The Office of the National Coordinator for
Health Information Technology

# Synthea<sup>TM</sup> Module Companion Guide

## SEPSIS

**January 2021**

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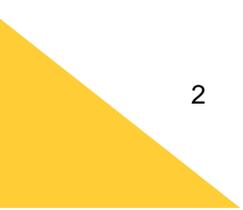
# Introduction

Synthea<sup>TM</sup> is an open-source, synthetic patient generator created by MITRE that models the medical history of synthetic patients. Clinical disease modules are created using a combination of clinical care protocols and publicly available disease incidence and prevalence statistics. Synthea uses these modules to generate individual synthetic patient records, simulating the progression and treatment of disease from birth to death. Synthea Module Companion Guides serve to orient users to a specific Synthea module. The intended audience includes those reviewing a module under development and/or interested in utilizing the module to generate synthetic patient data.

This document summarizes the scope and intent of the Sepsis module. It provides details of the module states and contains a full list of references and data sources used to develop the module.
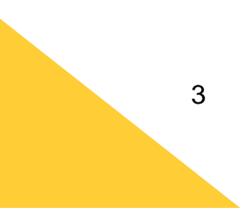
# Module Description

Table 1: Sepsis Module Metadata contains a list of metadata attributes that help describe the module including, but not limited to, module steward, module developer, date of last update, and other descriptive information.

*Table 1: Sepsis Module Metadata*

| Metadata | Description |
|---|---|
| Title | Sepsis |
| Module File Name | sepsis |
| Version Number | 1.0 |
| Last Updated | January 7, 2021 |
| Module Steward | Office of the National Coordinator for Health Information Technology (ONC) |
| Module Developer | Clinovations Government + Health |
| Description | Sepsis is a leading cause of death in critically ill patients in the United States.(1) This module models the treatment of sepsis in patients >=18 years of age. It is based on the Surviving Sepsis Campaign clinical care guidelines for sepsis, including the guidelines for the Hour-1 Bundle for initial resuscitation of sepsis and septic shock.(2) |
| Disclaimer | Synthea<sup>TM</sup> is an open-source synthetic patient generator, created by MITRE, that models the medical history of synthetic patients. This module is developed using the Synthea Module Builder and is limited to the capabilities of Synthea and the Synthea Module Builder. <br><br> This Synthea module is not a clinical guideline, does not establish a standard of medical care, and has not been tested for all potential applications. THIS MODULE IS PROVIDED "AS IS" WITHOUT WARRANTY OF ANY KIND. |
| Related Module(s) | None |
| Reference(s) | Surviving Sepsis Campaign: International Guidelines (2) <br> A Users' Guide to the 2016 Surviving Sepsis Guidelines (3) |
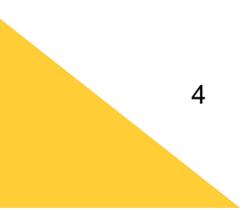
# Module Diagram

A [Synthea](#)<sup>TM</sup> module diagram within the Synthea Module Builder is often large and complex to view because it includes both clinical states and control states. It may be challenging for users to understand and navigate the module within Synthea, especially those who are new to the process. The purpose of the following Visio diagram is to provide a high-level, simplified view of the module contents and flow so users understand the scope and main components of the module before delving into details.

