# Modeling Biomedical Burdens in Basic Formal Ontology

Paul Smart[1,*,†], Nic Fair[1,†] and Michael Boniface[1,†]

[1]Electronics and Computer Science, University of Southampton, Highfield, Southampton, SO17 1BJ, UK

**Abstract**

The term "biomedical burden" refers to a number of types of burden that have been discussed in the medical literature. This includes the burdens that stem from the presence of disease (e.g., disease burden and symptom burden), as well as the burden associated with healthcare interventions (e.g., treatment burden and side-effect burden). The present paper describes an ontology of biomedical burdens that uses Basic Formal Ontology (BFO) as an upper-level ontology. The ontology provides support for the representation of burden-related cognitions, the classification of burden types, and the representation of burdensome situations. The ontology also captures our current theoretical understanding of burden, thereby serving as the basis for future analytic and definitional work.

**Keywords**

Basic Formal Ontology, Medical Ontology, Treatment Burden, Symptom Burden

## 1. Introduction

The term "biomedical burden" refers to a number of types of burden that have been discussed in the medical literature. These include the burdens associated with disease and illness (e.g., disease burden, symptom burden), as well as the burdens associated with healthcare interventions (e.g., treatment burden, side-effect burden).

While the study of burden has long been a feature of medical research—with studies dating back to at least the 1940s [1]—recent years have seen a renewed interest in burden. This is partly due to shifts in the demographic and epidemiological landscape, which has meant that more people are living with chronic, life-limiting conditions. Other changes relate to the provision of healthcare, with patients expected to play a greater role in the prevention, management, and treatment of disease. As May et al. [2] note:

> Healthcare services increasingly seek to position patients and their supporters as accountable for this work. In turn, this shift in accountability involves adding the burden of treatment to the burden of symptoms, as patients experience new and growing demands to organize and co-ordinate their own care, to comply with complex treatment and self-monitoring regimens, and to meet a whole range of expectations of personal motivation, expertise and self-care. (p. 2)

*15th International Conference on Biological and Biomedical Ontology, July 17–19 2024, Enschede, The Netherlands*

*Corresponding author.

†These authors contributed equally.

ps02v@ecs.soton.ac.uk (P. Smart); N.S.Fair@soton.ac.uk (N. Fair); M.J.Boniface@soton.ac.uk (M. Boniface)

0000-0001-9989-5307 (P. Smart); 0000-0003-1566-4689 (N. Fair); 0000-0002-9281-6095 (M. Boniface)

Despite the interest in burden, there has been little attempt to subject burden-related concepts to analytic scrutiny. This has complicated efforts to arrive at a common understanding of burden, leading to confusion about the meaning of burden-related terms and the absence of univocal definitions [see 3, 4].

Paralleling the lack of theoretical attention, there is, at present, little support for burden-related terms within medical ontologies. The Ontology Lookup Service (OLS) search engine, for example, yields no results for the terms "symptom burden" or "treatment burden."[1] This lack of support is problematic, for it complicates efforts to assimilate burden-related data into wider nexus of biomedical datasets and biomedical applications.

In the present paper, we aim to address these twin concerns by describing the Biomedical Burden Ontology (BBO)—a theoretically-grounded ontology of biomedical burdens.[2] To support interoperability with other medical ontologies, the BBO is implemented in the Web Ontology Language (OWL) and uses Basic Formal Ontology (BFO) [see 5] as an upper-level ontology. The BBO also relies on a number of ontologies that form part of the Open Biological and Biomedical Ontology (OBO) Foundry. These include the Ontology for General Medical Science (OGMS) [6], the Mental Functioning Ontology (MFO) [7], the Emotion Ontology (MFOEM) [8], and the Information Artifact Ontology (IAO) [9].

The bulk of the paper is devoted to a description of the BBO. This is presented in Section 3. In Section 2, we describe the theoretical grounding of the BBO, reporting the results of an initial analysis of the burden concept. Throughout the paper, we rely on typographic conventions to distinguish between ontology elements. OWL classes are rendered **`LIKE THIS`**, OWL properties **`likeThis`**, and OWL individuals `:LIKE THIS`. Property instances are rendered in italic font, *`likeThis`*.

## 2. Understanding Burden

One of the main challenges in developing an ontology of biomedical burdens is that burden-related concepts have seldom been at the forefront of analytic attention. This makes it difficult to answer questions that are relevant to the ontology development effort. What, for example, is a burden? Are burdens members of a common ontological kind (such as the category of continuants), or are they of different kinds? What, moreover, of the nature of burdensomeness? What is it that makes some things burdensome, while others are not burdensome?

A useful starting point is to consider a dictionary definition of burden. According to Merriam-Webster, the term "burden" can refer to multiple things.[3] Firstly, it may refer to a heavy load, as in the case of someone who is forced to carry a heavy backpack. Call this the *load-based view* of burden. Secondly, a burden may refer to a certain duty or responsibility, as when one reluctantly agrees to water a neighbor's plants while they are on vacation. Call this the *obligation-based view* of burden. Finally, a burden may refer to something oppressive or worrisome, as when an individual is burdened by a persistent sense of guilt or regret. Call this the *emotion-based view* of burden.

