

Defining ‘sign’ and ‘symptom’

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Abstract—The terms ‘sign’ and ‘symptom’ have proven difficult to define and represent in a biomedical ontology. Medical professionals use ‘sign’ and ‘symptom’ to refer to medically relevant information about patients; however, they do not agree on the definitions. In particular, while medical professionals agree that there is an important distinction between signs and symptoms, they do not agree on the precise nature of this distinction. It is unsurprising then that attempts to provide ontological representations of these entities have repeatedly fallen short. As an added complication, a variety of entities—including material entities, qualities, and processes—may reasonably be understood as signs or symptoms. Thus, the ontological nature of a sign or symptom raises many questions about the meanings and proper use of these terms. We discuss specific challenges to defining ‘sign’ and ‘symptom’, identify essential features of these entities, explore the ontological implications of existing definitions, and propose our own definitions. We evaluate several competing ontological representations and present our proposed representation within the framework of the Ontology for General Medical Science. The proposed representation of sign and symptom is ontologically sound, provides precise definitions of each term, and enables users to easily create customized groups of signs and symptoms. Our experience highlights general issues about developing definitions in ontologies.

Keywords—*sign; symptom; definition; clinical finding; OGMS; ontology*

I. INTRODUCTION

Clinicians and other medical professionals regularly use the terms ‘sign’ and ‘symptom’ to refer to medically relevant information about patients. Yet, the use of these terms is often imprecise, inconsistent, or both. This is due, in part, to the tendency to use these terms loosely. For example, by broadly referring to both signs and symptoms as symptoms [1]. As a further complication, many medical texts—including those dedicated to the study of signs and symptoms—fail to provide even preliminary definitions for these terms [2, 3]. When definitions are provided, they are not always consistent with one another. See TABLE I for a list of definitions.

Comparison of lists of signs and symptoms that are presented in the absence of definitions reveals numerous potentially inconsistent applications of ‘sign’ and ‘symptom’. According to [2], examples of symptoms include: fatigue, dizziness, fever, headache, insomnia, lymphadenopathy, night sweats, muscle weakness, weight gain, weight loss, pain, nausea, bloating, itching, sore throat, hearing loss, diarrhea, constipation, confusion, memory loss, tremor, anxiety, cough, and jaundice. According to [1], examples of signs include:

jaundice, swollen joints, and cardiac murmurs. According to [4], examples of vital signs include: temperature, respirations, pulse, and blood pressure. Notice that jaundice appears on both a list of symptoms and on a list of signs. While some definitions of ‘sign’ and ‘symptom’ allow certain features of the patient to be both a sign and a symptom, others do not. Additionally, which features can be both a sign and a symptom can change based on which definition is used.

Representing sign and symptom in an ontology is an ideal means by which to enforce their precise definitions and encourage their consistent application. At the same time, it emphasizes the importance of these terms to the medical community. Our goal is to precisely define the terms ‘sign’ and ‘symptom’ and to provide sound ontological representations of these entities. In doing so, we hope that our experience will serve as a primer on some of the challenges involved in developing rigorous definitions in ontologies.

II. METHODS

There are theoretical concerns regarding definition formation that must be considered prior to an attempt to define a term or set of terms. Definition formation is goal-driven and, as such, there are certain desiderata for what typically constitutes a “good” definition. These desiderata often depend on the type of definition one is seeking to provide as well as on the field one is working in [5, 6]. Nonetheless, we can identify certain desiderata that should hold irrespective of these concerns. In general, definitions ought to be: a) sufficiently inclusive so as to include or capture all of the actual instances of their definiens, b) sufficiently exclusive so as to exclude or discount all of the instances that are not their definiens, and c) informative enough to impart information to the audience [7]. We acknowledge that many groups may require additional desiderata. The considerations listed here are minimal desiderata for definitions.

