

Signs, Symptoms, and Clinical Manifestations

This document was developed by the Data Standardization Work Group (DSWG) of the Council of State and Territorial Epidemiologists (CSTE) Surveillance Practice and Implementation Subcommittee (SPIS) as a part of a larger data harmonization effort. It will be published and maintained in a repository on the CSTE website.

More information about the DSWG and data harmonization can be found here: [link to DSWG Core Surveillance Project Brief (pending)].

Background

Signs, symptoms, and clinical manifestations are often-overlapping concepts that are key to public health surveillance to describe cases of disease, establish trends, and identify potential outbreaks. Although dictionary definitions of signs and symptoms draw a distinction between those two terms, clinical manifestations is more all-encompassing and may be used as a synonym for either term.

To support collection of this information during a case investigation, questions about a person's clinical manifestations may be listed out individually in a surveillance system to ensure as much information as possible is collected. However, within the Message Mapping Guides (MMGs) used to define the structure for case notifications to CDC, a repeating group for either "signs and symptoms" or "clinical manifestations" is the most used structure for this type of information. The repeating group structure is essentially the same, regardless of if it is called signs and symptoms (Figure 1) or clinical manifestations (Figure 2). There are no MMGs that include both types of repeating groups.

Data Element (DE) Name	DE Identifier Sent in HL7 Message	Data Element Description	Value Set Name (VADS Hyperlink)
START: Signs and Symptoms Repeating Group			
Signs and Symptoms	56831-1	Sign and symptoms associated with the illness being reported	Signs and Symptoms (Mumps)
Signs and Symptoms Indicator	INV919	Indicator for associated signs and symptoms	Yes No Unknown (YNU)
END: Signs and Symptoms Repeating Group			

Figure 1. Data elements in Signs and Symptoms Repeating Group from the Mumps MMG.

Data Element (DE) Name	DE Identifier Sent in HL7 Message	Data Element Description	Value Set Name (VADS Hyperlink)
START: Clinical Manifestations Repeating Group			
Clinical Manifestation	INV929	Clinical manifestation of Lyme disease	Clinical Manifestations (Lyme)
Clinical Manifestation Indicator	INV930	For each clinical manifestation reported, indicate whether the subject developed the specified manifestation as a result of the illness.	Yes No Unknown (YNU)
END: Clinical Manifestations Repeating Group			

Figure 2. Data elements in the Clinical Manifestations Repeating Group from the Lyme Disease MMG.

The primary data element in the repeating group is associated with a unique value set that captures the signs and symptoms or clinical manifestations that are relevant to the condition being reported. In both types of repeating groups, the concepts included in the associated value sets range from more general terms (e.g., fever, headache, cough) to more condition-specific signs (e.g., thrombocytopenic disorder, submandibular salivary gland swelling). Most concepts are condition-specific and included in only one value set per repeating group.

An alternative structure to the repeating group is for any type of clinical finding to be included in the MMG as an individual data element. This structure is used in the Arboviral MMG, in which a “Clinical Section” contains approximately 30 discrete data elements representing various clinical findings. Each data element is associated with a Yes/No/Unknown value set to indicate if that finding was present (Figure 3). A third structure not commonly used for signs, symptoms, or clinical manifestations is the repeating element. This would be a single data element with a value set that lists all clinical findings appropriate to the condition, and the ability to “select all that apply” to indicate a positive response for findings that are present.

PHIN Variable	Data Element (DE) Name	Data Element Description	Value Set Name (VADS Hyperlink)
START: Clinical Section			
386661006	Fever	Fever	Yes No Unknown (YNU)
43724002	Chills or Rigors	Chills/ Rigors	Yes No Unknown (YNU)
271795006	Fatigue or Malaise	Fatigue and Malaise	Yes No Unknown (YNU)
271807003	Rash	Rash	Yes No Unknown (YNU)
68962001	Myalgia	Myalgia	Yes No Unknown (YNU)
57676002	Arthralgia	Arthralgia	Yes No Unknown (YNU)
3723001	Arthritis	Arthritis	Yes No Unknown (YNU)
25064002	Headache	Headache	Yes No Unknown (YNU)
44695005	Paralysis or Paresis	Paralysis or Paresis	Yes No Unknown (YNU)
161882006	Stiff Neck	Stiff Neck	Yes No Unknown (YNU)

Figure 3. Sample of the data elements in the Clinical Section of the Arboviral MMG.

