Abstract

Hepatitis C (HCV) is the most common bloodborne infection in the United States. Although the incidence of HCV is declining, the burden of the disease is rising, driven by the increasing rates of end-stage liver disease and other consequences of advanced HCV infection. According to a 2009 report, the number of patients with advanced liver disease will quadruple over the next 20 years; in that time, total medical costs for patients with HCV infection are expected nearly to triple, from $30 billion to more than $85 billion.

Given the limitations of current treatments and diagnostic technologies, HCV often goes undiagnosed and/or untreated. With new therapies in the pipeline that offer the promise of increased efficacy and improved side effect profiles, there likely will be a demand for improved diagnostics to more quickly and accurately identify patients in need of treatment. Daktari Diagnostics, Inc., based in Cambridge, Massachusetts, is developing a point-of-care, microfluidic diagnostic system that could be used both to diagnose HCV patients and to monitor treatment response.

This thesis hypothesizes that Daktari’s HCV diagnostic system can generate revenue in the United States, given the dynamics of the market. To explore this hypothesis, a background on the current diagnostic and treatment standards in HCV is presented, followed by an analysis of diagnostics and treatments currently in development. The thesis then defines the current paradigm of HCV testing and treatment and explores one potential future paradigm. Finally, a model of the HCV diagnostic market from 2012-2019 is generated. This model demonstrates that, under conservative assumptions, the Daktari diagnostic system could generate a minimum of $25MM in revenue in the United States over its first five years on the market, from 2015-2019.
Dedication

To my sixth grade science teacher, Jane Patterson, whose lessons both inside and outside the classroom I carry with me to this day.
The Biomedical Enterprise Program has provided me with incredible opportunities over the last three years. I owe a great deal to the program's founders, Dr. Ernie Berndt and Dr. Richard Cohen, for recognizing the power of a joint education in business and medicine. Thanks as well to Traci Anderson, who supports all of us in BEP; without her, many of us may not have graduated! And of course, thanks to the professors who have imparted a small part of their wisdom on me over the last few years: Prof. Stan Lapidus, Dr. Howard Golub, Dr. Rox Anderson, Dr. Warren Zapol, Prof. Carl Berke, Prof. Richard Anders, Dr. Rick Mitchell, Dr. Bobby Padera, and Dr. Shiv Pallai made this experience more valuable even than I hoped it would be.

My thesis advisors, Dr. Berndt and Dr. Bill Rodriguez, believed in me and in this project throughout the process. I feel privileged to have worked so closely with Daktari throughout my time at MIT.

My fellow BEP students and alumni have supported, challenged, and encouraged me throughout the program. Jeff Behrens, Will Crawford, Alan Braly, Elizabeth Wagner, Drew Cronin-Fine, Heather Vital, Sung You, Hewmun Lau, Jordanna Polis Schuz, Elyssa Campbell, Julia Kay Preis, and Mauricio Camargo played particularly significant roles; for their support they have my eternal thanks.

Finally, thank you to my parents, Carol and Chris Rocker, and my sister, Katie Rocker, who consistently reminded me of the value of education, and who let me follow a love of science in a family of liberal arts majors.
# Table of Contents

Abstract ................................................................................................................................. 2  
Dedication ............................................................................................................................. 3  
Acknowledgements ............................................................................................................... 4  
List of Tables and Figures .................................................................................................... 6  
Chapter 1: Introduction ........................................................................................................ 7  
Chapter 2: Background ......................................................................................................... 9  
  Pathology and epidemiology of HCV .................................................................................... 9  
  Treatment of HCV: 1990-2011 .......................................................................................... 11  
  Treatment of HCV: 2011 and beyond .............................................................................. 14  
  The relationship between therapeutic and diagnostic innovation: a case study from HIV .... 17  
  Diagnosis of HCV: Current standard of care .................................................................... 18  
  Diagnosis of HCV: Pipeline technologies ......................................................................... 23  
  The Daktari system ............................................................................................................ 26  
  Daktari & HCV .................................................................................................................... 29  
  Summary ......................................................................................................................... 32  
Chapter 3: Methodology ...................................................................................................... 34  
Chapter 4: Results ............................................................................................................... 36  
  HCV testing and treatment: Current paradigm .................................................................... 36  
  Number of HCV tests required: Current paradigm ............................................................. 38  
  HCV testing and treatment: Future paradigm .................................................................... 40  
  Number of HCV tests required: Future paradigm ............................................................... 44  
  Daktari HCV market share model: 2015-2019 .................................................................. 46  
  Sensitivity Analyses .......................................................................................................... 52  
Chapter 5: Discussion .......................................................................................................... 56  
  Limitations .......................................................................................................................... 56  
  Areas for future research .................................................................................................... 57  
Chapter 6: Conclusion ......................................................................................................... 59  
References ............................................................................................................................ 60
List of Tables and Figures

Table 1: Qualitative HCV RNA Assays ................................................................. 20
Table 2: Quantitative HCV RNA Assays .............................................................. 21
Figure 1: HCV Testing Process ......................................................................... 22
Figure 2: Daktari CD4 Instrument and Cartridge ............................................. 27
Figure 3: Daktari CD4 Cartridge (detail) ............................................................. 28
Figure 4: Daktari Testing Process ..................................................................... 29
Table 3: Daktari System Specifications: CD4 v. HIV ....................................... 30
Table 4A: Current Paradigm of HCV Testing ..................................................... 30
Table 4B: Current Paradigm of HCV Treatment ............................................... 38
Table 4C: Number of HCV Tests Required: Current Paradigm ......................... 40
Table 5A: Future Paradigm of HCV Testing ....................................................... 42
Table 5B: Future Paradigm of HCV Treatment .................................................. 44
Table 5C: Number of HCV Tests Required: Future Paradigm ......................... 45
Table 6A: HCV Testing and Treatment, 2012-2019 (Lower Bound) ..................... 50
Table 6B: HCV Testing and Treatment, 2012-2019 (Upper Bound) ..................... 51
Table 7A: Sensitivity Analysis: Adherence ......................................................... 52
Table 7B: Sensitivity Analysis: POC Competition .............................................. 53
Table 7A: Sensitivity Analysis: Discount Rate .................................................... 54
Chapter 1: Introduction

Hepatitis C, a bloodborne disease caused by the hepatitis C virus (HCV), is the most common bloodborne infection in the United States. Although specific prevalence estimates vary among sources, five times as many Americans are infected with HCV as with HIV. One significant reason for this inconsistency is that the populations with the highest rates of HCV infection, such as prisoners and the homeless, are excluded from most epidemiologic surveys. For example, the most recent NHANES data from 1999-2002 estimated that 3.2MM Americans were living with chronic HCV, but these data excluded the homeless and incarcerated populations, as well as persons on active military duty. When these populations were accounted for in a separate study, the estimate of the HCV-infected population rose by 60% to 5.2MM.

Despite this high prevalence, hepatitis C receives little media attention and disproportionately little federal funding relative to the disease burden. Within the Centers for Disease Control and Prevention (CDC), activities related to viral hepatitis are overseen by the Division of Viral Hepatitis (DVH), which is part of the National Center for HIV/AIDS, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Prevention (NCHHSTP). As the name would suggest, the NCHHSTP also oversees federal activity for HIV/AIDS. Although HCV affects five times more Americans than does HIV, in FY2008 2% of the NCHHSTP budget was allocated to HCV activities, while 69% of the budget was allocated to HIV. Furthermore, the services that do exist for HCV are inconsistent and fragmented, varying widely in terms of oversight, quality, and accessibility.

As I will discuss later in this thesis, recent innovations in pharmacotherapy for HCV are poised to dramatically improve treatment outcomes. However, in order for patients to be effectively treated, they must first be identified. Although the CDC recommends that all at-risk populations be tested for HCV
infection, the government acknowledges that as many as 75% of HCV patients in the United States are unaware of their infection status.\textsuperscript{6} Screening and diagnosing patients with HCV has proved to be a significant challenge for several reasons. First, the pathophysiology of the disease is such that patients with a chronic infection may remain asymptomatic for years, even decades, but still be able to infect others. Second, the limited efficacy and low tolerability of standard therapies has provided little incentive for patients to be accurately diagnosed. In the next sections, I will explore both of these challenges and their implications for diagnostics.
Chapter 2: Background

Pathology and epidemiology of HCV

Like other forms of hepatitis, hepatitis C is a bloodborne infection that is transmitted through contact with the body fluids of an infected person. Within the United States, the most common cause of infection is injection drug use, which is estimated to be responsible for as many as 60% of HCV infections.\(^7\) This mode of transmission is responsible in particular for HCV infections in patients born between 1945-1964, who may have been injection drug users (IDUs) in the 1960s, 1970s, or 1980s.\(^1\)

Another common cause of infection, reported in more than half of all HCV cases in patients over 60 in the United States, is a history of a blood transfusion or solid organ transplant prior to 1992, when screening standards for donated blood became more stringent. According to the CDC, other risk factors for transmission include chronic hemodialysis, HIV infection, and birth to an HCV-infected mother.\(^8\)

Sexual transmission, while possible, is a lower-risk mode of transmission, and is not thought to contribute significantly to the burden of disease in the United States.

Once a person has been exposed to HCV, the infection has two stages: acute and chronic. The acute phase is often asymptomatic; indeed, some sources say as few as 20-30% of patients infected with HCV will display acute symptoms.\(^8\) When symptoms do occur, they are often mild and non-specific. If symptoms appear, they will present 4-12 weeks after infection and may include fever, fatigue, abdominal pain, jaundice, nausea, and loss of appetite.\(^9\) Although some patients will clear the virus after the acute phase of infection, 75-85% of patients will go on to develop chronic hepatitis.\(^8\)

Chronic hepatitis C often remains asymptomatic for decades. During this time, however, patients may be progressively developing liver disease. Indeed, among those patients who develop chronic hepatitis...
C, 60-70% will develop chronic liver disease and 5-20% will go on to develop cirrhosis. In addition, HCV infection is responsible for one-third of hepatocellular carcinoma (HCC) cases in the United States; in the case of hepatitis C, patients usually go on to develop HCC secondary to cirrhosis. Again, these patients may remain asymptomatic until the late stages of liver disease.

Advanced liver disease already represents a serious economic burden in the United States; that burden will only grow as those in the baby boomer generation, who represent two-thirds of chronic HCV infections in the United States, progress to advanced liver disease over the next few decades. According to a 2009 report, the number of patients with advanced liver disease will quadruple over the next 20 years, with the price tag to match. Within that time frame, total medical costs for patients with HCV infection are expected nearly to triple, from $30 billion to more than $85 billion. This looming economic threat provides a major incentive to improve diagnosis of HCV, with the hope that these patients can be treated before they progress to the most advanced stages of the disease, when therapy is both more costly and much less likely to be effective, given the extensive liver complications that present in the late stages of the disease.

The fact that both the acute and chronic phases of HCV are largely asymptomatic is a major reason why people remain unaware of their infection status. Patients who do not consider themselves at risk for HCV infection will see no reason to discuss possible infection with their physician or healthcare provider. As noted earlier, more than 75% of those patients with HCV in the United States are unaware of their infection status. Without knowing who these patients are, healthcare providers have no opportunity to treat or manage their disease as it progresses. As I discuss in the next section, this knowledge gap is particularly costly because many HCV infections could be cured with a single course of therapy, and recent treatment advances are poised to deliver even more promising outcomes.
Of note, research suggests that many physicians are not aware of what factors in a patient's history would warrant testing for HCV. In one survey of family physicians, researchers found that although 95% of respondents would recommend HCV testing in patients who report a history of injection drug use, only 81% would recommend it for people who received blood transfusions before 1992, and only 65% would recommend testing of incarcerated persons, despite the fact that both of these are significant risk factors. If diagnosis could be improved – made faster, easier, or more accessible – it follows that healthcare providers might be more inclined to test their patients. Of course, even if diagnostic and treatment options continue to be improved, neither innovation will be sufficient to combat the HCV epidemic without significant education of both at-risk populations and the healthcare workers who care for them.

