

Fuzzy logic in clinical practice decision support systems

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Abstract

Computerized clinical guidelines can provide significant benefits to health outcomes and costs, however, their effective implementation presents significant problems. Vagueness and ambiguity inherent in natural (textual) clinical guidelines is not readily amenable to formulating automated alerts or advice. Fuzzy logic allows us to formalize the treatment of vagueness in a decision support architecture. This paper discusses sources of fuzziness in clinical practice guidelines. We consider how fuzzy logic can be applied and give a set of heuristics for the clinical guideline knowledge engineer for addressing uncertainty in practice guidelines. We describe the specific applicability of fuzzy logic to the decision support behavior of Care Plan On-Line, an intranet-based chronic care planning system for General Practitioners.

1. Introduction

Medical knowledge is vast and constantly changing, as well as expanding. The doubling time of medical knowledge is currently about 19 years [1], yet a recent survey found that textbooks available to physicians in their workplace were often more than 10 years old [2]. Leaving aside both basic and specialized medical knowledge, a General Practitioner (GP) in Britain is expected to practice in accordance with the contents of numerous policies, referral protocols, government circulars, adverse drug effect warnings, etc. that form a stack 18 inches tall [3]. It is unrealistic to believe that the typical GP has read all these materials; it is a cognitive impossibility that all these rules are accurately operationalized on every patient when each consult lasts just several minutes.

Information overload in medicine has long been acknowledged and remedies sought. One option is to devise medical expert system programs that reason for the doctor. A more modern approach is not to supplant but to support human reasoning (i.e., to build decision support

systems, DSS). Such systems may still be expert systems in the sense of having highly sophisticated reasoning capabilities. An anti-infectives DSS that links to hospital clinical data was recently demonstrated to lower cost, reduce adverse events and reduce length of hospital stay [4]. For complex specialized areas we may be content to compartmentalize the knowledge and embed it in a machine that provides doctors with high-quality solutions (as long as the machine can explain those solutions to the doctor's satisfaction). In many cases, however, we would prefer to educate the doctor with "just in time" clinical information [5]. In particular, we may design a system that provides decision support such that it contributes to the doctor's continuing medical education [6]. This requires that the doctor have access to not just the decision, but also the set of clinical rules from which it was derived, and the literature that explains the underlying principles and scientific evidence for the decision rules.

It has been recognized that simply making natural language *clinical practice guidelines* available on-line is not a complete solution to doctors' information management problems. The doctors must still know to seek out the right guideline information and take the time to find it. More significant practice improvements are achieved when guidelines are structured as algorithms that can trigger specific recommendations based on the content of an Electronic Medical Record (EMR) [7]. Comprehensive development of such algorithms, however, is frustrated because natural and relevant expressions of clinical guidance are apt to be somewhat imprecise in their context and phrasing.

Fuzzy logic has a history of application for clinical problems including use in automated diagnosis [8], control systems [9], image processing [10] and pattern recognition [11]. Liu and Shiffman [12] have demonstrated the application of fuzzy logic to model the imprecision of a published clinical practice guideline, which is cited by Zielstorff [7] as a promising direction for future development of computer-based decision

support in medicine; however, the work is still quite far from revealing a general approach to applying fuzzy logic to clinical guidelines.

The Care Plan On-Line (CPOL) system has been developed to assist GPs in development of care plans for the chronically ill [13]. CPOL runs over a wide area intranet and is an integrated with the SA HealthPlus coordinated care trial enrolling 5000 chronically ill South Australians in 10 disease-centered project groups. SA HealthPlus nominates GPs to act as the individual Care Coordinators for patients. In this role the GP is expected to consider a broad spectrum of planned services (such as dietician and physiotherapy) and clinical investigations (e.g., chest x-rays and bone density studies) to include in the patient's *care plan*. The goal is to engender a holistic and proactive model of care that stabilizes the patient's chronic conditions and improves their overall quality of life. Toward this end each disease-centered project group has assembled a Care Mentor team that has consolidated the latest medical findings to arrive at a set of specific care guidelines. To support this model of care, the CPOL system is not so much focused on sophisticated reasoning as informing the GPs of current "best practice" recommendations from the Care Mentor groups. There is a priority on encouraging GPs to understand and "buy into" the advice. Based on an EMR collected from an initial medical assessment and ongoing reviews, the system alerts the GP to possible issues providing links to topic guidelines.

The essence of CPOL decision support is human-to-human (e.g., Mentor to GP) communication through the medium of the on-line guidelines. Forcing the guidelines to adhere to be expressed with the precision of computer algorithms is contrary to their nature – they are meant to be interpreted by intelligent, clinically savvy human beings. Moreover, they are meant to be respected as statements by the Care Mentor groups -- regional opinion leaders who have worked through a process of surveying the literature worldwide and arriving at a consensus of recommendations that define "best practice." As such it is important that the on-line guidance resembles the Care Mentor advice rather than seeming to come from the computer or a computer analyst. The machine task is to identify guidelines that appear sufficiently relevant to bring to the GP's attention. Graphical alert flags are then displayed to encourage the GP to investigate the guidance available for these particular concepts. The guidance itself includes a display of the decision rules where the truth or falsehood of particular decision predicates and recommendations are graphically marked in accordance with the content of the EMR. In this way the GP can follow the decision logic for themselves and make their own choice as to whether they "buy into" the advice.