When compared to other data classes, there is relatively better standardization in how information on signs, symptoms, and clinical manifestations is transmitted to CDC. However, as described above, variations in the structure and naming of that data remain. In discussions surrounding these concepts, the DSWG considered the following questions:

- Is it necessary to maintain the signs and symptoms and clinical manifestations repeating groups as distinct repeating groups? If not, how should a single data class representing this concept be named and defined?
- For this data class, is the repeating group the preferred structure?
- Is there a need for an overall data element representing whether or not the patient was symptomatic?
- Should information such as condition complications, sequelae, and infection types be defined and standardized as additional core data elements, or implemented in a condition-specific manner as needed?

Core Surveillance Immunization Data Elements for Routine Case Notifications

The data elements below are those that the DSWG recommends be defined as core surveillance data for case notifications to CDC. Data elements marked with an asterisk (*) did not reach the 80% consensus mark within the group but were supported by more than half of the participants. These are included here as core data elements with weak support from the DSWG. For each of these data elements, there is no pre-defined default value for what should be transmitted when the data element has not been populated. Refer to Tables 1-3 below for definitions and additional information for each data element.

- Clinical Manifestations (as a data class)
- Summative Clinical Manifestations Indicator*
- Symptomatic Indicator*

Clinical Manifestations was voted as core as a data class rather than a data element. The individual clinical manifestations for a condition are unique, but the group agreed with consensus that there should be a standard place in a message mapping guide for sending this information for all applicable conditions. The structure of the Clinical Manifestations data class was discussed along with the data classes of Exposure, Risks, and Underlying Conditions. From participants from CDC there was a strong preference for the repeating group structure, as it is easier to make adaptations to data elements without a lengthy review process and updates to value sets may not require jurisdictions to go through an onboarding process for an updated MMG. From jurisdictions, the preferred structure was split between repeating group, repeating element, and individual questions, likely reflecting differences in surveillance systems used across the US. Ultimately, consistency in structure across conditions for a data class is what's most important, more than what the exact structure is.

One of the perceived benefits of the repeating group structure is that additional "child" data elements can be added into a data class more simply. However, detailed structure conversation revealed that a repeating group dependency structure of parent/child/child is more feasible than parent/child/grandchild. To demonstrate with an example: a parent element in a repeating group is to select a clinical manifestation (e.g. fever), and then the child element indicates yes/no/unknown for whether the person had a fever. Adding an additional data element of onset date is simpler if it is not dependent on the answer of "yes" (making it a grandchild) and is instead an additional answer to fever (making it a second child).

For Clinical Manifestations, from an epidemiologic perspective the group was polled on the importance of transmitting "No" and "Unknown" responses for each individual clinical manifestation. The majority of the group (74%) agreed that it is at least potentially helpful to allow for a structure that transmits this level of granularity. This excludes the structure of repeating element for this data class, leaving individual data elements or the repeating group format. Given the benefits outlined above for the flexibility of the repeating group format, this is likely the most advantageous structure for the Clinical Manifestations data class.

There was a long discussion regarding the Summative Clinical Manifestations Indicator and the Symptomatic Indicator. The Summative Clinical Manifestations Indicator conveys if the person had any of the clinical manifestations specified within the Clinical Manifestations data class. However, clinical manifestations may not all be perceived as symptoms, so someone with some clinical manifestations (e.g. low white blood cell count) may still consider themselves asymptomatic. The Symptomatic Indicator conveys if the person is symptomatic and is part of the Minimum Dataset for Case Notification to CDC during an Emergency. Both data elements were perceived by the group to be important for different reasons, and while over half the group believed both should be core neither reached 80% consensus.

The summative data class indicator may make it unnecessary to transmit information about individual manifestations if the overall answer is “no” or “unknown”. In addition, whether a person has any of the clinical manifestations associated with a condition may be epidemiologically important. Separately, whether or not a person with a condition considers experiences symptoms may be important from a public education perspective. Depending on the listed clinical manifestations these data elements may transmit the same information. Implementation of these data elements should make considerations for potential redundancy.