*Figure 1: Sepsis Visio Diagram*
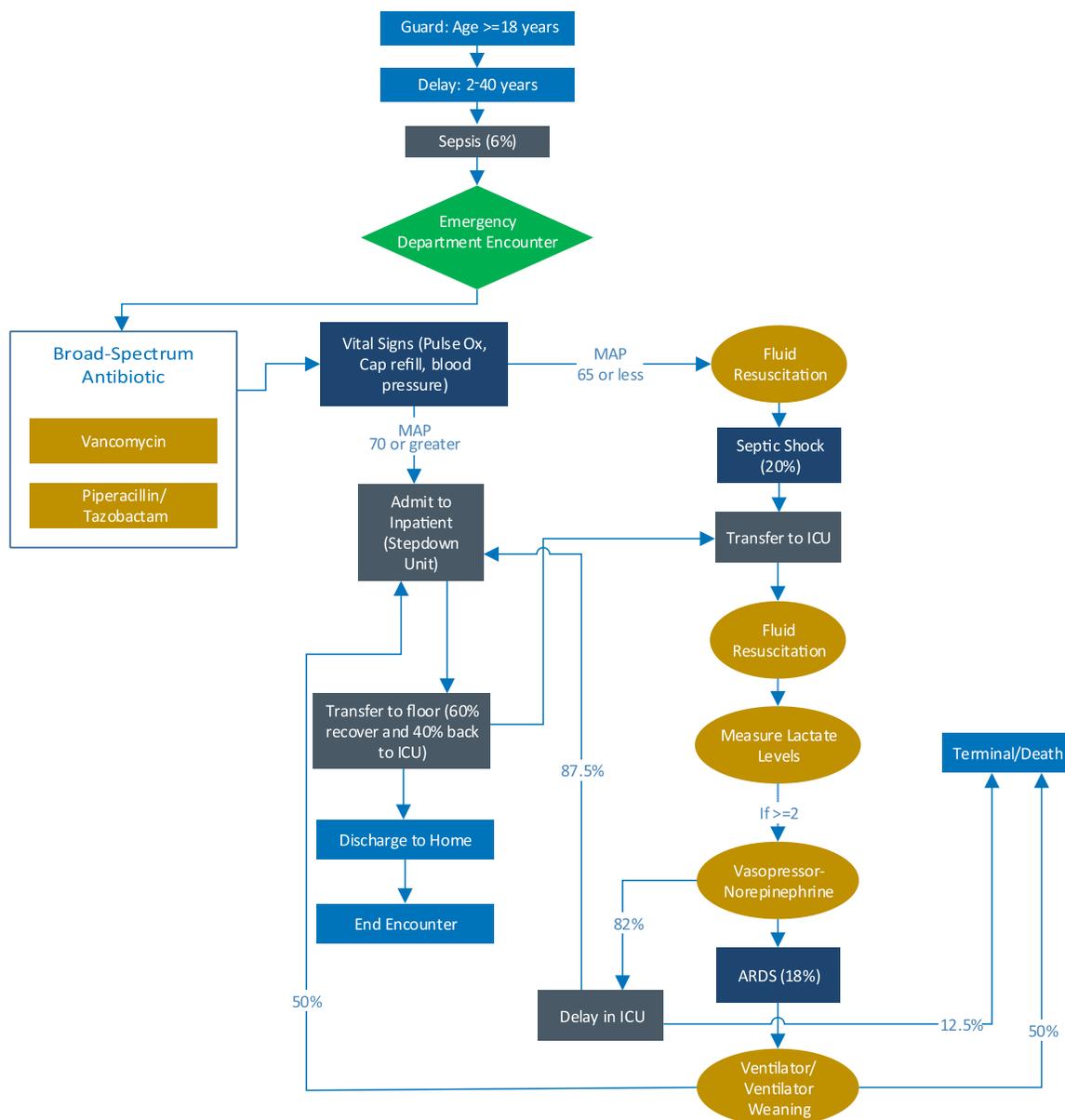
# Module States

Table 2: Sepsis Module States provides details about each clinical state modeled within the module. State Names are modeled in the Sepsis Module. The Type column indicates the Synthea state type used to define the state. State Remarks provide detailed documentation for each state, including notes, references, and data sources used to define probabilities. The Terminology column identifies the standard codes used to model the clinical states.

*Table 2: Sepsis Module States*

| State Name | Type | State Remarks | Terminology |
|---|---|---|---|
| **Initial** | Initial | Initial state of a module required by Synthea. | n/a |
| **Age_Guard** | Guard | This Guard state ensures that the module applies to patients age >=18 years. | n/a |
| **Delay** | Delay | This state delays the onset of sepsis for the patient. Random delay set 2-40 years. | n/a |
| **Sepsis** | Condition Onset | This state diagnoses the patient with sepsis. Probability set to 6% of the Synthea population.<br>Reference: (4) | System: SNOMED-CT<br>Code: 91302008<br>Display: Sepsis (disorder) |
| **Sepsis_ED_Encounter** | Encounter | This state is the Emergency Department (ED) encounter for a patient presenting with sepsis. Direct transition to Blood_Cultures. | System: SNOMED-CT<br>Code: 185347001<br>Display: Encounter for problem (procedure)<br>Reason: Sepsis |
| **Blood_Cultures** | Diagnostic Report | This state will generate a report with positive blood culture results for the patient with sepsis. Whenever possible, blood cultures should be drawn before antibiotics are administered.(5) Direct transition to Administer_Broad_Spectrum_Antibiotics. | System: LOINC<br>Code: 600-7<br>Display: Blood Culture, routine |
| **Administer_Broad_Spectrum _Antibiotics** | Simple | This simple state introduces the administration of antibiotics. The sepsis population directly transitions to the administration of piperacillin/tazobactam and vancomycin. These two drugs are common first-line treatments for sepsis.(6) Both drugs administered based on recommendations on guidelines and confirmed by expert feedback. (7) | n/a |

