Genotype _____

HCV RNA
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

Did subject achieve an undetectable HCV VL?
No ( ) (0)
Yes ( ) (1)
Unknown ( ) (8)

Did subject achieve a sustained virologic response?
No ( ) (0)
Yes ( ) (1)
Unknown ( ) (8)

ALT
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

Liver Biopsy Findings: _____

HIV Co-Infection:
( ) No (0)
( ) Yes (1)
( ) Unknown (8)

For HIV coinfected inmates please complete the following:

HIV RNA
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

CD4 cell count		Baseline: _____ Week 12: _____ Week 24: _____ Week 48: _____
	Other Date:	Week ( ): _____
CD4 %		Baseline: _____ Week 12: _____ Week 24: _____ Week 48: _____
	Other Date:	Week ( ): _____
HIV Antiretroviral Therapy		( ) None (0) ( ) Yes on treatment (1) ( ) Unknown (8)
	IF yes, specify	_____ _____ _____ _____
Were HIV medications changed while on HCV treatment?		( ) No (0) ( ) Yes (1) ( ) Don't Know (8)
	IF yes, reason:	_____ _____

Complete the following on everyone:

Hepatitis B status		( ) immune (1) ( ) active (2) ( ) not immune (3) ( ) unknown (8)
Hepatitis A status		( ) immune (1) ( ) not immune (2) ( ) unknown (8)
AFP		_____
WBC:		Baseline: _____ Week 12: _____ Week 24: _____ Week 48: _____
	Other Date:	Week ( ): _____
Hgb:		Baseline: _____

Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

HCT
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

PLT
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

Other Labs: _____
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____
Other Date: Week ( ): _____

Other Labs: _____
Baseline: _____
Week 12: _____
Week 24: _____
Week 48: _____

Other Health Conditions
( ) None (0)
( ) Yes (1)
( ) Unknown (8)

IF YES please check all that apply:

Arthritis	Yes ( ) (1)	No ( ) (0)
Cancer	Yes ( )	No ( )
Diabetes	Yes ( )	No ( )
Hypertension	Yes ( )	No ( )
Asthma/COPD	Yes ( )	No ( )
GERD	Yes ( )	No ( )
PPD +	Yes ( )	No ( )

Other (list): Yes ( ) No ( )

_____

_____

_____

_____

Medications at Baseline (list): (request med profile print- out and attach to data sheet for entry) ( ) Done

_____

_____

_____

_____

Mental Health Diagnoses ( ) No (0)
( ) Yes (1)
( ) Unknown (8)

If YES please check the following:

Depression	Yes ( ) (1)	No ( ) (0)
PTSD	Yes ( )	No ( )
Anxiety	Yes ( )	No ( )
Bipolar	Yes ( )	No ( )
Schizophrenia	Yes ( )	No ( )
Personality Dis	Yes ( )	No ( )
OCD	Yes ( )	No ( )
Other (list)	Yes ( )	No ( )

_____

_____

_____

_____

History of Substance Abuse ( ) No (0)
( ) Yes (1)
( ) Unknown (8)

History of Alcohol Abuse ( ) No (0)
( ) Yes (1)
( ) Unknown (8)

History of IV Drug Use ( ) No (0)
( ) Yes (1)
( ) Unknown (8)

If yes, onset of IV drug use: _____(year)
( ) unknown (88)

HCV Treatment Information

HCV Treatment Regimen:

Interferon alone ( ) (1)
Interferon plus Ribavirin ( ) (2)
Peg-Intron plus Ribavirin ( ) (3)
Pegasys plus Ribavirin ( ) (4)
Peg-Intron alone ( ) (5)
Pegasys alone ( ) (6)
Other ( ) (7) : _____
Unknown ( ) (8)

Length of Treatment

24 weeks ( ) (1)
48 weeks ( ) (2)
Other: ( ) (3) _____weeks
Unknown ( ) (8)

Any Treatment Interruptions? ( ) No (0)
( ) Yes (1)

If yes, specify reason: _____
_____
_____

Any does reductions? ( ) No (0)
( ) Yes (1)

IF yes, indicate med: ( ) interferon (1)
( ) Ribavirin (2)

Early Treatment Discontinuation? ( ) No (0)
( ) Yes (1)

If yes, Reason: ( ) poor virologic response (1)
( ) severe side effects (2)
Specify: _____
_____
_____
( ) poor compliance with RX (3)
( ) Other: specify below (4)
_____
_____
( ) Unknown (8)

Rate Treatment Adherence:

( ) Excellent (reported for Treatments) (1)
( ) Good – missed 1 or 2 (2)
( ) Fair – missed more than 2 But less than 5 (3)
( ) Poor – missed >5 (4)
( ) Unknown (8)

Was Epogen used
( ) No (0)
( ) Yes (1)
IF yes, specify length of time: _____
( ) Unknown (8)

Was Neupogen used?
( ) No (0)
( ) Yes (1)
IF yes, specify length of time: _____
( ) Unknown (8)

Treatment Limiting Side Effects:
Please list All side effects that resulted in a dose change or the need to interrupt or completely discontinue Hepatitis C Treatment

Side Effect	Week on Treatment	Management Strategy

Comments:

Data extracted by: _____ on _____
Initials Date

DOC Summary FY09

	July-08	August-08	Sep-08	October-08	Nov-08	Dec-08	Jan-09	Feb-09	Mar-09	Apr-09	May-09	Jun-09	TOTAL FY	AVG FY 09
Census	11424	11422	11419	11443	11335	11240	11237	11279	11289	11330	11,304	11,299	136,021	11,335
A. Medication Orders														
New	8,845	6,845	7,239	8,432	6,126	8,164	8,068	8,880	8,366	10,810	8,282	9,231	99,288	8,274
Refill (exception)	25,316	21,616	21,560	28,621	21,968	27,445	21,979	21,972	21,745	26,306	21,469	25,400	283,397	23,616
Total Orders	34,161	28,461	28,799	37,053	28,094	35,609	30,047	30,852	30,111	37,116	29,751	32,631	382,685	31,890
B. Medication Use														
# Inmates on medication	7,125	6,739	6,802	7,231	6,621	6,777	6,529	6,637	6,601	7,040	6,834	6,966	[redacted]	6,825
% Inmates on medication	62%	59%	60%	63%	58%	60%	58%	59%	58%	62%	60%	62%	[redacted]	60.2%
Medications/Inmate	3.0	2.5	2.5	3.2	2.5	3.2	2.7	2.7	2.7	3.3	2.6	2.9	[redacted]	3
Stock Orders	577	608	566	703	905	1182	549	545	585	660	554	771	[redacted]	684
% of Orders for Stock	1.7%	2.1%	2.0%	1.9%	3.2%	3.3%	1.8%	1.8%	1.9%	1.8%	1.9%	2.4%	[redacted]	2.1%
# Inmates on Non-Form	1,089	1,080	1,204	1,223	1,166	1,271	1,173	1,114	1,144	1,156	1,076	1,154	[redacted]	1,156
% of Orders Non-Form	3.2%	3.8%	4.2%	3.3%	4.2%	3.6%	3.9%	3.6%	3.8%	3.1%	3.6%	3.5%	[redacted]	3.7%
# Inmates on antidepressants	2,137	2,056	2,035	2,201	2,009	2,085	1,974	2,021	2,052	2,150	2,075	2,187	[redacted]	2,082
# Inmates on antipsychotics	1,190	1,048	1,085	1,108	949	984	955	956	941	985	908	986	[redacted]	1,006
# Inmates on Rebetron/Peglntr	75	79	80	74	77	74	75	90	91	93	88	60	[redacted]	81
** # Inmates on Controlled Subs	714	658	656	725	1,056	1,112	1,029	1,074	1,066	1,148	1,087	1,205	[redacted]	861
% Inmates on Controlled Subs	6.3%	5.8%	5.7%	6.3%	9.3%	9.9%	9.2%	9.5%	9.4%	10.1%	9.6%	10.7%	[redacted]	8.5%
C. Billing Composition														
Total Monthly Billing	$1,187,503.00	$999,006.63	992,918.87	$1,278,378.44	$792,673.53	$1,038,174.49	$882,059.05	$849,899.06	$790,565.35	$971,957.44	$818,246.46	$987,415.06	$11,488,797	$957,399.78
Billing per Inmate	$103.95	$87.46	$86.95	$111.72	$69.93	$92.37	$78.50	$75.35	$70.03	$85.79	$72.39	$87.54	$1,013	$84.41
Billing Non-Formulary	$304,485	$202,864	$202,865	$329,821	$267,097	$385,433	$312,093	$243,911	$258,053	$312,030	$251,208	$310,381	$3,380,241	$281,686.75
% Billing Non Formulary	25.6%	20.3%	20.4%	25.8%	33.7%	37.1%	35.4%	28.7%	32.6%	32.1%	30.7%	35.0%	[redacted]	29.8%
Billing HIV Meds	$415,634	$352,526	$338,131	$451,838	$267,122	$370,962	$369,517	$374,700	$323,179	$395,988	$351,091	$369,924	$4,380,612	$365,051.00
% Billing HIV Meds	35.0%	35.3%	34.1%	35.3%	33.7%	35.7%	41.9%	44.1%	40.9%	40.7%	42.9%	41.7%	[redacted]	38.4%
Billing Antipsych's	$311,488	$275,098	$278,756	$303,915	$191,550	$215,329	$146,731	$131,870	$121,465	$126,614	$101,831	$117,996	$2,322,643	$193,553.58
%Billing Antipsych's	26.2%	27.5%	28.1%	23.8%	24.2%	20.7%	16.6%	15.5%	15.4%	13.0%	12.4%	13.3%	[redacted]	19.7%
Billing Hep-C Meds.	$104,840	$83,345	$89,865	$88,306	$77,015	$81,629	$77,696	$91,657	$78,796	$111,631	$80,866	$72,839	$1,038,295	$86,524.58
% Billing Hep-C Meds	9%	8%	9%	7%	10%	8%	9%	11%	10%	11%	10%	8%	[redacted]	9.2%
Billing All Antidepressants	$35,850	$29,870	$31,685	$39,795	$21,551	$25,896	$20,689	$21,945	$23,084	$26,271	$23,662	$25,874	$329,182	$27,431.00
% Billing All Antidepressants	3%	3%	3%	3%	3%	2%	2%	3%	3%	3%	3%	3%	[redacted]	2.8%
	33 days			5 weeks		5 weeks				5 weeks		31 days		

	July-09	August-09	Sep-09	October-09	Nov-09	Dec-09	Jan-10	Feb-10	Mar-10	Apr-10	May-10	Jun-10	TOTAL FY
Census	11345	11300	11,305	11275	11229	11184	11188	11194	11195	11214	11,209	11,217	134,655
A. Medication Orders													
New	8,960	7,377	9,909	7,999	7,744	8,678	7,878	7,629	10,304	9,349	8,878	9,141	104,046
Refill (exception)	24,255	21,427	27,199	21,793	21,549	27,808	22,145	21,609	27,511	23,539	23,321	25,312	287,468
Total Orders	33,215	28,804	37,108	29,792	29,293	36,686	30,023	29,238	37,815	32,888	32,199	34,453	391,514
B. Medication Use													
# Inmates on medication	7,150	6,681	7,228	6,753	6,543	6,895	6,689	6,665	7,189	7,347	6,756	7,018	
% Inmates on medication	63%	59%	64%	60%	58%	62%	60%	60%	64%	66%	60%	63%	
Medications/inmate	2.9	2.5	3.3	2.6	2.6	3.3	2.7	2.6	3.4	2.9	2.9	3.1	
Stock Orders	627	545	623	545	572	549	495	505	790	552	597	613	
% of Orders for Stock	1.9%	1.9%	1.7%	1.8%	2.0%	1.5%	1.60%	1.7%	2.1%	1.7%	1.9%	1.8%	
# Inmates on Non-Form	1,242	1,185	1,270	1,131	1,127	1,229	1,203	1,204	1,409	1,335	1,304	1,312	
% of Orders Non-Form	3.7%	4.1%	3.4%	3.8%	3.8%	3.4%	4.00%	4.1%	3.7%	4.1%	4.0%	3.8%	
# Inmates on antidepressants	2,192	2,069	2,215	2,042	2,011	2,158	2,019	1,999	2,235	2,107	2,017	2,186	
# Inmates on antipsychotics	1,000	928	1,023	923	900	993	979	973	1,067	978	974	994	
# Inmates on Rebetron/PegIntron	82	84	84	77	70	68	64	66	65	58			
** # Inmates on Controlled Subs.	1,249	1,213	1,315	1,242	1,127	1,332	1,343	1,263	1,386	1,339	1,264	1,310	
% Inmates on Controlled Subs.	11.0%	10.7%	11.6%	11.0%	10.0%	11.9%	12.00%	11.3%	12.4%	11.9%	11.3%	11.7%	
C. Billing Composition													
Total Monthly Billing	$900,812.12	$751,590.13	$961,411.31	772,484.88	$724,279.96	$960,209.02	$754,911.15	$767,182.00	$987,877.00	$740,688.74	$751,999.60	$877,137.00	$9,950,583
Billing per Inmate	$79.40	$66.51	$85.04	$68.51	$64.50	$85.86	$67.48	$68.54	$88.24	$66.05	$67.09	$78.20	
Billing Non-Formulary	$287,606	$247,988	$317,760	$243,384	$249,762	$310,107	$257,042	$276,588	$356,741	$276,175	$278,237	$324,763	$3,426,153
% Billing Non-Formulary	31.9%	33.0%	33.1%	31.5%	34.5%	32.3%	34.00%	36.1%	36.1%	37.3%	37.0%	37.0%	
Billing HIV Meds	$395,430	$335,940	$427,335	$320,950	$316,074	$435,677	$313,690	$331,587	$413,444	$330,155	$324,375	$367,455	$4,312,112
% Billing HIV Meds	43.9%	44.7%	44.4%	41.5%	43.6%	45.4%	41.60%	43.2%	41.9%	44.6%	43.1%	41.9%	
Billing Antipsych's	$102,755	$91,521	$114,649	$88,059	$84,496	$108,745	$92,740	$100,243	$118,058	$90,728	$95,124	$106,007	$1,193,126
%Billing Antipsych's	11.4%	12.2%	11.9%	11.4%	11.7%	11.3%	12.30%	13.1%	12.0%	12.2%	12.6%	12.1%	
Billing Hep-C Meds.	$78,197	$62,825	$69,319	$75,152	$51,721	$83,850	$48,189	$38,079	$59,562	$48,858	$45,693	$62,442	$723,887
% Billing Hep-C Meds	9%	8%	7%	10%	7%	9%	6%	5%	6%	7%	6%	7%	
Billing All Antidepressants	$31,512	$27,278	$34,528	$30,227	$30,041	$39,362	$31,273	$32,334	$39,081	$29,481	$27,202	$27,978	$380,297
% Billing All Antidepressants	3%	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%	3%	
	32 days		***5 weeks***			***5 weeks***			*5 weeks* $12,000 error to be reflected next month (combivent)*			***32 days***	

	July-10	August-10	Sep-10	October-10	Nov-10	Dec-10	Jan-11	Feb-11	Mar-11	Apr-11	May-11	Jun-11	TOTAL FY 11
Census	11,217	11239	11,180	11215	11182	11143	11,127	11,235	11344	11370	11,428	11495	123,680
New Admissions	632	628	674										
A. Medication Orders													
New	8,955	7,682	9,777	8,067	7,373	8,378	7,344	7,561	9,599	7,046	7,402	8,329	97,513
Refill (exception)	24,157	21,984	27,167	21,853	21,778	27,129	22,140	22,475	27,850	29,708	23,091	26,540	295,872
Total Orders	33,112	29,666	36,944	29,920	29,151	35,507	29,484	30,036	37,449	36,754	30,493	34,869	393,385
B. Medication Use													
# Inmates on medication	6,926	6,722	7,068	6,739	6,672	6,970	6,696	6,702	7,209	6,735	6,964	7,266	
% Inmates on medication	62%	60%	63%	60%	60%	63%	60%	60%	64%	59%	61%	65%	
Medications/inmate	3.0	2.6	3.3	2.7	2.6	3.2	2.6	2.7	3.3	3.2	2.7	3.0	
Stock Orders	682	651	699	627	611	601	538	591	814	567	584	722	
% of Orders for Stock	2.1%	2.2%	1.9%	2.1%	2.1%	1.7%	1.8%	2.0%	2.2%	1.5%	1.9%	2.1%	
# Inmates on Non-Form	1,297	1,509	1,590	1,454	1,469	1,597	1,485	1,676	1,823	1,530	1,660	1,700	
% of Orders Non-Form	3.9%	5.1%	4.3%	4.9%	5.0%	4.5%	5.0%	5.6%	4.9%	4.2%	5.4%	4.9%	
# Inmates on antidepressants	2,153	2,098	2,234	2,017	2,065	2,172	2,096	2,121	2,324	2,114	2,161	2,295	
# Inmates on antipsychotics	1,023	970	905	828	551	576	938	550	1,105	956	1,005	1,010	
# Inmates on Rebetron/Peglntron	n/a	52	52	49	51	50	52	53	54	58	59	61	
** # Inmates on Controlled Subs.	1,269	1,227	1,240	1,056	990	1,129	1,083	1,107	1,179	1,029	1,071	1,106	
% Inmates on Controlled Subs.	11.3%	10.9%	11.1%	9.4%	8.9%	10.1%	9.7%	9.9%	10.4%	9.1%	9.4%	9.9%	
C. Billing Composition													
Total Monthly Billing	$862,595.00	$744,672.37	$986,900.28	$777,331.60	$725,658.41	$913,538.00	$762,025.00	$765,788.00	$996,576.00	$792,825.00	$810,320.68	$ 890,622.95	$10,028,853
Billing per Inmate	$76.90	$66.26	$88.27	$69.31	$64.90	$81.98	$68.48	$68.16	$87.85	$69.73	$70.91	$77.48	
Billing Non-Formulary	$319,207	$284,119	$347,336	$274,773	$270,758	$355,633	$306,158	$296,762	$402,918	$300,358	$331,298	$340,869	$3,830,189
% Billing Non-Formulary	37.0%	38.2%	35.2%	35.3%	37.3%	38.9%	40.2%	38.8%	40.4%	37.9%	40.9%	38.3%	
Billing HIV Meds	$386,237	$329,675	$424,867	$340,438	$343,857	$387,543	$330,125	$343,146	$413,088	$340,416	$341,086	$373,100	$4,353,578
% Billing HIV Meds	44.8%	44.3%	43.1%	43.8%	47.4%	42.4%	43.3%	44.8%	41.5%	42.9%	42.1%	41.9%	
Billing Antipsych's	$105,159	$89,936	$111,602	$76,541	$70,762	$91,980	$91,602	$77,635	$114,933	$85,996	$99,086	$105,642	$1,120,874
%Billing Antipsych's	12.2%	12.1%	11.3%	9.8%	9.8%	10.1%	12.0%	10.1%	11.5%	10.8%	12.2%	11.9%	
Billing Hep-C Meds.	$40,597	$47,949	$46,022	$48,735	$45,639	$40,048	$34,030	$49,254	$54,745	$42,347	$49,867	$65,983	$565,216
% Billing Hep-C Meds	5%	6%	5%	6%	6%	4%	4%	6%	5%	5%	6%	7%	
Billing All Antidepressants	$26,607	$23,289	$33,508	$24,508	$22,350	$24,129	$20,675	$19,127	$22,361	$17,319	$17,511	$26,064	$277,448
% Billing All Antidepressants	3%	3%	3%	3%	3%	3%	3%	2%	2%	2%	2%	3%	
	31 days		*5 weeks*			*5 weeks*			*5 weeks*			*33 days*	

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FY 2012	July-11	August-11	Sep-11	October-11	Nov-11	Dec-11	Jan-12	Feb-12	Mar-12	Apr-12	May-12	Jun-12	TOTAL FY 12
Census	11,572	11,523	11,490	11,502	11,470	11,456	11,501	11,545	11,592	11,630	11,614	11,624	138,519
New Admissions	UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK	UNK	0
A. Medication Orders													
New	6,890	8,043	6,503	7,427	7,911	7,622	6,977	9,094	7,415	6,844	8,906	10,837	90,469
Refill (exception)	23,898	28,069	21,993	23,726	24,050	20,850	21,310	27,077	22,213	22,934	28,613	26,196	270,929
Total Orders	30,788	36,112	28,496	31,153	31,961	28,472	28,287	36,171	29,628	29,778	37,519	37,033	361,398
B. Medication Use													
# Inmates on medication	6,981	7,206	6,835	6,707	7,124	6,719	6,679	7,263	6,832	6,917	7,497	7,058	
% Inmates on medication	60%	63%	59%	58%	62%	59%	58%	63%	59%	59%	65%	61%	
Medications/inmate	2.7	3.1	2.5	2.7	2.8	2.5	2.5	3.1	2.6	2.6	3.2	3.2	
Stock Orders	606	685	552	611	761	902	984	1295	1132	1027	1626	893	
% of Orders for Stock	2.0%	1.9%	1.9%	2.0%	2.4%	3.2%	3.5%	3.6%	3.8%	3.4%	4.3%	2.4%	
# Inmates on Non-Form	1,550	1,673	1,458	1,689	1,015	1,932	1,745	1,772	1,502	1,499	1,688	1,551	
% of Orders Non-Form	5.0%	4.6%	5.1%	5.4%	3.2%	6.8%	6.2%	4.9%	5.1%	5.0%	4.5%	4.2%	
# Inmates on antidepressants	2,256	2,325	2,132	2,082	2,199	2,132	1,935	2,152	1,952	1,968	2,707	2,864	
# Inmates on antipsychotics	567	594	976	905	1,015	839	981	1,066	938	923	1,161	1,347	
# Inmates on Rebetron/PegIntron	59	55	55	55	50	49	47	45	UNK	47	45	45	
# Inmates on Controlled Subs.	1,024	1,080	1,236	931	1,219	937	889	807	1,033	407	496	432	
% Inmates on Controlled Subs.	8.8%	9.4%	10.8%	8.1%	10.6%	8.2%	7.7%	7.0%	8.9%	3.5%	4.3%	3.7%	
C. Billing Composition													
Total Monthly Billing	$890,621.19	$1,039,223.38	$785,906.61	$837,832.43	$1,043,981.14	$809,538.60	$831,035.31	$1,077,427.65	$861,083.55	$261,108.24	$972,916.24	$ 811,059.53	$10,221,734
Billing per Inmate	$76.96	$90.19	$68.40	$72.84	$91.02	$70.67	$72.26	$93.32	$74.28	$22.45	$83.77	$69.77	
Cost Per Patient Day	$2.57	$2.58	$2.44	$2.60	$2.60	$2.52	$2.58	$2.67	$2.65	$0.80	$2.39	$2.49	
Billing Non-Formulary	$360,159	$437,145	$329,716	$363,427	$448,595	$373,902	$330,619	$432,467	$346,086	$331,697	$357,136	$291,514	$4,402,462
% Billing Non-Formulary	40.4%	42.1%	42.0%	43.4%	43.0%	46.2%	39.8%	40.1%	40.2%	127.0%	36.7%	35.9%	
Billing HIV Meds	$378,028	$424,392	$332,076	$344,668	$426,223	$348,646	$369,728	$433,330	$339,803	$385,573	$457,276	$362,391	$4,601,135
% Billing HIV Meds	42.4%	40.8%	42.3%	41.1%	40.8%	43.1%	44.5%	40.2%	39.5%	147.7%	47.0%	44.7%	
Billing Antipsychotics	$91,939	$108,217	$99,016	$100,230	$107,158	$85,013	$92,889	$110,378	$84,763	$61,890	$62,407	$62,959	$1,066,959
% Billing Antipsychotics	10.3%	10.4%	12.6%	12.0%	10.3%	10.5%	11.2%	10.2%	9.8%	23.7%	6.4%	7.8%	
Billing Hep-C Meds.	$42,234	$63,642	$44,727	$46,519	$65,311	$41,802	$36,786	$63,029	$67,676	$48,918	$54,344	$51,762	$626,781
% Billing Hep-C Meds	4.7%	6.1%	5.7%	5.6%	6.3%	5.2%	4.4%	5.8%	7.9%	18.7%	5.6%	6.4%	
Billing All Antidepressants	$27,298	$28,108	$20,571	$18,173	$20,927	$14,462	$13,601	$16,986	$12,936	$13,780	$15,564	$12,622	$214,047
% Billing All Antidepressants	3.1%	2.7%	2.6%	2.2%	2.0%	1.8%	1.6%	1.6%	1.5%	5.3%	1.6%	1.6%	
Weeks Per Fiscal Month	4 weeks	5 weeks	4 weeks	4 weeks	5 weeks	4 weeks	4 weeks	5 weeks	4 weeks	4 weeks	5 weeks	4 weeks	

DOC Summary - FY 2013	July	August	September	October	November	December	January	February	March	April	May	June	FY 2013 - AVG
Census	11,682	11,654	11,558	11,415	11,180	11,089	11,053	11,041	10,988	10,949	10,881	10,836	*11,194*

Medication Orders	July	August	September	October	November	December	January	February	March	April	May	June	FY 2013 - AVG
New	8,150	10,734	8,301	9,770	7,728	9,605	10,126	7,641	8,135	7,723	10,098	7,736	*8,812*
Refill (exception)	26,090	29,570	23,525	28,747	21,415	21,315	27,778	22,189	22,525	23,137	27,627	23,213	*24,761*
Total Orders	**34,240**	**40,304**	**31,826**	**38,517**	**29,143**	**30,920**	**37,904**	**29,830**	**30,660**	**30,860**	**37,725**	**30,949**	*33,573*

