

Risk Factors for HCV Infection Among Young Adults in Rural New York Who Inject Prescription Opioid Analgesics

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Hepatitis C virus is the most common blood-borne infection in the United States, with an estimated 4.1 million people HCV antibody (anti-HCV) positive and 3.2 million living with chronic infection.¹ Infection with hepatitis C is the leading cause of chronic liver disease, and mortality rates associated with HCV infection now surpass those associated with HIV disease.² HCV infection prevalence has reached epidemic proportions and is endemic among people who inject drugs (PWID).³ HCV is transmitted primarily by percutaneous exposure to contaminated blood, with injection drug use being the most common risk factor and the leading cause of incidence in the United States.⁴ Estimated seroprevalence among PWID ranges from 30% to 70%, depending on frequency and duration of use,^{3,5} and HCV incidence among PWID is high (≤ 40 per 100 person-years), especially among younger PWID (aged 18–29 years).⁶

Anti-HCV prevalence among the population of young PWID has historically been lower than among older PWID, between 10% and 36%.^{7,8} Over the past decade, however, state-level and national reporting staff have identified the largest increase in newly reported HCV cases to be among adolescents and young adults (aged 15–29 years).⁹ This increase is occurring predominantly in rural and suburban regions of the country, with clusters reported in Massachusetts,¹⁰ Pennsylvania,¹⁰ Wisconsin,¹¹ Washington,¹² and Upstate New York,¹³ and similar findings have recently been reported in the Appalachia region.^{14,15} Taken together, these reports suggest a significant change in the demographics of newly infected PWID.

In contrast to the late 1990s, when national surveys identified anti-HCV cases among PWID as highest among men, African Americans, urban residents, and people aged 40 to 49 years,¹ the more recent, cluster-associated cases are more likely to be young adults (aged 20–29 years), most of whom are White and

Objectives. We investigated a cluster of new hepatitis C cases in rural New York among a cohort of young people who inject drugs (PWID) and misuse prescription opioid analgesics (POA).

Methods. We recruited a purposive sample of PWID from Cortland County for an in-person survey and HCV rapid antibody test (March–July 2012). We examined sociodemographics, drugs currently injected, and lifetime and recent injection behaviors to ascertain associations with HCV antibody (anti-HCV) positivity.

Results. Of 123 PWID, 76 (61.8%) were younger than 30 years, and 100 (81.3%) received HCV rapid testing. Of those tested, 34 (34.0%) were positive. Participants who reported injecting POA in the past 12 months were 5 times more likely to be anti-HCV positive than those who injected drugs other than POA, and participants who reported sharing injection equipment in the past 12 months were roughly 4 times more likely to be anti-HCV positive than those who did not.

Conclusions. Our analysis suggests people injecting POA may be at higher risk for HCV infection than people who inject heroin or other drugs but not POA. (*Am J Public Health.* 2014;104:2226–2232. doi:10.2105/AJPH.2014.302142)

reside in rural and suburban areas. In addition to the change in both age distribution and geographic location, another distinguishing feature of these newly reported cases is the relatively high proportion of adolescents and young adults who report the nonmedical use of prescription opioid analgesics (POA) before initiating injecting.^{16,17}

Correspondingly, an increase in the number of young adults from rural areas who are injecting POA has also been reported. In a study of PWID from rural Appalachia, for example, two thirds of young PWID report injecting POA,¹⁸ and these people are young, White, and aged 18 to 29 years and report injecting drugs that differ significantly from those injected by their urban counterparts, most of whom inject heroin and cocaine or crack.¹⁹ Similar reports of POA injection among this age cohort have been reported in Massachusetts, Wisconsin, and Tennessee.^{10,20,21} In all, these recent reports and data portend a nascent intersection between the United States' prescription drug epidemic²² and what has been described as an emerging HCV epidemic.²³

Consistent with this developing trend was a recent cluster of newly reported HCV cases among a cohort of young PWID in Cortland County, New York (Cortland County Health Department, oral communication, 2011). Cortland is a rural county in central New York just south of Syracuse, with an estimated population of 49 000. In 2011, the Cortland County Health Department reported 18 new HCV cases among people aged younger than 35 years (New York State Department of Health, Bureau of Communicable Disease Control, unpublished statistics, 2012), whereas only 1 case was reported in this age group in 2010 (New York State Department of Health, Bureau of Communicable Disease Control, unpublished statistics, 2012). In response, the New York State Regional Health Department, in conjunction with the Cortland County Health Department, launched an investigation into the 18 new cases and discovered, through targeted interviews, a correlation among age, injection drug use, POA misuse, and anti-HCV positivity. The pressing need to further comprehend the behavioral risk factors associated with this increase—beyond the original 18

cases—was the motivation for conducting this follow-up survey investigation.