There is also an issue of conceptual priority underpinning our process. Since we acknowledge that there are general desiderata for definitions before we engage in analysis of the current literature, these concerns are conceptually prior to any considerations discovered in the process of evaluating existing efforts. We also acknowledge that there may emerge more desiderata for specific definitions or types of definitions as a result of the evaluation of a set of attempted definitions. These should also be considered when determining whether a definition is adequate. For example, if a definition meets the three initial desiderata listed above but is criticized for obscurity or inconsistency with dominant views expressed in the literature, then one should seek to find a consistent and

TABLE I. DEFINITIONS OF ‘SIGN’ AND ‘SYMPTOM’ FROM THE MEDICAL LITERATURE

Source	Definition of ‘sign’	Definition of ‘symptom’
DeGowin’s Diagnostic Examination [4]	Abnormalities detected by the examiner.	Abnormalities the patient perceives.
MedlinePlus www.merriam-webster.com	An objective evidence of disease especially as observed and interpreted by the physician rather than by the patient or lay observer.	Subjective evidence of disease or physical disturbance observed by the patient; broadly: something that indicates the presence of a physical disorder.
The Free Dictionary www.thefreedictionary.com	A body manifestation, usually detected on physical examination or through laboratory tests or x-rays, that indicates the presence of abnormality or disease.	A sign or an indication of disorder or disease, especially when experienced by an individual as a change from normal function, sensation, or appearance.
MediLexicon www.medilexicon.com	Any abnormality indicative of disease, discoverable on examination of the patient; an objective indication of disease.	Any morbid phenomenon or departure from the normal in structure, function, or sensation, experienced by the patient and indicative of disease; a subjective indication of disease.
MedicineNet www.medterms.com	Any objective evidence of disease. It is evidence that can be recognized by the patient, physician, nurse, or someone else.	Any subjective evidence of disease; only the patient can perceive them.
Towards an Ontology of Pain [20]		A restricted family of phenomena, which are of their nature experienced in the first person. Symptoms can be reported to, and associated behaviors and bodily qualities can be observed by, the clinician; but the symptoms themselves cannot be observed or objectively measured.
Signs and Symptoms: Applied Pathologic Physiology and Clinical Interpretation [1]	Signs are detectable by another person and sometimes by the patient himself.	(a) As broadly and generally employed, the word symptom is used to name any manifestation of disease. (b) Strictly speaking, symptoms are subjective, apparent only to the affected person. (c) In ordinary clinical usage, the term symptom refers to what the patient experiences and reports as manifestations of illness. Thus, symptoms are subjective (psychological) in the sense that the patient can report only that of which he is aware.
Textbook of Diagnostic Medicine [24]	As opposed to revealing symptoms, physical examination reveals information that is comparatively more objective, measurable, and reproducible.	Symptoms are clinical manifestations of the disorder of organs or systems as experienced by patients. Symptoms are subjective and often difficult to quantify.
Rational Diagnosis and Treatment: Evidence-based Clinical Decision-making [25]	(a) Physical signs comprise all those observations which are made by the doctor during the physical examination. (b) Some of the recorded ‘signs’ fall into a special group: provoked symptoms. They are subjective symptoms which are only noticed by the patient during the physical examination.	(a) Subjective symptoms are the sensations noted by the patient and the patient’s mood. (b) Objective symptoms are observations made by the patient or the relatives concerning the patient’s body and its products.
The Mosby Medical Encyclopedia [26]	Something seen by an examiner. Many signs go along with symptoms, as bumps and rashes are often seen when a patient complains of itching.	Something felt or noticed by the patient that can help to detect a disease or disorder.

non-obscure definition; thus adding to our initial set of desiderata. Considerations such as these are not universal for definitions as they are relative to a community or sub-community. In contrast to general desiderata, let us call these subject-specific desiderata. Both general and subject-specific desiderata should be considered equally when determining the success of a definition or set of definitions [8].

Sources for the definitions of ‘sign’ and ‘symptom’ were gathered by performing a literature review. The literature review drew primarily from medical dictionaries and medical texts—especially those texts whose asserted focus is on signs or symptoms. These texts typically discussed the diagnostic process, clinical encounters, identification of diseases, or lists of signs and symptoms based on their relative importance and possible etiology. It is notable that many texts failed to provide definitions of either ‘sign’ or ‘symptom’ and thereby implicitly presumed familiarity on the part of their readers with the meanings of these terms. We compiled a list of available definitions and present a representative selection in TABLE I.

