Hepatitis C Care Cascade Incarcerated or Detained Persons and General Population in California, 2011-2021

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Abstract

Objective: To evaluate the Centers for Disease Control and Prevention hepatitis C care cascade, that assesses hepatitis C follow-up testing and laboratory evidence of likely clearance/cure and recurrent viremia, among Californian incarcerated or detained persons (IDP) and general populations.

Methodology: Laboratory test results were analyzed for hepatitis C virus (HCV) antibody, RNA, and genotyping from Quest Diagnostics among IDP and general populations in California, 2011-2021.

Results: Overall, 27.4% (115,353/421,459) of the California IDP population who had HCV testing were initially HCV test positive. Of those with follow-up HCV RNA testing, 59.4% (24,694/41,539) had evidence of clearance/cure and of these 19.4% (4,793/24,694) had subsequent evidence of recurrent viremia or reinfection. For the general population 6.2% (246,620/3,961,225) with HCV testing were initially positive. Of those with follow-up HCV RNA testing, 63.7% (45,819/71,965) had evidence of clearance/cure and 6.7% (3,068/45,819) had subsequent evidence of recurrent viremia or reinfection.

Conclusions: Californian IDP population had a higher HCV positivity rate than the general population and evidence of subsequent recurrent viremia or reinfection. More resources and aggressive approaches are needed to successfully confront HCV in correctional facilities and after IDP community return.

Introduction

Hepatitis C virus (HCV) is a blood-borne virus, commonly transmitted through shared injecting equipment. Due largely to the criminalization of injection drug use, the hepatitis C epidemic has disproportionately affected the incarcerated and detained person (IDP) (“correctional”) population where many individuals originate from high-risk environments and engage in high-risk behaviors in their communities. Earlier estimates, from studies covering from 1994 to 2006, were 30% to 40% of the United States (U.S.) IDP population were infected with the HCV at some point in their lives, the majority of whom were infected before incarceration [1-5]. Recent estimates from the California Department of Correctional Health Care Services (CCHCS), based on testing from July 2018 through June 2019, found at entry, 18% of California-state IDP were HCV antibody

positive confirmed by HCV RNA presence of whom 72% had evidence of chronic hepatitis C [6]. This rate is similar to a 2015 U.S. study of HCV infection among IDP [7]. The HCV care cascade provides uniformity to track frequency of presumed clearance/cure in the populations, including lack of follow-up, and recurrent viremia-based solely on clinical laboratory test results. This care cascade provides a valuable public health perspective on the hepatitis C epidemic and may be applied to benchmark performance compared to World Health Organization elimination goals [8].

Although access to appropriate healthcare services is a right for U.S. IDP, HCV infection identification and treatment are challenging due to IDP turnover rates and inadequate follow-up care after return to the community. Many IDP are hepatitis C infected prior to becoming incarcerated or detained and some IDP may not be diagnosed with hepatitis C until after release or while on parole. Such individuals with undiagnosed and untreated hepatitis C may perpetuate community spread. Another challenge for correctional facilities to implement robust HCV treatment is the cost of these highly effective medications.

Given the prevalence of hepatitis C among IDP, and the advent of highly effective antiviral treatments, addressing hepatitis C clearance among IDP prior to and after release is critical if the U.S. is to achieve HCV elimination goals. Efforts must focus on establishing an accurate knowledge of who is infected and implementing education, policies, and procedures for the prevention and treatment of hepatitis C among IDP during their confinement and following their return to the community [9]. The CCHCS became a national model by expanding HCV testing statewide in 2016 and expanding treatment access to the general IDP population in 2018-2019.6 In 2022, the CCHCS developed detailed plans for addressing the burden of hepatitis C including expanding eligibility for treatment [10]. Based on analysis of Quest Diagnostics clinical laboratory test results, this study aims to determine prevalence of hepatitis C and presumed clearance/cure rates among IDP, inclusive of state and other correctional facilities based in California, and for comparison, among the general population in that state.

