Identifying and Reporting Outbreaks of Viral Hepatitis,

Considerations for Health Departments

BACKGROUND

Viral hepatitis outbreaks can be detected through a variety of methods. Unlike some other pathogens, molecular surveillance has not been routinely and systematically integrated into viral hepatitis surveillance programs to detect outbreaks in the United States to date. Instead, viral hepatitis outbreaks are typically detected through routine case surveillance, by observations from astute health department staff or health care providers, or during case interviews or contact tracing investigations. In practice, many suspected viral hepatitis clusters (defined as a higher than expected aggregation of reported health events in time and space) are only confirmed as outbreaks after several weeks or months of investigation.

In this guidance document, we review some key considerations based on literature review, experience from health departments, and CDC's experience providing technical assistance for detecting viral hepatitis outbreaks. Key considerations include when to initiate intensified case investigation, mobilize resources necessary to stop transmission, and report an outbreak to CDC. Clusters and suspected outbreaks should prompt additional investigation outside of routine surveillance activities. However, given that many local factors need to be considered when investigating cases of potential public health importance, the decision of what constitutes an "outbreak" is ultimately at the discretion of the health department. The information in this document is meant to serve as a general guide for health departments.

PURPOSE

To share key considerations and solicit input from health departments for developing standardized definitions of viral hepatitis outbreaks and to facilitate outbreak reporting to CDC. Jurisdictional approaches to viral hepatitis outbreak detection and confirmation may vary widely.

There are several reasons to investigate outbreaks, including:

- To identify the cause of the outbreak and inform prevention and control efforts
- To provide new insights or research (e.g., defining new modes of transmission or characterizing the risk to disproportionately affected populations)
- To evaluate existing public health programs or prevention strategies (e.g., to understand gaps in vaccination, harm reduction, or testing and linkage to care services)
- To respond to public, political, or legal concerns and minimize disruptions to society and health care systems
- To support public health workforce development (e.g., train staff to conduct outbreak investigations)

Deciding whether to investigate an outbreak often depends on several factors, including severity of illness, potential for spread, availability of prevention and control measures, and financial/ human resources. Jurisdictions should consider the resources required to investigate an outbreak along with other competing demands and prioritize those investigations or programmatic activities that are likely to be most impactful.

Jurisdictions are encouraged to monitor data regularly (e.g., weekly or monthly) as part of routine surveillance practices to identify outbreaks. When potential outbreaks are detected, multiple hypotheses should be explored to explain increases in observed cases of viral hepatitis; these might include increased reporting, changes to

surveillance processes or definitions, improved access to testing, or true increases in the incidence of viral hepatitis.

When and how to report an outbreak to CDC, for jurisdictions funded under the Integrated Viral Hepatitis Surveillance and Prevention Cooperative Agreement (IVHSP) PS21-2103

A cluster or suspected outbreak should be reported to CDC at any time if assistance is requested or if a multistate outbreak is suspected, although a report form is not necessary unless an outbreak is confirmed.

- Local health departments should follow their established procedures with the state/ jurisdictional health department for reporting to CDC.

- CDC staff assigned to the IVHSP **regional jurisdiction support teams** are readily available for technical assistance to share considerations and best practices for outbreak investigation and confirmation.

- Prompt outreach to CDC allows for more efficient communication and dissemination of prevention measures to neighboring jurisdictions where indicated.

Confirmed outbreaks should be reported to CDC within 5 days of being confirmed by jurisdictions, as specified in the IVHSP cooperative agreement.

1. Initial Outbreak Report

Use the IVHSP **Initial Outbreak Report Form** found at: https://airc.cdc.gov/surveys/?s=C4ADAHDKPXFDDM3P

2. Outbreak Summary Report

By the end of each IVHSP reporting period, submit an **Outbreak Summary Report Form** for each outbreak that was ongoing during that reporting period and was previously reported via the Initial Outbreak Report Form. Use the IVHSP Outbreak Summary Report Form found at: https://airc.cdc.gov/surveys/?s=FJ7EFWWJHFACF44A

Current challenges

During recovery of health care and public health systems from the COVID-19 pandemic, reported numbers and rates of viral hepatitis infections are likely to fluctuate. For example, Kaufman et al (Am J Prev Med 2021; 1: 369-376) reported that the volume of hepatitis C antibody and RNA testing and prescriptions for hepatitis C treatment decreased markedly during early-to-mid 2020 compared with the same time periods during 2018 and 2019. Also, most jurisdictions did not receive CDC/DVH funding for viral hepatitis surveillance prior to 2021, which may impact baseline case counts and rates used for outbreak detection. These challenges may initially diminish the ability to detect outbreaks through comparisons of surveillance data over time in some settings.

VIRAL HEPATITIS OUTBREAKS

I. HEPATITIS A

Hepatitis A community outbreaks associated with person-to-person transmission

Considerations for identifying suspected outbreaks. Examples include the following:

- An increase in reported hepatitis A cases that meet the CSTE/CDC hepatitis A surveillance case definition within a common geographic area or population above baseline (1 standard deviation or more) over a 4-week period. Baseline cases should be calculated from a non-outbreak, nadir period (e.g., 4-week average during 2011–2015).
- Three or more hepatitis A cases are reported during a 50-day period (one incubation period) among people within a common geographic area with common epidemiologic, social, or behavioral characteristics [e.g., injection or non-injection drug use, homelessness, male to male sex, or time spent in the same congregate living facility (jail, substance use treatment, group home, homeless shelter, etc.)]. Jurisdictions should consider that documentation of epidemiologic links between people with hepatitis A virus (HAV) infection are not required to suspect or declare an outbreak associated with person-to-person transmission.
- Two or more hepatitis A cases with an identical HAV RNA sequence are reported within a 50-day period from a common geographic area with common epidemiologic, social, or behavioral characteristics [e.g., injection or non-injection drug use, homelessness, male to male sex, or time spent in the same facility (jail, substance use treatment, group home, homeless shelter, etc.)].
- Jurisdictions might consider that hepatitis A cases are not part of a community outbreak associated with person-to-person transmission if any of the following apply:
    - Any case in a person who reports travel to a country or US territory with endemic hepatitis during the 15–50 days before symptom onset AND does not report other known risk factors, OR
    - Any case in a person who is linked to a hepatitis A foodborne outbreak by related HAV RNA sequencing (see next section, *Hepatitis A foodborne outbreak*), OR
    - Any case in a person who is epidemiologically linked to a foodborne outbreak AND does not report other known risk factors.
    - Any case with a serum or plasma specimen collected within four weeks of symptom onset that has undetectable HAV RNA (CDC staff are available for consultation about how to interpret laboratory results)

Hepatitis A foodborne outbreak

Considerations for identifying suspected outbreaks. Examples include the following:

- An increase in reported hepatitis A cases within a common geographic area or population above baseline (1 standard deviation or more) over a 4-week period and there are no known risk factors

(e.g., injection or non-injection drug use, male to male sexual contact, homelessness, or international travel) among the cases.

- Three or more primary hepatitis A cases are reported during a 50-day period among people in a common geographic area with common epidemiological exposures (e.g., grocery store, restaurant, or unusual food source/food item, etc.).
- Two or more hepatitis A cases with an identical HAV RNA sequence are reported within a 50-day period from a common geographic area with no known risk factors (e.g., injection or non-injection drug use, male to male sexual contact, homelessness, or international travel).
- Note: Hepatitis A foodborne outbreaks can be associated with contaminated food, infected food handlers, or both.

Considerations for outbreak confirmation. Examples include the following:

Two or more primary hepatitis A cases

- Meet **all** of the following criteria:
  - Meet the 2019 CSTE / CDC hepatitis A case definition, AND
  - Have illness onset within a defined time period (this will be outbreak-specific and should be defined in relation to the suspected exposure period [e.g., the dates when an infected food handler worked, the dates when a suspected contaminated food item was available for purchase, etc.])
- AND have **at least one** of the following criteria:
  - Report consumption of a common food item purchased from a common food retailer/distributor during the 15–50 days before symptom onset without a more likely, alternative exposure, OR
  - Have a similar HAV RNA sequence to a foodborne cluster case without a more likely, alternative exposure.

- Laboratory evidence (e.g., Nucleic Acid Test for HAV RNA, sequencing to determine the viral genotype and relatedness of viral sequences) from suspected contaminated food and traceback evidence from FDA investigations can help to confirm the contaminated food vehicle but are not necessary prerequisites to report hepatitis A foodborne outbreaks to CDC.

Additional considerations for both community and foodborne hepatitis A outbreaks

- A single hepatitis A case still warrants investigation and consideration of postexposure prophylaxis for close contacts (see *Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020, MMWR 2020*)

- Jurisdictions do not need to submit an Initial Outbreak Report Form for any hepatitis A clusters related to a hepatitis A outbreak that has already been declared for that jurisdiction associated with widespread person-to-person transmission. (For example, it is not necessary to report a hepatitis A outbreak associated with person-to-person transmission in a congregate living facility located in a community where a widespread hepatitis A outbreak has already been declared.)

Considerations for use of viral molecular sequencing for hepatitis A:

Nucleic acid testing for HAV RNA followed by sequencing and phylogenetic analysis of sequences from viremic hepatitis A cases may be useful for confirming or investigating an outbreak during some circumstances depending on availability of specimens. Sequencing of viral isolates from HAV RNA positive samples has been used to support hepatitis A outbreak investigations and can be particularly useful for confirming associations with foodborne outbreaks (see Viray MA et al, Epidemiology & Infection 2018; 147: e28). In the midst of hepatitis A outbreaks associated with person-to-person transmission, DVH encourages submission of specimens from hepatitis A cases without known risk factors (e.g., injection or non-injection drug use, male to male sexual contact, homelessness, or international travel) for nucleic acid testing, sequencing, and phylogenetic analysis. DVH staff are available for consultation about the role of sequencing of HAV isolates in outbreak investigations.

II. Hepatitis B or hepatitis C community-based or congregate living facility (non-health care) outbreaks

Considerations for identifying suspected outbreaks. Examples include the following:

- An increase in acute hepatitis B or hepatitis C cases above what is normally expected in a geographic area or population during a particular period AND evidence of recent transmission (e.g., within the previous six months) of HBV, HCV, or HIV among case-patients. This definition assumes that jurisdictions are routinely monitoring surveillance data to detect outbreaks. Source, for HCV: *CDC. Managing HIV and Hepatitis C Outbreaks Among People Who Inject Drugs A GUIDE FOR STATE AND LOCAL HEALTH DEPARTMENTS.*

  Because of lack of sensitivity of hepatitis C case definitions, investigators have sometimes defined outbreaks on the basis of increased number of acute and chronic cases diagnosed in young persons, e.g., CDC (see MMWR 2008; 57:517-21, MMWR 2011; 60: 537-41, MMWR 2011 60:1457-8, and MMWR 2012; 61: 358.) Please review "*Considerations for monitoring surveillance data for detection of community outbreaks of hepatitis B and hepatitis C*," below.