Medication Use	July	August	September	October	November	December	January	February	March	April	May	June	FY 2013 - AVG
# Inmates on medication	6,550	7,315	6,932	7,266	6,592	6,498	7,024	6,483	6,566	6,627	7,038	6,578	*6,789*
% Inmates on medication	56%	63%	60%	64%	59%	59%	64%	59%	60%	61%	65%	61%	*61%*
Medications/inmate	2.9	3.5	2.8	3.4	2.6	2.8	3.4	2.7	2.8	2.8	3.5	2.9	*3.0*
Stock Orders	1052	1010	893	1011	799	692	910	836	697	592	899	794	*849*
% of Orders for Stock	3.1%	2.5%	2.8%	2.6%	2.7%	2.2%	2.4%	2.8%	2.3%	1.9%	2.4%	2.6%	*2.5%*
# Inmates on Non-Form	1,470	1,585	1,424	1,527	1,325	1,339	1,484	1,324	1,281	1,241	924	1,205	*1,344*
% of Orders Non-Form	4.3%	3.9%	4.5%	4.0%	4.5%	4.3%	3.9%	4.4%	4.2%	4.0%	2.4%	3.9%	*4.0%*
# Inmates on antidepressants	1,983	2,167	2,064	2,206	1,970	1,978	2,189	1,953	2,008	2,047	2,169	1,974	*2,059*
# Inmates on antipsychotics	973	902	805	881	770	773	830	761	766	756	826	764	*817*
# Inmates on Rebetron/Peglintron	38	39	37	35	29	28	25	27	21	24	26	24	*29*
# Inmates on Controlled Subs.	408	446	393	377	264	261	271	273	252	256	270	219	*308*
% Inmates on Controlled Subs.	3.5%	3.8%	3.4%	3.3%	2.4%	2.4%	2.5%	2.5%	2.3%	2.3%	2.5%	2.0%	*2.7%*

Billing Composition	July	August	September	October	November	December	January	February	March	April	May	June	FY 2013 - AVG
Total Monthly Billing	$802,176.81	$972,850.68	$783,006.39	$961,558.62	$766,039.52	$767,585.28	$902,347.11	$726,348.97	$769,386.19	$780,721.87	$1,036,197.72	$ 861,632.51	*$844,246*
Billing per Inmate	$68.67	$83.48	$67.75	$84.25	$68.52	$69.22	$81.64	$65.97	$69.93	$71.31	$95.23	$79.52	*$75*
Cost Per Patient Day	$2.45	$2.39	$2.42	$2.41	$2.45	$2.47	$2.33	$2.36	$2.50	$2.55	$2.72	$2.74	*$2.48*
Billing Non-Formulary	$287,657.56	$341,530.19	$254,063.02	$327,497	$310,699.44	$275,084	$302,556.34	$239,331.91	$281,779.54	$303,744.53	$379,589.26	$335,669.14	*$303,267*
% Billing Non-Formulary	35.9%	35.1%	32.4%	34.1%	40.6%	35.8%	33.5%	32.9%	36.7%	38.9%	36.6%	39.0%	*36%*
Billing HIV Meds	$360,724.97	$430,548.33	$343,914.09	$422,192.20	$360,054.83	$339,158.88	$412,178.44	$333,338.27	$324,905.51	$325,913.11	$420,813.91	$333,648.41	*$367,283*
% Billing HIV Meds	45.0%	44.3%	43.9%	43.9%	47.0%	44.2%	45.7%	45.8%	42.3%	41.7%	40.6%	38.7%	*44%*
Billing Antipsychotics	$63,809.80	$65,724.40	$54,388.57	$63,255.90	$44,678.65	$55,721.87	$65,155.19	$47,264.90	$49,833.89	$54,391.14	$79,496.48	$69,494.44	*$59,435*
% Billing Antipsychotics	8.0%	6.8%	6.9%	6.6%	5.8%	7.3%	7.2%	6.5%	6.5%	7.0%	7.7%	8.1%	*7%*
Billing Hep-C Meds	$38,356.42	$38,146.16	$27,834.87	$30,691.10	$33,942.37	$23,916.80	$22,518.290	$26,032.07	$44,070.89	$51,882.10	$73,711.40	$71,725.20	*$40,236*
% Billing Hep-C Meds	4.8%	3.9%	3.6%	3.2%	4.4%	3.1%	2.5%	3.6%	5.7%	6.6%	7.1%	8.3%	*5%*
Billing All Antidepressants	$12,958	$16,428	$14,734	$18,160	$14,081	$15,261	$19,233	$14,163.43	$15,093	$15,551.9	$18,015.63	$14,489.34	*$15,681*
% Billing All Antidepressants	1.6%	1.7%	1.9%	1.9%	1.8%	2.0%	2.1%	1.9%	2.0%	2.0%	1.7%	1.7%	*2%*
Weeks Per Fiscal Month	**4**	**5**	**4**	**5**	**4**	**4**	**5**	**4**	**4**	**4**	**5**	**4+1day**	
# Days per Fiscal Month	**28**	**35**	**28**	**35**	**28**	**28**	**35**	**28**	**28**	**28**	**35**	**29**	

*Note: At the time of reporting, the number of patients taking Hep-C medications was unavailable.

Census	July	August	September	October	November	December	January	February	March	April*	May	June	FY 2014 - YTD TTL
Census	10,803	10,758	10,729	10,712	10,638	10,561	10,623	10,639	10,613	10,591	10,553	10,551	127,771

Medication Orders	July	August	September	October	November	December	January	February	March	April	May	June	FY 2014 - YTD TTL
New	6,377	9,312	7,387	9,576	8,863	6,553	7,791	6,195	6,694	6,828	9,247	7,920	92,743
Refill (exception)	21,296	27,421	22,564	27,768	26,259	21,447	28,068	23,062	30,331	24,505	30,328	24,780	307,829
Total Orders	27,673	36,733	29,951	37,344	35,122	28,000	35,859	29,257	37,025	31,333	39,575	32,700	400,572

Medication Use	July	August	September	October	November	December	January	February	March	April	May	June	FY 2014 - YTD TTL
# Patients on medication	6,447	6,977	6,556	6,402	6,776	6,208	6,816	6,424	6,515	6,459	6,911	6,694	79,185
% Patients on medication	60%	65%	61%	60%	64%	59%	64%	60%	61%	61%	65%	63%	62%
Medications/patient	2.8	3.4	2.8	3.5	3.3	2.7	3.4	2.7	3.5	3.0	3.8	3.1	3.1
# Patients on antipsychotics	742	820	748	699	801	716	777	732	757	728	778	729	9,027
% Patients on antipsychotics	6.87%	7.62%	6.97%	6.53%	7.53%	6.76%	7.31%	6.88%	7.13%	6.87%	7.37%	6.91%	7.06%
# Patients on Hep-C medication	21	20	21	20	23	11	12	13	13	12	11	11	188
# Patients on HIV medication	154	174	153	159	173	152	165	144	160	158	165	156	1,913

Nonformulary Requests	July	August	September	October	November	December	January	February	March	April	May	June	FY 2014 - YTD TTL
# Nonformulary requests	357	288	237	291	264	285	295	268	309	345	384	363	3,686
# Approved requests (%)	285 (80%)	214 (74%)	182 (77%)	231 (79%)	214 (81%)	243 (85%)	241 (82%)	212 (79%)	246 (80%)	265 (77%)	307 (80%)	299 (82%)	2939 (80%)
# Denied requests (%)	72 (20%)	74 (26%)	55 (23%)	60 (21%)	50 (19%)	42 (15%)	54 (18%)	56 (21%)	63 (20%)	80 (23%)	77 (20%)	64 (18%)	747 (20%)
Medical approved requests # (%)	227 (77%)	184 (73%)	139 (73%)	172 (75%)	175 (80%)	199 (84%)	217 (81%)	167 (78%)	217 (78%)	229 (74%)	267 (78%)	268 (81%)	2461 (78%)
Medical denied requests # (%)	66 (23%)	68 (27%)	52 (27%)	58 (25%)	43 (20%)	37 (16%)	52 (19%)	47 (22%)	63 (22%)	79 (26%)	75 (22%)	64 (19%)	704 (22%)
Psych approved requests # (%)	58 (91%)	30 (83%)	43 (93%)	59 (97%)	39 (85%)	44 (90%)	24 (92%)	45 (83%)	25 (86%)	36 (97%)	40 (95%)	31 (100%)	474 (91%)
Psych denied requests # (%)	6 (9%)	6 (17%)	3 (7%)	2 (3%)	7 (15%)	5 (10%)	2 (8%)	9 (17%)	4 (14%)	1 (3%)	2 (5%)	0 (0%)	47 (9%)

Billing Composition	July	August	September	October	November	December	January	February	March	April	May	June	FY 2014 - YTD TTL
Total Monthly Utilization	$778,838.08	$1,052,083.00	$847,600.24	$872,180.50	$1,053,899.41	$822,171.89	$1,115,677.77	$839,919.76	$837,155.76	$866,352.68	$1,141,534.89	$982,549.64	$11,209,963.62
Total Monthly Return & Reuse	$26,695.94	$42,738.48	$63,117.54	$31,951.02	$56,794.80	$69,363.98	$52,985.80	$50,813.34	$60,772.75	$61,640.90	$70,672.08	$83,088.88	$670,635.51
Monthly Billing Grand Total	$752,142.14	$1,009,344.52	$784,482.70	$840,229.48	$997,104.61	$752,807.91	$1,062,691.97	$789,106.42	$776,383.01	$804,711.78	$1,070,862.81	$899,460.76	$10,539,328.11
Billing/patient	$69.62	$93.82	$73.12	$78.44	$93.73	$71.28	$100.04	$74.17	$73.15	$75.98	$101.47	$85.25	$82.49
Billing HIV Meds	$296,974.00	$389,774.23	$311,710.72	$338,651.64	$400,456.67	$302,519.80	$433,574.60	$314,121.01	$329,078.70	$331,907.19	$435,958.38	$363,544.94	$4,248,272.08
Billing Hep-C Meds	$56,145.81	$90,073.13	$84,352.71	$84,059.80	$90,420.28	$78,399.68	$71,066.920	$45,828.36	$46,485.65	$59,349.95	$71,203.63	$53,845.96	$831,231.88
Weeks Per Fiscal Month	4	5	4	4	5	4	5	4	4	4	5	4+2	
# Days per Fiscal Month	28	35	28	28	35	28	35	28	28	28	35	30	

Census	July	August	September	October*	November	December	January	February	March	April*	May	June	FY 2015 - YTD TTL
Census	10,493	10,449	10,451	10,451	10,395	10,375	10,379	10,276					83,269

*At the time of report submission, the DOC October census was not available; census for September was used.

Medication Orders	July	August	September	October	November	December	January	February	March	April	May	June	FY 2015 - YTD TTL
New	8,172	7,625	6,476	7,678	5,813	7,636	6,201	5,648					55,249
Refill (exception)	27,669	23,694	25,262	30,119	28,938	29,350	24,489	23,900					213,421
Total Orders	35,841	31,319	31,738	37,797	34,751	36,986	30,690	29,548					268,670

Medication Use	July	August	September	October	November	December	January	February*	March	April	May	June	FY 2015 - YTD TTL
# Patients on medication	6,740	6,494	6,498	6,755	6,331	6,752	6,313	6,178					52,061
% Patients on medication	64%	62%	62%	65%	61%	65%	61%	60%					63%
Medications/patient	3.4	3.0	3.0	3.6	3.3	3.6	3.0	2.9					3.2
# Patients on antipsychotics	771	742	732	855	753	823	782	696					6,154
% Patients on antipsychotics	7.35%	7.10%	7.00%	8.18%	7.24%	7.93%	7.53%	6.77%					7.39%
# Patients on Hep-C medication	11	9	6	6	4	2	2	3					43
# Patients on HIV medication	153	140	145	152	142	156	140	137					1,165

*At the time of report submission, the number of patients on hepatitis C medications was not available; an estimated patient count was used based on reported utilization.

Nonformulary Requests	July	August	September	October	November	December	January	February	March	April	May	June	FY 2015 - YTD TTL
# Nonformulary requests	319	278	281	272	208	297	286	334					2,275
# Approved requests (%)	290 (91%)	228 (82%)	212 (75%)	217 (80%)	168 (81%)	222 (75%)	209 (73%)	265 (79%)					226 (80%)
# Denied requests (%)	29 (9%)	50 (18%)	69 (25%)	55 (20%)	40 (19%)	75 (25%)	77 (27%)	69 (21%)					58 (20%)
Medical approved requests # (%)	255 (90%)	198 (80%)	167 (73%)	166 (76%)	139 (79%)	177 (71%)	171 (71%)	224 (77%)					187 (77%)
Medical denied requests # (%)	27 (10%)	48 (20%)	62 (27%)	51 (24%)	36 (21%)	73 (29%)	71 (29%)	66 (23%)					54 (23%)
Psych approved requests # (%)	35 (95%)	30 (94%)	45 (87%)	51 (93%)	29 (88%)	45 (96%)	38 (86%)	41 (93%)					39 (91%)
Psych denied requests # (%)	2 (5%)	2 (6%)	7 (13%)	4 (7%)	4 (12%)	2 (4%)	6 (14%)	3 (7%)					4 (9%)

Billing Composition	July	August	September	October	November	December	January	February	March	April	May	June	FY 2015 - YTD TTL
Total Monthly Utilization	$1,133,716.22	$992,940.81	$854,063.12	$1,113,394.66	$927,097.02	$1,143,830.36	$974,164.90	$898,661.42					$8,037,868.51
Total Monthly Return & Reuse	$68,310.67	$97,159.32	$66,064.49	$65,715.09	$74,686.08	$67,022.43	$51,920.28	$53,967.04					$544,845.40
Monthly Billing Grand Total	$1,065,405.55	$895,781.49	$787,998.63	$1,047,679.57	$852,410.94	$1,076,807.93	$922,244.62	$844,694.38					$7,493,023.11
Billing/patient	$101.53	$85.73	$75.40	$100.25	$82.00	$103.79	$88.86	$82.20					$89.99
Billing HIV Meds	$433,033.66	$327,981.52	$320,054.19	$380,726.88	$317,960.45	$407,543.67	$325,479.17	$300,239.42					$2,813,018.96
Billing Hep-C Meds	$60,733.67	$50,666.51	$17,612.26	$28,685.62	$6,275.59	$150.27	$116.87	$121,952.87					$286,193.65
Weeks Per Fiscal Month	5	4	4	5	4	5	4	4	4	5	4	4+3	
# Days per Fiscal Month	35	28	28	35	28	35	28	28	28	35	28	31	

MMARS DOCUMENT ID: CT – DOC – 9004UMCHPRISONMEDICL

COMMONWEALTH OF MASSACHUSETTS
INTERDEPARTMENTAL SERVICE AGREEMENT (ISA) FORM

This Form is issued and published by the Office of the Comptroller (CTR) pursuant to 815 CMR 6.00 for use by all Commonwealth Departments. Departments may add non-conflicting additional terms, but changes to the official printed language of this Form shall be void.

BUDGET FISCAL YEAR: **2010**	RFR REFERENCE NUMBER ENTER RFR NUMBER: **RFR# 08-9004-R21**
MMARS ALPHA *BUYER/PARENT* DEPARTMENT CODE: **DOC**	MMARS ALPHA *SELLER/CHILD* DEPARTMENT CODE: **N/A HIGHER EDUCATION**
BUSINESS MAILING ADDRESS: **BRIAN KEARNAN** **50 MAPLE STREET, SUITE 3, MILFORD, MA 01757**	BUSINESS MAILING ADDRESS: **55 LAKE AVENUE NORTH, WORCESTER, MA 01655**
FISCAL ISA MANAGER: **BRIAN J. KEARNAN, CONTRACT MANAGER** PROGRAM ISA MANAGER: **TERRE MARSHALL, ASSISTANT DEPUTY COMMISSIONER, CLINICAL SERVICES**	ISA MANAGER: **THOMAS MANNING, DEPUTY CHANCELLOR** **UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL**
PHONE: **508-279-8633** FAX: **508-279-8654**	PHONE: **508-856-2770** FAX: **508-856-8181**
E-MAIL ADDRESS: **TERRE.MARSHALL@STATE.MA.US**	E-MAIL ADDRESS:

Purpose of ISA: (Check one option only and complete applicable information) (Attachment A required for New ISAs and all ISA Amendments.)

___ New ISA. Current Maximum Obligation for total duration of ISA $ **Rate Contract** (Use "N/A" for Non-Financial ISA.) (Complete Attachment B)

__X__ Amendment to Existing ISA. What is being amended? (Attachment C required for all Federal and Bond Account Amendments)

__X__ Amend Budget/Accounts. Change **Capitation Rate** from: **$15.2393** to New **Capitation Rate to $14.5816, effective January 1, 2010.**

___ Amend Budget/Accounts. No Change in Maximum Obligation (Attachment B)

___ Amend Dates of Performance. New Dates of Service: Start Date:_____ End Date:_____ (Subject to execution dates below.)

___ Amend Scope of Services/Performance

BRIEF DESCRIPTION OF PERFORMANCE GOALS TO BE ACCOMPLISHED BY ISA, OR IF AMENDMENT, IDENTIFY WHAT IS BEING AMENDED:

MEDICAL AND DENTAL SERVICES TO INMATES. RATE CONTRACT AMENDMENT # 5. REDUCTION IN CONTRACT DUE TO 9C CUTS. EFFECTIVE JANUARY 1, 2010, CAPITATION RATE = 14.5816. **(CWM#DOC004-A5)**

WILL SELLER/CHILD DEPARTMENT STATE EMPLOYEES (AA OBJECT CLASS) BE FULLY OR PARTIALLY FUNDED UNDER THIS ISA? ___ No __X__ Yes. If Yes, Seller/Child certifies that the ISA is not being used as an alternative funding mechanism for state employees, that the identified personnel in Attachment A are necessary for completion of the ISA due to particular expertise or other factors that can not be obtained through the use of contractors, and that if federal funds are being used, funds shall not be used to supplement the regular salary or compensation of any officer or employee of the Commonwealth for services performed during their regular working hours. M.G.L. c. 29, § 6B.

ACCOUNT INFORMATION. Complete for all new ISAs and Amendments (even if account information is not changing) Check one option, indicate "add", "delete" or "no change" and enter account, fund, major program code and program code.

___ BGCN – non-subsidiarized (federal, capital, trust). Attachment C required for any new ISA or ISA Amendment involving federal funds.

___ BGCS – subsidiarized (budgetary)

__X__ Other (CT, RPO as authorized by CTR): **Higher Education/UMMS**

___ Non-Financial ISA (no funds are transferred from Buyer/Parent to Seller/Child), however, resources are committed to ISA.

___ Amendment with no Accounting Changes to Budget/Accounts or to Attachments B or C. (Indicate no change below and complete account information.)

X ADD ___ DELETE ___ NO CHANGE	Account:89000001	Fund: 0010	Major Program Code: N/A	Program Code: N/A
___ ADD ___ DELETE ___ NO CHANGE	Account:	Fund:	Major Program Code:	Program Code:
___ ADD ___ DELETE ___ NO CHANGE	Account:	Fund:	Major Program Code:	Program Code:
___ ADD ___ DELETE ___ NO CHANGE	Account:	Fund:	Major Program Code:	Program Code:

ISA ANTICIPATED START DATE: **July 1, 2007**, provided that the Seller/Child certifies that it will not incur any obligations related to this ISA prior to the date that this ISA is executed, NOR prior to the date that sufficient funding for the obligations for this ISA is available in the Seller/Child account for expenditure.

TERMINATION DATE OF THIS ISA: This ISA shall terminate on **June 30, 2012** unless terminated or properly amended in writing by the parties prior to this date.

BUYER/PARENT AND SELLER/CHILD DEPARTMENT CERTIFICATIONS. IN WITNESS WHEROF, by executing this ISA below, the Buyer/Parent and Seller/Child certify, under the pains and penalties of perjury, that Buyer/Parent and Seller/Child understand and agree that any Buyer/Parent or Seller/Child officer or employee who knowingly violates, authorizes or directs another officer or employee to violate any provision of state finance law relating to the incurring of liability or expenditure of public funds, including this ISA, may be considered to be in violation of M.G.L. c. 29, § 66, and therefore the Buyer/Parent and the Seller/Child agree to ensure that this ISA complies with, and that all staff or contractors involved with ISA performance are provided with sufficient training and oversight to ensure compliance with 815 CMR 6.00, CTR applicable policies and the ISA Terms and Conditions which are incorporated by reference into this ISA, in addition to the performance requirements identified in Attachment A of this ISA, and that all terms governing performance of this ISA are attached to this ISA or incorporated by reference herein, and the Buyer/Parent and Seller/Child agree to maintain the necessary level of communication (including immediate notification of any amendments to accounting information, program codes or performance needs), coordination, access to reports and other ISA information, and cooperation to ensure the timely execution and successful completion of the ISA, amendments, and state finance law compliance; and that the Buyer/Parent certifies it will ensure that sufficient funds are timely made available in the Seller/Child account(s), with the proper accounting codes, prior to the Seller/Child's need to begin initial or amended performance; and that the Seller/Child will not allow initial or amended performance to begin until the ISA is executed AND the ISA Seller/Child account is sufficiently funded to support encumbrances and payments for performance (including payroll), and the Seller/Child will make encumbrances and payments (including payroll) only from the authorized ISA Seller/Child account(s) and shall not be entitled to transfer charges made from any other account not approved in writing by CTR in advance of expenditures by the Seller/Child.

BUYER/PARENT DEPARTMENT'S AUTHORIZED SIGNATURE: Harold W. Clarke DATE: 5-18-10 (Date must be handwritten by signatory at time of signature)	**SELLER/CHILD DEPARTMENT'S AUTHORIZED SIGNATURE:** Thomas Manning DATE: 5-14-10 (Date must be handwritten by signatory at time of signature)
PRINT NAME: **HAROLD W. CLARKE**	PRINT NAME: **THOMAS D. MANNING**
PRINT TITLE: **COMMISSIONER**	PRINT TITLE: **DEPUTY CHANCELLOR**

Commonwealth Medicine
UMASS MEDICAL SCHOOL
Applied Knowledge in Public Service

Correctional Health and Criminal Justice Programs
333 South Street
Shrewsbury, MA 01545
508-793-1220 (phone) 508-793-1270 (fax)
A Program of Commonwealth Medicine

ATTACHMENT C

UMass Correctional Health
FY 2010 -9C Budget Reductions
Table of Reductions

January 1, 2010

Reduction Idea	Potential Annual Savings
MASAC staffing redesign and reassumption of services	$390,000
Revise staffing plans at minimums to reduce coverage and clinical mix	$652,280
Reduce Hep C treatment cap from 96 to 70, with additional inmates to be added as clinically appropriate	$390,000
Implement new radiology vendor 1/1/2010	$100,000
Eliminate ID Director and consolidate duties under Chief Nursing Officer (CNO) and Eliminate Director Business Ops	$225,200
Infirmary reorganization	$444,184
Total Annual Savings	**$2,201,664**

From: "Barbara McGovern" <bmcgovern@uptodate.com>
To: Judith.Steinberg@umassmed.edu; Linda.Clayton@state.ma.us; Kevin.Cranston@state.ma.us; Bonnie.Burke@umassmed.edu; mmutinga@partners.org; . . .
CC: Jean.Foran@umassmed.edu; Patti.Onorato@umassmed.edu; Christine.Brazauskas@umassmed.edu; Michelle.Houle@umassmed.edu; Michelle.Houle@umassmed.edu
Date: 2/15/2009 9:13 AM
Subject: RE: Hepatitis C Task Force Kick Off Meeting Scheduled 2/25/09

Dear Patti:

As we had discussed previously, I would like to request that we have a small meeting regarding the DOT program from 3:00 to 3:30 to open discussions about how the outcomes of this program will be monitored.

Best regards,
Barbara

-----Original Message-----
From: Small, Nicole G [mailto:Nicole.Small@umassmed.edu]
Sent: Wed 2/11/2009 4:16 PM
To: Sweet, Charles (MD); DeMaria, Alfred (DPH); Terre Marshall; Cohen, Joseph (DPH); Kenneth.Freedman@state.ma.us; Barbara McGovern; mmutinga@partners.org; Burke, Bonnie; kevin.cranston@state.ma.us; linda.clayton@state.ma.us; Steinberg, Judith
Cc: Houle, Michelle; Houle, Michelle; Brazauskas, Christine; Patti.Onorato@umassmed.edu; Foran, Jean
Subject: Hepatitis C Task Force Kick Off Meeting Scheduled 2/25/09

Please note this email is being sent on behalf of Patti Onorato, Executive Director of Correctional Health & Criminal Justice Programs, CWM.

Good Afternoon,

Please be advised that the Hepatitis C Task Force will reconvene on Wednesday, February 25, 2009 and will be facilitated by Dr. Alfred DeMaria, Director of the Bureau of Communicable Disease Control State Epidemiologist William A. Hinton State Laboratory Institute. This meeting will be held at Lemuel Shattuck Hospital in the Administrative Conference Room on the first floor from 3:30 – 5:00 p.m.

The first meeting will consist of introduction of members, an overview of the current literature regarding Hepatitis C and a comparative review of the current Hepatitis C Guideline for Treatment. An agenda will follow under separate cover but the current guideline has been attached for your review prior to the meeting.

Future meeting dates will be decided on February 25th so please bring your calendars for planning purposes.

Please find attached the current guideline.

