Improving the Semantics of Drug Prescriptions with a Realist Ontology

Jean-Francois Ethier, Ryeyan Taseen, Luc Lavoie and Adrien Barton
Département de Médecine & Département d'Informatique
Université de Sherbrooke
Corresponding authors: ethierj@gmail.com, ryeyan.taseen@usherbrooke.ca, adrien.barton@gmail.com
Sherbrooke, Canada

***Abstract*—Electronic prescriptions are supported as a means to reduce adverse drug events, but the ambiguities and overspecificities of prescription semantics along with their lack of standardization reduce adoption, limit interoperability and are potential sources of error. Ontologies in the OBO Foundry, founded on realist methodology, have been successful in fostering the logical, scientifically accurate data standards that the domain of drug prescriptions is currently in need of. This paper illustrates some problems regarding the structuration of current electronic prescriptions, and demonstrates how the Prescription of Drugs Ontology (PDRO) addresses these issues with improved semantics founded on OBO and realist principles. PDRO reuses classes and object properties from IAO, OBI, OGMS, OMRSE and DRON, introducing new entities within its scope and proposing entities within those of its imported domains that may be useful to other health care and information artifact-related ontologies in the OBO Foundry. PDRO aims at improving the semantics of drug prescriptions and prospectively enabling the interoperability of prescription data.**

Keywords—Prescription; e-Prescribing; Drug product; Dosing Instructions; Ontological Realism; Informational Entity; Deontic Entity; OBO Foundry

I. Background

Modern health care extensively uses pharmaceutical drugs. But while the administration of a drug can mitigate, prevent, treat and cure disease, it can also cause unintended harm. Adverse drug events[1] (ADE) cause about 5% of all hospital admissions [3], [4] and are estimated to be the 4th to 6th leading cause of death in the US [4], [5].

Prescription errors that can result in ADE are a compelling target of patient safety improvement due to their susceptibility to interception by health IT systems [6]. There is evidence of benefit in the use of electronic prescriptions for detecting inappropriate prescriptions and thereby reducing the incidence of ADE [7]–[9], but important challenges remain in the implementation and adoption of these systems. Among the most frequently cited of these issues is the lack of data standardization [10]. This reduces system quality, hinders adoption and limits interoperability [11].

In recent years, open source, applied ontologies have emerged as a reliable solution to the Tower of Babel problem in medical informatics [12] as exemplified by ontologies in the consortium of the Open Biomedical Ontologies (OBO). As a whole, OBO aims to prospectively standardize biomedical data by using a shared, tested set of best practices in the building of ontologies. Each ontology aims at providing a logical, scientifically accurate and orthogonal representation of each domain [13]. Currently, the OBO Foundry includes ontologies for the domains of drug products (DRON: the drug ontology) [14], adverse events (OAE: Ontology of adverse events) [1], and potential drug-drug interactions (DIDEO: Drug Interaction and Evidence Ontology) [15], but a realist ontology for drug prescriptions is still missing.

Such an ontology could help standardize a key source of data for the potential clinical applications that motivated the afore-mentioned ontologies. Conversely, the adoption of a data standard that is within the fold of the OBO Foundry would facilitate the development of cross-domain health care applications, such as those for detecting inappropriate prescriptions by comparing electronic prescriptions against diagnosis data, demographic data, lab data, and drug-drug interaction data.

This paper will introduce a realist ontology for the prescription of drugs, the Prescription of Drugs Ontology (PDRO: pronounced 'Pedro'), which is available online and open for discussion at https://www.github.com/openLHS/PDRO. A first part of the article will describe certain challenges in the representation of drug prescriptions based on problems with current implementations of e-prescribing platforms. A second part will present the methodology that was adopted. A third part will expose how the PDRO ontology addresses those requirements. And finally, a fourth part will conclude the article.

II. Challenges

A. *Levels of generality in drug product specifications*

Consider two prescriptions[2] for metoprolol:

DAS_1 = 'Metoprolol 50 mg PO bid'

DAS_2 = 'Apo-Metoprolol 50 mg tab, 1 tab PO bid'

[1] An adverse drug event is a pathological bodily process that occurs after a drug administration and results in unintended harm to the patient [1], [2, p. 37]. We use this term in preference to 'adverse drug reaction', which has more variable definitions in drug safety literature [2, p. 38].