**Treatment of HCV: 1990-2011**

HCV was first identified as a distinct form of hepatitis in 1989. Research in the 1970s had suggested that most of the cases of hepatitis resulting from blood transfusions were not caused by the hepatitis A virus (HAV) or the hepatitis B virus (HBV), nor by any other known virus. They identified this virus as a "non-A, non-B hepatitis" (NANBH). This clumsy nomenclature stood until, in a study published in *Science* in 1989, Choo and colleagues distinguished the HCV genome from other known viral forms of hepatitis. As a result of this relatively recent discovery, and the fact that HCV cannot be grown in culture and therefore is difficult to study, R&D efforts directed towards the treatment of HCV have lagged.

Since the identification of HCV, interferon (IFN) has been the mainstay of HCV treatment. In fact, IFN was used to treat HCV before the virus was even named, although physicians did not — and in fact, still do not — understand why the treatment was effective. Although IFN treatment reduced serum
aminotransferase (ALT) and liver enzyme levels—indicators of a damaged liver—it was associated with a poor overall response rate and multiple adverse effects. Furthermore, it had to be administered via parenteral injection three times a week. Nonetheless, with no other options available, IFN was approved for the treatment of HCV in 1992.\textsuperscript{12}

However, even with a year-long course of IFN, only 10-25\% of patients achieved prolonged disease remission as measured by sustained virologic response (SVR).\textsuperscript{13,a} The next advance in therapy came with the 1998 approval of ribavirin as an adjunctive therapy to IFN. Ribavirin is a broad-spectrum antiviral drug active against a family of viruses known as flaviviruses, of which HCV is one. Although its precise mechanism of action remains unknown and it is not effective as a monotherapy, ribavirin is synergistic when combined with IFN in the treatment of HCV. The combination improved SVR to 40-50\% following a 48-week course of therapy. Ribavirin was approved for use in combination with IFN in 1998.\textsuperscript{12}

The next advance came in 2001, when pegylated IFNs were introduced. Pegylation—the process of attaching polyethylene glycol (PEG) molecules to IFN—prolongs the half-life of IFN and allows for less frequent administration. As a result, patients were able to transition to once-weekly injections, a significant improvement over the prior thrice-weekly formulation. The combination of pegylated interferon (PEG IFN) and ribavirin achieved SVR of 80\% in patients with genotypes 2 and 3 at 24-week follow-up following 48 weeks of therapy. In patients with genotype 1, SVR was improved to 54\% with the PEG IFN/ribavirin combination compared to 42\% with the combination of conventional IFN and ribavirin.\textsuperscript{14} Thus, this combination became the standard of care in HCV, and has remained in this position for the last decade.\textsuperscript{13}

---

\textsuperscript{a} SVR is defined as continued undetectable HCV viral load after cessation of therapy. It is usually measured either 12 or 24 weeks following treatment. SVR is used as a surrogate endpoint for cure in HCV clinical trials.
Even with these advances, several deficiencies remain. HCV is a heterogeneous disease, made up of distinct genotypes (1-6, plus subtypes) that correlate to treatment response. Nearly 75% of HCV infections in the United States are genotype 1, which is the genotype least likely to respond well to treatment. The PEG IFN/ribavirin combination did not overcome this challenge: only 40-50% of genotype 1 patients showed SVR after 48 weeks of therapy, compared to 70-80% SVR in patients with genotypes 2 and 3 after 24 weeks of therapy. At only 19%, the SVR in African-American patients with genotype 1 is even lower. Overall, fewer than half of HCV patients in the United States will achieve SVR following treatment with PEG IFN/ribavirin. In addition, the combination is associated with significant adverse events, including nausea, vomiting, diarrhea, anemia, rash, and pruritus (itching). Side effects like these impede patient compliance with the treatment regimen, which in turn further lowers efficacy. An annual price tag of $15,000-$30,000, depending on treatment length, makes the PEG IFN/ribavirin combination quite costly for a therapy that is effective in less than 50% of patients.

With three-quarters of HCV patients unaware of their diagnosis, and the standard treatment least effective in the genotype that is most prevalent in the US, it is not surprising that few HCV patients actually receive treatment. Indeed, “standard of care” may be an overly charitable term to describe PEG IFN, because it implies that it is standard for patients to receive treatment; rather, the opposite is true. The lack of efficacy and significant adverse events associated with PEG IFN provide little incentive for accurate diagnosis, let alone treatment.

In the last few years, though, exciting advances in the HCV treatment pipeline have brought the promise of more effective, safer treatments – and with that promise will come a necessity for improved diagnostics.
Treatment of HCV: 2011 and beyond

Perhaps because our understanding of HCV trailed that of other forms of hepatitis, innovations in treatment lagged as well. As discussed above, the PEG IFN/ribavirin combination regimen has several drawbacks that make it less than ideal for the treatment of HCV: reduced efficacy in genotype 1 patients, weekly intravenous administration, a long course of treatment, significant side effects, and high cost. The last several years, though, have seen a flurry of activity in HCV drug R&D. The first novel therapy developed specifically for the treatment of HCV was approved in 2011, and several even more promising therapies are expected to reach the market in the next few years. In this section, I will explore these new therapies and their implications for the importance of rapid, accurate, and accessible diagnostics.

As of 2011, there were 60 drugs in clinical development for the treatment of HCV. Some of these compounds have already been tested or approved for either HIV or hepatitis B (HBV), while others have been developed specifically to treat HCV. Of these 60 drugs, 66% were small-molecule antivirals. Broadly, these antivirals have two main targets. The first, NS5B polymerase, is involved in RNA synthesis. The second, NS3/4A protease, cleaves viral proteins necessary for HCV replication. By inhibiting these targets, the drugs prevent the virus from multiplying.

After seeing no approvals for the treatment of HCV in a decade, in May 2011 two drugs received FDA approval within ten days of each other. The first was Merck's Victrelis® (boceprevir), and the second was Vertex's Incivek® (telaprevir). Both compounds are NS3/4 protease inhibitors rationally designed specifically for the treatment of HCV; that is, scientists first mapped the structure of the HCV protease enzyme and then created a drug to inhibit it.
Importantly, both compounds achieve significantly higher response rates in genotype 1 patients than had been seen previously with PEG IFN/ribavirin. In RESPOND-2, the boceprevir pivotal trial in previously treated genotype 1 patients, subjects received either triple-therapy with boceprevir, PEG IFN and ribavirin, or double-therapy with PEG IFN and ribavirin alone. Patients in the boceprevir arm underwent a four-week lead-in with PEG IFN and ribavirin before boceprevir was added to the treatment regimen; the total length of treatment was 48 weeks in both groups. The SVR was 66% in the boceprevir arm and 21% in the control arm, a statistically significant difference in favor of boceprevir. Patients in the boceprevir arm had higher rates of anemia than those in the control arm and required erythropoietin therapy more frequently (46% vs. 21%).

In the REALIZE study, the telaprevir pivotal trial in previously treated genotype 1 patients, subjects received either the triple-therapy with telaprevir, PEG IFN, and ribavirin or double-therapy with PEG IFN and ribavirin alone. Patients were divided into prior relapsers, prior partial responders, and prior non-responders. The SVR in the triple- vs. double-therapy arms were 83% vs. 24% in the prior relapsers, 59% vs. 15% in the partial responders, and 29% vs. 5% in the null responders. Therapy with telaprevir achieved statistically significantly improved outcomes compared to double-therapy across all treatment arms. Once again, this increased efficacy came with a price: the telaprevir arm was associated with a significant increase (37% vs. 22%) in serious adverse events, particularly anemia, neutropenia (decrease in circulating neutrophils), and leukopenia (decrease in circulating leukocytes).

While the two compounds have never been tested head-to-head, a perception that Incivek is more efficacious has led it to dominate the US market. As of the end of 2011, Incivek had achieved sales of $876MM, while Victrelis had sales of only $140MM.
The biggest drawback to Incivek and Victrelis is that they must be used in combination with PEG IFN and ribavirin. While both achieve significant improvements over standard therapy, particularly in genotype 1 patients, adding either Victrelis or Incivek to this regimen does not mitigate the dosing challenges of weekly PEG IFN injections, poor tolerability, or long course of therapy.

The pace of anti-HCV drug innovation, however, has quickened. In November 2011 at the annual meeting of the American Association for the Study of Liver Diseases (AASLD), biotechnology company Pharmasset stunned the HCV world with the announcement of Phase II data for its NS5B nucleotide analog, PSI-7977. A 12-week, all-oral regimen of once-daily PSI-7977 combined with ribavirin in genotype 2/3 patients achieved 100% SVR at 24-week follow-up. Furthermore, safety and tolerability were improved compared to treatment arms that incorporated IFN. Earlier trials have demonstrated that PSI-7977 and ribavirin can achieve a cure rate as high as 91% in patients with genotype 1. These data were nothing short of revolutionary, offering the promise of an all-oral, short duration, well-tolerated treatment option for HCV, including for the most difficult-to-treat genotype 1 patients.

Less than two weeks after AASLD, Gilead announced its intention to acquire Pharmasset for $11B, or $137 per share, an 89% premium over the stock price at the time. Pharmasset had no products on the market at the time of the acquisition; essentially, Gilead made a bet on the promise of the company’s HCV pipeline. PSI-7977 (now GS-7977, following the Gilead acquisition) entered into Phase III trials in genotype 2/3 patients in late 2011 and will enter a Phase III trial in genotype 1 patients in the first half of 2012. Analysts believe that GS-7977 could be approved as part of the first all-oral regimen for HCV as early as 2014, and that GS-7977 sales in the top seven pharmaceutical markets (US, England, France, Spain, Italy, Germany, and Japan) could peak at $7B annually.
The relationship between therapeutic and diagnostic innovation: a case study from HIV

What is the relationship between innovations in treatment and diagnostic paradigms? There is precedent for improved treatments driving demand for improved diagnostics in several infectious diseases, including HIV. Similar to HCV, early diagnosis of HIV is critical to prevent viral transmission and to prevent or delay the onset of complications from serious immunologic damage. A major advancement in HIV therapy was the introduction of highly active antiretroviral therapy (HAART). HAART consists of treatment with three antiretroviral agents, typically two nucleoside reverse transcriptase inhibitors plus an additional drug from a second class. HAART, which became available in 1996, was the first treatment regimen that significantly delayed progression to AIDS and prolonged life in HIV patients.

Prior to HAART, there were few incentives for individuals to get tested. However, even after HAART became available, the cost-effectiveness of broad, community-level screening for HIV in the era of improved treatments was unknown.

The need for improved HIV screening and diagnosis proved to be dramatic: research in the mid-2000s suggested that 57% of HIV patients in large urban settings in the US had CD4 counts below 350 at initial presentation, suggesting a time lapse from infection to diagnosis of five years. Even worse, nearly 30% of patients were not identified until they presented with their first opportunistic infection—a point at which HAART may be less effective. In the context of these more effective HIV therapies, researchers were curious about the cost effectiveness and impact of expanded screening on treatment outcomes. In one study that measured costs, quality of life, and survival, while controlling for behavior changes due to counseling and treatment, diagnostic screening programs reduced rates of lifetime transmission of HIV.

While the statistics for the US are striking, it is important to note that the lack of diagnosis of HCV is an even more serious problem in the developing world. An analysis of those countries is beyond the scope of this thesis, though it will be addressed in the discussion.
by 20%. Furthermore, in high-risk populations (defined by the CDC as a prevalence of 1% or more), one-time screening was associated with an incremental cost of $15,078 per quality-adjusted-life-year (QALY). As a basis for comparison, the National Institute for Clinical Excellence (NICE) in the United Kingdom considers an intervention “cost effective” if its $/QALY ratio is less than £20,000-30,000, or $30,000-45,000. In the United States, the acceptable threshold has been established at $100,000.

Expanded screening for HIV met this threshold; indeed, it did so even when assumed prevalence rates were as low as 0.05%.

Thus, innovations in HIV therapy drove demand for improved screening and diagnostic practices. This same paradigm is now evolving in HCV, especially since, as I will explore in the next section, current HCV diagnostic practices are associated with significant challenges.