**Methods**

Results of HCV-related laboratory testing performed by Quest Diagnostics were analyzed from client accounts identified as being from all jurisdictions within Californian jail, prison, and correctional (collectively referred to as “correctional”) facilities from 2011 through 2021. For comparison, specimens from individuals tested by Quest Diagnostics in California who were not tested, the mean age was 44.7 years (standard deviation 16.7) and 93.9% were male, 6.0% were female, and 0.17% were sex undeclared.

The hepatitis C care cascade was applied to assign individuals into the defined categories [11]. For clarity, categories with no testing are listed and displayed first. Category 1 is defined as ever HCV infected, category 2 is based on HCV RNA testing (2a with no subsequent HCV RNA test and 2b as with subsequent HCV RNA testing), category 3 is based on the HCV RNA test result (3a with negative result and 3b as positive result), category 4 defines cured or cleared (4a1 no record of subsequent HCV RNA test, 4a2 subsequent HCV RNA test result remain positive, and 4b any subsequent HCV RNA negative test result after initial HCV RNA positive result), and category 5 includes people who had HCV RNA positive test result followed by negative and then subsequently a positive HCV RNA test result. In addition, because Quest Diagnostics also records HCV negative test results and the absence of subsequent testing performed within this laboratory network, absolute rates for testing and positivity were calculated. An individual with any initial HCV testing (antibody, RNA, and genotyping) results were accepted for study inclusion. A presumed HCV clearance/cure event was someone defined as having an HCV RNA negative result subsequent to an initial HCV RNA positive result, who was followed over a minimum of one year (category 4b). A presumed rebound infection or reinfection were those individuals having a subsequent HCV RNA positive result after HCV clearance/cure, who was followed over a minimum of one year (category 5).

Qualitative immunoglobulin G HCV antibody testing was performed using the U.S. Food and Drug Administration (FDA)-cleared automated VITROS Eci Immunodiagnostic System (Ortho Clinical Diagnostics). HCV RNA test methods included the quantitative COBAS AmpliPrep/COBAS TaqMan HCV v2.0 method and quantitative COBAS HCV nucleic acid test on the COBAS 6800/6880 systems (both from Roche Diagnostics). HCV genotyping was based on real-time reverse transcription and amplification of the 5′untranslated region and core region of the viral genome (Quest Diagnostics laboratory developed test and Siemens Healthcare Diagnostics). WCG Institutional Review Board deemed this Quest Diagnostics Health Trends® study as exempt.

**Results**

For the initial HCV testing for the IDP population at Quest Diagnostics, the individual’s mean age was 36.2 years (standard deviation 11.9) and 93.9% were male, 6.0% were female, and 0.06% were sex unspecified. For the general population tested, the mean age was 44.7 years (standard deviation 16.7) and 43.3% were male, 56.1% were female, and 0.17% were sex unspecified. For the IDP population, 27.4% (115,353/421,459) of those with any HCV test (i.e., antibody, RNA or genotyping) were initially positive (Table 1, 2011-2015 and 2016-2020 displayed separately, Figure 1 (IDP) and Figure 2 (general population)). Of these individuals, 86.1% (99,351) had any subsequent HCV RNA testing (category 2b); 13.9% (16,002/115,353) had no evidence of subsequent testing performed (category 2a). The rate of HCV RNA testing of specimens from antibody positive individuals increased from 54.4% (21,777/39,973) in 2011-2015 to 98.3% (58,387/59,378) in 2016-2020 after implementation of a single HCV antibody testing algorithm wherein all antibody positive results were automatically reflexed to HCV RNA testing in November 2015. Of those HCV RNA positive individuals with subsequent HCV RNA testing, 19.3% (19,197/99,351) had only negative HCV RNA test result(s) during the follow-up period (presumed self-limiting infection or an unconfirmed initial HCV antibody test result) (category 3a) whereas 80.7% (80,164/99,351) had positive HCV RNA test results (category 3b). No documented follow-up HCV RNA testing (category
4a1) was found in 69.6% (38,625/55,470) individual and 30.4% (16,856/55,470) had only positive HCV RNA results (presumed non-viral clearance/cured, category 4a2). Of those who had HCV RNA testing, 59.4% (24,694/41,539) with an initial positive HCV RNA test result had one or more subsequent negative HCV RNA test results (presumed viral clearance/cured) (category 4b): 44.8% (6,225/13,989) in 2011-2015 and 66.9% (18,429/27,550) in 2016-2020. Of the 24,694 individuals with presumed viral clearance/cured, 66.6% (4,793/7,206) of HCV tests performed were positive for an initial HCV antibody test result (presumed self-limiting infection or an unconfirmed initial HCV antibody test result) (category 3a), whereas 66.8% (130,872/192,064) had a subsequent positive HCV RNA test result (category 3b).