Biomedical ontologies that represent signs or symptoms were identified by performing queries in BioPortal for the terms ‘sign’ and ‘symptom’ [9]. Each search result was screened to identify and eliminate ontologies that returned inappropriate matches. The remaining results were reviewed to

identify and set aside ontologies that reused the relevant term from another ontology. Finally, we recorded the representations and definitions of sign and symptom in each remaining ontology. TABLE II displays the pertinent information for each ontology that provides a unique definition for at least one of these terms.

At the time of our research, querying the term ‘symptom’ returned 30 results in BioPortal. 9 results were screened out as irrelevant to our project. Of the remaining 21 results, 8 projects reused the symptom class from another ontology. Of the remaining 13 ontologies, only 6 provide a definition of ‘symptom’. 2 projects, the Translational Medicine Ontology (TMO) and the Ontology for General Medical Science (OGMS), use the same source and therefore give identical definitions [10]. This leaves 5 ontologies that uniquely define ‘symptom’. Querying the term ‘sign’ returned 21 results in BioPortal. 8 results were screened out as irrelevant to our project. Of the remaining 13 results, 5 projects reused the sign class from another ontology. Of the remaining 8 ontologies, only 4 provide a definition of ‘sign’. Again, TMO and OGMS give identical definitions. This leaves 3 ontologies that uniquely define ‘sign’.

Of the 8 reuses of ‘symptom’ and 5 reuses of ‘sign’, OGMS: ‘symptom’ is reused by 5 ontologies and OGMS: ‘sign’

TABLE II. DEFINITIONS OF ‘SIGN’ AND ‘SYMPTOM’ FROM ONTOLOGIES IN BIOPORTAL

Ontology	Term	Definition	Parent Class
Ontology for General Medical Science (OGMS)	symptom	A quality of a patient that is observed by the patient or a processual entity experienced by the patient, either of which is hypothesized by the patient to be a realization of a disease.	entity
	sign	A quality of a patient, a material entity that is part of a patient, or a processual entity that a patient participates in, any one of which is observed in a physical examination and is deemed by the clinician to be of clinical significance.	entity
National Cancer Institute Thesaurus (NCIT)	Symptom	Subjective evidence of disease perceived by the patient.	Sign or Symptom
	Sign	Objective evidence of disease perceptible to the examining healthcare provider.	Sign or Symptom
International Classification for Nursing Practice (ICNP)	Symptom	Phenomenon: Change in the body, subjective experience of change in bodily sensation, function or appearance.	Phenomenon
	Sign	N/A	Phenomenon
Symptom Ontology (SYMP)	symptom	A symptom is a perceived change in function, sensation, loss, disturbance or appearance reported by a patient indicative of a disease.	(Root Term)
Computer Retrieval of Information on Scientific Projects Thesaurus (CRISP)	sign/symptom	Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient.	pathology

is reused by 3 ontologies, which makes OGMS the most widely reused source of both classes. The Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) has the second most reuses. SNOMED CT boasts a massive medical terminology with over 300,000 classes and is designed for the primary purpose of improving Electronic Health Records (EHRs) [11]. In contrast, OGMS is a small mid-level ontology that is compliant with the Basic Formal Ontology (BFO) and is designed to be easily imported and used by other biomedical ontologies [12, 13]. While SNOMED CT currently has more end users, there are reasons to doubt that it has the logical capacity to meaningfully assist in automated reasoning over its classes [14]. Thus, OGMS’s versatility and compatibility with other biomedical ontologies makes it better suited to enable term reuse and is the best candidate ontology for hosting the representations of sign and symptom. For these reasons, we focus on the representation of these entities within the OGMS framework.