<<Management of Chronic Hepatitis C - Clinical Guideline.pdf>>

Patti Onorato, RN, ANP, MS

Executive Director

Correctional Health & Criminal Justice Programs

Commonwealth Medicine, UMMS

office 508 793-1266

fax 508 793-1248

email: <mailto:patti.onorato@umassmed.edu> patti.onorato@umassmed.edu

Nicole Small

Executive Assistant to Patti Onorato

Ad Comp Coordinator

Commonwealth of Massachusetts
Department of Correction
Pharmacy and Therapeutics Committee

Meeting Minutes

Meeting Date: March 3, 2011

Recorded by: Erik Hamel

Next Meeting: April 7, 2011

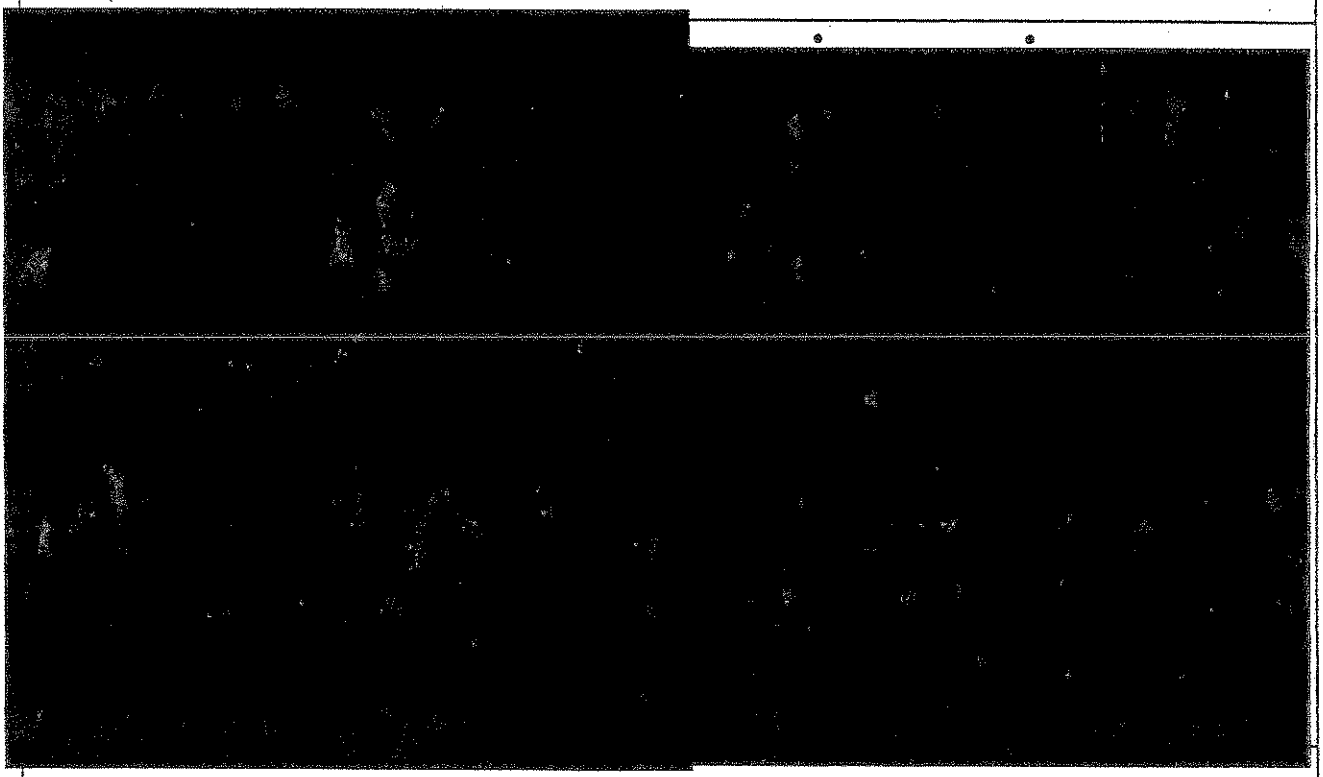
Members Present: E. Hamel, N. Zilban, G. Puffenberger, D. Manning, T. Cummins, L. Davis, T. Groblewski, L. Dell'Olio, K. Nelson

Members Absent: L. McGuire, E. Chase, K. Freedman, D. Rogers, R. Cantelli, R. Diener

Guests: Maria Ousterhout, Pavel Lavitas (Clinical Pharmacy Services), C. Gonzalez (UMass Correctional Health)

Members Excused:

Agenda Item	Discussion Points	Action Items/ Follow Up	Responsible Person	Date Due
I. Approval of January meeting minutes	• A motion was put forth to approve the January P&T minutes; the minutes were unanimously approved	• None	• E. Hamel	
II. CONTINUING BUSINESS				
a. Formulary / non-formulary statistics review	• Formulary and nonformulary summaries were provided for the months of December 2010 and January 2011 due to the cancellation of the February 2011 P&T meeting because of inclement weather. • For December 2010, total pharmacy expenditure was $913,538. December 2010 represented a 5 week reporting month. • For January 2011, the total pharmacy expenditures amounted to $762,205. January represented a typical 28-day reporting period. [redacted]	• None required	• E. Hamel, D. Rogers, N. Zilban	• Continuous



[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
b. *Pegylated interferons/ ribavirin update*	• Currently, there are 53 patients on treatment as of 1/31/2011 The average cost/patient/week was ~$160/patient/week in January. L. Davis inquired if the reduction in cost was impacted stock returns from sites. N. Zilban indicated that returns did impact the total treatment costs.	• UMCH and SOPS will continue to report the current status of antiviral therapy for hepatitis C patients and update the Committee of developments in the reporting and ordering process.	• E. Hamel, N. Zilban	• Continuous
c. *Contracting Update* i. Contracting/Pricing Updates	[redacted]	[redacted]	[redacted]	[redacted]

d. WebRx and Tote Validation Statistics				
d. HIV Summary Update	• For December, SOPS reported that reclaim and reuse of HIV medications amounted to $19,332 from a total of 36 orders and 775 units. • For January, the reported reclaim and reuse of HIV medications amounted to $19,966 from a total of 42 orders and 1,085 units.	• E. Hamel and SOPS will continue to update the committee of the HIV compliance status	• E. Hamel, D. Rogers	• Continuous
e. MHM update				
III. NEW BUSINESS				
a. 2011 Formulary				

b. Pharmacy Pipeline	[redacted]	[redacted]	[redacted]	[redacted]
• M. Oosterhout, consultant pharmacist from CPS presented on the 2011 pharmacy pipeline. Key highlights of the presentation included: o Impending generic entry dates for "blockbuster" medications used to treat endocrine cardiovascular, infectious, central nervous system and respiratory disorders o Overview of novel agents in late-phase development for use in hepatitis C, HIV, anticoagulation, hypercholesterolemia, infections, pain management, mental health, diabetes and COPD anticipated to be submitted for FDA review within the next 1-2 years.	• CPS, SOPS and MHM will use the information provided in the presentation to identify opportunities within the MA DOC formulary	• E. Hamel, N. Zilban, R. Diener.	• TBD	
c. Etanercept/Adalimumab Comparison	[redacted]	[redacted]	[redacted]	[redacted]

Respectively Submitted by Erik Hamel, Pharm.D. BCPS
April 7, 2011

[redacted]

Analysis of Health Care Costs in the DOC

DOC

DEPARTMENT OF CORRECTION

MGT OF AMERICA, INC.

502 East 11th Street
Suite 300
Austin, Texas 78701
www.mgtcriminaljustice.com

Final Report | December 2011

12. Hepatitis C Treatment

The University of Massachusetts Medical School has a proposal with associated costs for the use of the medications which have been recently approved for treatment of both new patients and previously treated patients for the disease of Hepatitis C. In the UMass proposal, there is a recommendation to spend $7,478,063 in the first year, $8,189,805 in year two and $9,008,785 in year three. The methodology utilized was based on selecting a number of patients to treat and then costing out how much that would cost. The first year includes 207 patient prorated months to treat 59 previously untreated patients, 141 previously treated and failed patients and seven patients with cirrhosis.

The projected annual cost, each year for three years, approaches the MDOC's entire annual medication expense for all medications ($10 M per year). Although it is reasonable to use the methodology proposed by UMass, this does not take into account two very important items. Number one, for the overwhelming majority of patients and especially those without access to alcohol and other chemicals that damage the liver, Hepatitis C is overwhelmingly an indolent disease. The majority of patients with this disease 40 years after infection are likely to have died from some other cause. A second important factor is cost. In this time of ever shrinking budgets, dollars spent for this newly approved treatment will be taken away from health services to treat other diseases, such as diabetes or hypertension or any one of a variety of other problems. This money is likely to result in staffing reductions which could delay access for other patients in need.

Because this medicine has just been approved this year and therefore the US experience with it is quite underdeveloped, and because this is overwhelmingly an indolent disease, it would be reasonable to carefully manage spending on this treatment. Development of an approach to prioritize patients most in need of treatment will be critical. The criteria should target those patients who are most advanced but still treatable along with those patients who are determined to be the most rapidly progressing with their disease. Both tissue and clinical parameters should be used to make these determinations. In fact, it would make sense to maintain a registry to insure that timely treatment is provided to those in greatest need.

Monitoring the early stages of Hepatitis C rather than immediately proceeding to treatment is an acceptable medical practice and mirrors actual treatment trends in the free world[5]. Actual treatment is conditioned on the progression of the disease, as monitored through liver function tests and biopsies.

For patients with earlier stages of fibrosis and sentences less than 5 years, condition monitoring is an appropriate treatment approach. If fibrosis progression indicates treatment, patients should be tried on the current therapy first. If that therapy is found to be futile at 12 weeks, patients may then be tried on new medical regimen, provided there are no contraindications

[5] *Fibrosis & Disease Progression in Hepatitis C.* Marcellin, et al. Hepatology, 2002, *Hepatitis C.* Centers for Disease Control & Prevention, 2011, *Hepatitis Treatment and Management.* Mukherjee, et al. Medscape Reference, 2011.

PRISONERS' LEGAL SERVICES
formerly known as
Massachusetts Correctional Legal Services
10 Winthrop Square, 3rd Floor
Boston, MA 02110

617-482-2773; WATS 800-882-1413
FAX 617-451-6383
State Prisoner Speed Dial *9004#
County Collect Calls 617-482-4124

April 13, 2012

The Honorable Governor Deval Patrick
Massachusetts State House
Office of the Governor – Room 280
Boston, MA 02133

Mary Elizabeth Heffernan, Secretary
Executive Office of Public Safety and Security
Office of the Secretary
One Ashburton Place, Suite 2133
Boston, MA 02108

Dr. JudyAnn Bigby, Secretary
Executive Office of Health and Human Services
Office of the Secretary
One Ashburton Place, 11th Floor
Boston, MA 02108

RE: Hepatitis C Treatment in the Department of Correction

Dear Governor Patrick, Ms. Heffernan, and Dr. Bigby:

Having repeatedly requested information about the status of Hepatitis C treatment in the Department of Correction, only to be denied any substantive response, our office asks that you intervene.

Hepatitis C is a chronic disease that damages the liver. Over 100,000 Massachusetts residents are likely afflicted with Hepatitis C, though most of them may not be aware that they have it. Some 8,000 to 9,000 new cases are diagnosed in the Commonwealth each year. Nationally, deaths from Hepatitis C now outnumber those from HIV. The prevalence of Hepatitis C in prison is believed to be several times that of the general population. In 2003, it was reported that some 3,000 of the 10,000 Massachusetts state prisoners were infected with Hepatitis C.

The high prevalence of Hepatitis C in prisons represents a challenge but also a public health opportunity. Hepatitis C treatment can be very effective in the prison setting. Such treatment improves patient health and community health, by reducing the spread of the disease and the future costs associated with cirrhosis, cancer, and liver transplants.

In May of 2011, the Food and Drug Administration approved two new medications – Boceprevir and Telaprevir. Either one of these drugs substantially improves the chances of successful treatment for certain Hepatitis C patients, when administered with traditional combination therapy (Ribavirin and Peginterferon).

Our clients followed the approval process with great interest, as the new "triple" therapy offers a much higher success rate than traditional combination therapy. In addition, triple therapy has proven effective with patients who have undergone combination therapy in the past and

experienced treatment failure or relapse. Where previously there was no further treatment option for these people, now there is hope. Our clients began asking their providers from UMass Correctional Health about their prospects for treatment. When those questions went unanswered, this office began asking DOC and UMass on their behalf. We have been told repeatedly that the "new" therapy is "under review," and that an "agency course of action" has not yet been determined. That message has never changed, even as the months have passed and the inquiries mounted. Neither DOC nor UMass has ever offered a timetable for offering triple therapy, or any explanation of why this "review" continues nearly a year after the medications were approved. At this point, their continued reliance on the "new"-ness of the therapies rings hollow.

The lack of candor from these public entities is disheartening. Everyone was aware of these new medications and their path toward FDA approval. The prisoners who suffer from Hepatitis C knew about these medications well before their approval, as did their families and loved ones. Anyone who read or watched the local news was aware of them, particularly with local company Vertex reporting on its development of Telaprevir. For some time, DOC and UMass have known all they need to know in order to make these medications available in a timely way. The means by which they gather, analyze, and discuss information about Hepatitis C are many, and they include the following:

- Hepatitis C is one of the most closely monitored diseases in the DOC. Data is collected and reported monthly as to how many prisoners are receiving combination therapy, how many prisoners are approved and waiting for therapy (there are a limited number of "treatment slots"), how many prisoners are being evaluated for possible treatment, and how much money has been spent on combination therapy.
- A Task Force has been meeting to review Hepatitis C treatment of DOC prisoners since 2009 (as UMass itself touts on its website). Representatives from DOC, UMass, and the Department of Public Health have participated in the work of this task force, including GI and Infectious Disease specialists from Lemuel Shattuck Hospital. One of these specialists, Barbara McGovern, is a member of the Antiviral Drugs Advisory Panel that recommended approval of the new medications to the FDA.
- The DOC's Pharmacy and Therapeutics Committee regularly reviews the monthly data concerning Hepatitis C treatment and cost. Representatives from DOC, UMass, and the State Office of Pharmacy Services sit on the P&T Committee. UMass enlists its pharmacy consulting division, Clinical Pharmacy Services, to offer advice about pharmacy procedure and information about new drugs, such as the development of the new Hepatitis C medications.
- SOPS similarly offers information and advice about pharmacy practices, along with reports on pricing and procurement of specific medications.

To suggest that all of these participants in the management of Hepatitis C require more time to "review" the new therapy is an insult to our intelligence. We understand that a revised treatment protocol was completed months ago. The real issue is cost. Triple therapy is expensive, just as traditional combination therapy has always been expensive. DOC and UMass anticipated these costs well before the FDA approved the new medications. A January 2010 addendum to the contract between DOC and UMass implemented service and staffing reductions, necessitated by the Governor's Section 9C budget cuts for FY2010. This addendum reduced the number of treatment slots for combination therapy from 96 to 70, and it amended the contract to acknowledge the likelihood of costs associated with "new emerging therapies" for Hepatitis C. The parties chose to postpone any decisions about how to pay for such therapies, agreeing only to "discuss a plan of action" at an unspecified future time.

That was a year and a half before the FDA's approval of Boceprevir and Telaprevir. Today, nearly a year after FDA approval, we do not know if DOC and UMass are still discussing a plan, but we do know that there is no plan of action, only inaction. The failure to implement a new treatment protocol is itself a new protocol, one that denies this treatment to all DOC prisoners. A blanket policy denying triple therapy for Hepatitis C is unconscionable. Triple therapy is available to federal prisoners, such as those at FMC Devens. Triple therapy is also available to MassHealth recipients, meaning that virtually everyone in the Commonwealth has access to this potentially lifesaving treatment. The only segment of the Massachusetts population to be completely denied this treatment is the prison population. Prisoners, it bears remembering, are also the only segment of the population with a constitutional right to adequate health care. For all the deference generally afforded to executive branch agencies when it comes to prison policy, courts have not been so deferential to blanket denials of standard care. The courts have also made clear that cost is no excuse for failing to provide adequate medical care.

Legalities aside, state prisoners with Hepatitis C are people – people who have been sentenced to a term of incarceration, not to unnecessary suffering or death. For most, the term of incarceration will end, and these people will return to their families and their Massachusetts communities, whether in good health and able-bodied, or in poor health and dependent on others.

With so many state officials reviewing, analyzing, and discussing this issue, we were optimistic that triple therapy would be made available to our clients in a timely fashion. That optimism has faded. Accordingly, we turn to you and ask that this administration intervene to do what is right. Thank you for your attention to this important matter.

Sincerely,

Joel H. Thompson
Staff Attorney
Co-Chair, PLS Health Care Project

The Commonwealth of Massachusetts
Executive Office of Public Safety & Security

Department of Correction
Health Services Division
PO Box 426
Bridgewater, Massachusetts 02324

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Deval L. Patrick
Governor

Timothy P. Murray
Lieutenant Governor

Mary Elizabeth Heffernan
Secretary

Luis S. Spencer
Commissioner

Peter A. Pepe, Jr.
Katherine A. Chmiel
Deputy Commissioners

Paul L. DiPaolo
Acting Deputy Commissioner

July 2, 2012

Joel Thompson, Esq.
Prisoner Legal Services
10 Winthrop Square, 3rd Floor
Boston, MA 02110

Re: Hepatitis C Treatment in the Department of Correction

Dear Mr. Thompson:

Your April 13, 2012 letter to Governor Patrick, Secretary Heffernan, and Secretary Bigby regarding Hepatitis C treatment in the Department of Correction (DOC) has been referred to me for a response.

DOC and UMass share your concern for, and commitment to, addressing the needs of inmates infected with Hepatitis C. Towards that end, I can inform you that the Hepatitis C Task Force which you reference in your letter continues to meet, most recently on June 7, 2012, to discuss a variety of issues, including screening for the HCV antibody, verification of chronic infection, education regarding HCV and liver disease, harm reduction counseling, and linkage to care, including the potential use of emergent therapies Boceprevir or Telaprevir, for those identified as having evidence of progressive liver damage.

The general consensus at that meeting was that DOC and UMass should look to and consider adopting as appropriate the March 2012 Federal Bureau of Prisons Clinical Practice Guidelines for the Evaluation and Treatment of Hepatitis C and Cirrhosis, which guidelines incorporate for the first time a framework for the application of emergent therapies (prior federal guidelines had issued in March 2011, two months before the new therapies were approved by the FDA). UMass has committed to completing its revised protocol for Hepatitis C treatment by July 31, 2012. DOC will then

be addressing operational issues surrounding the revised protocol. The task force intends to meet again sometime between now and July 31.

As you are undoubtedly aware, and as the federal guidelines amply attest, assessments of need and determinations of suitability for a particular form of treatment can be complicated, and contraindications for any particular treatment, emergent or not, must be weighed. DOC will continue to work with UMass and the Hepatitis C task force to advance the development of guidelines and protocols for the treatment of Hepatitis C.

Sincerely,

Lawrence Weiner
Assistant Deputy Commissioner

Cc: The Honorable Governor Deval Patrick
Dr.JudyAnn Bigby, Secretary, EOHHS
Mary Elizabeth Heffernan, Secretary, EOPSS

DOC

Non-Formulary Utilization

June 2013

	MHM	UMASS	Grand Total
GABAPENTIN	42	166	208
BUPROPION HCL	117		117
OMEPRAZOLE		97	97
DICLOFENAC SODIUM	2	40	42
TAMSULOSIN HCL	1	40	41
METHADONE HCL		37	37
MESALAMINE	1	34	35
CLONAZEPAM	33	2	35
FLUTICASONE PROPIONATE (N	4	31	35
METOPROLOL SUCCINATE	1	32	33
FINASTERIDE	1	27	28
FENOFIBRATE		28	28
SUMATRIPTAN SUCCINATE	2	25	27
RALTEGRAVIR POTASSIUM		25	25
INSULIN DETEMIR	7	18	25
QUETIAPINE FUMARATE	25		25
POLYETHYLENE GLYCOL 3350		24	24
MONTELUKAST SODIUM		24	24
OXYCODONE HCL	4	19	23
ARIPIPRAZOLE	19	1	20
OLANZAPINE	19		19
OXCARBAZEPINE	6	12	18
DARUNAVIR ETHANOLATE		18	18
ZIPRASIDONE HCL	18		18
LABETALOL HCL	2	15	17
ERGOCALCIFEROL	2	15	17
INSULIN GLARGINE	3	14	17
ATOMOXETINE HCL	16		16
MOMETASONE FUROATE-FORMOT		14	14
ATORVASTATIN CALCIUM		14	14
KETOCONAZOLE (TOPICAL)	1	11	12
B-COMPLEX W/ FOLIC ACID		11	11
LORAZEPAM	9	2	11
CLARITHROMYCIN	1	10	11
CALCIPOTRIENE		11	11
FLUNISOLIDE (NASAL)	2	8	10
CARBIDOPA-LEVODOPA	1	9	10
FLUTICASONE-SALMETEROL	2	8	10
NIFEDIPINE		9	9
MORPHINE SULFATE		9	9
FENOFIBRATE MICRONIZED		9	9
PIOGLITAZONE HCL		8	8
EZETIMIBE		8	8
LACTULOSE	8		8
TIOTROPIUM BROMIDE MONOHY	3	5	8
BOCEPREVIR		7	7
SODIUM CHLORIDE	3	4	7

MPCH
Massachusetts Partnership for Correctional Healthcare

Commonwealth of Massachusetts
Department of Correction
Pharmacy and Therapeutics Committee
Meeting Minutes

The MA DOC Pharmacy & Therapeutics (P&T) Committee Meeting was held April 3, 2014 at the MPCH regional office in Westborough Massachusetts from 9 AM to 11 AM.

The following individuals attended the meeting in person: Mark Waitkevich, Bonnie Damigella, Keelin Garvey, Erik Hamel, Jeffrey Fisher, Laura Vasconcellos, Tom Groblewski, Donna Jurdak, David Chantal, Rhonda Cantelli, Don Rogers, Aysha Hameed, Gina Spencer and David Stone

Attending by teleconference: Alki Nacopoulos

Guests: None

Excused member(s): Claudia Gonzalez, Robert Diener

Approval of March Meeting Minutes: The minutes from the March 2014 P&T meeting were reviewed. **A motion made to approve. The minutes were approved.**

Review of Statistics: Erik presented February's statistical data (Note-28-day reporting period):

- The census increased slightly to 10,639 in February. In December the census was 10,561, 10,638 in November and 10,712 in October). M Waitkevich noted that the census may continue to decrease as additional cases are being dismissed tied to the MA drug testing laboratory.
- Total prescription volume for January was 6,195 new orders and 23,062 refills.
- Total pharmaceutical expenditures amounted to $839,919.
    - Medical medication costs were $723,580. Top cost drivers were HIV medications Atripla, Reyataz, Raltegrevir and Truvada and the hepatitis C medication boceprevir.
    - Psych (post credit and fees) costs were $50,787. Cost drivers in this sector include aripiprazole, the typical antipyschotics chlorpromazine and prochlorperazine and the antidepressant, bupropion.
    - Bridgewater State Hospital (post credit and fees) costs were $65,552. Primary cost drivers included atypical antipsychotics aripiprazole, clozapine, lurasidone, and quetiapine extended-release. The quetiapine extended-release tabs were previously reviewed and approved for use.

- E. Hamel provided a summary of the cost avoidance figures from the formulary transition to levalbuterol and ciclesonide from October 2013
  - Ciclesonide yearly cost avoidance is estimated to be $101,392
  - Levalbuterol yearly cost avoidance is estimated to be $60,889

- Nonformulary requests-268 requests with 79% approved (212 requests)
  - Medical Requests-214 requests with 22% approved (167 requests)
  - Psych Requests-54 with 83% approved (45 requests)
  - New requests-132 with 70% approved (93 requests).
- SOPS report detailed data on the top non formulary drugs, by expenditure (top 3): boceprevir ($33,258), glatiramer ($24,264), and eltrombopag ($22,044).
- HIV and Hepatitis C patient statistics for February:
  - Hepatitis C
    - 5 currently undergoing treatment with dual therapy (average weekly cost-$243).
    - 6 patients are undergoing triple therapy.
  - The Committee discussed the new hepatitis C medication Sofosbuvir. The current hepatitis C guidelines have not been updated to incorporate the use of this medication.
    - Dr. Groblewski noted that the guidelines are under development
    - In the event a patient is admitted on the medication, data is being gathered from the manufacturer regarding gaps in therapy and efficacy to ensure appropriate continuity of therapy.
    - Currently medications from outside the system, including those from Houses of Corrections, are not permitted for use within the system; however, it was asked if an exception may be made for Sofosbuvir due to time to acquire the medication and costs.

Naltrexone Extended-Release Program Proposal: M. Waitkevich provided the Committee an update of a narcotic treatment pilot program in development.

- A final clinical draft of the program has been completed. MA DOC, MPCH and SOPS are reviewing the policy

- The proposed method of delivery requires finalization. The manufacturer wishes to deliver the medication directly to the facilities as samples, but wants the State Office for Pharmacy Services to coordinate the orders and patient information. This will increase workload and responsibilities for SOPS for a medication that they are not dispensing.
  - SOPS recommends that the medication be delivered to SOPS for labeling and delivery

Insulin pumps and medical devices: Dr. Groblewski summarized a new intake patient that has an insulin pump. The patient was admitted to an infirmary setting so he was transitioned to IV insulin, but the question arose as to how to handle these medical devises for new intake.

- M. Waitkevich noted that MA DOC does not have a specific policy on outside medical devices, including insulin pumps and CPAP machines.

- Dr. Groblewski stated that a policy will be drafted and presented to MA DOC.