METHODS

We administered anonymous surveys and HCV rapid antibody tests to identify risk factors associated with anti-HCV positivity. Eligibility criteria included being aged 18 years or older, having injected drugs within the previous 12 months, and residing in Cortland County. The Southern Tier AIDS Program, a community-based AIDS organization that provides health services to PWID, administered the study in Cortland from March through July 2012. Given that PWID are a hard-to-reach population and could be difficult to recruit for research, especially in rural settings, we used a modified snowball sampling methodology to maximize enrollment.²⁴

Initial recruitment involved posting flyers describing the project in the Cortland County Health Department and throughout the city of Cortland. Individuals were offered incentives for completing the survey (\$10) and being screened for HCV antibodies (\$10), and they could receive an additional \$30 by recruiting as many as 3 eligible participants via referrals; each participant could receive a total of \$50 for participation and referrals (tracked via coupons). Participants were screened for antibodies to HCV using the OraQuick HCV rapid antibody test, which provides point-of-care results within 20 minutes. Participants were assigned unique identification numbers to ensure anonymity. Identification numbers appeared on referral coupons to facilitate linkage of referrals to the referring participant. People who self-referred (or were not referred with a coupon) were considered “seeds”; that is, study participants who were not referred themselves but who might recruit from their peer groups.

Trained personnel administered the survey in private or semiprivate settings; the survey took between 20 and 40 minutes to complete. All participants receiving an anti-HCV rapid test were provided an explanation of their results along with other appropriate counseling messages. For people found to be anti-HCV positive, a follow-up appointment was made with a health care provider for HCV diagnostic testing (HCV RNA by polymerase chain

reaction). The study protocol was granted exemption from New York State Department of Health’s institutional review board because of the use of anonymous data.²⁵ Given the anonymous nature of the survey, a waiver of informed consent was requested; an informational sheet providing all necessary elements of an informed consent was reviewed with each participant and offered to them for their records.

Measures

The survey, designed by us for study purposes, collected sociodemographic data (age, gender, race/ethnicity, education, housing status, HIV status) and lifetime and recent (within the past 12 months) behavioral data. HIV status was determined on the basis of self-report. Lifetime behavioral factors included age at first injection, front or back loading (when sharing drugs, the process of transferring a drug solution from one syringe to another), injecting with others, and fishing for a vein (probing with one’s needle to find a vein). Recent behavioral factors included needle sharing, preparation equipment sharing (cookers, cotton, and water), and visiting a syringe exchange program. In addition, we collected information on type of drugs injected within the past 12 months and defined it as “drugs currently injected.”

We collected data for frequency of sharing needles, cookers, filters, and water within the past year and collapsed them into dichotomous categories because of small cell sizes; we dichotomized the variables on the basis of ever versus never having shared needles, cookers, filters, or water. To enable a more robust multivariable analysis, we collapsed variables measuring preparation equipment sharing by combining reports of sharing filters, cookers, and water into a single variable of sharing preparation equipment. In the analysis, we considered sharing of needles separately from sharing preparation equipment. Although it is possible that these behaviors may be correlated, they can also be mutually exclusive, thus warranting the separation.²⁶ See Table 1 for categories of independent variables.

Statistical Analysis

We conducted univariate analyses on lifetime and recent behavioral factors and drugs

currently injected. Associations with HCV rapid test positivity were assessed using the χ^2 test or the Fisher exact test, where appropriate. We conducted multivariable predictive modeling using variables associated with anti-HCV rapid test positivity ($P < .2$) in the bivariate analysis and those chosen on the basis of a priori criteria (age and gender). We chose age and gender on the basis of evidence that both are associated with anti-HCV positivity.^{6,27} Effect modification was evaluated using interaction terms in the model, and variables were assessed as effect modifiers on the basis of subject matter knowledge.

