

19-ID-06**Committee:** Infectious Disease**Title:** Revision of the Case Definition for Hepatitis C

☒ Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: 15-ID-03.

Synopsis: This position statement updates the confirmed and probable acute, and probable chronic case definitions for hepatitis C (previous position statement 15-ID-03) through modification of clinical/laboratory criteria and recommends that hepatitis C continue to be nationally notifiable.

I. Statement of the Problem

The revision of the hepatitis C acute classification is being proposed to address the following issues: Even with improvements from the prior revision of the HCV case classification, most acute cases are not captured and therefore the scope of the epidemic among people who inject drugs is not well understood. This revision increases the sensitivity of case classification based on current understanding of the disease. Use of bilirubin test results are proposed to allow for objective measures of jaundice as has been approved for other acute viral hepatitis infections. Clarification is made as to classification of chronic probable cases in consideration of NAT for HCV RNA testing.

II. Background and Justification

Hepatitis C is a major public health issue that causes higher annual mortality than 60 other nationally notifiable diseases combined, including HIV (1). The 2015 Revision of the Case Definition of Hepatitis C for National Notification position statement (2) that established revised case classifications for acute and chronic hepatitis C virus (HCV) infection continued to require the discrete onset of symptoms suggesting acute hepatitis, even though 70-80% of people acutely infected with HCV are asymptomatic (3). The symptoms that were included in the classification were not all strictly related to acute hepatitis (e.g. headache) which has led to variable practice in case classification between jurisdictions, as has interpretation of “discrete onset.” Use of a strict definition for acute HCV infection has led to more specific classification at the expense of sensitivity. This has, in part, allowed most cases of acute HCV to not be captured as such. For example, while most jurisdictions have seen a marked increase of cases in younger age groups due to the opioid epidemic, most of those cases have not been identified as acute cases. While CDC corrects for this in reporting estimates of acute infection (4), these rates are still lower than would account for the number of cases in the younger cohort. This has led to a national underestimate of the scope of the problem of HCV among people who inject drugs. Curative treatments are now available for HCV, and recent evidence suggests that treatment during the acute phase of illness may be achieved in a shorter, and therefore less expensive, time frame (5). However, currently treatment with direct acting HCV antivirals is not recommended for people while acutely infected until spontaneous clearance can be assessed, although close medical monitoring is recommended for this population. (6) Treatment of people with recent acute HCV infection, particularly for those exposed via injection drug use, may support prevention efforts by reducing viremia among people with ongoing risk (7). Treatment restrictions, put in place initially to control costs, have been eliminated or reduced in a number of jurisdictions, although some still remain (8). Expanding treatment to people who are actively using drugs will likely lead to some reinfection among at-risk populations. Cases of acute HCV infection due to reinfection were not possible to report to CDC under the 2015 position statement. Adoption of a more sensitive classification will allow jurisdictions to report a higher volume of acute HCV infection that is more in line with what is known to be occurring. As the reporting of negative NAT for HCV RNA test results has become more widely adopted, a clarification is being made regarding the classification of chronic probable cases of HCV infection. The prior revision of the HCV classification did not take into account the presence of negative NAT for HCV RNA test results which has led to variable practice in interpreting and reporting those cases.

III. Statement of the desired action(s) to be taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for hepatitis C.
 - A. Utilize standard sources (e.g. reporting*) for case ascertainment for acute and chronic HCV infection. Surveillance for acute and chronic HCV infection should use the recommended sources of data to the extent of coverage presented in Section V.
 - B. Utilize standardized criteria for case ascertainment for acute and chronic HCV infection presented in Section VI and Table VI in Technical Supplement.
 - C. Utilize standardized criteria for case classification for acute and chronic HCV infection presented in Sections VII and Table VII in Technical Supplement.
2. Utilize standardized criteria for case ascertainment and classification (based on Sections VI and VII and Technical Supplement of accompanying position statement) for hepatitis C and retain hepatitis C on the *Nationally Notifiable Condition List*
 - ☐ Immediately notifiable, extremely urgent (within 4 hours)
 - ☐ Immediately notifiable, urgent (within 24 hours)
 - ☒ Routinely notifiable
 - ☐ No longer notifiable
3. CSTE recommends that all States and Territories enact laws (statute or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.
4. Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: the National Notifiable Diseases Surveillance System (NNDSS) is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends a new condition be made nationally notifiable, CDC must obtain Office of Management and Budget Paperwork Reduction Act (OMB PRA) approval prior to accepting case notifications for the new condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new MMWR year following the CSTE annual conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMGs.
5. CDC should publish data on acute and chronic HCV infection as appropriate (see Section IX for additional information).

