

Bridging the Gap between Informal and Formal Guideline Representations

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Abstract. Clinical guidelines are important means to improve quality of health care while limiting cost and supporting the medical staff. They are written as free text with tables and figures. Transforming them into a formal, computer-processable representation is a difficult task requiring both computer scientist skills and medical knowledge.

To bridge this gap, we designed an intermediate representation (or ontology) which serves as a mediator between the original text and different formal guideline representations. It is easier to use than the latter, structures the original prose and helps to spot missing information and contradictions.

In this paper we describe the representation and a practical evaluation thereof through the modelling of a real-world clinical guideline.

1 Introduction

Clinical guidelines are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" [2]. A guideline describes the optimal care for patients and therefore, when properly applied, it is assumed that they improve the quality of care. Evidence-based guidelines are becoming an important and indispensable part of quality health care.

Translating guidelines into a computer-processable form brings several advantages. It makes them more accessible to browsing as in DeGeL [8], it allows their execution, i.e., the selection of the appropriate treatment steps based on the patient condition, and it is a precondition to various quality assurance techniques such as those pursued by the Protocure project [1].

While producing a formal model of a guideline is desirable, it is difficult and expensive. In addition, the resulting model is often difficult to compare to the original. If a guideline is revised, the modeling effort is lost and it is not easy to detect which changes in the formal model are required by the changes in the original text.

The main reason for this is that there is a large gap between natural language and the currently available formal representations. To close this gap in a versatile manner we designed an *intermediate representation* called MHB (Many-Headed Bridge). It can be seen as a small and versatile *ontology* of guideline components. It groups the statements in the guideline into chunks with predefined dimensions such as control flow, data flow, temporal aspects and evidence. The aspects of each dimension are described using natural language. Af-

ter building the initial model in MHB, the content of the aspects is reviewed to eliminate deliberate use of synonyms and to describe the knowledge missing to arrive at a model.

As the name suggests, MHB is not designed as a unidirectional bridge from a certain type of natural language guideline to a certain formal representation. Instead it is designed as a versatile device to improve guideline quality. Modeling a guideline in MHB makes important aspects such as control and data flow, resources, and patient aspects explicit. They can easily be grouped in various overview lists. Using the MHB model helps in locating and acquiring knowledge which is missing in the guideline text and inconsistencies such as contradicting definitions or recommendations.

In the next section we describe related work in the field of guideline modelling. In Section 3 we describe MHB in detail. In Section 4 we describe its evaluation. Section 5 concludes the paper.

2 Related Work

There are several guideline representations. Asbru, EON, GLIF, Guide, Prodigy and ProForma have been compared by [4]. Further representation are Glare [11] and GEM [9]. Although the degree of formalization varies between these approaches, the majority of them represents the guideline in a format which is precise enough to execute it (semi-)automatically. In practice, it is very difficult and error-prone to translate the original guideline into such a precise format in one step. Except for GEM and NewGuide, the mentioned languages do not explicitly model the evidence level of the each part of the guideline.

The tool which is used to generate and maintain the guideline's version in MHB forms an important background for the design of the representation itself. This tool is called Document Exploration and Linking Tools with Add-ons (DELT/A) [12]. DELT/A allows for explicit linking between pairs of guideline parts in textual and formal representations. DELT/A supports a multi-step modeling process. E.g., in a first step, the original guideline text is displayed at the left-hand side and the MHB model at the right-hand side. In a second step, the (then complete) MHB model is displayed at the left and a newly created translation of MHB to Asbru, GLIF, or ProForma is shown at the right-hand side. Tools similar to DELT/A are GEM Cutter [9], Degel [8], and Stepper [10]. DELT/A differs from GEM Cutter and Degel in maintaining explicit links between the original text and the formal representation. In contrast to Stepper it does not prescribe a fixed number of modeling steps from the informal text to the formal model.

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3 Our Solution: A Many-Headed Bridge

This section describes our solution to the afore described challenges in detail. Several teams try to bridge the gap between different kinds of representation building bridges between pairs of isles. Our vision is to connect all these isles by a single bridge having more than two heads. We therefore call it the *many-headed bridge* (MHB).

The syntax of MHB is based on XML, which allows us to use a range of available tools to create and process it, most importantly DELT/A.