We used a backward selection process to determine the best fit of the model.²⁸ This was accomplished by first removing interaction terms that were not significant ($P \geq .05$); then, in a stepwise fashion, beginning with the least significant variable, we removed independent variables from the model if insignificant. We performed this process until all variables retained in the model were significantly associated with HCV rapid test positivity. Multicollinearity was assessed by calculating Pearson partial correlation coefficients; we determined multicollinearity to not be problematic given that none of the correlation coefficients were larger than 0.65.²⁹ Model fit was assessed using Hosmer–Lemeshow’s goodness-of-fit test. We performed all analyses using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

A total of 123 individuals completed the survey, of whom 36 were seeds. Respondents were mostly male (68.3%), aged younger than 30 years (61.8%), and non-Hispanic White (88.6%; Table 1). Lifetime and recent behavioral factors for all participants are presented in Table 1. More than half of the respondents (59.3%) reported that they knew their HIV status, of whom none reported being HIV positive. Most participants initiated injection drug use before age 30 (83.7%); 44.4% reported most often injecting with 2 or more people. More participants reported sharing preparation equipment than sharing needles in the past year (68.3% compared with 44.4%, $P < .001$). The most commonly reported equipment shared was the cooker (63.3% compared

TABLE 1—Demographics and Injection Behaviors of Survey Respondents Overall and by Hepatitis C Antibody Rapid Test Results: Cortland County, NY, March–July 2012

Variable	Overall (n = 123), No. (%)	Reactive (n = 34), No. (%)	Nonreactive (n = 66), No. (%)	P
Age, y				
< 30	76 (61.8)	25 (73.5)	34 (51.5)	.03
≥ 30	47 (38.2)	9 (26.5)	32 (48.5)	
Gender				
Female	39 (31.7)	8 (23.5)	23 (34.8)	.25
Male	84 (68.3)	26 (76.5)	43 (65.2)	
Race/ethnicity				
Non-Hispanic White	109 (88.6)	30 (88.2)	57 (86.4)	.4
Non-Hispanic African American	3 (2.4)	1 (2.9)	2 (3.0)	
Hispanic	1 (0.8)	1 (2.9)	0 (0.0)	
Other	10 (8.2)	2 (5.9)	7 (10.6)	
Housing status				
Rent or own a home or apartment	91 (74.0)	25 (73.5)	48 (62.7)	.1
Living in a residential program	9 (7.3)	0 (0.00)	7 (10.6)	
Homeless or living with friends	23 (18.7)	9 (26.5)	11 (16.7)	
HIV status ^a (n = 113)				
Knows status	67 (59.3)	16 (50.0)	40 (63.5)	.21
Does not know status	46 (40.7)	16 (50.0)	23 (36.5)	
Age at first injection, y (n = 110)				
< 18	19 (17.3)	2 (6.1)	11 (20.0)	.02
18–20	27 (24.6)	7 (21.2)	12 (21.8)	
21–29	46 (41.8)	22 (66.7)	19 (34.5)	
30–39	14 (12.7)	2 (6.1)	9 (16.4)	
40–49	4 (3.6)	0 (0.0)	4 (7.3)	
Frontload or backload (n = 116)				
Yes	74 (63.8)	17 (53.1)	40 (65.6)	.24
No	42 (36.2)	15 (46.9)	21 (34.4)	
Inject with others (n = 115)				
Mostly inject alone or with 1 other person	64 (55.7)	14 (46.7)	38 (59.4)	.25
Mostly inject with ≥ 2 people	51 (44.4)	16 (53.3)	26 (40.6)	
Fish for a vein (n = 121)				
Never	81 (66.9)	18 (52.9)	49 (76.6)	<.01
Sometimes or always	40 (33.1)	16 (47.1)	15 (23.4)	
Use syringe exchange program to obtain syringes in past 12 mo				
Yes	23 (18.7)	11 (32.4)	5 (7.6)	.02
No	100 (81.3)	23 (67.6)	61 (92.4)	
Share any equipment in past 12 mo (n = 120) ^b				
Yes	82 (68.3)	27 (79.4)	37 (58.7)	.04
No	38 (31.7)	7 (20.6)	26 (41.3)	
Share needles while injecting in past 12 mo (n = 115)				
Yes	51 (44.4)	18 (54.5)	26 (42.6)	.27
No	64 (55.7)	15 (45.5)	35 (57.4)	

