Terminology and Ontology Development for Semantic Annotation: A Use Case on Sepsis and Adverse Events

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Abstract. Annotations enrich text corpora and provide necessary labels for natural language processing studies. To reason and infer underlying implicit knowledge captured by labels, an ontology is needed to provide a semantically annotated corpus with structured domain knowledge. Utilizing a corpus of adverse event documents annotated for sepsis-related signs and symptoms as a use case, this paper details how a terminology and corresponding ontology were developed. The Annotated Adverse Event NOte TErminology (AAENOTE) represents annotated documents and assists annotators in annotating text. In contrast, the complementary Catheter Infection Indications Ontology (CIIO) is intended for clinician use and captures domain knowledge needed to reason and infer implicit information from data. The approach taken makes ontology development understandable and accessible to domain experts without formal ontology training.

Keywords: ontology development, clinical knowledge representation and reasoning, semantic annotation, sepsis, adverse events

1. Introduction

Many natural language processing (NLP) studies rely on annotated corpora to create models for text classification, information extraction, named entity recognition, question answering, summarization, and text generation. Often, semantic annotation is done to capture domain knowledge within the text. Annotated corpora are frequently generated by annotators based on an annotation guideline, which provides the standard and rules for how to label text using specified terms. This annotation guideline is usually similar to a terminology, unless the corpus was annotated using

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an ontology. To further enrich an annotated corpus by capturing, reasoning, and inferring the underlying associated domain knowledge, an ontology is needed.

To demonstrate semantic annotation terminology and ontology development, the use case is based on clinician-presented needs for identifying sepsis from adverse events (AEs). Improperly cared for peripheral intravenous catheter (PIVC) medical devices can lead to unwanted and unintentional events that harm patients, such as AEs like phlebitis, bloodstream infections (BSIs), and sepsis. However, PIVCs are poorly documented in clinical records because of routine use among inpatients, and sepsis is also poorly documented outside the intensive care units (ICUs). The lack of explicitly documented concepts makes it challenging to directly detect and annotate PIVC-related phlebitis, BSI, and sepsis for quality surveillance to improve care. Thus, indications for the presence of PIVCs, phlebitis, infections, and sepsis are annotated instead. Those annotations are structurally preserved as a terminology, and the clinical knowledge required to reason about the indications is represented in an ontology. Additional details for the use case are provided in Section 2.

This paper provides a detailed and concrete description of the methodology utilized for ontology development of an annotated corpus based on a use case from the clinical domain. The main contributions presented are:

1. Describing the development process for constructing a terminology that can represent an annotated corpus. Specifically, a terminology for indexing annotated AE documents.
2. Presenting the development process for the terminology's corresponding ontology, which represents domain knowledge and allows inference of implicit knowledge in a specific domain. The corresponding ontology in the use case represents clinical domain knowledge specifically for annotated catheter-related and infection-related signs in AE documents.
3. Releasing a terminology and ontology that can be applicable to identifying and reasoning about sepsis in an AE corpus.

This paper significantly extends the papers [1] and [2], by adding an ontology with instances and including evaluation of the correctness and ability to answer competency questions. In addition, instances from the annotated corpus in [2] were added into the terminology, the terminology was evaluated using competency questions, and an ontology was developed to answer competency questions with clinical knowledge.

Based on the presented use case in Section 2 and objective in Section 2.2, an Annotated Adverse Event NOte TErminology (AAENOTE) and corresponding Catheter Infection Indications Ontology (CIIO) were developed. Section 5 details the terminology construction and development process to represent annotated documents, and Section 6 presents the results and evaluations for the AAENOTE. To address shortcomings in the terminology for annotated documents, Section 7 describes the ontology development process for domain knowledge representation of documented content. Additionally, Section 8 presents the results and evaluations for the CIIO. Finally, Section 9 discusses the findings, limitations, representations, accessibility, and utility.

2. Use Case Background and Motivation

2.1. Sepsis from Peripheral Intravenous Catheter-related Phlebitis and Infection Adverse Events

As the most commonly used medical device in hospitals, PIVCs are inserted into the peripheral vein to administer intravenous (IV) fluids, IV medications, and blood transfusions [3]. Improper management of PIVCs or the infusions connected to the PIVC can lead to phlebitis, which is either infectious, mechanical, or chemical inflammation of the vein [4–6]. Independent of cause, all PIVC phlebitis share many symptoms like redness and swelling near a patient's infusion insertion site for infectious, mechanical, or chemical phlebitis, making it difficult to distinguish. Furthermore, all PIVC-related phlebitis causes AEs like significant pain, PIVC failure that delays treatment, and compromises future venous access. Infectious phlebitis may lead to BSI due to: 1. migration of bacteria at the insertion site, 2. bacteria migrating through the catheter tract or catheter hub, 3. contaminated infusate, or 4. bacteria from an existing infection in the bloodstream attaching to the catheter [7]. BSIs can potentially cause sepsis and occur when bacteria enter the bloodstream [8]. *Staphylococcus aureus* (*S. aureus*) is a lethal bacteria frequently found on skin that commonly causes BSIs [9], defined as a dysregulated host immune response to infection that results in organ failure and a mortality rate of 20% [10]. Ap-

proximately 7.6% to 35% of *S. aureus* BSIs are caused by PIVCs [11].

Even though PIVCs are frequently used, they are routinely not documented in clinical records [3]. Moreover, sepsis is also poorly documented outside the ICUs [12]. This lack of documentation makes it challenging to perform retrospective and real-time systematic quality surveillance of PIVC-related phlebitis or BSIs to identify learning opportunities for improving PIVC care to lower phlebitis-related, BSI-related, and PIVC-related AE incidents. Hence, AE reports or documents, which are customarily used to report PIVC failures, were selected as the clinical text for this project. To capture documented observable patient states and infer underlying knowledge of PIVC-related phlebitis or BSI from clinical text, an ontology that models clinical knowledge representation and reasoning is necessary.

2.2. Use Case Objective

The use case objective was to develop a model for representing and reasoning about PIVC-related BSIs in the unstructured free-text of AE reports, describe the development process, and discuss the discoveries and limitations. From the research question "is there a connection between BSIs and PIVCs at the hospital?", competency question requirements for an ontology representing and reasoning about PIVC-related BSIs were identified by clinicians as follows:

1. Does patientA have phlebitis, and was it infectious, chemical, or mechanical phlebitis?
2. Does patientA have an infection?
3. Does patientA have a BSI?
4. How many patients have an infection or BSI?
5. Which patients have sepsis?
6. Does patientB have a catheter?
7. Does patientB have a PIVC?
8. How many catheters does patientB have, where are they, and why does patientB need them?
9. Does patientC have an infection and catheter? If so, was patientC's infection associated with a catheter?

3. Related Work

3.1. Annotation, Tagging, and Ontologies for Natural Language Processing

Many studies focus on the relationship between annotation, tagging, and ontologies for NLP development. These studies include annotating corpora, NLP extraction, and classification tasks. Below are some studies that have shared their findings, issues, and possible solutions.

Annotated using the Uberon multi-species anatomical ontology [13], the Colorado Richly Annotated Full-Text (CRAFT) Corpus is a resource for NLP development which is also semantically annotated with concepts from eight Open Biomedical Ontologies (OBO) and terminologies [14, 15]. However, while annotating with the OBOs, they discovered that the OBOs are not developed for annotation because there are overlapping terms within the different OBOs, context-specific definitions, and semantic ambiguities. Additionally, some OBOs do not follow the OBO Foundry principle of using relations from the OBO Relation Ontology (RO) [16] to link concepts [17]. Therefore, to improve OBOs for semantic annotation of biomedical documents, the researchers proposed desirable ontology implementations such as, but not limited to, integrating overlapping OBOs terms, resolving ontology-specific ambiguities, and expanding relations [17].

A study comparing how anatomy ontologies are used for annotations discovered annotation and ontology issues [18]. Annotations from three public datasets were compared to anatomical terms in the Foundational Model of Anatomy (FMA) [19, 20] and Uberon [13] ontologies using the Zooma [1] and Ontology Mapper [2] software tools. Manual and semi-automated preprocessing were done to normalize terms, but there were few matches between the ontologies and annotations, mainly because of strict matching. Additionally, the user-provided annotation labels resulted in mismatches, such as annotating a phrase with multiple ontology terms or using an abbreviation or adjective for an anatomical part instead of the anatomical ontology term. Ontology issues include missing anatomical synonyms used by the annotators and differing anatomical terms in the ontologies because the ontologies are designed for different purposes and made by different design decisions. The study concluded that mapping terms to an ontology requires a large amount of time, effort, and manual curation. Furthermore, an ontology's design decisions and scope will affect users trying to match annotations to an ontology, and ontologies must be used to understand their potential.

[1] https://www.ebi.ac.uk/spot/zooma/
[2] http://www.ebi.ac.uk/efo/tools

The Unified Medical Language System (UMLS) is a collection of standard biomedical terminology [21], and it has been used to process text by extracting concepts, relations, and knowledge (i.e., link or annotate text with standard terminology) [22]. A software capable of finding and linking biomedical text to terminology concepts in the UMLS Metathesaurus is MetaMap [23]. However, the developers of MetaMap mention that improvement is required for detecting similar names, acronyms, and abbreviations and resolving ambiguities by possibly distinguishing concepts using word sense disambiguation.

In [24], an overview of studies using knowledge bases for entity coreference resolution were discussed. Among those studies was the OntoNotes project, which annotated a multilingual corpus for different levels of semantic structure in the text [25–27]. One of the annotation levels includes linking OntoNotes word senses to the Omega ontology [27–29]. Near-synonymous word sense pools were created by specialists who grouped sense distinctions from WordNet and dictionaries based on similar definitions. This enables machines to automatically tag senses more accurately and improves inter-annotator agreement due to difficulties determining WordNet distinctions directly in the text [29]. Before each sense pool was linked to a concept in the Omega ontology [30], each sense pool was verified by machine and humans [29].

3.2. Ontology Development Methods and Evaluation

There are many ontology development methods, such as: the Enterprise ontology's Uschold and King [31], the TOronto Virtual Enterprise (TOVE) ontology's Grüninger and Fox [32], METHONTOLOGY [33], the On-To-Knowledge Methodology (OTKM) [34], and NeOn [35]. Of those methods, Uschold and King [31] and Grüninger and Fox [32] follow a sequential sequence of phases, whereas METHONTOLOGY [33], OTKM [34], and NeOn [35] are iterative. Whether sequential or iterative, the previously mentioned methods and 2 reviews [36, 37] have shown that ontology development typically includes the phases: specification, conceptualization, formalization, implementation, and maintenance. During those phases, the knowledge acquisition, evaluation, and documentation phases also commonly occur either as a separate phase or concurrently with other phases. Appendix A provides a summary of the methods for each phase.

During and between phases, ontology evaluation judges an ontology's content to a reference, such as requirement specifications, competency questions [32], or the real-world [38, 39]. Evaluation includes: (1) verification that the ontology has the correct informal natural language definition and formal ontology language definition, and (2) validation that the ontology represents the world it was created for [38, 39]. In theory, there are many criteria for evaluation, but in practice, most studies only use the expressiveness and practical usefulness criteria [40]. Expressiveness is the number of competency questions answerable by the ontology [32, 40, 41], and practical usefulness is the number of problems an ontology can be applied to [40, 41].

3.3. Relevant Ontology Resources

There lacks an ontology specifically for sepsis-related BSI, infection signs, anatomical locations, medical devices, and procedures. However, pre-existing ontologies can contain relevant concepts. For example, the Infectious Disease Ontology (IDO) [42] has sepsis and hospital-acquired infection entities. Sign and symptom entities are present in the Ontology for General Medical Science (OGMS) [43], and vital sign entities exist in the Vital Sign Ontology (VSO) [44, 45]. Anatomical locations can be described using anatomical entities of the Foundational Model of Anatomy Ontology (FMA) [19, 46] and anatomical spatial location descriptor entities from the Biological Spatial Ontology (BSPO) [47]. Because AE reports are used, the adverse event entities in the Ontology of Adverse Events (OAE) [48, 49] might also be relevant. Furthermore, relationship object properties in the Open Biological and Biomedical Ontology (OBO) Relation Ontology [16, 50] could be used to link different entities together to capture more information.

In addition to ontologies, there are also potential relevant terminologies and taxonomies. For example, there are different procedure, medical device, and catheter terms in the National Cancer Institute Thesaurus (NCIT) [51, 52]. Potential relevant standardized nursing practice language is found in the International Classification for Nursing Practice (ICNP) terminology [53], Nursing Interventions Classification (NIC) taxonomy [54], and NANDA International Nursing Diagnoses Classification taxonomy [55]. Furthermore, infusion phlebitis-related information can be obtained from the 1998 Visual Infusion Phlebitis Scale [56] and the 2021 Infusion Therapy Standards of Practice Updates [57]. Concepts or terms from these resources can be used to expand the ontology if deemed necessary by ontology users. The relevant ontologies, terminolo-

Table 1
Overview of Relevant Resourses for This Study

Type	Resource	Relevant Concepts or Terms
Ontology	Infectious Disease Ontology (IDO)	Sepsis and hospital-acquired infection entities
	Ontology for General Medical Science (OGMS)	Sign and symptom entities
	Vital Sign Ontology (VSO)	Vital sign entities
	Foundational Model of Anatomy Ontology (FMA)	Anatomical entities
	Biological Spatial Ontology (BSPO)	Anatomical spatial location descriptor entities
	Ontology of Adverse Events (OAE)	Adverse event entities
	Open Biological and Biomedical Ontology (OBO) Relation Ontology	Relationship object properties
Terminology	National Cancer Institute Thesaurus (NCIT) terminology	Procedure and medical device terms
	International Classification for Nursing Practice (ICNP) terminology	Terms
Taxonomy	Nursing Interventions Classification (NIC) taxonomy	Terms
	NANDA International Nursing Diagnoses Classification taxonomy	Terms
Clinical Guideline	1998 Visual Infusion Phlebitis Scale	Visual infusion phlebitis grading scale
	2021 Infusion Therapy Standards of Practice Updates	Updated infusion therapy practice standards

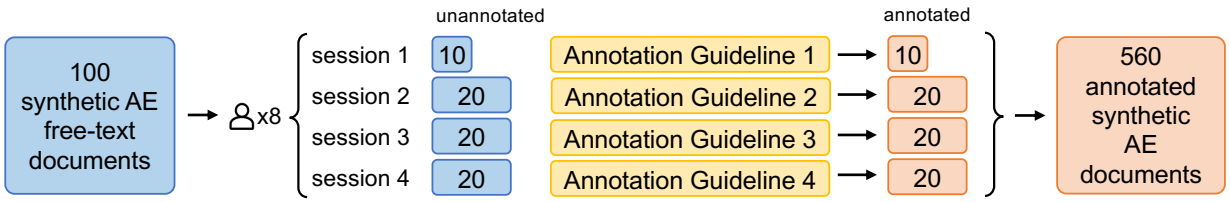


Fig. 1. From unannotated documents to an annotated corpus for populating instances in a terminology. 100 synthetic adverse event (AE) unstructured free-text documents were manually generated. Those synthetic documents were annotated by 8 annotators over 4 annotation sessions using revised annotation guidelines. Each annotator annotated 70 documents (i.e, 10 documents in session 1 and 20 documents in the remaining 3 sessions) to produce a total of 560 annotated synthetic AE documents.

gies, taxonomies, and clinical guidelines can be found in Table 1.

4. Materials

4.1. Synthetic Dataset

Documents for annotation are from an AE synthetic dataset. The documents are based on unstructured free-text AE notes within the extracted AE reports from the electronic incident reporting system at St. Olavs hospital, Trondheim University Hospital in Trondheim, Norway, between September 2015 to December 2019 [2]. The synthetic dataset contains 100 AE notes or documents manually created and verified by a nurse to ensure clinical data is anonymized. The Norwegian Regional Committees for Medical and Health Research Ethics (REK) has granted ethical approval to use AEs in this paper (approval no 2018/1201/REKmidt, 26814).

4.2. Annotated Synthetic Dataset

The synthetic documents were annotated by 8 annotators with clinical backgrounds over 4 annotation sessions [2]. Each annotator annotated 10 documents in session 1 and 20 documents in the remaining 3 sessions (i.e., 70 documents annotated over 4 annotation session). This resulted in 560 annotated synthetic AE documents, as shown in Fig. 1 (i.e., 8 annotators * 70 annotated documents * 4 sessions = 560 total annotated synthetic AE documents). In each annotation session, annotators followed the annotation guideline and used the Brat rapid annotation tool (BRAT) [58] to annotate the documents. Then, documents were evaluated and manually screened to identify ambiguities for revising the annotation guideline. This process was repeated 3 additional times with a new set of documents and a revised annotation guideline.

4.3. Annotation Guideline

An annotation guideline was developed based on the clinical research question: Is there a connection between BSIs and PIVCs at the hospital? Discussions with nurses provided insight into how catheters can be distinguished explicitly by the name or implicitly based on the anatomical insertion site or procedure mentioned. This formed into four domain-specific *questions of interest*:

1. What are the different signs of infections, specifically for BSIs, sepsis, or infected PIVCs?
2. What are the signs for different types of catheters?
3. Where are the anatomical insertion sites of catheters?
4. What procedures, interventions, and activities can be related to catheter use?

Answers to domain-specific questions were then sorted into the following 7 main categories:

1. **Sign**: infection signs.
2. **Location**: anatomical insertion sites.
3. **Device**: signs of catheter types.
4. **Procedure**: procedures, interventions, or activities related to catheters.
5. **Sensitivity**: protected health information.
6. **Person**: individuals mentioned, such as patient, clinician, or relative.
7. **Whole**: label representing the span of the whole document and given to indicate if the document contains information about infection, BSI, sepsis, faulty device malfunctioning, catheter, PIVC, or has sensitive protected health information.

All categories except **Whole** have a hierarchy with more specific subcategories to capture detailed granularity from text (e.g., the **Person** category has a **Patient** subcategory). Furthermore, to capture relationships between categories for downstream analysis (e.g., infection sign at a specific location), the following four relationships to link categories were included:

1. **Person** $\xrightarrow{\text{Person has}}$ **Sign**, **Location**, **Device**, or **Procedure**.
2. **Procedure** $\xrightarrow{\text{Procedure uses}}$ **Device**.
3. **Sign** $\xrightarrow{\text{Caused by}}$ **Device** or **Procedure**.
4. **Sign**, **Device**, or **Procedure** $\xrightarrow{\text{Located nearby/on/in}}$ **Location**.

A preliminary annotation guideline was created using the seven categories and four relationships. Annotation guidelines from each of the 4 annotation sessions are available online[3] [2].

[3] https://folk.ntnu.no/melissay/ae-guidelines/

5. Terminology Development for Annotations

In annotations, categories are known as entities for labeling a span of words or phrases. Whereas in ontologies and terminologies, categories are known as classes. To separate the annotation guideline from the terminology and ontology, the annotation categories and entities are in **bold font**, and the terminology and ontology classes are in `typewriter font`.

5.1. Design Decision for Annotations

The terminology was developed using the bottom-up approach based on the annotation guideline refinement process from 4 iterations. Competency questions were not used to create this terminology. This terminology is meant to assist annotators who want to label text and allow users interested in performing downstream analyses to adjust the granularity of labels. The objective is solely to represent the annotated corpus and provide structure to the terminology used by annotators. Thus, included individuals are based on concrete examples from the annotated corpus. A simplified example of how annotation labels in annotated documents are added to the terminology as individuals is provided in Fig. 2.