**Diagnosis of HCV: Current standard of care**

There is no single tool to diagnose hepatitis C. Presently, at both the acute and the chronic stages of infection, multiple tests are needed to arrive at a definitive diagnosis. In this section, I will examine the current diagnostic paradigm in HCV, highlighting the significant challenges healthcare providers face in arriving at an actionable diagnosis.

As discussed above, the most significant risk factor for contracting HCV is a personal history of injection drug use—at any point in the past, and at any frequency, even once. By some estimates, the prevalence of HCV among persons with a history of injection drug use is approximately 90%. The next most significant risk factor is receipt of a blood or blood product transfusion, or an organ transplant, prior to

---

The QALY is a gold standard measurement for determining intervention cost-effectiveness.
Other risk factors include exposure of healthcare workers to HCV-contaminated blood, exposure to an infected sexual partner, and body piercing or tattooing. With an estimated HCV prevalence in these populations of only 1-5%, these factors are less significant than either drug use or blood transfusion/organ transplantation. HCV also is associated with several co-morbid conditions, including HIV, hemophilia, and idiopathic elevated ALT. Current guidelines recommend that patients who report any of these risk factors or co-morbid conditions be screened for HCV. Importantly, despite the close tie between age cohort and HCV prevalence—as noted above, two-thirds of those infected with HCV in the US are baby boomers—there currently are no guidelines recommending HCV testing based on age.

Once a person has been selected for HCV testing, they begin diagnostic testing—an uncertain process, since there is no single test that can accurately and reliably diagnose HCV infection. A complete assessment of the state of HCV infection typically requires three separate tests.

The first step is to perform a serologic (blood-based) assay to test for the presence of anti-HCV antibodies. This test is conducted using an enzyme immunoassay (EIA), in which a serum sample is added to a membrane treated with recombinant HCV antigens that trap HCV antibodies, which are then detected by secondary antibodies against immunoglobulins. The first generation of these assays could detect antibodies approximately 16 weeks after viral transmission; current tests can detect antibodies four to six weeks after transmission, with specificity greater than 99% (AASLD). The newest EIAs that are commercially available include the Abbott HCV EIA 2.0 from Abbott Laboratories and the Ortho HCV Version 3.0 ELISA from Ortho Clinical Diagnostics. More recently, the OraQuick® HCV Rapid Antibody Test from OraSure was approved for the measurement of anti-HCV antibodies in February 2011.33

---

1992. After 1992, testing to screen potential donors for anti-HCV antibodies improved significantly, which is why recipients after that year are not considered to be at significant risk.

* For historical reasons, these are general referred to as "second-generation" anti-HCV assays.
OraQuick is a lateral flow assay, similar to a home pregnancy test, that can deliver a result from a finger stick or venous blood sample after 20 minutes.\textsuperscript{34}

A positive result on any of these tests indicates that a person has been exposed to HCV; problematically, it does not shed light on the current infection status. Since 15-25\% of patients will spontaneously resolve HCV without progressing to a chronic infection, confirming \textit{active} HCV infection is a crucial next step before initiating treatment.\textsuperscript{35} Furthermore, in immunocompromised individuals, such as patients on dialysis, transplant recipients, or HIV-positive patients (all of whom are at increased risk for contracting HCV), anti-HCV antibodies may not be detectable by EIA or rapid antibody tests, despite infection. Thus, further testing may be necessary in these patients even in the absence of a positive EIA.\textsuperscript{36}

The second step, then, is to test for \textit{active} HCV infection. The standard test for \textit{active} HCV infection is HCV RNA detection. Historically, RNA detection has been performed by nucleic acid amplification, either qualitatively or quantitatively. Qualitative testing has been used more broadly to monitor response to therapy, because it is able to detect lower levels of HCV in the blood. Quantitative assays have emerged more recently as the diagnostic standard; indeed, in its latest clinical guidelines, the AASLD stated that there is “no longer need for qualitative assays.”\textsuperscript{27} Of course, qualitative tests remain commercially available; a list can be found in Table 1.\textsuperscript{27, 37}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{Assay} & \textbf{Manufacturer} & \textbf{Method} & \textbf{Indication} \\
\hline
Amplicor HCV v2.0 & Roche Molecular Systems & Manual RT-PCR & Diagnosis of \textit{active} infection; monitoring \\
\hline
Cobas Amplicor HCV v2.0 & Roche Molecular Systems & Semi-automated RT-PCR & Diagnosis of \textit{active} infection; monitoring \\
\hline
Cobas Ampliscreen & Roche Molecular Systems & Semi-automated RT-PCR & Blood screening \\
\hline
Versant HCV Qualitative Assay & Siemens Healthcare Diagnostics & Semi-automated TMA & Diagnosis of \textit{active} infection; monitoring \\
\hline
\hline
\end{tabular}
\caption{Qualitative HCV RNA Assays}
\end{table}
The latest quantitative RNA assays are based on either real-time polymerase chain reaction (PCR) or transcription-mediated amplification (TMA). Both PCR and TMA involve amplifying the HCV RNA present in a sample to a level where it can be easily detected and quantified. These tests can detect HCV levels as low as 10-50 IU/mL with a specificity of 98-99%. A full list of commercially available quantitative assays is shown in Table 2.

### Table 2: Quantitative HCV RNA Assays

<table>
<thead>
<tr>
<th>Assay</th>
<th>Manufacturer</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobas Amplicor HCV Monitor v2.0</td>
<td>Roche Molecular Systems</td>
<td>Manual RT-PCR</td>
</tr>
<tr>
<td>Versant HCV RNA 3.0 Assay</td>
<td>Siemens Healthcare Diagnostics</td>
<td>Semi-automated bDNA signal amplification</td>
</tr>
<tr>
<td>LCx HCV RNA-Quantitative Assay</td>
<td>Abbott Diagnostics</td>
<td>Semi-automated RT-PCR</td>
</tr>
<tr>
<td>SuperQuant</td>
<td>National Genetics Institute</td>
<td>Semi-automated RT-PCR</td>
</tr>
<tr>
<td>Cobas Taqman HCV Test</td>
<td>Roche Molecular Systems</td>
<td>Semi-automated RT-PCR</td>
</tr>
<tr>
<td>Abbott RealTime</td>
<td>Abbott Diagnostics</td>
<td>Semi-automated RT-PCR</td>
</tr>
</tbody>
</table>

Following diagnosis of active HCV infection, a third test, genotype identification, is generally recommended. This test is often recommended because different HCV genotypes exhibit variable responses to currently available therapies. As discussed previously, pipeline therapies may be pan-genotypic, achieving the same treatment outcomes regardless of genotype. In that case, genotype testing might no longer be necessary; however, given the limitations of currently available treatments, genotype testing remains an important part of the diagnostic paradigm. Combined, these three tests cost more than $600, according to 2012 reimbursement data from the Centers for Medicare and Medicaid Services (CMS). The complexities of this diagnostic process are well-illustrated in visual form, as shown in Figure 1.

---

1 The IU, or international unit, is the global standard established by the World Health Organization for diagnostic assays. Requiring that all assays report their results in the same unit allows for comparability of results across different assays.
Aside from the technical challenges involved in administering three tests, there are several additional reasons why HCV remains infrequently diagnosed. First, patients with chronic HCV tend to remain asymptomatic for decades. Second, because of the lack of federal funding for HCV screening, diagnosis, and treatment, there are wide disparities in the reimbursement for, and availability of, HCV testing and treatment services, both among states and within states, across care settings. New HCV infections are most likely to occur in marginalized populations, including incarcerated persons and the homeless, who are treated in settings with limited resources. None of these settings can reliably afford the expensive technology required for an accurate diagnosis of HCV.

Given the shortcomings of the available tests, it appears a significant need exists for a method to diagnose active HCV infection that is simple, affordable, and accessible, especially in resource-constrained settings. Point-of-care (POC) diagnostics may offer a solution to these challenges. In the next section, I will review some of the pipeline POC systems currently under development before moving to a more in-depth analysis of the Daktari system.
Diagnosis of HCV: Pipeline technologies

While POC diagnostics are a major area of research and development, there are few companies specifically developing diagnostics for HCV. However, companies developing viral load or nucleic acid tests are potential entrants to the HCV diagnostics marketplace, since these technologies could be adapted for use in the diagnosis of HCV. In this section, I provide a brief overview of eight molecular diagnostics companies and their technologies, and discuss their potential application in HCV.

**Akonni Biosystems:** Akonni Biosystems is a privately held molecular diagnostics company based in Maryland that develops, manufactures, and markets integrated molecular diagnostics systems. The company has a dual focus on both clinical and research applications of their technologies. Akonni’s clinical molecular testing system is called TruDiagnosis*. The company describes the system as “near” point-of-care, since it must be used in a laboratory setting. The core of the TruDiagnosis* system is the TruArray* test, which automates processes such as nucleic acid extraction and data analysis on a relatively simple, bench-top platform. Currently, the TruArray* system is available for research purposes only; however, Akonni’s website states that they are discussing clinical applications of the technology with the FDA. The system has been developed for identification of several bacterial infections (tuberculosis, MRSA) as well as for qualitative detection of herpes simplex virus (HSV) 1 and HSV-2. There is no indication that the company is developing a quantitative viral testing platform, nor a test specific to HCV.

**Cepheid:** Cepheid is a global, publicly held, molecular diagnostics company based in California. Cepheid’s platform is the GeneXpert* system, which automates sample preparation and nucleic acid amplification and detection within one hour. The modular system allows for scalability; the most portable systems can conduct one test at a time, while larger systems can analyze up to sixteen tests in
parallel. Although the GeneXpert® system is simpler than current PCR tests, it is still based on PCR technology, meaning that the system remains both technically complex and expensive. Cepheid’s currently markets in vitro diagnostic tests in healthcare acquired infections (MRSA, C. difficile), epidemic infectious diseases (influenza, enteroviral meningitis), and women’s health (Group B Streptococcus).

While Cepheid does not currently have a virology platform, the company’s 2011 annual report indicates that they expect to launch a quantitative HCV test for clinical use in 2015-2016. The company is also developing quantitative tests in HBV, cytomegalovirus (CMV), and Epstein-Barr virus (EBV), as well as an HCV genotype test; all are expected to come to market in 2015-2016.

**GnuBIO:** GnuBIO, based in Massachusetts, is a privately-held company developing next-generation sequencing technology for clinical and research applications. The microfluidic, cartridge-based system automates nucleic acid sequencing, amplification, and analysis within three hours. GnuBIO is currently focused on DNA sequencing in oncology and sudden cardiac death. There is no indication that the company is currently pursuing a virology platform; however, the sequencing technology could in theory be applied to HCV.

**iQuum:** iQuum is a privately held company based in Massachusetts. The company’s platform, the Liat® system, automates purification and analysis of a fluid sample, delivering results in 20 minutes to 1 hour, depending on the assay. The workstation, which is based on PCR technology, can run up to eight samples simultaneously. iQuum currently does not have FDA approval for any products. The company is developing tests for influenza, dengue, HIV, and CMV; there is no indication it is developing a quantitative test for HCV. However, both the HIV and CMV test under development are quantitative, so it could theoretically adapt its technology for use in HCV.
TwistDx: TwistDx is a medical diagnostics company based in the United Kingdom which has recently become a subsidiary of Alere. Its DNA diagnostics platform is based on a proprietary method called recombinase polymerase amplification (RPA). Through RPA, enzymes known as recombinases target specific primers in a DNA sample and initiate amplification if those primers are present, resulting in detectable levels within 5-10 minutes. The system is designed as a replacement for PCR. Alere and TwistDx are currently exploring applications of the technology in medical diagnostics (MRSA), HIV, industrial applications (water quality testing), agriculture, and biodefense.