[2] More specifically, DAS_1 and DAS_2 are parts of a prescription specifying the administration of a drug, that we will later call *Drug administration specification* – see IV.A.

Certain e-prescribing platforms can only prescribe a uniquely registered drug (e.g., Apo-Metoprolol[3] 50 mg tab) as in **DAS$_2$**, which artificially restricts the collection of drugs that satisfy the intention of the prescriber (e.g., any drug product containing the active ingredient metoprolol and suitable for an administration by mouth of 50 mg of active ingredient at a time) [16]. This inability of the prescriber to specify a drug at different levels of generality poses several problems for different users. For the pharmacist, it means having to contact the prescriber and/or modify the prescription when the drug that was specified is not in stock or when it does not match patient insurance claims. This reduces efficiency and increases the risk of error [11], [17], [18]. For prescribers, it is frustrating to have to deal with the mismatch between the initial prescription and what appears on the prescription returned from the pharmacy, since there may not be any resemblance between the written names of the drug product specified and the drug product dispensed [16]. For the patient, if the medication that is prescribed is not covered by their insurance, it can increase out-of-pocket costs [18].

To address these issues, a representation of drug prescriptions should formalize the specification of a drug product such that the informational entity referring to the collection of drug products acceptable to dispense and administer on a prescription can be as general (or as specific) as the prescriber's intention.

B. Homonymy

Modelling informational entities that are commonly viewed as chains of characters, such as prescriptions, requires distinguishing between homonyms: strings that are identical in their composition and order of characters, but have different meanings. For example, "Metoprolol" in **DAS$_1$** would usually refer to any drug product containing metoprolol, although in some cases it might refer to the generic drug product branded with the name 'Metoprolol' [19].

Thus, a representation of drug prescriptions must not only consider the nominal value of the chains of characters that a prescription may be composed of, but must consider the intention behind them, that is, what these chains of characters might refer to.

C. Human & Machine Readable Dosing Instructions

Instructions for administering a drug (e.g. '1 tab PO bid' in **DAS$_2$**), are traditionally termed the "Sig." (for "signatura") [19]. We will refer to this as "dosing instructions". The importance of unambiguous information in this part of a prescription is demonstrated by the medication errors and adverse drug events that result from unclear dosing instructions on drug product labeling [20], [21, Ch. 5], [22], [23].

Despite their key role in influencing patient outcomes, dosing instructions are inadequately captured in electronic prescriptions, including in e-prescribing standards by the NCPDP [19] and in the province-wide electronic prescribing system implemented in Quebec, Canada [16]. Electronic prescribing systems accommodate this inadequacy by allowing free-text instructions, however there is often a discrepancy between these instructions (assumed to comprise the prescriber's actual intent) and their structured counterparts (the formalization of that intent) [24]. This reduces the validating ability of CPOE systems, and could potentially result in ADE [25], [26].

We will now present the OBO Foundry methodology used by our ontology of drug prescriptions, PDRO, in order to address the above-mentioned issues.

III. Methods

PDRO uses BFO 2.0 as a top ontology and classes from IAO, OBI, DRON, OMRSE and VO were imported. 167 classes were created and classified in accordance with these ontologies as per the OBO principle of orthogonality [13]. BFO makes the distinction between *Independent continuant*, which encompasses e.g. *Material object* – like an aspirin 81mg tablet; *Occurrent,* which encompasses e.g. *Process* – like the process of Mr. Martin taking aspirin 81 mg once a day for the rest of his life; and *Dependent continuant*, which encompasses e.g. *Quality* – like the shape of an aspirin 81 mg tablet. IAO:*Information content entity* (abbreviated "ICE") is a subclass of BFO:*Dependent continuant*[4] and has the property of being about something – for example, the ICE 'aspirin' on a drug product monograph is about the class of aspirin drug products [27]. PDRO classifies *Prescription*[5] as a subclass of IAO:*Document*, defined as an *ICE* intended to be understood as a whole.