| State Name | Type | State Remarks | Terminology |
|---|---|---|---|
| **Piperacillin_Tazobactam** | MedicationOrder | This state administers piperacillin/tazobactam to the sepsis patient. Set at 100% of the sepsis population. Direct transition to Vancomycin. | System: RxNorm<br>Code: 1659131<br>Display: piperacillin 2000 MG / tazobactam 250 MG Injection |
| **Vancomycin** | MedicationOrder | This state administers vancomycin to the sepsis patient. Set at 100% of the sepsis population. Direct transition to Vitals_and_Labs. | System: RxNorm<br>Code: 1807510<br>Display: 150 ML vancomycin 5 MG/ML Injection |
| **Vitals_and_Labs** | Simple | This simple state introduces vital signs and laboratory tests for sepsis within the module. Direct transition to Capillary_refill. | n/a |
| **Capillary_refill** | Observation | This state records the capillary refill time of the patient's nailbed. Direct transition to Pulse_oximetry. | System: LOINC<br>Code: 44963-7<br>Display: Capillary refill [Time] of Nail bed |
| **Pulse_oximetry** | Observation | This state records oxygen saturation as a vital sign percentage for the patient with sepsis. Direct transition to Set_Systolic_Blood_Pressure. | System: LOINC<br>Code: 2713-6<br>Display: Oxygen Saturation |
| **Lactate_Level1** | Observation | This state records a lactate level laboratory result for the patient with sepsis in mmol/L. Direct transition to Fluid_Resuscitation. | System: LOINC<br>Code: 59032-3<br>Display: Lactate [Mass/volume] in Blood |
| **Fluid_Resuscitation** | Procedure | This state records patients receiving fluid resuscitation. All sepsis patients will receive fluid resuscitation. To decrease mortality in sepsis patients, patients are treated, by fluid resuscitation with either crystalloid or colloid; vasoactive agents; and intubation, sedation, and paralysis as necessary (8). Direct transition to Check_Septic_Shock. | System: SNOMED-CT<br>Code: 430701006<br>Display: Resuscitation using intravenous fluid (procedure) |
| **Check_Septic_Shock** | Simple | This simple state introduces septic shock in the patient with sepsis. Twenty percent of sepsis patients develop septic shock.(6). Twenty percent of patients will transition to Low_MAP. The remaining 80% of patients will transition to Normal_MAP. | n/a |
| **Low_MAP** | Observation | This state sets the low range for mean arterial pressure (MAP) for the patient to be diagnosed with septic shock. Mean Arterial Pressure range set to 20-60 mmHg. Direct transition to Septic_Shock. | n/a |