Vivacta: Vivacta is a privately held company based in the United Kingdom. The company’s microfluidic, cartridge-based diagnostic platform uses piezoelectric materials to measure antibody/analyte binding in an assay within 10 minutes, using blood samples less than 30 μL. In the Vivacta system, a piezofilm is coated with antibodies which specifically bind to a target analyte. The antibody-target binding on the surface of the film generates an electric charge, which is used to measure the concentration of the analyte in the sample. Vivacta has successfully developed a diagnostic test for thyroid stimulating hormone (TSH) and is currently developing a cardiac diagnostic panel for use in the emergency room and acute care settings. While the company is not specifically developing a test for HCV, Vivacta believes its technology has potential applications in identification, diagnosis, or monitoring of endocrine/hormonal imbalances, vitamin deficiency, sepsis, kidney disease, stroke, and cardiovascular disease, and it may be applicable to HCV.

Veredus Laboratories: Veredus is a privately held life sciences company based in Singapore. The VerelD* Biosystem runs on proprietary VereChips®, which combine PCR and microarray technologies. Veredus currently markets two applications of its technology, one for influenza and one combined
biothreat test for anthrax, plague, smallpox, and tularemia. The company is working on a “full pipeline” of VereChips® in other molecular diagnostic indications, though it does not name specific applications.

**Wave 80 Biosciences:** Wave 80 Biosciences, Inc. is a privately held company based in California. The company develops next-generation molecular diagnostics products for infectious disease, cancer, autoimmune disease, and other human health conditions. Its EOSCAPE® diagnostic platform is a portable, cartridge-based system; minimal information is available on the specifics of the system. Wave 80’s most advanced platform is the EOSCAPE-HIV® system, which is scheduled to begin testing in Kenya and South Africa in 2012. Depending on the success of this platform, the company will advance its pipeline in a number of infectious and non-infectious diseases, including HCV, HBV, cardiovascular disease, certain autoimmune diseases, and cancer.

Thus, although several molecular diagnostics companies are developing platforms that could theoretically be applicable in HCV, only two companies (Cepheid, Wave 80) have specifically identified HCV in their product development pipelines. Additionally, these systems continue to face certain challenges; many are not truly point-of-care, while others continue to rely on complex, expensive PCR technology. In the next section, I will introduce the Daktari POC diagnostic platform and discuss the ways in which it may offer a solution to the challenges in HCV diagnosis.

**The Daktari system**

The goal of the Daktari platform is to provide an affordable, easy-to-operate alternative to standard diagnostic technologies. Diagnostic blood tests face two issues that make them complex to operate and

---

8 The Daktari CD4 test is the most advanced version of the system and is the basis for the patents that have been filed to date. Thus, this section will discuss the Daktari technology in the context of the CD4 test before explaining how the technology will be adapted for HCV testing.
expensive to manufacture and maintain. The first issue is sample preparation. After a venous blood sample is drawn, a series of reagents must be added, often manually, in a specific series of steps to isolate the target of interest. Second, once that target has been isolated, it must be detected, typically using laser-based or similar optical technologies. The Daktari platform offers simple, elegant solutions to both of these challenges, enabling Daktari's diagnostics to be used in places that could never support the complex equipment used for sample preparation and optical detection.

**Figure 2: Daktari CD4 instrument and cartridge**

As shown in Figure 2, Daktari's platform consists of two main components: the instrument and the cartridge. The instrument weighs less than 3kg and runs on a rechargeable battery, allowing it to be transported virtually anywhere. It contains a mechanical pump to move a blood sample and reagents through the cartridge and an electrical impedance meter to conduct analyte measurement (these processes will be explained in further detail below). The cartridge, shown in detail in Figure 3, contains all the reagents necessary to prepare and analyze a sample, in pre-measured blister packs. Once the sample has been collected on the cartridge and the cartridge has been inserted into the instrument, no more manual work is required; the system automatically runs the analysis and displays the result.

The technological innovation behind Daktari's cartridge is a process known as *microfluidic shear chromatography*. Each cartridge is made up of microfluidic channels no more than 50 microns tall, about

---

*See Table 3 for additional system specifications.*
half the width of a human hair. In the case of the CD4 test, these channels are lined with anti-CD4 antibodies. The instrument’s mechanical pump has been calibrated to achieve a flow rate that optimizes the shear stress applied to the sample as it moves through the network of microfluidic channels and chambers. Thus, as the sample flows through the cartridge, the CD4-positive T lymphocytes are captured while the other cells and contaminants in the sample can pass through to a waste chamber. Importantly, in future versions of the system, different channels could be coated with different binding moieties, and the flow rate could vary between channels, allowing for multiple tests to be conducted in the same cartridge.

Just as microfluidic shear chromatography provides a simple solution to the challenge of sample preparation for isolating cells (or other targets), lysate impedance spectroscopy solves the challenge of designing a simple method of detecting targets – or in the case of Daktari’s CD4 test, counting cells. Once the CD4 cells have been captured, the instrument takes a baseline electrical impedance measurement using a simple electrode and voltmeter. A lysis buffer is then released, rupturing the CD4 cells and releasing charged ions into the chamber. At this point, a second electrical measure is taken. The change in the electrical current between the measurement at baseline and the measurement after cell lysis provides an indirect count of CD4 cells without needing to employ fragile, expensive optics, such as lasers and microscope lenses. A graphic representation of this entire process,
including the relevant patents at each stage, can be found in Figure 4. All told, it takes approximately eight minutes to deliver a result from the time of the finger prick.

**Figure 4: Daktari Testing Process**

1. **Finger prick**
   - 10 sec

2. **Blood entry**
   - 10 sec

3. **Cell Capture**
   - 120 sec

4. **Differential Shear**
   - 90 sec

5. **Wash**
   - 90 sec

6. **Cell Lysis**
   - 30 sec

7. **Electrical Sensing**

8. **Result**
   - Total = <8 mins

**Daktari & HCV**

With a few important changes, the basic concept of Daktari’s microfluidic assay can be applied to the diagnosis of HCV. A side-by-side comparison of the CD4 and HCV systems can be seen in Table 3. There are several important differences. First, while the CD4 system is counting cells, the HCV system will be counting viral particles in a given sample of blood. Cells are 10 microns in diameter and 30 nanoliters in volume, while hepatitis C virus is 100 nanometers in diameter and 4 picoliters in volume; thus, capturing and detecting viruses poses a significant technical challenge. Compounding this issue, viral particles may be present at a lower concentration than cells in a microliter of blood, meaning that a larger blood sample is needed (200 μL via venous blood draw for HCV vs. 10 μL via fingerstick for CD4 cells) to achieve a clinically relevant detection threshold. Because a 200 μL sample is too large to be collected by finger stick, a venous blood draw will be necessary. As a result, some additional technician training is
required, although the test can still be completed by a person with a sixth-grade reading level. The size of the sample also impacts the assay time, increasing it from eight to 20 minutes. The added steps involved in viral load detection require some adjustments to the cartridge and instrument as well. The cartridge has an additional detection reagent and an additional chamber; the instrument is slightly larger and weighs slightly more (3.0 vs. 2.8 kg), although it remains fully portable.

### Table 3: Daktari System Specifications: CD4 vs. HCV

<table>
<thead>
<tr>
<th>Sample</th>
<th>CD4</th>
<th>HCV Active Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample volume</td>
<td>10 µL</td>
<td>200 µL</td>
</tr>
<tr>
<td>Preparation reagents</td>
<td>R1, R2 on chip</td>
<td>R1, R2 on chip</td>
</tr>
<tr>
<td>Detection reagents</td>
<td>R3 on chip</td>
<td>R3, R4, R5 on chip</td>
</tr>
<tr>
<td>Indication</td>
<td>Treatment Eligibility</td>
<td>Treatment Eligibility</td>
</tr>
<tr>
<td>Dynamic range</td>
<td>&gt;200 cells/µL / &gt;350 cells/µL</td>
<td>&gt;50,000 IU/mL</td>
</tr>
<tr>
<td>Dynamic range</td>
<td>Monitoring</td>
<td>Monitoring</td>
</tr>
<tr>
<td>Dynamic range</td>
<td>100 - 800 cells/µL</td>
<td>50,000 - 500,000 IU/mL</td>
</tr>
<tr>
<td>Assay Time</td>
<td>8 minutes</td>
<td>20 minutes</td>
</tr>
<tr>
<td>Instrument size</td>
<td>25 x 18 x 12 cm</td>
<td>30 x 20 x 12 cm</td>
</tr>
<tr>
<td>Instrument weight</td>
<td>2.8 kg</td>
<td>3.0 kg</td>
</tr>
<tr>
<td>Operating temperature</td>
<td>10 to 40 °C</td>
<td>10 to 40 °C</td>
</tr>
<tr>
<td>Operating environment</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>Cartridge shelf life</td>
<td>24 months</td>
<td>24 months</td>
</tr>
<tr>
<td>Hands-on operator time</td>
<td>30 seconds</td>
<td>60 seconds</td>
</tr>
<tr>
<td>Battery-powered operation</td>
<td>100 tests / 3 days</td>
<td>72 tests / 3 days</td>
</tr>
<tr>
<td>User skill</td>
<td>6th grade education</td>
<td>6th grade education</td>
</tr>
<tr>
<td>User training</td>
<td>3 hours</td>
<td>6 hours</td>
</tr>
<tr>
<td>Data</td>
<td>Screen display and local printer: USB, network or wireless data transmission</td>
<td>Screen display and local printer: USB, network or wireless data transmission</td>
</tr>
<tr>
<td>On-board memory</td>
<td>1000 assays</td>
<td>1000 assays</td>
</tr>
</tbody>
</table>

While the specifications of the Daktari CD4 system were intended to meet a crucial unmet need in the developing world, those same attributes make the system promising for fast and efficient diagnosis anywhere, including diagnosis of HCV in the United States. The issues underlying the diagnosis of HCV in this country are similar, in some ways, to the challenges of CD4 monitoring. HIV and HCV follow a similar natural history: a person becomes infected, may show non-specific symptoms early on, and then remains asymptomatic until the disease has progressed to such an advanced stage that treatment becomes difficult and expensive. The technological challenges are similar as well. In HIV, patients may
not have access to CD4 monitoring, because flow cytometers are capital-intensive, must be operated by skilled laboratory technicians, and require regular and expensive maintenance; most healthcare facilities cannot support one. In HCV, while an enzyme immunoassay is relatively inexpensive and easy to conduct, RNA detection assays are complex, creating a similar access gap. Furthermore, as shown in Figure 1 above, the current diagnostic paradigm in HCV requires as many as three tests before a physician can determine the correct course of treatment; no single result provides all the necessary information. When the Daktari system is considered within the context of each of these challenges, it appears to offer a simple, convenient solution.

**Cost of equipment:** While market pricing has not yet been determined, the manufacturing costs for Daktari are sufficiently low that the system stands to be 50-75% less expensive than the current equipment needed for RNA-based testing. There are two components to Daktari’s manufacturing costs: the instrument itself and the disposable cartridges. The device will cost approximately $1,000 - 1,500 to manufacture. The cartridge is projected to cost $10 to manufacture at market entry, including all pre-packaged reagents; that cost should fall to approximately $8/cartridge as Daktari achieves economies of scale in manufacturing. Furthermore, many of the hidden costs associated with RNA-based testing, including training, technician time, and maintenance, will either be reduced or eliminated due to the simplicity of the Daktari system.¹

**Technical complexity:** The blood volume required to conduct the Daktari HCV test is such that a venous blood draw will be required. Once the sample has been taken, though, the healthcare worker need only load it onto the cartridge. Because all of the necessary reagents are prepackaged within the cartridge,

¹ As shown in Table 3, the Daktari system can be operated by anyone with a sixth-grade education. Flow cytometers, on the other hand, must be operated by technicians with advanced degrees and training.
no manual sample preparation is required. Furthermore, the cartridge requires no refrigeration, eliminating the need for costly transportation and storage methods.

**Access:** Weighing only 3 kg at a size of 30 x 20 x 12 cm, the Daktari instrument is small and portable; it could be used in any level of healthcare facility. In addition, the battery will last for 70 tests, or approximately three days of constant use. As a result, the Daktari system could be taken into any level of health facility, from a hospital to a mobile clinic, to conduct testing on a variety of relevant patient populations.