- Additional epidemiological information obtained during case investigation indicates potential cases or clusters of public health importance (See "Considerations for outbreak detection by front-line public health investigators and epidemiologists). These might include:
  - **Congregate living facilities**
    - A single case of acute hepatitis B, hepatitis C, or test conversion in a resident of a correctional or detention facility or other closed residential institution.
    - Note that in the outbreak investigation setting, case definitions for acute hepatitis B or hepatitis C may be based on laboratory and clinical evidence rather than CSTE/CDC surveillance case definitions, which may omit asymptomatic cases, or those with a negative serologic or nucleic acid test for infection followed by a newly positive test over a longer span of time than included in the surveillance case definitions for acute hepatitis B or hepatitis C. Two or more acute cases of hepatitis B or hepatitis C with an epidemiological link to the same correctional or detention facility, homeless shelter, or other residential facility

- **Community-based**
  - Two or more acute cases of hepatitis B or hepatitis C epidemiologically linked to the same network of persons who inject drugs or men who have sex with men, or persons within a sexually transmitted infection network (e.g., syphilis or HIV).
  - When an outbreak of HIV is reported among persons who inject drugs (PWID) in a jurisdiction. High rates of viral hepatitis coinfection have been documented in some of these outbreaks.

Although acute hepatitis B and hepatitis C cases are ascertained using the 2012 CSTE acute hepatitis B case definition and the 2020 CSTE acute hepatitis C case definition for surveillance reporting, potential hepatitis B or hepatitis C outbreak cases may also be identified by laboratory or clinical evidence which may not meet criteria outlined in surveillance case definitions.

For instance, some clinicians or front-line public health investigators may have additional evidence to suggest seroconversion or are aware of other information (e.g., common exposures in time and place) that suggest cases may be recent and part of the same cluster. Decisions to include or exclude cases should always be made on the basis of criteria in the *outbreak* case definition, regardless of whether they meet the surveillance case definition.

- **Examples of community-based and congregate living facility (non-health care) hepatitis B (Table 1) and hepatitis C (Table 2) outbreak and cluster investigation publications are summarized at the end of this document.** These tables highlight how index cases were recognized, outbreak modes of transmission, and case criteria.

- **Examples of community-based outbreaks and clusters of HIV with HCV coinfection among cases are summarized in Table 3.** This table shows how hepatitis C coinfection was defined, how hepatitis C coinfection data were collected, and the temporal relationship between HCV diagnosis and HIV diagnosis

Considerations for use of sequencing of HBV DNA and HCV RNA from clinical samples

Sequencing of HCV RNA from hepatitis C cases may be useful for confirming or investigating an outbreak in some circumstances. Global Hepatitis Outbreak Surveillance Technology (GHOST) has been used to support outbreak investigations (see Ramachandran S et al, eBioMedicine 2018; 37:P374-381and Longmire AG et al, BMC Genomics 2017; 18: 916). Sequencing of HBV DNA from hepatitis B cases has limited utility because of the lack of adequate variability sufficient to establish linkages between cases in the HBV genome; however, sequencing has provided useful contextual information in some past outbreaks. CDC staff are available for consultation about the role of molecular sequencing in outbreak investigation.

Considerations for monitoring surveillance data for detection of community outbreaks of hepatitis B and hepatitis C:

US jurisdictions vary widely by size, demographics, health system capacity, access to harm reduction services, treatment for substance use disorder (SUD), and capacity to investigate outbreaks and clusters. Surveillance

system capacity, reporting statutes and mandates also vary by state, which influences the completeness of reporting. There is unlikely a single strategy for detection of community outbreaks of hepatitis B or hepatitis C that will be effective across all jurisdictions. This section offers some considerations for jurisdictions seeking to improve detection of community outbreaks of hepatitis B and hepatitis C.

- The literature on community outbreaks of hepatitis B and hepatitis C is sparse and dated (see Tables); however, many of the hepatitis B and hepatitis C outbreaks recorded in the literature have been identified on the basis of a noted increase in cases in person, place, and time. Routine (e.g., weekly or monthly) monitoring of data might increase recognition of outbreaks and clusters.
- Routine (e.g., weekly or monthly) review of data e.g., three years of data organized in a spreadsheet by geographic subdivision (county, jurisdiction, zip code, census tract) might be the simplest way to accomplish this task.
    - This approach might be preferable to other sophisticated methods such as automated cluster detection algorithms, for which many jurisdictions might not have sufficient case burden to benefit from, and may be particularly useful in settings with sparse data, for example:
        - in smaller jurisdictions or jurisdictions with few reports of hepatitis B or hepatitis C,
        - as the jurisdiction is becoming familiar with patterns of hepatitis B or hepatitis C transmission, and/or
        - during times when baseline viral hepatitis rates might be unstable due to changes in health care system or testing capacity.

- For hepatitis C, because jurisdictions may lack the capacity to adequately ascertain acute or 'recent' infections, some jurisdictions have analyzed trends among younger persons (e.g., <30 years of age) with acute ***or*** chronic hepatitis C in order to characterize trends and detect outbreaks. The assumption with this approach is that younger persons with newly identified infection, whether classified as acute or chronic, are more likely to have been acquired infection recently.
- Jurisdictions might consider routine (e.g., quarterly) or as-needed review of data collaboratively with syndemic surveillance partners such as HIV, STI, and overdose surveillance staff. This additional context might be helpful to identify clusters of overdose or infectious disease transmission that merit further investigation. Because overlapping risk behaviors in these populations may contribute to more than one poor health outcome, increases in one disease/ outcome might signal potential increases in another syndemic disease, even if not yet evident in surveillance data.
- Jurisdictions might also consider routine review of national hepatitis summary reports provided annually by CDC for context regarding ongoing epi-trends, especially among neighboring jurisdictions or regions with similar demographic characteristics.
- Because laboratory reporting gaps may hinder ability to detect outbreaks, jurisdictions might consider periodically assessing laboratory reporting completeness. Improving the number of laboratories that are participating in electronic laboratory reporting (ELR), in addition to improving the timeliness and completeness of ELR data, might improve speed and accuracy of outbreak detection.
- While there are no reports in the literature of hepatitis B or hepatitis C outbreaks detected exclusively using automated space-time cluster detection software, jurisdictions have attempted to use automated space-time cluster detection software to detect outbreaks and clusters of hepatitis B and hepatitis C. These strategies include:
    - Software for the spatial, temporal, and space-time statistics: https://www.satscan.org/

- Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE): https://publichealth.jmir.org/2021/6/e26303

Further research is needed to evaluate the sensitivity, specificity, and accuracy of these programs in detecting viral hepatitis outbreaks.