Following [27], an *ICE* can be concretized by some BFO:*Quality*; for example, a prescription can be concretized by the outline of a string of characters on a sheet of paper, by some pixels on a computer screen or even by some neuronal configuration inhering in the doctor or the patient. In the following, when we speak of e.g. the entity 'Amoxicillin'[6], we refer to an *ICE* that can be concretized by the string of characters "Amoxicillin" (whereas the class *Amoxicillin* is a subclass of DRON:*Active ingredient*, subclass of BFO:*Independent continuant*).

PDRO focuses on describing various parts of a *Drug prescription*, such as *Drug administration specification* (e.g. 'Amoxicillin 500 mg PO tid') or *Drug product specification* (e.g. 'Amoxicillin'). We use the relations BFO:*has_part* and BFO:*part_of* to describe mereological associations between universals that hold for all their instances.

[3] This is a generic drug brand name. Note that non-generic drugs are often referred to as "brand name drugs", yet what is referred to as a "generic drug" is also branded by its production company.

[4] More specifically, it is a BFO:*Generically dependent continuant*: it can migrate from one bearer to another. For example, a prescription can first inhere in the brain of a doctor, then in the screen of a computer, and finally in a printed paper.

[5] In the following, whenever the ontology name is omitted in an entity name, this means that the entity is introduced by PDRO - so we will write e.g. "*Prescription"* instead of "PDRO:*Prescription*".

[6] We will use single quotes to refer to an *ICE*.

IV. RESULTS

A. Drug administration specification as a Normative specification

While medical prescriptions can have many uses, e.g. physiotherapy, we differentiate a *Drug prescription* as a type of *Prescription* that has as part a *Drug administration specification* (abbreviated "DAS") that specifies how to realize the administration of a drug. An ontology of the records pertaining to the dispensing of a drug and the administration of a drug would classify such records under *Data item*, as they are intended to be truthful statements about a process. In contrast, a *DAS* cannot be considered to be a truthful statement, as it is intended to indicate how to realize a process, which might not occur, in case, for example, the patient is not compliant. Therefore, *DAS* is classified under OBI:*Directive information entity* (abbreviated "DIE") which is an *ICE* that intends to direct some process realized[7] by some agent(s). For example, a recipe for chocolate cake is a *DIE* that directs the process of making a chocolate cake by following the instructions described in this recipe.

In modern health care systems there is a background prohibition to take any prescribed drug unless explicitly permitted by a prescription. A *DAS* specifies instructions that imply permissions[8] overriding this background prohibition. For example, it may instruct the patient to take nitroglycerine if feeling chest pain, or to take an antibiotic if a certain time has elapsed since the previous dose. The nature of entities such as permissions has been investigated elsewhere [28], [29]. PDRO focuses instead on investigating the ontology of *DAS*, which specify such norms (and *DAS* is therefore formalized as a subclass of *Normative specification*[9], defined as a *DIE* specifying such norms).

B. Drug product specification and dose administration specification

Each *DAS* has as part one *Drug product specification* and at least one *Dose administration specification*: the former specifies the collection of drug product(s) that can be dispensed and administered, and the latter directs the administration of a dose.

In **DAS$_1$**, the chain of characters "Metoprolol" specifies a class of drug products, namely those who contain the active ingredient metoprolol, thus it is a *Drug product specification*. **DAS$_1$** also has as part an instance of *Dose administration specification* written '50 mg PO bid', which has parts that specify that '50 mg' should be the quantity in a dose (*Dose quantification specification*) and that 'PO' should be the route of administration (*Route of administration specification*). The part 'bid' informs when a dose should be taken; this is covered in section D.

The '50 mg' that appears in **DAS$_2$**, on the other hand, specifies the strength of the drug product intended by the prescriber, i.e., that 50 mg of active ingredient should be contained in one pill – and not split, for example, between two pills of 25 mg each. Accordingly, it is part of '50 mg tab', an instance of *Drug strength specification*, which is a part of the *Drug product specification*, along with 'Apo-Metoprolol'. The *Dose administration specification* in **DAS$_2$** is '1 tab PO', where '1 tab' specifies the quantity in a dose and is therefore an instance of *Dose quantification specification*.