In this paper we describe sources of uncertainty in clinical practice guidelines and review how fuzzy logic

can model the natural ambiguity of clinical guideline statements. We show how fuzzy logic can fit the CPOL decision support framework and give a set of heuristics for application of fuzzy logic to manage uncertainty in clinical guidelines.

2. Clinical practice guidelines

Clinical practice guidelines (hereafter *clinical guidelines* or simply *guidelines*) are standardized specifications for care developed by a formal process that incorporates the best scientific evidence of effectiveness with opinions of experts in the fields [14]. In general, they have been developed in an effort to reduce escalating health care costs without sacrificing quality and have been shown to improve health care outcomes when followed [15]. Many clinical practice guidelines are available for an extensive range of clinical problems, and several bodies have been established as clearinghouses [16-17].

To be effective, guidelines need to be integrated into the physician's decision-making process in daily practice [18]. The acceptance of guidelines by medical practitioners, however, depends on several factors, including awareness, availability, relevance, applicability in specific circumstances, mutual agreement, supporting evidence, etc.

Most current guidelines are implemented in printed form, or as direct translations of the printed text-based narratives [19], however there have been a number of attempts to provide effective electronic representations of clinical guidelines [7,18-25]. In this process several key factors affecting their use have been established.

The highest probability of an effective guideline implementation occurs when patient-specific advice is provided at the time and place of a consultation [7,15,25]. It has been recognized that the guideline statements should be linked to the actual patient data, and therefore be integrated into an electronic medical record. The most predictable impact is achieved when "the guideline is made accessible through computer-based, patient-specific reminders that are integrated into the clinician's workflow" [7]. Why then "don't we see more examples of it in the literature and in practice?" - asks Zielstorff [7]. The reason is that there are many obstacles on the way to making guidelines available in the form of patient-specific reminders. One such obstacle is the uncertainty and imprecision, inherent in clinical guidelines.

Guidelines in medicine are rarely represented as algorithms. We understand an algorithm in its general sense, regardless of its presentation, to be a collection of *If...Then...* rules, a diagram, a flowchart, a sequence of statements in a procedural language, etc. Usually clinical guidelines are implemented in the form of text narratives, describing possible medical conditions and signs with the

appropriate recommendations. One profound reason we do not see guidelines represented as algorithms is that such narrative recommendations may not have traditional algorithmic representations. Some authors suggest that guidelines are not intended to be literally and directly applied, they specify a “mixture of procedural and criterion-based knowledge, which the clinicians are tacitly expected to adjust and adapt according to the specific of a case” [26]. This fact creates a significant obstacle for computerising clinical guidelines, their electronic exchange and assessment. Despite recent progress in developing formal syntax for guideline representation [20-21,24], in the computerised form the guidelines are mostly translations of text-based narratives.

3. Sources of uncertainty in clinical practice guidelines

Uncertainty plays a major role in the problem of guidelines representation. While natural languages (e.g., English) are quite suitable to express the uncertainty, present algorithmic languages call for precise recipes, and the translation from the first representation to the second presents a significant challenge. There are several types of uncertainty that may appear in clinical guidelines.

First, it is *lack of information*. Not every observation of relevance to a guideline may be available or has been collected, in which case an educated guess sometimes has to be made. Even if collected, the information can be unreliable.

Second, it is *non-specificity*, connected with sizes (cardinalities) of relevant sets. Frequently guidelines refer to “other conditions,” “other risk factors,” “other significant comorbidities,” leaving it up to the doctor to decide what they are. To be translated into an algorithmic language, an explicit list of those conditions is required [7].

Third, it is the *probabilistic nature of data and outcomes*. There are few clinical signs that unequivocally point to a medical condition, and therefore to a predefined course of actions. Sensitivity and specificity of most clinical tests are far from ideal, and consequently they point to a likelihood, rather than presence or absence of medical condition. The outcome of any non-trivial recommendation is also, in a sense, a gamble. The words “usually”, “likely”, “commonly”, “possibly”, etc., express this type of uncertainty in natural languages.

Fourth, it is *vagueness in the formulation of recommendations*. What is the meaning of such phrases as “suggested,” “recommended,” “should be strongly considered” or “not routinely warranted?” The guidelines, in contrast to precise recipes suitable for direct translation into a computer language, allow for situations in which the recommendation may not be appropriate, without specifying the exact conditions. They urge but not force

doctors to follow the recommendations, and thus do not supplant their decision making process.