Continued

with 52.5% and 40.8% who shared water and filters, respectively). The 2 most commonly reported drugs injected by participants were

POA (58.0%)—which included Opana (oxycodone), Oxycontin (oxycodone), Dilaudid (hydromorphone), Roxycontin (oxycodone),

morphine (morphine sulfate), Vicodin (hydrocodone and acetaminophen), and Percocet (oxycodone and acetaminophen)—and heroin

TABLE 1—Continued

Drugs currently injected ^c				
Prescription opiates ^d	71 (57.7)	26 (76.5)	27 (40.9)	< .001
Heroin	41 (33.3)	9 (26.5)	24 (36.4)	.32
Cocaine	22 (17.9)	9 (26.5)	11 (16.7)	.25
Bath salts	13 (10.6)	7 (20.6)	3 (4.6)	.01
Crack	6 (4.9)	2 (5.9)	2 (3.0)	.49
Methamphetamine	3 (2.4)	2 (5.9)	1 (1.5)	.23
Other	7 (6.3)	0 (0.0)	6 (10.7)	.08

Note. Not all variables have information for all respondents; percentages are out of the total number of respondents with complete information.

^aBy self-report; no individuals reported being HIV-positive.

^bRefers to injection equipment except needles.

^cNot mutually exclusive.

^dReported prescription opioids injected include Opana (n = 58), Oxycotin (n = 21), Dilaudid (n = 7), Roxycontin (n = 3), morphine (n = 4); Vicodin (n = 1), and Percocet (n = 1). Categories were not mutually exclusive.

(33.3%; Table 1). HCV rapid testing was administered to 100 participants. Of these, 34 were anti-HCV reactive (34.0%; 95% confidence interval [CI] = 24.8%, 44.2%; Table 1). Qualitative feedback from study participants indicated that the most common reason for refusing the test was believing they already knew their status.

Bivariate analysis results are presented in Tables 1 and 2. The following were significantly associated with HCV rapid test positivity at a *p* value of less than .05: younger age, currently injecting POA, currently injecting bath salts, initiating injecting before age 30, visiting a syringe exchange program in the past 12 months, fishing for a vein, and sharing equipment in the past 12 months. Although we did not consider housing status significant in the bivariate analysis at that level, it met the criteria for inclusion in the initial multivariate model. After the backward stepwise selection process, not all variables remained in the multivariable model; age, age at first injection, using a syringe exchange program, fishing for a vein, and housing status were no longer significantly associated with anti-HCV rapid test reactivity. Adjusting for gender and the other variables in the model, we found the following to be significantly associated with anti-HCV positivity: (1) injecting POA (adjusted odds ratio [AOR] = 5.53; 95% CI = 1.92, 15.91; Table 2) and (2) sharing preparing equipment in the past 12 months (AOR = 3.79; 95% CI = 1.20, 12.00). Overall, the model had adequate fit on the basis of

Hosmer–Lemeshow’s goodness-of-fit test ($P > .05$).

DISCUSSION

In this investigative study, we examined behavioral risk factors associated with injection drug use in Cortland County, New York, to assess why PWID, and young adults in particular, are increasingly being infected with hepatitis C. Overall, our analysis identified several risk factors associated with anti-HCV positivity, and young PWID made up almost three quarters of the people in our sample population testing positive for anti-HCV (none of the respondents reported being HIV positive). With similar clusters occurring in numerous other states, this study sheds additional light on what appears to be, in certain regions of the country,^{9–14} an emerging trend of increased HCV infections among young adults who report injecting drugs and misusing POA.²³

Our most notable finding is the strong association between the injection of POA and anti-HCV positivity. Although respondents reported injecting myriad drugs over the previous 12 months, those who reported injecting POA were 5 times more likely to be anti-HCV positive than those who injected other drugs. This finding is consistent with recent studies identifying POA injection as an independent predictor of HCV infection,^{15,30} suggesting that risks associated with preparing and injecting POA place PWID at increased risk

for HCV infection. Also noteworthy is the finding of an association between anti-HCV positivity and the sharing of injection equipment, also a well-established risk factor for HCV infection.³¹

Age, when adjusting for other variables, was not significantly associated with anti-HCV positivity in this cohort. Yet, it is worth noting that almost three quarters (25 of 34) of anti-HCV positive people in our sample were younger than 30 years. This finding is consistent with recent evidence identifying a rapid increase in newly reported hepatitis C cases among people aged 18 to 29 years and among populations with similar demographic characteristics and behavioral risk factors.⁹ Of the 25 young people who tested anti-HCV positive, all reported being recent initiates to injecting (< 2 years) while injecting POA and sharing injection equipment (cookers and syringes) over the previous 12 months.