| State Name | Type | State Remarks | Terminology |
|---|---|---|---|
| **Normal_MAP** | Observation | This state sets the normal range for the mean arterial pressure for the sepsis patient. Mean Arterial Pressure range set to 70-100mmHg. Direct transition to Admit_to_Inpatient. | n/a |
| **Septic_Shock** | ConditionOnset | This state diagnoses sepsis patients with low blood pressure with septic shock. Direct transition to Transfer_to_ICU. | System: SNOMED-CT<br>Code: 76571007<br>Display: Septic shock (disorder) |
| **Admit_to_ICU** | Procedure | This state is a code to indicate the patient is admitted to the intensive care unit (ICU). Direct transition to Fluid_Resuscitation2. | System: SNOMED-CT<br>Code: 397821002<br>Display: Transfer to ICU (procedure) |
| **Fluid_Resuscitation2** | Procedure | This state records patients receiving fluid resuscitation. All sepsis patients will receive fluid resuscitation. To decrease mortality in sepsis patients, patients are treated, by fluid resuscitation with either crystalloid or colloid; vasoactive agents; and intubation, sedation, and paralysis as necessary (8). Direct transition to Lactate_Level. | System: SNOMED-CT<br>Code: 430701006<br>Display: Resuscitation using intravenous fluid (procedure) |
| **Lactate_Level** | Observation | This state records the lactate level for patients. Lactate may be useful in identifying an otherwise unrecognized population of critically ill patients with normal blood pressure.(9) Although serum lactate is not a direct measure of tissue perfusion, it can serve as a surrogate because increases may represent tissue hypoxia, accelerated aerobic glycolysis driven by excess beta-adrenergic stimulation, or other causes associated with worsening outcomes. Randomized controlled trials have demonstrated a significant reduction in mortality with lactate-guided resuscitation.(10) This state is set to randomly record a level between 0 and 4 for lactate level. Transition to Administer_Vasopressors if lactate level >=2. Otherwise, patients transition to Set_Systolic. | System: LOINC<br>Code: 59032-3<br>Display: Lactate [Mass/volume] in Blood |
| **Administer_Vasopressors** | Simple | This simple state introduces the administration of vasopressors for patients. Direct transition to vasopressin. | n/a |
| **Norepinephrine** | MedicationOrder | This state administers norepinephrine (NE) to the patient. Currently set at 100% of the septic shock population. NE remains the most commonly used vasopressor and is recommended as the first-line agent by the Surviving Sepsis Campaign (SSC) experts. As a strong α-adrenergic agonist, NE increases blood pressure primarily through its vasoconstrictive properties with little effect on heart rate.(11) | System: RxNorm<br>Code: 242969<br>Display: 4 ML norepinephrine 1 MG/ML Injection |

| State Name | Type | State Remarks | Terminology |
|---|---|---|---|
| **Set_Systolic** | VitalSign | This state sets the range for the systolic blood pressure for the patient. Systolic blood pressure range set to 40-120mmHg. Direct transition to Set_Diastolic. | n/a |
| **Set_Diastolic** | VitalSign | This state sets the range for the diastolic blood pressure for the patient. Diastolic blood pressure range set to 40-120mmHg. Direct transition to Record_Blood_Pressure. | n/a |
| **Record_Blood_Pressure** | MultiObservation | This state records the systolic and diastolic blood pressure of the patient. Direct transition to Check_ARDS. | System: LOINC<br>Code: 85354-9<br>Display: Blood Pressure |
| **Check_ARDS** | Simple | This state checks for acute respiratory distress syndrome (ARDS) in the patient with septic shock. The incidence of ARDS is approximately 18% in patients with septic shock, and mortality approaches 50%.(12)<br>Eighteen percent of patients will transition to Acute_Respiratory_Distress_Syndrome_ARDS. Remaining 82% of patients will transition to Delay_in_ICU state. | n/a |
| **Acute_Respiratory_Distress_Syndrome_ARDS** | ConditionOnset | This state diagnoses a certain percentage of septic shock patients with ARDS. All patients diagnosed with ARDS transition to Ventilator state. | System: SNOMED-CT<br>Code: 67782005<br>Display: Acute respiratory distress syndrome (disorder) |
| **Ventilator** | Procedure | This state initiates mechanical ventilation for the ARDS patient. Direct transition to Ventilator_Weaning. | System: SNOMED-CT<br>Code: 40617009<br>Display: Artificial respiration (procedure) |
| **Ventilator_Weaning** | Procedure | This state encompasses weaning from the ventilator for the ARDS patient. Since mortality is 50% for the ARDS patient, 50% of patients transition from this state to Death.(12) The other 50% transition to Delay_in_ICU state. | System: SNOMED-CT<br>Code: 243174005<br>Display: Weaning from mechanically assisted ventilation (procedure) |
| **Delay_in_ICU** | Delay | This state sets a delay of 1-2 days to accommodate an ICU stay. After this delay, 12.5% of patients will die (transition to Death state) and the remaining 87.5% will transition to the Admit_to_Inpatient state to begin the recovery process. | n/a |
| **Death** | Death | This state indicates death of the patient with sepsis. Overall mortality for sepsis is 12.5%.(13) Rate is higher, as noted above, for ARDS patients. Direct transition to Terminal state. | n/a |