[1] See https://www.ebi.ac.uk/ols4/ [Accessed: 09 April 2024].
[2] The current version of the BBO is available via GitHub: https://github.com/ps02v/BBO.
[3] See https://www.merriam-webster.com/dictionary/burden [Accessed: 16 March 2024].

At first sight, these views suggest that burdens are unlikely to belong to a common ontological kind, such as the category of continuants or occurrents. Under the load-based view, for example, the thing that is deemed to be a burden is a physical load of some sort, such as a heavy backpack. Given that backpacks are material entities (and thus independent continuants), the load-based view suggests that some burdens can qualify as independent continuants.

The emotion-based view yields a different result. In this case, the thing that is deemed to be burdensome is a particular sort of experience, such as a feeling of guilt or regret. This suggests that some burdens are best understood as occurrent or processual entities, at least according to contemporary BFO-conformant ontologies, such as the MFO and MFOEM. Much the same could be said of the obligation-based view. If, for example, one is burdened because one has an obligation to water a neighbor's plants, then it is hard to resist the conclusion that processes (specifically, plant-watering processes) must have something to do with this.[4]

The problem, then, is that different views yield different conclusions regarding the ontic nature of burdens. The load-based view suggests that burdens are best understood as continuant entities, while the emotion- and obligation-based views suggest that burdens are best understood as occurrent entities. Having said this, it should be noted that occurrent entities are not entirely absent from cases that fall under load-based view. Consider, again, the backpack case. While the backpack is readily understood to be a burden (or the thing that is burdensome), it cannot be the mere presence of the backpack that establishes its status as a burden. What makes the backpack burdensome is not so much the fact that it exists; it is more the fact that one is obliged to *carry* it. In short, the backpack is burdensome because one must enter into some sort of relationship with the backpack. This relationship is established courtesy of one's participation in a process, specifically, a carrying process. This is important, for it highlights a point of commonality between the load-based, obligation-based, and emotion-based views: In all these cases, we encounter state-of-affairs in which some individual is obliged to participate in a process of some sort. In the backpack case, that process is a carrying process; in the plant-watering case, it is a watering process, and, in the guilt-ridden case, it is an emotional process.

This insight serves as the basis for a view of burden we call the *Atlassian view*.[5] According to the Atlassian view, burdens are best understood as situations or states-of-affairs in which some entity (e.g., a human individual) is obliged to participate in a process. This notion of obligatory participation is central to the Atlassian view. According to the Atlassian view, what makes something burdensome is the fact that an individual is obliged to participate in a process. This might be because an individual has no control over the process, as is often the case with symptom processes.[6] Alternatively, there might be a substantial cost associated with one's refusal to participate in a process, as when one is obliged to participate in a particular course of treatment as the a means of ridding oneself of a disease.[7]

[4] An alternative reading of the obligation-based view stems from Arp et al. [5, p. 103]. They suggest that obligations are best understood as relational qualities. This would place burdens (under the obligation-based view) in the category of specifically-dependent continuants.

[5] The Atlassian view is named after the Titan, Atlas, who was condemned (obliged) to hold up the heavens after the Titanomachy.

[6] Pain, for example, is something that happens to us; we do not choose to participate in a pain-related process, nor is it easy to suspend our participation in pain-related processes whenever we wish to do so.

[7] For more on the notion of participation, and the different types of participatory relationship included in BFO, see Smith and Grenon [10].

**Table 1**
Biomedical burdens according to the Atlassian view. Different types of burden are distinguished according to the nature of a process in which a human individual is obliged to participate.

| Burden Type | Process Type | Comments |
|---|---|---|
| Disease Burden | Pathological Bodily Process | Pathological bodily processes correspond (either wholly or in part) to the realization of diseases. Diseases are represented as dispositions in BFO. |
| Symptom Burden | Symptom Process | A process that often occurs as part of a disease course (e.g., pain, fatigue, nausea, or anxiety). |
| Treatment Burden | Treatment Process | A process that is performed as part of a treatment regimen or treatment plan (e.g., the process of injecting insulin). |
| Side-Effect Burden | Side Effect | A process that occurs as the consequence of (i.e., as the *effect* of) a treatment process. |

One virtue of the Atlassian view is that it is readily applicable to many of the burdens discussed in the medical literature. In respect of treatment burden, for example, the burden arises as the result of an individual's obligatory participation in processes that are intended to treat an ongoing illness or disease (i.e., treatment processes). The same applies to other types of biomedical burden, such as symptom burden, side-effect burden, and disease burden (see Table 1). What is common to these burdens, we suggest, is that a given individual (e.g., a patient) is obliged to participate in a certain sort of process. It is then the nature of this process (e.g., a treatment process) that serves as the basis for the distinction between burden types.