Instead of reusing and re-defining existing ontologies, it was easier and simpler to develop a terminology based on what is documented in the data. For instance, although the FMA contains relevant anatomical parts, the ontology was too complex and detailed to be incorporated easily into the terminology to fit the use case's purpose. Additionally, the purpose was to include only concrete items documented in the terminology and not provide terminology for all existing items. By opting to simplify the terminology, it was easier to build the terminology directly based on the annotation guideline and then modify the terminology to incorporate feedback from discussions with clinicians.

5.2. Convert Annotation Guideline To Terminology

The categories, attributes, and relationships in annotation guidelines described in Section 4.3 correspond to classes, data properties, and object properties in terminologies (Table 2 and Fig. 3).

The terminology was developed from the annotation guideline by translating each hierarchy of entities into a class hierarchy, using attribute information to add data properties, and converting relationships into object properties. During development, the terminology

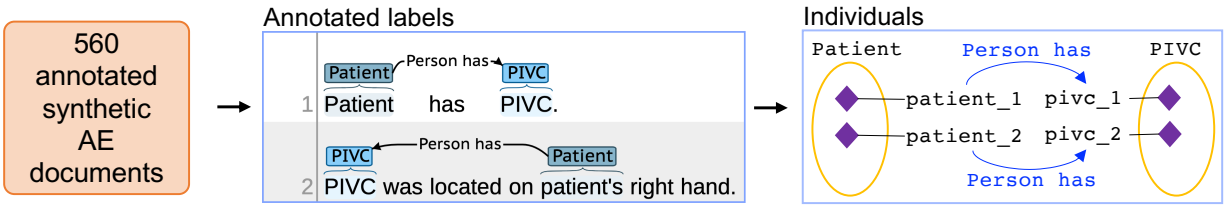


Fig. 2. Using an annotated corpus to populate individuals in a terminology. Each of the 560 documents were translated into an individual, and each label within a document was also translated into an individual. In the simplified example, an annotated document has 2 **patient** labels, 2 **PIVC** labels, and 2 $\xrightarrow{\text{Person has}}$ relationships linking the labels. Each label is converted into an individual (i.e., a purple diamond) of the corresponding class (i.e., `Patient` or `PIVC` yellow circle). Then the labels are linked using the $\xrightarrow{\text{Person has}}$ object property, similarly to how the $\xrightarrow{\text{Person has}}$ relationship links labels in the annotated text.

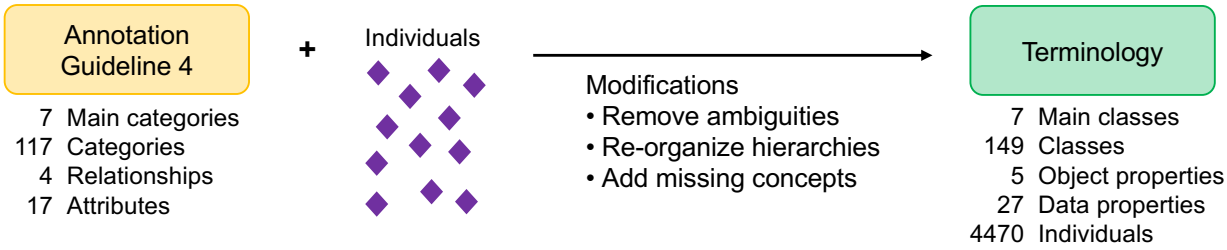


Fig. 3. Terminology development. The annotation guideline from the fourth annotation session was converted into a terminology. Annotation categories were converted into ontology classes, relationships into object properties, and attributes into data properties. Then the individuals of documents and labels were added. Additional modifications were incorporated as needed, such as removing ambiguities, re-organizing hierarchies, and adding missing concepts. This resulted in the AAENOTE which models and provides an index of annotated documents.

Table 2
Convert Annotation Guideline to Terminology

Annotation Guideline	**Terminology**
Entity (category) hierarchies	Class hierarchies
Attributes which provide detailed entity information	Data properties
Relationships between entities	Object properties

was modified to remove ambiguities by adding new class hierarchies and modifying class names, object properties, and data properties. Specifically, to remove ambiguity between symptoms, infection signs, and device malfunction signs, the `Observation` class was introduced to encompass them. Additionally, the **Sensitive** category was revised to the `Identifier` class and the $\xrightarrow{\text{Caused by}}$ relationship was revised to the $\xrightarrow{\text{Is observed with}}$ relationship. A summary of the converted 7 main classes can be found in Table 3.

The results from all 4 annotation sessions were included as individuals in the terminology, but the terminology only reflects results based on the last annotation guideline. To accommodate revisions in the annotation guideline, annotation categories that were revised in the guideline are updated in the terminology correspondingly. For instance, removed annotation categories are reflected by changing the granularity of the removed category to a higher level. Annotation categories can also be re-organized to become subclasses of a different class. Moreover, newly added annotation categories are directly added as new classes in the terminology. An example is depicted in Fig. 4.

Although the terminology was not developed to answer competency questions, the competency questions were still used to determine what could be found in annotated documents. To answer competency questions, the annotated documents were imported into the terminology as individuals.

6. Terminology Results for Annotations

6.1. Annotated Adverse Event NOte TErminology (AAENOTE)

Annotated AE documents and their annotations are modeled by the Annotated Adverse Event NOte TErminology (AAENOTE). To increase accessibility, the terminology is in both English and Norwegian. There

Table 3

Annotation Guideline vs Annotated Adverse Event NOte TErminology (AAENOTE). Annotation categories and entities are in **bold font** and the terminology and ontology classes are in `typewriter font`

Annotation Categories	Category Description	Sub-categories	Terminology Classes	Class Description	Subclasses
Sign	Infection signs	29	`Observation`	Documented clinical observation including symptoms, infection signs, and device malfunctions	41
Location	Anatomical insertion sites	17	`Anatomical location`	Anatomical location	25
Device	Signs of catheter types	16	`Medical device`	Treatment equipment or part	19
Procedure	Procedures, interventions, or activities related to catheters	31	`Procedure`	Procedure, intervention, or activity for catheter-related versus non-catheter related	36
Sensitivity	Protected health information	14	`Identifier`	Protected health information	14
Person	Individuals	3	`Person`	Individual	3
Whole	Label representing whole text indicating the note contains infection, BSI, sepsis, faulty device malfunctioning, catheter, PIVC, or sensitive information	0	`Annotated document`	Representation of an AE note's filename, annotation session, annotator, and annotated labels	4

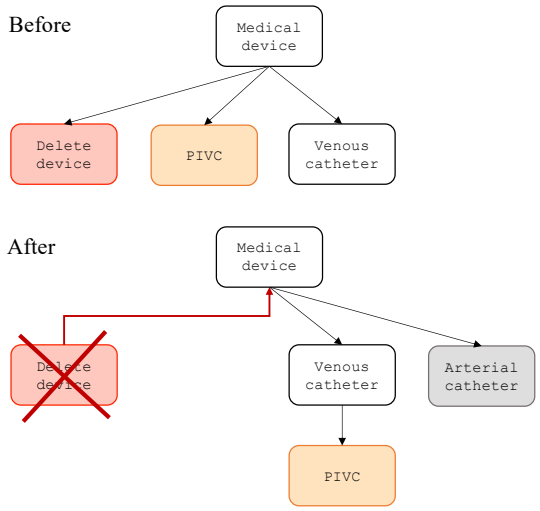


Fig. 4. Handling annotation guideline revisions in the terminology. If the **Delete device** annotation category in red is removed from the annotation guideline, then the `Delete device` class is removed from the terminology and all individuals of the `Delete device` terminology class are now part of the superclass `Medical device`. If the **PIVC** (peripheral intravenous catheter) annotation category in orange is re-organized to become the sub-category of **Venous catheter**, then the `PIVC` class is now a subclass of `Venous catheter` and the individuals remain as part of the `PIVC` class. If the **Arterial catheter** annotation category in gray is added, then the `Arterial catheter` class is added to the terminology and the corresponding individuals will be added as well.

are 149 classes, 5 object properties, 27 data properties, and 4470 individuals. The 7 classes which form the main hierarchies are:

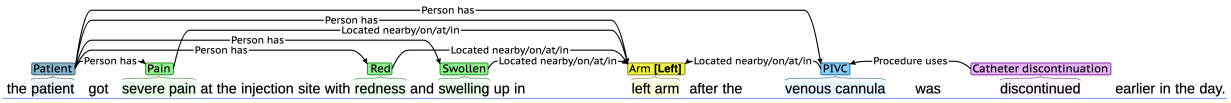
1. `Observation`: Any sign or symptom that can be monitored.
2. `Anatomical location`: Any anatomical body part, organ, or relative position of the body.
3. `Medical device`: Any instrument, device, or equipment used for a medical purpose.
4. `Procedure`: Any procedure, intervention, or activity related to catheters.
5. `Identifier`: Protected health information that can be used to identify an individual.
6. `Person`: An individual, such as a patient, clinician, or relative.
7. `Annotated document`: Annotated adverse event document metadata and labels.

Relationships between the 7 class hierarchies can be formed using the following 5 object properties:

1. `Person` $\xrightarrow{\text{Person has}}$ `Observation`, `Anatomical location`, `Medical Device`, or `Procedure`.
2. `Procedure` $\xrightarrow{\text{Procedure uses}}$ `Medical device`.
3. `Observation` $\xrightarrow{\text{Is observed with}}$ `Medical device` or `Procedure`.
4. `Observation`, `Medical device`, or `Procedure` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
5. `Annotated document` $\xrightarrow{\text{Has label}}$ `Anatomical location`, `Identifier`, `Medical device`, `Observation`, `Person`, or `Procedure`.

An example showing AAENOTE representing an annotated document using parts of the class hierarchies

(a)



(b)

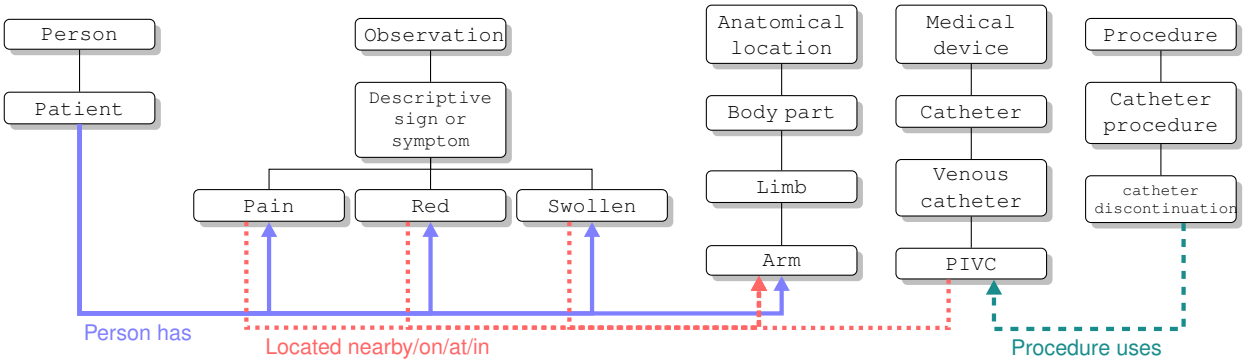


Fig. 5. Annotated Adverse Event NOte TErminology (AAENOTE) representing an annotated document. (a) Example of an annotated document with annotation categories and relationships that link the categories together. (b) Part of the terminology class hierarchies used within the annotation example are shown in the white boxes. The 3 annotated relationships (i.e., $\xrightarrow{\text{Person has}}$, $\xrightarrow{\text{Located nearby/on/at/in}}$, and $\xrightarrow{\text{Procedure uses}}$)are represented by the 3 object properties that link the classes together. Object properties are shown using the thicker colored lines with arrows.

and class properties is shown in Fig. 5. The complete class hierarchies of AAENOTE are in Appendix B.1.

Each annotated AE note or document is an individual of the `Annotated document` class and can have object properties linking the AE document to individual labels from the other 6 class hierarchies. Additionally, each AE document has data properties for the filename, annotation session, and annotator. The individuals of the other 6 hierarchies can also have object properties and data properties if an annotator provides that information.

6.2. AAENOTE Evaluation

The purpose of AAENOTE is to model and provide semantic meaning to annotated AE notes or documents. The terminology was not developed based on competency questions, but it would be interesting to see what competency questions could be answered. Hence, AAENOTE was evaluated using the competency questions as requirements. Competency questions using AAENOTE can only be answered based on explicitly annotated classes or subclasses. Words or phrases that lack annotation are excluded from this terminology. Thus, only the annotation category labels provided by annotators are included as individuals of the corresponding classes.

Knowledge represented by the terminology can either be found explicitly, based on the direct classes and relationships, or be inferred implicitly, based on underlying concrete knowledge and indirect classes and relationships. For example, the competency question "Does patientA have an infection?" can be answered explicitly by finding an individual of the patient class who has an infection (i.e., `Patient` $\xrightarrow{\text{Person has}}$ `Infection`). It can also be answered implicitly by finding an anatomical location that has an infection (i.e., `Infection` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`) because an anatomical location, in this terminology, must be part of a person. However, if the infection is not explicitly mentioned, this terminology cannot implicitly determine what other observations combined indicate an infection.

SPARQL query results vary depending on the clinician's interest in knowing how many instances a patient has for one class or a combination of that one class with other classes. For example, to find how many patients explicitly have an infection, the query can be written to find all instances where either: 1. individuals of the patient class have the object property "person has" to an individual of the infection class (i.e., `Patient` $\xrightarrow{\text{Person has}}$ `Infection`), or 2. the individuals of the patient class have the object property "person has" to an individual of the

Table 4
AAENOTE SPARQL Query Result: Patient has Infection

Query Result	Instances	# Observations	Person	Observation											
			patient	blood pressure	body temp	c reactive protein	conciousness level	infection	neurological and physiological	observation	pulse	red	respiratory rate	sepsis	swollen
1	14	1	✓					✓							
2	1	1	✓					✓							
3	1	2	✓				✓	✓							
4	1	2	✓					✓				✓			
5	1	2	✓					✓					✓		
6	1	3	✓		✓	✓		✓							
7	1	3	✓		✓			✓					✓		
8	1	3	✓			✓		✓	✓						
9	1	3	✓				✓	✓		✓					
10	2	3	✓					✓				✓			✓
11	1	4	✓			✓	✓	✓		✓					
12	1	5	✓	✓	✓	✓		✓			✓				
13	1	6	✓	✓	✓	✓		✓			✓			✓	
14	1	8	✓	✓	✓	✓		✓	✓	✓	✓		✓		

Query result 1: `Patient` $\xrightarrow{\text{Person has}}$ `Infection`.
Query result 2-14: `Patient` $\xrightarrow{\text{Person has}}$ `Infection` and other `Observation(s)`.

infection class and/or an individual of the observation class or it's subclass (i.e., `Patient` $\xrightarrow{\text{Person has}}$ `Infection` and other `Observation(s)`). The different number of instances is shown in Table 4. The first query has 14 instances where a patient has an infection regardless of other observations. In contrast, the second query divides the 14 instances into Query Result 2-14 to show the number of instances where a patient has an infection with different combinations of other observations. To implicitly find patients who have an infection, the infection must be located at an anatomical location of a person. Queries about infections at an anatomical location can be written using `Infection` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location` or using `Infection` and other `Observation(s)` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location` if the clinician is curious about additional observations that were documented with the infection. In AAENOTE, there is only 1 instance where an anatomical location (i.e., skin) has an infection, as shown in Query Result 1 of Table 5. However, it is more informative for clinicians to look at additional potential observations that can indicate infection around a certain location; Table 5 Query Results 2-10 provide other observations located on skin. In AAENOTE, there lacks clinical knowledge required to find indications of infections and catheters.

Overall, explicit queries and basic implicit queries in AAENOTE can answer 7 of the 9 competency questions. However, these queries still lack the clinical knowledge needed to include more implicit queries by combining additional observations, anatomical locations, and/or procedures to identify indications. In Appendix B, Table 7 provides the terminology classes and relationships used to form explicit and implicit queries to explicitly and implicitly answer each competency question. Additionally, concrete underlying knowledge used to make inferences is also provided. Results can be found in Appendix B.

7. Ontology Development for Domain Knowledge

7.1. Design Decision for Domain Knowledge

In this use case, the clinicians' need is to focus on identifying and inferring a patient's state based on documented observations in AE documents related to PIVCs and BSIs. A patient's underlying state can be

Table 5
AAENOTE SPARQL Results for Observations Located at the Skin

Query Result	Instances	Observations					
		edema	infection	pain	red	swollen	warm
1	1		✓				
2	3			✓			
3	3					✓	
4	2			✓		✓	
5	2			✓	✓	✓	
6	2				✓		
7	2				✓	✓	
8	1						✓
9	1				✓		✓
10	1	✓			✓	✓	

Query result 1: `Infection` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
Query result 2-10: `Observation` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Skin`.

measured by monitoring devices that measure vital signs (e.g., blood pressure, pulse, and respiratory rate) or exhibited by observable signs and symptoms (e.g., pain, fever, chills, and mobility impairment). Those measurable and observable signs and symptoms are then documented by clinicians in the electronic health record (EHR) to record patient conditions and communicate with other clinicians. When an AE incident could have or has happened, clinicians will go through the documentation to recall what occurred and report it in a separate AE document.

To limit the scope of modeling the clinical knowledge ontology, 15 documents were used as examples to form the classes and individuals. Each document was split into sentences to identify catheter and infection indications at the sentence-level and document-level. At the sentence-level, individual sentences were presented to clinicians who determined what observations, anatomical locations, or procedures within the text are needed to determine catheter and infection indication. Only clinician-identified sentences with indications were included as individuals in the ontology. At the document-level, individual sentences from a document were presented together, allowing clinicians to identify indications based on additional information from a more complete documented story. Presenting the document as separate sentences allowed clinicians to identify concepts within a limited example to determine what can and cannot be determined based on limited information. Whereas, allowing a clinician to see the whole document presented more possibilities and helped identify necessary data combinations for indications of catheters and infections.

The focus of the ontology includes catheter indications and the clinicians have identified that it is important to identify infusion phlebitis. Thus, infusion phlebitis was included in the ontology as rules based on the 1998 Visual Infusion Phlebitis Scale [56] mentioned in the 2021 Infusion Therapy Standards of Practice Updates [57]. Furthermore, causality is not within the scope because the exact reason for chemical and mechanical reactions resulting in infection-like signs are more likely found at the body's cellular or genetic-level in pathophysiology studies [59, 60] and unlikely to be documented in AE documents.

Anatomical locations in this ontology were kept simple and similar to the AAENOTE. Clinical guidelines for catheter insertion into anatomical locations are very specific (e.g., a central venous catheter is inserted in the jugular vein until it reaches the superior vena cava [61]) because clinical guidelines provide instructions on how to perform a task properly. However, clinical documentation is more general (e.g., central venous catheter in the chest) because this is common clinical knowledge, and the documentation is written for other clinicians to understand. To match the ontology with available documented data, this ontology relies on general anatomical location terminology. If clinicians deem it necessary, clinical guidelines can be included in a separate ontology focused on identifying catheter locations based on clinical guidelines and the FMA. Inclusion of clinical guidelines to identify specific catheter insertion sites and placement requires anatomical knowledge. For instance, to identify a central venous catheter's general anatomical location using a clinical guideline and the FMA anatomy ontology, the ontology would need to:

1. Identify the jugular vein insertion site and the superior vena cava placement.
2. Infer that the jugular vein is in the neck and the superior vena cava is present within the superior and middle mediastinum [62], annotated as anatomical location chest.
3. Convert the terms into more general terms that match the available data (i.e., vena cava is in the chest).