No documented follow-up HCV RNA testing (category 4a1) was found in 69.6% (38,625/55,470) of individuals and 30.4% (16,856/55,470) of individuals had only positive HCV RNA results (presumed non-viral clearance/cured, category 4a2). Of those who had HCV RNA testing, 59.4% (24,694/41,539) with an initial positive HCV RNA test result had one or more subsequent negative HCV RNA test results (presumed viral clearance/cured) (category 4b): 44.8% (6,225/13,989) in 2011-2015 and 66.9% (18,429/27,550) in 2016-2020.

No documented follow-up HCV RNA testing (category 4a1) was found in 69.3% (58,907/85,053) of individuals and 30.7% (26,146/85,053) of individuals had only positive HCV RNA results (presumed non-viral clearance/cured, category 4a2). Of those tested, 63.7% (45,819/71,965) with an initial positive HCV RNA test result had one or more subsequent negative HCV RNA test results (presumed viral clearance/cured) (category 4b): 62.7% (25,143/40,095) in 2011-2015 and 64.9% (20,676/31,870) in 2016-2020. Of the 45,819 individuals with presumed viral clearance/cured, 6.7% (3,068) had a subsequent positive HCV RNA result (category 3b).

In contrast, for the general population 6.2% (246,620/3,961,225) of HCV tests performed were positive for an initial HCV analyte (either antibody screen, RNA, or genotype) between 2011-2020. The rate of reflex HCV RNA testing of specimens from antibody positive individuals increased from 66.6% (92,858/139,400) in 2011-2015 to 96.3% (103,206/107,220) in 2016-2020 after implementation of a single HCV antibody testing algorithm option wherein all antibody positive results were automatically reflexed to HCV RNA testing in November 2015 (category 2b).

Table 1: Hepatitis C Care Cascade Definitions, Californian incarcerated and detained persons and general populations, 2011-2021.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Incarcerated or Detained Persons</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Ever tested</td>
<td>421,458</td>
<td>3,961,225</td>
</tr>
<tr>
<td>1</td>
<td>Ever HCV infected</td>
<td>55,975</td>
<td>59,378</td>
</tr>
<tr>
<td>2</td>
<td>HCV RNA testing</td>
<td>15,011</td>
<td>26.82 (2a/1)</td>
</tr>
<tr>
<td>3</td>
<td>Initial infection</td>
<td>6,388</td>
<td>15.59 (3a/2b)</td>
</tr>
<tr>
<td>3a</td>
<td>Initial reported HCV RNA negative during follow-up period</td>
<td>34,576</td>
<td>84.41 (3b/2b)</td>
</tr>
<tr>
<td>4</td>
<td>Cured or cleared</td>
<td>28,311</td>
<td>81.88 (4a/3b)</td>
</tr>
<tr>
<td>4a1 (subset of 4a)</td>
<td>Never tested after first HCV RNA positive</td>
<td>20,587</td>
<td>72.72 (4a1/4a)</td>
</tr>
<tr>
<td>4a2 (subset of 4a)</td>
<td>Tested after initial HCV RNA positive but remained viral positive</td>
<td>7,724</td>
<td>27.28 (4a2/4a)</td>
</tr>
<tr>
<td>4b</td>
<td>Any reported HCV RNA negative after initial testing positive during follow-up period</td>
<td>6,265</td>
<td>44.79 (4b/4a2+4b)</td>
</tr>
<tr>
<td>5</td>
<td>Persistent Infection or re-infection</td>
<td>1,280</td>
<td>20.43 (5/4b)</td>
</tr>
</tbody>
</table>
sequent HCV RNA positivity, thereby consistent with recurrent infection and clearance of infection, and of these 19.4% had sub-
sequent HCV RNA positivity, thereby consistent with recurrent or persistent infection was much higher than the observed 6.7% observed for the general population.