NNC data sharing/release and print criteria

CSTE recommends the following case statuses be included in the CDC Print Criteria:

- ☒ Confirmed
 - ☒ Probable
 - ☐ Suspect
 - ☐ Unknown
6. CSTE recommends that all jurisdictions (e.g. States, Localities, or Territories) with legal authority to conduct public health surveillance follow the recommended methods outlined in this recommendation and in the accompanying standardized surveillance position statement.

*Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local, state, or territorial public health. Note: notification is addressed in a Nationally Notifiable Conditions Recommendation Statement and is the process of a local, state, or territorial public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* TO CDC.

**Notification: process of a local or state public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* to CDC.

IV. Goals of Surveillance

The main goals of hepatitis C surveillance are to provide information on the temporal, geographic, and demographic occurrence of hepatitis C to facilitate its prevention and control, and to provide information about population burden of disease to inform policy and planning.

V. Methods for Surveillance: Surveillance for acute and chronic HCV infection should use the recommended sources of data and the extent of coverage listed in Table V.

The majority of hepatitis C cases are identified through laboratory and healthcare provider (e.g., clinicians and hospitals) reporting. Additional cases may also be ascertained from supplemental data sources including death certificates, hospital discharge or outpatient records, and electronic medical records (as referenced in Table V).

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of acute and chronic HCV infection.

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers), specify:		
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone survey		
School-based survey		
Other, specify: Birth certificates	X	

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VI. Criteria for case ascertainment

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

Report any person with or without symptoms that meets the following criteria for reporting:

A1. Clinical Criteria for Reporting N/A

A2. Laboratory Criteria for Reporting

A person who has tested positive for:

- Antibodies to hepatitis C virus (anti-HCV) OR
- RNA of hepatitis C virus by nucleic acid testing, OR
- Hepatitis C viral antigen(s).

A3. Epidemiologic Linkage Criteria for Reporting

None

A4. Vital Records Criteria for Reporting

- A person whose death certificate lists hepatitis C as a cause of death or a significant condition contributing to death.
- A person who is listed as a birth mother with hepatitis C infection on the birth certificate of a newborn.

A5. Other Criteria for Reporting

A person whose healthcare record contains a diagnosis of hepatitis C infection.

B. Disease-specific data elements to be included in the initial report

Symptoms of viral hepatitis:

Most people with acute hepatitis C infection are asymptomatic. Twenty percent of people will develop jaundice during the acute phase of illness. Other symptoms may include clay colored stools, dark urine, fever, malaise, anorexia, and nausea. Most people with chronic HCV infection are also asymptomatic until later in the disease process when there has been significant damage to the liver.

Serum alanine aminotransferase (ALT) levels

Total bilirubin levels

Epidemiological risk factors:

For acute HCV infections, cases should be interviewed to determine relevant risk history. Information to obtain includes (see section VII B for considerations on relevant timing of risk history):

Injection drug use

Intranasal drug use

Receipt of a blood transfusion, tissue product, or organ transplant

Surgery (other than oral)

Dental work or oral surgery

Hemodialysis

IV infusions or injections in an outpatient setting

Accidental stick/puncture with a needle or other object contaminated with blood

Employed in a medical, dental, or other field involving contact with human blood or other bodily fluids

Sexual activity that may have resulted in blood exposure

Receipt of a body piercing

Receipt of a tattoo

Other exposure to blood (not including risk factors listed above)

VII. Case Definition for Case Classification**A. Narrative: Description of criteria to determine how a case should be classified.**

All HCV cases in each classification category should be >36 months of age, unless known to have been exposed non-perinatally.

A1. Clinical Criteria

One or more of the following:

Jaundice, OR

Peak elevated total bilirubin levels ≥ 3.0 mg/dL, OR

Peak elevated serum alanine aminotransferase (ALT) levels >200 IU/L,

AND

The absence of a more likely diagnosis (which may include evidence of acute liver disease due to other causes or advanced liver disease due to pre-existing chronic HCV infection or other causes, such as alcohol exposure, other viral hepatitis, hemochromatosis, etc.)