That these risk factors were reported by all 25 anti-HCV-positive young people suggests that younger age, although not a risk factor in itself, may serve as a proxy for low levels of injecting competency characteristic of novice injectors.³² Recent initiates to injecting (< 2 years) have less experience with the practice of injecting than seasoned injectors,^{33,34} they are less knowledgeable of the HIV and HCV risks associated with preparing POA tablets for injection,³⁵ and they are more likely to develop unsafe injecting techniques,³⁶ many of which persist with duration.³⁷ Consequently, recent initiates also have high levels of risk for HCV

TABLE 2—Logistic Regression Model of Associations With Hepatitis C Antibody Positivity: Cortland County, NY, March–July 2012

Variable	Unadjusted OR (95% CI)	AOR ^a (95% CI)
Age, y		
< 30	2.61 (1.06, 6.44)	...
≥ 30 (Ref)	1.00	...
Gender		
Female	0.58 (0.22, 1.47)	0.27 (0.08, 0.88)
Male (Ref)	1.00	1.00
Housing		
Rent or own a home or apartment (Ref)	1.00	...
Living in a residential program
Homeless/living with friends	1.57 (0.58, 4.29)	...
Age at first injection, y		
< 18	0.12 (0.01, 1.26)	...
18–20	0.19 (0.02, 2.06)	...
21–29 (Ref)	1.00	...
30–39	0.67 (0.05, 9.47)	...
40–49
Use syringe exchange program to obtain syringes in the past 12 mo		
Yes	5.83 (1.83, 18.63)	...
No (Ref)	1.00	...
Fish for a vein		
Never fish for a vein	0.34 (0.14, 0.84)	...
Sometimes/always fish for a vein (Ref)	1.00	...
Share any equipment while injecting in the past 12 mo ^b		
Yes	2.71 (1.03, 7.16)	3.79 (1.20, 12.00)
No (Ref)	1.00	1.00
Inject prescription opiate		
Yes	4.69 (1.85, 11.92)	5.53 (1.92, 15.91)
No (Ref)	1.00	1.00
Inject bath salts		
Yes	5.40 (1.31, 22.65)	...
No (Ref)	1.00	...

Note. AOR = adjusted odds ratio; CI = confidence interval; OR = odds ratio.

^aAdjusted for all variables in the model.

^bRefers to equipment except needles.

infection,^{38,39} and the interval between initiating injection and HCV infection remains, for a significant portion (about 25%), extremely brief (< 2 y).⁵ That is to say, in contrast to HIV, for which the chance of becoming infected increases significantly after an initial 5-year window,⁴⁰ the average duration from when a person first initiates injecting to when he or she acquires HCV infection appears to be more truncated.⁵

The analysis of our survey data points to the possibility that behavioral risk factors specific to POA injection are placing PWID at increased

risk for HCV infection because respondents most commonly reported injecting POA (58%, compared with 33.3% using heroin), and this variable is most strongly associated with anti-HCV positivity. Whether this elevated risk is attributable to the mechanics required to prepare and inject prescription tablets⁴¹ or associated with the sharing of higher risk injection equipment such as high dead-space syringes⁴² is beyond the analytical scope of this investigation. Yet, because both associations (anti-HCV positivity and POA injection and

anti-HCV positivity and preparation equipment sharing) are consistent with the hepatitis literature,^{7,30} the findings from this investigation in Cortland County, New York, improve our understanding of an emerging syndemic between POA misuse and HCV infection, especially as it concerns young adults from rural areas who are recent initiates to injection.