Following OGMS and BFO, we employ the methodology of ontological realism in developing our representations of sign and symptom [15]. According to ontological realism, when developing an ontology, the goal is to identify the sorts of entities that exist in reality and then represent them according to the best current scientific understanding. We are committed to upholding the OBO (Open Biological and Biomedical Ontologies) Foundry principles for best practices in ontology development [8]. In particular, we adhere to the principles of avoiding redundancy, exploiting compositionality, and using common architecture [16, 17]. The existence of at least 13 distinct representations of symptom and 8 distinct representations of sign in ontologies available through BioPortal creates redundancy and multiple architectures. Making OGMS the sole host of sign and symptom respects these OBO Foundry principles. Our proposed representations exploit compositionality by using existing terms from multiple ontologies to define ‘sign’ and ‘symptom’.

III. RESULTS

Examination of particular signs and symptoms reveals that, taken as a whole, they are not instances of a single universal. That is, sign and symptom are not natural kinds. Rather, instances of each group are comprised of a variety of types of entities including material entities, processual entities, and

qualities. Adherence to ontological realism therefore requires that sign and symptom not be asserted as named universal classes in an ontology.

Our solution is to introduce relations to connect entities that can be a sign, symptom, or, in some cases, both to the diseases, disorders, or syndromes that they are a sign or symptom of. Given the frequent use of the terms ‘sign’ and ‘symptom’ in non-clinical settings, we chose to use the terms ‘clinical sign’ and ‘clinical symptom’. In addition to reducing confusion, the use of specialized terms emphasizes the need for specialized definitions and can reduce objections to the definitions’ potentially counter-intuitive entailments. Hence, we propose the relations ‘is clinical sign of’ and ‘is clinical symptom of’ as subtypes of the Information Artifact Ontology’s ‘is about’ object property, which relates an information artifact to an entity. We define these relations as follows:

is clinical symptom of =_{df} X is a symptom of Y if and only if: (i) X is a clinical finding about a patient that is reported by a patient, family member, caretaker, or other non-medical professional; (ii) Y is a disease, disorder, or syndrome; and (iii) X is hypothesized by a clinician to be of clinical significance to Y.

is clinical sign of =_{df} X is a sign of Y if and only if: (i) X is a clinical finding about a patient that is observed by a clinician or reported by another medical professional; (ii) Y is a disease, disorder, or syndrome; and (iii) X is hypothesized by a clinician to be of clinical significance to Y.

While we contend that these relations most accurately represent the meanings of ‘sign’ and ‘symptom’, users may find it desirable to have named classes. Named classes make it easier to annotate terms and to identify and compose lists of entities of interest. Adoption of our relational approach does not necessitate a loss of functionality. Anonymous defined classes (ADCs) can be created for this purpose [18, 19]. Unlike a named class, an ADC need not represent a natural kind. Thus, ADCs can be constructed to represent just those entities that ontology users are interested in. For example, if a user wants to query her ontology for a list of all clinical signs, she can create an anonymous class defined as (‘clinical finding’ and (‘is clinical sign of’ some (disease or disorder or syndrome))).

This approach can be used to generate lists of signs, symptoms, or both that are hypothesized to be of significance to specific diseases, disorders, or syndromes. For example, a user who is only interested in symptoms of cardiovascular disease can create an anonymous class defined as (‘clinical finding’ and (‘is clinical symptom of’ some ‘cardiovascular disease’)). If an ADC is of particular value to the user, it can be given a name—such as ‘clinical sign’ or ‘clinical symptom of cardiovascular disease’. Naming an ADC produces a named defined class. Although a named defined class need not be a universal type, users can interact with it in much the same way that they interact with named universal classes. In this way, our representations of sign and symptom can accommodate the diversity of users’ needs.

IV. DISCUSSION

A. Defining ‘sign’ and ‘symptom’

The definitions in TABLE I suggest the adoption of one of the following criteria for distinguishing signs from symptoms:

1. Who reported or observed the phenomenon.
2. Whether the patient or the clinician reported or observed the phenomenon.
3. Who is capable, at least in theory, of observing or experiencing the phenomenon.

The first distinction can, but need not, allow persons other than the patient to observe and report the patient’s symptoms. The second distinction limits symptoms to only those things the patient observes and reports. Both distinctions allow certain features of patients to be both signs and symptoms.