7.2. Representing Domain Knowledge

Discussions with clinicians about example documents and indications formulated the classes, object properties, data properties, and rules within the ontology. Then, the provided indications were sorted and summarized to match the ontology closely. Afterward, indications were verified by clinicians and included in the ontology using SPARQL queries. A list of indications can be found in Appendix C.3.1 to Appendix C.3.7.

8. Ontology Results for Domain Knowledge

8.1. Catheter Infection Indications Ontology (CIIO)

The Catheter Infection Indications Ontology (CIIO) represents clinical knowledge for signs of infections and catheters to identify PIVC-related BSIs and was developed to accompany the AAENOTE. Similar to AAENOTE, this ontology is also in both English and Norwegian. There are 57 classes, 10 object properties, 16 data properties, and 187 individuals. The 7 classes which form the main hierarchies are:

1. `Observation`: Any sign or symptom that can be monitored.
2. `Anatomical location`: Any anatomical body part, organ, or relative position of the body.
3. `Medical device`: Any instrument, device, or equipment used for a medical purpose.
4. `Procedure`: Any procedure, intervention, or activity related to catheters.
5. `Person`: An individual.
6. `Document`: Unstructured free-text report consisting of sentences documented to represent observable patient states.
7. `Sentence`: A set of words documented to represent observable patient states.

Relationships between the 7 class hierarchies can be formed using the following 10 object properties:

1. `Person`'s subclass `Patient` $\xrightarrow{\text{Patient has}}$ `Observation`, `Anatomical location`, `Medical device`, or `Procedure`.
2. `Procedure` $\xrightarrow{\text{Procedure uses}}$ `Medical device`.
3. `Observation` $\xrightarrow{\text{Is observed with}}$ `Medical device` or `Procedure`.
4. `Observation`, `Medical device`, or `Procedure` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
5. `Document` or `Sentence` $\xrightarrow{\text{Contains}}$ `Observation`, `Anatomical location`, `Medical device`, `Procedure`, or `Person`. Additionally, only `Document` $\xrightarrow{\text{Contains}}$ `Sentence`.
6. `Procedure`'s subclass `General IV` $\xrightarrow{\text{Is combined with}}$ a different `General IV`.
7. `Procedure`'s subclass `General IV` $\xrightarrow{\text{Is IV for}}$ `Procedure`'s subclass `Infusion`.
8. `Procedure`'s subclass `General IV` $\xrightarrow{\text{Medication should have been}}$ a different `General IV`.
9. `Observation`, `Anatomical location`, `Medical device`, `Procedure`, or `Person` $\xrightarrow{\text{Is documented in}}$ `Document` or `Sentence`. Additionally, only `Sentence` $\xrightarrow{\text{Is documented in}}$ `Document`.
10. `Anatomical location` $\xrightarrow{\text{Location has}}$ `Observation`, `Medical device`, or `Procedure`.

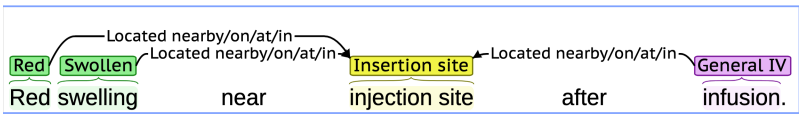
An example showing how a sentence is represented using the class hierarchies and class properties of CIIO to model documented clinical knowledge is shown in Fig. 6. The complete class hierarchies of CIIO are in Appendix C.1.

Each sentence documented in the report is an individual of the `Sentence` class. `Sentence` class individuals contain `Observation`, `Anatomical location`, `Medical device`, `Procedure`, or `Person` individuals present within the text. An individual of the `Document` class contains the `Sentence` individuals that form it and the content from those sentences. Similar to AAENOTE, individuals of `Observation`, `Anatomical location`, `Medical device`, `Procedure`, and `Person` can also have object properties and data properties.

8.2. CIIO Evaluation

Designed to capture and reason about clinical catheter-related and infection-related signs and symptoms documented in an AE report, the CIIO provides the missing clinical domain knowledge for the AAENOTE. CIIO can answer 8 of the 9 competency questions based on assumptions and indications. The assump-

(a)



(b)

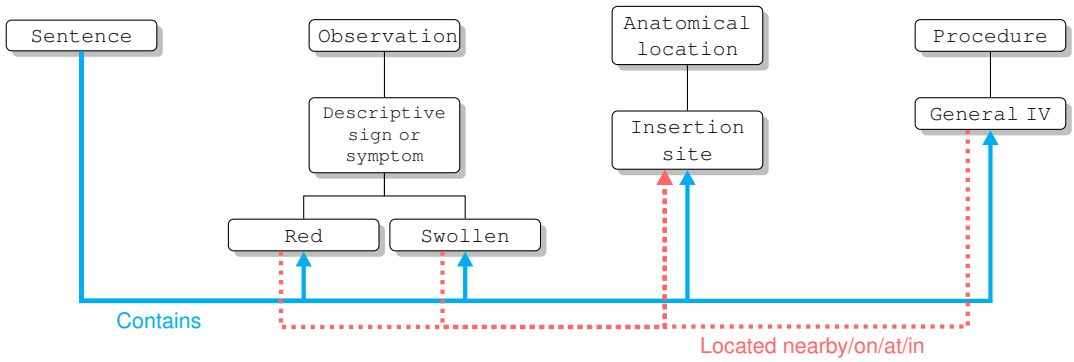


Fig. 6. Catheter Infection Indications Ontology (CIIO) clinical knowledge representation. (a) A sentence from a document used to identify documented clinical knowledge. Annotations are based on terms from the Annotated Adverse Event NOte TErminology (AAENOTE). (b) CIIO has a `Sentence` class and $\xrightarrow{\text{Contains}}$ relationship to link a sentence to documented observable patient states (i.e., AAENOTE terms). AAENOTE terms were used in CIIO to conceptualize the classes and object properties that represent documented knowledge and can be used in reasoning to identify catheters and infections. Part of the ontology class hierarchies and object properties used in knowledge representation are shown. Classes are in white boxes and object properties are shown using thicker colored lines with arrows.

tions are that 1 AE document represents 1 patient and all sentences within a document are likely to describe concepts within the same event (Appendix C.2). Indications for catheters and infections are provided in (Appendix C.3). Additionally, the ontology classes and relationships used to answer each competency question is detailed in Appendix C.4.

9. Discussion

9.1. Ontology Development Method Comparison

The clinical problem drove this study, and the objective was not to apply an ontology development method. Hence, a specific ontology development method was not applied. However, certain steps taken are similar to the pre-existing methods and this study does include the typical phases of specification, conceptualization, formalization, implementation, maintenance, knowledge acquisition, evaluation, and documentation. An overview of the process is shown in Fig. 7, and similarities to other methods can be found in Appendix A.

During the pre-development and specification phases of the terminology, clinicians provided the research question and use case. Those were utilized to define the competency questions. Additionally, the AE dataset was retrieved, and an AE synthetic dataset was created. The conceptualization phase was performed by iteratively developing the annotation guideline and annotation sessions. Afterward, the formalization and implementation phases of the terminology were developed iteratively based on the annotation guideline and using instances from the annotated corpus to answer competency questions for evaluation. Knowledge acquisition occurred during all phases with insight, guidance, and feedback from clinicians. Documentation is provided in the annotation guidelines, the annotated corpus, and the evaluation of competency questions. The annotation guidelines document changes in terms over time, and the annotated corpus documents knowledge acquisition from the text. Answers to each competency question are documented using natural language for clinicians and SPARQL queries for computer scientists.

Ontology development is similar to the terminology's pre-development, specification, and conceptualization phases. However, the formalization and implementation phases differ. The ontology iteratively incorporated clinical knowledge that can be annotated in AE documents using terminology terms to answer competency questions for evaluation. Knowledge

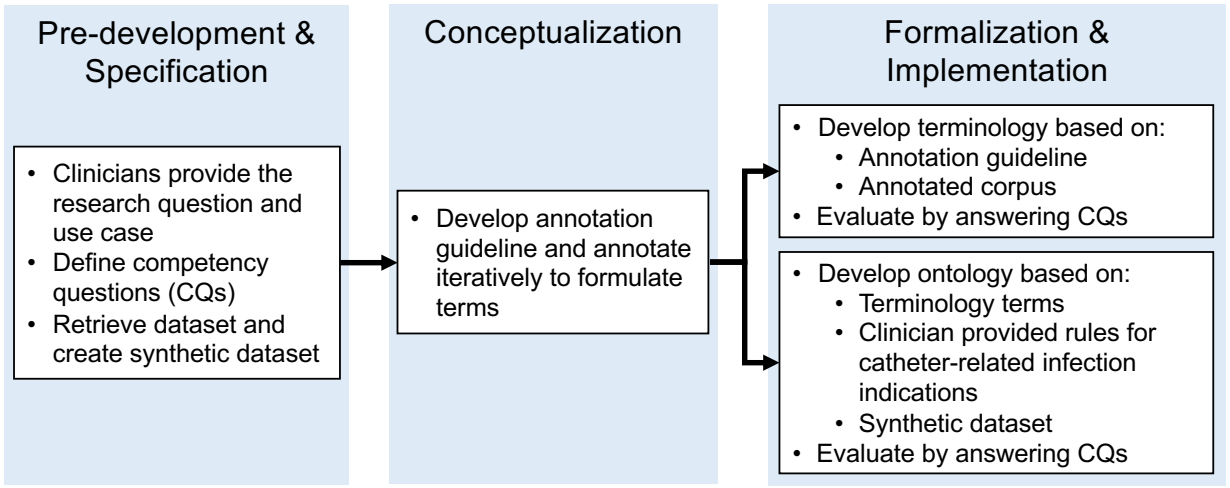


Fig. 7. Development phases for Annotated Adverse Event NOte TErminology (AAENOTE) and Catheter Infection Indications Ontology (CIIO).

acquisition was provided through the annotated corpus, clinician-provided catheter indication rules, and clinician-provided publications containing phlebitis rules. Additionally, clinicians iteratively reviewed and verified documented sentences to match the rules and competency questions. Ontology documentation includes the assumptions (Appendix C.2), rules for catheter and infection indications (Appendix C.3), and how competency questions were answered (Appendix C.4).

Although UMLS includes clinical terminology (i.e., SNOMED CT and ICD-10), the terms are often a combination of different concepts. For example, phlebitis has many options and is combined with different locations, such as “phlebitis of the lower limb vein,” “phlebitis of the portal vein,” and “retainal phlebitis.” Additionally, swollen has many options, such as “foot swelling,” “swollen nose,” and "tongue swelling.” The June 10, 2022 version of SNOMED CT has 361,907 classes[4]. It would require extensive time and effort to determine which classes are suitable for our purpose and to maintain a pre-determined class hierarchy. Introducing UMLS terminology would make it difficult for annotators to determine which term to use, introduce ambiguities for the use case, and decrease the precision needed. Furthermore, the UMLS MetaMap is software that finds and links biomedical text to terminology concepts [23]. Unfortunately, that software is for biomedical text and not clinical text. Clinical text differs from biomedical text because it is often ungrammatical and ambiguous, with many shorthand abbreviations and acronyms [63]. Additionally, the MetaMap developers have mentioned that detecting abbreviations and acronyms needs improvements [23].

[4]https://bioportal.bioontology.org/ontologies/SNOMEDCT/?p=summary

9.2. AAENOTE Scope and Limitations

The clinician asks questions about the condition of a physical patient and the patient’s PIVCs, but AAENOTE is about words in the AE document regarding a patient event. The correspondence between clinical condition and document content is represented by CIIO. So, the answer to a question about a patient’s condition will be answered using the document’s annotated text. Understanding a query means translating it from clinical concepts to concepts within the document’s content. Here, the terminology is used to fit and answer questions. SPARQL queries can answer most competency questions, and the results can be used as consistency checks. For example, SPARQL can be used to count and make quantitative queries about the number of catheters and devices. Likewise, qualitative results enabled clinicians to verify if results matched their expectations of clinical events (i.e., the anatomical location of specific catheters) or why the AE was reported (i.e., incorrect medical devices used in a particular procedure).

There are several limitations to the AAENOTE. Although this terminology does not cover sepsis, it does cover events that could lead to sepsis. This terminology lacks the clinical knowledge required to answer several competency questions more in-depth. Moreover, it is not always possible to determine what a patient

has because of the document's content or provided annotations. Most documents do not explicitly mention a patient because these are AE documents, and it is often implied that the adverse event has happened to a patient. Annotators will often not link the patient to all possible observations, anatomical locations, medical devices, or procedures because typically, one AE document refers to one event or patient. Furthermore, referent tracking and resolution are not handled by AAENOTE. Thus, multiple mentions of a label or individual do not indicate whether it is the same item or a different item. For example, given the annotated document in Fig. 2, the terminology cannot determine if the 2 `Patient` individuals refer to the same patient or not because each label is an individual. Similarly, the same also applies to the 2 `PIVC` individuals. In this example, a query counting how many patients have a PIVC will answer 2. However, based on the context, both sentences in the document likely refer to the same patient and PIVC and the answer should be 1.

9.3. CIIO Scope and Limitations

The CIIO is an abstract ontology with instances populated using the terminology. Only parts of the AAENOTE necessary for creating queries with clinician-provided indications were included or extended. This provides flexibility, allows for easier ontology maintenance, and separates the needs of clinicians who use CIIO and annotators who use AAENOTE.

Based on assumptions and indications, competency questions can be answered using SPARQL queries. The queries retrieve documents and translate the content for the user by identifying concepts necessary to answer the competency questions. Thus, the retrieved documents and concepts can provide sufficient information for clinicians to further decipher retrieved answers. For example, the exact reason why a patient needs a catheter cannot be determined by the query unless there is a direct relationship (i.e., `Procedure` $\xrightarrow{\text{Procedure uses}}$ `Medical device`) because the list of indications does not provide reasons for catheter usage. However, the clinician can view the retrieved list of medical devices and procedures within a document to determine why the medical devices were required.

The lack of detailed documentation inhibits the query's ability to answer certain questions. This includes why a patient needs a catheter as previously stated, counting catheters within a patient, and where the catheters are located in a patient. Counting the exact number of catheters per document is not possible because multiple sentences within a document could be describing the same catheter or multiple procedures could use the same catheter. The exact anatomical location of catheters per document cannot be determined for several reasons. First, multiple sentences within a document could be describing the same catheter at the same location but with more general terms (i.e., arm instead of hand). Second, the location's position not being documented makes it difficult to distinguish if a body part is on the same side. Finally, various procedures can be performed at the same location. For example, given an example document, "The patient received IV fluids in elbowA and IV antibiotics in right handB. Right armC showed signs of phlebitis." Here, handB is part of armC because both are on the right side, but elbowA might or might not be part of armC. Additionally, armC is likely a more general term for handB. Furthermore, an additional anatomical ontology is needed to infer the possible locations based on catheter type.

9.4. Purpose of Separate Terminology and Ontology

Even though the ontology uses terms from the terminology, the terminology and ontology are separate. They are separate because of their different purposes and functionalities. Additionally, separation provides downstream analysis flexibility for researchers. It also simplifies evaluation and allows for easier maintenance. Furthermore, separation enables a better understanding of the terminology's and ontology's limitations.

The terminology and ontology were developed for different purposes using different methods. AAENOTE is intended to be useful for annotators who are annotating documentation and a way to provide them a structured terminology with varying granularity. In comparison, CIIO is intended to be used by clinicians to clinically reason about a patient state. The design process of AAENOTE is heavily based on the explicit terms used in annotations and not on competency questions. It uses the bottom-up method and the annotation guideline development process to capture semantic annotations. In contrast, the design process of CIIO is based on the competency questions, which focus on patient states. Designed with a top-down method, it is based on concepts naturally used by clinicians to describe patients. Thus, the terminology and ontology have different purposes and functionalities.

Separating the terminology from the ontology enables annotators to annotate concepts with standard

terms and clinicians to reason about the annotated concepts. Here, the ontology does not impact the terminology annotators can use. Instead, the ontology provides knowledge for the terminology. Thus, our methods avoid the significant amount of time, effort, and manual curation previously required to map terms to an ontology [18]. Instead, our ontology utilizes concepts in the terminology and is limited by the competency questions, clinical guidelines used, and clinician-provided rules. In downstream analyses, researchers can freely choose to use the terminology to quickly retrieve documents with specific annotations, the ontology to reason and infer clinical knowledge, or both.

The terminology indicates concepts annotated in documents. Using terms from the terminology ensures that the included clinical knowledge within the ontology represents the knowledge documented in the text that can be annotated. As the ontology develops further, it is possible to conceptualize additional terms required to answer the competency questions. Those terms can then be added to the terminology and annotation guideline for additional data curation.

In this paper, separating the terminology made it easier and quicker to evaluate syntax and semantics because the ontology only has 187 instances compared to the terminology's 4470 instances. Mixing the indexed annotation terminology with a clinical knowledge ontology would be outside the ontology's scope, decrease ontology reusability, and increase the complexity of ontology maintenance. Additionally, the terminology can cover a broader scope of documents not in the ontology. Finally, using competency questions to evaluate the terminology and ontology separately reveals the distinct limitations of both. The inability to answer competency questions can be due to either the lack of knowledge or lack of necessary content within the data.

9.5. Representing Annotated Data and Revisions

Annotating data provides data meaning, and the corresponding annotation guideline and terminology provide additional structured semantic meaning. Additionally, the terminology can represent knowledge and disambiguate annotation entities and relationships. Each annotation session uses a slightly different annotation guideline that has been revised based on the previous annotation session. Hence, revisions in the annotation guidelines include added, re-organized, and removed categories. Since results from 4 different annotation sessions are included as individuals in the AAENOTE, this indicates the terminology can handle different versions of annotated data while preserving semantic meaning. It is also possible to easily customize the granularity (i.e., superclasses, classes, or subclasses) and extend or retract the terminology based on clinician needs without breaking the terminology.

To alleviate the problem with overlapping terms and ambiguities experienced by [17] and remove mismatches between the annotations and the terminology experienced by [18], all annotators in our study could only use provided annotation labels from the terminology. Using concrete concepts from the annotation guideline based on what can be found in the documentation instead of other pre-existing ontologies lowers the complexity and simplifies the terminology.

9.6. Representing Annotated Documents The Way Clinicians View Patients

The AAENOTE is a terminology that provides an index of what is annotated in a clinical document. It is not used to design a language's syntax, grammar, or terms because AAENOTE is a terminology for understanding the language and underlying meanings. Instead, it is the interpreted formalized language that has been translated into basic statements for reasoning. To capture relevant information, the underlying document was represented by annotated labels and relationships for the task of question answering and text understanding instead of solely retrieving information. Hence, the terminology focuses only on items of interest and is blind to items not within the terminology.

The corresponding CIIO is an ontology that models clinical knowledge missing from AAENOTE. It provides the missing clinical knowledge required to reason about the presence of catheters and infections documented in clinical text. Although the data modeled is documented text, it enables clinicians to think about the data as an individual patient because they already do this routinely when documenting patient states.

9.7. Understandability and Accessibility for Domain Experts

The approach in this study made ontology development understandable and accessible for the domain experts without formal ontology training. Furthermore, the employed approach made it possible for clinicians to understand and be part of the design process. In practice, the approach was a necessity to progress in developing the ontology to incorporate clinical knowledge.