Next, it is *strife* (or *discord*), which expresses conflicts among the various sets of alternatives. Often several guidelines may be applicable to the given patient circumstances, each pointing to a specific set of actions. Conflicting guidelines are not necessarily a feature of poor design or lack of expert agreement. The doctor then has to decide which action or combination of actions is the most appropriate.

Finally, it is *fuzziness in determination of clinical signs* that trigger the guidelines. It can be subjectivity in the *assessment* of a patient’s symptoms, or in the *interpretation* of precise objective data, such as laboratory test results or even a patient’s age. What exactly is the size of an “enlarged liver?” What exactly do we mean by “infants” or “middle-aged men?”

Several mathematical formalisms have been proposed to treat uncertainty. The oldest and best-studied approach is the probabilistic one. It has sound axiomatic foundations laid by Kolmogorov in the 1930s, and allows various interpretations, among which are frequentist and subjectivist approaches. In the framework of medical decision making and expert systems it has been used since the 1970s. The pitfall in using probabilities is that the vast majority of conditional probabilities required for the Bayes rule are not available, and their subjective estimations by medical experts tend to be inconsistent and inaccurate. Directions explored in the past 30 years include belief transfer in semantic networks, Dempster-Shafer evidence theory, fuzzy logic and possibility theory. These approaches frequently overlap and can be considered as different sides of the unifying Generalised Information Theory that we are just beginning to understand [27].

Fuzzy Set Theory (FST), introduced by Lotfi Zadeh in 1965, is the basis for Fuzzy Logic, Approximate Reasoning, Possibility Theory and other related disciplines. The main advantage of FST is that it allows transparency in knowledge representation. Formulation of decision rules mimics human thinking, and fuzzy logic permits one to construct fuzzy algorithms, flexible enough to represent the narratives of clinical guidelines. The key concept of FST is that of partial membership of elements in a set. In contrast to classical, “crisp” sets, where an element either belongs to the set or not, FST allows for degree of belonging to the set, usually real values taken from the range of 0 to 1, with 1 standing for complete membership and 0 for non-membership.

4. Fuzzy logic for clinical guidelines

In this section we analyze two particular types of uncertainty, fuzziness in determination of clinical signs

and vagueness in formulation of recommendations, and their treatment in the framework of fuzzy logic. Other mentioned types of uncertainty require different treatment, either in probabilistic framework or otherwise, and the interested reader is referred to [27],[33] and [7].

Consider the set of “obese men,” which usually includes men with Body Mass Index (BMI) greater than 30. This set is crisp. Fuzzy set “obese” includes not only men with BMI>30, but those with BMI<30 as well, with a smaller degree of membership. The lower the BMI the smaller the membership, smoothly decreasing to zero.

In FST, an object can partially belong to several mutually exclusive sets simultaneously. For instance, in addition to the set “obese,” let us define the fuzzy set “overweight” as the set of men with 25<BMI<30. Then, a person with BMI=29 is belonging to both classes, of “obese” and “overweight” men, although with different degrees of membership. There is no sharp transition between the two classes. With the increase of BMI, the person gradually becomes “less” overweight and “more” obese.

Suppose that the guideline states: “Obese men require the following course of action...” Does this not apply to a man with BMI=29.99? Let this person have two cups of tea, and his BMI will become 30.1 (based on 170cm height, 87 kg weight and 300g liquid intake). Thus, the recommended action would strongly depend on such things like what the patient did before coming into practice, rather than on his medical condition! Such an odd result; however, it is exactly what classical logic results in. In fuzzy logic, a person gradually passes from one class to another with the change of physical parameters. If guideline rules for these classes are different, the degree of membership in each class governs the degree of applicability of each rule. In some cases the rule with the strongest applicability should be followed, in other cases a weighted average is the correct answer.

A representation of clinical guidelines suitable for algorithmic purposes would be a collection of *If... then...* rules. Such rules can be easily followed, and also transformed to another representations, such as a decision table of a flowchart. The rules have the form:

$$\text{If } x \text{ is } A \text{ then } y \text{ is } B. \tag{1}$$

In such rule, x is a variable, whose value may represent a physical parameter, like in this case:

$$\text{If } BMI > 30 \text{ then provide dietary advice.}$$

In fuzzy logic, x can also be a *linguistic variable*, that is the variable whose possible values are fuzzy sets rather than numbers. Consider the statement:

$$\text{If } x \text{ is obese then provide dietary advice.}$$

Here “obese” is the label of a fuzzy set, the membership in which depends on the physical parameter

BMI. The linguistic variable x has possible values “obese”, “overweight”, “normal”, “underweight”.

As opposed to classical logic, in which the rules are “executed” if the antecedents are true, in fuzzy logic the rules are executed partially. The strength of the recommendation depends on the membership value of x in the set “obese.” The lower the value, the weaker the recommendation. For a person with BMI=35 the rule can read “necessarily provide dietary advice,” whereas for the one with BMI=28 it can read “consider providing dietary advice.”