| State Name | Type | State Remarks | Terminology |
|---|---|---|---|
| **Admit_to_Inpatient** | Procedure | This state indicates a patient is admitted from the ED to the stepdown unit within a hospital during the same encounter. Direct transition to Delay_3-10_days. | System: SNOMED-CT<br>Code: 449214001<br>Display: Transfer to stepdown unit (procedure) |
| **Delay_3-10_days** | Delay | This state indicates a delay of 3-10 days in the stepdown unit to accommodate a stepdown unit stay. Following this delay, 60% of patients will transition to Transfer_to_ICU to indicate a worsening in their condition, and the other 40% will transfer to Discharge_to_Home state. | n/a |
| **Discharge_to_Home** | EncounterEnd | This state indicates the patient is discharged to home and ends the sepsis encounter. Direct transition to Terminal state. | System: NUBC<br>Code: 01<br>Display: Transfer to stepdown unit (procedure) |
| **Terminal** | Terminal | Ending state required by Synthea. | n/a |

# Module Parameters

Table 3: Sepsis Module Parameters summarizes the probabilities used to construct distributed module states where branching occurs in the module flow. A value of 1.0 indicates 100%; 0 indicates 0%.

*Table 3: Sepsis Module Parameters*

| Parameter | Value | Notes and References |
|---|---|---|
| **Probability of sepsis in patients 18 years of age or older** | 0.06 | Sepsis shown to be present in 6% of hospital admissions, with a sensitivity of 69.7% (95% confidence interval [CI] 52.9% to 92.0%), 98.1% specificity (95% CI 97.7% to 98.5%), 70.4% positive predictive value (95% CI 64.0% to 78.8%), and 98.0% negative predictive value (95% CI 95.9% to 99.6%) when using Sepsis-3 criteria as the reference standard. Reference: (4) |
| **Probability of sepsis patient receiving a broad-spectrum antibiotic** | 1.0 | Vancomycin and piperacillin/tazobactam were recommended as first-line treatments for sepsis. Antibiotics A and B, respectively.(7) |
| 1.  Probability of receiving vancomycin | 1.0 | Vancomycin and piperacillin/tazobactam were recommended as first-line treatments for sepsis. Antibiotics A and B, respectively.(7) |
| 2.  Probability receiving piperacillin/tazobactam | 1.0 | Vancomycin and piperacillin/tazobactam were recommended as first-line treatments for sepsis. Antibiotics A and B, respectively.(7) |
| **Probability of septic shock** | 0.20 | Twenty percent of sepsis patients develop septic shock. Reference: (6) |
| **Probability of acute respiratory distress syndrome (ARDS) and ventilator support in septic shock patients** | 0.18 | The incidence of ARDS is approximately 18% in patients with septic shock, and mortality approaches 50%. Reference: (12) |
| **Probability of death** | 0.125-0.50 | Overall mortality from sepsis is 12.5%. Rate is higher, at 50%, for ARDS patients. Reference: (13) |
| **Probability of discharge to home from stepdown unit** | 0.60 | Prevalence data not available. Probability set at 60%. |
| **Probability of transferring back to ICU from stepdown unit** | 0.40 | Prevalence data not available. Probability set at 40%. |

# Sample Synthetic Data Results

Sample Synthea generated data results for this module are included below (see Table 4). The sample results are also displayed as a chart in Figure 3. Analysis was performed using 10,496 patients generated in CSV output from Synthea. The synthetic prevalence rates matched the prevalence benchmark defined in the module. For example, 5.983% of patients are diagnosed with sepsis which matches the 6% prevalence benchmark defined in the module.

*Table 4: Patients with Sepsis Synthetic Prevalence*

| Sepsis | Patients with Sepsis | Total Patients | Synthetic Prevalence | Benchmark Prevalence Defined in Module |
|---|---|---|---|---|
| **Sepsis (disorder)** | 628 | 10496 | 5.983% | 6%* |

* See Table 3: Sepsis Module Parameters

# References

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