A 1994 hepatitis C prevalence study of entrants to the California correctional system (n = ~5,000) found 41.8% of IDP HCV positive (males, 39.4%; females, 54.5%) [14]. A 20-year study of Los Angeles County IDP found 34.6% (27,881/80,681) had positive HCV antibody test results [15]. A 2015 estimate of sero-prevalence of HCV for U.S. IDP averaged 18% [7]. A recent study, including testing from July 2018 through June 2019, across California prisons, likewise found IDP at entry had approximately 18% HCV antibody positivity with opt-out screening [6].

In the current real world evidence-based study, 59.4% (24,694/41,539) of the IDP population and 63.7% (45,819/71,965) of general population participants were cleared/cured of their HCV infection based on a negative HCV RNA test result following an initial HCV RNA positive test result -ignoring the sizable 48.2% (38,625/80,164) of the IDP population and 45.0% (58,907/130,872) of the general population who were not subsequently HCV RNA tested after their initial HCV RNA positive result. In contrast, another real-world evidence study in the general population demonstrated achieving 97% sustained virologic response at 12 weeks post-treatment [16]. In the current study, 19.4% (4793/24,694) of initially HCV RNA positive IDP participants initially positive had evidence of HCV viremia after a negative HCV RNA test result. This compares to the recent CCHCS report: 51.1% (1,909/3,376) of those with sustained viral response had subsequent HCV RNA testing and of these 19.8% (378/1,909) had a return to a viremic status during follow up while incarcerated in a California State prison [6].

Although the time periods evaluated differ between the two investigations and there may be substantial overlap in the populations studied, the relative similarity between the two datasets suggest that both approaches may be employed to describe the HCV care cascade for the IDP population.

One analysis estimated risk-based and opt-out screening could diagnose one-third of new hepatitis C infections, compared to no screening practices, and therefore would reduce many more liver-related deaths [17]. Risk-based screening of new IDP could be effective in identifying who is HCV infected and likely eligible for curative treatment [18]. Nevertheless, universal screening of all new and released IDP may be justified based on the high prevalence of HCV infection in that population and to reduce community spread of HCV [19]. Further, in a study of Massachusetts hospitalized IDP, 15% individuals with HCV died within 2 years after hospitalization [20]. Hepatitis C infection was associated with a 61% increased risk of 2-year mortality even after controlling for severity of disease [20]. Given the U.S. targets to reduce and eradicate hepatitis C infections and deaths [21], and that most infections among IDP likely occur outside of correctional facilities, either prior to or after incarceration, routine HCV testing and treatment while incarcerated or detained and those on parole may play an important role in achieving said goals [23]. In reality, for some correctional facilities there is a fluid migration of IDP in and out of jails and prisons with approximately one third annual turnover and median time incarcerated being less than three years.
and re-incarceration more common among some communities [24,25]. Further, nearly half of all patients with HCV infection are unaware of their infection (and can pass infection onto others) according to National Health and Nutrition Examination Surveys [26]. Thus, screening and treatment of IDP should have broad community benefits in achieving HCV elimination goals [8].