At the same time, the strength of the recommendation depends on the pre-assigned rule strength, expressed as the membership of y in B in the Eq. (1). It models differences in statements like “Action is suggested,” “Action is recommended” and “Action must be taken” regardless of the rule antecedent. Thus, it is not only the antecedent of the rule that is fuzzy, but the rule itself may be fuzzy. Both types of fuzziness need to be combined. It results in *fuzzy implication*, the mathematical basis for which is provided within fuzzy logic.

Finally, the rule may have compound antecedents. For example:

$$\text{If } x \text{ is } A \text{ AND } y \text{ is } B \text{ AND } z \text{ is } C \text{ then } v \text{ is } V.$$

Here the membership values of x in A , y in B and z in C have to be combined to determine the overall strength of the antecedent, and therefore of the recommendation. Aggregation of membership values is performed by using *aggregation operators*, which may be simple operations like MIN and MAX or may be arbitrarily complex.

Let us summarize the above. Essentially, fuzzy logic translates vague algorithmic statements into numbers, and provides a mechanism to operate with these numbers in a consistent manner.

There are three principal steps in fuzzifying clinical guidelines: *fuzzification*, *fuzzy inference* and *defuzzification*. At the fuzzification stage, the antecedents of *if...then...* rules and the rules themselves are *fuzzified*: the antecedents become linguistic variables carrying the degree of membership of an object in the corresponding fuzzy set. For compound antecedents these membership values are combined with an appropriate aggregation operator. Fuzzy inference consists in determining the strength of the rule consequent based on its antecedent. The consequent (the recommendation of the rule) is assigned a degree of membership (or net strength of rule). The net strength of the rule is combined with the strength of the antecedents to determine the overall strength of the recommendation. The last stage, defuzzification, consists in determining the appropriate recommendation if two or more possibly contradicting rules are activated.

Consider the situation where key specific indications for dietary advice are: 1) underweight; 2) rapid weight loss. In this context underweight is defined as BMI<20

and rapid weight loss is defined as >10% weight loss in 3 months or less. This statement can be translated into the following *if-then* rule:

If x is *underweight* **or** x is *losing_weight*
then recommend *dietary advice*.

Given a specific patient, x , with BMI (20.2) and rate of losing weight (9% in 2.5 months), x could have, for instance, the following membership values: $m_{\text{underweight}}(x)=0.7$, $m_{\text{losing_weight}}(x)=0.9$. Assuming that “recommend” corresponds to the net strength of rule being 0.8, we obtain:

$$\text{IMPL}(\text{OR}(m_{\text{underweight}}(x), m_{\text{losing_weight}}(x)), \text{recommend}) = (0.9 + 0.7 - 0.9 * 0.7) * 0.8 = 0.97 * 0.8 = 0.776.$$

The value 0.776 gives us the overall strength of recommendation, which is a little less than the 0.8 for “recommend.” The IMPL and OR in the above construction denote fuzzy implication and aggregation operators, for which we used product and probabilistic OR, respectively, in this example.

The defuzzification stage consists in the adequate choice of the action to undertake when more than one rule is activated. Suppose that two rules are activated:

If x is *overweight* then *provide dietary advice*, and
If x is *obese* then *consider drug therapy*.

Let BMI of x be 29. The first rule activates dietary advice with the strength of 0.9, and the second rule activates drug therapy with 0.7. In this case, the first rule should be followed because it is the most appropriate. The defuzzification procedure selects the strongest recommendation. In other cases, however, it may not be the most appropriate recommendation, but a combination of various recommendations. For instance, let the rules be:

If x is *overweight* then *reduce fat intake by 30%*, and
If x is *obese* then *reduce fat intake by 50%*.

Here, something like “reduce fat intake by 40%” may be the appropriate recommendation (the weighted average is $(0.9 * 30\% + 0.7 * 50\%) / (0.7 + 0.9) = 38.7\%$). The Defuzzification procedure selects the weighted average of the rule consequents.

In this section we have considered how vague antecedents of *if-then* rules can be combined with vague rule recommendations and how conflicting recommendations can be combined together using fuzzy logic. Let us now briefly examine what are the conditions that make rule antecedents fuzzy in the first place.

There exist three main sources of fuzziness in determination and interpretation of clinical signs, which

transform even precise numerical parameters into fuzzy values [28, 33]. They are:

1. *Errors in measurement.* Inexactness in measuring physical parameters results in ambiguity when classifying according to these parameters. For example, measuring a person’s weight with the precision ± 1 kg results in an error in calculating BMI, which in turn leads to a possible error in classifying the person as obese ($\text{BMI} > 30$).
2. *Difference in expert opinion.* This is due to lack of agreement about the thresholds that separates one class from another. For example, in Australia the threshold for BMI for obese people is 30, whereas in Canada it is 27. FST allows us to average the value of the threshold across the experts and to define a fuzzy threshold.
3. *Lack or excess of information.* This kind of fuzziness arises when it is necessary to classify an object according to some criteria when either (a) not all of them are available, or (b) there are other criteria that may affect the classification. For instance, we can relatively easily determine the age group of a person, without knowing the precise age (missing criterion). On the other hand, knowing that another ten people in this area were recently diagnosed with an infectious disease, a person with a set of mild non-specific symptoms would probably be hospitalised for observation rather than sent home in normal circumstances (information not being an explicit criterion affects the classification and the decision).