C. Process of drug administration vs. dose administration

The administration of a drug aims at fulfilling some health-related objective such as curing a disease, alleviating a symptom, preventing a disease, etc. In order to fulfill this objective, a drug is often administered in several individual doses that will be taken over some period of time. Accordingly, the administration process of a drug involves two related processual entities: A *Dose administration* such as the administration of 500 mg of Amoxicillin on February 24th, 2016 at 1 PM; and a *Drug administration*, which is a mereological sum of one or several instances of *Dose administration*, such as the administration of 500mg of Amoxicillin three times a day during 7 days, starting on February 19th, 2016.

D. Drug administration and dose administration specifications

We will now analyze the ontological nature of normative specifications in prescriptions, which create permissions that override the background prohibition mentioned above [31]. A *DAS* specifies both the condition(s) for permitting a *Drug administration*, and the condition(s) for permitting the *Dose administration*(s) of that *Drug administration*. Consider the informational parts of the following *DAS* (Fig. 1):

DAS$_3$: 'Amoxicillin 500 mg PO q8h start PRN if symptoms of bronchitis x 7 days'

In common language, **DAS$_3$** allows the patient to start a treatment of Amoxicillin, 500 mg by mouth ('PO') in case of symptoms of bronchitis. If the patient decides to start such a treatment, he or she should continue the treatment for 7 days, and 500 mg of Amoxicillin should be taken every 8 hours ('q8h').

In order to analyze the logical structure of **DAS$_3$**, let us introduce the following time-indexed conditions **C$_1$**, **C$_2$** and **C$_3$**, all instances of *Statement,* which is a subclass of *ICE*:

[7] There are different views about the nature of this connection between a DIE and a process it directs. See OBI's definition and Smith & Ceusters (2015) [27] for various positions on what can be concretizations of *DIEs* and *ICEs*. We do not take a stance on this issue.

[8] The nature of the instructions specified by a DAS can be a matter of debate. Some of these instructions might be seen as a suggestion, while others might be seen as an obligation. Such an obligation could be ethical (e.g. to continue a treatment of antibiotics once started in order to avoid antimicrobial resistance, which would have negative consequences for society) or even legal (e.g. in some countries, it is compulsory to be treated for tuberculosis). More generally, those instructions may be seen as normative recommendations with various strengths – from sheer permission to strong obligations. Also, it might be a matter of debate towards which entity there is an obligation (the society? the doctor?). We leave those questions open here.

[9] This can be considered as a kind of "speech act" [30].

- **$C_1(t)$**: 'at t, symptoms of bronchitis are present'
- **$C_2(t)$**: 'at t, less than 7 x 24h have elapsed since the administration of a first dose or no first dose has been administered'
- **$C_3(t)$**: 'at t, 8 hours have elapsed since the administration of the last dose during the current drug administration or no first dose has been administered'

DAS_3 is synonymous[10] with **DAS_3'**, which reads as follows:

DAS_3': 'for every t_0, if **$C_1(t_0)$**, complete the administration of Amoxicillin as directed by **$PDS'(t_0)$**, in case such a drug administration is not already ongoing'

Where **$PDS'(t_0)$** is an instance of *Prescribed dosing specification*, defined as a *normative specification* that directs the dosing of a drug product:

$PDS'(t_0)$: 'for every t>t0, if **$C_2(t)$** and **$C_3(t)$** then administer a dose of 500 mg PO of drug at t'

The action[11] guided by **DAS_3'** is a drug administration over seven days in order to achieve some health-related objective, specifically that of treating an acute bronchitis. By contrast, **$PDS'(t_0)$** guides an action whose extension in time is much more limited, namely a dose administration at time t. When such a dose administration is not permitted, it is prohibited by the background prohibition.

C_1 is an instance of *Drug administration starting condition*[12]. Moreover, **C_1** is here an instance of *Presence of symptom statement*, but in another instance of *DAS*, the condition for starting the drug administration might be e.g., an instance of *Current time statement* (such as 'at t, it is July 2nd, 2016').

If **$C_2(t)$** and **$C_3(t)$** are both true at some time t, subsequent dose administration(s) should occur as part of a drug administration. However, once the drug administration has begun, **C_2** remains true until it becomes false, playing the role of an upper bound for the drug administration, whereas **C_3** can alternate truth values with some periodicity during the drug administration. This is why **C_2** is classified as a *Drug administration continuing condition* and **C_3** as a *Dosing condition*.