The overall structure of an MHB file is very flexible. It is a series of *chunks*. Each chunk corresponds to a certain bit of information in the natural language guideline text, e.g., a sentence, part of a sentence, or more than one sentence. Initially, the order of the chunks reflects the order of building blocks in the original version of the guideline. However, they can be moved freely in the MHB file. Such regrouping eases the construction of a more formal representation based on the MHB model.

The information in a chunk is structured in *aspects*. These aspects are grouped in *dimensions*, e.g., control flow, data flow, and evidence. The aspects of different dimensions are independent, i.e., a chunk can have any combination of aspects. However, some are related, e.g., the evidence aspects always refer to the aspects in the other dimensions of the same chunk. In practice, for most chunks only aspects of a few dimensions are given. The reason for this lies in the fact that chunks are a uniform representation for all the heterogeneous parts of the guideline.

In addition to the aspects grouped in dimensions, each chunk has optional fields for the context and the subject of the chunk. All aspects contain link elements which store the connection between each part of the MHB file and the original guideline text. In addition, most aspects contain an attribute *degree-of-certainty* to explicitly show the confidence the original guideline authors expressed in the particular statement, expressed in words like "should", "could", "is advisable", etc. This is completely independent of the evidence dimensions (Section 3.4) which describes the formal rating of the evidence base of a certain conclusion or the importance of a certain recommendation. The subsections below describe the representation of each of these dimensions.

3.1 Dimension: Control Flow

One of the most prominent aspects of a guideline is, *when* to do *what*. This is often shown (incompletely) by a clinical algorithm. *When* either relates to the condition under which something happens, or to the temporal order of actions relative to each other. *What* generally refers to a task⁵ to be performed under the described condition. A third issue is *decomposition*, i.e., the way in which larger tasks or activities are made up of smaller ones. Furthermore, some tasks are performed *repeatedly* as part of other tasks.

Ordering, decomposition, and repetition imply temporal aspects, e.g., one task being performed after the other. Still, they are included here, while the dimension *temporal aspects* deals with explicit and often quantitative descriptions of the timing of actions and also effects, etc. (see explanations in Section 3.3).

Decisions. From the formal modeling point of view, the main distinction is made between mutually exclusive and non-excluding options. In the first case, clear directives on how to arrive at exactly one

of the given options are specified, be it in a decision tree, a decision table, or simple if-then rules. In the second case, for each of the options there are one or more reasons to take it or not to take it and there is no a-priori safety that exactly one option will be taken.

In MHB the basic structure of a single decision is *if-then*. It consists of a *condition*, a *condition-modifier*, a *result*, a *result-modifier*, and a *degree-of-certainty*. All five are attributes formally containing any text. Semantically, the condition is described as precisely as possible based on the guideline text. It should – if possible – contain concepts described in the data dimension (compare Section 3.2). The *condition-modifier* supports various categories of choices, such as negative recommendations and strong and weak arguments pro and contra a certain option.

The *result* designates the recommended action, first in the words of the original guideline, later in terms of the more formal representation to which MHB will be translated. If omitted, *result-modifier* defaults to simply *do* but it can also take values describing the state of the task/plan/action. These depend on the target representation and on the precision of the information in the guideline. E.g., tasks in ProForma have three states (abandoned, terminated, performed) while plans in Asbru only have two (aborted, completed).

The words *should*, *can*, etc. which sometimes are found in a guideline's recommendations as well as phrases like "it seems appropriate" are stored in *degree-of-certainty* alternatively to the above.

Sometimes more than one recommendation or option are described together. In MHB the element *option-group* is used to group several *if-then* elements. The options can exclude each other or not. The attribute *selection-type* has the values *single-choice* or *multiple-choice* to represent this distinction. The additional (optional) attribute *other-selection-specification* can contain more complex constraints on the selection, such as the number of options to select together, e.g., "perform two of the following five tasks".

Ordering and Decomposition. A task can be *decomposed* into subtasks. *Ordering* defines constraints on their execution relative to each other. Both ordering and decomposition are modeled by the same element in MHB named *decomposition*.

It names a task as an attribute and the names of subtasks in separate elements.