A2. Laboratory Criteria

Confirmatory laboratory evidence:

Positive hepatitis C virus detection test: Nucleic acid test (NAT) for HCV RNA positive (including qualitative, quantitative, or genotype testing), OR

A positive test indicating presence of hepatitis C viral antigen(s) (HCV antigen)

Presumptive laboratory evidence:

A positive test for antibodies to hepatitis C virus (anti-HCV)

A3. Epidemiologic Linkage

No epidemiologic linkage is required for case classification.

A4. Case Classifications

Acute Confirmed:

A case that meets clinical criteria and has confirmatory laboratory evidence,

OR

A documented negative HCV antibody followed within 12 months by a positive HCV antibody test (anti-HCV test conversion) in the absence of a more likely diagnosis,

OR

A documented negative HCV antibody OR negative hepatitis C virus detection test (in someone without a prior diagnosis of HCV infection) followed within 12 months by a positive hepatitis C virus detection test (HCV RNA test conversion) in the absence of a more likely diagnosis,

Acute, probable

A case that meets clinical criteria and has presumptive laboratory evidence,

AND

Does not have a hepatitis C virus detection test reported,

AND

Has no documentation of anti-HCV or HCV RNA test conversion within 12 months,

Chronic, confirmed

A case that does not meet OR has no report of clinical criteria,

AND

Has confirmatory laboratory evidence,

AND

Has no documentation of anti-HCV or HCV RNA test conversion within 12 months.

Chronic, probable

A case that does not meet OR has no report of clinical criteria,

AND

Has presumptive laboratory evidence,

AND

Has no documentation of anti-HCV or RNA test conversion within 12 months,

AND

Does not have an HCV RNA detection test reported.

B. Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance

A new acute case is an incident case that is over the age of 36 months and has not previously been reported meeting case criteria for chronic hepatitis C or for whom there is laboratory evidence of re-infection. Cases under the age of 36 months should be classified under the Perinatal HCV Position Statement (17-ID-08) unless the exposure mode is not perinatal (e.g., healthcare acquired).

All jurisdictions are encouraged to track negative HCV viral detection tests to document both spontaneous clearance of infection or sustained viral response to HCV treatment. Cases that have evidence of having cleared the infection at time of initial report or are considered false positive should not be reported to CDC.

Acute cases determined via anti-HCV test conversion do not need to have a positive HCV viral detection test reported to be considered confirmed acute cases.

A new probable acute case may be reclassified as confirmed acute if a positive HCV viral detection test is reported in the same reporting year (e.g. prior to CDC closing reporting for the calendar year).

Collection of risk history data is recommended for probable and confirmed acute HCV cases. Timing of risk history data to collect ranges from 2 weeks to 12 months prior to symptom onset or diagnosis. The time frame to employ depends on the method of classification (e.g. if a case meets clinical criteria and has a positive HCV detection test, a risk history time frame of 2 weeks to 6 months following onset should be used; for a case classified via anti-HCV test conversion or HCV RNA test conversion, 2 weeks to 12 months following onset should be considered).

If evidence indicating resolution of infection is received after a confirmed acute or confirmed chronic case has been reported to CDC, the case report does not need to be modified as it was a confirmed case at the time of initial report. However, negative HCV viral detection test results received on confirmed acute and chronic cases, subsequent to an initial positive result, should be appended to case reports, as feasible, and considered for the purpose of data analysis by each jurisdiction.

Evidence for re-infection may include a case of confirmed chronic HCV infection that has at least two sequential negative HCV viral detection tests reported, indicative of treatment initiation and sustained virologic response, followed by a positive HCV viral detection test. Under current treatment recommendations, those two negative tests should be at least three months apart, however, the timing may change as standard of care for HCV treatment evolves. Other evidence of reinfection should be considered, including a report of a new genotype on a case that has previously cleared a different genotype. Jurisdictions are encouraged to ensure that cases of HCV treatment failure are not classified as new cases of HCV infection to the extent that it can be determined. Jurisdictions tracking re-infection should also consider collecting data on prior treatment completion (when relevant and possible to document), treatment failure, change in reported genotype if that applies, and the known time frame for reinfection.