9.8. Clinical Utility

The collected competency questions and requirements are largely met. Thus, the main objective of developing a terminology and ontology that clinicians and hospital systems can use to get a systematic overview of identifying and reasoning about PIVC-related phlebitis, infection, and sepsis in an AE corpus has been met. Furthermore, our ontology is a step toward automated and continuous quality control that move beyond today's focus on repeated point prevalence quality controls, like the Peripheral Intravenous Catheter mini Questionnaire (*PIVC-miniQ*) [64].

The developed ontology is of value for sepsis because of its purpose, clinician involvement during development, and intended use. The ontology focuses on identifying indicators of catheter-related phlebitis or infections that can lead to sepsis by utilizing the clinicians' documentation and perspectives. Throughout the whole development, clinicians were involved as the users, domain experts, and data annotators. Furthermore, clinical knowledge within the ontology was captured similarly to how clinicians ask questions, document observations, and view documents as patients. The intent is to eventually implement the ontology into a quality surveillance system to automatically detect the presence of PIVC-related phlebitis and BSIs to improve PIVC care and lower sepsis incidents. Thus, only documented content can be included as data, and the ontology must directly correspond to and represent concepts documented within the AE documents from the clinician's perspective.

10. Future Work

For the sepsis-related use case, the synthetic AE dataset used for annotations is a placeholder for the real Norwegian AE dataset and clinical records from the EHR. Future work includes utilizing the current AAENOTE to annotate the real Norwegian AE dataset and clinical records. And to evaluate if clinical knowledge from the CIIO can still be applied and expanded on new data. Additionally, the ontologies could be applied to AE documents at other Norwegian hospitals to assess how similar documentation and knowledge are between different hospitals. The ontologies can be directly translated to other Scandinavian languages (e.g., Swedish and Danish) and applied similarly at other Scandinavian hospitals. The design and representations are largely language-independent and should be easy to transform for English clinical text about adverse events. After all, international literature suggests that the phenomena related to PIVC and devices are language-independent [3]. It would also be possible to provide multi-language querying over multi-language AE documents to enable cross-language repositories [65]. Furthermore, supervised machine learning methods can be employed to identify PIVC-related BSIs and classify patients requiring additional monitoring.

11. Conclusion

The development process resulted in a terminology and an ontology, specifically, the Annotated Adverse Event NOte TErminology (AAENOTE) which models annotated classes in annotated documents and the Catheter Infection Indications Ontology (CIIO) which models clinical knowledge for catheter and infection indications. Although there is a clinical focus here, the methodology for creating a terminology from an annotation guideline for semantically annotated data and a domain knowledge ontology to represent knowledge can be utilized in other domains to provide additional semantic meaning to annotated datasets in other domains.

12. Data Availability

The AAENOTE, CIIO, and SPARQL queries for this paper are in the GitHub repository branch "swj" of https://github.com/melissayan/aaenote_and_ciio. Detailed specifications for AAENOTE and CIIO were generated using WIzard for DOCumenting Ontologies (WIDOCO) [66] and are available in English and Norwegian at https://folk.ntnu.no/melissay/ontology/index.html.

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Appendix A. Ontology Development Methods and Evaluation Similarities

There are various ontology development methods and the steps in this study have some similarities to other methods Table 6.

Table 6
Ontology Development Methods Versus This Paper

	Uschold and King [31]	**Grüninger and Fox** [32]	**METHONTOLOGY** [33]	**On-To-Knowledge** [34]	**NeOn** [35]	**This Paper**
Pre-development				Feasibility study phase to identify problems.	Initiation phase to specify ontology requirements, intended use, users, and formal language in the form of competency questions and glossary of terms.	Use clinician identified research question to form competency questions. Form terms for annotation, perform data screening and pre-annotation, develop annotation guideline, schedule annotation, implement annotation sessions, and evaluate annotations.
Specification	Identify ontology purpose, intended use, and users.	Define ontology requirements as competency questions based on a scenario or user provided problem.	Specification phase to produce ontology specifications.	Kickoff phase to document ontology requirements and semi-formal ontology.	Part of pre-development.	Part of pre-development.
Conceptualization	Identify terms and relationships of interest.	Define terminology of ontology.	Conceptualization phase to build glossary of terms.	Refinement phase to refine semi-formal ontology and formalize ontology iteratively based on domain expert interviews.	Design phase to produce an informal and formal model to meet requirements.	Annotation and annotation guideline revision phases determine the terms and concepts that are documented in data.
Formalization	Codify ontology into formal language.	Specify terminology definitions using first order logic.	Part of conceptualization.	Part of conceptualization.	Implementation phase to implement the formal model into an ontology language.	Codify terminology and ontology in Protégé using OWL.
Implementation	Part of formalization.	Represent terminology in a formal language.	Implementation phase to codify ontology into formal ontology.			Part of formalization.

Table 6
(continued)

	Uschold and King [31]	**Grüninger and Fox** [32]	**METHONTOLOGY** [33]	**On-To-Knowledge** [34]	**NeOn** [35]	**This Paper**
Management				Apply the ontology and manage it's evolution and maintenance.	Use the ontology to detect errors or missing knowledge for design phase of the next ontology version.	Terminology can be updated to a new annotation guideline version and its corresponding annotated corpus. Ontology can include new clinical knowledge.
Knowledge Acquisition			Interview experts and/or analyze text.	Knowledge creation, capture, retrieval and access, and use.	Knowledge is introduced by domain experts and ontology practitioners at different development phases.	Knowledge was acquired iteratively with users and domain experts. Discussions with users and domain experts resulted in annotation guideline revisions and discovering the knowledge needed for ontology reasoning and inferences. Annotations by domain expert annotators to capture knowledge from text.
Evaluation	Adapt what has been done in the knowledge based systems field for ontologies.	Evaluate the ontology by proving completeness theorems to answer competency questions.	Evaluate the ontologies, software environment, and documenation with the requirement specification document during and between each phase. Document how the ontology was evaluated, errors detected, and knowledge sources for evaluation.	Proposed technology-focused (i.e., the development tool's evaluation of syntax and semantics of the ontology and the evaluation of tools and applications for interoperability and scalability), user-focused (i.e., user satisfaction with the application and comparing the ontology based application to pre-existing ones), and formal evaluation.	Evaluate the ontology using 5 different tasks [67] which includes selecting individual ontology network components for evaluation, selecting the evaluation goal and approach, identifying the reference and evaluation metric, applying the selected evaluation, and presenting the combined results of the individual components.	Ability to answer competency questions and if the ontology is useful from the perspective of the user.
Documentation	Document ontology type and purpose		Document ideally all phases, knowledge acquisition, and evaluation.	Document kickoff phase ontology requirements.	Document ontology requirement specifications, ontology description, and evaluation.	Annotation guidelines record changes, annotations document knowledge acquisition, and evaluation documentation answers competency questions in a format understandable to the users and developers.

Appendix B. Annotated Adverse Event NOte TErminology (AAENOTE) Hierarchy Competency Questions (CQs), SPARQL Queries, and Results

B.1. AAENOTE Hierarchy

The AAENOTE classes and their subclasses can be found in the following figures:

1. Fig. 8 `Observation`
2. Fig. 9 `Anatomical location`
3. Fig. 10 `Medical device`
4. Fig. 11 `Procedure`
5. Fig. 12 `Identifier`
6. Fig. 13 `Person`
7. Fig. 14 `Annotated document`