**Transparency of result:** Instead of needing three separate tests to determine a patient's HCV status, the Daktari system will report all necessary information in one simple, easy-to-interpret result.\(^1\)

**Summary**

Several factors are driving change in the way HCV is managed in the United States. First, the epidemiology of the epidemic is shifting. Baby boomers, who contracted HCV decades ago, make up the largest segment of the infected population. As these patients progress to symptomatic disease, the costs of their treatment pose a major burden to the healthcare system. Second, more effective therapies with reduced side effect profiles offer the first real possibility that the majority of these patients could be effectively managed, perhaps even cured. Third, the current diagnostic process is complex, taking multiple steps to differentiate between cleared and chronic infections. The next generation of therapies will not reach those who need them unless patients can be accurately and reliably diagnosed.

\(^1\) Currently, the Daktari system is not being developed to detect HCV genotype. However, given the probability that pipeline therapies will be pan-genotypic, genotype testing likely may not be standard practice by the time the Daktari system comes to market.
Given its attributes, Daktari's diagnostic technology may be one solution to providing a fast, reliable
diagnosis of active HCV that would allow patients to receive the correct therapy. The hypothesis of this
thesis is that, in light of these market factors, Daktari will successfully generate revenue marketing its
platform for the diagnosis of HCV in the United States. In the next section, I will outline the methodology
I will use to explore this hypothesis.
Chapter 3: Methodology

The first step in understanding Daktari’s market opportunity is to quantify the number of patients who may require HCV testing in the United States. Under the current paradigm, this number is limited. The CDC currently recommends that the following populations be screened for HCV infection:

a) Current or former injection drug users, including those who injected only once many years ago;

b) Persons with conditions associated with a high prevalence of HCV infection, including persons with HIV infection, recipients of clotting factor concentrates made before 1987, chronic hemodialysis patients, and patients with unexplained abnormal ALT (a marker of liver disease);

c) Patients with known exposures to HCV, such as healthcare workers who may have been exposed to HCV-positive blood via needlestick, or recipients of blood or organs from donors who later tested HCV positive;

d) Children born to HCV-positive mothers.

Screening by age cohort currently is not recommended, despite the high rate of infection in the baby boomer population. However, there are indications that the CDC is poised to recommend age-based screening, specifically one-time screening for baby boomers. This step would significantly increase the number of subjects receiving HCV screening, which, as a consequence, should increase the number of patients who are diagnosed and enter treatment.

Thus, I construct a model of the current HCV testing and treatment paradigms, and propose future testing and treatment paradigms, to identify how many subjects might be eligible for screening, receive a diagnosis of HCV, and initiate treatment. The current HCV testing paradigm reflects the algorithm in Figure 1, and includes estimates of the aforementioned CDC criteria. The current treatment paradigm

---

1 For the remainder of this thesis, when I refer to “the market,” I am referring to the United States.

1 I will use the phrase “current paradigm” to refer to the current standard for the diagnosis and management of HCV.
makes assumptions on the proportion of screened patients who are identified to be HCV positive and subsequently receive treatment. Using these numbers as a baseline, I then estimate the number of HCV screening and monitoring tests that are conducted under the current paradigm, based on current clinical guidelines.

I next repeat each of these steps for the future testing and treatment paradigms, making assumptions on the ways that certain dynamics may shift in light of impending market changes. For example, the proposed future testing paradigm includes baby boomers as a recommended screening population, and the proposed future treatment paradigm assumes that a higher proportion of patients will seek treatment once more effective, more tolerable therapies are on the market. The number of tests conducted under the future paradigm will also be influenced by these new therapies, which likely will be administered over a shorter course of treatment. I compare the current and future paradigms to identify the main differences, and consider the impact those differences would have on the market for HCV diagnostics.

Last, taking the projections from the future paradigm as a baseline, I construct a model of the HCV RNA testing market from 2012 to 2019. The model takes into account both the introduction of new therapies for HCV and the introduction of new diagnostics, including the Daktari system. Both of these advances are forecast to take place in approximately 2015, so the model was built to examine the five years following the commercialization of new drugs and diagnostics. Sensitivity analyses were conducted to test the impact of certain assumptions built into the model.
Chapter 4: Results

HCV testing and treatment: Current paradigm

The model representing the number of patients captured in the current paradigm of HCV testing and treatment can be found in Tables 4A and 4B. To populate the model, estimates for the at-risk populations identified in the current CDC screening criteria for HCV were culled from the literature. I arrived at the estimates shown in the table as follows:

- **History of IDU**: The National Household Survey on Drug Abuse conducted a survey from 2000-2002 to obtain an estimate of the prevalence of IDU at any time in the past. Interestingly, of 1.5% of the population (or 3.4MM persons) who reported a lifetime history of IDU, the majority were from the baby boomer generation, placing them at increased risk for contracting HCV as a result of their drug use.\(^{51}\)

- **Persons with HIV infection**: The CDC estimates that there are 1.2MM people living with HIV in the United States.\(^{52}\) However, approximately 25% of HIV-positive patients report a history of IDU; thus, to avoid double-counting, this group was excluded and the total number of non-IDU, HIV-positive patients included in the model was 1,200,000 \(\times 0.75 = 900,000\).

- **Clotting factor recipients before 1987**: The population of hemophiliacs was used as a surrogate for recipients of clotting factors. According to a CDC epidemiologic study conducted in 1994, the prevalence of hemophilia at that time was 17,000.\(^{53, m}\)

- **Hemodialysis patients**: The United States Renal Data System issues an annual report of the number of patients receiving dialysis each year, as well as the number of deaths among patients receiving dialysis. I added the incident (new) dialysis each year from 1980-2008 (1,817,623) and

\(^{m}\) I use an older estimate to reflect the screening requirement that patients must have received clotting factors prior to 1987; however, realistically, a significant percentage of these patients likely have died since 1994. Thus, 17,000 may represent an overestimate of the patients alive today.
subtracted the number of deaths across the same time period (1,246,367). The resultant estimate of dialysis patients alive in the United States was 571,000.54

- **Patients with unexplained elevated LFTs**: This is the largest category of HCV screening eligibility. A recent analysis of NHANES data by Ioannou and colleagues found that 7.3% of the population over 20 years old has unexplained elevated ALT levels, defined as >43 IU/L without a history of alcoholism, or a diagnosis of HBV, HCV, or diabetes.55,n I multiplied this percentage by the total US population over the age of 20 per the United States Census Bureau to arrive at an estimate of 16.3MM.56

- **Organ/blood recipients pre-1992, persons with known exposure to HCV, and children born to HCV-positive mothers**: These populations were excluded from the model due to their small size. Given that the testing population is in the millions, these populations, which number in the low thousands, do not affect the final estimate by a significant amount.

- **Number of patients with chronic HCV**: The estimate of 5.2MM patients with chronic HCV comes from the paper by Chak and colleagues, referenced in the introduction, which augmented the NHANES estimate of the HCV population in the United States by adding incarcerated, homeless and active military populations.4

- **Percentage of patients who receive a diagnosis**: This is based on estimates by the US Department of Health and Human Services that only 25% of patients with chronic HCV are aware of their infection status.6

---

43 IU/L is a fairly liberal definition of “elevated” ALT. Furthermore, its clinical meaning may be limited, since most physicians define elevated ALT as a percentage of normal rather than as a discrete number. In its risk factors for HCV, the CDC simply mentions “unexplained elevated ALT” without providing a threshold. Given the large sample size and the rigor of the NHANES study, I decided to use this definition, though I acknowledge that it may overestimate the screening population.
Percentage of patients who begin treatment: According to the market research firm Frost and Sullivan, only 5.5% of patients who are diagnosed actually initiate treatment, largely due to the low efficacy and significant toxicity associated with current therapies.  

**Table 4A: Current Paradigm of HCV Testing**

<table>
<thead>
<tr>
<th>Persons needing HCV screening</th>
<th>Current paradigm</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of IDU</td>
<td>3,400,000</td>
</tr>
<tr>
<td>Persons with HIV infection (non-IDU)</td>
<td>900,000</td>
</tr>
<tr>
<td>Clotting factor recipients before 1987</td>
<td>17,000</td>
</tr>
<tr>
<td>Hemodialysis patients</td>
<td>517,000</td>
</tr>
<tr>
<td>Patients with unexplained elevated LFTs</td>
<td>16,300,000</td>
</tr>
<tr>
<td><strong>Total # of persons needing screening</strong></td>
<td><strong>21,134,000</strong></td>
</tr>
</tbody>
</table>

**Table 4B: Current Paradigm of HCV Treatment**

<table>
<thead>
<tr>
<th># of patients with chronic HCV</th>
<th>5,200,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of patients who receive a diagnosis</td>
<td>25%</td>
</tr>
<tr>
<td># of diagnosed HCV patients</td>
<td>1,300,000</td>
</tr>
<tr>
<td>% of diagnosed patients who begin treatment per year</td>
<td>5.5%</td>
</tr>
<tr>
<td># of patients who begin treatment per year</td>
<td>71,500</td>
</tr>
</tbody>
</table>

As this model shows, 3.9MM people with HCV have not received a diagnosis. Furthermore, despite the fact that a significant number of HCV patients could be cured with a 48-week course of therapy, only 71,500 patients – less than 1.5% of the population with chronic HCV – actually initiate treatment. These numbers highlight the inadequacy of the current testing and treatment paradigm to deal with the steadily increasing burden of HCV in the United States.

**Number of HCV tests required: Current paradigm**

Two sets of patients require HCV testing: patients undergoing screening, and patients on treatment who require regular monitoring. Screening is performed using an HCV antibody test, while testing to confirm
diagnosis and monitor response to therapy is performed with an HCV RNA test. Since monitoring is conducted throughout the course of therapy, the number of HCV RNA tests needed during treatment is influenced by the amount of time the patient is on treatment, which will vary depending on two main factors: the patient’s genotype and his/her compliance with the treatment regimen (i.e., those patients who drop out before receiving the full course of therapy will no longer be monitored). The AASLD recommends that patients receiving treatment for HCV have their HCV RNA levels measured at the beginning of therapy, at week 4, at 4-12 week intervals over the course of treatment, at the end of the treatment cycle, and 24 weeks after cessation of therapy to monitor response. The previous tables established the size of the testing and treatment populations under the current treatment paradigm of relatively ineffective therapies. In this section, I will use these estimates as a basis to obtain the number of HCV tests needed for both screening and monitoring.

Under current treatment regimens, genotype 1 patients (approximately 75% of the US HCV population) receive a 48-week course of therapy, while genotype 2/3 patients (approximately 25% of the US HCV population) receive a 24-week course of therapy. Given the clinical recommendation that patients be monitored every 4-12 weeks during treatment, under the assumption that patients are monitored on average every 8 weeks, genotype 1 patients would receive HCV RNA testing eight times (treatment initiation, week 4, week 12, week 20, week 28, week 36, week 44, treatment cessation, 24 weeks post-treatment) and genotype 2/3 patients would receive HCV RNA testing six times (treatment initiation, week 4, week 12, week 20, treatment cessation, 24 weeks post-treatment). Applying these testing rates to the HCV patient population identified under the current testing and treatment paradigm, the number of HCV tests currently conducted for screening and monitoring is as follows:

---

See Figure 1 for additional detail.
Table 4C: Number of HCV Tests Required: Current Paradigm

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening population (per Table 4A)</td>
<td>21,134,000</td>
</tr>
<tr>
<td># HCV antibody tests needed per screen</td>
<td>1</td>
</tr>
<tr>
<td>Total # screening tests (HCV antibody)</td>
<td>21,134,000</td>
</tr>
<tr>
<td># antibody-positive patients$^1,^4,^8$</td>
<td>1,530,000</td>
</tr>
<tr>
<td># HCV RNA tests needed per confirmation of diagnosis</td>
<td>1</td>
</tr>
<tr>
<td>Total confirmation tests (HCV RNA)</td>
<td>1,530,000</td>
</tr>
<tr>
<td># of patients diagnosed with chronic HCV$^4$</td>
<td>1,300,000</td>
</tr>
<tr>
<td>Monitoring population (total treatment population; based on Table 4B)</td>
<td>71,500</td>
</tr>
<tr>
<td>Genotype 1 patients (75% of HCV population)$^{15}$</td>
<td>53,600</td>
</tr>
<tr>
<td># tests required for genotype 1</td>
<td>8</td>
</tr>
<tr>
<td>Total genotype 1 tests</td>
<td>429,000</td>
</tr>
<tr>
<td>Genotype 2/3 patients (25% of HCV population)$^{15}$</td>
<td>17,900</td>
</tr>
<tr>
<td># tests required for genotypes 2/3</td>
<td>6</td>
</tr>
<tr>
<td>Total genotype 2/3 tests</td>
<td>107,000</td>
</tr>
<tr>
<td>Total monitoring tests (HCV RNA)</td>
<td>536,000</td>
</tr>
<tr>
<td>Total HCV RNA tests (confirmation + monitoring)</td>
<td>2,066,000</td>
</tr>
</tbody>
</table>

Given the promising HCV therapies currently in development, a new standard for treatment may be on the horizon. To fully realize the potential of these therapies, they must be supported by new diagnostics that simplify the process of identifying HCV patients and helping them to receive treatment. The next section explores one such paradigm, built on major advances in treatment, and its impact on management of HCV.