Considerations for outbreak detection by front-line public health investigators and epidemiologists:

- Although published reports are sparse and dated (see tables), many of the hepatitis B and hepatitis C outbreaks recorded in the literature have been recognized and reported by front-line public health investigators or clinicians.
- Investigation protocols and investigation worksheets might help front-line public health investigators ask the right questions of case-patients and identify and report clusters to the jurisdictional health authority.
- Training of front-line investigators might also help these staff recognize and report outbreaks and clusters to the jurisdictional health authority. Training can occur through conference calls, webinars, state epi conferences, and other activities.
- Routine check-ins with investigators might build relationships between jurisdiction viral hepatitis staff and front-line investigators and empower and engage front-line staff to improve outbreak recognition and reporting.
- Routine training might be needed if there is staff turnover.

IV. Hepatitis B or hepatitis C health care-associated outbreaks

Considerations for identifying suspected outbreaks. Examples include the following:

One or more cases of acute hepatitis B or hepatitis C in a person without known risk factors represents a sentinel event for possible health care-associated infection and warrants evaluation for possible health care exposures during the likely incubation period. Even a single case, particularly among repeat blood donors, dialysis patients, elderly persons, or residents of long-term care facilities has led to the detection of outbreaks by jurisdictions. A single case of viral hepatitis might also be the sentinel event that leads to recognition of an outbreak of viral hepatitis related to diversion of injection drugs in a health care setting. Collaboration between health department viral hepatitis programs and health care-associated infections programs is recommended to support investigation efforts of health care-associated outbreaks of hepatitis B or hepatitis C; such collaborations are also important to cross-train front-line investigators and build subject matter expertise in overlapping program areas.

A publicly available table summarizing all confirmed health care-associated outbreaks of HBV and HCV infection reported to CDC during 2008-2019, highlighting index case recognition, outbreak modes of transmission, and case criteria may be found at: https://www.cdc.gov/hepatitis/outbreaks/healthcarehepoutbreaktable.htm

- Suspected or confirmed health care-associated outbreaks should be reported to CDC at haioutbreak@cdc.gov, in addition to reporting to the IVHSP regional team.

Consideration should be given to training front-line investigators in local and state public health departments to recognize and report suspected health care-associated hepatitis B or hepatitis C cases. Investigation protocols and investigation worksheets could be modified to assist front-line investigators in recognizing

potential health care exposures during the incubation periods for hepatitis B and hepatitis C. Note that in the outbreak investigation setting, case definitions may be based on laboratory and clinical evidence rather than CSTE/CDC surveillance case definitions, which may omit asymptomatic cases, or those with a negative serologic or nucleic acid test followed by a newly positive test for infection over a longer span of time than included in the surveillance case definitions for acute hepatitis B or hepatitis C.

A **toolkit** for evaluating and responding to potential health care-associated viral hepatitis infections is available at: https://www.cdc.gov/hepatitis/outbreaks/Healthcare-associatedOutbreaks.htm. Case definitions and criteria for confirming health care-associated infections may vary by setting and investigation.

Considerations for use of viral molecular sequencing

Molecular sequencing is especially useful as one component of an epidemiologic investigation for health care-associated outbreaks of hepatitis C, less so for hepatitis B. CDC staff can link jurisdiction staff to resources for molecular testing of outbreak specimens.

Tables. Community-based or Congregate Living Facility (non-health care) Outbreaks or Clusters of Hepatitis B and Hepatitis C

Table 1a. Selected Community-based or Congregate Living Facility (non-health care) Outbreaks or Clusters of Hepatitis B Reported in the Literature, United States, through 2021[a]

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timeframe]
a. Community-based					
CDC. MMWR Morb Mortal Wkly Rep, 1984; 33:70, 76-7	Kentucky	Injection drug use, sexual contact	Clusters of fulminant hepatitis B deaths limited to persons who inject drugs (PWID) and their sexual contacts.	Acute clinical symptoms compatible with hepatitis B; acute elevation of AST or ALT two or more times greater than the upper limit of normal; and (3) positive HBsAg	17 cases [Jan - Sep 1983]
	California	Injection drug use, sexual contact	same	same	19 cases [Jun - Dec 1983]
CDC. MMWR Morb Mortal Wkly Rep, 1986; 35:481-2	Durham, North Carolina	Injection drug use, sexual contact	86 cases reported in 1985, compared with 24 cases in 1984 and eight in 1983.	Not specified	86 cases [1985]
Lettau L, N Engl J Med, 1987; 317:1256-62	Worchester, Massachusetts	Injection drug use, sexual contact	Increase in cases of acute hepatitis B with deaths	Acute clinical illness; (+) HBsAg; ALT or AST twice the level of normal; residence in Worcester.	190 cases, including 11 deaths [Sep 1983 – May 1985]
Khan. AJPH, 2005; 95:1793 MMWR, 2001; 50:529	State correctional facility, Georgia	Sexual contact, injection drug use, tattoos, shared personal items	Single acute case in a correctional facility, 2000; Second acute case, 2001	Seroconversion between 2000 and 2001 serosurveys	18 incarcerated persons seroconverted[b] [2000 – 2001]