HCV opt-in testing in Massachusetts led to only 22% of IDP/detainees being tested [27]. Opt-out testing tends to be more effective [28,29]. In a modeling study, risk-based and universal opt-out hepatitis C screening in prisons, followed by treatment of those infected can avert many cases of hepatitis including avoiding 90% of infections would have occurred outside of prisons [30]. In another modeling study, a model based upon test all, treat all, and linkage to care at inmate release led to increased lifetime sustained hepatitis C virologic response, decreased cirrhosis, and an additional cost of $1,440 per inmate entrant and deemed cost-effective [31]. Further, co-infection of IDP with hepatitis B, hepatitis C, and/or human immunodeficiency virus is relative common and all three infections may warrant routine testing [32]. Likewise, tuberculosis is more common among IDP than the corresponding general population and such testing should also be considered [33,34]. Novel approaches may include, as suggested by the World Health Organization in 2007, prison needle and syringe programs if there is evidence that injecting drug use is taking place in prisons [35]. Such programs are rare due to many obstacles though considered effective [36,37].

The rate of persistent or recurrent infection was similar in both time periods for the correctional population (20.4% in 2011-2015 and 19.1% in 2016-2020). In contrast, it fell from 9.3% in 2011-2015 to 3.6%, a 61% relative decrease, in the general population during the period of 2016-2020. This may reflect improved therapeutics available in the later time period. However, the minimal change and relatively higher rate of persistent or recurrent infection among the correctional population is of concern particularly since effective antiviral therapeutics were available in that latter period.

As we still grapple with the coronavirus disease-2019 (COVID-19) pandemic, we are reminded that IDP recently released back into their communities may be especially vulnerable to social and structural barriers that increase risk to COVID-19 and other infections [38]. In addition, released IDP have higher rates of several chronic medical conditions than does the general population which adds stress to those affected and our entire healthcare systems [39].

There are several limitations of this study. The evaluated HCV-related testing was limited to that performed at Quest Diagnostics and there are other clinical laboratory test providers in California. Secondly, California IDP and correctional facilities practices may not be representative of testing and treatment in place at such facilities in other states. Additionally, there may be differences among the various correctional facilities within California. The IDP population members may alternatively receive care prior to and after release from incarceration and such HCV test results would be unavailable for this study. Most significantly, some IDP may spend a limited time within the correctional facility system and therefore not been available for follow-up testing. Additionally, this study was unable to identify where or when HCV infection and rebounds or reinfec tions occurred. Any HCV treatment prescription data were unavailable to these authors so laboratory test results were relied upon to determine persistence of initial infection, cure, and potential re-infection or viral rebound after an initial infection. Differences in HCV infection detection and treatment practices likely exist during the interval before and after the introduction of highly-effective direct-acting antiviral therapies that were first approved by the U.S. Food and Drug Administration in 2013. Guidelines from American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) in 2018 introduced major changes in treatment eligibility [40]. Although the California Department of Corrections and Rehabilitation serves as a model for advancing IDP screening and treatment of hepatitis C, a direct comparison between the IDP and general populations in this study is burdened with different criteria for HCV testing and different shares of testing of each group.

In summary, this study findings demonstrated that HCV infection was more common among Quest Diagnostics-tested Californian IDP population than in the general California population and provide evidence that HCV clearance was lower than generally recognized for available treatments [16]. Lastly evidence of recurring viremia (HCV RNA positive results with intervening negative HCV RNA test results) was higher than for the general population. Due to availability of effective treatments and expanding testing and treatment services, current results should be more promising, although always challenging, due to the continual flux of the IDP population in and out of these facilities. This study found HCV treatment response rates and recurrent viremia rates similar to that reported by the CCHCS in 2020 [6]. Maximizing the effectiveness of community-wide HIV viral suppression programs requires correctional/community coordination. Likewise, reduction and elimination of hepatitis C will depend on a thoughtful, well-funded effort to manage this disease for IDP populations involving coordination among the criminal justice system, community health systems, and others [41].

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Summary box

What is the current understanding of this subject?

Hepatitis C virus (HCV) infection and treatment as evaluated by clinical laboratory data differ for the correctional and general populations.

What does this report add to the literature?

Unique comparison of the HCV care cascade of the Californian correctional and general populations, 2011-2021.

What are the implications for public health practice?

HCV eradication goals can only be achieved by addressing HCV diagnosis and treatments among incarcerated and detained persons and after their reentry into the general population.
References


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