Notwithstanding the merits of the Atlassian view, there are reasons to think that it cannot be the whole story of burden. In particular, while obligatory participation may be a common (perhaps universal) feature of burden, it cannot be sufficient for burden. Consider that one may be obliged to participate in an eating process, but this does not mean that the eating process (or one's participation in the eating process) is thereby rendered burdensome. In order for the eating process to qualify as burdensome, something more must be added. The missing ingredient, it seems, is something to do with the 'hedonic tone' of the process in which one is obliged to participate. If one wants to eat, and the food is palatable, then there is no reason to think the eating process will be burdensome. If, by contrast, one is forced to eat despite the fact that one is full, then the eating process is apt to acquire more burdensome 'flavor'.

In addition to obligatory participation, then, the apparent 'goodness' or 'badness' of a process looks to be important to our understanding of burden. In particular, we suggest that an individual's obligatory participation in a process only counts as burdensome if the process is non-preferred, by which we mean, the individual would much prefer not to be participant in the process in which they are obliged to participate. Ideally, of course, the appeal to non-preferred processes would benefit from an account that explicates the distinction between preferred and non-preferred processes. While we have explored this issue in recent research, a detailed discussion of this issue would take us too far afield.[8] For present purposes, then, we will simply

[8]In brief, our approach relies on predictive processing (aka. active inference) accounts of motivated and goal-directed

acknowledge that the distinction between preferred and non-preferred processes is likely to be important to our theoretical understanding of burden.

Putting all this together, yields the following working definition of burden: A burden is a situation (*O*) in which a subject (*S*) is obliged to participate in a process (*P*) and *P* is a non-preferred process, meaning that *S* would much prefer they were not a participant in *P*.

We can now make a distinction between what we call the *object of burden* and the *subject of burden*. The object of burden is the situation in which an individual is obliged to participate in a (non-preferred) process (i.e., *O* in the above definition). The subject of burden is the entity that is being burdened (i.e., *S* in the above definition). For present purposes, we will assume that the subject of burden is always a human individual (as opposed to a collective entity, such as a nation state). Accordingly, when we talk of treatment burden, what we mean is that a human individual is obliged to participate in one or more treatment processes (e.g., a kidney dialysis process). Likewise, when we talk of symptom burden, what we mean is that a human individual is obliged to participate in one or more symptom processes (e.g., a chronic pain process or chronic fatigue process).

Having summarized the effort to advance our theoretical understanding of burden, our attention now turns to the BBO. In the next section, we describe how the various elements of the Atlassian view of burden are accommodated by the BBO.

## 3. Representing Burden

The BBO is implemented as an extension of existing ontologies, some of which are included in the OBO Foundry. Aside from BFO, the BBO incorporates entities from OGMS [6], MFO [7], MFOEM [8], and the Cognitive Process Ontology (CPO) [12, 13]. The BBO also relies on entities from the IAO [9], as well as the more recent information modeling extensions provided by the Common Core Ontologies (CCO) suite [14].

At the heart of the BBO is the **BURDEN PROCESS** class. This is represented as a subtype of **AFFECTIVE PROCESS**, which is one of the classes included in the MFOEM. Different types of biomedical burden (e.g., **TREATMENT BURDEN** and **SYMPTOM BURDEN**) are represented as subtypes of the **BURDEN PROCESS** class (see Figure 1).

As with the modeling of other affective phenomena, such as emotions [8], we assume that additional processes occur as part of burden processes. These include the likes of physiological processes (e.g., those associated with a stress response), cognitive processes (e.g., appraisal processes), and experiential processes (e.g., the subjective feeling of burden). While these processes need not occur at the same time, we assume they occur as part of burden processes, which is to say that they all occur (if they occur) within the **TEMPORAL REGION** occupied by the burden process.

Although it is not explicitly represented in the BBO, we allow for the possibility that burden processes may be linked to phenomena that are typically studied as part of research into

behavior [e.g., 11]. In particular, we suggest that preferred processes are tied to neurally-realized predictions that govern the choice between action policies. In the BBO, these predictions are represented via a **CONATIVE REPRESENTATION** class (see Figure 3). Non-preferred processes are then the processes that disrupt an individual's capacity to bring about the state-of-affairs denoted by conative representations.