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timeframe]
Garfein, Hepatology, 2004; 40:865-873	North Central Montana	Injection drug use	Four deaths in five months from acute hepatitis B among Native Americans who injected drugs	Acute hepatitis B: (+) IgM anti-HBc with or without symptoms Fulminant hepatitis B: IgM anti-HBc (+) progressing to liver failure (increased PTT and hepatic encephalopathy) within 12 weeks of onset	12 cases of acute hepatitis B, 10 cases of fulminant hepatitis B [1998-2000]
Bialek, J Urban Health, 2005; 82:468 MMWR, 2001; 50:388	Pierce County, Washington	Injection drug use	Twelve cases of acute hepatitis B were reported in the first four months of 2000, compared to seven cases in all of 1999	(+) IgM anti-HBc	58 cases; 28 (34.5%) were coinfected with HDV [2000]
Vogt. Addiction, 2006;101:726	Wyoming, 2003	Injection drug use, sexual contact	21 cases Jan-Jun 2003 versus 9 cases in 2002 and 0 cases in 2001	(+) IgM anti-HBc or symptoms	45 cases [Jan – Aug 2003]
Devasia. Vaccine, 2006; 24:1354	Five counties, Tennessee	Injection drug use, sexual contact, tattoo while incarcerated	150% increase in cases of hepatitis B in five counties, from 16 to 42 during 2002-2003.	(+) IgM anti-HBc	48 cases [2002 – 2003]
Harris AM. MMWR Morb Mortal Wkly Rep 2016; 65:47–50.	Kentucky, Tennessee, and West Virginia, 2010 to 2013	Injection drug use	20% increase in incident HBV infections was observed from 2009 to 2010	Surveillance case definition	2,062 cases [2012 – 2013]
Comer, MMWR, 2018; 67: 230-231	Pascoe County, Florida, 2016	Injection drug use	Increase in one county between 2011 and 2016 from 1.5 to 17.28 per 100,000 residents	Surveillance case definition	275 cases [2011 – 2016]

b. Congregate living facility (non-health care)

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timeframe]
Devasia. Vaccine, 2006; 24:1354	Community, Tennessee	Injection drug use, sexual contact, tattoo while incarcerated	Two index cases were epidemiologically linked to individuals incarcerated in a jail	(+) IgM anti-HBc	4 cases outside of the jail, 3 inside the jail [2003]

[a] Note that in June 1982, the Advisory Committee on Immunization Practices (ACIP) published the first official recommendations on the use of hepatitis B vaccine, recommending pre-exposure vaccination initially for groups with a high risk for HBV infection e.g., men who have sex with men, injection-drug users, and heterosexual persons with multiple partners. In 1991 recommendations were updated to include universal childhood vaccination, prevention of perinatal HBV transmission, vaccination of adolescents and adults in high-risk groups, and catch-up vaccinations for susceptible children in high-risk populations. (See MMWR 2002)

[b]A total of 230 incarcerated individuals had evidence of hepatitis B at baseline and were excluded from further analysis, including 11 with acute hepatitis B, 11 with chronic hepatitis B, and 208 with resolved hepatitis B.

Table 1b. Selected Non-US Community Outbreaks or Clusters of Hepatitis B Reported in the Literature, through 2021

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timespan]
Kirk AP. Scand J Infect Dis, 1980; 12:251-6.	Small market town in South-East England	Injection drug use and sexual contact	Fulminant hepatitis B in a sexual contact of a person who injects drugs (PWID)	"Acute hepatitis B"	4 cases [Jun – Aug 1977]
Streetly A, Journal of Public Health 1988 Vol. 10 Issue 2 Pages 147-55	Medway area of Kent, England	Injection drug use, sexual contact	Three reports of hepatitis B in PWID in one week	Jaundice and HBsAg (+)	13 cases [Oct 1985 – Aug 1986]
Baxter DN, Journal of Public Health, 1988; 10:298-305	Stockport, England	Injection drug use, tattoos, sexual contact	Three-fold increase in acute hepatitis B between 1982-1983 to 1984-1985.	(+) HBsAg and anti-HBc IgM or (+) HBsAg and equivocal anti-HBc IgM with clinical findings	51 cases [1984 – 1985]

P. B. Christensen, J Clin Virol 2001; 22:133-41	County of Funen, Denmark	Injection drug use, sexual contact	From a yearly average below 10 cases (2.1/100 000), the number of reported cases rose to 38 in 1994 (8.1/100 000).	jaundice and (+) HBsAg or anti-HBc IgM. For asymptomatic cases, seroconversion for HBsAg or (+) anti-HBc IgM was required.	127 cases [1992 – 1998]
Stevenson J. Commun Dis Public Health 2001 Vol. 4 Issue 1 Pages 60-3	Inverclyde, Scotland, 1997	Injection drug use, sexual contact, household contact	From a baseline of 10 cases per year, five cases were identified in June 1997 alone	Anti-HBs IgM (+)	92 cases [1996 – 1999]
Mackenzie AR. *Scott Med J,* 2003; 48: 73-5.	Aberdeen, Scotland	Injection drug use, sexual contact	Increase from an average of 3.3 patients per year during 1991–1996 to 46 patients per year in 2000	"acute hepatitis B"	119 cases [1991-2000]
Andersson MI. Epidemiol. Infect, 2012; 140:47–57. Andersson MI. J Clin Virol, 2012; 53: 125-9.	Avon, England	Injection drug use, sexual contact	Increased number of cases reporting injection drug use as a risk factor beginning July 2001	HBsAg (+) and anti-HBc IgM (+), or seroconverted to total anti-HBc, with or without discrete onset of jaundice or other symptoms	237 cases [Jul 2001 – Dec 2005]
Shankar AG. Sex Transm Infect, 2016; 92: 227.	East of England	Male-to-male sexual contact (MMSC)	Cluster of five acute hepatitis B cases in men, median age 55	"acute hepatitis B"	5 cases [Jan – Aug 2015]