“The distinction between symptoms and signs is frequently unclear. For instance, jaundice may be a symptom that brings the patient to the physician, but it is also a sign visible to the clinician. [...] Vomiting, although it can be witnessed, is more often a symptom, while tenderness, although it may be noted by the patient, is a sign that can be elicited by the examiner.” [4]

The third distinction makes a stronger claim. According to this distinction, signs can, at least in theory, be observed by more than one person, but symptoms can only ever be observed by the patient [20]. Thus, nothing can be both a sign and a symptom. What is essential is who *could* have observed the feature, not who *actually* observed or reported it.

Yet, an historically compelling reason for creating and continuing to use the sign/symptom distinction is that observations made by medical professionals are, as a whole, typically considered to be more reliable than reports made by the patient, a family member, or someone who is not trained in medicine [4]. Thus, while the third distinction is *prima facie* ontologically superior because it does not allow the same feature of the patient to be both a sign and a symptom, it fails to account for the primary motivation for making the distinction. More significantly, the third account relies on a distinction between objectivity and subjectivity that may be metaphysically untenable.

Consider pain. Pain is arguably the archetypical symptom because, while people can observe behavioral cues and then infer that another individual is in pain, only that individual can definitively say whether he or she is experiencing pain. Yet, neuroscientists have made incredible progress both in imaging

the human brain and in mapping specific functions to specific areas of the brain [21]. In some cases, such as neurons in the hippocampus called place cells, precise locations of specific memories have been identified [22, 23]. Thus, it is becoming increasingly plausible that neuroscientists will eventually be able to objectively observe pain and other features of the patient. If this is possible, then, according to the third distinction, pain and other archetypical symptoms are—and always have been—signs. For this reason, we reject the third distinction in favor of an account of sign and symptom based on who reported the feature.

This leaves either the first or the second proposal. The second distinction is more restrictive since only the patient can report a symptom. If signs are similarly restricted to reports made by clinicians, then observations reported by a family member, caretaker, or other non-clinician fall outside the range of signs and symptoms. One implication of this is that, while a parent can report observations about his or her child and a doctor can use these reports to aid in diagnosing the child, a parent cannot report his or her child’s symptoms. Rejecting the second distinction and allowing non-clinicians to report symptoms avoids this oddity while preserving the initial motivation for the sign/symptom distinction. On the resulting view, symptoms are reports about the patient’s health made by a non-clinician; signs are reports about the patient’s health made by a clinician. This can be refined to allow reports made by certain non-clinicians, namely those persons who play related medical roles, to report signs. Identifying what these roles are, who has them, and in what settings they are realized are important issues that we set aside for the purposes of this paper.

Having distinguished signs from symptoms, it remains to distinguish them from other entities. We contend that an essential criterion of both signs and symptoms is that they be hypothesized to be clinically significant. A competing view is that signs and symptoms are clinically significant regardless whether anyone ever hypothesizes them to be so. We reject this view because we take signs and symptoms to have an important epistemic component. That is, something cannot be a sign or symptom unless it is known by someone. For example, a genetic mutation may be the material basis of a particular genetic disease, but it is not a sign of that disease until a test has detected the presence of the mutation and a qualified professional has interpreted the test results. Prior to that, the genetic mutation is simply a disorder. The epistemic component of signs and symptoms is due to the social construction of clinical settings. Determining clinical significance requires interpretation by clinicians. Furthermore, clinicians use signs and symptoms as part of the diagnostic process—the goal of which is to arrive at a diagnosis, which is a hypothesis about the patient’s health. Hence, it would be a mistake to divorce signs and symptoms from their clinical interpretation.

It is a further question whether the role of the person who formulates the hypothesis of clinical significance matters. There are three plausible answers:

- (i) It does not matter who hypothesizes the feature to be of clinical significance as long as someone does.
- (ii) It only matters whether the person who reported the feature hypothesizes that it is clinically significant.

- (iii) It only matters whether the clinician hypothesizes that the feature is clinically significant.

We reject (ii) because it entails that, if a patient reports something but fails to postulate that it is important, it is not a symptom. This is true even if the clinician correctly identifies the reported feature as important. We reject (i) because it permits too many things to be signs or symptoms. For example, any observation a clinician makes about a patient, regardless of its relevance to the patient's health, can become a sign simply because another person hypothesizes that it is clinically significant.

