# Ontology of early warning signs of Cytokine Release Syndrome (CRS)

**CRS** 

As defined by:

**Early warning sign** 

## **Definition**

A supraphysiologic response following any immune therapy that results in the activation or engagement of endogenous or infused T cells and/or other immune effector cells

# **Definition**

The change in a characteristic measure over a period of time prior to a critical transition to a clinically diagnosable disease state

DE-RISKING CYTOKINE RELEASE SYNDROME



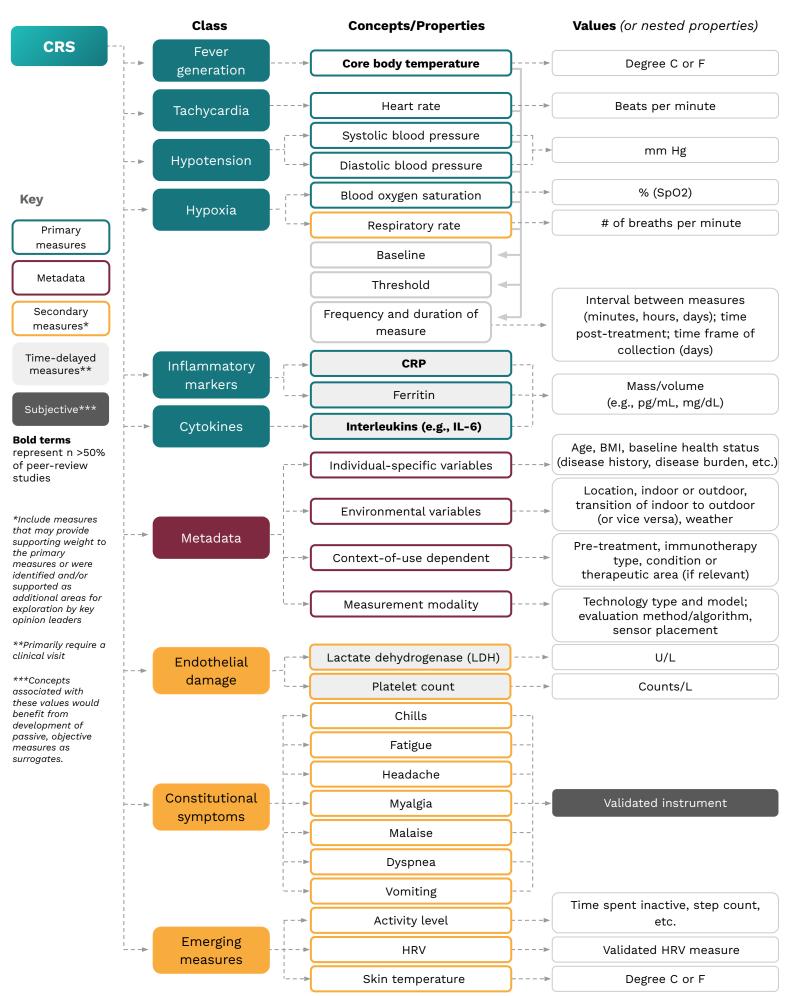
Digital Measures Development



Digital Health Measurement Collaborative Community



# Ontology of early warning signs of Cytokine Release Syndrome (CRS)



# **Measure considerations**

### Fever Generation

Increased core body temperature is a hallmark feature of CRS onset.

### Hypotension

Hypoxia

Drops in blood pressure or oxygen levels are associated with higher grade CRS.

CRP

Ferritin

Interleukins (e.g., IL-6)

IL-6 and other cytokine profiles as well as the surrogates, CRP and ferritin, are inflammatory markers associated with the onset of CRS and may express differently based on several factors including treatment type and disease.

### Metadata

Pre-treatment factors captured in the metadata such as the type and round of treatment, disease type, and disease burden may influence the development of CRS.

- The median onset of CRS for each therapy can inform when CRS may occur.
- Comorbidities such as COPD may be associated with a <u>higher risk</u> of severe CRS.

### Constitutional symptoms

Patients may present with a multitude of symptoms at the time of CRS onset that may be indicative of the onset or presence of CRS. Symptoms may be collected by the clinical staff or reported by the patient or caregiver.

# **Examples of measures in action**

Baseline

**Baseline**: Temperature at pre-infusion time; temperature over last two days

Threshold

**Threshold**: Definition for CRS grade (e.g., fever of 38 °C); two standard deviations from baseline

Frequency and duration of measure

**Frequency**: every four hours (standard of care); continuous monitoring

**Duration**: 14 days (recommended observation period for CRS)

More CRS resources are available to support you.

Full ontology of early warning signs of CRS

Ontology of fever generation

Ontology of tachycardia

Ontology of hypotension

Ontology of hypoxia

Visit the project page