FST provides the techniques to construct membership functions for the previously mentioned sources of fuzziness, whose role is to transform the value of a numerical parameter into the grade of membership in the relevant fuzzy set. These techniques are described in [30-33, 28].

In the previous discussion we mentioned such notions as *aggregation operators*, *fuzzy implication*, *defuzzification* and *membership function* while intentionally not going into detail. From the semantics point of view, the role of these concepts is clear:

- *aggregation operators* combine membership values of rule antecedents,
- *fuzzy implication* (or *fuzzy inference*) refers to determining the strength of recommendation based on the strength of the antecedents and that of the rule,
- *defuzzification* procedures select the appropriate action based on fuzzy recommendations,
- *membership functions* assign a degree of membership to an object in a set based on a measurable parameter.

However, in contrast to classical logic, the mathematical expression for these concepts is not uniquely defined. This means that one can select fairly arbitrarily the form of aggregation and implication

operators, defuzzification procedures and membership functions, without affecting their semantics. Different operators will lead, of course, to different results. There are no abstract theoretical criteria that make some operators better than the others - it all comes down to empirical validation. On the one hand, this is the strength of the theory because it allows one to treat many different situations within the same semantic framework. The price for such universality is the lack of straightforward selection rules for those mathematical operators. For every particular guideline one has to select different operators and verify them for consistency with human decision making.

Among the advantages of fuzzy algorithms is that they can be written in a form similar to natural language. Although the internal execution of the algorithm may be quite different from the way we think (apparently we do not crunch numbers when asked to follow a guideline full of uncertain information), it can provide recommendations consistent with our thinking. A consequence of this transparency is that fuzzy rules are easy to develop and understand.

The consistency of fuzzy logic with classical logic in the limit is also a significant bonus. When uncertainty disappears (when there is no doubt about assigning an object to a particular class), the deduction chain and the end result are identical to those in classical bi-valued logic [30, 32]. Thus, one can use the classical algorithms and flowcharts to follow the guidelines, adjusting for fuzziness in the borderline cases. Classical logic becomes a rough approximation to our reasoning process, and fuzzy logic becomes its refinement rather than an alternative.

5. Fuzzy logic for decision support in chronic disease care planning

With respect to the CPOL system, we have been able to craft crisp (i.e., classic, not fuzzy) logic guidelines that in fact provide a useful approximation to specialist recommendations for the same patients. In particular, CPOL recommends a number of services and investigations (in concurrence with the specialist Care Mentors), which GPs working without the benefit of electronic guidance have largely ignored. It is not particularly surprising that we have been able to construct a useful facsimile of the expert decision logic -- thousands of successful expert systems have been developed since the 1970's, many in medicine. Moreover, as is human nature, our implementation and evaluation to date avoids some of the guideline recommendations that have been particularly hard to formulate satisfyingly as crisp algorithms.

What is more at issue is the lack of a coherent formalism in the specification of the decision logic. While many guidelines were adequately expressed by

simple Boolean logic, in some cases we needed arbitrary additions to the system's decision predicates to fit the specialists' intentions (see examples below). A long-term goal of the CPOL project is to create a general architecture for intranet-based clinical guidance that integrates with the EMR and physician workflow. The client side of CPOL is a relatively generic shell that receives guideline and EMR specifics from the central server. This reconfigurability is made much more difficult to achieve when we lack a formalism that encompasses all our guideline modeling requirements (i.e., when we cannot predict if we might need to hack a new class of function into the client). Similarly, analysis and evaluation are ad hoc without a structuring formalism. Introducing a fuzzy logic formalism does not make the complexity go away, but it can provide a more unified framework for representing the issues, making it easier to achieve a generic DSS shell. Moreover, once we have a unifying decision framework, we can begin to organize our analysis methods, a first attempt at which is offered in the next section.

A particular benefit to a fuzzy logic framework is that we can readily unify our approach to CPOL's decision support responses to the end user based on the output value of the membership functions. CPOL provides three classes of user feedback:

1. Attention/alert triggers that signal that a topic should be investigated by the user (see figure 1 where several service triggers and a body mass index (BMI) alert are shown);
2. Predicate truth/falsehood is graphically marked on the guideline's Checklist display (see figure 2);
3. Recommendations are graphically marked on Checklist and Status displays (the Status tab provides a problem-oriented EMR summary plus recommendations).