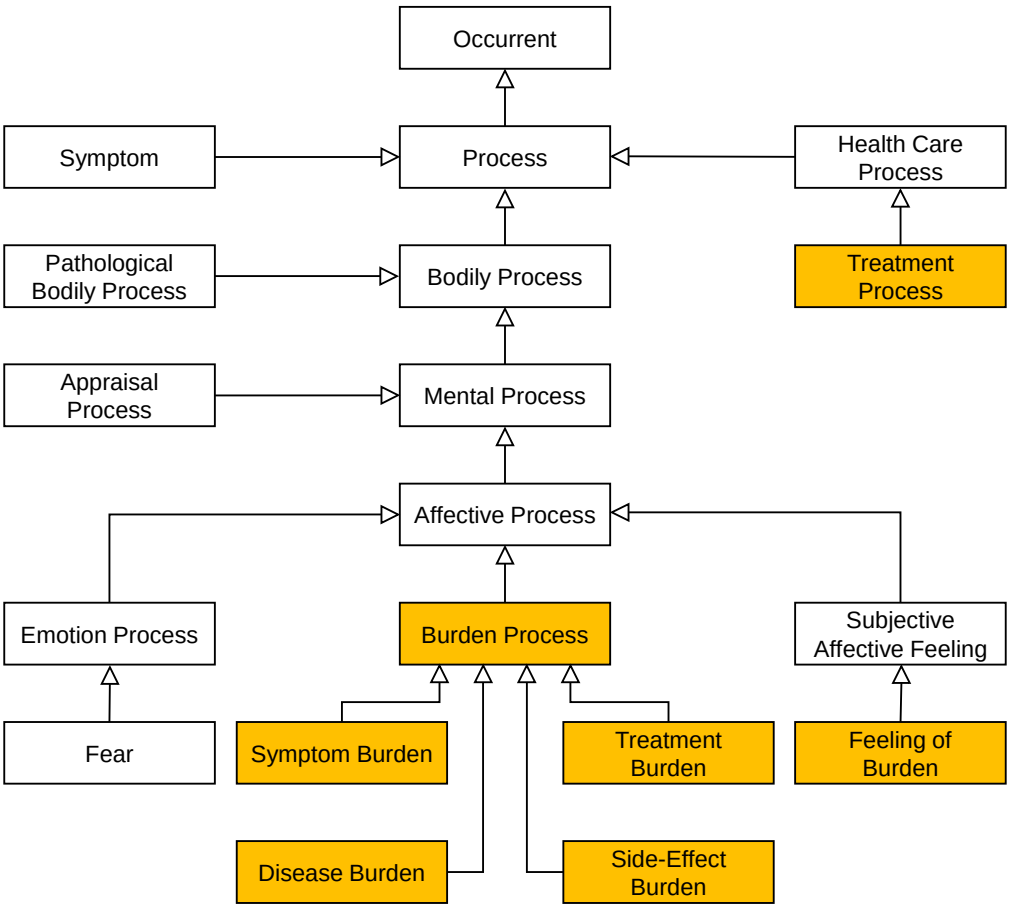



**Figure 1:** Different types of biomedical burden (e.g., treatment burden) are represented as subtypes of the **BURDEN PROCESS** class. Colored boxes indicate classes that are specific to the BBO, while non-colored boxes indicate classes sourced from other ontologies, such as BFO, OGMS, MFO, and MFOEM.

biomedical burdens. In respect of treatment burden, for example, there is considerable interest in the relationship between treatment burden and medical non-adherence [e.g., 15]. Indeed, non-adherence is one of the most widely cited consequences of treatment burden [e.g., 16]. Figure 2 illustrates one way of representing this relationship in the BBO. In this case, a **BURDEN PROCESS** causes a **GAIN OF REALIZABLE ENTITY**, which represents the gain of a particular tendency, namely, **TREATMENT NON-ADHERENCE TENDENCY**.[9] [Note that the nodal elements (or boxes) in Figure 2 correspond to OWL individuals, not OWL classes.]

Appraisal processes are of central importance to burden processes, for they are the means by which individuals appraise certain situations as being burdensome. In the MFOEM, appraisal processes are represented by the **APPRAISAL PROCESS** class, which is a type of **MENTAL**

[9]See Jansen [17], for more on the ontological characterization of tendencies and their relation to other types of realizable entity (e.g., dispositions).