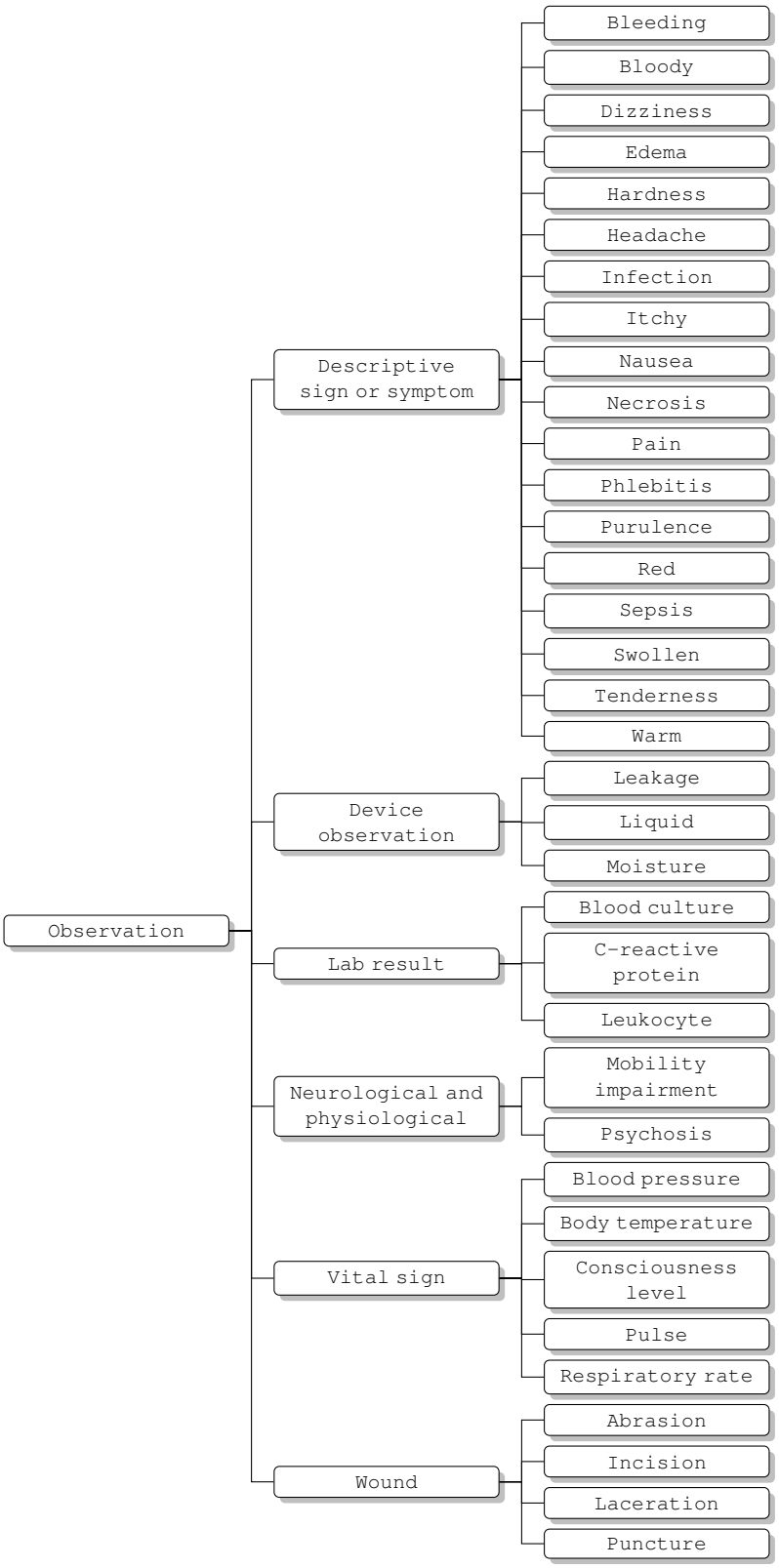

Fig. 8. AAENOTE Observation Class Hierarchy

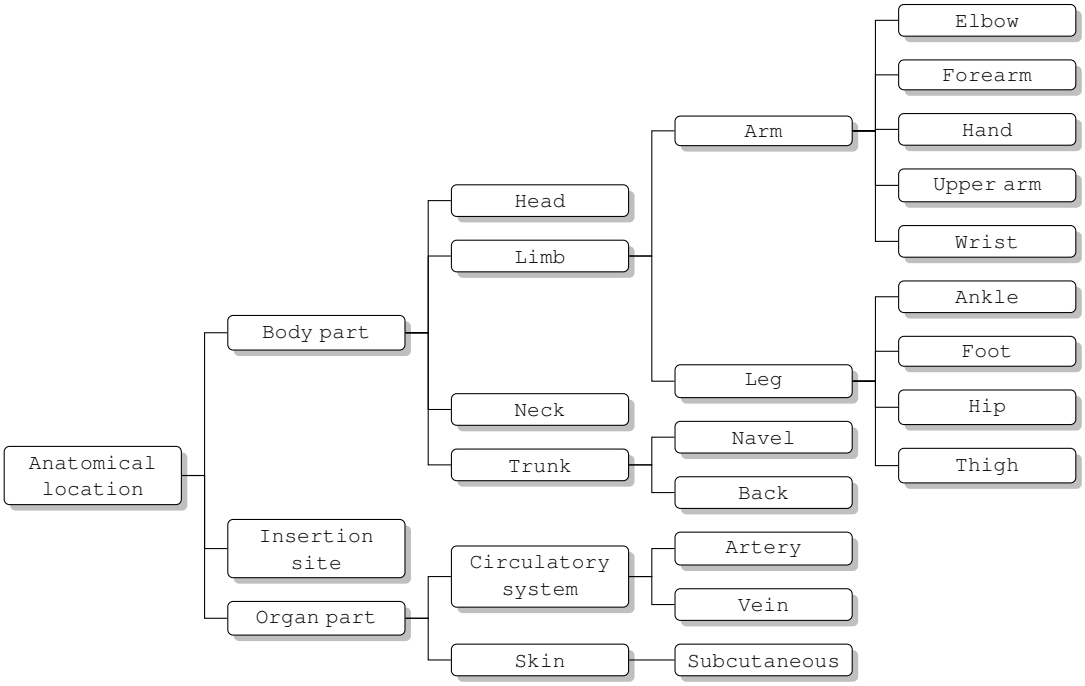

Fig. 9. AAENOTE Anatomical Location Class Hierarchy

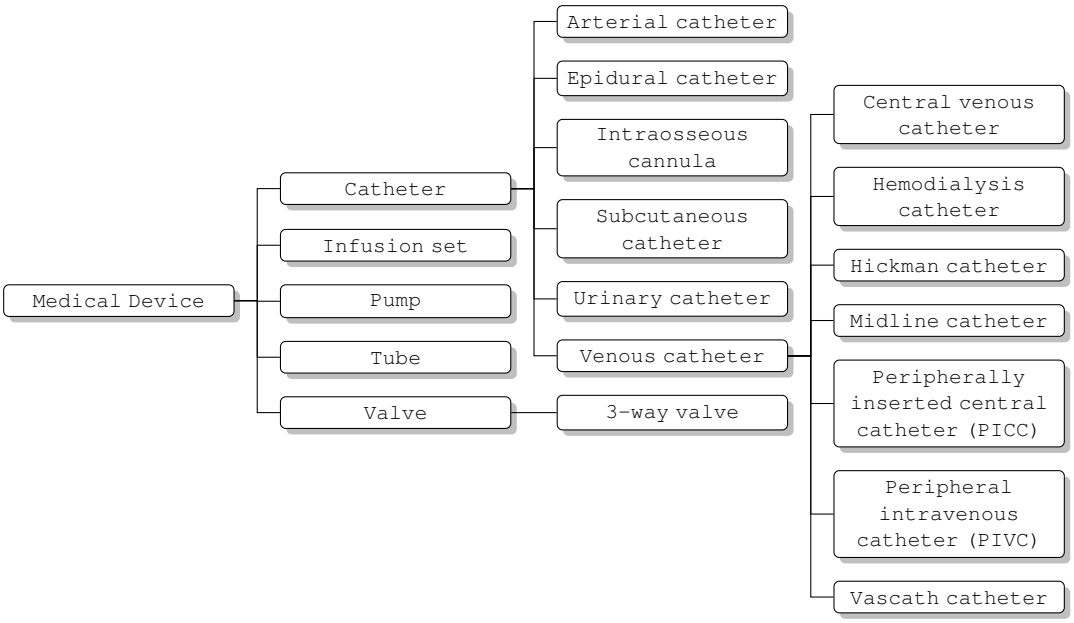

Fig. 10. AAENOTE Medical Device Class Hierarchy

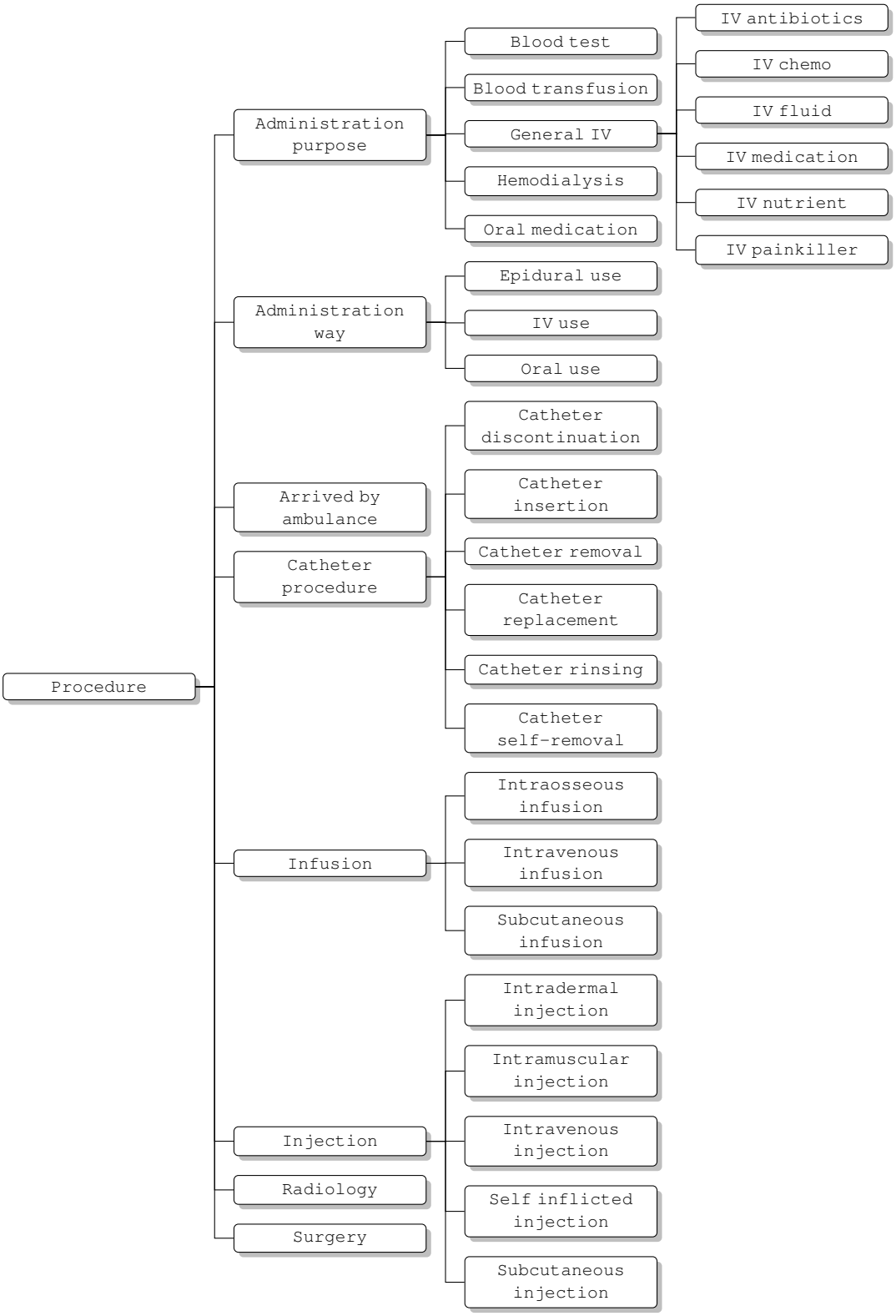

Fig. 11. AAENOTE Procedure Class Hierarchy

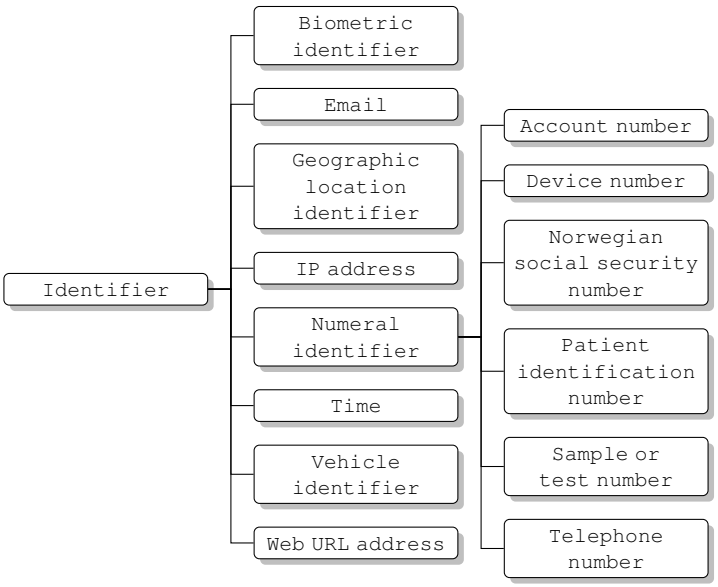

Fig. 12. AAENOTE Identifier Class Hierarchy

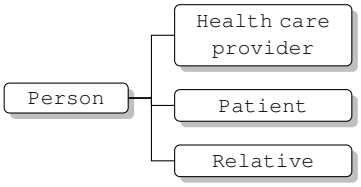

Fig. 13. AAENOTE Person Class Hierarchy

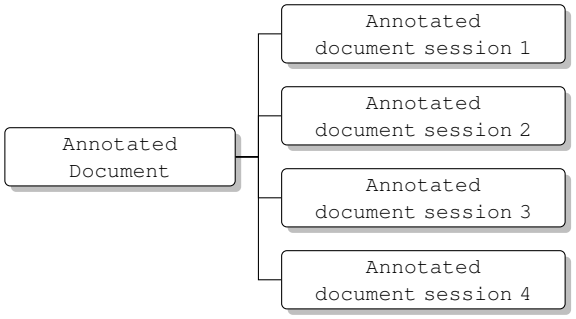

Fig. 14. AAENOTE Annotated Document Class Hierarchy

B.2. Details About Converting Annotation Guideline to Terminology

To further differentiate observations, `Descriptive sign or symptom`, `Vital sign`, `Neurological and physiological`, `Wound`, `Lab result`, and `Device observation` subclasses were introduced. In addition, `Insertion site` was introduced because some documents document a catheter's insertion site without mentioning a specific body part. Similarly, `Organ parts`, such as `Skin` and `Circulatory system`, were also introduced because they are documented instead of body part. For `Medical device`, additional catheters were included (i.e., `Intraosseous cannula` and `Subcutaneous catheter` for specificity. The category for device parts was removed because the terminology only covers catheter and catheter parts; thus, it is a part of a medical device if it is not under a catheter. For `Procedure`, `Administration way` was introduced to describe how a substance was administered into the patient, `Catheter procedure` subclasses all include "catheter" to indicate the action is for catheters only, and different `Infusion` types were included to differentiate from `Injection` types.

A hierarchy for certain data properties was introduced to organize the anatomical location descriptors, contents within a document, and document identity. For instance, document identity-related data properties were included for identification, such as annotator ID, filename, and annotation session. Unlike the data property values for body temperature (i.e., hyperthermia, normal, and hypothermia) and severity level (i.e., high, normal, and low), `Conciousness level` required a separate data property with values of alert, confusion, painfully responsive, unresponsive, and verbally responsive). The "observation is diagnosed by" and "observation said by" data properties were added to distinguish signs from symptoms because signs are what a clinician observes and symptoms are what a patient says.

B.3. AAENOTE Competency Questions and Terminology Usage

Table 7: AAENOTE Competency Questions and Terminology Usage

Competency Question	**Terminology Classes and Relationships to Find Instances***
1. Does patientA have phlebitis, and was it infectious phlebitis, chemical phlebitis, or mechanical phlebitis?	Explicit: `Patient` $\xrightarrow{\text{Person has}}$ `Phlebitis`. Implicit: `Phlebitis` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. †`Anatomical location` is part of a person, and typically a patient given the context is an AE note. ‡Need clinical knowledge to determine if the `Phlebitis` is infectious phlebitis, chemical phlebitis, or mechanical phlebitis.

2. Does patientA have an infection?

Explicit:

`Patient` $\xrightarrow{\text{Person has}}$ `Infection`.
`Patient` $\xrightarrow{\text{Person has}}$ `Infection` and other `Observation(s)`.

Implicit:

`Infection` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
`Infection` and other `Observation(s)` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
†`Anatomical location` is part of a person, and typically a patient given the context is an AE note.
‡Need clinical knowledge to determine if the `Observations` combined indicate infection without `Infection` explicitly included.

3. Does patientA have a BSI?

§ Cannot determine if there is a BSI without a microbiology laboratory result of a positive blood culture and the cultured bacteria name.

4. How many patients have an infection or BSI?

Same as Competency Question 1 and 2.

5. Which patients have sepsis?

Explicit:

`Patient` $\xrightarrow{\text{Person has}}$ `Sepsis`.
`Patient` $\xrightarrow{\text{Person has}}$ `Sepsis` and other `Observation(s)`.

Implicit:

‡Need clinical knowledge to determine if the `Observations` combined indicate `Sepsis`.

6. Does patientB have a catheter?

Explicit:

`Patient` $\xrightarrow{\text{Person has}}$ `Catheter`.

Implicit:

`Catheter` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
†`Anatomical location` is part of a person, and typically a patient given the context is an AE note.
‡Need clinical knowledge to determine if the `Observations`, `Anatomical locations`, and/or `Procedures` combined indicate a `Catheter` is present.

7. Does patientB have a PIVC?

Explicit:

`Patient` $\xrightarrow{\text{Person has}}$ `PIVC`.

Implicit:

`PIVC` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
†`Anatomical location` is part of a person, and typically a patient given the context is an AE note.
‡Need clinical knowledge to determine if the `Observations`, `Anatomical locations`, and/or `Procedures` combined indicate a `PIVC` is present.

8a. How many catheters does patientB have?

Same as Competency Question 5.

8b. Where are the catheters in patientB?	Explicit: `Patient` $\xrightarrow{\text{Person has}}$ `Anatomical location` (X). `Patient` $\xrightarrow{\text{Person has}}$ `Catheter` (Y). `Catheter` (Y) $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location` (X). Implicit: `Catheter` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. †`Anatomical location` is part of a person, and typically a patient given the context is an AE note.
8c. Why does patientB need the catheter(s)?	Explicit: (a) Patient has a catheter and the catheter is used in the procedure. `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter` (Y). `Procedure` $\xrightarrow{\text{Procedure uses}}$ `Catheter` (Y). (b) Patient has a catheter, patient has a procedure, and that procedure uses that catheter. `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter` (Y). `Patient` (X) $\xrightarrow{\text{Person has}}$ `Procedure` (Z). `Procedure` (Z) $\xrightarrow{\text{Procedure uses}}$ `Catheter` (Y). Implicit: (a) Patient has a catheter and patient has a procedure. `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter`. `Patient` (X) $\xrightarrow{\text{Person has}}$ `Procedure`. ‡Need clinical knowledge to determine which `Procedure` is likely to use or involve a specific type of `Catheter`.
9a. Does patientC have an infection and catheter?	Explicit: `Patient` (X) $\xrightarrow{\text{Person has}}$ `Infection`. `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter`. Implicit: ‡Need clinical knowledge to determine if the `Observations` combined indicate `Infection`. ‡Need clinical knowledge to determine if the `Observations`, `Anatomical locations`, and/or `Procedures` combined indicate a `Catheter` is present.
9b. Was patientC's infection associated with a catheter?	§ Cannot determine if an infection is associated with a catheter unless that catheter is tested in the microbiology lab.

B.4. AAENOTE CQ 1: Does patientA have phlebitis, and was it infectious phlebitis, chemical phlebitis, or mechanical phlebitis?

The patients who have phlebitis are listed in Table 8 using Listing 1. And anatomical locations with phlebitis in Table 9 were queried using Listing 2.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT DISTINCT ?indv_patient ?class_phlebitis
WHERE {
        ?indv_patient rdf:type :patient ;
                rdf:type ?class_patient .
        FILTER(?class_patient != owl:NamedIndividual) .
        ?indv_phlebitis rdf:type* :phlebitis ;
                rdf:type ?class_phlebitis .
        FILTER(?class_phlebitis != owl:NamedIndividual) .
        FILTER(REGEX(str(?class_phlebitis), "phlebitis")) .
        ?indv_patient :person_has ?indv_phlebitis .
}
ORDER BY ?indv_patient
```

Listing 1: Patient has phlebitis.

Table 8
AAENOTE SPARQL Query Result: List patients that have phlebitis

Query Result	Patient	Phlebitis
1	patient.T1.2.lo22a.SD_0003	✓
2	patient.T1.3.do13a.PO_0005	✓
3	patient.T2.2.do13a.SP_0008	✓
4	patient.T2.2.lo12a.SD_0003	✓
5	patient.T2.2.lo22a.PO_0005	✓
6	patient.T2.3.do23a.PO_0005	✓
7	patient.T2.3.po24a.SD_0003	✓
8	patient.T2.4.lo22a.SP_0008	✓
9	patient.T3.3.po14a.SD_0003	✓
10	patient.T4.1.po14a.PO_0005	✓

Query result 1-10: `Patient` $\xrightarrow{\text{Person has}}$ `Phlebitis`.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT DISTINCT ?indv_location ?class_phlebitis
WHERE {
        ?indv_phlebitis rdf:type :phlebitis ;
                rdf:type ?class_phlebitis .
        FILTER(?class_phlebitis != owl:NamedIndividual) .
        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                rdf:type ?class_location .
        FILTER(?class_location != owl:NamedIndividual) .
        ?indv_phlebitis :located_nearby_on_at_in ?indv_location .
}
ORDER BY ?indv_location
```

Listing 2: List phlebitis located nearby/on/at/in an anatomical location.

Table 9
AAENOTE SPARQL Query Result: List phlebitis at an anatomical location

Query Result	Anatomical Location	Phlebitis
1	elbow.T1.4.lo22a.DO_0010	✓
2	elbow.T2.1.do13a.DO_0010	✓
3	elbow.T2.4.lo12a.DO_0010	✓
4	elbow.T3.3.so11a.DO_0010	✓
5	elbow.T3.3.so21a.DO_0010	✓
6	hand.T3.4.lo12a.SP_0008	✓
7	hand.T4.3.do13a.PO_0005	✓
8	hand.T7.2.lo22a.PO_0005	✓
9	wrist.T4.2.do13a.SP_0008	✓
10	patient.T4.1.po14a.PO_0005	✓

Query result 1-10: Listing 5 SPARQL query: `Phlebitis` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.

B.5. AAENOTE CQ 2: Does patientA have an infection?

B.5.1. AAENOTE CQ 2 Explicit

The patients who have infection are listed in Table 10 using Listing 3. Whereas, patients who have infection and/or other observations are listed in Table 11 using Listing 4.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT DISTINCT ?indv_patient ?class_infection
WHERE {
        ?indv_patient rdf:type :patient ;
                rdf:type ?class_patient .
        FILTER(?class_patient != owl:NamedIndividual) .
        ?indv_infection rdf:type* :infection ;
                rdf:type ?class_infection .
        FILTER(?class_infection != owl:NamedIndividual) .
        FILTER(REGEX(str(?class_infection), "infection")) .
        ?indv_patient :person_has ?indv_infection .
}
ORDER BY ?indv_patient
```

Listing 3: List patients who have infection.

Table 10
AAENOTE SPARQL Query Result: List patients that have infection

Query Result	Patient	Infection
1	patient.T1.2.lo22a.SD_0006	✓
2	patient.T1.4.lo22a.SP_0002	✓
3	patient.T10.2.do23a.SP_0007	✓
4	patient.T12.4.lo12a.SP_0007	✓
5	patient.T2.2.do23a.SP_0006	✓
6	patient.T2.2.lo12a.SD_0006	✓
7	patient.T2.3.do23a.PO_0010	✓
8	patient.T2.3.po14a.SD_0006	✓
9	patient.T3.2.do13a.SP_0007	✓
10	patient.T4.4.lo22a.DO_0008	✓
11	patient.T4.4.so11a.DP_0010	✓
12	patient.T5.2.po24a.DO_0008	✓
13	patient.T5.4.lo22a.SP_0007	✓
14	patient.T7.3.po24a.SD_0006	✓

Query result 1-14: `Patient` $\xrightarrow{\text{Person has}}$ `Infection`.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT DISTINCT ?indv_patient ?observations
WHERE {
        {
                # Group ?class_observations alphabetically by ?indv_patient
                SELECT ?indv_patient ?class_patient
                    (GROUP_CONCAT (DISTINCT str(?class_observation); separator=", " ) as ?observations)
                WHERE {
                        # Organize alphabetically ?class_observations
                        SELECT ?indv_patient ?class_patient ?class_observation
                        WHERE {
                                ?indv_patient rdf:type :patient ;
                                        rdf:type ?class_patient .
                                FILTER(?class_patient != owl:NamedIndividual) .
                                FILTER(REGEX(str(?class_patient), "patient")) .
                                ?indv_observation rdf:type/rdfs:subClassOf* :observation ;
                                        rdf:type ?class_observation .
                                FILTER(?class_observation != owl:NamedIndividual) .
                                ?indv_patient :person_has ?indv_observation .
                        }
                        GROUP BY ?indv_patient ?class_patient ?class_observation
                        ORDER BY ?class_observation
                }
                GROUP BY ?indv_patient ?class_patient
        }
        FILTER REGEX(str(?observations), "infection")
}
ORDER BY ?indv_patient
```

Listing 4: List patients who have infection and/or other observations.

Table 11

AAENOTE SPARQL Query Result: List patients that have infection and/or another observation

Query Result	Person	Observation											
	Patient	blood pressure	body temp	c reactive protein	conciousness level	infection	neurological and physiological	observation	pulse	red	respiratory rate	sepsis	swollen
1	patient.T1.2.lo22a.SD_0006	✓	✓	✓		✓			✓				
2	patient.T1.4.lo22a.SP_0002		✓			✓					✓		
3	patient.T10.2.do23a.SP_0007				✓	✓							
4	patient.T12.4.lo12a.SP_0007				✓	✓		✓					
5	patient.T2.2.do23a.SP_0006					✓							
6	patient.T2.2.lo12a.SD_0006		✓	✓		✓							
7	patient.T2.3.do23a.PO_0010					✓				✓			
8	patient.T2.3.po14a.SD_0006	✓	✓	✓		✓	✓	✓	✓		✓		
9	patient.T3.2.do13a.SP_0007			✓	✓	✓		✓					
10	patient.T4.4.lo22a.DO_0008					✓				✓			✓
11	patient.T4.4.so11a.DP_0010					✓					✓		
12	patient.T5.2.po24a.DO_0008					✓	✓			✓			✓
13	patient.T5.4.lo22a.SP_0007			✓		✓	✓						
14	patient.T7.3.po24a.SD_0006	✓	✓	✓		✓			✓			✓	

Query result 1-14: `Patient` $\xrightarrow{\text{Person has}}$ `Infection` and other `Observation(s)`.

B.5.2. AAENOTE CQ 2 Implicit

By using anatomical locations it is possible to implicitly identify infection within a patient because the anatomical locations refer to a place on a human and in the context of AE notes anatomical locations commonly refer to a place on a patient. As shown in Table 12, only 1 instance where infection is located at an anatomical location was found using either Listing 5 or Listing 6.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT DISTINCT ?indv_location ?class_infection
WHERE {
        ?indv_infection rdf:type :infection ;
                rdf:type ?class_infection .
        FILTER(?class_infection != owl:NamedIndividual) .
        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                rdf:type ?class_location .
        FILTER(?class_location != owl:NamedIndividual) .
        ?indv_infection :located_nearby_on_at_in ?indv_location .
}
ORDER BY ?indv_location
```

Listing 5: List infection located nearby/on/at/in an anatomical location.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT DISTINCT ?indv_location ?observations
WHERE {
        {
                SELECT ?indv_location ?class_location
                    (GROUP_CONCAT (DISTINCT ?class_observation; separator=", " ) as ?observations)
                WHERE {
                        {
                                SELECT ?indv_location ?class_location ?class_observation
                                WHERE {
                                        ?indv_observation rdf:type/rdfs:subClassOf* :observation ;
                                                rdf:type ?class_observation .
                                        FILTER(?class_observation != owl:NamedIndividual) .
                                        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                                                rdf:type ?class_location .
                                        FILTER(?class_location != owl:NamedIndividual) .
                                        ?indv_observation :located_nearby_on_at_in ?indv_location .
                                }
                                GROUP BY ?indv_location ?class_location ?class_observation
                                ORDER BY ?class_observation
                        }
                }
                GROUP BY ?indv_location ?class_location
                ORDER BY ?class_location
        }
        FILTER REGEX(str(?observations), "infection")
}
ORDER BY ?indv_location
```

Listing 6: List infection and other observations located nearby/on/at/in an anatomical location.

Table 12
AAENOTE SPARQL Query Result: List infections and/or observations at an anatomical location

Query Result	Anatomical Location	Infection
1	skin.T4.2.po14a.SL_0006	✓

Same results for Listing 5 and Listing 6 SPARQL query.
Query result 1 from Listing 5 SPARQL query: `Infection` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.
Query result 1 from Listing 6 SPARQL query: `Infection` and other `observation(s)` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.

B.6. AAENOTE CQ 3: Does patientA have a BSI?

Cannot determine if there is a BSI without a microbiology laboratory result of a positive blood culture and the cultured bacteria name.

B.7. AAENOTE CQ 4: How many patients have an infection or BSI?