The ordering of the children is specified in attribute *ordering* of element *decomposition*. Its values should map to plan orderings available in the targeted formal representation. Binary temporal relations between child tasks are modelled in the temporal dimension (Section 3.3).

Synchronization. When several tasks are performed in parallel or otherwise independent from each other, the question arises when to pursue the rest of the guideline. Several formal guideline representation allow to define those subtasks (*awaited-subtasks* in MHB) which must be completed before the next step is taken in a logical expression, or the number of completed subtasks can be given alternatively.

Repetition. Often one task is performed more than once – either for a certain number of times or at certain times during another task. In any case, there is a task ("envelope task") which lasts during all the repetitions and a subtask ("repeated task") which is performed repeatedly.

⁵ The word *task* is used in this text as a synonym for action, plan, activity, procedure, etc. used by different guideline modelling groups.

Atomic Actions. Some activities or tasks are only described in a sentence without further detailing it. In these cases, they are generally called *atomic actions* which may be too strict if taken literally. Therefore, the MHB element to model such cases is called `clinical-activity`.

3.2 Dimension: Data Flow

Interwoven with control flow is the description of the data processing involved in the diagnosis and treatment of the patient. While the processing of data seems of little importance in the treatment of many diseases, it is often prominently described in the diagnosis part of a guideline. As control flow describes the gathering of information, data flow describes how one piece of information is abstracted from other ones. In MHB, we distinguish the following:

- The `definition` of a data item is rarely found in the guideline in explicit form. Still, it is necessary for the formal version of the guideline. It consists of a name, a type, and often a range of plausible values and a preferred unit.
- The `usage` of a data item is made explicit to varying degrees in actions described in the guideline and calculation of other values.
- The `input` of a data item is sometimes explicitly described in the description of the patient interview or diagnosis.
- `abstraction-rules` describe the calculation or abstraction of one data item based on others. It is found mostly in descriptions of diagnosis. The time at which the calculation or abstraction is performed may be explicitly stated or not. In the first case, the statement in question has a data flow aspect and a control flow aspect at the same time. In the second case, abstraction is assumed to take place automatically whenever necessary.

3.3 Dimension: Temporal Aspects

Both data and control flow may have temporal aspects. They can be qualitative or quantitative. MHB covers the complexity of Asbru (which has the most complex means to model the temporal dimension) in modeling temporal aspects, but adds more standard concepts such as average or precise duration. For each of start, end, and duration, the minimum, maximum, estimate, and precise value can be given. Of course the precise value excludes others, but the other three values can be combined, i.e., minimum, maximum, and estimate can be given together, if ever found in a guideline. The difference between estimate and precise value lies in the semantic given in the guideline. If start or end are given relative to a certain starting point and it is not obviously the start of the task described, then the reference point must be noted together with the offset in the respective attribute.

In addition to the above, the temporal dimension also models qualitative temporal relations such as "A is started after the end of B". While this could be implemented using the above elements, we provide a distinct element for qualitative relations to improve comprehensibility of the model.

3.4 Dimension: Evidence

An evidence-based guideline builds a bridge from carefully examined pieces of evidence which are obtained for the problem to generally applicable recommendations. While it might be an interesting task to document the foundation of each sentence in the guideline, it will be too tiresome in practice. However, it can be useful for certain parts of the guideline.

Evidence for a statement can appear in explicit and implicit form. For *explicit* references with defined format (summary statement of the evidence, literature references) MHB provides the attributes `grade`, `level`, `importance` and `literature-reference`. They are all optional and can be combined as suitable.

Implicit references in the guideline can be made explicit in the MHB file to help improve the quality of the guideline. To this end, the attribute `is-based-on` contains a reference to another MHB element.

3.5 Dimension: Background Information

Background information describes various aspects of the topic. Their potential to be formally encoded largely varies – some information is aimed at motivating the reader to follow the guideline, while other information complements the statements in the recommendation part.