Here, **C_2** is an instance of *Time elapsed since first dose statement* and **C_3** is an instance of *Time elapsed since previous dose statement.* In another instance of *DAS*, the condition for continuing a drug administration might be e.g., an instance of *Number of doses statement* (such as 'at t, less than 21 doses of this drug have been given') or *Current time statement* (such as 'at t, it is before July 2nd, 2016'), and the dosing condition might be e.g., an instance of *Presence of symptom statement* (such as 'at t, the patient has chest pain') or *Total dosage statement* (such as 'at t, less than 4 grams of this drug have been administered in the last 24 hours').

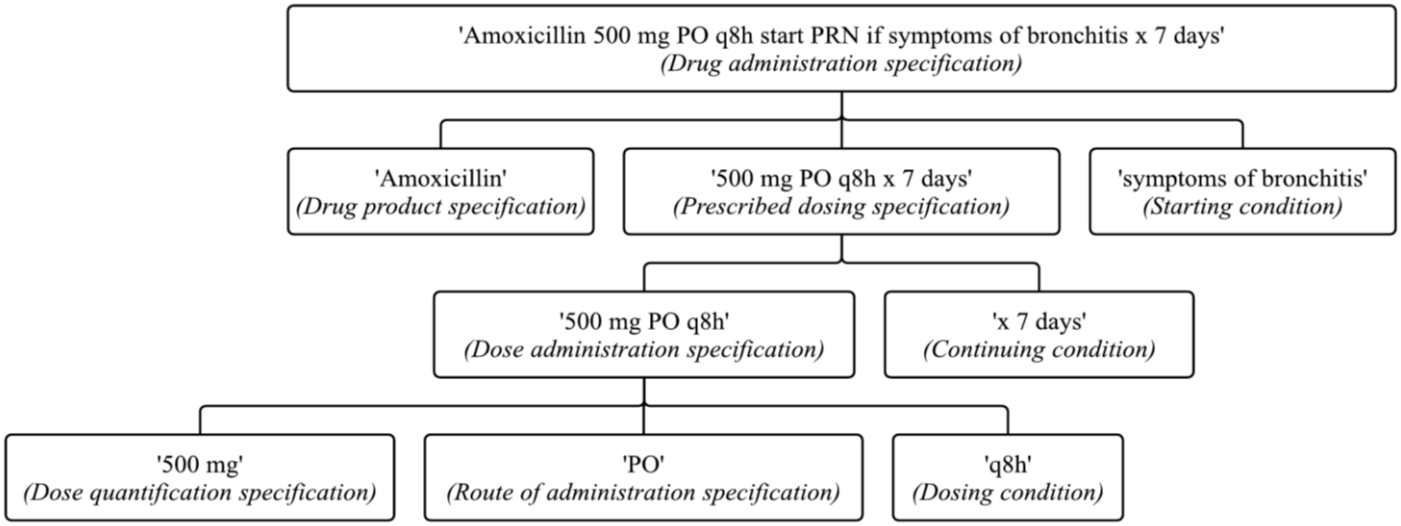

Fig. 1. Mereology of particulars and corresponding universals in DAS3. Note that the labels of *Drug administration starting condition* and *Drug administration continuing condition* have been truncated.

[10] Note that **DAS_3** is not the same *ICE* as **DAS_3'**: they are different entities as they are concretized by different chains of characters. For more on synonymy, see section V.B.

[11] We refer here informally to an 'action', without taking a position on whether an action is a process or some other entity.

[12] Note that $C_1(t)$ is a *Drug administration starting condition* only because it is used in some way in the prescription. Therefore, *Drug administration starting condition* can be seen as equivalent to an *ICE* that is BFO:*bearer_of* a *Drug administration starting condition role* (and similar considerations could hold for $C_2(t)$ and $C_3(t)$ defined above). Since the use of roles has not yet been systematized in BFO and IAO for *ICEs*, we have not defined these role classes in PDRO yet.