Antipsychotic Weight Gain and Metformin Formulary Updates:

- Dr. Garvey proposed beginning the use of metformin to address weight gain and metabolic issues arising from chronic antipsychotic use.
  - Available information notes that use of metformin is effective in preventing further weight gain and improving insulin sensitivity in patients on long-term antipsychotic therapy.
  - Dr. Garvey requested input from the committee as to which prescribers would oversee the therapy-psychiatrists or the medical prescribers.
    - It was recommended that psychiatrists oversee metformin prescribing and adjust therapy as part of their psychiatric evaluation.
    - Dr. Garvey requested pharmacy to provide information at an upcoming medical staff meeting on metformin prescribing. E. Hamel will provide that in-service.

The following changes were proposed for the MA DOC formulary:

- **Additions**
  - Hydrocortisone 1% Lotion
  - Dolutegrevir (Tivicay®)
  - Paricalcitol (Zemplar®) 2 mcg/mL
- **Deletions**
  - Fluocinolone 0.01% Solution
- **Additions C-6 Bridgewater State Hospital**
  - Perphenazine 16 mg tablets
  - Vancomycin IV Premixed
  - Doxycycline 100 mg
  - Ondansetron IM

Dr. Stone recommended removing vancomycin from the proposed list for stock use. His concern surrounding adverse reactions associated with the medication with improper dosing and monitoring, particularly renal complications.

A motion made to approve the proposed additions with the exception of vancomycin. The proposed additions with the exception of vancomycin were approved.

Medication Backorders: Updates to the current backorder medications were provided. Venlafaxine backorders were resolved. Notable backordered medications included calcitriol injections.

Discussion Points:

The addition of the HIV medications raltegrevir, emtricitabine/tenofovir, and lopinavir/ritonavir to facilities' C-6 stock box for post-exposure prophylaxis has not taken place. It was determined that a memo will be sent out to facilities to expect the additions at a TBD date.

Adjournment & Next Meeting:
The meeting adjourned at 11am and the next meeting is scheduled for May 1 2014 at the MPCH Regional Office location in Westborough MA.

MPCH
Massachusetts Partnership for Correctional Healthcare

Commonwealth of Massachusetts
Department of Correction
Pharmacy and Therapeutics Committee
Meeting Minutes

The MA DOC Pharmacy & Therapeutics (P&T) Committee Meeting was held August 7, 2014 at the MPCH regional office in Westborough Massachusetts from 9 AM to 11 AM. Note the July P&T meeting was cancelled due to scheduling conflicts.

The following individuals attended the meeting in person: Erik Hamel, Robert Diener, Gene Chaissen, Alki Nacopoulos, Laura Vasconcellos, Bonnie Damigella, Claudia Gonzalez, Mark Waitkevich, and David Stone

Attending by teleconference: Karen Lee

Guests: None

Excused member(s): Don Rogers Tom Groblewski, Keelin Garvey,

Approval of June Meeting Minutes: The minutes from the June 2014 P&T meeting were reviewed. **A motion made to approve. The minutes were approved.**

Review of Statistics: Erik presented May and June's pharmacy utilization data (Note-May was a 35 day reporting period and June was a 30 day reporting period. Reporting periods are typically 28 days):

- The census was 10,553 patients in May and 10,551 June.
- Total prescription volume was 9,247 new orders and 30,328 refills in May and 7,920 new orders and 24,780 refills in June.
- May pharmaceutical costs was $1,141,535
    - Medication costs after credits and returns were $1,070,863. Top cost drivers for medications ordered for medical indications were the HIV medications Atripla ($136,293, 71 orders), Truvada ($84,832, 69 orders), Boceprevir ($43,078, 7 orders) and Prezista ($42,800, 38 orders). The top non-HIV medication was the hepatitis C medication boceprevir ($43,078, 7 orders).
    - Psychiatric medication costs were $85,949. Cost drivers in this sector include aripiprazole ($11,039, 14 orders), the typical antipyschotics chlorpromazine ($8,791, 134 orders) and perphenazine ($7,107, 141 orders).

- Bridgewater State Hospital medication costs were $84,637. The primary cost drivers included risperidone ($5,387, 224 orders), quetiapine ($5,137,
- 30 orders), and perphenazine ($5,048, 77 orders).

- June pharmaceutical costs was $982,550
  - Medication costs after credits and returns were $899,461. Top cost drivers for medications ordered for medical indications were the HIV medications Atripla ($111,637, 59 orders), Truvada ($63,993, 52 orders), Boceprevir ($42,643, 7 orders) and Prezista ($39,421, 35 orders). The top non-HIV medication was the hepatitis C medication boceprevir ($42,643, 7 orders).
  - Psychiatric medication costs were $82,550. Cost drivers in this sector include aripiprazole ($9,550, 12 orders), the typical antipyschotics chlorpromazine ($7,025, 115 orders) and perphenazine ($6,232, 120 orders).
  - Bridgewater State Hospital medication costs were $65,762. The primary cost drivers included Truvada ($6,153, 4 orders), perphenazine ($4,156, 77 orders), and risperidone ($3,848, 159 orders).
- Nonformulary requests for June-363 requests with 82% of the requests approved (299 requests)
  - Medical Requests-332 requests with 81% approved (268 requests)
  - Psych Requests-31 with 100% approved (31 requests)
  - New requests-192 with 77% approved (147 requests).
- SOPS report detailed data on the top non formulary drugs, by expenditure (top 3): boceprevir ($42,643, 6 patients), Sorafenib ($26,312), glatiramer ($19,573, 4 patients).
- Top requested nonformulary medications were: Gabapentin (70 requests), fluticasone nasal (18 requests), Oxcarbazepine (11 requests), metoprolol ER (7 requests) and methadone (9 requests).

Infectious Disease Updates

- HIV and Hepatitis C patient statistics for June
  - 170 HIV + patients.
    - 104 HIV + patients are reported to be co-infected with hepatitis c.
    - 151 patients are undergoing HAART therapy
    - 148 patients on stable therapy have an undetectable viral load
    - Facilities with the highest number of HIV + patients include: Norfolk (27), Old Colony (23), and Concord (19).
  - For Hepatitis C
    - 5 patients are currently undergoing treatment with dual therapy (average weekly cost-$208).
    - 6 patients are currently undergoing triple therapy.
  - The Committee discussed the new hepatitis C medication Sofosbuvir. Interim guidelines have been drafted and there are 3 patients that have been evaluated and cleared to start sofosbuvir therapy in August. Patient handouts and consent forms were

- Laura Vasconcellos outlined a proposal for a keep-on-person KOP program for stable HIV patients. Feedback from the committee were raised that will require further information and/or follow-up:
  - MA DOC legal will require additional information on the KOP programs and the benefits over the current medline administered method.
  - SOPS noted that the medication will be required to be repackaged for KOP. Currently the medication is packaged differently for medical staff administration and operations is set for one method or another (hydrid packaging being time/cost prohibitive).
  - It was noted NECC (Concord Farm) currently administers these medications under officer observation due to medical staff scheduling. The labels currently contain indications and it was asked if they can be removed.
- Discussion continued regarding permitting an exception for using medications from outside the system, (including those from Houses of Corrections and patient's personal medications) for sofosbuvir from new intakes due to time to acquire the medication and costs. Currently policy does not permit use of outside medications. Erik will draft up a letter outlining a verification process to ensure the medication is genuine and not adulterated and present that document to Mark Waitkevich.
- Health and Human Services updated the Adult treatment guidelines in May 2014. Erik summarized the major changes included:
  - CD4 count frequency changes
  - Recommended regimen changes
  - Principles for changing regimens

Naltrexone Extended-Release Program Proposal:

- Rhonda Cantelli requested that lockable cold storage boxes be provided to secure the stores of injectable naltrexone while on site. There was a question whether the boxes would be supplied by the manufacturer, the pharmacy or MPCH. MPCH and SOPS will investigate who would be responsible for supplying the lock boxes.

Testosterone Multidose:

- There was a request to clarify the "do not use beyond date" for multidose testosterone and use of alternative formulations to reduce inventory of opened vials and waste of remaining medication past the expiration in 10 mL vials
  - Erik clarified that beyond use date is 28-days after 1st use or as specified by manufacturer
    - Since the manufacturer does not specify a date, opened vials should be discarded 28 days after 1st use.
  - A summary of common testosterone formulations were presented. It was found that testosterone vials were still the most cost effective and the use of 1 mL vials would reduce waste and/or need for inventory.

Formulary Updates:
The following changes were proposed for the MA DOC formulary:

- **Additions**
  - Aclidinium 30 dose units (Tudorza)-anticholinergic inhaler indicated for COPD and cleared by DOC for KOP use. Current anticholinergic inhalers for COPD, tiotropium and ipratropium, are medline administered and more costly. Current utilization is expected to be ~30 patients and result in ~$60k cost savings per year.
  - Labetalol-beta-blocker used by the consultant cardiologist for refractory hypertension. Current utilization is 10-12 patients/month
- **Deletions**
  - Ipratropium inhalers (Atrovent/Combivent). To be replaced with aclidinium.
  - Doxepin. Tricyclic antidepressant with a high rate of use as a hypnotic. Removal was approved in January and the effective date was August 1.
  - Omeprazole 40 mg capsules. This strength was found to be disproportionately more costly than using 20 mg capsules. Interchanging with the 20 mg capsule is estimated to result in ~$60k cost savings/year
- **C-6 Stock Box**
  - Methylprednisolone. Increase stock levels from 2 vials to 6 vials to facilitate more on site injections by orthopedic specialists.

A motion made to approve. The proposed formulary changes were approved.

Adjournment & Next Meeting:
The meeting adjourned at 11am. The next meeting is scheduled for September 4, 2014 at the MPCH Regional Office location in Westborough MA.

MPCH
Massachusetts Partnership for Correctional Healthcare

Commonwealth of Massachusetts
Department of Correction
Pharmacy and Therapeutics Committee
Meeting Minutes

The MA DOC Pharmacy & Therapeutics (P&T) Committee Meeting was held October 2, 2014 at the MPCH regional office in Westborough Massachusetts from 9 AM to 11 AM.

The following individuals attended the meeting in person: Erik Hamel, Claudia Gonzalez, David Stone, Tom Groblewski, Linda Hermann-Gomes, Rhonda Cantelli

Attending by teleconference: None

Guests: None

Excused member(s): Keelin Garvey, Robert Diener, Alki Nacopoulos, Don Rogers, Karen Lee, Dave Chantal, Mark Waitkevich

Approval of September P&T Meeting Minutes: The minutes from the September 2014 P&T meeting were reviewed. **A motion made to approve. The minutes were approved.**

Review of Statistics: Erik presented August pharmacy utilization data (Note-August was a 28 day reporting period):

- The census was 10,449 patients in August.
- Total prescription volume was 7,625 new orders and 23,694 refills in August.
- August pharmaceutical costs were $992,940
    - Medication costs after credits and returns were $895,781. Top cost drivers for medications ordered for medical indications were the HIV medications Atripla ($90,521, 46 orders), Truvada ($61,532, 50 orders), Nexavar ($53,704, 4 orders).
    - Psychiatric medication costs were $87,700. Cost drivers in this sector include aripiprazole ($8,369, 12 orders), the typical antipyschotics chlorpromazine ($8,365, 157 orders) and perphenazine ($5,593, 111 orders). Psychiatric costs overall are increasing due increased costs and shortages to risperidone amitriptyline and carbamazepine.
    - Bridgewater State Hospital medication costs were $52,250. The primary psychiatric cost drivers included clozapine ($4,451, 265 orders), rifaxamin ($3,789, 3 orders and perphenazine ($3,751, 71 orders). Non-psychiatric

medications driving BSH medication costs include: the aforementioned rifaxamin, cinacalcet ($2,484, 1 order) and Complera ($1,968, 1 order).

- Nonformulary requests for August-278 requests with 82% of the requests approved (228 requests)
  - Medical Requests-246 requests with 80% approved (198 requests)
  - Psych Requests-32 with 94% approved (2 requests)
- The top non formulary drugs, by expenditure (top 3): sorafenib ($53,704), boceprevir ($30,459), and epoetin ($26,876).

Infectious Disease Updates

- HIV and Hepatitis C patient statistics for August
  - 169 HIV + patients.
    - 102 HIV + patients are reported to be co-infected with hepatitis c.
    - 152 patients are undergoing HAART therapy
    - 149 patients on stable therapy have an undetectable viral load
    - Facilities with the highest number of HIV + patients include: Norfolk (28), Old Colony (24), and Concord (18).
  - 1541 Hepatitis C +patients
- Hepatitis C
  - The Committee discussed the new hepatitis C medication Sofosbuvir . There are 5 patients that have been evaluated and are cleared to initiate sofosbuvir treatment once operational processes are put into place.
  - HIV keep-on-person (KOP) program for stable HIV patients proposal. This agenda topic is a continuation from the July and August P&T meeting. Additional clarification and/or follow-up required:
    - Currently DOC policy is for directly observed therapy. It was noted some NECC (Concord Farm) patients have these medications ordered as "keep on person" through physician orders. It is unclear if the patients were using these medications KOP or if they were administered under officer/medical staff supervision (medications still stored at nursing stations).
    - The current decision by the committee that the DOT policy applies to all patients, regardless of housing condition. All providers will be reminded to ensure that these medications are ordered as DOT for all patients.
    - Further information is waiting from MA DOC legal regarding if any patient did receive the medication KOP in the interim.
- HDAP
  - A question was raised on HIV Drug Assistance Programs (HDAP) eligibility in Massachusetts for House of Correction (HOC) patients housed at MA DOC facility. Currently county HOC programs are able to participate in this program that assists low income patients to receive their HIV-related medications. Currently DOC patients are not eligible to receive this benefit, but clarification was requested if HOC patients in DOC custody are eligible. C. Gonzalez will follow-up.

Naltrexone Extended-Release Program:

- Currently there is an approved patient list for the naltrexone extended-release program has been developed and will be updated and forwarded to the PDC pharmacy. Only patients on that list are to receive medications supplied by Alkermedes under this program.
- Two sites have already received injectable naltrexone extended-release deliveries. Those sites that already have injectable naltrexone on site will submit orders to the pharmacy but will note "DO NOT SEND" to indicate they are using existing stock on site.
- Operationally, the medication is to be written as a stock order and not patient specific through the State Office of Pharmacy Services.

Operational Updates/Discussion

- Clonidine-there has been 6 reported incidences of diversion at the OCCC of clonidine. Currently policy does not require clonidine to be crushed or to be ordered for medline and administered directly observed only.
- Further discussion was tabled until the November meeting when psychiatry can provide input on the use and impact of ordering clonidine DOT and by crushing only.

Formulary Updates:

The following changes were proposed for the MA DOC formulary:

- **Deletions**
  - Clobetasol cream and ointment was proposed to be removed from stock due to drastic ingredient cost increases. Currently there is no alternative very high potency topical steroid alternative on the formulary. It was recommended that as an alternative treatment, providers utilize the high potency alternatives and if medically necessary submit nonformulary requests for limited duration of use of very high potency steroids. This decision would affect
- **C-6 Stock Box-Updates**
  - Naltrexone-A proposal was made to add naltrexone to facilities stock boxes. The naltrexone will be used primarily for patients approved for naltrexone extended-release injection prior to receiving their injection to safely test for possible recent opiate use.
  - Glucagon-A proposal was made to increase the facility's par level from 2 injections to 4 injections. At one facility, their supply was depleted over the weekend and they required a 3rd injection prior to resupply which obtained from another facility.

A motion made to approve the above proposals. The proposed formulary changes were approved.

Backorders/Shortages:

E. Hamel updated the committee of the current backorders. Currently the most impactful has been the hepatitis B vaccine. Memos were sent to medical staff updating them of the supply

issues and recommending routine vaccinations be held until supply issues are resolved. Information from the CDC was relayed that informed medical staff that the series may be continued as is when the vaccine is made available without additional shots needed.

Adjournment & Next Meeting:

The meeting adjourned at 11am. The next meeting is scheduled for November 6, 2014 at the MPCH Regional Office location in Westborough MA.

MPCH
Massachusetts Partnership for Correctional Healthcare

Commonwealth of Massachusetts
Department of Correction
Pharmacy and Therapeutics Committee
Meeting Minutes

The MA DOC Pharmacy & Therapeutics (P&T) Committee Meeting was held December 4, 2014 at the MPCH regional office in Westborough Massachusetts from 9 AM to 11 AM.

The following individuals attended the meeting in person: Claudia Gonzalez, Tom Groblewski, Rhonda Cantelli, Keelin Garvey, Erik Hamel, Robert Falk, Jeff Fisher, Alki Nacopoulos, Robert Diener

Attending by teleconference: Karen Lee, Don Rogers, Joe Calamo

Guests: None

Excused member(s): Mark Waitkevich, David Stone, Laura Vasconcellos

Approval of September P&T Meeting Minutes: The minutes from the November 2014 P&T meeting were reviewed. A **motion made to approve. The minutes were approved.**

Review of Statistics: Erik presented October's pharmacy utilization data (Note-October was a 35 day reporting period):

- The census was 10,451 patients in October.
- Total prescription volume was 7,678 new orders and 30,119 refills in October.
- August pharmaceutical costs were $1,113,394
    - Medication costs after credits and returns were $1,047,680. Top cost drivers for medications ordered for medical indications were the HIV medications Atripla ($112,168, 57 orders), Truvada ($70,310, 58 orders), Reyataz ($40,548, 38 orders).
    - Psychiatric medication costs increased $105,629 were $83,032. Besides the 5 week reporting week, there was an overall increase in expenditures due to increase in perphenazine costs ($13,479, 156 orders) and chlorpromazine ($11,479, 242). Other cost drivers in this sector include aripiprazole ($11,347, 16 orders) and amitriptyline ($5,903, 271).
    - Bridgewater State Hospital medication costs were $80,470. The primary psych cost drivers included chlorpromazine ($5,518, 84 orders), clozapine ($4,977, 249 orders), and aripiprazole ($4,030, 5 orders). Non-psychiatric medications driving

BSH medication costs include: the rifaxamin ($7,732, 5 orders) and elvitegrevir ($2,356, 1 order).

- Nonformulary requests for October-272requests with 80% of the requests approved (217 requests)
  - Medical Requests-217 requests with 24% approved (166 requests)
  - Psych Requests-55 with 93% approved (51 requests)
- The top non formulary drugs, by expenditure (top 3): Sorafenib ($28,285, 2 orders), sofosbuvir ($26,852, 1 order) and Complera ($25, 592, 12 orders).
- A. Nacopoulos provided an overview of a program that SOPS has with Invega Sustena and the potential benefit to pysch patients. The program permits doses of 254 mg and 156 mg injections to be provided to DOC patients at no costs without restrictions and would be an alternative to other long-acting antipsychotics.

Infectious Disease Updates

- HIV and Hepatitis C patient statistics for August
  - 166 HIV + patients.
    - 103 HIV + patients are reported to be co-infected with hepatitis c.
    - 147 patients are undergoing HAART therapy
    - 134 patients on stable therapy have an undetectable viral load
    - 1560 patients have been identified as hepatitis C positive
  - 1 patient has initiated treatment with sofosbuvir/Peg/RBV in October. Early viral load reports indicate he is responding well to treatment.
  - Dr. Stone noted that there is a significant increase in Harvoni use in the community and recommended the MA DOC be prepared for new intakes that may be on the medication.

Drug Price Increases

- E. Hamel summarized recent significant price increases to medications within the DOC formulary
  - Generic Elavil prices have increased >2000% over what was charged ~6 months ago. Due to this price increase, the added cost may increase $60k/year. MPCH is recommending providers to switch their patients from amitriptyline to nortriptyline for the most common indication used in the medical side-neuropathy. Dosing guidance and medication information were distributed to providers.
- Clobetasol-Clobetasol, a very high potency steroid underwent a near 5000% increase in cost and was removed from the formulary in October. Providers were asked to identify patients to convert to formulary alternatives.
- Fluocinonide-Fluocinonide has recently undergone a similar price increase, as clobetasol and is being recommended to be removed from the formulary. In the meantime, providers were informed ahead of time to begin the transition where suitable.

Operational Updates/Discussion

- Auxiliary labels for new dose- A request was made to see if SOPS can add auxiliary labels when the dose of a medication changes or if the manufacturer changes to prevent

confusion. Currently auxiliary labels are not being used and are usually used when a large conversion is conducted, but the order label does contain a description of the tablet for confirmation. Another issue with pill changes are the MARs are not updated when labels are changed. Current practice is to send notification of a new manufacturer to the prescriber, but the information is not being relayed to nursing.

- Medication Event Trends-K. Lee provided an overview of medication events over a 12 month period ending in October 2014. The PDC pharmacy noted an increase number of orders being processed during the period (~32,500 to 37,000), but has seen a decreasing trend in total events reported by DOC sites and dispensing event reported and one-third to one-half are non-dispensing events.
- Medication repackaging-D. Rogers informed the committee in November that many medications that are repackaged in unit dose blister packs are recommended to be dispensed in their original container in the product information. SOPS noted that repackaging these medications are still standard practice for DOC and long-term facilities.
- Pharmacy Information Systems-D. Rogers summarized the latest progress on the implementation of the pharmacy information system (PIS) including updates to the availability of new scanners (projected to be January 2015), the use of new scanner bar coding.

New Business -The following changes were proposed for the MA DOC formulary:

- Additions-Human papillomavirus vaccine was recommended for addition due to the 100% approval rate in the nonform process.
- Deletions-Fluocinonide cream and ointment was proposed to be removed from formulary due to drastic ingredient cost increases. Currently there is one other high potency topical steroid alternative on the formulary.

A motion made to approve the above proposals. The proposed formulary changes were approved.

The review and vote of the 2015 DOC formulary draft was tabled to include the new updates and identify how to incorporate the BSH medications into one document.

Backorders/Shortages:

- E. Hamel updated the committee of the current backorders. Currently the most impactful has been the hepatitis B vaccine. Memos were sent to medical staff updating them of the supply issues and recommending routine vaccinations be held until supply issues are resolved. Information from the CDC was relayed that informed medical staff that the series may be continued as is when the vaccine is made available without additional shots needed.

Adjournment & Next Meeting:

The meeting adjourned at 11am. The next meeting is scheduled for January will be cancelled due to the holiday season and those agenda items will be presented at the February 5, 2015 meeting at the MPCH Regional Office location in Westborough MA.

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981 **Account Number:**
LS0004383147
Ordering Doctor: SMITH, BENJAMIN MD
Associated Orders: GI CLINIC EST PT LEVEL 4 **Adm/**
Date: 01/15/14
Date/Time Report Entered: 01/15/14 1607 **Patient Location:** GAS.L

REFERRING PHYSICIAN:

DATE OF SERVICE:
January 15, 2014

REASON FOR FOLLOWUP:
A 62-year-old with history of chronic hepatitis C, cirrhosis and portal hypertension, seen for followup of high alpha-fetoprotein tumor marker.

HISTORY OF PRESENT ILLNESS:
The patient is a 62-year-old with history of chronic hepatitis C, genotype 1B complicated by cirrhosis and grade 1 esophageal varices, documented by Dr. Mutinga on 04/05/2012. He also had portal gastropathy. He has been followed since 2009 for an elevated alpha-fetoprotein tumor marker. His alpha-fetoprotein tumor marker was 141.41 back on 02/19/2009. It has been as high as 202.35 on January 30, 2013. The value was 141.5 most recently on December 19, 2013. He underwent a CT scan of the abdomen on 12/17/2002. The findings included a new lesion measuring approximately 5 mm medial to the middle hepatic vein. Dr. Polak, who read the study, noted that the lesion was suspicious for neoplasm given the new appearance of this lesion compared with his prior scans from 10/14/2008 and 03/19/2012. Per the notes of Dr. Mutinga of 06/26/2013, the patient had an MRI performed at Boston Medical Center in February of 2013, which showed a 6 mm hypointense lesion thought likely to represent a dysplastic nodule. He was seen at Boston Medical Center Liver Tumor Clinic and the plan was for followup MRI in a few months per patient report. He was also suppose to be seen in followup at Boston Medical Center as recommended by Dr. Mutinga. The patient reports that he has not been seen back there, but he did undergo another MRI scan here at the Shattuck Hospital on 11/12/2013. The examination shows an enlarged liver measuring 18 cm and spleen measuring 17 cm. The liver has a nodular contour and diffuse heterogeneous enhancement consistent with cirrhosis.

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There were no focal liver lesions seen. The patient has had grade 1 esophageal varices. He has had very limited tolerance for beta blockers, which caused bradycardia at doses greater than 20 mg every other day. He also has developed lower extremity edema, but has not been able to tolerate diuretics. He reports that even low-dose of diuretic causes a dry and sore throat, and has also caused confusion. I discussed the patient's management with Carlos Flores at Shirley who corroborated the history in terms of the diuretic use. He noted that multiple diuretics have been tried at low dose, including furosemide, spironolactone, hydrochlorothiazide as well as chlorthalidone and the patient developed throat soreness, dryness or other side effects which he found intolerable. He notes that the diet is suppose to be a low sodium high-protein per the dietitian there, but that higher sodium items are accessible in the canteen if someone wants access to them. Our lab work reveals that the patient is immune to hepatitis A and hepatitis B. His most recent lab work on 12/17/2013 and 12/19/2013 showed WBC 3.6, hemoglobin 14.8, hematocrit 44, platelet 51,000. Total bilirubin was 3.4 with direct 1.6, alkaline phosphatase 190. AST and ALT were 204 and 127 respectively. Albumin was 2.8.

PAST MEDICAL HISTORY:
Includes the above. He has hepatitis C genotype 1B and did not respond to pegylated interferon and ribavirin therapy. He also has history of sore throat, and GERD symptoms. He has chronic arthritic pain. He has history of cervical spine therapy with bone grafting.