- *Intentions* of the described actions or recommendations inform and motivate the reader about the reason of certain steps.
- *Effects* are relations between data or phenomena and other phenomena which are not seen as events or actions.
- *Relations* are similar to effects, but do not postulate that one of the two named entities is the cause of the other.
- Other *educational information* can target at the physician or the patient to discuss the recommendations in detail. To some extent, it is related to evidence, as it is an alternative backing for the recommendations in the guideline.
- *Explanations* contain information directly explaining recommendations or other (important) statements in the guideline. When executing a guideline in a computer-based form, it might be useful to show them to the user (patient or physician) – in contrast to the education information above which is not as directly related to the actions resulting from following the guideline.
- *Indicators* are measurable elements of health care that give an indication about the quality. One way to develop indicators is to derive them from key recommendations of a guideline. They are not yet part of many guidelines but will be integrated in the future.

3.6 Dimension: Resources

Each action consumes resources of various nature: *Personnel* resources such as the working time of clinical staff; *Devices*, such as treatment facilities; and *Financial cost*, which can be given independent of qualitative or quantitative information on the above items. It includes also drug cost, etc.

3.7 Dimension: Patient Related Aspects

While the resources dimension mostly represents the view of the care provider, there are several other general issues mentioned in a guideline which see treatment from the patient perspective. *Risk* connected to a certain treatment option or diagnostic action. *Patient discomfort* is often described as free text and refers to undesired side effects of treatments, such as chemotherapy against cancer. *Health prospective* can be seen as a resource which is gained by the treatment process, while it is consumed by waiting.

3.8 Dimension: Document Structure

While the position of a statement in the guideline document could be considered a formal property, its status (narrative, displayed recommendation) certainly forms an important context for its interpretation. This means that a statement found in the recommendations or

control	decomposition	parent-task	mastectomy
		child-task(s)	deciding whether to carry out primary or secondary reconstruction
	if-then	condition	higher risk of requiring postoperative radiotherapy
		result	consider the increased risk of complications
degree-of-certainty		should	
data	usage	name	is there higher risk of postoperative requiring radiotherapy
structure		status	recommendations

Figure 1. Model of a vague recommendation.

the scientific conclusions has more weight than one in the introduction or other parts of the guideline.

Example. Figure 1 shows the MHB model of the statement “*In women who have a higher risk of requiring postoperative radiotherapy, the increased risk of complications should be considered when deciding whether to carry out primary or secondary reconstruction.*” This statement is made in the context of mastectomy interventions. It can be modelled as a decomposition stating that “deciding whether to carry out primary or secondary reconstruction” is a child-task of task “mastectomy”. This child-task is performed under the condition of “higher risk of requiring postoperative radiotherapy”. There is one data item used here – the information whether there is a higher risk of requiring postoperative radiotherapy.

MHB is intended for the use with various guideline representations. In the first practical evaluation, carried out as part of the Procedure II project, it was used together with Asbru, bridging the gap between this representation and the English text in a real-world guideline of more than 100 pages. This is described in the next section.

4 Evaluation

Evaluation of MHB is performed on a theoretical and on a practical level.

Theoretical evaluation. This consisted of three parts complementing each other:

- The mapping between MHB and various formal representations for clinical guidelines and protocols is analyzed in detail in [7].
- The suitability of MHB to represent guidelines was discussed with domain experts.
- It was shown that MHB can represent the guideline constructs on a list of prototypical patterns developed as another part of the Procedure II project [6].

Each of the three activities led to the conclusion that MHB is sufficiently expressive. The discussion with domain experts also showed that MHB is easier to comprehend than Asbru or other formal guideline representations.

Dimension	Aspect	Chapter						Total
		1	2	3	4	5	6	
control	clinical-activity	13	1	1	1	0	9	25
	decomp.	32	2	4	2	4	4	48
	if-then	39	0	2	2	5	12	60
	option-group	1	6	1	1	1	2	12
	repetition	3	2	1	6	0	0	12
	<i>subtotal</i>	88	11	9	12	10	27	157
data	abstraction	1	0	3	0	2	0	6
	definition	4	8	1	0	2	0	15
	usage	52	31	2	3	14	22	124
	<i>subtotal</i>	57	39	6	3	18	22	145
time	end	1	0	0	0	0	0	1
	qualitative-rel.	4	0	2	1	0	0	7
	start	1	3	0	0	0	0	4
	<i>subtotal</i>	6	3	2	1	0	0	12
evidence	grade	28	5	9	11	7	9	69
	level	37	5	9	11	8	13	83
	literature-ref.	43	4	9	11	8	13	88
	<i>subtotal</i>	108	14	27	33	23	35	240
back-ground	educational	17	7	4	9	2	6	45
	effect	10	8	10	6	3	4	41
	explanation	2	1	1	1	2	0	7
	intention	3	1	2	2	2	3	13
	relation	1	5	6	0	0	0	12
	<i>subtotal</i>	33	22	23	18	9	13	118
patient-aspects	discomfort	1						1
	health-impr.	7						7
	risk	10						10
	<i>subtotal</i>	18						18
resources	personal-needed	1	2		1			4
	req.-devices		1					1
	<i>subtotal</i>	1	3		1			5
Total		311	92	67	68	60	97	695