Although **PDS′(t_0)** specifies here the administration of some dose at some time t, other specifications may be more temporally extended in their instruction. For example, if a *DAS* were to specify to take a medication "bid" (i.e. twice per day), it would be synonymous with a *DIE* having as part the condition: 'less than two doses have been administered during the day of which t is part', which, if true, would instruct the administration of two doses during the day of which t is part, without specifying the time at which these dose administrations should occur.

Note that a *DAS* will only have prescriptive power and specify authentic instructions in case the current time is during the period of validity of the prescription. For example, in Québec, this is by default 24 months after the prescription has been written [32].

V. Conclusion and Future Work

A. Conclusion

By formalizing the informational parts of a prescription, PDRO enables the annotation of real-world prescriptions at various levels of mereological granularity. It supports, for example, the specification of a drug product based on its active ingredient(s), its branded name, its strength(s) or its form, avoiding the ambiguities and overspecificities often encountered in e-prescribing systems. Complex dosing instructions can be represented in a coherent manner, as illustrated by the example of Amoxicillin for bronchitis. This is achieved by dissociating the instructions for an entire drug administration from the instructions for a single dose administration. In addition, we distinguish the conditions determining those normative specifications and illustrate how interchangeable statements can play the role of these conditions in order to cover the variety of expressions found on prescriptions.

PDRO could both improve the semantics of electronic prescriptions and prospectively enable the interoperability of prescription data. Used in conjunction with other OBO Foundry ontologies, it can be used to express complex decision-support rules to identify potentially inappropriate prescriptions among hospitalized elderly patients [33]. With the introduction of normative specifications and conditions, we can also envision, for example, smartphone applications that guide patients with polypharmacy in safely taking their medication as directed, and thereby reduce adverse drug events.

B. Future work

The question of aboutness is currently left open by PDRO. The relation IAO:*is_about* could be used to define synonymy: several ICEs are synonyms if they are about the same portion of reality (as defined by [27]). However, some challenges need to be addressed before PDRO can consistently use aboutness. A first one is a representational issue: a drug product specification, such as 'Lopresor', is an instance of *ICE* which is about the class of drug product branded as "Lopresor". However, an instance cannot be related to a class in OWL using an object property [34] (some propositions have been put forward by [35]). Another problem is raised concerning what prescriptions are about. Since parts of prescriptions are *DIEs*, they are not about some future processes, as such process may never occur, as stated earlier. In this respect, future work would include articulating PDRO with the Document Acts Ontology [28] by linking a *Normative specification* with the deontic entity it gives rise to.

Note also that a doctor's prescription does not only permit the administration of a drug to a patient: it also permits a pharmacist to distribute those drugs. A pharmacist may also further specify the original prescription, for example, by selecting a particular brand of drug product intended to be dispensed to the patient.

Finally, while PDRO is a reference ontology formalizing the various parts of a drug prescription, additional requirements specific to a given jurisdiction might be required to create or validate prescriptions in this context. To formalize this, various application ontologies can be built upon PDRO in order to describe how a prescription should be structured according to local norms. We will clarify this articulation in a subsequent article.

Acknowledgment

We thank Thomas Joly-Mischlich for the invaluable insight into the impact of drug prescription semantics on clinical pharmacy. We also thank team member Christina Khnaisser for the useful discussions on e-prescribing platforms. AB's research was supported by the "Bourse de fellowship du Département de médecine de l'Université de Sherbrooke".

References

[1] Y. He, S. Sarntivijai, Y. Lin, Z. Xiang, A. Guo, et al., "OAE: The Ontology of Adverse Events.," *J. Biomed. Semant.*, vol. 5, no. 1, p. 29, Jan. 2014.

[2] Institute of Medicine, P. Aspden, J. Wolcott, J. L. Bootman, and L. R. Cronenwett, *Preventing Medication Errors: Quality Chasm Series*. Washington, D.C.: The National Academies Press, 2007.

[3] M. Pirmohamed, S. James, S. Meakin, C. Green, A. K. Scott, et al., "Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients.," *BMJ*, vol. 329, no. 7456, pp. 15–9, Jul. 2004.

[4] J. Lazarou, B. H. Pomeranz, and P. N. Corey, "Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies.," *JAMA*, vol. 279, no. 15, pp. 1200–5, Apr. 1998.