Explicitly, Table 4 shows the number of patients with infection and the number of patients with infection and/or other observations (Listing 7). Implicitly, there was only 1 anatomical location that had infection (Appendix B.5.2), so the results are not shown for the query in Listing 8. If there was clinical knowledge, it could provide the insight required to determine if combinations of observations at certain anatomical locations are indications of an infection (Listing 9 and Table 13). As previously stated in Appendix B.6, BSI cannot be determined because this requires microbiology laboratory blood test results.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?class_patient ?observations ?n_patients
WHERE {
        {
                SELECT ?class_patient
                    (GROUP_CONCAT (DISTINCT str(?class_observation); separator=", " ) as ?observations)
                    (COUNT (DISTINCT ?indv_patient ) as ?n_patients)
                WHERE {
                        ?indv_patient rdf:type :patient ;
                                rdf:type ?class_patient .
                        FILTER(?class_patient != owl:NamedIndividual) .
                        ?indv_infection rdf:type :infection ;
                                rdf:type ?class_observation .
                        FILTER(?class_observation != owl:NamedIndividual) .
                        ?indv_patient :person_has ?indv_infection .
                }
                GROUP BY ?class_patient ?class_observation
                ORDER BY ?class_observation
        }
        UNION
        {

                SELECT ?class_patient ?observations (COUNT (DISTINCT ?indv_patient ) as ?n_patients)
                WHERE {
                        {
                                SELECT ?indv_patient ?class_patient
                                    (GROUP_CONCAT (
                                        DISTINCT str(?class_observation); separator=", " ) as ?observations)
                                WHERE {
                                        SELECT ?indv_patient ?class_patient ?class_observation
                                        WHERE {
                                                ?indv_patient rdf:type :patient ;
                                                        rdf:type ?class_patient .
                                                FILTER(?class_patient != owl:NamedIndividual) .
                                                ?indv_observation rdf:type/rdfs:subClassOf* :observation ;
                                                        rdf:type ?class_observation .
                                                FILTER(?class_observation != owl:NamedIndividual) .
                                                ?indv_patient :person_has ?indv_observation .
                                        }
                                        GROUP BY ?indv_patient ?class_patient ?class_observation
                                        ORDER BY ?class_observation
                                }
                                GROUP BY ?indv_patient ?class_patient
                        }
                        FILTER REGEX(str(?observations), "infection")
                }
                GROUP BY ?class_patient ?observations
        }
}
```

Listing 7: Count the number of patients with infection and number patients with infection and other observations.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?class_location ?observations (COUNT (DISTINCT ?indv_location) as ?n_instances)
WHERE {
        {
                SELECT ?indv_location ?class_location
                    (GROUP_CONCAT (DISTINCT ?class_observation; separator=", " ) as ?observations)
                WHERE {
                        {
                                SELECT ?indv_location ?class_location ?class_observation
                                WHERE {
                                        ?indv_observation rdf:type/rdfs:subClassOf* :observation ;
                                                rdf:type ?class_observation .
                                        FILTER(?class_observation != owl:NamedIndividual) .
                                        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                                                rdf:type ?class_location .
                                        FILTER(?class_location != owl:NamedIndividual) .
                                        ?indv_observation :located_nearby_on_at_in ?indv_location .
                                }
                                GROUP BY ?indv_location ?class_location ?class_observation
                                ORDER BY ?class_observation
                        }
                }
                GROUP BY ?indv_location ?class_location
                ORDER BY ?class_location
        }
        FILTER REGEX(str(?observations), "infection")
}
GROUP BY ?class_location ?observations
ORDER BY ?class_location
```

Listing 8: Count the number of anatomical locations where infection and other observations are located nearby/on/at/in that anatomical location.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?class_location ?observations (COUNT (DISTINCT ?indv_location) as ?n_instances)
WHERE {
         {
                 SELECT ?indv_location ?class_location
                     (GROUP_CONCAT (DISTINCT ?class_observation; separator=", " ) as ?observations)
                 WHERE {
                         {
                                 SELECT ?indv_location ?class_location ?class_observation
                                 WHERE {
                                         ?indv_observation rdf:type/rdfs:subClassOf* :observation ;
                                                 rdf:type ?class_observation .
                                         FILTER(?class_observation != owl:NamedIndividual) .
                                         ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                                                 rdf:type ?class_location .
                                         FILTER(?class_location != owl:NamedIndividual) .
                                         ?indv_observation :located_nearby_on_at_in ?indv_location .
                                 }
                                 GROUP BY ?indv_location ?class_location ?class_observation
                                 ORDER BY ?class_observation
                         }
                 }
                 GROUP BY ?indv_location ?class_location
                 ORDER BY ?class_location
         }
}
GROUP BY ?class_location ?observations
ORDER BY ?class_location
```

Listing 9: Count the number of anatomical locations with the same observations located nearby/on/at/in that anatomical location.

Table 13
AAENOTE SPARQL Results for Anatomical Location with Combinations of Observations

Query Result	Instances	Anatomical Location				Observation										
		arm	elbow	hand	skin	body temp	edema	infection	mobility impairment	pain	phlebitis	purulence	red	swollen	warm	wound
1	12	✓								✓						
2	7	✓												✓		
3	6	✓											✓	✓		
4	4	✓								✓				✓		
5	3	✓								✓			✓	✓		
6	2	✓								✓			✓			
7	2	✓											✓			
8	1	✓							✓	✓						
9	1	✓							✓	✓		✓				
10	1	✓				✓			✓	✓		✓				
11	1	✓										✓				
12	1	✓											✓		✓	
13	1	✓					✓						✓			
14	1	✓											✓	✓	✓	
15	7		✓												✓	
16	7		✓										✓			
17	7		✓										✓	✓	✓	
18	6		✓							✓			✓	✓		
19	5		✓							✓				✓		
20	4		✓								✓					
21	3		✓											✓		
22	2		✓										✓		✓	
23	1		✓							✓						
24	1		✓									✓				
25	4			✓										✓		
26	3			✓							✓					
27	2			✓									✓	✓		✓
28	1			✓						✓						
29	1			✓						✓				✓		
30	1			✓									✓	✓		
31	3				✓					✓						
32	3				✓									✓		
33	2				✓					✓				✓		
34	2				✓					✓			✓	✓		
35	2				✓								✓			
36	2				✓								✓	✓		
37	1				✓										✓	
38	1				✓			✓								
39	1				✓								✓		✓	
40	1				✓		✓						✓	✓		

Query result 1-40: `Observation(s)` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`.

B.8. AAENOTE CQ 5: Which patients have sepsis?

Explicitly, 5 patients have sepsis (Table 14, Listing 10) and 3 of the 5 patients with sepsis have sepsis and another observation (Table 15, Listing 11). Additional clinical knowledge is needed to determine if other observations combined without the sepsis class are indications of sepsis.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?class_sepsis
WHERE {
        ?indv_patient rdf:type :patient .
        ?indv_sepsis rdf:type :sepsis ;
                rdf:type ?class_sepsis .
        FILTER(?class_sepsis != owl:NamedIndividual) .
        ?indv_patient :person_has ?indv_sepsis .
}
ORDER BY ?indv_patient
```

Listing 10: List patients who have sepsis.

Table 14
AAENOTE SPARQL Query Result: List patients that have sepsis

Query Result	Patient	Sepsis
1	patient.T1.2.do13a.SP_0006	✓
2	patient.T1.4.lo12a.SP_0006	✓
3	patient.T6.3.lo22a.DP_0010	✓
4	patient.T7.2.po24a.SL_0004	✓
5	patient.T7.3.po24a.SD_0006	✓

Query result 1-5: `Patient` $\xrightarrow{\text{Person has}}$ `Sepsis`.

Table 15
AAENOTE SPARQL Query Result: List patients that have sepsis and/or another observation

Query Result	Person	Observation								
	Patient	blood pressure	body temp	c reactive protein	infection	pulse	red	respiratory rate	sepsis	swollen
1	patient.T1.2.do13a.SP_0006								✓	
2	patient.T1.4.lo12a.SP_0006								✓	
3	patient.T6.3.lo22a.DP_0010							✓	✓	
4	patient.T7.2.po24a.SL_0004		✓				✓		✓	✓
5	patient.T7.3.po24a.SD_0006	✓	✓	✓	✓	✓			✓	

Query result 1-5: `Patient` $\xrightarrow{\text{Person has}}$ `Sepsis` and other `Observation(s)`.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?observations
WHERE {
        {
                SELECT ?indv_patient ?class_patient
                    (GROUP_CONCAT (DISTINCT str(?class_observation); separator=", " ) as ?observations)
                WHERE {
                        {
                                SELECT ?indv_patient ?class_patient ?class_observation
                                WHERE {
                                        ?indv_patient rdf:type :patient ;
                                                rdf:type ?class_patient .
                                        FILTER(?class_patient != owl:NamedIndividual) .
                                        ?indv_observation rdf:type/rdfs:subClassOf* :observation ;
                                                rdf:type ?class_observation .
                                        FILTER(?class_observation != owl:NamedIndividual) .
                                        ?indv_patient :person_has ?indv_observation .
                                }
                                GROUP BY ?indv_patient ?class_patient ?class_observation
                                ORDER BY ?class_observation
                        }
                }
                GROUP BY ?indv_patient ?class_patient
        }
        FILTER REGEX(str(?observations), "sepsis")
}
ORDER BY ?indv_patient
```

Listing 11: List patients that have sepsis and/or other observations.

B.9. AAENOTE CQ 6: Does patientB have a catheter?

The patient and the type of catheter a patient has can be found explicitly using Listing 12. A subset of the results are in Table 16, where each patient individual is listed with a type of catheter and how many catheters of that specific type are present. Thus, the same patient can be listed multiple times as seen in Table 16's Query Result 28-30 where the same patient is listed 3 times because the patient has 3 catheters of different types. Implicitly, an anatomical location with a catheter indicates a person has a catheter (Listing 13, Table 17). Additional clinical knowledge is needed to determine if other observations combined indicate a catheter is present.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?class_catheter (COUNT (DISTINCT ?indv_catheter ) as ?n_catheters)
WHERE {
        ?indv_patient rdf:type :patient ;
                rdf:type ?class_patient .
        FILTER(?class_patient != owl:NamedIndividual) .
        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                rdf:type ?class_catheter .
        FILTER(?class_catheter != owl:NamedIndividual) .
        ?indv_patient :person_has ?indv_catheter .
}
GROUP BY ?indv_patient ?class_catheter
ORDER BY ?indv_patient ?class_catheter
```

Listing 12: List patients that have a catheter, the catheter's type, and the number of that catheter type.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_location ?class_catheter
WHERE {
        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                rdf:type ?class_catheter .
        FILTER(?class_catheter != owl:NamedIndividual) .
        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                rdf:type ?class_location .
        FILTER(?class_location != owl:NamedIndividual) .
        ?indv_catheter :located_nearby_on_at_in ?indv_location .
}
ORDER BY ?indv_location
```

Listing 13: List the anatomical location and the type of catheter located nearby/on/at/in there.

Table 16
AAENOTE SPARQL Query Result: List of patients with a catheter

Query Result	Number of specific catheters	Person	Catheter								
		Patient	catheter	central venous catheter	epidural catheter	hickman catheter	hemodialysis catheter	peripheral intravenous catheter	urinary catheter	vas catheter	venous catheter
1	1	patient.T1.1.lo12a.LO_0007						✓			
2	1	patient.T1.1.lo22a.LO_0007						✓			
3	1	patient.T1.1.lo22a.LO_0009					✓				
4	1	patient.T1.2.do13a.LO_0001						✓			
5	1	patient.T1.2.do13a.SP_0001							✓		
6	1	patient.T1.2.do13a.SP_0005						✓			
7	1	patient.T1.2.do13a.SP_0006						✓			
8	1	patient.T1.2.do13a.SP_0010						✓			
9	1	patient.T1.2.lo12a.PO_0005						✓			
10	1	patient.T1.2.lo12a.SD_0007								✓	
11	1	patient.T1.2.lo22a.SD_0002						✓			
12	1	patient.T1.2.lo22a.SD_0007								✓	
13	1	patient.T1.2.po24a.DO_0001			✓						
		...									
22	1	patient.T1.4.lo12a.SP_0003		✓							
23	1	patient.T1.4.lo22a.DO_0003									✓
24	1	patient.T1.4.lo22a.SP_0005						✓			
25	1	patient.T1.4.lo22a.SP_0006						✓			
26	1	patient.T1.4.lo22a.SP_0010						✓			
27	1	patient.T1.4.po24a.LD_0004				✓					
28	1	patient.T1.4.po24a.LD_0009	✓								
29	1	patient.T1.4.po24a.LD_0009		✓							
30	1	patient.T1.4.po24a.LD_0009			✓						
		...									
93	1	patient.T3.4.so11a.LO_0003									✓
94	1	patient.T3.4.so21a.LO_0004						✓			
95	2	patient.T4.1.lo22a.LO_0003						✓			
		...									
138	1	patient.T9.2.so11a.LD_0003						✓			
139	1	patient.T9.3.po24a.SD_0005						✓			

Query result 1-139: `Patient` $\xrightarrow{\text{Person has}}$ `Catheter`. And provide the specific type of `Catheter`.
Query result 28-30, same patient but different catheters.
Query result 95, the patient has 2 PIVCs.

Table 17
AAENOTE SPARQL Query Result: List anatomical locations with catheters

Query Result	Anatomical Location	Catheter		
	Individuals under class	catheter	venous catheter	peripheral intravenous catheter
1	arm.T14.3.po24a.SD_0002			✓
2	arm.T2.3.po24a.LO_0002			✓
3	arm.T2.3.po24a.SD_0001			✓
4	arm.T3.3.po24a.LO_0005			✓
5	arm.T5.3.po24a.LO_0004			✓
6	arm.T5.3.po24a.SD_0003			✓
7	arm.T5.3.so11a.DO_0002			✓
8	arm.T5.4.lo12a.DO_0003			✓
9	arm.T5.4.lo22a.DO_0003		✓	
	...			
14	arm.T9.4.lo12a.DO_0003			✓
15	body_part.T8.3.po14a.LO_0004			✓
16	elbow.T2.2.lo12a.SD_0001			✓
	...			
69	hand.T9.2.so21a.LD_0003			✓
70	navel.T5.3.so11a.LP_0010	✓		
71	navel.T5.4.do23a.LP_0010	✓		
72	skin.T11.3.po24a.LO_0001			✓
73	skin.T5.2.do23a.LO_0005			✓
74	subcutaneous.T12.2.do23a.LO_0004			✓
75	wrist.T2.2.do13a.LO_0005			✓
76	wrist.T3.2.do23a.LO_0005			✓
77	wrist.T3.4.so11a.LO_0005			✓
78	wrist.T7.3.po14a.LO_0005			✓

Query result 1-78: `Catheter` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. And provide the specific `Anatomical location` and type of `Catheter`.

B.10. AAENOTE CQ 7: Does patientB have a PIVC?

This competency question (CQ) can be answered similarily to Appendix B.9. Explicitly using Listing 14 (Table 18) and implicitly using Listing 15 (Table 19). Likewise, additional clinical knowledge is needed to determine if other observations combined indicate a PIVC is present.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?class_pivc (COUNT (DISTINCT ?indv_pivc) as ?n_catheters)
WHERE {
        ?indv_patient rdf:type :patient ;
                rdf:type ?class_patient .
        FILTER(?class_patient != owl:NamedIndividual) .
        ?indv_pivc rdf:type/rdfs:subClassOf* :peripheral_intravenous_catheter ;
                rdf:type ?class_pivc .
        FILTER(?class_pivc != owl:NamedIndividual) .
        ?indv_patient :person_has ?indv_pivc .
}
GROUP BY ?indv_patient ?class_pivc
ORDER BY ?indv_patient
```

Listing 14: List patients that have a PIVC and number of PIVCs.

Table 18
AAENOTE SPARQL Query Result: List patients that have a PIVC

Query Result	Number of PIVCs	Patient	peripheral intravenous catheter
1	1	patient.T1.1.lo12a.LO_0007	✓
2	1	patient.T1.1.lo22a.LO_0007	✓
3	1	patient.T1.2.do13a.LO_0001	✓
4	1	patient.T1.2.do13a.SP_0005	✓
5	1	patient.T1.2.do13a.SP_0006	✓
		...	
31	1	patient.T2.1.lo22a.LO_0001	✓
32	2	patient.T2.1.lo22a.LO_0003	✓
33	1	patient.T2.2.do23a.LO_0001	✓
		...	
91	1	patient.T8.4.lo22a.SP_0010	✓
92	1	patient.T9.2.so11a.LD_0003	✓
93	1	patient.T9.3.po24a.SD_0005	✓

Query result 1-93: `Patient` $\xrightarrow{\text{Person has}}$ `PIVC`.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_location ?class_pivc
WHERE {
        ?indv_pivc rdf:type/rdfs:subClassOf* :peripheral_intravenous_catheter ;
                rdf:type ?class_pivc .
        FILTER(?class_pivc != owl:NamedIndividual) .
        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                rdf:type ?class_location .
        FILTER(?class_location != owl:NamedIndividual) .
        ?indv_pivc :located_nearby_on_at_in ?indv_location .
}
ORDER BY ?indv_location
```

Listing 15: List anatomical locations with a PIVC.

Table 19
AAENOTE SPARQL Query Result: List anatomical locations with a PIVC

Query Result	Anatomical Location: Individuals under class	Catheter: peripheral intravenous catheter
1	arm.T14.3.po24a.SD_0002	✓
2	arm.T2.3.po24a.LO_0002	✓
3	arm.T2.3.po24a.SD_0001	✓
4	arm.T3.3.po24a.LO_0005	✓
5	arm.T5.3.po24a.LO_0004	✓
...		
14	body_part.T8.3.po14a.LO_0004	✓
15	elbow.T2.2.lo12a.SD_0001	✓
16	elbow.T2.2.lo22a.SD_0001	✓
...		
67	hand.T7.2.lo22a.PO_0005	✓
68	hand.T9.2.so21a.LD_0003	✓
69	skin.T11.3.po24a.LO_0001	✓
70	skin.T5.2.do23a.LO_0005	✓
71	subcutaneous.T12.2.do23a.LO_0004	✓
72	wrist.T2.2.do13a.LO_0005	✓
73	wrist.T3.2.do23a.LO_0005	✓
74	wrist.T3.4.so11a.LO_0005	✓
75	wrist.T7.3.po14a.LO_0005	✓

Query result 1-75: `PIVC` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. And provide the specific `Anatomical location`.

B.11. AAENOTE CQ 8a: How many catheters does patientB have?

Listing 16 is used to explicitly query the number and types of catheters a patient has as shown in Table 20. Sometimes there is a direct relationship between a person and multiple catheters such as in Query Result 28, 30, 45, and 52 of Table 20. Whereas, typically there is only one direct relationship between one catheter and an anatomical location when using the implicit query Listing 17 (Table 21). Similarly to Appendix B.7 where with clinical knowledge it could be possible to identify infection indications based on a combination of observations at a certain anatomical location, it could also be possible to determine if combinations of observations at certain anatomical locations are indications of a catheter.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
# Group ?class_catheters alphabetically by ?indv_patient
SELECT ?indv_patient (GROUP_CONCAT (DISTINCT str(?class_catheter); separator=", " ) as ?catheters)
    (COUNT (DISTINCT ?indv_catheter ) as ?n_catheters)
WHERE {
        {
                # Organize alphabetically ?class_catheter
                SELECT ?indv_patient ?indv_catheter ?class_catheter
                WHERE {
                        ?indv_patient rdf:type :patient ;
                                rdf:type ?class_patient .
                        FILTER(?class_patient != owl:NamedIndividual) .
                        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                                rdf:type ?class_catheter .
                        FILTER(?class_catheter != owl:NamedIndividual) .
                        ?indv_patient :person_has ?indv_catheter .
                }
                GROUP BY ?indv_patient ?indv_catheter ?class_catheter
                ORDER BY ?class_catheter
        }
}
GROUP BY ?indv_patient
ORDER BY ?indv_patient
```

Listing 16: Count the number of catheters a patient has and provide the types of catheters.