Figure 2. Usage count for each dimension and aspect.

Practical evaluation. Scientific conclusions, other considerations, and recommendations in the Dutch Guideline for the Treatment of Breast Carcinoma [3] were modeled in MHB in a shared effort by three teams in different countries [5]. Parts of the guideline not relevant for the subsequent formal representation of the guideline were omitted. These parts mostly described background information regarding the disease and the details of the studies which form the evidence for the recommendations. All recommendations were modeled.

Table 2 shows the number of element used for each of the aspects in the various dimensions.

The greatest count of elements is given for dimension evidence which was expected for an evidence-based guideline such as the modeled one. As assumed from the beginning, the control dimension proved to be the most prominent one. The data dimension is also frequently used.

In the background dimensions, educational information and description of effects were equally frequent while all other aspects of that dimension were rarer.

Some rare aspects were not used at all in the guideline. They are omitted for space consideration, as is the structure dimension which

is trivially present in every chunk.

The evaluation of the data dimensions confirms the assertion that data input is only implied in the guideline. There was not a single bit of information found for any chunk. This is in part due to the fact that the guideline deals with treatment and not with diagnose or screening. Besides this, it is assumed that the reader of the guideline knows about the usual data flow during diagnosis and treatment.

The fact that little information regarding patient aspects and resources were found is in line with the common opinion that future guidelines should focus more on these issues. The fact that they were mostly found in chapter 1 hints at an inter-modeler deviation.

Indicators were not contained in the guideline because they are a future development of guidelines.

Overall, the evaluation confirmed the suitability of the representation. All the necessary information was captured in the modelling process.

Unfortunately, the nature of the chapters proved to be rather dissimilar. Therefore, deviations between chapters or teams can be caused by the nature of the chapter or by the preference of the team. However, when reading chapters from other teams, we found a very large degree of consistency of the modeling. This was also due by a set of written recommendations which directed the modeling process.

5 Conclusions

Our experience has shown that MHB is appropriate to model the statements found in the significant guideline parts. MHB not only provides constructs to express the essential knowledge we intended to model, but also allowed for a modeling with the degree of detail necessary for our purposes. An initial problem was the variation observed across the MHB models obtained initially. To solve this, we elaborated a series of basic MHB modeling recommendations. Thanks to these recommendations, the degree of variation was greatly decreased, regardless of the different background of the modelers.

In the Protocure II project we showed that MHB is easier to understand than Asbru by persons without computer background. However, a significant effort in training was necessary.

It is easier to create an MHB model from the original guideline text than an Asbru model. The main reason for this is that MHB does not demand complete information. Also, MHB can be structured like the guideline, while formal representations such as Asbru and others model a guideline as a hierarchy of tasks which is not easy to detect in the original guideline text.

In addition, it is easier to create an Asbru model based on MHB than based on the original text alone. While missing knowledge and vague information in the guideline text still cause modeling problems, they are more efficiently handled since they are already displayed in the MHB model. Using a cross-reference table of all task and data items mentioned in the guideline, we were able to spot countless instances of slightly deviating names for the same entity used in different places of the guideline.

The major drawback of MHB compared to other, more formal representations such as Asbru or GLIF lies in the fact that the syntax of MHB does not impose strict rule for the usage of each attribute (or aspect). The usage is only described in a guidelines [7] and it is the author's responsibility to follow them. While this is an advantage in the early modeling phase, it takes considerable effort to arrive at a uniform naming scheme for tasks and data items in the guideline. However, this is a known problem shared by all formal guideline representations.