Also discussed on the call were clinical data elements currently transmitted as “Complications”, “Clinical Findings”, or “Infection Type”. These data classes convey information that is similar to Clinical Manifestations but routinely captured as separate data elements within MMGs. The group did not support making a separate core data class for this type of clinical information. However, while it should be handled in a condition-specific manner, the group does support the standardization of structure of these data elements across MMGs when used. Several other clinical manifestations-related data elements are included in existing MMGs but are only relevant to specific conditions and would be outside the scope of core surveillance data for case notifications to CDC. Such data elements were mentioned briefly during workgroup meetings but not discussed at length in the context of core surveillance data.

The recommendations outlined in this document focus on data element definitions and their associated value sets. Implementation of these recommendations will be addressed in future guidance. These future implementation notes will include recommendations on setting up and mapping data elements at the jurisdictional level, as well as how CDC program areas should incorporate these recommendations when developing new and updated reporting mechanisms, such as case report forms and message mapping guides.

Table 1. Core Surveillance Data Class for Routine CDC Case Notification – Clinical Manifestations

Clinical Manifestations	
Definition	Clinical manifestations, including signs and symptoms, associated with the condition being reported
Standard Code for Transmission to CDC	Utilizing the repeating group format, clinical manifestations would be transmitted as two data elements: - Clinical Manifestations- LOINC: 56831-1 Problem associated signs and symptoms - Clinical Manifestations Indicator- TBD
Value Set or Coding System for Transmission to CDC	Individual clinical manifestations should be represented using SNOMED-CT when available. Local codes may be created as needed. The Clinical Manifestations Indicator would take values of Yes/No/Unknown.
Abstracted/ Derived/ Created	Abstracted
Derived from (examples)	N/A
Recommendations for Input Data Source(s)	Case investigation eCR
Notes	This data class includes transmission of signs, symptoms, and any other clinical manifestations associated with a condition. The value set for which clinical manifestations are associated with a condition is condition dependent. This value set may contain a response option for “other, please specify” to capture any associated clinical manifestations.
Data Source Details*	
eCR CDA	HL7 CDA R2 Implementation Guide: Public Health Case Report, Release 2 STU Release 1.1 - US Realm - ClinicalDocument/component/Problem Section/Problem Concern Act/Problem Observation/code - ClinicalDocument/component/Problem Section/Encounter Diagnosis/Problem Observation/code HL7 CDA R2 Implementation Guide: Public Health Case Report – eICR Release 2, STU Release 3.1 - US Realm Available as a coded field: - ClinicalDocument/component/Problem Section/Problem Concern Act/Problem Observation/code - ClinicalDocument/component/Problem Section/Encounter Diagnosis/Problem Observation/code Uncoded text that may contain relevant information: - ClinicalDocument/component/Reason for Visit Section/text - ClinicalDocument/component/Review of Systems Section/text
eCR FHIR	Resource Profile: eICR Composition - Composition.section:sliceProblemSection - Composition.section:sliceHistoryOfPresentIllnessSection - Composition.section:sliceReviewOfSystemsSection Resource Profile: US Public Health Condition

	Condition.code
ELR	N/A
USCDI v4	Problems - Definition: Condition, diagnosis, or reason for seeking medical attention. - Applicable Vocabulary Standard(s): SNOMED-CT, ICD-10-CM - Part of the Problems data class.
USCDI+ Public Health: Case Reporting Use Case	Symptoms (list) - Definition: List of patient symptoms (structured) for the reportable event. - Part of the Problems data class.

* Additional information on input data sources for immunizations data can be found in Appendix A.

Table 2. Core Surveillance Data Element for Routine CDC Case Notification – Summative Clinical Manifestations Indicator

Summative Clinical Manifestations Indicator	
Definition	Indicator that the person experienced any listed clinical manifestations associated with the condition being reported
Standard Code for Transmission to CDC	TBD
Value Set or Coding System for Transmission to CDC	Yes/No/Unknown
Abstracted/ Derived/ Created	Derived
Derived from (examples)	If a person has any listed clinical manifestations associated with the condition being reported, the response would be “Yes”. If the person does not have any of the listed clinical manifestations, this response is “No”. If this is not known, the response is “Unknown”.
Recommendations for Input Data Source(s)	Case Investigation eCR
Notes	This data element is a summative indicator that communicates if the person has any clinical manifestations associated with the condition as listed in the Clinical Manifestations value set. If the Clinical Manifestations value set includes a response option for collecting “other” manifestations, the definition of this data element would encompass any clinical manifestations associated with the condition regardless of explicit inclusion in the value set.
Data Source Details	
eCR CDA	N/A
eCR FHIR	N/A
ELR	N/A
USCDI v4	N/A
USCDI+ Public Health: Case Reporting Use Case	N/A