Table 20
AAENOTE SPARQL Query Result: List how many catheters and type of catheter a patient has

Query Results	Number of catheters	Person	Catheter								
		Patient	catheter	central venous catheter	epidural catheter	hickman catheter	hemodialysis catheter	peripheral intravenous catheter	urinary catheter	vas catheter	venous catheter
1	1	patient.T1.1.lo12a.LO_0007						✓			
2	1	patient.T1.1.lo22a.LO_0007						✓			
3	1	patient.T1.1.lo22a.LO_0009					✓				
4	1	patient.T1.2.do13a.LO_0001						✓			
5	1	patient.T1.2.do13a.SP_0001							✓		
6	1	patient.T1.2.do13a.SP_0005						✓			
7	1	patient.T1.2.do13a.SP_0006						✓			
8	1	patient.T1.2.do13a.SP_0010						✓			
9	1	patient.T1.2.lo12a.PO_0005						✓			
10	1	patient.T1.2.lo12a.SD_0007								✓	
11	1	patient.T1.2.lo22a.SD_0002						✓			
12	1	patient.T1.2.lo22a.SD_0007								✓	
13	1	patient.T1.2.po24a.DO_0001			✓						
		…									
26	1	patient.T1.4.lo22a.SP_0010						✓			
27	1	patient.T1.4.po24a.LD_0004						✓			
28	4	patient.T1.4.po24a.LD_0009	✓	✓	✓				✓		
29	1	patient.T1.4.po24a.SO_0009							✓		
30	2	patient.T1.4.so11a.DP_0002						✓	✓		
		…									
45	2	patient.T2.1.lo22a.LO_0003						✓			
46	1	patient.T2.2.do13a.SP_0003		✓							
47	1	patient.T2.2.do23a.LO_0001						✓			
48	1	patient.T2.2.do23a.LO_0007						✓			
49	1	patient.T2.2.do23a.SP_0006						✓			
50	1	patient.T2.2.lo22a.PO_0005						✓			
51	1	patient.T2.2.po14a.DO_0002						✓			
52	3	patient.T2.2.so11a.LD_0009	✓	✓					✓		
53	1	patient.T2.2.so11a.PO_0005						✓			
		…									
70	1	patient.T3.2.do23a.SP_0003		✓							
71	1	patient.T3.2.po14a.DO_0001			✓						
72	1	patient.T3.2.po14a.DO_0003									✓
73	1	patient.T3.2.so11a.LD_0003						✓			
74	1	patient.T3.2.so11a.LD_0004				✓					
75	1	patient.T3.3.do13a.SL_0002						✓			
		…									
131	1	patient.T9.2.so11a.LD_0003						✓			
132	1	patient.T9.3.po24a.SD_0005						✓			

Query result 1-132: `Patient` $\xrightarrow{\text{Person has}}$ `Catheter`. And count how many `Catheter(s)` of a specific type the `Patient` has.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
# Group ?class_catheters alphabetically by ?indv_location
SELECT ?indv_location (GROUP_CONCAT (DISTINCT str(?class_catheter); separator=", " ) as ?catheters)
    (COUNT (DISTINCT ?indv_catheter ) as ?n_catheters)
WHERE {
        {
                # Organize alphabetically ?class_catheter
                SELECT ?indv_location ?indv_catheter ?class_catheter
                WHERE {
                        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                                rdf:type ?class_catheter .
                        FILTER(?class_catheter != owl:NamedIndividual) .
                        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                                rdf:type ?class_location .
                        FILTER(?class_location != owl:NamedIndividual) .
                        ?indv_catheter :located_nearby_on_at_in ?indv_location .
                }
                GROUP BY ?indv_location ?indv_catheter ?class_catheter
                ORDER BY ?class_catheter
        }
}
GROUP BY ?indv_location
ORDER BY ?indv_location
```

Listing 17: Count the number of catheters located nearby/on/at/in an anatomical location and provide the types of catheters.

Table 21

AAENOTE SPARQL Query Result: List how many catheters and type of catheter an anatomical location has

Query Results	Number of catheters	Anatomical Location	Catheter		
		Individuals under class	catheter	peripheral intravenous catheter	venous catheter
1	1	arm.T14.3.po24a.SD_0002		✓	
2	1	arm.T2.3.po24a.LO_0002		✓	
3	1	arm.T2.3.po24a.SD_0001		✓	
4	1	arm.T3.3.po24a.LO_0005		✓	
5	1	arm.T5.3.po24a.LO_0004		✓	
6	1	arm.T5.3.po24a.SD_0003		✓	
7	1	arm.T5.3.so11a.DO_0002		✓	
8	1	arm.T5.4.lo12a.DO_0003		✓	
9	1	arm.T5.4.lo22a.DO_0003			✓
		...			
14	1	arm.T9.4.lo12a.DO_0003		✓	
15	1	body_part.T8.3.po14a.LO_0004		✓	
16	1	elbow.T2.2.lo12a.SD_0001		✓	
		...			
67	1	hand.T6.3.do23a.PO_0005		✓	
68	1	hand.T7.2.lo22a.PO_0005		✓	
69	1	hand.T9.2.so21a.LD_0003		✓	
70	1	navel.T5.3.so11a.LP_0010	✓		
71	1	navel.T5.4.do23a.LP_0010	✓		
72	1	skin.T11.3.po24a.LO_0001		✓	
73	1	skin.T5.2.do23a.LO_0005		✓	
74	1	subcutaneous.T12.2.do23a.LO_0004		✓	
75	1	wrist.T2.2.do13a.LO_0005		✓	
76	1	wrist.T3.2.do23a.LO_0005		✓	
77	1	wrist.T3.4.so11a.LO_0005		✓	
78	1	wrist.T7.3.po14a.LO_0005		✓	

Query result 1-78: `Catheter` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. And count how many `Catheter(s)` of a specific type the specific `Anatomical location` has.

B.12. AAENOTE CQ 8b: Where are the catheters in patientB?

Explicitly Listing 18 and Table 22. Implicitly, it is the same as Appendix B.9's Listing 13 and Table 17 where catheter located at an anatomical location indicates a person has the catheter. Here also, additional clinical knowledge is needed to determine if other observations combined indicate a catheter is present.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?indv_catheter ?indv_location
WHERE {
        ?indv_patient rdf:type :patient ;
                rdf:type ?class_patient .
        FILTER(?class_patient != owl:NamedIndividual) .
        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                rdf:type ?class_catheter .
        FILTER(?class_catheter != owl:NamedIndividual) .
        ?indv_location rdf:type/rdfs:subClassOf* :anatomical_location ;
                rdf:type ?class_location .
        FILTER(?class_location != owl:NamedIndividual) .
        ?indv_patient :person_has ?indv_catheter ;
            :person_has ?indv_location .
        ?indv_catheter :located_nearby_on_at_in ?indv_location .
}
ORDER BY ?indv_patient
```

Listing 18: List patients that have an anatomical location, a catheter, and the patient's catheter is located nearby/on/at/in the patient's anatomical location.

Table 22

AAENOTE SPARQL Query Result: Patient has an anatomical location, patient has a catheter, and that catheter is at the patient's anatomical location.

Query Result	Patient	Catheter	Anatomical Location
1	patient.T1.4.lo22a.DO_0003	venous_catheter.T6.4.lo22a.DO_0003	arm.T5.4.lo22a.DO_0003
2	patient.T4.2.lo22a.SD_0003	peripheral_intravenous_catheter.T5.2.lo22a.SD_0003	hand.T6.2.lo22a.SD_0003

Query result 1-2: `Patient` (X) $\xrightarrow{\text{Person has}}$ `Anatomical location` (Y), `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter` (Z), and `Catheter` (Z) $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location` (Y).

B.13. AAENOTE CQ 8c: Why does patientB need the catheter(s)?

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?class_catheter
    (GROUP_CONCAT (DISTINCT str(?class_procedure); separator=", " ) as ?procedures)
WHERE {
        {
                SELECT ?indv_patient ?class_catheter ?class_procedure
                WHERE {
                        ?indv_patient rdf:type :patient ;
                                rdf:type ?class_patient .
                        FILTER(?class_patient != owl:NamedIndividual) .
                        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                                rdf:type ?class_catheter .
                        FILTER(?class_catheter != owl:NamedIndividual) .
                        ?indv_procedure rdf:type/rdfs:subClassOf* :procedure ;
                                rdf:type ?class_procedure .
                        FILTER(?class_procedure != owl:NamedIndividual) .
                        ?indv_patient :person_has ?indv_catheter .
                        ?indv_procedure :procedure_uses ?indv_catheter .
                }
                GROUP BY ?indv_patient ?class_catheter ?class_procedure
                ORDER BY ?class_procedure
        }
}
GROUP BY ?indv_patient ?class_catheter
ORDER BY ?indv_patient
```

Listing 19: List patients that have a catheter and the procedures which use that catheter.

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?class_catheter
    (GROUP_CONCAT (DISTINCT str(?class_procedure); separator=", " ) as ?procedures)
WHERE {
        {
                SELECT ?indv_patient ?class_catheter ?class_procedure
                WHERE {
                        ?indv_patient rdf:type :patient ;
                                rdf:type ?class_patient .
                        FILTER(?class_patient != owl:NamedIndividual) .
                        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                                rdf:type ?class_catheter .
                        FILTER(?class_catheter != owl:NamedIndividual) .
                        ?indv_procedure rdf:type/rdfs:subClassOf* :procedure ;
                                rdf:type ?class_procedure .
                        FILTER(?class_procedure != owl:NamedIndividual) .
                        ?indv_patient :person_has ?indv_catheter ;
                            :person_has ?indv_procedure .
                        ?indv_procedure :procedure_uses ?indv_catheter .
                }
                GROUP BY ?indv_patient ?class_catheter ?class_procedure
                ORDER BY ?class_procedure
        }
}
GROUP BY ?indv_patient ?class_catheter
ORDER BY ?indv_patient
```

Listing 20: List patients that have a catheter, a procedure, and the patient's procedure uses the patient's catheter.

Table 23
AAENOTE SPARQL Query Result: List patients that have a catheter which was used for a procedure

Query Results	Person	Catheter					Procedure											
	Patient	central venous catheter	epidural catheter	peripheral intravenous catheter	venous catheter	urinary catheter	administration purpose	catheter discontinue use	catheter rinse	catheter self removal	general iv	iv antibiotics	iv chemo	iv fluid	iv medication	iv nutrient	subcutaneous injection
1	patient.T1.1.lo12a.LO_0007			✓								✓					
2	patient.T1.1.lo22a.LO_0007			✓								✓		✓			
3	patient.T1.2.do13a.LO_0001			✓								✓					
4	patient.T1.4.lo12a.DO_0003			✓				✓									
5	patient.T1.4.lo12a.SP_0003	✓													✓		
6	patient.T1.4.lo22a.DO_0003				✓			✓									
7	patient.T1.4.lo22a.SP_0010			✓								✓			✓		
8	patient.T1.4.so11a.DP_0002			✓						✓							
9	patient.T1.4.so11a.DP_0002					✓				✓							
10	patient.T1.4.so11a.LO_0001			✓								✓					
11	patient.T11.1.lo22a.LO_0004			✓									✓				
12	patient.T12.4.so11a.LO_0003				✓				✓								
13	patient.T2.2.do23a.LO_0007			✓								✓		✓			
14	patient.T2.3.so11a.LP_0007			✓						✓							
15	patient.T2.3.so21a.LP_0004			✓										✓			
16	patient.T2.4.lo22a.DO_0001		✓				✓										
17	patient.T2.4.so11a.DP_0001			✓												✓	
18	patient.T2.4.so11a.LO_0007			✓								✓					✓
19	patient.T3.2.so11a.LD_0003			✓										✓			
20	patient.T3.4.po24a.SO_0002			✓						✓							
21	patient.T3.4.so11a.LO_0003				✓				✓								
22	patient.T4.3.po14a.SD_0005			✓						✓							
23	patient.T4.3.so11a.LP_0004			✓										✓			
24	patient.T5.3.po24a.LO_0003			✓					✓					✓			
25	patient.T5.4.lo12a.SP_0010			✓								✓					
26	patient.T6.1.lo22a.LO_0007			✓								✓		✓			
27	patient.T6.3.lo22a.DP_0001	✓									✓						
28	patient.T7.2.do23a.LO_0004			✓									✓				
29	patient.T7.3.po24a.SD_0007				✓				✓								
30	patient.T7.4.so11a.LO_0007			✓								✓					✓
31	patient.T8.4.lo22a.SP_0010			✓								✓					
32	patient.T9.3.po24a.SD_0005			✓						✓							

Query result 1-32: `Patient` $\xrightarrow{\text{Person has}}$ `Catheter` (Y) and `Procedure` $\xrightarrow{\text{Procedure uses}}$ `Catheter` (Y).

Table 24
AAENOTE SPARQL Query Result: List patients that have a catheter, have a procedure, and where the catheter was used for that procedure

Query Result	Person	Catheter	Procedure		
	Patient	peripheral intravenous catheter	iv antibiotics	iv fluid	iv medication
1	patient.T1.1.lo22a.LO_0007	✓	✓	✓	
2	patient.T1.4.lo22a.SP_0010	✓	✓		✓
3	patient.T2.2.do23a.LO_0007	✓	✓	✓	
4	patient.T6.1.lo22a.LO_0007	✓	✓	✓	

Query result 1-14: `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter` (Y), `Patient` (X) $\xrightarrow{\text{Person has}}$ `Procedure` (Z), and `Procedure` (Z) $\xrightarrow{\text{Procedure uses}}$ `Catheter` (Y).

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient (GROUP_CONCAT (DISTINCT str(?class_catheter); separator=", " ) as ?catheters)
    (GROUP_CONCAT (DISTINCT str(?class_procedure); separator=", " ) as ?procedures)
WHERE {
        {
                SELECT ?indv_patient ?class_catheter ?class_procedure
                WHERE {
                        ?indv_patient rdf:type :patient ;
                                rdf:type ?class_patient .
                        FILTER(?class_patient != owl:NamedIndividual) .
                        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                                rdf:type ?class_catheter .
                        FILTER(?class_catheter != owl:NamedIndividual) .
                        ?indv_procedure rdf:type/rdfs:subClassOf* :procedure ;
                                rdf:type ?class_procedure .
                        FILTER(?class_procedure != owl:NamedIndividual) .
                        ?indv_patient :person_has ?indv_catheter ;
                            :person_has ?indv_procedure .
                }
                GROUP BY ?indv_patient ?class_catheter ?class_procedure
                ORDER BY ?class_catheter ?class_procedure
        }
}
GROUP BY ?indv_patient
ORDER BY ?indv_patient
```

Listing 21: List patients that have a catheter and a procedure, and all catheters and all procedures the patient has.

Table 25
AAENOTE SPARQL Query Result: List patients that have a catheter and a procedure

Query Result	Person	Catheter					Procedure								
	Patient	catheter	central venous catheter	hemodialysis catheter	peripheral intravenous catheter	urinary catheter	administration purpose	blood test	general iv	iv antibiotics	iv chemo	iv fluid	iv medication	procedure	surgery
1	patient.T1.1.lo22a.LO_0007				✓					✓					
2	patient.T1.1.lo22a.LO_0009			✓				✓							
3	patient.T1.2.do13a.SP_0001					✓									✓
4	patient.T1.2.do13a.SP_0010				✓					✓				✓	
5	patient.T1.2.lo22a.SD_0002				✓				✓				✓		
6	patient.T1.4.do13a.LP_0004				✓							✓			
7	patient.T1.4.lo22a.SP_0006				✓			✓							
8	patient.T1.4.lo22a.SP_0010				✓			✓		✓			✓		
9	patient.T12.2.lo22a.SD_0002				✓				✓						
10	patient.T15.3.po24a.SD_0002				✓				✓						
11	patient.T2.1.lo22a.LO_0001				✓					✓					
12	patient.T2.2.do13a.SP_0003		✓										✓		
13	patient.T2.2.do23a.LO_0001				✓					✓					
14	patient.T2.2.do23a.LO_0007				✓					✓		✓			
15	patient.T2.2.lo22a.PO_0005				✓										✓
16	patient.T2.3.do23a.PO_0005				✓										✓
17	patient.T3.2.do13a.LO_0007				✓					✓					
18	patient.T3.2.do23a.SP_0003		✓										✓		
19	patient.T3.3.lo22a.SO_0008	✓											✓		
20	patient.T3.3.po14a.SD_0002				✓								✓		
21	patient.T3.4.lo22a.SP_0003		✓										✓		
22	patient.T4.2.po24a.DO_0002				✓		✓								
23	patient.T5.2.do13a.LO_0003				✓							✓			
24	patient.T5.3.po24a.LO_0001				✓					✓					
25	patient.T6.1.lo22a.LO_0007				✓					✓		✓			
26	patient.T6.2.do13a.LO_0004				✓						✓				
27	patient.T6.4.do13a.LP_0002				✓		✓								
28	patient.T6.4.do23a.LP_0004				✓							✓			
29	patient.T8.4.lo22a.SP_0010				✓			✓							

Query result 1-29: `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter` and `Patient` (X) $\xrightarrow{\text{Person has}}$ `Procedure`.

B.14. AAENOTE CQ 9a: Does patientC have an infection and catheter?