These user feedback features are currently implemented using ad hoc crisp logic functions that download from the CPOL server in a prefix notation processed by the CPOL client on the end-user's desktop. If all predicates and recommendations were fuzzy, we could simplify the feedback functions and more easily change the system behavior if we had a new idea about the decision support user interface. Also we could make the system more or less conservative simply by adjusting the threshold values. Figure 3 summarizes the mapping of output membership functions to CPOL system response icons.

We are not sponsoring the use of fuzzy logic as a substitute for providing scientific evidence. Access to evidence is provided in CPOL by the Evidence tab present in each guideline. CPOL exploits the power of HTML-based hypertext for provision of supporting materials for the guidelines. This includes purpose built text (devised by the Care Mentors) held on the CPOL server, and links to external Web-based sources as well as conventional literature citations. One cannot predict just when the GP

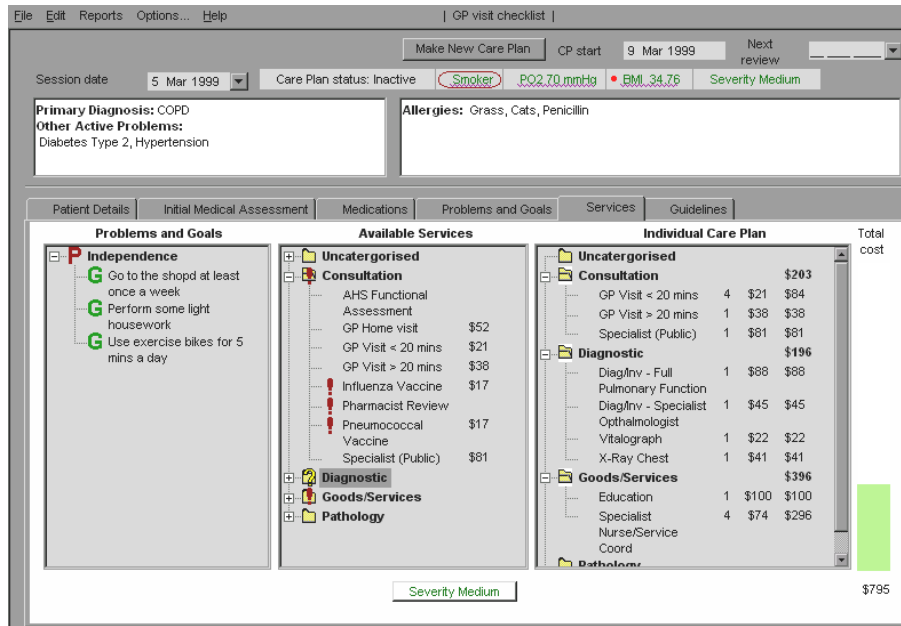


Figure 1. Care Plan On-Line (CPOL) main screen showing several service triggers and an alert on Body Mass Index (BMI).

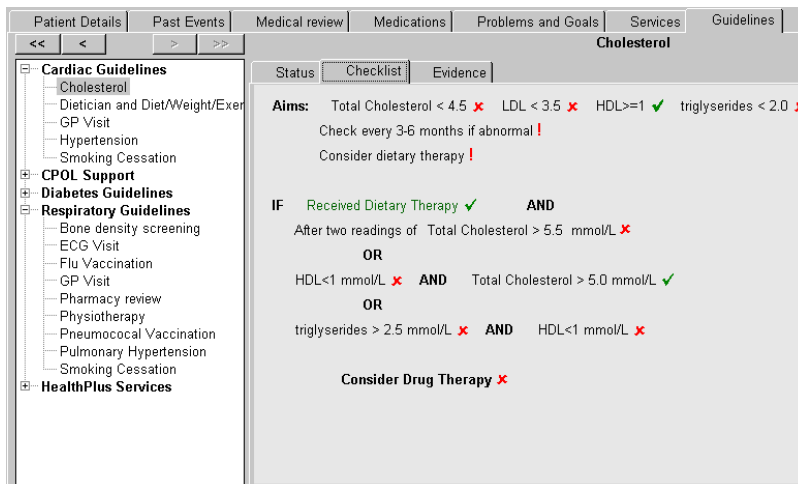


Figure 2. Cholesterol guideline checklist showing aims and drug therapy recommendations and related advice with graphic marks in accordance with patient's data.

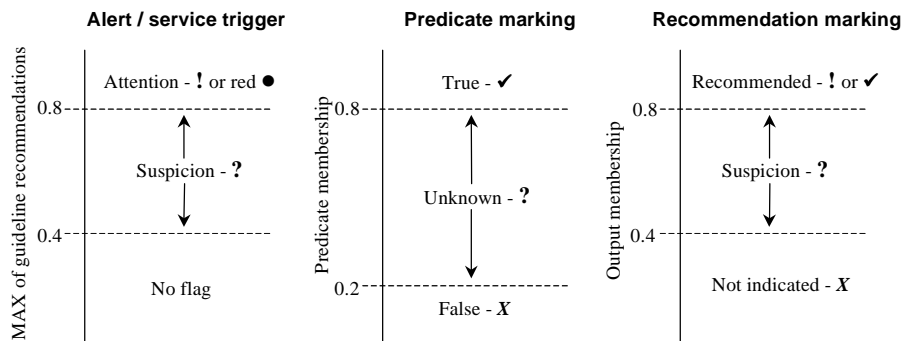


Figure 3. Mapping fuzzy membership to CPOL decision support responses.

will decide to have a look at the evidence – perhaps when there is a lull in the queue of patients, or in the evening. For this reason we provide both triggered and user-initiated access (via a topic index) to the guidelines.