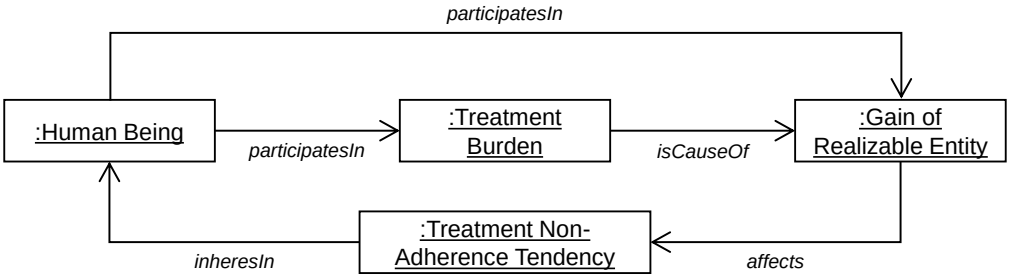



**Figure 2:** Using the BBO to represent the relationship between treatment burden and non-adherence.

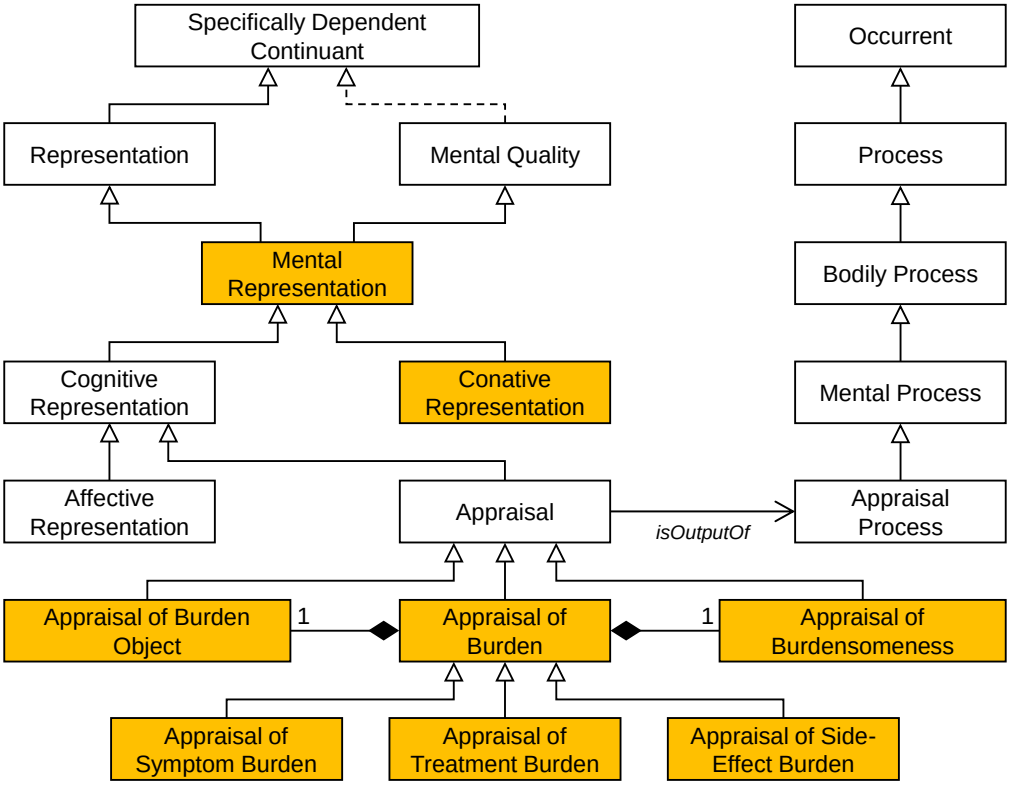



**Figure 3:** Burden appraisals are represented as subtypes of the **APPRAISAL** class. Each **APPRAISAL OF BURDEN** consists of an **APPRAISAL OF BURDEN OBJECT** and an **APPRAISAL OF BURDENSOMENESS**. [Dashed lines represent indirect taxonomic relationships.]

**PROCESS** (see Figure 1). The output of an **APPRAISAL PROCESS** is an **APPRAISAL OF BURDEN**, which is represented as a type of **COGNITIVE REPRESENTATION** (see Figure 3). The **APPRAISAL OF BURDEN** is a composite representation, which consists of at least two further representational entities. These are the **APPRAISAL OF BURDEN OBJECT** and the **APPRAISAL OF BURDENSOMENESS** (see Figure 3). The former entity (i.e., **APPRAISAL**

**OF BURDEN OBJECT**) represents what we earlier referred to as the object of burden (see Section 2). That is to say, it represents the situation or (state-of-affairs) that an individual deems to be burdensome (e.g., a situation in which the individual is obliged to carry a heavy backpack). The latter entity (i.e., **APPRAISAL OF BURDENSOMENESS**) represents the reason why the object of burden is deemed to be burdensome. In the BBO, this is understood in terms of the impact or effect of one's (obligatory) participation in a process. Specifically, situations are appraised as burdensome when they threaten to disrupt (or interfere with) an agent's capacity to bring about the state-of-affairs denoted by instances of the **CONATIVE REPRESENTATION** class (see Figure 3 and Footnote 8). Due to space constraints, we will refrain from further discussion of the **CONATIVE REPRESENTATION** class and its link to negative impacts. For present purposes, we will limit our attention to the **APPRAISAL OF BURDEN OBJECT** class.