**HCV testing and treatment: Future paradigm**

The model representing the number of patients captured in the future paradigm of HCV testing and treatment can be found in Table 5. The categories under “Persons needing HCV screening” are the same as in the current paradigm model, with one exception: the addition of baby boomers. The estimate of

$^p$ 1.3MM patients are currently diagnosed with chronic HCV in the US. According to Chak and colleagues, if 85% of patients who contract HCV go on to develop chronic illness, an additional 15% of patients will test positive for HCV antibody but will not be actively infected; thus, the total number of patients in the US who would test positive for HCV antibody under the current paradigm is $1,300,000 / 0.85 = 1,530,000$. 

40
the baby boomer population – 78,000,000 – comes from US Census data taken in 2006 and includes both US-born and immigrant populations.\textsuperscript{58}

Since baby boomers are now being included in the screening population, they must be subtracted from the other categories to avoid double-counting. This was achieved across categories as follows:

- **History of IDU**: According to Armstrong and colleagues, baby boomers are significantly more likely than the general population to report a lifetime history of IDU. Indeed, in their sample, the prevalence of lifetime IDU in persons aged 35-49 (a baby boomer cohort) was 3.1\%.\textsuperscript{51} If we apply this prevalence to the estimate of the baby boomer population, the number of baby boomers with a history of IDU is: \(3.1\% \times 78\text{MM} = 2.4\text{MM}\).

- **Persons with HIV infection**: Of the 1.2MM people in the United States living with HIV in 2008, 533,000 were baby boomers.\textsuperscript{59}

- **Clotting factor recipients**: The total population is estimated to be only 17,000, and eliminating baby boomers from this group would have no significant impact on the final estimate. Thus, no double-counting correction was performed.

- **Hemodialysis patients**: Approximately 40\% hemodialysis patients are baby boomers; thus, the total number of baby boomers in this category is: \(40\% \times 517,000 = 207,000\).\textsuperscript{54}

- **Unexplained elevated ALT**: According to the Ioannou paper, the prevalence of unexplained elevated ALT was 11.4\% in persons ages 40-49 and 7.7\% in persons ages 50-59. According to US Census data, of the 78MM baby boomers in the US in 2006, 55\% were ages 40-49 while 45\% were ages 50-59. Thus, the total number of baby boomers with elevated unexplained ALT would be: \((11.4\% \times 43\text{MM}) + (7.7\% \times 35\text{MM}) = 7.6\text{MM}\).
- Baby boomers: Given the US Census estimate of 78MM baby boomers, the baby boomer population after correcting for double counting is: $78,000,000 - 2,400,000 - 533,000 - 207,000 - 7,600,000 = 67,260,000$.

Under these assumptions, the future paradigm of HCV testing appears as follows:

**Table 5A: Future Paradigm of HCV Testing**

<table>
<thead>
<tr>
<th>Persons needing HCV screening</th>
<th>Current paradigm</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of IDU $^{51}$</td>
<td>3,400,000</td>
</tr>
<tr>
<td>Persons with HIV infection (non-IDU) $^{52}$</td>
<td>900,000</td>
</tr>
<tr>
<td>Clotting factor recipients before 1987 $^{53}$</td>
<td>17,000</td>
</tr>
<tr>
<td>Hemodialysis patients $^{54}$</td>
<td>517,000</td>
</tr>
<tr>
<td>Patients with unexplained elevated ALT $^{55,56}$</td>
<td>8,700,000</td>
</tr>
<tr>
<td>Baby boomers $^{58}$</td>
<td>67,260,000</td>
</tr>
<tr>
<td><strong>Total # of persons needing screening</strong></td>
<td><strong>80,800,000</strong></td>
</tr>
</tbody>
</table>

As one can see, the addition of baby boomers as a relevant population drives nearly a four-fold increase in the HCV screening population. With this new, higher baseline, the next step is to explore the main differences in treatment between the current and future paradigms.

Aside from the addition of the baby boomer population as a screening group, it is my hypothesis that the future testing and treatment paradigm will see a significant increase in the percentage of patients who receive a diagnosis of HCV. The increase in the percentage patients receiving a diagnosis will be influenced by a number of factors. First, public health campaigns will raise both physician and consumer awareness of HCV. According to Bryce Smith of the CDC's Division of Viral Hepatitis, the organization will launch just such an initiative, called "Know More Hepatitis," in May 2012. The agency estimates that the initiative will lead to approximately 80MM baby boomers being screened, with 2.68MM receiving a diagnosis. $^{60}$ This number was added to the baseline level of people receiving a diagnosis in Table 4 to arrive at the new estimate of total patients diagnosed: 3,980,000. Since the total number of HCV cases
in the US remains 5.2MM (because this estimate included diagnosed and undiagnosed cases), the CDC’s campaign would result in 76.5% of HCV patients being diagnosed, a dramatic increase over today’s 25%. Additionally, the efficacy and tolerability profiles of new medications likely will increase the percentage of patients who choose to initiate treatment. New therapies likely will offer four specific advantages: increased efficacy across genotypes, including genotype 1; improved tolerability; reduced length of treatment; and, eventually, the possibility of an all-oral, interferon-free regimen. The most conservative, lower-bound assumption would be that the new therapies will have no impact on the percentage of patients treated, and that the percentage will therefore remain stable at 5.5%. Even under this assumption, with the higher rate of patients receiving a diagnosis, nearly 220,000 HCV patients would begin treatment in the future paradigm, a threefold increase over the current paradigm.

To determine an appropriate upper bound, we can turn again to the treatment of HIV. While the comparison is not perfect, there are several parallels that make it attractive: HIV, like HCV, is a chronic infectious disease, and HIV treatment was transformed with the approval of HAART in the mid-1990s. In 1998, the HIV Cost and Services Utilization Study issued a report stating that up to two-thirds of HIV patients did not receive regular medical care. A significant percentage of these patients were assumed to have either undiagnosed or early-stage HIV infection. Applying the same proportion to the HCV population, the upper bound of patients receiving treatment would be: 33% * 5.2MM = 1.7MM, or approximately 43% of the diagnosed population. Thus, the future HCV treatment paradigm is as follows:

---

9 The timing of this study offers a convenient analogy to the current state of HCV treatment in the United States. In 1998, HAART had been introduced only recently and the clinical community was still adjusting its treatment standard. HCV treatment is facing a similar shift today, with the recent introduction of Incivek/Vicretis and the promise of even more efficacious therapies in late-stage clinical development.
Table 5B: Future Paradigm of HCV Treatment

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td># of patients with chronic HCV</td>
<td>5,200,000</td>
</tr>
<tr>
<td># of screening tests to be conducted under CDC campaign</td>
<td>80,000,000</td>
</tr>
<tr>
<td>% of patients who receive a diagnosis</td>
<td>76.5%</td>
</tr>
<tr>
<td># of diagnosed HCV patients</td>
<td>3,980,000</td>
</tr>
<tr>
<td>% of diagnosed patients who begin treatment (lower bound)</td>
<td>5.5%</td>
</tr>
<tr>
<td>% of diagnosed patients who begin treatment (upper bound)</td>
<td>43%</td>
</tr>
<tr>
<td># of patients who begin treatment (lower bound)</td>
<td>219,000</td>
</tr>
<tr>
<td># of patients who begin treatment (upper bound)</td>
<td>1,700,000</td>
</tr>
</tbody>
</table>

Number of HCV tests required: Future paradigm

In table 4C, I arrived at an estimate of the number of HCV screening and monitoring tests that are conducted under today’s testing and treatment paradigm. I used the monitoring standards of current HCV therapies as the basis for this estimate. Given my assumption that the future paradigm of HCV treatment will be impacted by the availability of new, improved therapies, it follows that new monitoring standards will be a part of this shift in treatment. Thus, I need to make new assumptions on the frequency of monitoring in the future treatment paradigm to arrive at an estimate of the total number of HCV tests that may be conducted.

Therapies currently under development for the treatment of HCV are expected to offer a shorter course of therapy for patients of all genotypes. Specifically, genotype 2/3 patients, who currently undergo 24 weeks of therapy, likely will require only 12 weeks of therapy. Genotype 1 patients, who currently require 48 weeks of therapy, likely will require between 12-24 weeks of therapy. The length of treatment of genotype 1 patients remains more uncertain because clinical trial results to date have been mixed; however, there is a strong possibility that a therapy which allows for cure of genotype 1 HCV within 12 weeks will be developed in the next several years. I therefore assume that all HCV patients will receive treatment for 12 weeks, regardless of genotype. Under a 12-week treatment regimen, I assume
that patients will have their HCV RNA levels monitored five times (treatment initiation, week 4, week 8, treatment cessation, 24 weeks post-treatment). Under a 24-week regimen, I assume that patients will have their HCV RNA levels monitored six times (treatment initiation, week 4, week 12, week 20, treatment cessation, 24 weeks post-treatment).

Applying these testing rates to the number of patients requiring monitoring generates an estimate of the number of HCV tests conducted under the future paradigm:

**Table 5C: Number of HCV Tests Required: Future Paradigm**

<table>
<thead>
<tr>
<th>Description</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening population (per Table 5A)</td>
<td>80,800,000</td>
</tr>
<tr>
<td># HCV antibody tests needed per screen</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total # screening tests (HCV antibody)</strong></td>
<td>80,800,000</td>
</tr>
<tr>
<td># antibody-positive patients(^{4,8})</td>
<td>6,100,000</td>
</tr>
<tr>
<td># HCV RNA tests needed per confirmation of diagnosis</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total # confirmation tests (HCV RNA)</strong></td>
<td>6,100,000</td>
</tr>
<tr>
<td># of patients with chronic HCV(^4)</td>
<td>5,200,000</td>
</tr>
<tr>
<td>Monitoring population (lower bound; based on table 5B)</td>
<td>219,000</td>
</tr>
<tr>
<td>Monitoring population (upper bound; based on table 5B)</td>
<td>1,700,000</td>
</tr>
<tr>
<td># tests required for monitoring per patient</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total # monitoring tests (HCV RNA) – lower bound</strong></td>
<td>1,095,000</td>
</tr>
<tr>
<td><strong>Total # monitoring tests (HCV RNA) – upper bound</strong></td>
<td>8,500,000</td>
</tr>
<tr>
<td><strong>Total # HCV RNA test (confirmation + monitoring) – lower bound</strong></td>
<td>7,195,000</td>
</tr>
<tr>
<td><strong>Total # HCV RNA tests (confirmation + monitoring) – upper bound</strong></td>
<td>14,600,000</td>
</tr>
</tbody>
</table>

I assume that Daktari’s platform will be used only for confirmation and monitoring, not for HCV screening. As discussed earlier, testing for anti-HCV antibodies is inexpensive and can already be done at the point of care with the OraQuick HCV Rapid Antibody Test. Daktari’s potential market is HCV RNA tests, which in this model ranges from 7.2MM to 14.6MM tests, depending on the number of patients who enter therapy.