[5] Linda T. Kohn, Janet M. Corrigan, and Molla S. Donaldson, Eds., *To Err Is Human: Building a Safer Health System*. Washington, D.C.: National Academies Press, 2000.

[6] P. G. Shekelle, R. M. Wachter, P. J. Pronovost, K. Schoelles, K. M. McDonald, et al., "Making health care safer II: an updated critical analysis of the evidence for patient safety practices.," *Evid. ReportTechnology Assess.*, no. 211, pp. 1–945, Mar. 2013.

[7] E. Ammenwerth, P. Schnell-Inderst, C. Machan, and U. Siebert, "The effect of electronic prescribing on medication errors and adverse drug events: a systematic review.," *J. Am. Med. Inform. Assoc. JAMIA*, vol. 15, no. 5, pp. 585–600, Jan. 2008.

[8] T. K. Nuckols, C. Smith-Spangler, S. C. Morton, S. M. Asch, V. M. Patel, et al., "The effectiveness of computerized order entry at reducing preventable adverse drug events and medication errors in hospital

settings: a systematic review and meta-analysis.," *Syst. Rev.*, vol. 3, p. 56, Jan. 2014.

[9] J. Kannry, "Effect of e-prescribing systems on patient safety.," *Mt. Sinai J. Med. N. Y.*, vol. 78, no. 6, pp. 827–33, Jan. 2011.

[10] M.-P. Gagnon, É.-R. Nsangou, J. Payne-Gagnon, S. Grenier, and C. Sicotte, "Barriers and facilitators to implementing electronic prescription: a systematic review of user groups' perceptions," *J. Am. Med. Inform. Assoc.*, vol. 21, no. 3, pp. 535–541, 2014.

[11] M.-P. Gagnon, J. Payne-Gagnon, C. Sicotte, J.-A. Langué-Dubé, and A. Motulsky, "Connecting primary care clinics and community pharmacies through a nationwide electronic prescribing network: a qualitative study," *J. Innov. Health Inform.*, vol. 2222, no. 3, pp. 359–367, Jan. 2015.

[12] R. Arp, B. Smith, and A. D. Spear, *Building Ontologies with Basic Formal Ontology*. The MIT Press, 2015.

[13] B. Smith, M. Ashburner, C. Rosse, J. Bard, W. Bug, et al., "The OBO Foundry: coordinated evolution of ontologies to support biomedical data integration," *Nat. Biotechnol.*, vol. 25, no. 11, pp. 1251–1255, Nov. 2007.

[14] J. Hanna, E. Joseph, M. Brochhausen, and W. R. Hogan, "Building a drug ontology based on RxNorm and other sources," *J. Biomed. Semant.*, vol. 4, p. 44, Dec. 2013.

[15] Mathias Brochhausen, Jodi Schneider, Daniel Malone, Philip E. Empey, William R. Hogan, et al., "Towards a foundational representation of potential drug-drug interaction knowledge," in *Drug Interaction Knowledge Management (DIKR 2014)*, Houston, Texas, 2014.

[16] A. Motulsky, C. Sicotte, M.-P. Gagnon, J. Payne-Gagnon, J.-A. Langué-Dubé, et al., "Challenges to the implementation of a nationwide electronic prescribing network in primary care: a qualitative study of users' perceptions.," *J. Am. Med. Inform. Assoc. JAMIA*, vol. 22, no. 4, pp. 838–48, Jul. 2015.

[17] O. Odukoya and M. a. Chui, "Retail pharmacy staff perceptions of design strengths and weaknesses of electronic prescribing," *J. Am. Med. Inform. Assoc.*, vol. 19, no. 6, pp. 1059–1065, Jan. 2012.

[18] K. L. Lapane, R. K. Rosen, and C. Dubé, "Perceptions of e-prescribing efficiencies and inefficiencies in ambulatory care.," *Int. J. Med. Inf.*, vol. 80, no. 1, pp. 39–46, Jan. 2011.

[19] H. Liu, Q. Burkhart, and D. S. Bell, "Evaluation of the NCPDP Structured and Codified Sig Format for e-prescriptions," *J. Am. Med. Inform. Assoc.*, vol. 18, no. 5, pp. 645–651, Sep. 2011.