Table 3. Core Surveillance Data Element for Routine CDC Case Notification – Symptomatic Indicator

Symptomatic Indicator	
Definition	Indicator that the person was symptomatic with symptoms associated with the condition being reported
Standard Code for Transmission to CDC	TBD
Value Set or Coding System for Transmission to CDC	Yes/No/Unknown
Abstracted/ Derived/ Created	
Derived from (examples)	N/A
Recommendations for Input Data Source(s)	Case investigation eCR
Notes	If the value set for Clinical Manifestations associated with a condition does not include the response option “other”, it is possible that the listed manifestations may only include symptoms perceived by the patient. During implementation of the Clinical Manifestations data element, it should be considered if this symptomatic indicator is redundant.
Data Source Details*	
eCR CDA	N/A
eCR FHIR	N/A
ELR	N/A
USCDI v4	N/A
USCDI+ Public Health: Case Reporting Use Case	N/A

* Additional information on input data sources for immunizations data can be found in Appendix A.

Appendix A. Input Data Sources for Immunization Data

Electronic Case Reporting (eCR)

Data related to clinical manifestations of a condition may be captured in several locations within an eCR transmission. The most common templates used to transmit this data in an electronic initial case report (eICR) are as follows.

- The Problem Observation template reflects a discrete observation about a patient's problem using SNOMED or ICD10 codes. This template is used across multiple sections within the eICR, and the ones most relevant to the current condition are the Problem Concern Act and the Encounter Diagnosis.
- Codes in the Problem Concern Act may persist within eICR documents as active, even if entered during previous encounters. Utilizing the fields of effectiveTime/high and effectiveTime/low may be necessary to ensure listed codes are relevant to the current instance of an illness.
- Within the STU Release 3.1 additional document sections may transmit text based narratives that contain information about clinical manifestations. These include the Reason for Visit Section and Review of Systems Section.

Electronic Laboratory Reporting (ELR)

Information on clinical manifestations is typically not collected or transmitted in ELR. Relevant content may be found in or derived from the Reason for Study field (OBR-31), but this field is unlikely to be comprehensive and may contain information unrelated to clinical manifestations (such as exposures or diagnoses of medical conditions).

United States Core Data for Interoperability (USCDI) and USCDI+

The Problems data class contains the following data elements that may relate to the transmission of clinical manifestations information:

Table 4. Data elements within the Problems data class of USCDI or USCDI+ that relate to the transmission of clinical manifestations.

Data Element	Definition	Status	USCDI+
Problems	Condition, diagnosis, or reason for seeking medical attention.	USCDI V1 and subsequent	No
Date of Diagnosis	Date of first determination by a qualified professional of the presence of a problem or condition affecting a patient.	USCDI v2 and subsequent	Yes – Case Reporting
Date of Resolution	Date of subsiding or termination of a symptom, problem, or condition.	USCDI v2 and subsequent	No
Date of Onset	Date when a problem/condition started.	Level 2	Yes – Case Reporting
Symptoms (list)	List of patient symptoms (structured) for the reportable event.	N/A	Yes – Case Reporting

The USCDI guidance indicates that the applicable value sets and codes for Problems should utilize the SNOMED-CT and ICD-10-CM coding systems. While Date of Diagnosis and Date of Resolution are not part of the core data elements recommended here, these data elements may contain information that can help interpret if a problem is historical or associated with a current instance of a condition. Date of Onset is not yet included within a version of USCDI and is listed as maturity level 2, indicating that it has broad standardization and guidance for its collection, existing terminology standards or technical

specifications for its representation, is already being captured and exchanged in multiple EHRs, and can be applied to most care settings.

Within USCDI+ there is a Problems data class, but the data element “Problems” is replaced by a data element “Symptoms (list)”, specifying that this is a structured list of patient symptoms for the reportable event. Date of Onset is also included in USCDI+ for Case Reporting, where it is defined as the date when a problem/condition started.

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