Abbreviations: anti-HBc, antibody to hepatitis B core antigen; ALT, alanine transaminase; AST, aspartate transaminase; HBV, hepatitis B virus; HDV, hepatitis delta virus; IgM immunoglobulin M; MMSC Male-to-male sexual contact; PTT, partial thromboplastin time

Table 2a. Selected US Community-based Outbreaks or Clusters of Hepatitis C among Persons who Inject Drugs (PWID) through 2021

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timespan]
Trooskin SB. Public Health, 2005; 119:1042-7	Connecticut	Not determined	Six clusters of HCV laboratory reports were identified by geographic information systems cluster analysis	Non-institutionalized individuals with positive laboratories for hepatitis C during 1999; 97% anti-HCV (+) and 3% RIBA or RNA (+)	1184 cases in six towns with incidence ranging from 138 – 366 per 100,000 population [1999].
CDC. MMWR Morb Mortal Wkly Rep, 2008; 57:517-21	Suburban Buffalo	Injection drug use	High number of newly identified HCV infections among persons aged <30 years who resided in the same postal code	Age < 30 years, current CDC case definitions for acute and chronic hepatitis C	20 cases [Nov 2004 – Apr 2007]
CDC. MMWR Morb Mortal Wkly Rep 2011; 60: 537-41. CDC. *MMWR Morb Mortal Wkly Rep* 2011; 60:1457-8.	Massachusetts	Injection drug use	Newly diagnosed HCV infection increased from 65 to 113 cases per 100,000 population among persons aged 15–24 years between 2002–2009.	Surveillance case definitions for probable and confirmed HCV infection, persons aged 15 – 24 years	1,925 cases [2007 – 2009]
CDC. MMWR Morb Mortal Wkly Rep 2012; 61: 358.	Six contiguous rural counties of Wisconsin	Injection drug use	Increase from eight cases per year during 2004–2008 to an average of 24 cases per year during 2009–2010 among persons aged <30 years	Confirmed (anti-HCV [+]) and elevated signal-to-cut-off ratio or HCV RNA (+) or probable (anti-HCV [+]) HCV infection in persons aged < 30 years	25 cases [2010]
Zibbell JE. MMWR Morb Mortal Wkly Rep, 2015; 64: 453-8.	Kentucky, Tennessee, Virginia, West Virginia	Injection drug use	364% increase in the number of cases of acute HCV infection from 2006 to 2012 among persons aged ≤30 years	Surveillance case definition	1,377 cases [2006–2012]
Stopka TJ. BMC Infect Dis, 2017; 17: 294.	Massachusetts	Not addressed	GIS, spatial epidemiological, and statistical modeling approaches to identify and characterize statistically significant geographic HCV hotspot clusters	Using cases that met confirmed and probable case definitions, clusters were defined by hot spot analysis including case density per mile, case count hot spots, case rate hot spots and space-time cluster analyses	Hot-spot clusters: 8 cluster for case density 9 clusters for case counts 3 clusters for case rates 2 clusters for space-time cluster analysis [2002 -- 2013]

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timespan]
Hochstatter KR. *Emerg Infect Dis,* 2021; 27: 480-89.	Wisconsin	Not addressed	Clustering by quasispecies analysis for samples tested by Wisconsin Department of Health Laboratory from syringe services programs [SSPs], correctional facilities, local health departments, community-based organizations, and public health clinics	Among 379 samples available, quasispecies analysis was used to define clusters of HCV infection	42 clusters comprising 126 persons; cluster sizes ranged from 2 to 11 persons [2016–2017]

Table 2b. Selected Non-US Community-based or Congregate Living Facility (non-health care) Outbreaks or Clusters of Hepatitis C among Persons who Inject Drugs (PWID) through 2021

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timespan]
a. Community-based					
Patrick DM. Cmaj, 2001; 165:889-95	Vancouver, British Colombia, Canada	Injection drug use	Observation of elevated seroconversion rates of HCV among PWID also experiencing an HIV outbreak	HCV seroconversion	62 cases [Dec 1996 – Nov 1999]
Gambotti L. Euro Surveill, 2005; 10: 115-7. Ghosn J. HIV Med, 2004; 5: 303-6.	Paris, France	Sexual contact (MMSC), non-injection drug use	Three hospital wards reported an increase in cases of HCV infection among gay men with HIV infection One ward had reported cases of acute HCV among gay men who were HIV (+) and with primary or secondary syphilis	HIV+ gay men with acute hepatitis C defined as HCV test conversion within 6 months, or a positive HCV-RNA PCR and ≥10-fold the ULN of ALT with documented normal levels during the preceding year	29 cases [Ma 2001 -- Oct 2004]