As with other types of appraisal (e.g., the appraisal of pleasantness), the **APPRAISAL OF BURDEN** is intended to represent the appraisal-related cognitions that individuals have about certain situations. This notion of 'aboutness' is what is sometimes referred to as the *content* of a representation. In the BBO, the content of burden appraisals is given by a particular type of **INFORMATION CONTENT ENTITY**, called **REPRESENTATIONAL INFORMATION CONTENT ENTITY** (RICE). This class is taken from the CCO suite, specifically, the Information Entity Ontology [see 14]. Instances of the **REPRESENTATIONAL INFORMATION CONTENT ENTITY** class are used to connect burden appraisals to particular situations or states-of-affairs. In the case of the **APPRAISAL OF BURDEN OBJECT** class, this situation is what we understand to be the object of burden; i.e., a situation in which an individual is obliged to participate in a particular process. In the BBO, the object of burden is represented by instances of the **SITUATION** class, which is asserted as a subtype of the (top-level) BFO **ENTITY** class.[10] The 'aboutness' of burden appraisals is then established via the use of two relations: **concretizes** (which connects a burden appraisal to a **REPRESENTATIONAL INFORMATION CONTENT ENTITY**) and **isAbout** (which connects a **REPRESENTATIONAL INFORMATION CONTENT ENTITY** to a **SITUATION**). The elements of a **SITUATION** are then specified via a custom BBO relation, namely, **hasSituationPart**. In the case of appraisals relating to the object of burden (i.e., **APPRAISAL OF BURDEN OBJECT**), we assume that the relevant **SITUATION** will consist of at least one **PROCESS**. We then rely on participatory relationships (e.g., **participatesIn**, **agentIn**, **isAffectedBy**, etc.) to represent the involvement of continuant entities in the **PROCESS**.[11] One such (continuant) entity is the individual that is obliged to participate in the **PROCESS**. This individual is what we earlier referred to as the subject of burden (see Section 2). If the subject of burden is the individual entertaining burden-related cognitions (i.e., the same individual who is appraising a situation as burdensome), then we have a form of self-referential cognition—i.e., a state-of-affairs in which the individual appraises themselves as being the subject of burden.

[10] In the current version of the BBO, a situation is defined as "… a Portion of Reality that refers to a configuration of entities."

[11] Note that processes can have *multiple* participants. The process of carrying a backpack, for example, would have both the individual who is tasked with carrying the backpack and the backpack itself as participants in the carrying process.

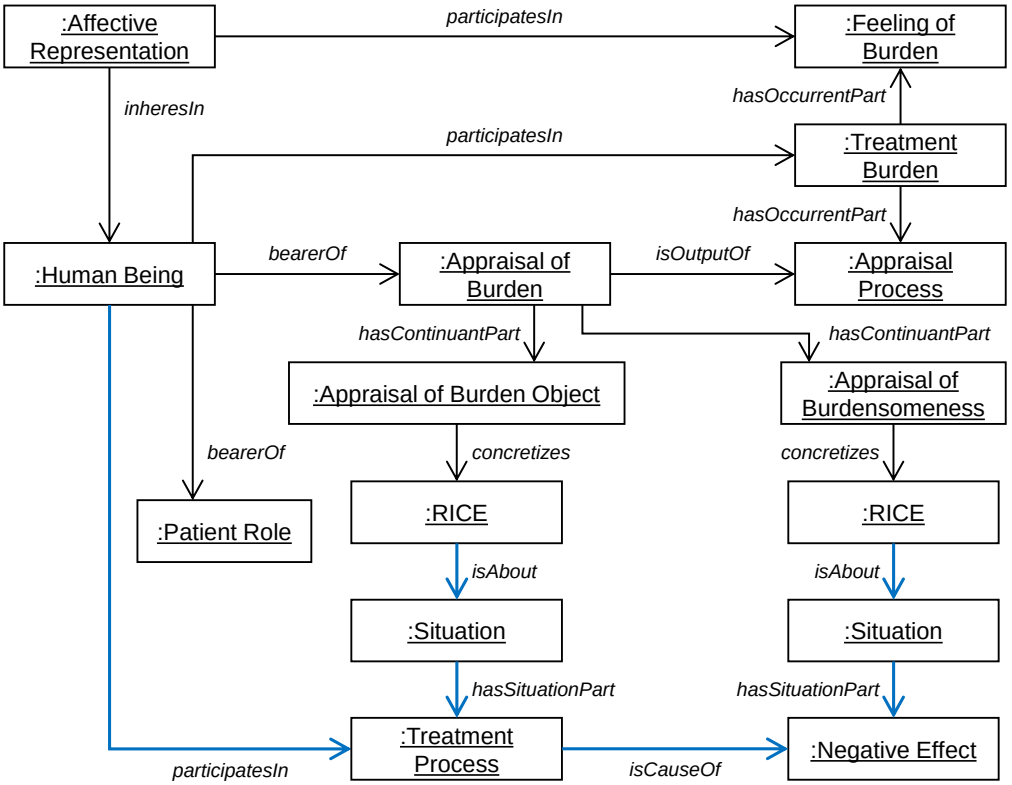
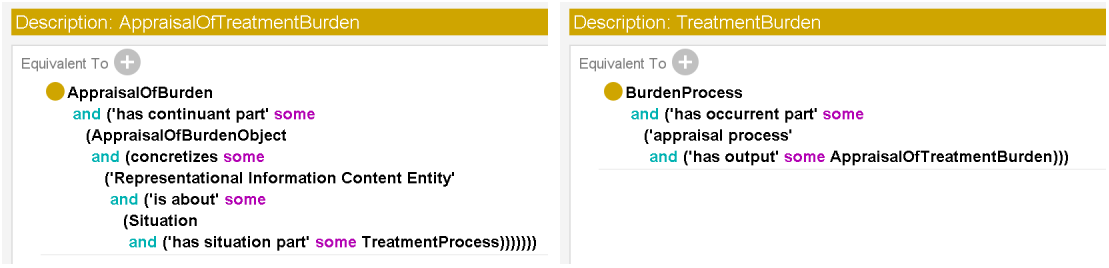



**Figure 4:** Using the BBO to represent a case of treatment burden. Blue arrows indicate relations from the Modal Relation Ontology (see main text for details).