Limitations

The findings in this study are subject to a number of limitations. First, our relatively small sample size limits the ability to detect true associations, specifically with regard to a multivariable analysis. Because data were measured cross-sectionally, we were unable to examine causality. Second, our sample was not randomly selected and thus may not adequately represent the population of young PWID in Upstate New York; results may not be generalizable to the larger population of young PWID or in other rural or suburban counties. Even so, our sample represents an understudied cohort that needs to be included in future studies so we can better understand the behavioral risk factors for HCV infection associated with POA injection. Third, because the survey was taken anonymously, it is possible that some respondents could have participated twice. We suspect subject duplication was minimal given the short time frame of the study (5 months). Fourth, a number of survey respondents refused HCV rapid testing (n = 23), reporting knowing their HCV status as the reason, and these people could differ from people who agreed to be tested. Still, tested and untested people did not significantly differ on any sociodemographics, drugs injected, or injection behaviors evaluated. Last, duration of injection could not be determined from the survey as administered; however, it is likely that younger respondents are relatively new injectors, though this cannot be confirmed.

Public Health Implications

The recent increase in the nonmedical use of POA in North America poses new challenges for public health.²⁰ Although the need to investigate the sequelae of opioid addiction is clear, most new cases of hepatitis C in the United States result from parenteral exposure by way of illicit drug injecting.³ Given this primary risk factor, and in light of the recent

increase in newly reported HCV cases among young PWID, we offer several measures to strengthen primary prevention for PWID, with a particular focus on young people and recent initiates residing in rural areas.

First, it is critical that primary prevention focus on the risks associated with injection drug use because parenteral exposure is the primary driver of HCV incidence in the United States. Second, with the recent discovery that HCV infectivity can persist on inanimate objects well after the initial injection event,^{43–45} it is important for prevention interventions to emphasize the risks associated with sharing preparation equipment, in which the sharing of cookers, filters, water, injecting surfaces, and so forth are put on equal footing with the hazard of sharing syringes. This way, PWID who are either unable or unwilling to cease injecting will have the most up-to-date knowledge on how to protect themselves and their injecting partners from acquiring or transmitting HCV.

Third, in those areas in which SEPs operate, they may serve as an important point of contact to engage PWID because they provide injection-related health services to people currently injecting.⁴⁶ Fourth, timely prevention strategies, designed specifically for recent initiates to injecting, are important given the brief window of time between when a person begins injecting to when the person can become exposed to HCV.⁴⁷ Fifth, innovative ways to reach young PWID and effective models for integrating delivery of interventions are needed to reduce the incidence of HCV, such as multicomponent interventions⁸ and community-wide responses like Project Lazarus.⁴⁸ This may be especially relevant in rural settings in which people are thinly settled and sterile injection equipment and drug treatment programs may not be easily available.

Finally, the increase in newly reported HCV infections among young people from rural areas who report injecting POA suggests a geographic and circumstantial intersection between the illicit use of prescription drugs and an emerging HCV epidemic in this population.²⁷ Scientists and scholars whose injection-related research has traditionally involved older, urban-based residents and inner-city, drug-using networks may want to consider placing additional emphasis on rural areas to examine the social networks of rural (and suburban) injectors

and the health risks associated with the injection of POA. This rural focus could generate an influx of mixed-methods research to examine the behavioral factors contributing to the recent increase in newly reported HCV infections involving young PWID. It may also allow us to investigate why people who report injecting POA seem to be at higher risk for HCV infection than people who report injecting other drugs. ■

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This article was accepted June 16, 2014.

Note: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Contributors

J. E. Zibbell, R. Hart-Malloy, and C. Flanigan designed the study and wrote the protocol. J. E. Zibbell managed the literature searches and summaries of previous related work. R. Hart-Malloy conducted statistical analyses, and J. E. Zibbell and R. Hart-Malloy drafted the article. J. Barry and L. Fan were coinvestigators and provided technical assistance and managed data collection. C. Flanigan provided clinical and editorial comments throughout. All authors have seen and approved the final article.

Acknowledgments

As with any work, this investigation could not have been possible without the generous support of many people. We thank Project Safe Point and Keith Brown for their work on this study in Albany, NY. Additionally, we thank the Cortland County Health Department, particularly Catherine Feuerherm and her staff; Dan Casler, Amy Burns, Lisa Harder, and Kelly Firenze from the New York State Regional Office for the initial investigation in Cortland County; Maxine Philips and Nkechi Oguagha from the New York State Department of Health AIDS Institute for their sustained commitment to harm reduction; and Geoff A. Beckett, Rajiv Patel, Bryce D. Smith, and Anthony K. Yartel of the Division of Viral Hepatitis at the Centers for Disease Control and Prevention for their editorial and methodological counsel.

Human Participant Protection

This study was approved by the New York State Department of Health institutional review board.

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