In practical work with non-IT persons such as epidemiologists it showed that MHB when used in an XML editor like DELT/A is very difficult to understand for them. Therefore, future work will go into developing a user-friendly editing environment, which guides the user by means of context-sensitive help and shields away the complexity of XML. Also, the integration of knowledge extraction to automatically generate parts of the model is an interesting option. Standard vocabularies such as UMLS can be used together with MHB (including compliance checks), however the editor does not yet include browsing and picking items per mouse click.

Weighing the advantages and limitations of MHB, we conclude that MHB is a suitable solution to bridge the gap between the original guideline text and formal representations such as Asbru.

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REFERENCES

- [1] M. Balsler, O. Coltell, J. van Croonenborg, C. Duelli, F. van Harmelen, A. Jovell, P. Lucas, M. Marcos, S. Miksch, W. Reif, K. Rosenbrand, A. Seyfang, and A. ten Teije, 'Protocure: Supporting the development of medical protocols through formal methods', in *Computer-based Support for Clinical Guidelines and Protocols*, eds., K. Kaiser, S. Miksch, and S. Tu, pp. 103–107. IOS Press, (2004).
- [2] M. J. Field and K. H. Lohr, 'Clinical practice guidelines: Directions for a new program', (1990).
- [3] Nationaal Borstkanker Overleg Nederland (NABON), *Guideline for the treatment of breast carcinoma*, Van Zuiden Communications B.V., 2002.
- [4] M. Peleg, S. Tu, J. Bury, P. Ciccarese, J. Fox, R. Greenes, R. Hall, P. Johnson, N. Jones, A. Kumar, S. Miksch, S. Quaglioni, A. Seyfang, E. Shortliffe, and M. Stefanelli, 'Comparing computer-interpretable guideline models: A case-study approach', *JAMIA*, **10**(1), (2003).
- [5] C. Polo, M. Marcos, A. Seyfang, J. Wittenberg, S. Miksch, and K. Rosenbrand, 'Assessment of MHB: an intermediate language for the representation of medical guidelines', in *Proceedings of CAEPIA05*, (2005).
- [6] R. Serban, A. ten Teije, F. van Harmelen, M. Marcos, C. Polo, J. C. Galan, P. Lucas, A. Homersom, K. Rosenbrand, J. Wittenberg, and J. van Croonenborg, *Deliverable D2.5: Library of design patterns for guidelines*, EU Project Protocure, 2004. Available at www.protocure.org (Accessed: 1 May 2006).
- [7] A. Seyfang, S. Miksch, P. Votruba, K. Rosenbrand, J. Wittenberg, J. van Croonenborg, W. Reif, M. Balsler, J. Schmitt, T. van der Weide, P. Lucas, and A. Homersom, *Deliverable D2.2a: Specification of Formats of Intermediate, Asbru and KIV Representations*, EU Project Protocure, 2004. Available at www.protocure.org (Accessed: 1 May 2006).
- [8] Y. Shahr, O. Young, E. Shalom, A. Mayaffit, R. Moskovitch, A. Hessing, and M. Galperin, 'DeGeL: A hybrid, multiple-ontology framework for specification and retrieval of clinical guidelines', in *Proceedings in Artificial Intelligence in Medicine*, (2003).
- [9] R. N. Shiffman, B. T. Karras, A. Agrawal, R. Chen, L. Marenco, and S. Math, 'GEM: A proposal for a more comprehensive guideline document model using xml', *Journal of the American Medical Informatics Association*, **7**(5), 488–498, (2000).
- [10] V. Svatek and M. Ruzicka, 'Step-by-step mark-up of medical guideline documents', *International Journal of Medical Informatics*, **70**(2-3), 329–335, (2003).
- [11] P. Terenziani, G. Molino, and M. Torchio, 'A modular approach for representing and execution clinical guidelines', *Artificial Intelligence in Medicine*, **23**, 249–276, (2001).
- [12] P. Votruba, S. Miksch, A. Seyfang, and R. Kosara, 'Tracing the formalization steps of textual guidelines', in *Computer-based Support for Clinical Guidelines and Protocols*, eds., K. Kaiser, S. Miksch, and S. W. Tu, pp. 172–176. IOS Press, (2004).