```
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX : <http://www.semanticweb.org/2022/04/aaenote#>
SELECT ?indv_patient ?class_catheter ?class_infection
WHERE {
        ?indv_patient rdf:type :patient ;
                rdf:type ?class_patient .
        FILTER(?class_patient != owl:NamedIndividual) .
        ?indv_catheter rdf:type/rdfs:subClassOf* :catheter ;
                rdf:type ?class_catheter .
        FILTER(?class_catheter != owl:NamedIndividual) .
        ?indv_infection rdf:type :infection ;
                rdf:type ?class_infection .
        FILTER(?class_infection != owl:NamedIndividual) .
        ?indv_patient :person_has ?indv_catheter ;
                :person_has ?indv_infection .
}
ORDER BY ?indv_patient
```

Listing 22: List patients that have an infection and a catheter.

Table 26
AAENOTE SPARQL Query Result: List patients that have a infection and a catheter

Query Result	Patient	peripheral intravenous catheter	infection
1	patient.T2.2.do23a.SP_0006	✓	✓

Query result 1: `Patient` (X) $\xrightarrow{\text{Person has}}$ `Infection` and `Patient` (X) $\xrightarrow{\text{Person has}}$ `Catheter`.

B.15. AAENOTE CQ 9b: Was patientC's infection associated with a catheter?

Cannot determine if a patient's infection is associated with a catheter unless that catheter is tested in the microbiology lab.

Appendix C. Catheter Infection Indications Ontology (CIIO) Hierarchy, Assumptions, Indications, and Competency Questions

C.1. CIIO Hierarchy

The CIIO classes and their subclasses can be found in the following figures:

1. Fig. 15 `Observation`
2. Fig. 16 `Anatomical location`
3. Fig. 17 `Medical device`
4. Fig. 18 `Procedure`
5. Fig. 19 `Person`
6. Fig. 20 `Document`
7. Fig. 21 `Sentence`

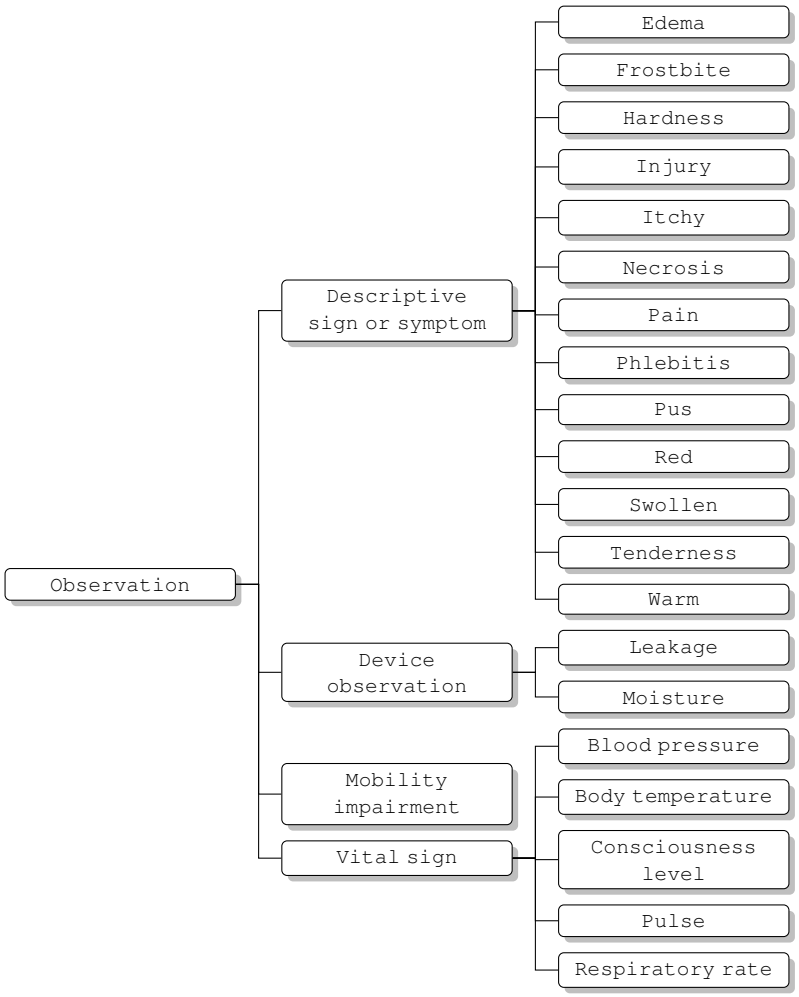

Fig. 15. CIIO Observation Class Hierarchy

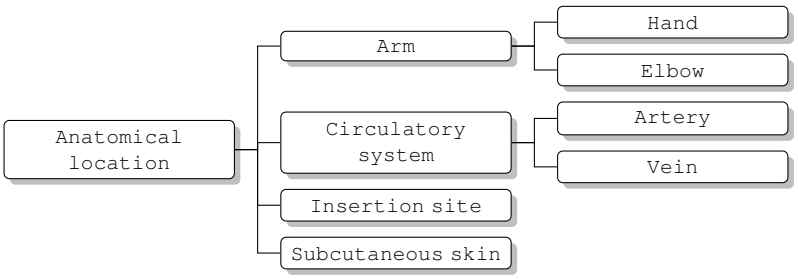

Fig. 16. CIIO Anatomical Location Class Hierarchy

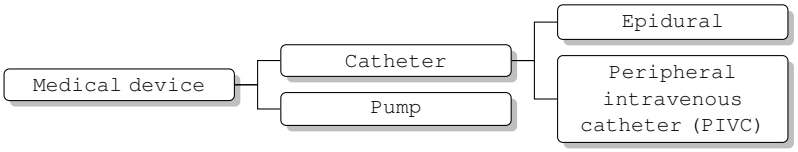

Fig. 17. CIIO Medical Device Class Hierarchy

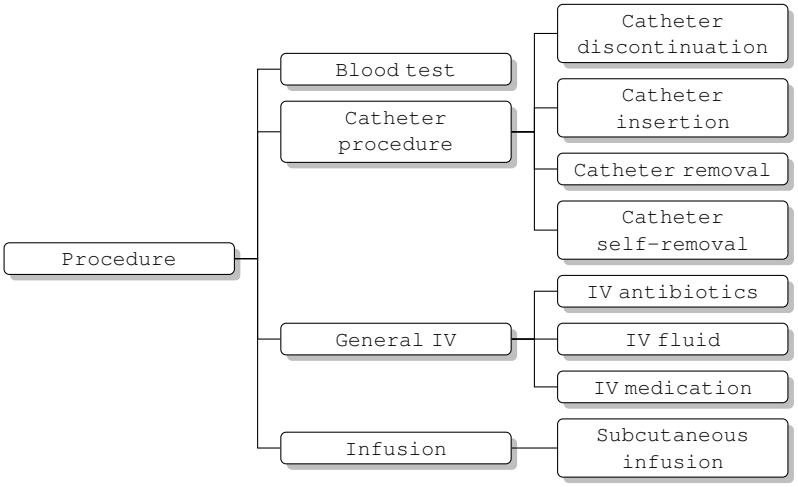

Fig. 18. CIIO Procedure Class Hierarchy

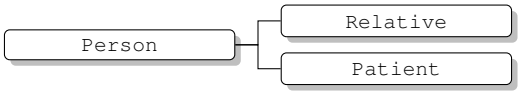

Fig. 19. CIIO Person Class Hierarchy

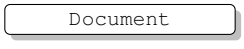

Fig. 20. CIIO Document Class Hierarchy

Fig. 21. CIIO Sentence Class Hierarchy

C.2. CIIO Assumptions

To address the competency questions (CQs) which ask about patients and not documents and alleviate the problem of patients being implicitly mentioned, 1 AE document represents 1 patient. In the actual electronic incident reporting system database, if the reported AE is related to a patient, there will be a patient ID. This allows users to know if the AE is about 1 patient, more than 1 patient, or no patients. Additionally, concepts that are documented within different sentences of the same document are likely describing concepts that occurred in the same event for the same patient. Furthermore, concepts documented in the same sentence that are linked together by a relationship are directly related. Certain relationships can provide the reason for why a concept was or is needed (i.e., procedureA $\xrightarrow{\text{Procedure uses}}$ deviceX, therefore deviceX was needed to perform procedureA).

C.3. Catheter and Infection Indications

C.3.1. Catheter Indications

1. A patient has a specific catheter documented.
2. Any IV usage or infusion indicates some type of catheter is used. IV usage includes general IV, IV medication, IV fluid, and IV antibiotics. Infusion includes infusion, intraosseous infusion, intravenous infusion, and subcutaneous infusion. Based on the type of IV usage or infusion alone, it is not enough to determine what type of catheter was used.
3. Catheter procedures indicate that a catheter is or was present because they require a catheter. Catheter procedures include catheter insertion, catheter discontinued use, catheter removal, catheter replacement, and catheter self-removal.
4. Infusion phlebitis indication indicates that some type of catheter is used.

C.3.2. Peripheral Intravenous Catheter (PIVC) Indications

1. PIVCs are rarely documented, so any PIVC explicitly documented indicates a PIVC was used or in use.
2. Leaking IV or an infusion at the arm, elbow, or hand indicates a PIVC is used. IV includes general IV, IV medication, IV fluid, and IV antibiotics. Infusion includes infusion, intraosseous infusion, intravenous infusion, and subcutaneous infusion. Central venous catheters (CVCs) are deep, so there should not have leakage on the skin. PIVC leakage typically occurs because the catheter dressing is not properly secured or the PIVC is placed near a movable joint (i.e., elbow) and becomes dislodged.

C.3.3. Epidural Indication

1. Epidural usage will explicitly be documented.
2. A epidural catheter is the only catheter located nearby/on/at/in the back (i.e., spinal cord).

C.3.4. Infusion phlebitis

As previously stated, infusion phlebitis can be mechanical, chemical, or infectious [6]. Regardless of cause, it is documented similarly and can either be a catheter-related infection or complication.

1. Early stage of infusion phlebitis is indicated by an insertion site or infusion with 2 of the following signs: (i) pain or tenderness, (ii) red, (iii) swollen or edema, or (iv) warm.
2. Medium stage of infusion phlebitis is indicated by (1) a vein with pain and (2) an insertion site or infusion with 2 signs: (i) red, (ii) swollen or edema, or (iii) warm.
3. Advanced stage of infusion phlebitis is indicated by (1) a vein with pain and hardness and (2) an insertion site or infusion with 2 signs: (i) red, (ii) swollen or edema, or (iii) warm.

C.3.5. Infection

1. Pus at an insertion site indicates an infection. Because pus present is a sure sign of infection.

C.3.6. Bloodstream Infection (BSI)

1. A bloodstream infection is indicated by a blood test with a positive test result and/or the name of the cultured bacteria.

C.3.7. Sepsis

1. Infection combined with mobility impairment, high body temperature, and frostbite indicates sepsis.
2. Meeting the Quick Sequential Organ Failure Assessment Score (qSOFA) [68] sepsis criteria is indicated if there is an infection indication and at least 2 of the following: (1) high respiratory rate, (2) low blood pressure, or (3) a consciousness level that is either confusion, verbally responsive, painfully responsive, or unresponsive.
3. Sepsis is indicated if there is an infection indication and the National Early Warning Score 2 (NEWS2) [69] criteria for clinical deterioration is met by a combination of (1) high respiratory rate, (2) low blood pressure, (3) high pulse, (4) low body temperature or high body temperature, and (5) consciousness level = confusion, verbally responsive, painfully responsive, or unresponsive.

C.4. CIIO Competency Questions and Ontology Usage

SPARQL queries for answering the CIIO competency questions are available on GitHub at https://github.com/melissayan/aaenote_and_ciio/wiki/Ontology-SPARQL-Queries.

Table 27: CIIO Competency Questions and Ontology Usage

Competency Question	**Ontology Classes and Relationships to Find Instances**
1. Does patientA have phlebitis, and was it infectious phlebitis, chemical phlebitis, or mechanical phlebitis?	Early stage infusion phlebitis (a or b): (a) (`Pain` or `Tenderness`), `Red`, (`Swollen` or `Edema`), `Warm` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Injection site`. (b) `Infusion` $\xrightarrow{\text{Is observered with}}$ (`Pain` or `Tenderness`), `Red`, (`Swollen` or `Edema`), `Warm`. Medium stage infusion phlebitis (a) and (b or c): (a) (`Pain` or `Tenderness`) $\xrightarrow{\text{Located nearby/on/at/in}}$ `Vein`. (b) `Red`, (`Swollen` or `Edema`), `Warm` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Injection site`. (c) `Infusion` $\xrightarrow{\text{Is observered with}}$ `Red`, (`Swollen` or `Edema`), `Warm`. Advanced stage infusion phlebitis: (a) `Hardness` and (`Pain` or `Tenderness`) $\xrightarrow{\text{Located nearby/on/at/in}}$ `Vein`. (b) `Red`, (`Swollen` or `Edema`), `Warm` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Injection site`. (c) `Infusion` $\xrightarrow{\text{Is observered with}}$ `Red`, (`Swollen` or `Edema`), `Warm`. ‡Need additional documentation or pathophysiology studies at the body's cellular or genetic-level to determine if the `Phlebitis` is infectious phlebitis, chemical phlebitis, or mechanical phlebitis.
2. Does patientA have an infection?	Pus at an insertion site indicates infection. `Sentence` $\xrightarrow{\text{Contains}}$ `Pus` and `Insertion site`. `Pus` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Insertion site`.
3. Does patientA have a BSI?	Documentation with a blood test with (a) a positive test result and/or (b) name of cultured bacteria. `Sentence` $\xrightarrow{\text{Contains}}$ `Blood test`. (a) `Blood test` $\xrightarrow{\text{Has blood test result}}$ Positive. (b) `Blood test` $\xrightarrow{\text{Has cultured bacteria}}$ bacteria name (i.e., Streptococcus, Staphylococcus, *S. aureus*, etc.).

4. How many patients have an infection or BSI?

Same as Competency Question 1 and 2.

5. Which patients have sepsis?

Sepsis is indicated by (a) an infection indication combined with (b): (1) mobility impairment, (2) high body temperature (i.e., hyperthermia), and (3) frostbite:

(a) `Sentence` $\xrightarrow{\text{Contains}}$ `pus` and `Insertion site`.
`Pus` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Insertion site`.
(b) `Sentence` $\xrightarrow{\text{Contains}}$ `Mobility impairment`, `Body temperature`, and `Frostbite`.
`Body temperature` $\xrightarrow{\text{Has body temperature range}}$ hyperthermia.

Meeting the Quick Sequential Organ Failure Assessment Score (qSOFA) criteria of (a) an infection indication and (b) at least 2 of the following: (1) high respiratory rate, (2) low blood pressure, or (3) a consciousness level that is either confusion, verbally responsive, painfully responsive, or unresponsive:

(a) `Sentence` $\xrightarrow{\text{Contains}}$ `pus` and `Insertion site`.
`Pus` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Insertion site`.
(b) `Sentence` $\xrightarrow{\text{Contains}}$ `Respiratory rate`, `Blood pressure`, and/or `Consciousness level`.
`Respiratory rate` $\xrightarrow{\text{Has severity}}$ high.
`Blood pressure` $\xrightarrow{\text{Has severity}}$ low.
`Consciousness level` $\xrightarrow{\text{Has consciousness state}}$ confusion, verbally responsive, painfully responsive, or unresponsive.

Meeting (a) an infection indication and (b) the National Early Warning Score 2 (NEWS2) criteria for clincial deterioration by having a combination of: (1) high respiratory rate, (2) low blood pressure, (3) high pulse, (4) low body temperature or high body temperature (i.e., hypothermia or hyperthermia), and (5) consciousness level = confusion, verbally responsive, painfully responsive, or unresponsive:

(a) `Sentence` $\xrightarrow{\text{Contains}}$ `Pus` and `Insertion site`.
`Pus` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Insertion site`.
(b) `Sentence` $\xrightarrow{\text{Contains}}$ `Respiratory rate`, `Blood pressure`, `Pulse`, `Body temperature`, and/or `Consciousness level`.
`Respiratory rate` $\xrightarrow{\text{Has severity}}$ high.
`Blood pressure` $\xrightarrow{\text{Has severity}}$ low.
`Pulse` $\xrightarrow{\text{Has severity}}$ high.
`Body temperature` $\xrightarrow{\text{Has body temperature range}}$ hypothermia or hyperthermia.
`Consciousness level` $\xrightarrow{\text{Has consciousness state}}$ confusion, verbally responsive, painfully responsive, or unresponsive.

6. Does patientB have a catheter?

Documentation of a specific catheter, IV usage, infusion, or catheter-related procedure:

`Sentence` $\xrightarrow{\text{Contains}}$ `Medical device(s)` or `IV`-related, `infusion`-related, or `Catheter procedure`-related procedures.

Early stage infusion phlebitis is indicated by (a) an injection site or (b) infusion with 2 of the following signs: (i) pain or tenderness, (ii) red, (iii) swollen or edema, or (iv) warm:

(a) `Sentence` $\xrightarrow{\text{Contains}}$ `Injection site` and `Pain` or `Tenderness`, `Red`, `Swollen` or `Edema`, and/or `Warm`.
`Pain` or `tenderness`, `Red`, `Swollen` or `Edema`, or `Warm` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Injection site`.

(b) `Sentence` $\xrightarrow{\text{Contains}}$ `Infusion` and `Pain` or `Tenderness`, `Red`, `Swollen` or `Edema`, and/or `Warm`.
`Pain` or `Tenderness`, `Red`, `Swollen` or `Edema`, or `Warm` $\xrightarrow{\text{Is observered with}}$ `Infusion`.

Medium stage infusion phlebitis is indicated by (a) a vein with pain or tenderness, and (b) an injection site or (c) infusion with 2 of the following signs: (i) red, (ii) swollen or edema, or (iii) warm:

(a) `Sentence` $\xrightarrow{\text{Contains}}$ `Vein` and `Pain` or `Tenderness`.
`Pain` or `Tenderness` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Vein`.

(b) `Sentence` $\xrightarrow{\text{Contains}}$ `Injection site` and `Red`, `Swollen` or `Edema`, and/or `Warm`.
`Red`, `Swollen` or `Edema`, or `Warm` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Injection site`.

(c) `Sentence` $\xrightarrow{\text{Contains}}$ `Infusion` and `Pain` or `Tenderness`, `Red`, `Swollen` or `Edema`, and/or `Warm`.
`Red`, `Swollen` or `Edema`, or `Warm` $\xrightarrow{\text{Is observered with}}$ `Infusion`.

Advanced stage infusion phlebitis is indicated by (a) a vein with (i) hardness and (ii) pain or tenderness, and (b) an injection site or (c) infusion with 2 of the following signs: (i) red, (ii) swollen or edema, or (iii) warm:

(a) `Sentence` $\xrightarrow{\text{Contains}}$ `Vein`, `Hardness`, and `Pain` or `Tenderness`.
`Hardness` and `Pain` or `Tenderness` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Vein`.

(b) `Sentence` $\xrightarrow{\text{Contains}}$ `Injection site` and `Red`, `Swollen` or `Edema`, and/or `Warm`.
`Red`, `Swollen` or `Edema`, or `Warm` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Injection site`.

(c) `Sentence` $\xrightarrow{\text{Contains}}$ `Infusion` and `Pain` or `Tenderness`, `red`, `Swollen` or `Edema`, and/or `Warm`.
`Red`, `Swollen` or `Edema`, or `Warm` $\xrightarrow{\text{Is observered with}}$ `Infusion`.

7. Does patientB have a PIVC?

PIVCs are rarely documented, so any PIVC explicitly documented indicates a PIVC was used or in use:

`Sentence` $\xrightarrow{\text{Contains}}$ `PIVC`.

Leaking IV or infusion at the arm, elbow or hand indicates PIVC usage:

`Sentence` $\xrightarrow{\text{Contains}}$ `Leakage` and `IV`-related or `Infusion`-related procedures.
`Leakage` $\xrightarrow{\text{Is observed with}}$ `IV`-related or `Infusion`-related procedures.

8a. How many catheters does patientB have?	Same as Competency Question 5's documentation of a specific catheter, IV usage, infusion, or catheter-related procedure: `Sentence` $\xrightarrow{\text{Contains}}$ `Medical device(s)` or `IV`-related, `Infusion`-related, or `Catheter procedure`-related procedures. * The exact number of catheters per document cannot be counted because multiple sentences within the document could be describing the same catheter and documented procedures can use the same catheter.
8b. Where are the catheters in patientB?	Medical device located nearby/on/at/in an anatomical location: `Sentence` $\xrightarrow{\text{Contains}}$ `Anatomical location` and `Medical device`. `Medical device` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. IV usage, infusion, or catheter-related procedure located nearby/on/at/in an anatomical location: `Sentence` $\xrightarrow{\text{Contains}}$ `Anatomical location` and `IV`-related, `Infusion`-related, or `Catheter procedure`-related procedures. `IV`-related, `Infusion`-related, or `Catheter procedure`-related procedures $\xrightarrow{\text{Located nearby/on/at/in}}$ `Anatomical location`. * The exact anatomical location of catheters per document cannot be determined because multiple sentences within a document could be describing the same catheter at the same location but with more general terms (i.e., arm instead of hand), the location's position was not documented (e.g., If a sentence contains elbowA, right handB, and right armC, then handB is part of armC, but elbowA might or might not be part of armC), multiple procedures can be performed at the same location, and an additional anatomical ontology is needed to infer the location based on catheter type.
8c. Why does patientB need the catheter(s)?	The medical device is needed and used in a specific procedure. `Sentence` $\xrightarrow{\text{Contains}}$ `Medical device` and `Procedure`. `Procedure` $\xrightarrow{\text{Procedure uses}}$ `Medical device`. Document has sentences with medical devices and/or procedures: `Sentence` $\xrightarrow{\text{Contains}}$ `Medical device` and/or `Procedure`. * The exact reason cannot be determined unless the $\xrightarrow{\text{Procedure uses}}$ object property links `procedure` and `medical device` because the indications do not provide a list of reasons for why a specific catheter can be used. However, a clinician can view the retrieved list of devices and procedures to determine if the devices in a document could be used for the procedures documented.
9a. Does patientC have an infection and catheter?	Document with (a) infection indication and (b or c) catheter indication : (a) `Sentence` $\xrightarrow{\text{Contains}}$ `Pus` and `Insertion site`. `Pus` $\xrightarrow{\text{Located nearby/on/at/in}}$ `Insertion site`. (b) `Sentence` $\xrightarrow{\text{Contains}}$ `Medical device`. (c) `Sentence` $\xrightarrow{\text{Contains}}$ `Anatomical location` and `IV`-related, `Infusion`-related, or `Catheter procedure`-related procedures.
9b. Was patientC's infection associated with a catheter?	§ Cannot determine if an infection is associated with a catheter unless that catheter is tested in the microbiology lab.

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