An example of this representational scheme is depicted in Figure 4. In particular, Figure 4 shows how the BBO can be used to model a case of treatment burden. The subject of burden in this figure is represented by :HUMAN BEING. :HUMAN BEING is the bearerOf a :PATIENT ROLE, which establishes the status of :HUMAN BEING as a patient. In addition to :PATIENT ROLE, :HUMAN BEING is also the bearerOf an :APPRAISAL OF BURDEN, which is produced by :APPRAISAL PROCESS.[12] The :APPRAISAL OF BURDEN OBJECT concretizes a :RICE, which isAbout a :SITUATION. Within this :SITUATION, we find a :TREATMENT PROCESS that involves :HUMAN BEING as a participant. Figure 4 thus depicts a state-of-affairs in which a patient (i.e., an individual who is the bearer of a patient role) appraises a situation as being burdensome, and this situation is one that features the patient as a participant in a treatment process. This establishes :HUMAN BEING as the subject of (treatment) burden, while the object of burden is the :SITUATION that is being appraised as burdensome.[13]

[12] For reasons of simplicity, we have represented burden appraisals as inhering in a human individual. Readers should, however, note that the more correct characterization is one of burden appraisals (*qua* mental qualities) inhering in some part of the cognitive system of a human individual. See Limbaugh et al. [13], for more on this.

[13] Figure 4 also shows how the subjective experience of burden (or the feeling of burden) is represented within the BBO. Here, the BBO follows the strategy adopted by the MFOEM. Specifically, the feeling of burden is represented by the **FEELING OF BURDEN** class, which specializes the MFOEM **SUBJECTIVE AFFECTIVE FEELING**




(a) Appraisal of Treatment Burden

(b) Treatment Burden

**Figure 5:** The characterization of **APPRAISAL OF TREATMENT BURDEN** and **TREATMENT BURDEN** in the Protégé ontology editor.

Note that some of the relations depicted in Figure 4 are rendered in blue font (e.g., `isAbout`, `hasSituationPart`, `participatesIn`, and so on). These relations are so-called modal relations, which form part of the CCO, specifically, the Modal Relation Ontology [see 14]. The use of these modal relations enables the BBO to refer to non-actual states-of-affairs, as when an individual who is obliged to water their neighbor's plants appraises themselves as being burdened, even though they have not (as yet) begun to water the plants. In short, the use of modal relations enables the BBO to refer to expected (i.e., future) states-of-affairs. At present, it remains unclear whether all burden appraisals are about future states-of-affairs; nevertheless, we suspect that modal relations will be a common feature of burden modeling efforts. This is not to say that the past (or present) is irrelevant to our understanding of burden; it is merely to note that burden appraisals are often tied to things that will happen in the future (i.e., beyond the present moment).[14]

While one can explicitly denote burden processes as being of a particular type (as is the case in Figure 4), it is also possible to rely on the semantic description of classes within the BBO to support the automatic classification of burden instances via subsumption reasoning. Figure 5 shows the logical expressions that support subsumption reasoning in respect of treatment burden. In this case, an **APPRAISAL OF BURDEN** is classified as an **APPRAISAL OF TREATMENT BURDEN** based on the type of **PROCESS** that features as part of the **SITUATION** that is being appraised as burdensome (see Figure 5a). This classification then serves as the basis for classifying a (generic) **BURDEN PROCESS** as a particular instance of **TREATMENT BURDEN** (see Figure 5b).

## 4. Conclusion

In recent years, the assessment and management of biomedical burdens has emerged as an important focus area for both scientific research and clinical practice. As a means of supporting this effort, the present paper describes an ontology of biomedical burdens—the BBO—that uses BFO as an upper-level ontology. The ontology provides support for the representation

class (see Figure 1).

[14] See Cassell [18] for a similar (future-oriented) approach to suffering.

of burden-related cognitions, the classification of burden types, and the representation of burdensome situations. It also demonstrates the way in which recent information modeling practices, specifically those associated with the CCO [14], can be applied to the modeling of cognitive/affective phenomena.

Future work will seek to extend and refine the BBO. One of the aims for future work is to extend the scope of the BBO, providing support for the representation of entities that feature as part of research into burden (examples include health literacy, demographic factors, education background, early life experiences, and so on). A second focus area for future work relates to the representation of data emanating from scientific studies of burden. This includes the data emanating from survey instruments such as the Patient Experience with Treatment and Self-management (PETS) [19]. Finally, we aim to use the BBO to support the data-driven analysis of burdensome health conditions, combining the BBO with ontologies that specialize in the representation of diseases, symptoms, treatments, and other types of patient data.