\(^{4}\) Given 5.2MM patients with chronic HCV (as per Chak and colleagues), if 85% of patients who contract HCV go on to develop chronic illness, an additional 15% of patients will test positive for HCV antibody but will not have acute infection; thus, the total number of patients in the US who would test positive for HCV antibody is 5,200,000/0.85 = 6,117,647.
I thus have established an estimate of the market size (in terms of number of tests) of HCV RNA tests in the United States. The next step is to examine the potential for the Daktari HCV system within this market.

**Daktari HCV market share model: 2015-2019**

Daktari anticipates that its HCV diagnostic system will become available in the US in 2015. This timing aligns well with the introduction of novel oral therapies for the treatment of HCV, such as GS-7977 and other therapies discussed above. Furthermore, the CDC will already have initiated its campaign to increase HCV screening, meaning more patients will be accurately diagnosed and will enter treatment, therefore requiring monitoring. Thus, I have constructed a potential market share model for the Daktari HCV system once it enters the market. This model is based on the following assumptions:

- **Timeframe:** Daktari will launch its HCV diagnostic system in 2015. The model was limited to a five-year window following 2015 because, if Daktari cannot generate an acceptable level of revenue in that time, pursuing commercialization of the HCV system in the US would not be practical. Based on market research discussed above, I assume that novel HCV therapies will become available in 2015 as well.

- **Screening:** The CDC's Know More Hepatitis campaign expects to screen 80MM people. For the purposes of this model, I assume 10MM people are screened per year from 2012-2019. In Table 5C above, of 80,800,000 patients screened, 6,100,000 patients – or 7.5% – will test positive for anti-HCV antibody. Applying this percentage to the assumed annual screening rate, for every 10MM people screened, 760,000 people will be HCV antibody-positive and require an HCV RNA test to confirm diagnosis of chronic HCV.

- **Treatment and monitoring by HCV genotype:** As discussed above, the next generation of HCV therapies is expected to be administered for the same duration of treatment regardless of
patient genotype. Therefore, per Table 4C above, from 2012-2014, I assume that genotype 1 patients will be monitored eight times and genotype 2/3 patients will be monitored eight times over the course of therapy. From 2015-2019, per Table 5C above, I assume that all patients will receive the same 12-week course of therapy and will be monitored five times.

- **Percentage of patients entering treatment**: In the discussion of the future paradigm above, I established a lower and an upper bound for the percentage of diagnosed HCV patients who would enter care. The lower bound assumption was that, if no new therapies enter the market, the percentage of diagnosed patients to initiate treatment would remain flat at 5.5%. The upper bound assumption was that, with the successful entry of new therapies, 43% of diagnosed patients would enter treatment. I have therefore created two separate models of the diagnostic market based on these bounds. For the model based on the upper bound, I assume that the percentage of patients entering treatment will rise to 10% in 2015, coinciding with the commercialization of new drugs and diagnostics. The percentage will then rise by 10% each year in 2015-2018 before peaking at 43% in 2019.

- **Treatment adherence**: Population-based studies have suggested that adherence with HCV therapy is approximately 50%. However, even those patients who end up being non-adherent will go through at least a portion of their treatment. I therefore assume that 50% of the patient population is fully adherent and 50% of the population is non-adherent. I define non-adherent as completing, on average, half the course of therapy. Non-adherent patients will therefore receive half the number of monitoring tests that compliant patients receive.

- **Incident cases**: I assumed that the number of incident HCV cases will remain flat at the current rate of approximately 17,000 cases/year.

- **HCV-specific mortality**: At the time of the model, the annual mortality rate from HCV-related chronic liver disease or HCC is predicted to be approximately 19,000 persons/year.
mortality and incidence rates are so similar, for the purposes of the model I assume that the number of incident HCV cases is equal to the number of HCV-specific deaths in a given year.

- **Population mortality:** The annual death rate in the United States is approximately 793.8 per 100,000 population. I applied this rate to the screening eligible population throughout the model to account for deaths from non-HCV causes.

- **Retreatment:** Current clinical guidelines recommend against retreatment in HCV patients who fail to respond to the first line of therapy. Thus, for the purposes of the model I assume that patients only receive treatment once; patients who receive treatment in a given year are removed from the model in the following year.

- **Maintenance therapy:** Treatment guidelines recommend against maintenance therapy with either IFN or RBV due to a lack of demonstrated efficacy. Thus, for the purposes of the model I assume that patients remain on treatment for a maximum of 48 weeks (depending on HCV genotype and treatment response).

- **Daktari manufacturing capacity:** By the time the Daktari HCV system comes to market, the company will have already scaled up manufacturing capacity for its CD4 diagnostic, which is expected to launch in the developing world in late 2012. Thus, Daktari will already have significant manufacturing capacity. Specifically, the company expects to be able to produce 3MM HCV cartridges each year in 2015 and 2016 before increasing capacity to 8MM HCV cartridges in 2017.

- **Daktari price:** Daktari anticipates setting a price of $44 per test (cartridge) in the US. There will not be a separate price for the instrument; this charge is bundled into the price of the cartridge. The standard protocol for reimbursement of in vitro diagnostics in the US is that CMS sets a reimbursement threshold that private insurers generally follow. CMS currently reimburses
quantitative HCV RNA tests approximately $60; Daktari assumes that CMS will reimburse its more rapid, more convenient test for $44.38

- **POC Competition**: Daktari will face competition both from standard nucleic acid tests (those currently manufactured by Roche, Siemens, and Abbott) as well as from other novel POC diagnostics. Based on the competitive analysis conducted above, Cepheid and Wave 80 are the companies most likely to have an HCV RNA test available at the same time as Daktari; these three companies will split the POC market. Relative market share will be based on a number of factors, including manufacturing and distribution capacity, partnerships with larger companies, accuracy of the diagnostic system compared to the reference standard, pricing, and reimbursement. For the purposes of this model, I assume that all three competitors enter the market in 2015 and that they evenly split the POC share of the HCV diagnostic market.

- **POC market share**: I assume that the POC diagnostics will take 10% of the total HCV diagnostics market in 2015, 20% in 2016, and an additional 5% per year through 2019.

- **Discount rate**: Given that Daktari is still an early-stage company with no products currently on the market, I apply a standard 30% discount rate to calculate the net present value of the revenue generated by the Daktari HCV system from 2015-2019.

Incorporating all of these assumptions, the model of the HCV testing and treatment market from 2012-2019 is as follows:
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population screened</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
</tr>
<tr>
<td>Screened pop. requiring HCV RNA test</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
</tr>
<tr>
<td>Total confirmation tests</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
</tr>
<tr>
<td>Total Untreated HCV Population</td>
<td>5,200,000</td>
<td>4,870,000</td>
<td>4,560,000</td>
<td>4,270,000</td>
<td>4,010,000</td>
<td>3,760,000</td>
<td>3,520,000</td>
<td>3,300,000</td>
</tr>
<tr>
<td>Mortality</td>
<td>40,000</td>
<td>40,000</td>
<td>40,000</td>
<td>30,000</td>
<td>30,000</td>
<td>30,000</td>
<td>30,000</td>
<td>30,000</td>
</tr>
<tr>
<td>% Patients entering therapy</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
</tr>
<tr>
<td># Patients entering therapy</td>
<td>290,000</td>
<td>270,000</td>
<td>250,000</td>
<td>230,000</td>
<td>220,000</td>
<td>210,000</td>
<td>190,000</td>
<td>180,000</td>
</tr>
<tr>
<td># Genotype 1 patients</td>
<td>220,000</td>
<td>200,000</td>
<td>190,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># Genotype 2/3 patients</td>
<td>70,000</td>
<td>70,000</td>
<td>60,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># Genotype 1 monitoring tests</td>
<td>1,760,000</td>
<td>1,600,000</td>
<td>1,520,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># Genotype 2 monitoring tests</td>
<td>420,000</td>
<td>420,000</td>
<td>360,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gross monitoring tests</td>
<td>2,180,000</td>
<td>2,020,000</td>
<td>1,880,000</td>
<td>1,150,000</td>
<td>1,100,000</td>
<td>1,050,000</td>
<td>950,000</td>
<td>900,000</td>
</tr>
<tr>
<td>Tests lost to nonadherence</td>
<td>545,000</td>
<td>505,000</td>
<td>470,000</td>
<td>287,500</td>
<td>275,000</td>
<td>262,500</td>
<td>237,500</td>
<td>225,000</td>
</tr>
<tr>
<td>Net monitoring tests</td>
<td>1,635,000</td>
<td>1,515,000</td>
<td>1,410,000</td>
<td>862,500</td>
<td>825,000</td>
<td>787,500</td>
<td>712,500</td>
<td>675,000</td>
</tr>
<tr>
<td>Total HCV RNA tests (conf. + mon.)</td>
<td>2,395,000</td>
<td>2,275,000</td>
<td>2,170,000</td>
<td>1,622,500</td>
<td>1,585,000</td>
<td>1,547,500</td>
<td>1,472,500</td>
<td>1,435,000</td>
</tr>
<tr>
<td>Market share - SOC diagnostics</td>
<td>2,395,000</td>
<td>2,275,000</td>
<td>2,170,000</td>
<td>1,460,000</td>
<td>1,270,000</td>
<td>1,160,000</td>
<td>1,030,000</td>
<td>930,000</td>
</tr>
<tr>
<td>Market share - Daktari</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>50,000</td>
<td>110,000</td>
<td>130,000</td>
<td>150,000</td>
<td>170,000</td>
</tr>
<tr>
<td>Market share - POC Competitors</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>112,500</td>
<td>205,000</td>
<td>257,500</td>
<td>292,500</td>
<td>335,000</td>
</tr>
<tr>
<td>Daktari price/test</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td></td>
</tr>
<tr>
<td>Daktari revenue</td>
<td>$2,200,000</td>
<td>$4,840,000</td>
<td>$5,720,000</td>
<td>$6,600,000</td>
<td>$7,480,000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daktari revenue NPV (30% discount)</td>
<td>$11,490,000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6B: HCV Testing and Treatment, 2012-2019 (Upper Bound)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population screened</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
<td>8,000,000</td>
</tr>
<tr>
<td>Screened pop. requiring HCV RNA test</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
</tr>
<tr>
<td>Total confirmation tests</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
<td>760,000</td>
</tr>
<tr>
<td>Total untreated HCV population</td>
<td>5,200,000</td>
<td>4,870,000</td>
<td>4,560,000</td>
<td>4,270,000</td>
<td>3,810,000</td>
<td>3,020,000</td>
<td>2,090,000</td>
<td>1,230,000</td>
</tr>
<tr>
<td>Mortality</td>
<td>40,000</td>
<td>40,000</td>
<td>40,000</td>
<td>30,000</td>
<td>30,000</td>
<td>20,000</td>
<td>20,000</td>
<td>10,000</td>
</tr>
<tr>
<td>% Patients entering therapy</td>
<td>5.5%</td>
<td>5.5%</td>
<td>5.5%</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
<td>43%</td>
</tr>
<tr>
<td># Patients entering therapy</td>
<td>290,000</td>
<td>270,000</td>
<td>250,000</td>
<td>430,000</td>
<td>760,000</td>
<td>910,000</td>
<td>840,000</td>
<td>530,000</td>
</tr>
<tr>
<td># Genotype 1 patients</td>
<td>220,000</td>
<td>200,000</td>
<td>190,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># Genotype 2/3 patients</td>
<td>70,000</td>
<td>70,000</td>
<td>60,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># Genotype 1 monitoring tests</td>
<td>1,760,000</td>
<td>1,600,000</td>
<td>1,520,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># Genotype 2 monitoring tests</td>
<td>420,000</td>
<td>420,000</td>
<td>360,000</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gross monitoring tests</td>
<td>2,180,000</td>
<td>2,020,000</td>
<td>1,880,000</td>
<td>2,150,000</td>
<td>3,800,000</td>
<td>4,550,000</td>
<td>4,200,000</td>
<td>2,650,000</td>
</tr>
<tr>
<td>Tests lost to nonadherence</td>
<td>545,000</td>
<td>505,000</td>
<td>470,000</td>
<td>537,500</td>
<td>950,000</td>
<td>1,137,500</td>
<td>1,050,000</td>
<td>662,500</td>
</tr>
<tr>
<td>Net monitoring tests</td>
<td>1,635,000</td>
<td>1,515,000</td>
<td>1,410,000</td>
<td>1,612,500</td>
<td>2,850,000</td>
<td>3,412,500</td>
<td>3,150,000</td>
<td>1,987,500</td>
</tr>
<tr>
<td>Total HCV RNA tests (conf. + mon.)</td>
<td>2,395,000</td>
<td>2,275,000</td>
<td>2,170,000</td>
<td>2,372,500</td>
<td>3,610,000</td>
<td>4,172,500</td>
<td>3,910,000</td>
<td>2,747,500</td>
</tr>
<tr>
<td>Market share - SOC diagnostics</td>
<td>2,395,000</td>
<td>2,275,000</td>
<td>2,170,000</td>
<td>2,140,000</td>
<td>2,890,000</td>
<td>3,130,000</td>
<td>2,740,000</td>
<td>1,790,000</td>
</tr>
<tr>
<td>Market share - Daktari</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>80,000</td>
<td>240,000</td>
<td>350,000</td>
<td>390,000</td>
<td>320,000</td>
</tr>
<tr>
<td>Market share - POC Competitors</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>152,500</td>
<td>480,000</td>
<td>692,500</td>
<td>780,000</td>
<td>637,500</td>
</tr>
<tr>
<td>Daktari price/test</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
<td>$44</td>
</tr>
<tr>
<td>Daktari revenue</td>
<td>$3,520,000</td>
<td>$10,560,000</td>
<td>$15,400,000</td>
<td>$17,160,000</td>
<td>$14,080,000</td>
<td>$25,770,000</td>
<td>$25,770,000</td>
<td>$25,770,000</td>
</tr>
<tr>
<td>Daktari revenue NPV (30% discount)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In Table 6A, under the conservative, lower-bound assumption that new treatments will not come to market, the Daktari HCV system could generate nearly $11.5MM in its first five years on the market. In Table 6B, under the less conservative – but perhaps more realistic – assumption that new therapies will come to the market and will increase the proportion of patients who enter therapy, the Daktari HCV system could generate nearly $26MM in the same timeframe. Importantly, because the HCV-infected population is expected to remain stable (since incidence and mortality will be roughly equal), the number of untreated patients drops every year. If the current standard that patients who have already received treatment are ineligible for additional rounds of therapy persists, the size of the market will continue to decline. However, if this standard changes and these patients remain eligible for therapy, Daktari’s revenue could be significantly higher even under the remaining constraints of the model.\footnote{It is important to note that this model represents Daktari’s revenue potential in the United States, where approximately 5MM people are infected with HCV. Globally, nearly 200MM people are infected with HCV, representing a significant additional market opportunity for Daktari. However, an analysis of this market is outside the scope of this thesis.}