MEDICATIONS:
1. Amlodipine 5 mg a day.
2. Chlorthalidone 25 mg every day, which he has not been taking.
3. Nadolol 20 mg every other day.
4. Oxycodone 5 mg tablets, 3 tablets twice a day.
5. Protonix 40 mg a day.

ALLERGIES: IBUPROFEN.

SOCIAL HISTORY:
He is incarcerated and not smoking or drinking.

FAMILY HISTORY:
No reported family history of colonic polyps or gastrointestinal malignancy.

The patient has not had a colonoscopy, which he states is because he will not stay in the health services unit for the prep, but he would consider it, if he had the preparation in his room.

REVIEW OF SYSTEMS:
Negative for headache or stiff neck. He does have the sore throat. No exertionally related chest pain or shortness of breath. No fevers or chills. He has had intermittently dark urine. No light-colored stools. He reports chronic joint pains, but no other focal neurologic symptoms. No oral ulcers. No heat or

cell. If this is possible, I would recommend scheduling a colonoscopy with a 2-day preparation in his room. Please continue a low-sodium diet. We would like to see him back in the GI clinic in 2-3 months' time. I greatly appreciate the opportunity to continue to assist in his care.

Signed by: <<Signature on File>>
Signed by date/time: 02/26/14 1824

Dictated By: SMITH, BENJAMIN MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By:

Dictated Date/Time: 01/15/14 1458

CC:

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Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004489738
Ordering Doctor: MUTINGA, MUTHOKA L MD
Associated Orders: GI CLINIC EST PT LEVEL 3
Date: 04/22/14
Date/Time Report Entered: 04/22/14 1700

Account Number:

Adm/

Patient Location: GAS.L

REFERRING PHYSICIAN: Carlos Flores, NP

DATE OF SERVICE:
04/22/2014

REFERRING PHYSICIANS:
Carlos Flores, Nurse Practitioner

REASON FOR REFERRAL:
Followup after recent hospitalization for decompensated cirrhosis.

HISTORY OF PRESENT ILLNESS:
Mr. Paszko is a 62-year-old gentleman with advanced cirrhosis secondary to chronic hepatitis C. He was admitted to Lemuel Shattuck Hospital last month for decompensated cirrhosis manifested with anasarca and significant ascites. The decompensation occurred in the setting of the patient self discontinuing his diuretic medications for several weeks in an effort to "cleanse his body." Diuretics were reinstituted, and he had an ultrasound-guided paracentesis as well. He reports that his weight at the facility has been fluctuating between about 170-175 pounds without change in other equipment.

REVIEW OF SYSTEMS:
He reports no melena or hematochezia. Occasionally he has seen a little bit of bright red blood when he strains. He reports that his thinking is not always clear, that he sometimes feels like his brain is a little foggy. He admits that he is not taking lactulose as prescribed. He is prescribed 30 mL twice per day, but he only takes 30 mL once per day because he finds that taking the evening dose makes him have bowel movements in the middle of the night. He thinks that the lower extremity edema has been diminishing, and his ascites has also significantly diminished. He complains of a lot of arthritis involving his hands

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and his ankles and knees. He feels lightheaded sometimes in the morning. He occasionally has some dyspnea on exertion. He feels tired a lot. He is dissatisfied with his diet in that he feels that he is not given a sodium-restricted diet, and when he was offered a sodium-restricted diet it was more of a renal diet which was very bland and low in calories and led to some further weight loss. He complains of dry skin.

DATA REVIEWED:
He had an MRI in November 2013. This was notable for the absence of any focal liver lesions. His last alpha-fetoprotein level that was measured here at the Shattuck was 123.9 in May of 2013.

CURRENT MEDICATIONS:
He takes nadolol 20 mg every other day. He is not able to tolerate a daily dose. He is prescribed lactulose 30 mL twice per day, but he takes 30 mL once per day. He has rifaximin 550 mg twice per day. He takes amlodipine 10 mg daily, nadolol 20 mg every other day, as mentioned; Protonix 40 mg daily; Metamucil 1 tablespoon daily; eplerenone 50 mg twice per day; furosemide 80 mg daily. It looks like he is prescribed Keflex 500 mg 3 times a day for 10 days.

ALLERGIES: MOTRIN CAUSES GI BLEED.

EXAM:
Today, height 5 feet 10 inches, weight 182 pounds. He was 187 pounds the last time he was seen in the clinic in October 2013. Blood pressure 116/83, heart rate of 55, respiratory rate of 20, sats 98% room air. Temperature 97.4.
HEENT EXAM: He has faint scleral icterus. Neck is supple. No lymphadenopathy. He has some spider angiomas on his face. He has no thyromegaly.
LUNGS: Clear to auscultation. He has mild bilateral gynecomastia. Some spider angiomas on his chest.
CARDIOVASCULAR EXAM: Regular rate and rhythm.
ABDOMEN: Soft. There is no flank bulging to suggest ascites. He has a small reducible umbilical hernia.
EXTREMITIES: Reveal 1+ edema at the level of the ankles.
NEUROLOGICALLY: He has a clear sensorium. Oriented x3. No asterixis.

IMPRESSION/RECCOMENDATIONS:
1. Advanced cirrhosis with elevated alpha-fetoprotein and previously noted hepatic nodules. His most recent MRI in November 2013 did not reveal any liver lesions. He has previously been followed at Boston Medical Center Liver Tumor Clinic. I recommend that he have a followup MRI in May 2014, that is next month, which would be a 6-month interval from his last MRI, and alpha-fetoprotein should also be checked at that time.
2. With regard to the advanced cirrhosis, I recommend that he maintain a low-sodium (maximum 2 grams of sodium per day) diet. I suggest that he be seen by a dietitian to give further recommendations on how to optimize his diet and maintain adequate caloric intake. I recommend that he continue to take the nadolol and that he avoid aspirin or NSAIDs. I would consider reducing

the amlodipine dose in case it is contributing to his lightheadedness and fatigue, especially in light of his relatively low blood pressure.
3. Chronic hepatitis C genotype 1b, prior nonresponder to pegylated interferon and ribavirin. Given his advanced liver disease, at this time he is not a good candidate for the antiviral therapy that is currently available.
4. Colorectal cancer screening: He has had no prior colonoscopy. Please confirm that EGD and colonoscopy with Anesthesia support have been scheduled. I believe these may have been scheduled earlier this year, but may have been postponed because of his acute illness. He may require admission for bowel preparation at Lemuel Shattuck Hospital if he is unable to safely do the bowel preparation at the facility. I would recommend that he have both an upper endoscopy and colonoscopy with Anesthesia support as previously recommended.
5. I also recommend that he have continued followup in the Liver Tumor Clinic at Boston Medical Center.
6. Lastly, he should follow up in the GI clinic in approximately 3 months for continued close monitoring.

Signed by: <<Signature on File>>
Signed by date/time: 04/29/14 1618

Dictated By: MUTINGA, MUTHOKA L MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By:

Dictated Date/Time: 04/22/14 1520

CC:

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Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH MEDICAL CONSULTATION RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS0057981 **Account Number:**
LS0004546537
Ordering Doctor: ARMSTRONG, CATHARINA MD
Associated Orders: PCC/MEDICAL NEW PT LEVEL 3
Adm/Reg Date: 06/12/14
Date/Time Report Entered: 06/12/14 1420 **Patient Location:** 8NO.L

REFERRING PHYSICIAN:

DATE OF SERVICE:
June 12, 2014

PRESENTING COMPLAINT:
Lower extremity edema, abdominal edema, scrotal edema, and intermittent noncompliance with diuretics in the setting of end-stage liver disease secondary to previously treated and failed hepatitis C.

HISTORY OF PRESENTING COMPLAINT:
This is a 62-year-old man with a known history of hepatitis C genotype 1B, previously treated with PEG interferon and relapsed, with a background history of grade 1 esophageal varices noted in 2012 who had been refusing to take his Lasix approximately 4 weeks ago, as he was feeling better, and then a week and a half ago he restarted it. But in the setting of this, he has gained; he has gone from a weight of 196 on the 22nd of May to 220 today. He also has significant abdominal swelling and scrotal edema as well as lower extremity swelling. The patient is now being admitted for further management for his increased ascites. Also of note, the patient reports that he had a fall and had a fracture to his left leg and has been walking on this leg and has had an increased amount of swelling in his left leg as well as pain. The patient is also intermittently not taking his lactulose. The patient comes in today.

MEDICATIONS:
Med list includes the following meds: Lasix, which was taken as late as last night, 80 mg p.o. b.i.d., recently brought up from 60 mg, 80 mg started yesterday; Prilosec p.o. 20 mg daily; amlodipine 10 mg p.o. daily; lactulose 30 mL p.o. 4 times a day; Cipro 500 mg p.o. b.i.d., assuming for SBP prophylaxis; lactulose 10 mg daily; nadolol 20 mg p.o. daily; oxycodone 4 tablets for chronic

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pain t.i.d.; pantoprazole 40 mg p.o. daily; clobetasol 0.05% cream b.i.d.

LABORATORY DATA:
Last labs were done in the facility on the 10th of June. They include a CBC with diff. A white count of 3.63, H and H 12.5 and 37.5, platelets of 49. Absolute neutrophils 3500.
Comprehensive metabolic panel: Creatinine 0.59, BUN 12. Alk phos 296, AST 296, ALT 121. Sodium 135, potassium 3.8, chloride 103. no other the testing done.

IMAGING:
Patient also reports he had imaging of the left leg. I do not see it included here.

PHYSICAL EXAMINATION:
VITAL SIGNS: Last set of vital signs are reported on this sheet from today. Temperature 98.4, heart rate 79, respiratory rate 16, and 95% on room air for an O2 sat. Blood pressure 129/82. Weight on 06/04/2014 was 209, that is up from 196 on 05/22, and today he is 122.

Therefore, in the setting of the patient's increased weight gain, abdominal ascites, scrotal ascites, left lower extremity worse than great lower extremity edema, recent fracture, he was sent over for further management.

PAST MEDICAL HISTORY:
Hypertension, BPH, psoriasis, lower extremity edema, arthritis, GERD, surgery to C-spine for fusion, tonsillectomy, left ankle recent fracture.

MEDICATIONS:
As listed.

ALLERGIES: MOTRIN.

IN TERMS OF THE PATIENT'S PAST MEDICAL HEPATITIS C HISTORY, HE WAS TREATED IN OLD COLONY CLINIC. HE HAS HEPATITIS C GENOTYPE 1B. PRIOR TREATMENT WITH PEG INTERFERON. PATIENT WAS A PRIOR NONRESPONDER TO PEG INTERFERON. HE HAS BEEN FOLLOWED BY DR. MUTINGA, AND GIVEN HIS ADVANCED LIVER DISEASE, HE IS A GOOD CANDIDATE AT THIS TIME FOR DIRECT-ACTING ANTIVIRALS, AS MENTIONED IN DR. MUTINGA'S NOTES MOST RECENTLY AS 04/29/2014.

OTHER ISSUES, IS THE PATIENT HAS NOT HAD A PRIOR COLONOSCOPY/ENDOSCOPY, AND THIS WAS SUPPOSED TO BE SCHEDULED IN THE OUTPATIENT, AND THIS DID NOT OCCUR, AND HE HAS HAD EPISODES OF HEMATEMESIS AND GUAIAC-POSITIVE STOOL. THEREFORE, THIS HAS BEEN POSTPONED, AND THIS NEEDS TO BE DONE.

ASSESSMENT AND PLAN:
This is a 62-year-old man with advanced cirrhosis secondary to chronic hepatitis C genotype 1B, prior relapser, now with abdominal ascites, lower extremity swelling, scrotal ascites all secondary to end-stage liver disease.
1. Scrotal and abdominal ascites: Patient has ascites. He does not report any fevers, chills, but in the setting of ascites, he should have at least a diagnostic paracentesis to rule out spontaneous bacterial peritonitis. He

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is on spontaneous bacterial peritonitis prophylaxis with a quinolone, although this does not completely rule this out. The patient does not have an significant O2 requirement, but there are reports in the outside records that his O2 sats have decreased to 94%-95%. Therefore, a therapeutic tap to rule ourt SBP and better understand the ascities fluid cell makeup, if possible, would be recommended though I suspect he will have a significant amount of ascities will be present and provide relief if removed via therapuetic tap. I have sent him down for an abdominal ultrasound including a scrotal ultrasound, including coags.

2. Cirrhosis: Patient is on nadolol. Also on lactulose, although he has not taken it consistently. I have asked for one of the labs to be an ammonia level to assess his ammonia level in the setting of intermittently taking his lactulose. He should continue his nadolol.
3. Diuresis: Needs abdominal ascites, lower extremity ascites. Patient has recently been brought up from 60 mg p.o. b.i.d. to 80 mg p.o. b.i.d. He has intermittently not been taking. He likely will need IV Lasix at this point, as his weight is at 220, up from 196 on May 22nd. The patient is extremely fluid overloaded. Although he does not have an O2 requirement right now, he has had reports of low O2 saturation.
4. Hepatitis C: Patient, as mentioned, is a good candidate for treatment at this point, even with advanced liver disease, with direct-acting antivirals. He is genotype 1B. This has been discussed with him between himself and Dr. Mutinga. I would advise that Dr. Mutinga be alerted to his admission here.
5. Left lower extremity fracture: The patient reports that he fell and was told that he fractured his left lower extremity. He notes that he has had increased pain and increased swelling in the left lower extremity and has been walking on this fracture site. I did order a left lower extremity plain film.

DISPOSITION:
The patient will be admitted to he acute service. I have talked to Dr. Stone, the admitting attending, and the admitting team has been paged, and he will be admitted to the acute service.

LABS ORDERED:
Full CBC with diff, coags including albumin, comprehensive metabolic panel, ammonia level.

Signed by: <<Signature on File>>
Signed by date/time: 06/24/14 0142

Dictated By: ARMSTRONG, CATHARINA MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By:

Dictated Date/Time: 06/12/14 1317

CC:

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Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004674032
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 11/20/14 1432

Account Number:

Adm/Reg Date: 11/14/14
Patient Location: 8NO.L

REFERRING PHYSICIAN:

DATE OF SERVICE:
November 20, 2014

HISTORY OF PRESENT ILLNESS:
Emilian Paszko is a 63-year-old man with a past medical history significant for cirrhosis secondary to hepatitis C that has been complicated by esophageal varices, hepatic encephalopathy, and recurrent ascites, who is being seen in consultation for evaluation of management of cirrhosis as well as further discussion of treatment for hepatitis C virus. At the current time, the patient appears to be diuresing well. He notes that he has lost approximately 22 pounds during this admission. He has had good urine output over the past few days and notes that his urine output is significantly better with IV Lasix than it is with p.o. Lasix. He notes that he has continued to have intermittent periods where he gains a significant amount of abdominal fluid and has required intermittent paracenteses, as recently as last week. He notes that he is not having significant abdominal pain when this occurs; although, his hernias cause him significant problems, particularly his inguinal hernia. He reports some nausea in the mornings after he receives his dose of Lasix, but this tends to go away and he is able to maintain his appetite, for the most part. He notes that in addition to his ascites improvements, he has noticed improvement in his lower extremity edema, as well. He denies any recent encephalopathy and notes that his thinking has been relatively clear for the past 3 months. He reports that his breathing is relatively comfortable at this point in time. He notes that he is aware of the need for a low-salt diet. However, he has trouble with this at his facility because all the foods are high in salt, per his report. The patient has had multiple hospitalizations over the past few months for complications related to his cirrhosis, and he has been frustrated by the repeat hospitalizations, per his report.

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REVIEW OF SYSTEMS:
The balance of the 12-system review was negative other than as described in the HPI.

PAST MEDICAL HISTORY:
1. Cirrhosis secondary to hepatitis C, genotype 1B. Previously attempted treatment with interferon, which failed per patient's report.
2. Esophageal varices status post most recent banding in June 2014.
3. Recurrent ascites requiring intermittent paracenteses.
4. Umbilical hernia.
5. Hypertension.
6. Chronic arthritis.
7. History of hepatic encephalopathy.
8. History of SBP.

MEDICATIONS ON ADMISSION:
1. Amiloride 5 mg p.o. b.i.d.
2. Nadolol 40 mg p.o. daily.
3. Eplerenone 80 mg b.i.d.
4. Rifaximin 550 mg p.o. b.i.d.
5. Lactulose 60 mL p.o. 4 times a day, titrated for 4 to 5 soft bowel movements.
6. Double-strength Bactrim tablet p.o. daily.
7. Oxycodone 10 mg p.o. every 4 hours p.r.n. pain.
8. Omeprazole 20 mg p.o. b.i.d.
9. Colace 100 mg p.o. b.i.d.
10. Senna 2 tablets p.o. at bedtime.
11. Lasix 120 mg p.o. b.i.d.

ALLERGIES: PATIENT IS INTOLERANT TO NSAIDS.

SOCIAL HISTORY:
Prior tobacco user, as well as a remote history of alcohol and IV drug use.

PHYSICAL EXAMINATION:
VITAL SIGNS: Temp 97.9, pulse 60, respiratory rate 18, blood pressure 114/73, O2 sat 97% on room air.
GENERAL: The patient is an ill-appearing 63-year-old man in no apparent distress.
HEENT: Sclerae anicteric.
NECK: Supple.
CARDIOVASCULAR: Normal rate, normal rhythm. No murmurs, rubs, or gallops.
LUNGS: Clear to auscultation bilaterally. No wheezes, rales, or rhonchi.
ABDOMEN: Bowel sounds present. Abdomen soft, distended, with notable dullness to percussion consistent with a large amount of ascites on board.
EXTREMITIES: 2 to 3+ pitting edema of the lower extremities with trace pitting edema all the way up to the upper thigh area in dependent areas.
NEURO: No evidence of asterixis. No focal neurologic deficits on exam.

LABORATORY STUDIES:
White blood cell count 3.4, hemoglobin 10.2, hematocrit 29.8, platelet count 48.

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Sodium 133, potassium 4, chloride 100, bicarb 29, BUN 18, creatinine 1.4, glucose 100, calcium 8.3, INR is 1.5.

ASSESSMENT:
Emilian Paszko is a 63-year-old man with past medical history significant for cirrhosis secondary to hepatitis C virus, complicated by ascites, esophageal varices, SBP, hepatic encephalopathy in the past, who is now being seen in consultation for evaluation and management of cirrhosis, as well as consideration of hepatitis C treatment. We had a long discussion with the patient regarding the potential for hepatitis C treatment and the fact that, the newest therapies are not approved in the DOC system at this point in time; although, the patient would certainly be a candidate for consideration of therapy once these are approved. This would be done on an outpatient basis. The patient would need to follow up in GI clinic following his hospitalization for further discussion of this. He does have a longstanding history of cirrhosis that appears decompensated at this point in time, with the multiple complications listed above. At this point in time, the most pressing issue appears to be his fluid balance and his increasing requirement for paracenteses and a lack of response to p.o. diuretics. While he is continuing to diurese heavily with IV Lasix, his creatinine is at 1.4 now and we would recommend close monitoring of his renal function as well as his electrolytes with these high doses of Lasix therapy. Although the patient certainly has a large amount of fluid on board, if he were to develop worsening kidney injury, this would be a significant detriment given his poor liver function at this point in time. We discussed all these recommendations with the patient at length, including his need for strict low-sodium diet. He expressed understanding. He is to be commended for his adherence to the lactulose and rifaximin regimen, as evidenced by his lack of hepatic encephalopathy, which been a significant problem for him in the past. It appears that he has been over 3 months without any confusion, which is a significant achievement for him.

RECOMMENDATIONS:
1. Patient should follow up in GI clinic following this admission for further discussion regarding the potential for treatment for his hepatitis C virus. Again, once the newer therapies are approved, he would be a patient that would receive consideration of treatment.
2. Continue to monitor patient's diuresis with close monitoring of electrolytes and renal function for the reasons detailed above.
3. If patient becomes refractory to diuretic therapy, he may simply require standing paracenteses as often as once every 2 weeks. He has not declared himself at that point currently; however, this remains a consideration moving forward. He would be less likely as a candidate for TIPS therapy, given his history of profound hepatic encephalopathy.
4. Agree with continued treatment for prophylaxis for SBP, given his history.
5. Would continue to monitor his ins and outs strictly.
6. Continue to avoid any hepatotoxic agents.
7. We did discuss with the patient that he is not a good candidate for hernia repair at this point in time, given the massive amount of ascites. Although this would ultimately be the decision for the surgeons, this would be a risky procedure given the stage of his liver disease and the amount of ascites present.

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Date Report Last Updated: 11/28/14
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The patient was seen and examined with Dr. Alene Conant who agrees with the assessment and plan.

GI STAFF ADDENDUM:
I have seen and evaluated the patient. I have discussed with the resident/fellow and agree with the resident/fellow's findings and plan as documented in the above note. Mr. Emilian Paszko is a 63 yo male with hepatitis C cirrhosis presenting with weight gain, edema, and ascites. The most likely etiology is dietary indiscretion (sodium intake over 2 grams per day). I agree with closely monitoring his renal function with aggressive IV diuresis. If his ascites is refractory to diuretics, then standing paracentesis would be needed as he is not a good candidate for TIPS given his history of encephalopathy. He should follow up in GI Clinic to discuss hepatitis C treatment. He would be considered for treatment when the new medications become available.

Alene Conant, MD

Signed by: <<Signature on File>>
Signed by date/time: 11/28/14 0946

Dictated By: BARNES, EDWARD L MD

Co-Signed by: <<Signature on File>>
Co-Signed by date/time: 11/21/14 1142
Co-Dictated By: CONANT, ALENE MD

Dictated Date/Time: 11/20/14 1318

CC:

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 11/28/14
W37791

Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004673448
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 12/03/14 1750

Account Number:

Adm/Reg Date: 12/03/14
Patient Location: GAS.L

REFERRING PHYSICIAN:

DATE OF SERVICE:
December 3, 2014

CHIEF COMPLAINT:
Followup after hospitalization, chronic hepatitis C, refractory ascites.

Mr. Paszko is a 63-year-old gentleman with a history of chronic hepatitis C cirrhosis with ascites and esophageal varices, presenting after his recent hospitalization for volume overload. At that time, the patient weighed 222 pounds. He came in and was aggressively diuresed with IV Lasix, down to a weight of 170 pounds. He was discharged on eplerenone as well as Bumex in addition to dietary restrictions and rifaximin and lactulose for encephalopathy. The patient reports that he has been unhappy at his current facility. He reports he has not seen anyone in regards to a physician or psychiatrist since his admission. He has been compliant with his medications. He had labs obtained as recommended on December 1, 2014. He reports that he is thirsty. He denies fevers or chills. His abdomen is not distended anymore than when he was discharged from the hospital. He denies GI bleeding.

REVIEW OF SYSTEMS:
As per HPI. Otherwise, all other review of systems are negative.

PAST MEDICAL HISTORY:
Chronic hepatitis C with decompensated cirrhosis, esophageal varices, status post banding with most recent procedure in early November with eradication of varices noted, hepatic encephalopathy, umbilical hernia, hypertension.

ALLERGIES: NO KNOWN DRUG ALLERGIES.

MEDICATIONS:
Lactulose 45 mL p.o. q.i.d., Bumex 3 mg in the morning 2 mg at bedtime, rifaximin 550 mg p.o. b.i.d., nadolol 40 mg daily, Bactrim 1 tablet daily, omeprazole 20 mg b.i.d., eplerenone 50 mg twice daily, amiloride 5 mg twice daily, senna 2 tablets b.i.d. p.r.n. constipation, oxycodone 10 mg p.o. q.4

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hours p.r.n. pain.

PHYSICAL EXAM:
VITAL SIGNS: Temperature 97.8, pulse 91, blood pressure 126/86, respiratory rate 18, O2 sat 100% on room air. Pain 0/10. Height 5 feet 11 inches, weight 165.6 pounds.
GENERAL: The patient is a chronically ill-appearing gentleman in no acute distress.
HEENT: Sclerae is mildly icteric. Conjunctiva is pink. Oral mucosa is moist. No oral ulcerations.
NECK: Supple without lymphadenopathy.
CARDIOVASCULAR: Regular rate. Normal S1, S2. No murmurs.
PULMONARY: Clear to auscultation bilaterally.
ABDOMEN: Soft, distended with ascites. Umbilical hernia present. No rebound or guarding.
EXTREMITIES: Trace edema.
NEURO: No asterixis.
SKIN: Telangiectasias on the upper chest.

LABORATORY DATA:
From December 1, 2014: BUN 24, creatinine 1.35. This is stable from the time of discharge. Sodium 130, also stable from time of discharge. Potassium 4.6, AST 134, ALT 54. White blood cell count 3.7, hematocrit 34.6, platelets 58.

ASSESSMENT:
Mr. Emilian Paszko is a 63-year-old gentleman with a history of chronic hepatitis C cirrhosis with ascites, hepatic encephalopathy and history of esophageal varices. His most recent hospitalization was in the setting of refractory ascites, most likely due to dietary indiscretion. He improved with aggressive IV diuresis and adjustment of his diuretics as well as limiting sodium in his diet. Since discharge, his weight has decreased by about 5 pounds based on his discharge weight of 170 pounds. His BUN and creatinine and sodium remain stable. The patient did not have asterixis on exam today. He is alert and oriented to person, place and time. He does not have symptomatic encephalopathy at this point. He is not happy about his current living situation, which as I told him, is something that is beyond my control. We are focusing on managing his chronic hepatitis C and decompensated liver disease. At this time, I would make the following recommendations:
1. The patient should continue Bumex 3 mg in the morning. I recommend decreasing the evening dose to 1 mg at bedtime.
2. Continue the eplerenone 50 mg twice daily.
3. Continue lactulose and rifaximin for treatment of hepatic encephalopathy.
4. Continue nadolol 40 mg daily for treatment of esophageal varices.
5. The patient to have labs checked twice per week. Please fax the results to the GI Clinic for review. Please check the patient's weight daily. I also recommend sending at the end of the week his weight summary for review to the GI Clinic at 617-971-3489.
6. The patient should follow up with us in clinic in 2 week's time. At that time, we can readdress scheduling the patient for a screening colonoscopy, if appropriate.