6. Dealing with uncertainty in guidelines

In the previous section we describe unified system response for CPOL based on the degree of fuzzy membership in the output variable, however, there are still many issues as to how one arrives at these membership functions. It is widely recognized that fuzzy membership functions are a very case-by-case thing (some would say a hack), however, we can introduce some structure to the process. Table 1 provides a set of indications and treatments for uncertainty in clinical guidelines categorized by source of uncertainty. We suggest that one should attempt any of the crisp solutions that seem applicable as long as it does not corrupt the nature of the guideline by forcing it to be crisp where the state of medical knowledge or practicability does not support that degree of structure. The fuzzy solutions then serve to formalize the remaining vagueness and imprecision.

Some issues stand out as particularly challenging and commonplace in fuzzy modeling of clinical guidelines:

Maximum membership. The maximum response of the output variable must be attuned to the specificity of the fuzzy predicate. Liu and Shiffman [12] illustrate this well. Their output variable is strength of recommendation for lumbar puncture (LP). A clear-cut Brudzinski sign is sufficient to recommend LP, so its maximum appropriateness value is 1.0. In contrast, an elevated white blood cell (WBC) count is also an indicator, but is only somewhat concerning, so its maximum value is set to 0.75.

Aggregation of antecedents (“ANDness”). English provides us with relatively few words to express logical relationships for combining evidence, chiefly (in addition to IMPLIES) we have AND and OR. MIN and MAX give good strict interpretations of AND and inclusive OR, respectively. There are many alternative operators. Beliakov [29] demonstrates a class of well formed AND operators in terms of similarity to (1 minus distance from) the “Ideal” – a point that defines perfect attainment on all the ANDed parameters. Using different distance metrics we can achieve different effects; e.g., city-block distance gives us the classic MIN operation, whereas Euclidean distance gives us a less strict AND. OR is similarly defined in terms of distance from the “anti-Ideal.” Another (less formal) possibility is to consider fuzzy ANDness as a weighting factor between AND and OR [30]. For instance, the hypertension guideline from SA HealthPlus requires that a patient show high blood pressure (above a certain threshold over repeated readings) and undergo lifestyle counseling before we recommend

that the GP consider drug therapy. If we have an 0.6 membership in AND between an 0.8 High Blood Pressure and 0.3 Counseling we could give an $0.6 * (\text{MIN}(0.8,0.3)) + 0.4 * (\text{MAX}(0.8,0.3)) = 0.5$ membership in Consider Drug Therapy.

Framing qualifiers. We need to be clear about exactly when a guideline applies. For instance, cholesterol management recommendations are substantially different for those with known cardiac disease (secondary prevention) than for others (primary prevention). This is a fairly clear-cut issue that can be considered as an initial crisp AND in front of an entire set of guidance rules. However, continuing with this example, the benefits of cholesterol treatment are less well-established for the elderly. In this case we may use a fuzzy AND simply modeled by a MAX operator that limits strength of recommendation. In all cases we would need to be sure to make these framing qualifiers visible to the doctor.

Role of time. Again referring to the SA HealthPlus hypertension guideline, with respect to counseling, how long does counseling go on before this antecedent is satisfied? In fact, the textual clinical guideline mentions at least 3 months dietary therapy as a prerequisite for hyperlipidaemia (cholesterol) drug therapy, but we would have to clarify the temporal extent of this requirement for hypertension. Also, there is the question of whether it has any fuzziness – do we have 0.5 membership after 1.5 months? Since humans lack perfect introspection into their decision-making capabilities, reviewing expert decisions over a range of test cases may be necessary.

7. Conclusion

We have described motivations and merits for use of fuzzy logic in representation of clinical practice guidelines for automated decision support. In particular, we have described the applicability of fuzziness for guidance alert flags in Care Plan On-Line, a chronic disease decision support tool for General Practitioners (GPs). We argue that it can be better to model the natural fuzziness in clinical guidelines than to force doctors to work with precise “crisp” logic algorithms. Fuzzy logic is an approach for describing vagueness and imprecision in a precise mathematical language, explicitly representing natural vagueness rather than abolishing it.

It can be argued that the best manifestation of Evidence Based Medicine is to remove fuzziness from clinical decisions. Experimentally proven risk factors and treatment benefits can be compiled through a Bayesian decision network to provide precise risks and costs. For instance, evidence based guidelines frequently provide as the “bottom line” the NNT (e.g., number of patients needing treatment for 10 years to prevent an event) and the cost of treatment to prevent an event (such as a serious

Table 1. Heuristics for dealing with uncertainty in clinical guidelines.