Of course, the upper-bound model is subject to several additional assumptions. In the next section, I conduct several sensitivity analyses to test their effect on Daktari’s revenue.

**Sensitivity Analyses**

In conducting sensitivity analyses on the model generated above, I use Table 6B (the upper bound model) as the baseline. I tested the impact of changing many of the baseline assumptions on the NPV of Daktari’s revenue. In all cases, I changed one variable at a time; the rest of the model remained consistent. Below I provide the rationale for conducting each sensitivity analysis and discuss the implications of the results.
Adherence: At baseline, the model assumes a 50% adherence rate, as found in population-based studies of HCV patients. However, these studies were conducted with current HCV treatment regimens, to which patients often are non-adherent due to the length of therapy and the frequency of significant side effects. Two scenarios are possible regarding future treatment regimens: either pipeline therapies will fail, in which case current treatments will remain standard of care and adherence rates will stay consistent, or pipeline therapies will succeed, in which case they will replace current treatments as the standard of care, and adherence rates will improve. I therefore conducted a sensitivity analysis using adherence rates of 60%, 70%, 80%, and 90%.

Not surprisingly, Daktari’s revenue increases as adherence increases, although the incremental revenue gain is relatively small. While these adherence rates represent a substantial increase over the current rates seen in HCV, they are realistic based on the precedent from HIV and HAART. Recent studies show that adherence to HAART may be as high as 91% if patients receive support from community organizations.64

Number of POC competitors: The baseline model assumes that Daktari will have at least two competitors in the POC space and that revenue will be divided equally among them. There is a chance that other POC competitors may fail, which would open up a greater percentage of the POC market for Daktari. Of course, there is also the chance that a larger number of competitors will enter the space, in which case Daktari’s revenue will be diluted. The sensitivity analysis below shows what would happen if Daktari had anywhere from zero to four competitors in the POC HCV diagnostic space.

<table>
<thead>
<tr>
<th>Adherence</th>
<th>Daktari NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>$25,770,000</td>
</tr>
<tr>
<td>60%</td>
<td>$26,970,000</td>
</tr>
<tr>
<td>70%</td>
<td>$28,660,000</td>
</tr>
<tr>
<td>80%</td>
<td>$29,860,000</td>
</tr>
<tr>
<td>90%</td>
<td>$30,750,000</td>
</tr>
</tbody>
</table>
While increased adherence resulted in only a small increase in Daktari’s revenue, the amount of competition in the POC landscape has a more dramatic effect. Daktari’s revenue increases by more than 50% if there is only one other POC competitor, and it more than doubles if there are no competitors. Of course, this analysis assumes that the market share of POC diagnostics remains the same. For Daktari to capture such a large portion of the market on its own, it likely would need to consider a strategic partnership with a company with an established presence in the US in either HCV or medical diagnostics. Without such a relationship, Daktari may struggle to secure the resources for marketing, sales, and distribution necessary to maintain such a significant market share.

**Discount rate:** A model’s discount rate is one of the variables that has the most significant impact on the final NPV. For an early-stage medical device company – one, like Daktari, that has secured funding but does not have any products yet on the market – 30% is a standard discount rate that accounts for risks inherent in R&D, regulatory affairs, and commercialization. However, Daktari has some advantages that, one could argue, justify a less conservative discount rate. First, the company expects to begin marketing its CD4 system in the developing world by the end of 2012. Second, it has already secured two rounds of funding. For these and other reasons, an analysis exploring the impact of an adjusted discount rate on the model is warranted.

<table>
<thead>
<tr>
<th># POC competitors</th>
<th>Daktari NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>$76,860,000</td>
</tr>
<tr>
<td>1</td>
<td>$38,630,000</td>
</tr>
<tr>
<td>2</td>
<td>$25,770,000</td>
</tr>
<tr>
<td>3</td>
<td>$19,240,000</td>
</tr>
<tr>
<td>4</td>
<td>$15,340,000</td>
</tr>
</tbody>
</table>
Similar to the effect seen in Table 7A, adjusting the discount rate has a relatively small effect on Daktari’s NPV. The fact that Daktari’s NPV is only marginally affected with an increased discount rate (i.e., from 30% to 40%) is encouraging; even if the risk to the success of the project increases, Daktari will still generate more than $20MM in revenue.

Table 7C: Sensitivity analysis - discount rate

<table>
<thead>
<tr>
<th>Discount rate</th>
<th>Daktari NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>$33,110,000</td>
</tr>
<tr>
<td>25%</td>
<td>$29,100,000</td>
</tr>
<tr>
<td>30%</td>
<td>$25,770,000</td>
</tr>
<tr>
<td>35%</td>
<td>$22,970,000</td>
</tr>
<tr>
<td>40%</td>
<td>$20,600,000</td>
</tr>
</tbody>
</table>
Chapter 5: Discussion

The hypothesis of this thesis was that Daktari could successfully generate revenue with its HCV diagnostic system in the United States, given likely market factors. As the results show, even with conservative assumptions around the market share of POC diagnostics, the percentage of patients who enter therapy, and the appropriate discount rate, Daktari will be able to generate substantial revenues. If some of these assumptions are relaxed – particularly the assumption on POC competition – Daktari could generate as much as $70MM in revenue over its first five years on the market.

Daktari largely has focused its commercialization efforts to date on bringing products to market in the developing world. The findings of this thesis suggest that Daktari’s products can also have a significant impact in the US market. As was seen in HIV in the 1990s, the intersection of improved treatments and simplified diagnostics can significantly expand the market potential within a given therapeutic area.

Limitations

There are several important limitations to this thesis. First and foremost, the uncertainty of future market dynamics limits the confidence of the current model. From a public health perspective, the CDC screening campaign could be cut short, leading fewer patients to be diagnosed and enter care. From a competitive perspective, another company could come out with a superior diagnostic solution, limiting Daktari’s market opportunity. From a treatment perspective, the new therapies currently in the pipeline for the treatment of HCV may not make it to market, which would remove a significant driver of the need for improved diagnostics. From a strategic perspective, Daktari could fail to secure a partnership with a major pharmaceutical or medical device company, limiting access to crucial distribution channel infrastructure. From a reimbursement perspective, future attempts to control healthcare costs could
lead to significant reduction in reimbursement for HCV diagnostics. Any one of these factors could negatively impact Daktari's market opportunity.

Second, the lack of firm epidemiologic data on HCV in the US may pose a challenge in reliably identifying the market size. As noted above, current estimates of the chronically infected HCV population in the US range from 3MM to more than 5MM. The diagnostic market opportunity could be substantially different depending on the true size of the infected population.

Finally, Daktari will not make the decision of whether or not to proceed with commercialization of a diagnostic solution in HCV based solely on the US market. Daktari's market orientation lies primarily in developing countries, where the lack of appropriate diagnostic solutions significantly limits patients' access to care. Thus, even if Daktari decides against commercializing its HCV diagnostic in the US, the company may pursue other markets where HCV is endemic, such as Egypt, China, or Brazil. An analysis of those markets was outside the scope of this thesis, but such research would be important in shaping Daktari's future strategy.

**Areas for future research**

This thesis could serve as the basis for additional research in a number of areas. As noted above, there may be a significant market opportunity for the Daktari system in several developing markets with a high prevalence of HCV infection; research into the dynamics of those markets is warranted.

Additionally, Daktari could expand its market opportunity in HCV by offering the option to run additional, concurrent diagnostic tests. The Daktari platform is designed in such a way that multiple diagnostic tests could be run on the same cartridge, using the same fluid sample. One possibility would
be to offer a co-diagnostic for HCV and HIV. The two infections commonly are comorbid; in fact, as many as 50-90% of HIV-positive patients with a history of IDU also are infected with HCV. Thus, a companion diagnostic for these two infections might be of interest. One option would be to pair HIV and HCV diagnostics. Alternatively, HIV patients need their CD4 levels monitored at regular intervals, similar to the monitoring that HCV patients must receive while on treatment; a diagnostic that could run both of these tests quickly and accurately from a single sample could be an interesting opportunity.
Chapter 6: Conclusion

The HCV landscape is poised to undergo a significant shift in the next several years. Although HCV incidence is declining, an increasing number of patients – driven by the high prevalence of infection among baby boomers – will present with advanced liver disease; thus, the economic burden of the disease is actually growing. Indeed, total medical costs for patients with HCV infection are expected to more than double, from $30 billion to more than $85 billion, over the next 20 years.²

New treatments are a necessary and important part of the solution to this growing public health burden. However, until the patients in need of those treatments can be identified quickly, accurately, and inexpensively across settings, the burden of HCV cannot effectively be addressed. This thesis establishes that the Daktari HCV platform is a promising solution to the challenge of HCV diagnosis. Furthermore, this thesis validates Daktari’s market opportunity in this space. Daktari’s diagnostic system could bring fast, reliable diagnosis of HCV to the patients who need it most, and could positively impact treatment outcomes by allowing for fast, accurate monitoring of treatment response.
References


7. Epidemiology: Hepatitis C; Hepatitis C virus will remain a prevalent bloodborne disease in the seven major markets, primarily transmitted through Injection Drug Use: Datamonitor; 2011.


44. iQuum. (Accessed April 6, 2012, at www.iquum.com.)

45. TwistDx. (Accessed April 6, 2012, at www.twistdx.co.uk.)


64