Option (iii) has its own potentially counter-intuitive consequences because it ignores patients' hypotheses. This entails that only reports made within a clinical setting can be signs or symptoms. Nonetheless, we endorse (iii) for several reasons. First, clinicians are in a privileged position to identify which features of a patient are clinically significant. Their knowledge and experience prevents a lot of irrelevant information from being misidentified as significant and limits the likelihood that something significant will be overlooked.

Second, the social nature of signs and symptoms is important. The clinician role is a special social entity that endows its bearer with the power to medically diagnose patients within a clinical setting. This is similar to how only a judge has the authority to sentence a defendant within an appropriate legal setting. Furthermore, since signs and symptoms are used to diagnose patients and determine treatment plans, they are only needed within a clinical setting. This does not, however, prevent people from using the terms 'sign' and 'symptom' in a very broad manner to refer to any number of things; however, the general application of these terms is technically incorrect and any meaning that is conveyed is derivative of their proper clinical usage. The prevalence of non-clinical applications of 'sign' and 'symptom' is ample reason to prefer the use of 'clinical sign' and 'clinical symptom' in order to avoid confusions of this sort. Once the terminological confusion is eliminated and the importance of the clinical setting is emphasized, we contend that the initial counter-intuitiveness of (iii) becomes negligible. Thus, we conclude that a health feature of a patient is only a sign or symptom if it is hypothesized by a clinician to be of clinical significance.

B. Representing Sign and Symptom

Recall from TABLE II that the Ontology for General Medical Science (OGMS) defines 'sign' as "A quality of a patient, a material entity that is part of a patient, or a processual entity that a patient participates in, any one of which is observed in a physical examination and is deemed by the clinician to be of clinical significance." OGMS defines 'symptom' as "A quality of a patient that is observed by the patient or a processual entity experienced by the patient, either of which is hypothesized by the patient to be a realization of a disease."

These definitions raise several issues. First, they allow material entities to be signs but not symptoms. If this is due to acceptance of the subjective/objective distinction, it has not been fully implemented because these definitions are consistent with a quality or processual entity being both a sign and a symptom. Yet, if the subjective/objective distinction is not

being employed, it is unclear why material entities, such as a rash or abnormal lump, cannot be symptoms. Second, it is not explicit whether being "deemed... to be of clinical significance" is the same as being "hypothesized... to be the realization of a disease". Third, OGMS is built using the Basic Formal Ontology (BFO), which states that qualities are not realizable entities. So OGMS's definition of 'symptom' is incorrect. Finally, and most significantly, these definitions combine fundamentally different types of entities. Qualities are dependent continuants, material entities are independent continuants, and processes are occurrents. As a result, these classes do not fit within BFO's representational structure. Hence, they are defined classes and are represented as direct subtypes of 'entity'.

The current representations of sign and symptom in OGMS limits what can be axiomatically asserted of these classes because anything that is asserted must hold for qualities, material entities, and processes. This means that not even the most fundamental relations, for example 'inheres in', 'bearer of', or 'realizes', can be asserted of either class. While this does not prevent simple annotation using these terms and these relations can still be asserted at the instance level, it severely limits the automatic reasoning power of any system that uses these OGMS terms. This undermines one of the major advantages of using an ontology. The problem is compounded because the meaning of many other OGMS terms depends on a clear account of sign and symptom. These include: syndrome, treatment, acute disease course, clinical picture, and clinical history.

Before presenting the reasoning for our representations of sign and symptom, we present four alternative representations and briefly discuss why each one should be rejected. First, eliminate 'sign' and 'symptom' from OGMS. Everything that is currently a sign or symptom could instead be represented as a clinical finding. This would require the redefinition of other OGMS terms that explicitly refer to signs and symptoms, which might lead to further difficulties. More importantly, it is highly unlikely that the medical community would accept the elimination of 'sign' and 'symptom'. So, even if the distinguishing characteristics of signs and symptoms were incorporated in OGMS using logical definitions to preserve important information about these clinical findings, this representation would fail to satisfy the desires of the ontology's intended user base. Nonetheless, of the four alternatives discussed here, this solution is ontologically superior because, unlike the others, it is ontologically self-consistent. Readers who are ultimately left with the sense that 'sign' and 'symptom' are overly confused or possibly indefinable, may be inclined to endorse this solution.