Alene Conant, MD

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LEMUEL SHATTUCK HOSPITAL
LSH GASTROINTESTINAL CONS. RPT

PASZKO, EMILIAN MEDICAL RECORD NUMBER: LS00057981

Signed by: <<Signature on File>>
Signed by date/time: 12/03/14 1811

Dictated By: CONANT, ALENE MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By:

Dictated Date/Time: 12/03/14 1606

CC:

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Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004696183
Ordering Doctor: MUTINGA, MUTHOKA L MD
Associated Orders: CLINIC EST LEV 1
Date: 12/16/14
Date/Time Report Entered: 12/16/14 1700
TELEGI.L

Account Number:

Adm/Reg

Patient Location:

REFERRING PHYSICIAN: Maria Angeles, MD

DATE OF SERVICE:
December 16, 2014.

REASON FOR REFERRAL:
Followup of end-stage liver disease with progressive ascites.

HISTORY OF PRESENT ILLNESS:
Mr. Paszko was briefly seen in Telemedicine Clinic, but we advised that he be seen in the physical clinic at the Lemuel Shattuck Hospital because of his complex medical problems, which also require physical exam. Of note, he is actually scheduled for a followup visit at the Lemuel Shattuck Hospital on December 23, 2014. I briefly spoke with him today.

Mr. Paszko was last seen in GI Clinic on December 3, 2014. He has chronic hepatitis C, and has had difficult to control ascites. He has required hospitalization for intravenous diuresis, and as detailed by Dr. Conant on her from December 3, 2014, when he was last discharged from the hospital, his weight was 170 pounds. He was discharged from the hospital on a combination of eplerenone and Bumex, and he was also supposed on sodium restriction, and was also prescribed rifaximin and lactulose for control of his ascites. When he was seen in clinic on December 3, 2014, his weight was 165.6 pounds.

Mr. Paszko states that he is weighed on a daily basis, and that his weight has been gradually increasing since his last clinic visit. In fact, today his weight was 184 pounds, an increase of close to 20 pounds over the last 2 weeks. He states that he is not on a sodium-restricted diet because of this is hard to adhere to in light of limitations with what he can be given in the cafeteria.

On review of his medications, he is prescribed Bumex 3 mg in the morning and 2 mg at 4 p.m. in the afternoon. According to the nurse who reviewed his records, there have been several days in which he has declined to take the Bumex in the

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morning, although Mr. Paszko states that he only recalls 1 day declining to take the medication. With regards to the afternoon dose of the Bumex that was just prescribed on December 8, and his 1st dose was administered on December 10. He is taking eplerenone 50 mg twice per day. He has not had any abdominal pain. He has not experienced any lower extremity edema, but his abdominal girth has been increasing. He has had he reports no shortness of breath.

LABORATORY DATA:
His most recent lab tests were from December 8, 2014. They were as follows: December 8, his BUN was 17, his creatinine was 1.03. His white count was 3.4, hematocrit 33.0, platelet count 55.

Prior to that on December 1, 2014, his BUN was 14, creatinine was 1.35. His potassium was 4.6, sodium was 130, chloride was 99, bicarb was 23. His hematocrit was 34.6.

FINDINGS:
VITAL SIGNS: At the facility today, temperature 97.9 heart rate 69, respiratory rate of 18, blood pressure 117/78, weight 184.4 pounds, sats 98% room air.

PHYSICAL EXAMINATION:
Physical exam was not performed. Patient seen in telemedicine.

CURRENT MEDICATIONS:
I have reviewed and confirmed that his current medications are as follows: He is taking eplerenone 50 mg twice per day, lactulose taking 60 mL 4 times a day. He takes rifaximin 550 mg twice per day. Nadolol 40 mg daily, omeprazole 20 mg twice per day. He is taking the Bumex 3 mg in the morning and 2 mg at 4 p.m. He is taking oxycodone 10 mg q.4 hours p.r.n. for pain.

RECOMMENDATIONS:
1. I strongly believe that he would benefit from a more closely adhered to sodium restricted diet. Patients with advanced cirrhosis are very sensitive to sodium intake, and it is difficult to control the ascites and peripheral edema without truly controlling their sodium intake and limiting it to no more than 2 g of sodium per day. I would strongly recommend working closely with the dietitian to see what provisions can be made to make it more likely that he can adhere to a sodium-restricted diet.
2. I would recommend continued daily weights and recording of these weights, and I would recommend that these weights be sent with him to the clinic.
3. He should follow up in the GI clinic in the physical clinic at the Shattuck Hospital for all future visits, and he is scheduled for 1 on December 23, 2014, which he should keep.
4. I recommend that prior to his upcoming visit a that is chem 7, which will include his electrolytes, BUN, and creatinine be checked. I also recommend that coagulation and platelet count be checked as well prior to that visit.
5. I recommend that he be scheduled for a therapeutic paracentesis in the medical clinic on the same day, December 23, 2014. I recommend that be done in the morning so that it will not interfere with his afternoon GI clinic visit. I have spoken today with that Dr. Arielle Adrien in the medical clinic to make sure that it would be okay to have him get a therapeutic paracentesis there in the clinic. Given his advanced liver

disease, I would suggest that he received some salt poor albumin either before or during the paracentesis. Also on December 23, 2014, before his GI clinic visit, that paracenteses should be arranged in the medical clinic on that day.

Signed by: <<Signature on File>>
Signed by date/time: 12/30/14 1647

Dictated By: MUTINGA, MUTHOKA L MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By:

Dictated Date/Time: 12/16/14 1523

CC:

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH DISCHARGE SUMMARY

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004699799
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 12/30/14 1339
Discharge Date/Time: 01/01/15 1130

Account Number:

Adm/Reg Date: 12/19/14
Patient Location: 8NO.L

DATE OF SERVICE:
January 1, 2015.

DISCHARGE DIAGNOSIS:
Ascites secondary to dietary noncompliance.

MEDICATIONS ON DISCHARGE:
1. Bumex 3 mg p.o. b.i.d.
2. Eplerenone 50 mg p.o. b.i.d.
3. Lactulose 60 mL p.o. q.6 hours.
4. Nadolol 40 mg p.o. daily.
5. Omeprazole 20 mg p.o. twice daily.
6. Polyethylene glycol 1 packet p.o. daily.
7. Rifaximin 550 mg p.o. twice daily.
8. Bactrim 800/160 mg 1 tablet p.o. daily.
9. Oxycodone 10 mg p.o. q.4 hours p.r.n. pain.
10. Clotrimazole 1% cream, 1 application twice daily.
11. Peroxide swish and spit.
12. Metolazone 5 mg p.o. once daily p.r.n. 5-pound weight gain.

Please check a basic metabolic panel to evaluate renal function after giving a dose of metolazone. Note this metolazone should only be given if the patient has a 5-pound weight gain.

ALLERGIES: IBUPROFEN.

CHIEF COMPLAINT:
Weight gain.

HPI:
Mr. Paszko is a 63-year-old gentleman with hepatitis C, cirrhosis, grade 2 esophageal varices status post banding, an umbilical hernia, and recurrent ascites, who presents from his facility after a 33-pound weight gain over the 15 days prior to admission. Per report from the facility, the patient's dry weight is 152 pounds which was documented on December 4, 2014, and they reported

noncompliance with a salt and fluid restriction at the facility. They note he gained 33 pounds since December 14th. He was 186 pounds on admission. After speaking with the patient, he noted that he had been gaining a couple pounds every day over the past 2 weeks. He noted that it was difficult to comply with the salt-restricted diet at his facility, and he noted that many of the foods that he had been served were high in salt. He did try to comply with the fluid restriction, but he noted that he felt dehydrated often and stated that he felt that he is doing okay with the fluid restriction.

Prior to admission on December 7th, the patient's Bumex had been increased from 2 mg b.i.d. to 2 mg in the afternoon and 3 mg in the morning due to weight gain. He noted that over the 2 weeks prior to admission he could feel his abdomen becoming more distended. He noted that his legs started swelling 2 days prior to admission. He did not have pain in his legs and abdomen but noted some pressure in the legs. He did note some shortness of breath secondary to the fluid in his abdomen and some wheezing as well. He did note dyspnea on exertion and some orthopnea. He tried to elevate his legs as much as possible prior to admission. Due to the increased dose of diuretic, he had noted increased urination but no pain, dysuria, hematuria, change in color or dark urine. He noted that he had not been constipated or had any diarrhea. He denies any hematochezia. He denied black stools. He denied nausea and vomiting, recent confusion, or changes in vision. He denied recent illness, fever, chills, or sweats. He denied any chest pain. He had not had subacute bacterial peritonitis in the past. He was previously scheduled for a therapeutic paracentesis the week following admission.

PAST MEDICAL HISTORY:
Hepatitis C diagnosed in 1989, cirrhosis, grade 2 esophageal varices status post banding June 2014, umbilical hernia, recurrent ascites.

PHYSICAL EXAMINATION:
VITAL SIGNS: On admission, weight 186.4 pounds. Temperature 97.5, heart rate 167, blood pressure 105/67, respiratory rate 18, oxygen saturation 100% on room air.
GENERAL: Patient is calm, cooperative, in no acute distress, lying supine in bed, pleasant and conversant.
HEENT: Slight scleral icterus is noted. Normocephalic, atraumatic. Mucous membranes appear slightly dry.
NEURO: Alert and oriented x3. No asterixis. Cranial nerves 2-12 are intact.
CARDIOVASCULAR: Regular rhythm. No murmur appreciated.
PULMONARY: Clear to auscultation bilaterally. No wheezing. Nonlabored.
ABDOMEN: Soft, distended, fluid wave is present. No tenderness. No firmness. Hernia is present. Bowel sounds are present and equal in all 4 quadrants.
EXTREMITIES: Radial and DP pulses are 2+ bilaterally. Pitting edema 2+ to the hip bilaterally.

FINAL PHYSICAL EXAMINATION:
VITAL SIGNS: Temperature 97.7, heart rate 64, blood pressure 106/62, respiratory rate 18, oxygen saturation 98% on room air. Weight 169 pounds.
GENERAL: The patient is in no acute distress, calm and cooperative, supine in bed, pleasant and conversant.
HEENT. Scleral icterus is present. Normocephalic, atraumatic. Mucous membranes are moist.
CARDIOVASCULAR: Regular rhythm. No murmur appreciated.
PULMONARY: Clear to auscultation bilaterally. No wheezing, nonlabored.

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Date Report Last Updated: 01/02/15

ABDOMEN: Soft, slightly distended, but improved. No tenderness. No firmness. Hernia is present. Bowel sounds are present and equal in all 4 quadrants.
NEURO: Alert and oriented x3. No asterixis.
EXTREMITIES: Radial and DP pulses are 2+ bilaterally. Pitting edema is 2+ to the knees bilaterally.

LABORATORY DATA:
White blood count 3.5, hemoglobin 11.2, hematocrit 31.9, platelet count 51. Sodium 133, potassium 3.7, chloride 99, CO2 of 26, BUN 12, creatinine 1.3, glucose 161, calcium 8.2.

Total bilirubin 3.5, AST 132, ALT 55, alkaline phosphatase 157, total protein 7.4, albumin 2.3, globulin 5.1.

Peritoneal fluid showed a white blood cell count of 62 negative for SBP. Peritoneal fluid culture and Gram stain were negative.

HOSPITAL COURSE:
1. Ascites. The patient presented with a 33-pound weight gain over a several-week period despite increasing his p.o. Bumex. He was initially scheduled for a therapeutic paracentesis several days after his admission. He was started on IV Bumex 3 mg b.i.d., and he was monitored with strict in's and out's and daily weights. He was placed on a salt-restricted and fluid-restricted diet. He was given a pen and a pad to keep track of his daily urine output. Upon admission, the patient's creatinine was found to be 1.2 in the evening. The next morning it was found to be slightly elevated at 1.5. We continued to trend his creatinine which remained at 1.5-1.6 for the majority of his stay. On the day of discharge, his creatinine was 1.3. The patient diuresed well during his admission. The 3 mg of Bumex b.i.d. was getting some response; however, it was not the desired 2 L negative that we had targeted, so he was given 2.5 mg of metolazone once on December 23rd, which did not have much effect, so the following day on the 24th he was given 5 mg of metolazone which had good effect on urine output. His electrolytes were monitored during his entire admission, and potassium was repleted as necessary. On December 26, the patient complained of some slight subxiphoid tenderness, and a diagnostic and therapeutic paracentesis was performed. 8 L of fluid was removed, and his vital signs remained stable. He was given 25 g of albumin during the procedure. His blood pressure remained stable during and after the procedure. The diagnostic paracentesis showed no evidence of SBP. Given that the patient had been seen by GI for quite some time and they had recommended a colonoscopy, which had been documented back to the spring of 2014 and he had since refused, he was scheduled for a colonoscopy on Monday, December 29th. He tolerated the prep well, and the colonoscopy was performed. The colonoscopy showed no masses, AVMs, polyp strictures, or mucosal erythema or ulceration. There were small internal hemorrhoids noted. The patient was transitioned to oral Bumex on December 29th. The patient, despite his fluid restriction and diuresis, began slowly reaccumulating fluid. He is to be discharged on 3 mg b.i.d. of Bumex, which can be titrated upwards if needed for weight gain depending on his renal function and electrolyte status. If the patient gains 5 pounds or more, the facility should feel free to give 5 mg of metolazone once that day and draw a basic metabolic panel the following day to evaluate renal function and electrolytes status. The patient appears to have refractory ascites and may need definitive therapy. He would likey benefit from an evaluation for a TIPS procedure.

The patient received an additional 5mg metolazone on 12/30/14 for fluid reaccumulation and had adequate diuresis.

2. Hepatitis C. The patient has had hepatitis C since 1989 and carries a diagnosis of cirrhosis. He has been followed by Dr. Mutinga of Gastroenterology. He was continued on his home lactulose, rifaximin, and Bactrim for SBP prophylaxis. He was also continued on his home nadolol for esophageal varices and portal hypertension. The patient remained asymptomatic from this standpoint while admitted.
3. Guaiac-positive stool. The patient tested positive for guaiac-positive stool while he was admitted. He had been refusing a colonoscopy in the past due to concerns of prepping at his facility. He was prepped successfully on Sunday, December 28th, and underwent colonoscopy on December 29th. He tolerated the procedure well, and there was no finding of masses, AVMs, polyp, strictures, ulcerations.
4. Diet. The patient was on a 1.5 L fluid-restricted diet with a 2 g sodium restriction. He was given Venodynes for DVT prophylaxis.

CONDITION ON DISCHARGE:
Stable.

FOLLOWUP PLAN:
The patient should follow up with gastroenterology at the next regularly scheduled appointment. The patient would also likely benefit from an evaluation for a TIPS procedure.

The patient should be seen by a dental clinic for complaints of gingival pain.

The patient should be seen by optometry, as he complained several times about not having his glasses.

If the patient gains 5 pounds, the facility should feel free to give 5 mg of metolazone once and evaluate renal function and electrolyte status the following day with a basic metabolic panel.

Time required for discharged greater than 60 minutes.

Signed by: <<Signature on File>>
Signed by date/time: 01/02/15 1413

Dictated by: VOLIN, SAMUEL D MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated by: ROY, DONNA MD

Dictated Date/Time: 12/30/14 1218

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH DISCHARGE SUMMARY

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004711628
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 01/14/15 1708
Discharge Date/Time: 01/14/15 1505

Account Number:

Adm/Reg Date: 01/12/15
Patient Location: 8NO.L

DATE OF SERVICE:
January 15, 2015

DISCHARGE DIAGNOSIS:
Hypokalemia.

MEDICATIONS ON DISCHARGE:
1. Prochlorperazine 10 mg p.o. t.i.d. p.r.n. nausea/vomiting.
2. Lactulose 60 mg p.o. q.2 h., goal three bowel movements per day.
3. Dulcolax suppository 10 mg p.r. b.i.d. p.r.n. constipation.
4. Bactrim Double-Strength 1 tablet p.o. daily.
5. Nadolol 40 mg p.o. daily.
6. Rifaximin 550 mg p.o. b.i.d.
7. Oxycodone 10 mg p.o. 4 times daily.
8. Bumex 2 mg p.o. b.i.d. (this was decreased from 3 mg b.i.d.). This may be increased back to 3 mg b.i.d. if the patient has weight gain and once the creatinine goes back to his baseline).
9. Senna 2 tabs p.o. at bedtime.
10. Docusate 100 mg p.o. b.i.d.
11. Eplerenone 50 mg p.o. b.i.d.
12. Omeprazole 20 mg p.o. b.i.d.
13. Metolazone 5 mg p.o. once daily as needed for 5-pound weight gain.

ALLERGIES: NSAIDS.

CHIEF COMPLAINT:
Altered mental status.

HISTORY OF PRESENT ILLNESS:
Mr. Paszko is a 63-year-old gentleman with a past medical history of hepatitis C cirrhosis, grade 2 esophageal varices, status post banding in June 2014, an umbilical hernia, as well as recurrent ascites, who presents from his facility with several days of altered mental status that did not improve with up-titrating lactulose dosing. Per reports from the facility, the patient has had altered mental status for several days and they had increased his lactulose

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Date Report Last Updated: 01/15/15

dosing to every 2 hours and then increased it further to every hour, with no improvement in his encephalopathy. He was sent to the emergency department for evaluation, where a head CT and chest x-ray were obtained which returned with no signs of acute pathology. The patient had a diagnostic paracentesis given concern for SBP. The peritoneal fluid resulted with 507 white blood cells, of which 7% were poiys, which is not consistent with SBP. When speaking with the patient, he complains of diarrhea for the past several days as a result of increased lactulose dosing. He also complains of some weakness and ataxia, as well. He does note that he is having dark urine which started about 1:00 a.m. on the morning of admission. He denied any recent illness or any fevers or any chills. He denied abdominal pain. He noted that he did not feel confused or lightheaded or dizzy at the time of admission. He denied chest pain or shortness of breath and noted that he was able to lie flat with no difficulty. He denied cough. He denied dysuria or hematuria or trouble starting or stopping. He denied any blood in his stool. He denied constipation. He denied back pain and flank pain. He noted that he had been eating and drinking a normal amount, although sodium and fluid restrictions are difficult to follow in the facility. He denied any increased swelling in his legs.

PAST MEDICAL HISTORY:
1. Hepatitis C diagnosed in 1989.
2. Cirrhosis.
3. Grade 2 esophageal varices, status post banding, June 2014.
4. Umbilical hernia.
5. Recurrent ascites.

PHYSICAL EXAMINATION:
VITAL SIGNS: Temperature 97.7, heart rate 76, blood pressure 117/77, respiratory rate 18, oxygen saturation 95% on room air.
GENERAL: The patient is calm, cooperative, in no acute distress, lying supine in bed. Pleasant and conversant, although appears not at his baseline mental status as compared with previous admissions. The patient seems to be having some slowness to his speech and difficulty finding words.
NEUROLOGIC: No asterixis noted. Resting tremors present bilaterally in bilateral hands. Cranial nerves II through XII are grossly intact. Muscle strength is 5/5 in upper and lower extremities bilaterally. Speech is slow and choppy. He is alert and oriented x3.
HEENT: Normocephalic, atraumatic. Scleral icterus is present. Mucous membranes are dry.
SKIN: Purpura and petechiae are present over much of his body. A notable large patch of purpura is noted over the anterior chest, beneath the right clavicle, extending into the midline.
CARDIOVASCULAR: Regular rhythm. No murmur appreciated.
PULMONARY: Clear to auscultation bilaterally. No wheezing. Nonlabored.
ABDOMEN: Soft, nontender to deep palpation. No guarding. No rebound. Bowel sounds are present and equal in all four quadrants. Umbilical hernia is present.
EXTREMITIES: Radial 2+ and DP 2+ pulses. No edema is noted.

FINAL PHYSICAL EXAMINATION:
VITAL SIGNS: Temperature 97.8, heart rate 59, blood pressure 100/64, respiratory rate 18, oxygen saturation 97% on room air.
GENERAL: The patient is calm, cooperative, in no acute distress, standing in his room. Pleasant and conversant.
NEURO: No asterixis. Alert and oriented x3. Speech is normal and back to

baseline. Gait is within normal limits.
HEENT: Scleral icterus is present. Normocephalic, atraumatic.
SKIN: Positive for jaundice and purpura over the chest. Multiple petechial lesions are noted.
CARDIOVASCULAR: Regular rhythm. No murmur appreciated.
PULMONARY: Clear to auscultation bilaterally. No wheezing. Nonlabored.
ABDOMEN: Soft. Not tender on deep palpation. Bowel sounds are present and equal in all four quadrants.
EXTREMITIES: Radial 2+ and DP 2+ pulses bilaterally. Trace edema of the calf bilaterally.

LABORATORY DATA:
White blood count 3.6, hemoglobin 9.7, hematocrit 29.0, platelet count 40.

Sodium 143, potassium 3.8, chloride 109, carbon dioxide 22, BUN 28, creatinine 1.7, glucose 129, calcium 8.4, magnesium 2.0.

HOSPITAL COURSE:
1. Altered mental status. The patient presented Lemuel Shattuck Hospital after his facility expressed concerns of altered mental status that was not responding to increased doses of lactulose. Upon presentation, the patient was alert and oriented x3; however, he did not seem to be at his baseline. He appeared to be slightly weak and noted that he was having trouble with his gait and also appeared to have some slowness and shakiness to his speech. The patient was continued on lactulose with a goal of three bowel movements per day. Given that his diagnostic paracentesis was not consistent with SBP, this was not repeated and no changes in his antibiotics were made. He was continued on Bactrim and rifaximin. The altered mental status could have been due to a GI bleed, which was less likely given no evidence or history of melena or hematochezia and the patient was not complaining of any hematemesis. In addition, his hemoglobin and hematocrit were stable. Electrolyte disturbances were felt to be the most likely cause of his altered mental status given that he was found to have hypokalemia to 2.4 at the outside facility, which after review of records, appears was only repleted with 10 mEq of potassium chloride. Repeat BMPs on admission were checked, and his potassium was repleted, with a goal to maintain potassium greater than 4. There was a question of infection that could also be causing his altered mental status. However, he did not have an elevated white count, was not having fevers, and chest x-ray and diagnostic paracentesis were negative. At the time of discharge, the patient was back to his baseline mental status and reported significant improvement in his weakness and gait, and his speech was back to baseline.
2. Hypokalemia. The patient was found at the outside hospital to have a potassium of 2.4. They repleted it with 10 mEq of potassium chloride. His hypokalemia could have been due to increasing doses of lactulose causing diarrhea, and also Bumex may have played a role in his hypokalemia. On admission, his potassium was noted to be 2.3. He was given 40 mEq for the potassium of 2.3. A repeat BMP showed his potassium had only improved to 2.4. At that time, 80 mEq of oral potassium chloride were given, and a repeat BMP was checked in the morning which showed a potassium level of 2.8. The patient received another 40 mEq of potassium chloride tablet and then 2 hours later received 40 mEq of the potassium chloride elixir. A repeat BMP showed potassium of 4.0. We repeated a BMP in the morning on the day of discharge, and his potassium was found to be 3.8. He was given

40 mEq of potassium. He reported vast improvement in his weakness and gait disturbance. His resting tremor that was present on admission had resolved by the time of discharge. His gait was improved, and his speech was back to baseline. We recommend following up a repeat BMP to evaluate his potassium and creatinine in several days. If he has evidence of hypokalemia, then he can be repleted with oral potassium chloride. A goal potassium for him should be above 4.0.

3. AKI. The patient presented with a creatinine of 1.7, and it trended up to 1.9 on the morning after admission and then dropped back down to 1.7. After review of records, it appears that his baseline creatinine appears to be between 1.2 and 1.5. Given his increased creatinine on admission, we decreased his dose of Bumex from 3 mg b.i.d. to 2 mg b.i.d. This can be increased to his previous dose of 3 mg b.i.d. if the patient experiences weight gain. On the day of discharge, he was 151 pounds. On admission, his weight was 149 pounds. In addition, regarding his fluid status, he can be given metolazone 5 mg p.o. if he has a 5-pound weight gain. It was felt that this AKI was likely due to hypovolemia and concurrent use of diuretics. The patient presented to Lemuel Shattuck Hospital below his baseline weight and had been having copious watery bowel movements due to increased doses of lactulose and was likely dehydrated while also still receiving Bumex.
4. Hepatitis C. The patient has had hepatitis C since 1989 and also has cirrhosis. He is followed by Dr. Mutinga of gastroenterology. We continued the patient on rifaximin and Bactrim. We continued nadolol, as well. The patient should follow up with Dr. Mutinga of gastroenterology at his regularly scheduled appointment. I believe that patient is supposed to have follow up with them regarding his hepatocellular carcinoma screening in February of 2015. At that time when he meets with Gastroenterology, he should also have a discussion about liver transplant or TIPS.

CONDITION ON DISCHARGE:
Stable.

FOLLOWUP PLAN:
The patient should follow up with Gastroenterology at the next regularly scheduled appointment. I believe he is scheduled to follow up for his hepatocellular carcinoma screening in February of 2014. At that time, he would also likely benefit from a discussion about liver transplant or TIPS, given that he has recurrent ascites and a fragile fluid balance.