Reference	Location	Transmission	Recognition of Index Case(s)	Clinical and Laboratory Case Criteria	Total Number of Cases [timespan]
Browne R. Sex Transm Infect, 2004; 80: 326-7. Danta M. Aids, 2007; 21: 983-91.	Three urban HIV units in Britain	Sexual contact, (MMSC), injection and non-injection drug use	Increased HCV seroconversions primarily among HIV (+) gay men in an HIV and sexual health clinic between 1997 and 2002	HCV seroconversion or symptoms, ALT level ≥10 times the ULN and positive HCV-RNA by PCR	111 cases [1999 – 2005]
Götz HM. Aids, 2005; 19: 969-74.	Rotterdam, Netherlands	Sexual contact (MMSC)	Seroconversion to HCV in a case-patient from an outbreak of LGV proctitis	HCV seroconversion of HCV positive and epi-linked to the LGV	7 cases [2003]
Bottieau E. Eurosurveillance, 2010; 15: 19673.	Antwerp, Belgium	Sexual contact (MMSC), another STI (mainly syphilis, LGV)	Annual incidence of HCV infection in HIV (+) gay men increased from 0.2% in 2001 to 1.51% in 2008, and 2.9% in 2009 at an HIV/STI reference clinic	Confirmed: anti-HCV test conversion within 24 months. Probable: anti-HCV test conversion within > 24 months plus ALT elevation and (+) confirmatory test	69 cases (including two reinfections) [2001 – 2009]
Paraschiv SL. PLoS One, 2017; 12: e0185866.	Romania	Injection drug use	Retrospective recognition of HCV clusters in the context of an HIV outbreak among PWID	Of 117 case-patients with HIV, those patients within clusters, as defined by molecular sequencing	97 HCV sequences clustered in 13 transmission clusters [2011-2014]
Ramière C. Clin Infect Dis, 2019; 69: 2127-35.	Lyon, France	Sexual contact (MMSC), injection and non-injection drug use	Increase in acute HCV infection from 1.1/100 person-years in 2014 to 2.4/100 person-years in 2017 in HIV-infected gay men	New HCV infections were defined by HCV RNA testing every 6 months and anti-HCV testing annually.	108 cases among 96 gay men (75% HIV infected) [2014 -- 2017]
b. Congregate living facility (non-health care)					
Maisa A. J Viral Hepat, 2019; 26: 1377-87.	Belfast, Ireland	Injection drug use	Acute or recent HCV infections among four young and unexperienced heroin users at a hostel frequented by people experiencing homelessness	PWID) currently or previously living in, or associated with a homeless hostel with (+) HCV RNA infection between were considered cases	45 cases [Jul 2016 -- Dec 2017]

Abbreviations: ALT, alanine transaminase; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LGV, Lymphogranuloma venereum; MMSC, male-male sexual contact; PWID, persons who inject drugs; STI, sexually transmitted infection; ULN, upper limit of normal

Table 3. Selected Outbreaks and Clusters of HIV with Documentation of HCV Coinfection among Cases, United States, 2015–2021

Reference	Location	Outbreak time period	Hepatitis C definition	Source of HCV data	HCV prevalence among HIV outbreak cases n/N (%)	Average time from HCV detection to HIV diagnosis
Hudson et al Hershaw RB MMWR Morb Mortal Wkly Rep 2022; 71(2): 66-68.	Kanawha County, West Virginia	2019-21	Any positive test for HCV	HCV registry	61/65 (93.8)	HCV detected on average 4 years prior to HIV
Atkins A, *MMWR Morb Mortal Wkly Rep* 2020; 69(16): 499-500. McClung RP, *American Journal of Preventive Medicine* 2021; 61(5): S143-S50.	Cabell County, West Virginia	2018-19	Any positive test for HCV	HCV registry	72/ 82 (87.8)	Not reported
Kim MM, J Infect Dis 2020; 222 (Suppl 5): S250-s58.	Philadelphia, Pennsylvania	2018	Not specified	Health department surveillance data	81/116 (69.8)	Not reported
Tookes et al	Miami/Dade County, Florida	2018	HCV antibody or RNA positive	Opt-out HCV screening at an SSP	4/7 (57.1)	Not reported, *although 3 of 4 HCV infections were detected at least one year prior to HIV*
State of Alaska Epidemiology Bulletin	Alaska	2018	Not specified	Health department surveillance data	2/7 (28.6)	Not reported
Alpren C , Am J Public Health 2020; 110 (1): 37-44.	Northeastern Massachusetts	2015-18	Any positive test for HCV	HCV registry	116/129 (89.9)	HCV detected on average 5 years prior to HIV
Samoff E, *Am J Public Health* 2020; 110 (3): 394-400.	Western North Carolina	2017-18	Positive HCV antibody with or without RNA	Testing of cases or surveillance records	9/ 14 (64.3)	Not reported
Sizemore L, *Public Health Rep* 2020; 135(3): 329-33.	Knox County or East Tennessee Public Health Region	2017	Positive HCV antibody with or without RNA	Self-reported test for HCV	3/8 (37.5) PWID[a]	Not reported

Reference	Location	Outbreak time period	Hepatitis C definition	Source of HCV data	HCV prevalence among HIV outbreak cases n/N (%)	Average time from HCV detection to HIV diagnosis
Peters PJ N Engl J Med 2016; 375 (3): 229-39. Ramachandran S, EBioMedicine 37 (2018): 374-81.	Scott County, Indiana	2014-15	HCV antibody or RNA positive	HCV testing of cases	167/181 (92.3)	Not reported, *although in some cases HCV infection preceded HIV diagnosis by at least 5 years*

Appendix. Sample document:

Oregon Health Authority, Hepatitis C Response Tier

Outbreak Criteria

To determine whether public health interventions more than routine case investigation and control methods are required, the Oregon Health Authority (OHA) will consider several criteria that depend on whether the increases seen occur among acute or chronic cases (Tables 2 and 3).

On a monthly basis, the Viral Hepatitis Program (VHP) Medical Director, Hepatitis Epidemiologist, and Viral Hepatitis Prevention Coordinator (VHPC) will review acute cases of hepatitis C that have been reported to Orpheus, OHA's Acute and Communicable Disease Prevention (ACDP) surveillance database. Table 2 outlines the thresholds for launching an outbreak investigation based on the number of acute cases and the number of syringe-sharing contacts they have. Since acute cases are rare, the threshold for elevating to a Tier 2 or Tier 3 response, which will require contacting syringe-sharing contacts of cases, will be lower than for launching an outbreak investigation into chronic cases of HCV infection.