Second, make 'sign' and 'symptom' roles. These roles may be played either by clinical findings or by qualities, processes, or material entities. Both representations fail because BFO does not permit qualities, processes, or dependent continuants to be the bearers of roles. Even if these entities were permitted to bear roles, this solution would create the logistical challenge of constructing a particular role for each disease, syndrome, and disorder. It is not sufficient to simply create the roles 'sign of' and 'symptom of' because each role is specific to the particular disease, disorder, or syndrome it is a sign or symptom of. Thus, the ontology would have to include

thousands of roles (e.g., ‘sign of Alzheimers disease’, ‘sign of heart attack’, ‘sign of influenza’, etc.), which is not an ontologically parsimonious solution.

Third, make ‘sign’ and ‘symptom’ subtypes of ‘clinical finding’. Yet, a clinical finding becomes a sign or symptom once it has been hypothesized to be of clinical significance to a particular disease, disorder, or syndrome. Thus, this solution permits clinical findings to shift their type simply because a clinician makes a hypothesis about it. This sort of type shifting is especially ontologically vicious because the “change” that occurs involves no change in the clinical finding itself. While a role can be acquired or lost without a corresponding change in its bearer, gaining or losing a role does not change the type of entity that its bearer is. Thus, this solution should be rejected.

Fourth, make ‘sign’ and ‘symptom’ relations between qualities, processes, or material entities and the diseases, syndromes, or disorders they are hypothesized to be of clinical relevance to. It is unclear that these relations are needed since more explicit relations already exist to connect these entities to their respective diseases, disorders, or syndromes. Pathological processes, such as tremors, are part of the disease course that realizes the disease. Pathological qualities, such as an elevated temperature, inhere in the patient as a result of certain pathological processes. Pathological material entities are part of the patient and can be a manifestation of the disease, such as a rash, or part of its material basis, such as neurofibrillary tangles. Furthermore, this solution is incompatible with the absence of a feature being a sign or symptom. For example, hyporeflexia, the lack of a deep tendon reflex, can be a sign of neuromuscular disease. Thus, material entities, qualities, and processes do not exhaust the domain of signs and symptoms.

Our solution is to represent sign and symptom as relations between clinical findings and the illnesses they are hypothesized to be of clinical relevance to. The result is X ‘is sign of’ Y and X ‘is symptom of’ Y where the domain X is a clinical finding and the range Y is a disease, disorder, or syndrome. These relations specify the nature of aboutness that holds between certain clinical findings and certain diseases, disorders, and syndromes. Which relationship is used depends on the role played by the person who reported the finding. Clinical findings reported by the patient, the patient’s family, or another non-clinician are potential symptoms. Clinical findings reported by a clinician are potential signs. In both cases, only findings hypothesized by a clinician to be of clinical significance to a disease, disorder, or syndrome will have one of these relations.

While laboratory tests, imaging techniques, and other medical procedures can provide diagnostically valuable clinical findings, they often are not performed by a clinician. Thus, it is necessary to allow the medical professionals who perform these procedures to report findings that may be hypothesized by a clinician to be signs. Additionally, while patients and non-clinician medical professionals must report their observations in order for them to be symptoms or signs, observations made by a clinician do not need to be reported in order to be signs. This is because a clinician must be informed about observations made by others in order to hypothesize that they are clinically significant, but does not need to report his own findings in order to hypothesize about them. If the clinician does not report his finding, the clinical finding is the clinician’s

mental representation. Thus, both features of the patient observed by a clinician and clinical findings about the patient that are reported by a medical professional can be signs.

Note that our representation is capable of handling cases where nonexistent entities are signs or symptoms. While there are no nonexistent entities, there can be a clinical finding about a feature that is not present. This clinical finding can then be hypothesized to be of clinical significance. In the case of hyporeflexia, the clinical finding would be the observation or report that no reflex occurred.