If the patient gains 5 pounds, the facility should feel free to give 5 mg of metolazone once and evaluate renal function and electrolytes status the following day with a basic metabolic panel.

If the patient gains weight on 2 mg of Bumex b.i.d., then they can return to the original 3 mg b.i.d. dose.

The patient should have a basic metabolic panel drawn within the next several days to evaluate potassium status as well as creatinine.

TIME REQUIRED FOR DISCHARGE:
Greater than 60 minutes.

Signed by: <<Signature on File>>

Signed by date/time: 01/15/15 0921

Dictated by: VOLIN, SAMUEL D MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated by: WORKUM, PETER (FIFIELD) MD

Dictated Date/Time: 01/14/15 1408

Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004718789
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 02/05/15 1551

Account Number:

Adm/Reg Date: 01/23/15
Patient Location: 8NO.L

REFERRING PHYSICIAN:

DATE OF SERVICE:
February 5, 2015

Followup labs were received for patient, Emilian Paszko, a 63-year-old male with a history of cirrhosis, and reviewed this morning. The labs were collected on February 3, 2015. Notably, the labs include a CBC that shows a white blood cell count of 2.2, which is down slightly from his most recent blood count of about 3.8. It also shows a hematocrit of 29.7, which is stable from prior, and a platelet count of 43, which is stable from prior. These labs also include an alpha fetoprotein marker of 6, which is in the normal range.

ASSESSMENT AND PLAN:
Given the decrease in the most recent white blood cell count down to 2.2 from prior value above 3 without clear reason, we would recommend repeating a CBC for Emilian in approximately 1 week's time, with those results again faxed to us for review. No other specific testing is warranted at this time.

Patient's laboratory tests discussed with Amy Lo, GI attending.

Agree with Dr. Borges' assessment and plan.

Amy Lo MD
Signed by: <<Signature on File>>
Signed by date/time: 02/06/15 1402

Dictated By: BORGES, LAWRENCE MD

Co-Signed by: <<Signature on File>>

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 02/06/15
W37791

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH DISCHARGE SUMMARY

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004733481
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 02/25/15 1519
Discharge Date/Time:

Account Number:

Adm/Reg Date: 02/18/15
Patient Location: 8NO.L

DATE OF SERVICE: 2/18/15 - 2/25/15

DISCHARGE DIAGNOSIS: Decompensated end-stage liver disease

MEDICATIONS ON DISCHARGE:
Bactrim DS 1 tab PO daily
Bumetanide 2mg PO BID
Eplerenone 50mg PO BID
Metolazone 5mg PO daily prn weight gain > 5lbs or anasarca
Lactulose 60ml PO QID. Titrate to 3-4 bowel movements/day
Rifaximin 550mg PO BID
Nadolol 40mg PO daily
Omeprazole 20mg PO BID
Senna/Docusate 8.6mg-50mg 2 tabs PO qhs prn constipation
Prochlorperazine 10mg PO TID prn nausea
Tylenol 650mg PO TID prn fever/pain. Not to exceed 2g/day
Mucinex LA 600 mg PO bid
Preparation H 1app TOP daily and prn. Apply to perianal area
Oxycodone 5mg PO q6h prn pain
KCl 40mEq PO TID

CHIEF COMPLAINT: Progressively worsening lower extremity edema, ascites, and altered mental status

ALLERGIES: NSAIDs

HISTORY OF PRESENT ILLNESS:
Mr. Paszko is a 63 year old male with past medical history of Hepatitis C cirrhosis and end-stage liver disease complicated by refractory ascities, history of hepatic encephalopathy, spontaneous

bacterial peritonitis, and esophageal varices who presented with progressive volume overload, ascites, and altered mental status. The patient was transferred from his facility to the urgent care primary care clinic for evaluation of a cough, worsening edema, ascites, and wheezing. The patient reported that he had developed a new productive cough of yellowish sputum that was occasionally streaked with blood, especially after excessive coughing. He also had associated SOB and a wheeze. He also reported that he had been gaining weight and lower extremity edema "for a while" but is unable to specify the timing. He complained that the diuretics make him thirsty and he drinks a lot. He reported he maintains a low-salt diet and takes his diuretics regularly. However, he did report that he had been refusing his lactulose for approximately 12 days. Only recently prior to admission (patient unable to give specific timeline) had the staff at his facility convinced him to restart taking his lactulose. He took it on the day of admission. The patient reported he recently had been slightly more confused and had "been unable to write anything" because of this. The patient denied any fevers or chills, abdominal pain worse than his baseline, nausea/vomiting, hematemesis, hematochezia, or melena. However he did admit to some bleeding in his gums and blood in his saliva, especially with tooth brushing. He denied dysuria or any changes in his urinary habits. He denied runny nose, sore throat, congestion, pleuritic chest pain, palpitations, or orthopnea. He stated that he has had fluid overload episodes more than once in the past.

Per his facility, over the past 2 weeks the patient has had difficulty with his disease. He had been progressively gaining weight with fluid accumulation despite multiple diuretics including metolazone, bumetanide, and eplerenone. On review of his MAR, it appeared as though he had not received many doses of his metolazone prn but had regularly received his bumetanide and eplerenone. He also was receiving Bactrim as spontaneous bacterial peritonitis prophylaxis. Of note, per his facility, the patient's dry weight was 165.6 lbs on 12/3/14. He was recently referred to BMC in the past for a TIPS procedure evaluation.

PAST MEDICAL HISTORY:
- End-stage liver disease with decompensated cirrhosis, tense ascites
- Intractable ascites
- History of encephalopathy
- Hepatitis C diagnosed in 2004 status post antiviral treatment
- Hypertension
- BPH
- Esophageal varices status post banding, June 2014
- Umbilical hernia, June 2014
- Has received his flu shot for 2014/2015 season

PAST SURGICAL HISTORY:
- cervical spine fusion
- tonsillectomy
- left ankle orthopedic procedure not otherwise specified.

PHYSICAL EXAMINATION ON ADMISSION:
VITAL SIGNS: T 99.0, P 74, RR 18, BP 114/75, O2 Sat 100% RA. Admission weight: 197lbs
GENERAL: Jaundiced male, sitting on edge of bed in no acute distress, calm
HEENT: Normocephalic, atruamatic. PERRL, EOMI, scleral icterus. Moist mucus membranes,

oropharynx clear
NECK: Soft, no thyrmoegaly, no LAD
CARDIOVASCULAR: Distant heart sounds, RRR. No M,R.G. Normal S1/S2
LUNGS: Mild rhonci diffusely heard, worst in bilateral bases. Good air movement. No accessory muscle use or respiratory distress.
ABDOMEN: Soft. Mildly tender to palpation without rebound or guarding, worse in epigastric region. Distended but not tense, tympanic. Normoactive bowel sounds. Stable umbilical hernia, reducible, nontender.
EXTREMITIES: Warm and well perfused, bilateral 2+ pitting edema over lower extremities to mid-thigh. No upper extremity edema.
SKIN: Jaundiced. Scattered bruises.
NEUROLOGIC: Alert, oriented x3. Very mild asterixis. Motor and sensation grossly intact. Gait is slow but steady.

FINAL PHYSICAL EXAMINATION OF PATIENT:
VITAL SIGNS: Temperature 97.8, pulse 66, respiratory rate 20, blood pressure 93/58, oxygen saturation 95% on room air. Discharge weight 160.1 pounds.
GENERAL: Jaundiced male, lying in bed, in no acute distress, calm.
HEENT: Normocephalic, atraumatic. Pupils equally round and reactive to light. Extraocular movements intact. Scleral icterus. Moist mucous membranes. Oropharynx clear.
NECK: Soft. No thyromegaly. No lymphadenopathy. Trachea midline.
CARDIOVASCULAR: Regular rate and rhythm with no murmurs, rubs, or gallops. Normal S1 and S2.
LUNGS: Good air movement throughout. Chest is clear to auscultation bilaterally with no wheezes, rales, or rhonchi. No accessory muscle use or respiratory distress.
ABDOMEN: Soft, nontender, nondistended. No rebound tenderness or guarding. Normoactive bowel sounds. Stable umbilical hernia, reducible, nontender.
EXTREMITIES: Warm and well perfused. No pitting edema in the shins bilaterally. Lower extremity skin shows some fine wrinkling. No upper extremity edema.
SKIN: Jaundice, scattered bruises. No diaphoresis, rashes, or pallor.
NEURO: Alert and oriented x3. No asterixis. Motor and sensation grossly intact. Gait is slow but steady.

LABORATORY DATA:
2/25/15
Na 134, K 3.3, Cl 97, CO2 33, BUN 34, Cr 1.5, Glu 105, Ca 8.4
2/24/15
Mg 1.8
2/23/15
WBC 4.2, Hgb 10.2, Hct 30.1, Plt 52

MICROBIOLOGY:
2/21/15 Urine culture: No growth

HOSPITAL COURSE:
Mr. Paszko is a 63-year-old male with a past medical history of hepatitis C cirrhosis complicated by

esophageal varices, intractable ascites, and a history of encephalopathy, who presented with progressive worsening of his ascites, weight gain, encephalopathy, and also with associated increased shortness of breath and productive cough.

Volume overload in the setting of end-stage liver disease
Given the patient's history of decompensated liver disease and recurrent intractable ascites we felt his weight gain, ascites, and edema were highly likely to be due to decompensated liver disease. His medical records indicated that his dry weight was 165.6lbs and he was admitted with a weight of 197lbs. He had not been routinely receiving his metolazone prn as an outpatient despite his weight gain. Based on admission labs, the patient's MELD score was 20. He was put on a Na-restricted diet with a 1.5L fluid restricted diet. Strict in and outs and daily weights were monitored. On the day of admission the patient underwent a therapeutic and diagnostic paracentesis, however only 1L of straw-colored clear fluid was able to be removed. Fluid analysis, gram stain, and culture were not consistent with spontaneous bacterial peritonitis. He was started on increased doses of his home diuretics (bumetanide and eplerenone) and his metolazone was changed to a standing medication. On 2/20/15, the patient underwent another therapeutic paracentesis with removal of 5L of ascitic fluid. He quickly improved and achieved a weight of 158.4, slightly better than his dry weight. Therefore his diuretics were converted back to his home regimen. On discharge the patient had no abdominal distention, lower extremity edema, or SOB/cough. The patient should continue his diuretics as prescribed (Bumetanide 2mg PO BID, Eplerenone 50mg PO BID, and Metolazone 5mg PO daily prn weight gain > 5lbs or anasarca). He should continue a sodium restricted and fluid restricted diet. If the patient has recurrent weight gain, consider changing his metolazone from prn to standing. He should followup with GI via telemedicine appointment next week. He may need to followup with hepatology for definitive treatment of his hepatitis C.

Altered Mental Status
The patient presented alert and oriented x3 but slightly altered and with mild asterixis. This is likely multifactorial from a combination of hepatic encephalopathy in the setting of lactulose noncompliance in addition to a urinary tract infection. An infectious workup was initially pursued which only revealed a positive urinalysis (negative for spontaneous bacterial peritonitis, negative chest x-ray, negative blood culture). The patient had a fecal occult blood test to rule out GI bleed as a cause of hepatic encephalopathy, which was negative. His TSH was within normal limits. We also restarted the patient on his lactulose, continued his rifaximin, and discontinued his oxycodone. His mental status cleared over the next day and his oxycodone was added back at a reduced dose (5mg PO q6h prn pain). His positive urinalysis was treated as a urinary tract infection (see below). On discharge the patient was alert and oriented x3 and did not show signs of altered mental status or asterixis.

Hypokalemia
The patient has a history of hypokalemia and was on standing KCl supplementation on admission. This problem is most likely secondary to his chronic diuretic use. The patient's potassium was frequently assessed and aggressively repleted during his hospitalization and he was kept on telemetry to monitor for arrhythmias. He did not complain of palpitations or chest pain but did have one short run of SVT at one point which self-resolved and did not recur. He does not have concurrent hypomagnesemia. The patient's home dose of KCl supplementation was increased to 40mEq PO TID. His labs on the day of discharge showed a potassium of 3.3. A potassium level

should be repeated on the morning of 2/26/15 and his potassium should be repleted orally as necessary.

Urinary tract infection, resolved
For the patient's altered mental status, an infectious workup was pursued which revealed positive leukocyte esterase and pyuria from a good sample. His records indicated that he had a prior UTI reportedly treated with ciprofloxacin. However, during this admission he was started on Keflex 500mg PO q12h and completed a 7 day course while in the hospital. A urine culture was obtained but was negative, most likely because he was started on treatment before the urine was able to be collected.

#Anemia: The patient was anemic on admission with a hemoglobin of 9.4. Iron studies, B12, folate levels suggested anemia of chronic disease and no further interventions were given. The patient was discharged with a hemoglobin of 10.2.

CONDITION ON DISCHARGE: Stable

FOLLOW UP PLAN:
- Continue Bumetanide 2mg PO BID, Eplerenone 50mg PO BID, and Metolazone 5mg PO daily prn weight gain > 5lbs or anasarca.
- Continue sodium restricted and fluid restricted diet
- If the patient has recurrent weight gain, consider changing his metolazone from prn to standing
- Repeat potassium level on the morning of 2/26/15 and replete as necessary
- GI telemedicine appointment next week. He may need to followup with hepatology for definitive treatment of his hepatitis C.
- Continue reduced oxycodone dose (5mg PO q6h prn pain). Consider holding or decreasing oxycodone dose if patient has altered mental status or is sedated.
- Patient may see general surgery as an outpatient for further management of his inguinal and umbilical hernias

TIME REQUIRED FOR DISCHARGE: 60 Minutes

ADDENDUM:
Patient was unable to be transported 2/25/15 and was kept overnight. On 2/26/14, the patient's potassium was 4.1. He was discharged back to MCI Shirley on the morning of 2/26/15. He should have a potassium level rechecked in 3-5 days and have his KCl redosed as necessary.

Signed by: <<Signature on File>>
Signed by date/time: 02/26/15 1202

Dictated by: PLEET, ALEXANDER L MD

Co-Signed by:
Co-Signed by date/time:

Co-Dictated by: FREEDMAN, KENNETH MD

Dictated Date/Time: 02/25/15 1519

ISigned

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004745675
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 03/26/15 0743

Account Number:

Adm/Reg Date: 03/07/15
Patient Location: 8NO.L

DATE OF SERVICE:
March 26, 2015

Laboratory results received on patient, Emilian Paszko, dated March 23, 2015:
Electrolyte panel notable for mild hyponatremia with a sodium of 133, down from 136 at discharge; BUN improved to 17 and creatinine improved to 1.09.
Complete blood cell count notable for a white blood cell count of 3.8k, stable from 3.8k at discharge; hematocrit 34.2, increased from 28.8 at discharge; and platelet count of 55k, up from 46k at discharge.

ASSESSMENT:
This is a 63-year-old male with a history of cirrhosis complicated by hepatic encephalopathy, ascites, and esophageal varices status post banding, with recent admission for altered mental status felt 2/2 hepatic encephalopathy. Laboratory results show improved kidney function and mild hyponatremia (within his baseline and improved from 128 on March 3, 2015).

PLAN:
-Patient should remain on a 2 gm Na restriction as well. May liberalize fluid intake.
-Please repeat basic metabolic panel in one week and fax results to the GI department at Shattuck Hospital (Fax number: 617-971-3489) for review
-If hyponatremia persists or worsens despite sodium restriction, we will first recommend a fluid restriction to 2L. If his sodium worsens despite fluid restriction, we will then consider decreasing his diuretic regimen.

Navin Kumar
GI Fellow

I agree with the plan as outlined.

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 03/26/15
W37791

Signed by: <<Signature on File>>
Signed by date/time: 03/26/15 1336

Dictated By: KUMAR, NAVIN L MD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By: SMITH, BENJAMIN MD

Dictated Date/Time: 03/26/15 0736

CC:

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 03/26/15
W37791

ISigned

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004745675
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 04/09/15 0821

Account Number:

Adm/Reg Date: 03/07/15
Patient Location: 8NO.L

Date of Service: 04/09/15

Review of Laboratory Data

Laboratory data performed on 4/8/15 reviewed as follows:
Na 131, K 3.3, Cl 98, CO2 25, BUN 14, Cr 0.99.
Hgb 11.1, Hct 32.3, Plts 48,000

ASSESSMENT:
63yo male with history of cirrhosis complicated by hepatic encephalopathy, ascites, and esophageal varices status post banding, recent admission for altered mental status 2/2 hepatic encephalopathy who presents with persistent hyponatremia. Sodium is decreased to 131mmol/L from discharge of 133mmol/L despite low sodium diet. Renal function is improved with Cr now 0.99. Hgb is stable at 11.1g/dL and thrombocytopenia is stable at 48,000.

PLAN:
- Continue low sodium diet (2g total daily)
- Please start fluid restriction at 2L daily (<1.25L if already drinking less than 2L daily)
- Re-check BMP in 1-2 weeks and fax results to the GI department at Shattuck Hospital (Fax number: 617-971-3489) for review
-If his sodium worsens despite fluid restriction, we will then consider decreasing his diuretic regimen.

Walter Kim
GI Fellow

****
GI STAFF:

Discussed above with Dr. Walter Kim, GI Fellow. Agree with above plan.

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 04/09/15
W37791

Signed by: <<Signature on File>>
Signed by date/time: 04/09/15 1305

Dictated By: KIM, WALTER M MD, PHD

Co-Signed by:
Co-Signed by date/time:
Co-Dictated By: MUTINGA, MUTHOKA L MD

Dictated Date/Time: 04/09/15 0816

CC:

Date Report Last Updated: 04/09/15
W37791

Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH MEDICAL CONSULTATION RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004833042
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 07/15/15 1509

Account Number:

Adm/Reg Date: 07/15/15
Patient Location: PCC.L

DATE OF SERVICE:
07/15/15

CHIEF CONCERN:
Therapeutic paracentesis

HISTORY OF PRESENT ILLNESS:
Mr. Paszko is a 63-year-old incarcerated male with h/o hepatitis C from intravenous drug use and cirrhosis complicated by esophageal varices, periods of encephalopathy, and ascites here for repeat therapeutic paracentesis. He currently resides at MCI-Shirley, and was last hospitalized for hepatic encephalopathy in March of 2015. His last therapeutic paracentesis on 06/30/15 was performed without complications, and approximately 8L (18.4 lbs) of translucent yellow fluid was removed from the abdomen after ultrasound. He tolerated the procedure well, and had no hypotension or side effects. He is currently takin Bactrim for prophylaxis of spontaneous bacterial peritonitis in the setting of chronic ascites with repeated therapeutic paracentesis. Today he has increased swelling of the lower extremities, and reports having eaten a larger amount of canned food than usual. Today he has no other specific complaints and denies fevers, abdominal pain, chills, night sweats, nausea, vomiting, and diarrhea.

ROS:
All other systems negative

PAST MEDICAL HISTORY:
End-stage liver disease due to hepatitis C, which caused cirrhosis complicated by esophageal varices s/p banding. The patient has had numerous paracenteses for ascites removal and episodes of hepatic encephalopathy.
Hypertension
Benign Prostatic Hypertrophy
Abdominal hernia
Right scrotal swelling

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 07/16/15
W37791

ALLERGIES: NONSTEROIDAL ANTI-INFLAMMATORIES.

MEDICATIONS:
Bumex 2 mg twice a day
eplerenone 50 mg twice a day
lactulose 60 mL 4 times aday, nadolol 40 mg daily
nadolol 40 mg PO daily
omeprazole 20 mg twice a day
potassium chloride, 80 mg 3 times a day
rifaximin 550 mg twice a day
senna
colace
Bactrim double strength 1 tablet by mouth daily
Tylenol 650 mg 3 times a day as needed for pain
oxycodone immediate release 5 mg 4 times a day,
hemorrhoidal ointment perianally daily as needed
nystatin 100,000 units/g of powder topically 3 times a day
compazine 10 mg PO TID PRN

SOCIAL HISTORY:
The patient is currently incarcerated.
History of IV drug use

PHYSICAL EXAMINATION:
VITAL SIGNS:
-BP: 123/86 before procedure, 106/71 (after procedure)
-T: 98.4
-HR: 70
-RR: 18
-SaO2: 97% on room air
-Wt: 210.7 (before procedure), 188.6 (after procedure)
GENERAL: Awake, alert, non-toxic, and in no apparent distress
HEENT: PERRL, EOMI, mild scleral icterus, moist mucous membranes, oropharynx clear
CV: RRR, normal S1 and S2, no MGR
GU: very large right testicular swelling that completely transilluminates
PULM: CTAB, no WRR
ABD: active bowel sounds, tense and distended abdomen, no peritoneal signs, no voluntary or involuntary guarding.
EXT: Pitting edema to mid calf

IMAGING:
Ultrasound (07/15/15): pocket of abdominal ascites visible. Center of pocket identified as 5 cm deep. Entry point marked.

LEMUEL SHATTUCK HOSPITAL
LSH MEDICAL CONSULTATION RPT

PASZKO,EMILIAN MEDICAL RECORD NUMBER: LS00057981

ASSESSMENT/PLAN:
ASSESSMENT AND PLAN: 63 year old incarcerated man with cirrhosis from hepatitis C here for repeat therapeutic paracentesis. The procedure was performed without complications using sterile technique. Following the procedure the patient had a slight drop in systolic blood pressure, which should be considered for any future large volume paracentesis

Progressive ascites.
- Repeat paracentesis performed today. Approximately eight liters of transparent yellow fluid removed from the abdomen. The patient tolerated the procedure well. The fluid appeared transudative without blood or purulence. He does not have any evidence of SBP, peritonitis, or other infection at this time. The abdomen was soft and non-tender but still distended following the procedure. Systolic blood pressure decreased from 123 to 106 after the procedure, but the patient remained asymptomatic and otherwise tolerated the procedure well.
-Approximately 8 L (22.1 lbs) fluid removed today
-We are not sending ascities for lab analysis today as the patient is well known to the clinic and there is no concern for SBP today.
-Procedure should be repeated as soon as abdomen becomes tense with ascites to minimize discomfort from abdominal and scrotal swelling

#LOWER EXTREMITY EDEMA
-Decrease salt intake and monitor

Scrotal Swelling
-Testicular swelling appears to be hydrocele communicating with the abdominal cavity based on the ability to drain the fluid back into the abdomen with gentle pressure and transillumination on exam. We did not attempt to reduce his hydroceole during this paracentesis, as it proved to have little benefit last time and the fluid quickly returned to the scrotum.

Liver disease.
- The patient appears to be fairly well stabilized on his current medication regimen.
- Can consider treatment for Hepatitis C

Attending addendum:
Patient seen and examined with Dr. Luther. History, physical exam is accurate and plan written as discussed. Paracentesis was performed by Dr. Luther under my supervsion using sterile technique. As patient presented without sign of encephalopathy, fever, hypotension or complaint of abd pain, the fluid was not sent for cytology. Pt tolerated procedure well and was discharged back to his facility.

Signed by: <<Signature on File>>
Signed by date/time: 07/16/15 1113

Dictated By: LUTHER, DANIEL J MD
Page: 3
LA: P.SHI;P.SHI2|
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LEMUEL SHATTUCK HOSPITAL
LSH MEDICAL CONSULTATION RPT

PASZKO,EMILIAN MEDICAL RECORD NUMBER: LS00057981

Co-Signed by: <<Signature on File>>
Co-Signed by date/time: 07/15/15 1829
Co-Dictated By: ADRIEN, ARIELLE MD

Dictated Date/Time: 07/15/15 1507

CC:

LA: P.SHI;P.SHI2|
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Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH MEDICAL CONSULTATION RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004839221
Account Number:
Ordering Doctor: KRSAK, MARTIN MD
Associated Orders: PCC/MEDICAL EST PT LEVEL 3
Adm/Reg Date: 07/27/15
Date/Time Report Entered: 07/27/15 1435
Patient Location: PCC.L

DATE OF SERVICE:
07/27/15

CHIEF CONCERN:
Abdominal ascites

HISTORY OF PRESENT ILLNESS:
Mr. Paszko is a 63-year-old incarcerated male with h/o hepatitis C from intravenous drug use and cirrhosis complicated by esophageal varices, periods of encephalopathy, and ascites here for repeat therapeutic paracentesis. He currently resides at MCI-Shirley, and was last hospitalized for hepatic encephalopathy in March of 2015. His last therapeutic paracentesis on 07/15/15 was performed without complications, and approximately 8L of translucent yellow fluid was removed from the abdomen after ultrasound. He tolerated the procedure well. He is currently takin Bactrim for prophylaxis of spontaneous bacterial peritonitis in the setting of chronic ascites with repeated therapeutic paracentesis. Today he reports increased swelling in his legs, left > right, and increasing fatigue with activity. Over the last month he has had difficulty walking very short distances. Previously he was able to walk for 30-40 minutes.

ROS:
Positive for fatigue
Denies fevers, chills, nausea, vomiting, abdominal pain, chest pain.