For both probable acute and probable chronic cases, the presence of a negative HCV viral detection test result, in the absence of criteria that would allow for confirmation, indicates that a case should not be classified as probable acute or probable chronic and should not be reported to CDC.

A new chronic case is a newly reported case that does not have evidence of being an acute case of HCV infection. A confirmed acute case may be classified as a confirmed chronic case if a positive HCV viral detection test is reported one year or longer after acute case onset. A confirmed acute case may not be reported as a probable chronic case (i.e. HCV antibody positive, but with an unknown HCV viral detection test). For purposes of incidence and prevalence calculations, confirmed acute and chronic HCV cases should be counted.

Jurisdictions are also encouraged to track and classify possible re-infection cases that may have been previously reported to CDC as a confirmed or probable chronic HCV infection case. Jurisdictions tracking re-infection should also consider collecting data on prior treatment completion (when relevant and possible to document), treatment failure, change in reported genotype if that applies, and the known time frame for reinfection.

VIII. Period of Surveillance

Surveillance for acute and chronic HCV infection is ongoing.

IX. Data sharing/release and print criteria

1. CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:

- ☒ Confirmed
- ☒ Probable
- ☐ Suspect
- ☐ Unknown

* Which case statuses are included in the case counts constitute the "print criteria."

2. Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report (<http://www.cste2.org/webpdfs/drgwgreport.pdf>) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.
- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

X. Revision History

Position Statement ID	Section of Document	Revision Description
15-ID-03	Section VII A1 – Clinical Criteria	EDITED to remove symptom requirement and include total bilirubin results
15-ID-03	Section VII A4 – Confirmed Acute Classification	EDITED clinical data requirements
15-ID-03	Section VII B – New Case Criteria	EDITED to include age limits and reinfection case criteria
15-ID-03	Table VII – Clinical Criteria for Confirmed and Probable Acute Cases	EDITED to remove symptoms and include total bilirubin test results and clarify role of negative HCV NAT test results with chronic cases
15-ID-03	Table VII – Criteria to Report a New Case	EDITED to remove limitation on reporting reinfection

XI. References

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Technical Supplement

Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Hepatitis C Virus
<i>Laboratory Criteria for Reporting</i>	
Antibodies to hepatitis C virus (anti-HCV) Positive test for hepatitis C antigen(s)*	S
Nucleic acid test (NAT) for HCV RNA positive	S
Positive test for hepatitis C antigen(s)*	S
<i>Vital Records Criteria for Reporting</i>	
Death certificate lists hepatitis C	S
Birth certificate lists birth mother as having hepatitis C	S
<i>Other Criteria for Reporting</i>	
Healthcare record contains a diagnosis of hepatitis C	S

Notes:

S = This criterion alone is SUFFICIENT to report a case.

* When and if a test for HCV antigen(s) is approved by FDA and available.

Table VII. Classification Table: Criteria for defining a case of Hepatitis C.

Criterion	Acute				Chronic	
	Confirmed			Probable	Confirmed	Probable
Clinical Evidence						
Jaundice	O			O		
Total bilirubin ≥ 3.0 mg/dL	O			O		
ALT >200 IU/L	O			O		
The absence of a more likely diagnosis	N	N	N	N		
> 36 months of age, unless known to have been exposed non-perinatally	N	N	N	N	N	N
Does not meet or has no report of clinical criteria					N	N
Laboratory Evidence						
Positive anti-HCV antibody				N		N
Positive NAT for HCV RNA test (including quantitative, qualitative, and genotype)	O				O	
Positive HCV antigen test	O				O	
Absence of a negative HCV viral detection test				N		N
A documented negative HCV antibody test result followed within 12 months by a positive HCV antibody or positive HCV viral detection test result		N				
A negative HCV viral detection test result followed within 12 months by a positive HCV viral detection test if not previously reported as having HCV infection			N			
Criteria to distinguish a new case						
Not previously reported as an acute case within one year	N	N	N	N	N	N
Not previously reported as a chronic case unless there is evidence of having cleared HCV infection since the initial report					N	N

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Notes:

N = All "N" criteria in the same column are NECESSARY to classify a case. A number following an "N" indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the absence of criterion as a necessary component.

O = At least one of these "O" (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) **in the same column**—in conjunction with all "N" criteria in the same column—is required to classify a case. A number following an "O" indicates that this criterion is only required for a specific disease/condition subtype.