One might object that, unlike the subjective/objective distinction for sign and symptom, our representation fails because it permits a single feature of a patient to be both a sign and a symptom. If this were the case, it would mean that our definitions are too inclusive. This could lead to confusion and violate ontology best practices. On our account, the same clinical finding cannot have both the ‘is clinical sign of’ and the ‘is clinical symptom of’ relations. This is because only those clinical findings that are reported by a patient or non-medical professional can have the ‘is clinical symptom of’ relation. Similarly, only those clinical findings that are observed by a clinician or reported by an appropriate medical professional can have the ‘is clinical sign of’ relation. Thus, while there can be two findings about the same feature of a particular patient, no single finding can be both a sign and a symptom.

What happens if the patient or family member who reports a clinical finding is a clinician? Can such reports be both a sign and a symptom? The answer depends on which conditions one accepts for the realization of a clinician role. It is reasonable to assert that a clinician role can only be realized in the context of a clinical encounter. It is a further question whether an individual can play both a patient role and a clinician role in a single clinical encounter. Since the clinician role is a social construct, limitations—such as prohibiting a doctor from diagnosing or treating himself—can easily be asserted to resolve this dilemma. Another solution would be to allow clinicians to self-diagnose, but assert that the clinician role takes priority over the patient role with regard to clinical findings. Thus, clinical findings made during these encounters would always be either a clinical sign or just a clinical finding. The precise explication of this scenario is left open for further debate.

Finally, one might object that our proposed definitions are overly strict because they exclude prognostic signs from being clinical signs. Prognostic signs are signs that are indicative of the patient’s health outcome. These signs assist clinicians in determining a patient’s likelihood of survival, recovery time, or possible loss of physical ability or mental functioning. This is opposed to diagnostic signs, which are indicative of the nature of the patient’s illness. If—as our definition of ‘is clinical sign of’ requires—some prognostic signs are not about a disease, disorder, or syndrome, then not all prognostic signs are clinical signs and our definition is too restrictive.

There are several things to consider here. First, even if prognostic signs cannot always be understood as clinical signs, this may be due to prognostic signs and diagnostic signs being distinct types of signs. If this is the case, then the mistake may lie in grouping two distinct kinds of clinical findings together

as a single thing. Second, our definition permits clinical signs to be signs of disorders or syndromes as well as of diseases. It is plausible that most, if not all, prognostic signs are signs of disorders. For example, a death rattle is a prognostic sign of imminent death, but it is also a clinical sign of the buildup of fluid in the throat and upper chest, which can be understood as a syndrome and is the result of a disorder. Similarly, a clinician may determine that a gunshot victim will make a full recovery based on observing that the bullet missed all major organs and arteries. The wound is a disorder and it is based on this clinical finding that the clinician is able to make a prognosis. Thus, according to our definition, all prognostic signs are clinical signs.

V. CONCLUSIONS

We have presented an ontologically sound representation of sign and symptom and developed precise definitions for relations that capture the meaning of each term. This is important for the biomedical community because it unifies the representation of two commonly used terms while providing a clear delineation of their instances that does not allow for confusing overlap between their members. Furthermore, our representation enables the easy formulaic creation of customized groups of signs and symptoms in order to identify information relevant to each user's needs. This is, perhaps, the most significant contribution our work provides to the biomedical ontologies community.

Our experience in developing this account of signs and symptoms is indicative of general issues that can arise when developing definitions in ontologies. For example, when the ontological representation requires a more restrictive definition than the colloquial definition, it is advisable to create a special label for the entity (e.g., 'clinical sign' instead of 'sign' and 'clinical symptom' instead of 'symptom'). Changing the label reduces the risk of confusion as well as the risk that the specialized definition will elicit resistance from users familiar with the old term. Ontology development is typically a descriptive exercise in representing entities such that the ontology is made to conform to our understanding of the world; however, our experience here has shown that the direction of fit can operate in reverse. This occurs when the only ontologically sound means of representing the entities in question requires changing our everyday understanding of the meaning of those terms. In these cases, the ontological definition should be used to prescriptively enforce a new, more precise, use of the term.

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