[20] M. S. Wolf, L. M. Curtis, K. Waite, S. C. Bailey, L. A. Hedlund, et al., "Helping Patients Simplify and Safely Use Complex Prescription Regimens," *Arch. Intern. Med.*, vol. 171, no. 4, pp. 300–305, Feb. 2011.

[21] Institute of Medicine, P. Aspden, J. Wolcott, J. L. Bootman, and L. R. Cronenwett, *Preventing Medication Errors: Quality Chasm Series*. Washington, D.C.: The National Academies Press, 2007.

[22] T. C. Davis, M. S. Wolf, P. F. Bass, J. A. Thompson, H. H. Tilson, et al., "Literacy and misunderstanding prescription drug labels.," *Ann. Intern. Med.*, vol. 145, no. 12, pp. 887–94, Dec. 2006.

[23] T. C. Davis, A. D. Federman, P. F. Bass, R. H. Jackson, M. Middlebrooks, et al., "Improving patient understanding of prescription drug label instructions.," *J. Gen. Intern. Med.*, vol. 24, no. 1, pp. 57–62, Jan. 2009.

[24] M. B. Palchuk, E. A. Fang, J. M. Cygielnik, M. Labreche, M. Shubina, et al., "An unintended consequence of electronic prescriptions: prevalence and impact of internal discrepancies," *J. Am. Med. Inform. Assoc. JAMIA*, vol. 17, no. 4, pp. 472–476, 2010.

[25] K. C. Nanji, J. M. Rothschild, C. Salzberg, C. A. Keohane, K. Zigmont, et al., "Errors associated with outpatient computerized prescribing systems.," *J. Am. Med. Inform. Assoc. JAMIA*, vol. 18, no. 6, pp. 767–73, Jan. 2011.

[26] T. K. Gandhi, S. N. Weingart, A. C. Seger, J. Borus, E. Burdick, et al., "Outpatient prescribing errors and the impact of computerized prescribing.," *J. Gen. Intern. Med.*, vol. 20, no. 9, pp. 837–41, Sep. 2005.

[27] B. Smith and W. Ceusters, "Aboutness: Towards foundations for the information artifact ontology," in *Proceedings of the Sixth International Conference on Biomedical Ontology (ICBO)*, 2015.

[28] Mathias Brochhausen, Mauricio Barcellos Almeida, and Laura Slaughter, "Towards a formal representation of document acts and resulting legal entities," in *Johanssonian Investigations: Essays in Honour of Ingvar Johansson on His Seventieth Birthday*, Walter de Gruyter, 2013.

[29] B. Smith, "How to Do Things with Documents," *Riv. Estet.*, vol. 50, no. 50, pp. 179–198, 2012.

[30] M. Green, "Speech Acts," *The Stanford Encyclopedia of Philosophy*. 2015.

[31] S.-E. Öhlund and G. Goldkuhl, "Towards a socio-pragmatic understanding of ePrescribing," in *5th Intl Conference on Action in Language, Organisations and Information Systems (ALOIS-2008)*, Venice, 2008.

[32] 41e Assemblée Nationale du Québec, *Règlement sur les normes relatives aux ordonnances faites par un médecin*. 2015.

[33] K. Arvisais, S. Bergeron-Wolff, C. Bouffard, A.-S. Michaud, J. Bergeron, et al., "A Pharmacist-Physician Intervention Model Using a Computerized Alert System to Reduce High-Risk Medication Use in Elderly Inpatients," *Drugs Aging*, vol. 32, no. 8, pp. 663–670, Aug. 2015.

[34] Boris Motik, Peter F. Patel-Schneider, and Bijan Parsia, "OWL 2 Web Ontology Language Structural Specification and Functional-Style Syntax (Second Edition)." [Online]. Available: https://www.w3.org/TR/owl2-syntax/. [Accessed: 13-May-2016].

[35] S. Schulz, C. Martínez-Costa, D. Karlsson, R. Cornet, M. Brochhausen, et al., "An Ontological Analysis of Reference in Health Record Statements.," in *FOIS*, 2014, pp. 289–302.