Table 2. Tiered response plan based on surveillance for *acute HCV*			
Tier	**Level of Response**	**Need for Incident Management Team (IMT)**	**Communications plan**
I. Sporadic cases (baseline)	Routine case investigation of acute cases	None	Routine posting of surveillance data on OHA website

II. Any acute case with 3 or more needle sharing contacts **Or** **2 acute cases in single county or 2 acute cases in different jurisdictions with epi links within a 4-week period** **Or** **A single case of acute HCV acquired in a carceral or residential setting**	As part of case investigation, if a case reports injection drug use in past 6 months, inquire about number of syringe-sharing contacts in past 6 months. Also obtain contact information for exposed persons and attempt to notify syringe-sharing contacts of their exposure and offer HCV testing, harm reduction counseling, and hepatitis A and hepatitis B vaccination. If resources permit, consider HIV/sexually transmitted infection (STI) (particularly syphilis) testing of cases and contacts, linkage to infectious disease care, as well as referral for medication for opioid use disorder (MOUD) and substance use disorder (SUD) treatment	VHP medical director notifies ACDP section manager and Health Security, Preparedness, and Response (HSPR) manager. Together, they consider need for incident management team (IMT) response	OHA public health information officer (PIO) assigned to the response does the following: establishes contact with local public health authorities (LPHAs), disseminates plain language information about HCV to cases and contacts in affected settings (as applicable), and considers need for press release in collaboration with LPHA

III. 3 or more epi-linked cases in a 4-week period	Continue follow up of acute cases and screening of exposed contacts, broaden screening program to include high risk groups (not just contacts), and consult with CDC about the need to obtain specimens for genotyping and sequencing. Will need to do the following: mobilize additional resources to offer screening (including HIV, syphilis, and other STIs) and linkage to care to individuals who screen positive; increase public and provider awareness of the importance of screening and the availability of highly effective treatment; broadly promote harm reduction measures; promote hepatitis A and hepatitis B vaccination of cases and their contacts; and increase awareness of local resources for medication for opioid use disorder (MOUD) and	VHP medical director consults with ACDP section manager, HSPR, Oregon Immunization Program (OIP) on scope of IMT response	OHA public information officer (PIO) activates communications plan, prepares press releases, plans social media campaign, provides updates to OHA leadership and other key stakeholders

	substance use disorder (SUD) treatment		

Because most acute cases of HCV in Oregon are not reported to OHA, trends in the incidence of chronic cases of HCV infection will help identify regions of the state with increases in HCV transmission (See Table 3).

The basic approach will be to monitor rates of cases reported with chronic HCV under the age of 30 years. This age group often acquires HCV through injection drug use and likely represents recently acquired HCV, since most people acquire HCV from drug use within 2-3 years of initiation. Since reports of chronic cases in persons under age 30 years are common, any recommendations to interview chronic cases under the age of 30 will be considered a Tier 2 response and will likely require assistance from OHA. If high numbers of cases are found among people reporting recent injection drug use and multiple syringe-sharing contacts, the response will be upgraded to Tier 3.

Additionally, the VHP Program Medical Director and VHP Epidemiologist will attend monthly meetings of the HIV cluster review team to exchange information about recent surveillance trends and maintain situational awareness of trends in transmission of bloodborne pathogens.

Table 3. Tiered response plan based on surveillance for *chronic* HCV

Tier	Level of Response	Need for IMT	Communications plan
I. Monthly rates of chronic cases in persons < 30 years are within baseline	Routine case investigation of acute cases only. If resources are available, consider conducting interviews of sample of chronic cases under 30 years	None	Routine posting of surveillance data on OHA website

II. **Occurrence of a rise in the number of chronic cases in persons under 30 years in a jurisdiction more than two standard deviations above the monthly average from the previous 3 years** **Or** **Cases of HCV infection found during HIV or HBV outbreak** **Or** **Time/space cluster detection noted**	Conduct enhanced surveillance of persons with chronic HCV infection under 30 years, consisting of either medical record review or interview of cases, with the goal of determining how many have injected drugs in the past 6 months and their numbers of syringe-sharing contacts (appendix A, "Brief chronic HCV interview form"). For interviewed cases, provide harm reduction counseling, hepatitis A and hepatitis B vaccination, testing for HIV, syphilis and other STIs, as well as linkage to infectious disease and MOUD/SUD treatment.	VHP medical director notifies ACDP section manager and HSPR manager, who considers need for IMT response.	OHA PIO assigned to the response establishes contact with LPHA PIO, disseminates plain language information about HCV to cases and contacts in affected settings as applicable, and considers need for press release in collaboration with LPHA.
III. High prevalence of HCV infection (>30%) in persons who inject drugs undergoing screening for HCV infection in settings serving individuals at high risk, such as syringe service programs (SSPs) and opioid treatment programs (OTPs)	Interview chronic HCV cases of any age identified in venues with high prevalence of HCV infection and offer HCV screening to syringe-sharing contacts of cases. Will need to mobilize additional resources to offer screening and linkage to care to individuals who screen positive, increase public and provider awareness of the importance of screening and the availability of highly effective treatment, broadly promote	VHP medical director consults with ACDP section manager, HSPR, OIP who will consider scope of IMT response	OHA PIO activates communications plan, prepares press releases, plans social media campaign, provides updates to OHA leadership and other key stakeholders

	harm reduction measures and hepatitis A and hepatitis B vaccination, and increase awareness of local resources for MOUD and SUD treatment.		