ALLERGIES:
NSAIDS

MEDICATIONS:
Bumex 2 mg twice a day
eplerenone 50 mg twice a day
lactulose 60 mL 4 times aday, nadolol 40 mg daily

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nadolol 40 mg PO daily
omeprazole 20 mg twice a day
potassium chloride, 80 mg 3 times a day
rifaximin 550 mg twice a day
senna
colace
Bactrim double strength 1 tablet by mouth daily
Tylenol 650 mg 3 times a day as needed for pain
oxycodone immediate release 5 mg 4 times a day,
hemorrhoidal ointment perianally daily as needed
nystatin 100,000 units/g of powder topically 3 times a day
compazine 10 mg PO TID PRN

PAST MEDICAL HISTORY:
End-stage liver disease due to hepatitis C, which caused cirrhosis complicated by esophageal varices s/p banding. The patient has had numerous paracenteses for ascites removal and episodes of hepatic encephalopathy.
Hypertension
Benign Prostatic Hypertrophy
Abdominal hernia
Right scrotal hydrocele

SOCIAL HISTORY:
The patient is currently incarcerated.
History of IV drug use

PHYSICAL EXAMINATION:
VITAL SIGNS:
-BP: 109/76
-T: 97.7
-HR: 65
-RR: 18
-SaO2: 99% on room air
-Wt: 211.5 (before procedure), 194.6 (after procedure)
GENERAL: Awake, alert, non-toxic, and in no apparent distress.
HEENT: Pupils equal round and reactive to light. Extra-ocular motion intact. Sclera non-icteric. Oropharynx clear. Moist mucous membranes. No erythema or exudate. Neck supple. No lymphadenopathy.
CV: regular rate and rhythm, normal S1 and S2, no murmurs gallops or rubs, 2+ pitting edema (L>R)
GU: large fluid collection in scrotum with transillumination
LUNGS: Clear to auscultation bilaterally; bronchial breath sounds
ABDOMEN: active bowel sounds, distended abdomen, tense ascites, umbilical hernia, no peritoneal sounds, no voluntary or involuntary guarding

IMAGING
Abdominal Ultrasound (07/27/15): pocket of abdominal ascites visible. Center of pocket identified as 5 cm deep. Entry point marked.
Lower Extremity Ultrasound (07/27/15): according to preliminary read with radiologist, no DVT or abnormalities seen

ASSESSMENT/PLAN
63 year old incarcerated man with cirrhosis from hepatitis C here for repeat therapeutic paracentesis. The procedure was performed without complications using sterile technique. Following the procedure the patient had a slight drop in systolic blood pressure, which should be considered for any future large volume paracentesis

ASCITES s/p multiple paracenteses.
- THERAPEUTIC PARACENTESIS performed today. Approximately six liters of transparent yellow fluid removed from the abdomen after ultrasound. The patient tolerated the procedure well. The fluid appeared transudative without blood or purulence. He did not have any evidence of SBP, peritonitis, or other infection. The abdomen was soft and non-tender but still distended following the procedure. Blood pressure dropped to 95 during the procedure, and the decision was made to stop the paracentesis at 6L. His blood pressure returned to pre-procedure levels immediately following the procedure
- Approximately 6 L (16.9 lbs) fluid removed today
- He did not present with altered mental status, fever, hypotension, abdominal pain, or ileus, and the fluid was not sent for analysis.
-Procedure should be repeated as soon as abdomen becomes tense with ascites to minimize discomfort from abdominal and scrotal swelling

#LOWER EXTREMITY EDEMA
-Decrease salt intake and monitor
-Negative lower extremity ultrasound today

SCROTAL SWELLING hydrocele communicating with the abdominal cavity based on the ability to drain the fluid back into the abdomen with gentle pressure during paracentesis and transillumination on exam.

LIVER DISEASE
- The patient appears to be fairly well stabilized on his current medication regimen.
- Can consider treatment for Hepatitis C

Signed by: <<Signature on File>>
Signed by date/time: 07/28/15 1341

Dictated By: LUTHER, DANIEL J MD
Page: 3
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LEMUEL SHATTUCK HOSPITAL
LSH MEDICAL CONSULTATION RPT

PASZKO,EMILIAN MEDICAL RECORD NUMBER: LS00057981

Co-Signed by: <<Signature on File>>
Co-Signed by date/time: 07/27/15 2127
Co-Dictated By: KRSAK, MARTIN MD

Dictated Date/Time: 07/27/15 1432

CC:

LA: P.SHI;P.SHI2|
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Signed

LEMUEL SHATTUCK HOSPITAL
170 Morton Street
Jamaica Plain, MA 02130
(617) 522-8110

LSH GASTROINTESTINAL CONS. RPT

Patient Name: PASZKO,EMILIAN
Medical Record Number: LS00057981
LS0004843322
Ordering Doctor:
Associated Orders:
Date/Time Report Entered: 08/03/15 1143
TELEGI.L

Account Number:

Adm/Reg Date: 08/03/15
Patient Location:

GI Telemedicine Clinic Note

Patient name: Paszko, Emilian
DOB: 9/19/1951
Date of Visit: 08/03/2014

Reason for Visit: HCV treatment questions, decompensated cirrhosis
Referring provider: ML Angeles, MD

HPI: 33yo male with male with history of HCV genotype 1b 2/2 IFN therapy with decompensations including thrombocytopenia, esophageal varices 2/2 banding (6/2/2014) who presents with questions for HCV treatment. The patient supplied the history. The patient reported being diagnosed in 1989 and being treated with PEG-IFN for 1 year while incarcerated (2003) with only 6 months of reported remission. He has since had evidence of esophageal varices with variceal banding performed in 6/2014 with negative reported EGD following. He has also developed worsening abdominal distension with worsening abdominal ascites requiring large volume paracenteses every 2 weeks for drainage. He denied fever, chills, nausea, vomiting, chest pain, frank abdominal pain, diarrhea, constipation, jaundice.

ROS: Please see HPI. Otherwise negative.

PMHx:
HCV, genotype 1b with decompensations including esophageal varices, thrombocytopenia
HTN
BPH
Umbilical hernia s/p repair

Medications:
Eplerenon
Lactulose
Nadolol
Omeprazole
Potassium
Rifaximin

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Colace
Bactrim
Oxycodone
Prochlorperazine

Social history: incarcerated.

Family history: Non-contributory. No known family history of colon cancer.

Physical Exam:
Weight 204lb
T 97.6
P 69
BP 116/86

GEN: well appearing, comfortably sitting in chair.
Exam otherwise limited due to video telemedicine visit.

Labs:
HCV genotype 1b, Platelets 45,000
APRI 5.389
WBC 3.1
Alb 1.7, AFP 6.6, Cr 1.26, INR 1.5

Imaging: none

Path: none

Assessment:
63yo male with history of ESLD 2/2 HCV with decompensations including abdominal ascites, esophageal varices, thrombocytopenia who presents with evidence of decompensated cirrhosis.

ESLD 2/2 HCV. The patient presents with ESLD 2/2 HCV with significant decompensations including esophageal varices, abdominal ascites requiring biweekly large volume paracentesis, thrombocytopenia, elevated INR and evidence of renal disease. Unfortunately, this constitutes decompensated cirrhosis with subacute to acute decompensations making his candidacy for anti-HCV therapy poor. The primary therapy for patients with decompensated cirrhosis is liver transplantation.

Plan
- Continue large volume paracentesis for comfort on scheduled basis
- Check RUQ ultrasound in 3 months to assess for HCC
- Continue home medications as tolerated
- Follow up in telemedicine GI clinic in 3 months

GI fellow: Walter Kim, MD
GI Attending: Ewa Preneta, MD

Signed by: <<Signature on File>>

LA: P.SHI;P.SHI2|
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Date Report Last Updated: 08/06/15
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LEMUEL SHATTUCK HOSPITAL
LSH GASTROINTESTINAL CONS. RPT

PASZKO,EMILIAN

MEDICAL RECORD NUMBER: LS00057981

Signed by date/time: 08/03/15 1147

Dictated By: KIM, WALTER M MD, PHD

Co-Signed by: <<Signature on File>>
Co-Signed by date/time: 08/06/15 0947
Co-Dictated By: PRENETA, EWA MD

Dictated Date/Time: 08/03/15 1142

CC:

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Date Report Last Updated: 08/06/15
W37791

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JEFFREY FOWLER, PAUL WHOOTEN, MICHAEL TURNER, and MICHAEL FITZPATRICK, on behalf of themselves and all others similarly situated,

Plaintiffs,

v.

THOMAS TURCO, Commissioner of Massachusetts Department of Correction, in his official capacity, and MASSACHUSETTS PARTNERSHIP FOR CORRECTIONAL HEALTHCARE, INC.,

Defendants.

C.A. NO. 1:15CV12298

AFFIDAVIT OF JEFFREY FOWLER

I, Jeffrey Fowler, do hereby swear and depose:

1. I am a prisoner in the custody of the Massachusetts Department of Correction. I am serving a life sentence without the possibility of parole.

2. I have had Hepatitis C, genotype 1A, for over 25 years. I have been told by my providers that I have evidence of liver cirrhosis.

3. I was treated with combination therapy in 1999-2000. I suffered side effects of a low white blood cell count (anemia) and my viral load did not come down enough so the treatment was stopped, and I was deemed a "non-responder" to treatment.

4. After being deemed a non-responder my Hepatitis C was basically forgotten about by my medical providers. They did no further testing that they shared with me and when I brought up that I still was infected with hepatitis C, I was told there was nothing that could be done.

5. In or around the late 2000s, when I finally convinced a Nurse Practitioner to check my viral load and order a complete blood count, I was told that "the committee" denied the request.

6. In 2012, after triple therapy was FDA-approved, I had a teleconference with Dr. Mutinga at Lemuel Shattuck Hospital and he believed that another liver biopsy would be beneficial. I didn't receive the second liver biopsy until August of 2013.

7. During this time I was suffering from extreme fatigue and felt drawn out all the time.

8. I was ultimately approved for triple therapy and began it in March or April of 2014. It was stopped in the end of August 2014. I was again a non-responder to treatment. My viral load came down at first, but it went back up. I lost thirty-five pounds during the treatment because I felt sick all the time. This medication regimen was very hard on my body. During the treatment, I had body aches and cold sweats, I became depressed, I developed sores in my mouth, and I had to take a Neupagen shot once a week to boost my white blood cell count.

9. Given my history and disease I was told that I would be a "high priority" for the newer treatment, but I am still waiting. I was told that the "cure rate" with the new medication is close to 100%, but I have not received it.

10. In February of 2015, I was told that my APRI score (0.38) and liver biopsy results did not meet MPCH criteria for further evaluation, even though MPCH decided to treat me with triple therapy based on those same biopsy results.

11. In March of 2015, lab tests were done and my APRI score had risen to 0.74.

12. In February of 2016, MPCH finally drew my blood again for lab tests. The lab numbers were worse than they had ever been before. My viral load was the highest it has ever been, and my ALT was over 180, when it had never been over 100 in any of the previous tests. The FibroTest had me at an F3 level of fibrosis, and an A3 level of inflammation.

13. I have been having abdominal pain for the past eight months, and a Lemuel Shattuck Hospital provider told me that the pain is explained by the high labs.

14. In May of 2016 I had a teleconference with the GI service at Lemuel Shattuck Hospital, where it was recommended that I be treated with Harvoni. I was told that LSH doctors would send this paperwork to the prison, but I am still waiting for treatment and do not know if the GI specialist□s recommendation has been or will be approved.

Sworn to upon the pains and penalties of perjury this 13th day of May, 2016.

/s/ Jeffrey Fowler
Jeffrey Fowler

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JEFFREY FOWLER, PAUL WHOOTEN, MICHAEL TURNER, and MICHAEL FITZPATRICK, on behalf of themselves and all others similarly situated,

Plaintiffs,

v.

THOMAS TURCO, Commissioner of Massachusetts Department of Correction, in his official capacity, and MASSACHUSETTS PARTNERSHIP FOR CORRECTIONAL HEALTHCARE, INC.,

Defendants.

C.A. NO. 1:15CV12298

AFFIDAVIT OF PAUL WHOOTEN

I, Paul Whooten, do hereby swear and depose:

1. I am a prisoner in the custody of the Massachusetts Department of Correction.

2. I have Hepatitis C.

3. Medical providers have advised me that I have Genotype 1a and 2b of the Hepatitis C virus.

4. I was previously treated for Hepatitis C in the mid-2000s, with Interferon and Ribavirin. I went through all 48 weeks of treatment and had obtained a viral response at that time, but the virus returned a few weeks later.

5. I had my most recent liver biopsy in 2011, which concluded that my liver fibrosis was at Stage 3 out of 6 on the Ishak scale.

6. I tried to obtain triple therapy (Interferon, Ribavirin, and either Teleprevir or Boceprevir) from the DOC when it became the standard. In July of 2013, MPCH staff advised me that because of my date of incarceration, which was deemed to be March of 2013, I would not even be considered for treatment until April of 2014.

7. I had actually been in DOC custody since 2011, as a pretrial detainee. At that time, I was told that Hepatitis C treatment was not available to me because of my pretrial status. March 2013 marked the beginning of my sentence, but I was already in DOC custody.

8. I have not had a gastroenterology consult since arriving in the DOC.

Sworn to upon the pains and penalties of perjury this 12th day of May, 2016.

/s/ Paul Whooten
Paul Whooten

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JEFFREY FOWLER, PAUL WHOOTEN, MICHAEL TURNER, and MICHAEL FITZPATRICK, on behalf of themselves and all others similarly situated,

Plaintiffs,

v.

THOMAS TURCO, Commissioner of Massachusetts Department of Correction, in his official capacity, and MASSACHUSETTS PARTNERSHIP FOR CORRECTIONAL HEALTHCARE, INC.,

Defendants.

C.A. NO. 1:15CV12298

AFFIDAVIT OF MICHAEL TURNER

I, Michael Turner, do hereby swear and depose:

1. I am a prisoner in the custody of the Massachusetts Department of Correction. I am due to be released in 2021 or 2022. I become eligible for parole in 2017 or 2018.

2. I have Hepatitis C.

3. According to my medical providers, I have Genotype 1b of the Hepatitis C virus.

4. My most recent liver biopsy was in 2011. I was found to have liver fibrosis at stage 3 out of 6.

5. I was treated for Hepatitis C in 2012, while in DOC custody. The treatment was Pegylated Interferon and Ribavirin. The treatment was discontinued, because it was not working. I was also having side effects from the medications.

6. In April 2014, I consulted with MPCH providers about treatment options. After discussing triple therapy and the potential for new, Interferon-free regimens that were coming soon, I agreed that we should wait until the new regimens had arrived.

7. In November 2014, I submitted a medical grievance requesting Hepatitis C treatment with the new medications. I was told that I was not eligible for treatment under MPCH s

current guidelines. It was also suggested that my liver function was normal, despite all the previous tests and my previously having been found eligible for treatment.

8. At that time, MPCH providers also advised that my APRI score was 0.621 and that their treatment protocol required that I have an APRI score of greater than or equal to 1.0. The APRI score was based on blood tests that were done in April 2014.

9. On September 1, 2015, I had a video appointment with a gastroenterologist. She advised me that I was approved for Hepatitis C treatment. She said I would be starting on the medications in the following week.

10. Since that time I have asked my MPCH providers about the schedule for treatment, but I was told there is no specific time when I will start treatment. In November 2015 and again in April 2016, I was told that I am on a waiting list and that I am lower priority on that list.

11. I had a FibroTest and ActiTest □blood tests □taken in January 2016. I had severe liver fibrosis (score of 0.78, or F4 on a scale of 0 □4), and some inflammation activity (score of 0.47, or A1-A2 on a scale of A0-A3).

Sworn to upon the pains and penalties of perjury this 12th day of May, 2016.

/s/ Michael Turner
Michael Turner

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JEFFREY FOWLER, PAUL WHOOTEN, MICHAEL TURNER, and MICHAEL FITZPATRICK, on behalf of themselves and all others similarly situated,

Plaintiffs,

v.

THOMAS TURCO, Commissioner of Massachusetts Department of Correction, in his official capacity, and MASSACHUSETTS PARTNERSHIP FOR CORRECTIONAL HEALTHCARE, INC.,

Defendants.

C.A. NO. 1:15CV12298

AFFIDAVIT OF MICHAEL FITZPATRICK

I, Michael Fitzpatrick, do hereby swear and depose:

1. I am a prisoner in the custody of the Massachusetts Department of Correction. I am due to be released in September of 2016.

2. I have Hepatitis C.

3. I suffer from advanced cirrhosis of the liver brought on by uncured Hepatitis C, genotype 1a. I also suffer from GAVE disease, which is associated with cirrhosis of the liver and causes me to bleed from my rectum. I have had esophageal varices, which occur when blood can't get through the liver and backs up in veins and arteries of the esophagus. Varices can rupture, which can be fatal if I don't receive immediate emergency medical care.

4. When I entered DOC custody in 2010, I told my medical providers that I had Hepatitis C and was seeking treatment.

5. In April of 2012, I was seen by an infectious disease specialist from Lemuel Shattuck Hospital. She noted that my viral load was high, and a FibroSure test showed cirrhosis of the liver. She recommended putting me □on the top of the list for triple therapy.□ She repeated this recommendation in June of 2012.

6. A year passed after that initial recommendation, before I finally began triple therapy in April of 2013.

7. The treatment began with combination therapy (Interferon and Ribavirin) and Boceprevir was added later, in May of 2013. I suffered from multiple side effects which worsened with time, including severe pancytopenia. The treatment was stopped in July 2013.

8. In April of 2014, a gastroenterologist concluded that I was a candidate for interferon-free therapy for Hepatitis C, and that the "treatment would include simeprevir [Olysio] and sofosbuvir [Sovaldi] for 12 weeks with minimal side effects."

9. I was hospitalized in May of 2014 with explosive diarrhea and fevers. A gastroenterologist noted that I continued to have esophageal varices, a CT scan showed signs of portal hypertension and splenomegaly, and a FibroSure test suggested that I had cirrhosis. My APRI score at the end of my hospitalization was 3.76.

10. In February of 2015, I was hospitalized at Lemuel Shattuck Hospital for an infection. At this point, I was periodically spitting up blood. I was told that I needed to see a liver specialist in order to manage treatment of my hepatitis C. The discharge papers recommended an appointment with gastroenterology in 3-4 weeks. This appointment never took place.

11. In or around April of 2015, I received disciplinary report for possession of homebrew. MPCH providers informed me that the disciplinary report made me ineligible for Hepatitis C treatment for twelve months.

12. In August of 2015 I was rushed to Norwood Hospital emergency room because I was vomiting blood and had bloody stool. Imaging found evidence of portal hypertension and varices, and it was thought that the bleeding was caused by GAVE disease. I was given medication to help with the varices but I have not been provided care for the cause of the varices, Hepatitis C.

13. In late December 2015 I was taken to the emergency room again, with abdominal pain, vomiting, and a low platelet count. The emergency room doctor evidently consulted with the prison medical staff about my Hepatitis C and treatment for it, and he was told that I needed to be not using alcohol for one year before they would consider treatment. They said it had been eight months.

14. I was readmitted four days later, in January 2016, with bloody stool, spitting up blood, vomiting, and severe abdominal pain. Imaging found esophageal, gastric, and splenic varices. I was transferred from Norwood Hospital to Lemuel Shattuck Hospital. I remained inpatient for weeks, and ultimately I was sent to Boston Medical Center for surgery on my stomach, for complications from the GAVE disease.

15. Despite all the medical complications I have had because of untreated Hepatitis C, I still am waiting for treatment. MPCH has not taken any action to have me receive the treatment I need and it appears they won't. They are waiting for me to be released or die. Either way, they will not have to spend the money.

Sworn to upon the pains and penalties of perjury this 15th day of May, 2016.

/s/ Michael Fitzpatrick
Michael Fitzpatrick

MPCH
assachusetts Partnership
r Correctional Healthcare

Commonwealth of Massachusetts
Department of Correction
Pharmacy and Therapeutics Committee
Meeting Minutes

MA DOC Pharmacy & Therapeutics (P&T) Committee Meeting was held March 5, 2015 at MPCH regional office in Westborough Massachusetts from 9 AM to 11:30 AM.

following individuals attended the meeting in person: Tom Groblewski, Rhonda Cantelli, Hamel, Jeff Fisher, Mark Waitkevich, Laura Vasconcellos, Claudia Gonzalez, Karen Lee, Don ers, Alki Nacopoulos, Robert Falk, and David Stone

nding by teleconference: Joe Calamo, Dave Chantal, Bonnie Damigella, Keelin Garvey

ts: Anita Jedwabski (CPS), Mellissa Putnam (SOPS)

sed member(s): Robert Diener,

oval of February P&T Meeting Minutes: The minutes from the February 2015 P&T ing were reviewed. A motion made to approve. **The minutes were approved.**

w of Statistics: Erik presented January pharmacy utilization data (Note-January was a 35 eporting period):

The census was 10,379 patients in January.
Total prescription volume was 6,201 new orders and 24,489 refills in January. Total orders were 36,986.
January pharmaceutical costs were $974,164
- Medication costs after credits and returns were $922,245. There was an error in billing for the month in January. A higher than anticipated charge for Foscarnet ($70,265 higher than delivered), and antiviral agent and an omitted charge for Harvoni ($30,208), a hepatitis C treatment. An overall credit of ($40,056) will be applied to the February statement.
- The top cost drivers for medications ordered for medical indications was Foscarnet (12 orders, $82,902), the HIV medications Atripla ($80,682, 42 orders), Truvada ($57,840, 31 orders), and Reyataz ($34,916, 31 orders). As previously

covered, a correction in medication charges and a credit of $40,056 will be reflected in the February pharmacy statement.
    - Complete January psychiatric medication costs were unavailable at the time of the meeting. Last reported costs in December were $134,052, an increase from $105,629 from the prior month. The primary cost driver was due to increase in unit cost for chlorpromazine ($33,224, 195 orders). MPCH is reviewing the patients currently on this medication and identifying ways to optimize therapy for these patients.
    - Bridgewater State Hospital medication costs were $99,057 in December. The primary psych cost drivers included chlorpromazine ($7,782, 30 orders), and perphenazine ($7,205, 82 orders). Non-psychiatric medications driving BSH medication costs include: rifaxamin ($5,019, 3 orders) and Truvada ($4,922, 3 orders).
- Nonformulary requests for January-286 requests with 73% of the requests approved (209 requests)
    - Medical Requests-242 requests with 71% approved (171 requests)
    - Psych Requests-44 requests with 86% approved (38 requests)
- The top non formulary drugs, by expenditure (top 3): Elvitegrevir-cobicistat-emtricitabine-tenofovir ($23,565, 10 orders), Ambresentan ($16,554, 2 orders) and Glatiramer ($15,996, 3 orders).

Infectious Disease Updates

- HIV and Hepatitis C patient statistics for January
    - 162 HIV + patients.
        - 103 HIV + patients are reported to be co-infected with hepatitis c.
        - 144 patients are undergoing HAART therapy
        - 131 patients on stable therapy have an undetectable viral load
        - 1560 patients have been identified as hepatitis C positive
    - 2 patients have initiated treatment with sofosbuvir/ledipasvir with 1 additional patient anticipated to begin in early March

Naltrexone Extended-Release Updates

- Since September the program has had:
    - 18 patients enrolled into the program
    - 5 patients are released in February, 5 more scheduled in March
    - 14 patients released still on medication in the community
    - 4 patients not on medication following release:
        - 1 re-incarcerated
        - 3 did not follow through with 2nd dose

New Business

Drug Pricing Increases:

Erik summarized some of the recent drug price increases that have impacted the system.

- Topical steroid had undergone significant increases. Fluocinonide and clobetasol had increases of 660% and 5072% respectively and would have resulted in an additional expenditure of $180k if alternative formulary agents were not utilized. It was decided in late 2014 that those agents be removed from the formulary and transition patients to formulary alternatives.
- Amitriptyline, a highly utilized antidepressant underwent a 2500% increase in cost. The agent was not removed from the formulary but an initiative is in place to transition eligible patients using amitriptyline for medical indications to alternative formulary

Operational Updates/Discussion

- Therapeutic Interchange Program
  - Anita Jedwabski provided an overview of a therapeutic interchange policy in use within the State Office of Pharmacy Services for other correctional facilities. It outlines the current medications that would be interchanged with formulary alternatives and the notification process that would be communicated to prescribers and facilities. She also identified nonformulary requests from August 2014 through January 2015 that may use the therapeutic interchange program. The benefits include minimal intervention from medical staff, streamlined nonformulary process, reduction in nonformulary requests and higher formulary compliance.
  - Operational barriers identified include updating medication administration records to reflect the interchanges.
  - It was proposed to review how the program was implemented at House of Correction facilities and identify a process to implement the program into DOC facilities through a pilot program and phase in the process.
- Medication Administration Records Printing Updates
- Patient Transfers and Ordering
  - Laura Vasconcellos summarized a transfer issue that occurred with a patient transferring between facilities and requested a policy be developed to standardize the process. Currently when a patient is transferred, medication ordering at the new facility can be done only after the patient is transferred. Current operational issues include required medications that unable to be transferred with the patient (e.g. scheduled medications) and timely delivery of medications to the ensure continuity of care.
  - Laura will draft an outline policy for the Committee to review.
- Pharmacy Information Systems-D. Rogers summarized the latest progress on the implementation of the pharmacy information system (PIS) including updates to the availability of new scanners; new MAR's and MAR printers.
- Medication Administration Records-New printers for the updated MAR's are in place and will begin use for the April MARs. The new printing system will resolve issues from the legacy system including lengthy printing times, printer malfunctions, and the ability to transmit them electronically in time-sensitive circumstances.

- Medication Tote returns-Several sites noted that medication totes are not being returned to the pharmacy. It was identified that the delivery courier is unable to return all totes due to space available in their delivery vehicles. SOPS will work with the facilities to arrange return of the totes.

Backorders/Shortages:

- E. Hamel updated the committee of the current backorders. Memos were sent to medical staff updating them of the supply issues and recommending alternative medications.

Adjournment & Next Meeting:

The meeting adjourned at 11:30 am. The next meeting is April 2, 2015 meeting at the MPCH Regional Office location in Westborough MA.