

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 (signs being objective evidence of disease especially as observed by the physician versus symptoms reported subjectively by the patient¹), clinical manifestations are 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.

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: 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			

¹ Merriam-Webster.com. 2024. <https://www.merriam-webster.com> (16 July 2024)

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

The primary data element in the repeating group has a value set that captures the signs and symptoms or clinical manifestations relevant to the condition being reported. In either repeating group, the concepts included in the value sets range from more common (e.g., fever, headache, cough) to more specific signs (e.g., thrombocytopenic disorder, submandibular salivary gland swelling).

An alternative structure to the repeating group is for any type of clinical manifestation to be included in the MMG as an individual data element. This approach 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 clinical manifestation 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 manifestations appropriate to the condition, and the ability to “select all that apply” to indicate a positive response for findings that are present.

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

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)

There is already some standardization across MMGs 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 signs and symptoms and clinical manifestations as distinct repeating groups? If not, how should a single data class representing this concept be named and defined?
- For this data class, what is 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 should they be 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)
- Clinical Manifestations Data Class Indicator*
- Symptomatic Indicator*

Clinical Manifestations was voted as core as a data class rather than a data element, meaning the group agreed with consensus that there should be a standard place in a message mapping guide for sending information on signs, symptoms, and other clinical manifestations for all applicable conditions. The name “Clinical Manifestations” was chosen over “Signs and Symptoms” as Clinical Manifestations is inclusive of signs and symptoms, as well as other manifestations (such as a laboratory finding like “high white blood cell count”). The individual clinical manifestations for a condition are unique, and the relevant clinical manifestations to be captured for each condition will be defined by CDC programs.

The structure of the Clinical Manifestations data class was discussed in conjunction 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 updates to only a value set can allow changes to be made in an expeditious fashion (without multi-agency federal review) to hasten public health response. Updates made within a value set also 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, the opinion voiced during the workgroup call was that consistency in structure across conditions for a data class is what’s most important, more than what the exact structure is. A majority of the group (74%) supported transmitting “No” and “Unknown” responses for each clinical manifestation due to the level of detail it provides. This favored using either individual data elements or the more flexible 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.

Two indicator values related to clinical manifestations were considered: the Clinical Manifestations Data Class Indicator and the Symptomatic Indicator. The Clinical Manifestations Data Class Indicator conveys if the person had any of the clinical manifestations specified within the Clinical Manifestations data class for the given condition. However, someone with certain clinical manifestations (e.g. low white blood cell count) may still be asymptomatic. The Symptomatic Indicator, separate from the previous variable, conveys if the person is symptomatic and is part of the Minimal Data Necessary for Case Notification During Emergency Response. Distinguishing between the presence of any clinical manifestations and symptomatic status is valuable epidemiologically and for public education. Despite the importance attached to both, neither reached the 80% consensus needed to be considered core, achieving 72% and 69%, respectively. Implementing these elements should consider potential redundancies as they might contain the same information.

The data classes of Complications, Clinical Findings, and Infection Type convey information that is similar to Clinical Manifestations but routinely captured as separate data elements within MMGs. These data classes should be handled in a condition-specific manner, and the structure of these data elements standardized 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 Manifestation- LOINC: 56831-1 Problem associated signs and symptoms - Clinical Manifestation Indicator- CDC Local Code: INV930 Clinical Manifestation Indicator See Interpretation Notes below.
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. These value sets will be defined by CDC programs. The Clinical Manifestation 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 the Clinical Manifestations data class can be found in Appendix A.

Interpretation Notes – Clinical Manifestations Data Class

An example of the two data element repeating group where responses of “Yes” for fever and “No” for cough are transmitted:

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OBX|nn|CWE|INV929^Clinical Manifestation^PHINQUESTION|1|386661006^Fever^SCT||||F
OBX|nn|CWE|INV930^Clinical Manifestation Indicator^PHINQUESTION|1|Y^Yes^HL70136||||F
OBX|nn|CWE|INV929^Clinical Manifestation^PHINQUESTION|2|49727002^Cough^SCT||||F
OBX|nn|CWE|INV930^Clinical Manifestation Indicator^PHINQUESTION|2|N^No^HL70136||||F
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A repeating group structure was noted for its ease in adding "child" data elements. For example, a parent element might denote a clinical manifestation like fever, and a child element could indicate yes/no/unknown regarding its presence (like Clinical Manifestations Indicator in Table 1). An additional data element of onset date would be simpler to add as an additional child (dependent only on the clinical manifestation of “fever”) rather than as a dependent "grandchild" element (dependent on the clinical manifestations indicator value of “yes”).

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

Clinical Manifestations Data Class 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. This data element is distinct from the Symptomatic Indicator as some clinical manifestations can be present when a person is asymptomatic.
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 the person exhibited 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	Abstracted
Derived from (examples)	N/A
Recommendations for Input Data Source(s)	Case investigation eCR
Notes	This variable is distinct from the Clinical Manifestations Data Class Indicator as it captures if a person with a condition is considered symptomatic or asymptomatic. During implementation of the Clinical Manifestations data class for a condition, it should be considered if this Symptomatic Indicator is redundant of the Clinical Manifestations Data Class Indicator. If all values listed within the Clinical Manifestation value set is are symptoms, these indicators would be 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

Appendix A. Input Data Sources for Clinical Manifestations 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 for Problems should utilize the SNOMED-CT and ICD-10-CM coding systems. Although Date of Diagnosis and Date of Resolution are not recommended as core data elements here, they may contain information that can help interpret if a problem is historical or associated with a current 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.

In USCDI+, the Problems data class has a data element “Symptoms (list)” that replaces the data element “Problems”. This data element is defined as 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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