## Acknowledgments

This paper is independent research funded by the National Institute for Health Research Artificial Intelligence for Multiple Long-Term Conditions (AIM) programme (Multidisciplinary Ecosystem to study Lifecourse Determinants and Prevention of Early-onset Burdensome Multimorbidity (MELD-B), award identifier NIHR203988). The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

## References

[1] J. Downes, Illness in the chronic disease family, American Journal of Public Health and the Nations Health 32 (1942) 589–600.

[2] C. R. May, D. T. Eton, K. Boehmer, K. Gallacher, K. Hunt, S. MacDonald, F. S. Mair, C. M. May, V. M. Montori, A. Richardson, Rethinking the patient: using Burden of Treatment Theory to understand the changing dynamics of illness, BMC Health Services Research 14 (2014) 1–11.

[3] M. Bastawrous, Caregiver burden—A critical discussion, International Journal of Nursing Studies 50 (2013) 431–441.

[4] A. Sav, M. A. King, J. A. Whitty, E. Kendall, S. S. McMillan, F. Kelly, B. Hunter, A. J. Wheeler, Burden of treatment for chronic illness: a concept analysis and review of the literature, Health Expectations 18 (2013) 312–324.

[5] R. Arp, B. Smith, A. D. Spear, Building Ontologies with Basic Formal Ontology, MIT Press, Cambridge, Massachusetts, USA, 2015.

[6] R. H. Scheuermann, W. Ceusters, B. Smith, Toward an ontological treatment of disease and diagnosis, Summit on Translational Bioinformatics 2009 (2009) 116–120.

[7] J. Hastings, W. Ceusters, M. Jensen, K. Mulligan, B. Smith, Representing mental functioning: Ontologies for mental health and disease, in: 3rd International Conference on Biomedical

Ontology: Towards an Ontology of Mental Functioning Workshop, Graz, Austria, 2012, pp. 1–5.
[8] J. Hastings, W. Ceusters, B. Smith, K. Mulligan, The emotion ontology: Enabling interdisciplinary research in the affective sciences, in: M. Beigl, H. Christiansen, T. R. Roth-Berghofer, A. Kofod-Petersen, K. R. Coventry, H. R. Schmidtke (Eds.), Modeling and Using Context, volume 6967, Springer, Karlsruhe, Germany, 2011, pp. 119–123.
[9] B. Smith, W. Ceusters, Aboutness: Towards foundations for the Information Artifact Ontology, in: F. M. Couto, J. Hastings (Eds.), 6th International Conference on Biomedical Ontology, volume 1515, CEUR Workshop Proceedings, Lisbon Portugal, 2015, pp. 1–5.
[10] B. Smith, P. Grenon, The cornucopia of formal-ontological relations, Dialectica 58 (2004) 279–296.
[11] G. Pezzulo, F. Rigoli, K. J. Friston, Hierarchical active inference: A theory of motivated control, Trends In Cognitive Sciences 22 (2018) 294–306.
[12] D. Limbaugh, D. Kasmier, W. Ceusters, B. Smith, Warranted diagnosis, in: A. D. Diehl, W. D. Duncan, G. Sanso (Eds.), 10th International Conference on Biomedical Ontology, volume 2931, CEUR Workshop Proceedings, New York, New York, USA, 2019, pp. 1–10.
[13] D. Limbaugh, J. Landgrebe, D. Kasmier, R. Rudnicki, J. Llinas, B. Smith, Ontology and cognitive outcomes, Journal of Knowledge Structures and Systems 1 (2020) 3–22.
[14] CUBRC, Modeling Information with the Common Core Ontologies, Technical Report, CUBRC, Inc., Buffalo, New York, USA, 2020.
[15] S. Demain, A.-C. Goncalves, C. Areia, R. Oliveira, A. J. Marcos, A. Marques, R. Parmar, K. Hunt, Living with, managing and minimising treatment burden in long term conditions: A systematic review of qualitative research, PLoS One 10 (2015) e0125457.
[16] D. T. Eton, R. T. Anderson, J. L. St Sauver, E. A. Rogers, M. Linzer, M. K. Lee, Longitudinal trajectories of treatment burden: A prospective survey study of adults living with multiple chronic conditions in the midwestern United States, Journal of Multimorbidity and Comorbidity 12 (2022) 1–14.
[17] L. Jansen, Tendencies and other realizables in medical information sciences, The Monist 90 (2007) 534–554.
[18] E. J. Cassell, The nature of suffering and the goals of medicine, New England Journal of Medicine 306 (1982) 639–645.
[19] D. T. Eton, K. J. Yost, J.-s. Lai, J. L. Ridgeway, J. S. Egginton, J. K. Rosedahl, M. Linzer, D. H. Boehm, A. Thakur, S. Poplau, Development and validation of the Patient Experience with Treatment and Self-management (PETS): A patient-reported measure of treatment burden, Quality of Life Research 26 (2017) 489–503.