Type of uncertainty	Indication	Treatment
Lack of information	Observations (obs) called for as predicates in a guideline are not present in EMR OR Needed obs are unattainable in relevant decision context OR obs are available but may be highly inaccurate	<u>crisp solutions</u> : amend EMR to include needed obs; include data entry areas on guideline for needed obs; consider communications network links to needed sources <u>fuzzy solutions</u> : avoid placing commonly missing obs in MIN expressions if a decision is in fact possible without it; limit output membership from other obs to <1 if missing obs is definitive test
Non-specificity of sets	Phrases such as “other risk factors”	<u>crisp solution</u> : get specialists to specify the likely “other risk factors” <u>fuzzy solution</u> : allow user to specify degree of presence of “other risk factors” -- must decide maximum output membership possible from this source
Probabilistic nature of data and outcomes	Use of qualifiers like “commonly” or “possibly”	<u>crisp solution</u> : extract known sensitivities and specificities of tests; obtain precise risk reduction and treatment cost data <u>fuzzy solution</u> : choose a mapping of words to membership values (can also map probabilities to membership values if desired)
Vagueness in the formulation of recommendations	Course of action is “suggested,” “recommended” or should be “considered”	<u>crisp solution</u> : make explicit the factors that make the recommendation vague <u>fuzzy solution</u> : factor risk, cost and expert opinion into output membership value; defuzzify to chosen words (or other system responses) based on level of membership
Strife or discord in recommendations	Guidelines provide conflicting recommendations for this patient	<u>crisp solution</u> : look for flaws in framing of required conditions for recommendations <u>fuzzy solution</u> : apply fuzzy aggregation of outcomes <u>in either case</u> : provide access to supporting and refuting arguments
Imprecision of clinical signs	Subjectivity or need for interpretation of measure	<u>crisp solution</u> : revise guideline to avoid subjective measures and provide precise quantitative bounds on measurable items <u>fuzzy solution</u> : design membership functions to map subjective terms to membership values; design membership function to reach minimum and maximum outside of likely scope of imprecision <u>in either case</u> : encourage repeating measure if practical and cost effective

acute myocardial infarction). However, existing Randomized Controlled Trials (RCTs) do not cover every combination of factors, and there still must be allowance for patient choice clinician judgement. Moreover, one cannot present all relevant facts in complete detail to the doctor all at once, thus there must be some filtering mechanism. We believe that an effective information filtering system can be devised from (a) passive alert flags, which on user request lead to (b) naturally-phrased guidance expression, which then link to (c) scientific supporting evidence.

Further reading

Although most of the fuzzy logic literature is written for specialists, there are a few monographs that do not require mathematical background yet go to a sufficient level of detail. The book by Lopez de Mantaras [31] offers introductory level reading. Excellent monographs

by Zimmermann [30] and Klir and Folger [32] provide more detailed and formal discussion. Recent issues of the *Journal of the American Medical Informatics Association* and *Proceedings of the Annual Symposia of AMIA* have several papers on application of fuzzy logic to medicine in general and clinical guidelines in particular (e.g., [7, 12]).

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References

- [1] Smith, R. (1996). What clinical information do doctors need? *BMJ* **313**(7064), 1062-1068.
- [2] Hubbs, R. et al. (1997). The Stanford health information network for education: integrated information for decision making and learning, *Proc. AMIA Ann. Fall Symp.*, pp. 505-508.
- [3] Hanka, R., O'Brien, C., Heathfield, H. & Buchan, I. (1999). WAX ActiveLibrary; a tool to manage information overload, *HICSS-32*.
- [4] Scott Evans, R. et al. (1998). A computer-assisted management program for antibiotics and other anti-infective agents, *NEJM* **338**(4), 232-238.
- [5] Chueh, H. & Barnett, O. (1997). 'Just in time' clinical information, *Academic Medicine* **72**(6), 512-517.
- [6] Godin, P. et al. (1999). A new instrument for medical decision support and education: the Stanford health information network for education. *HICSS-32*.
- [7] Zielstorff, R.D. (1998). Online practice guidelines, *JAMIA* **5**, 227-236.
- [8] Adlassnig, K-P. (1986), Fuzzy set theory in medical diagnosis, *IEEE Tr. On Syst., Man, and Cybernetics* **16**(2), March/April, 260-265.
- [9] Mason, D., Linkens, D. & Edwards, N. (1997), Self-learning fuzzy logic control in medicine, *Proc. AIME'97*, (E. Keravnou et al., eds.), *Lecture Notes in Artificial Intelligence* **1211**, Springer-Verlag: Berlin, pp. 300-303.
- [10] Lalonde, A. et al., (1997). Automatic detection of cardiac contours on MR images using fuzzy logic and dynamic programming, *Proc. AMIA Ann. Fall Symp.*, pp. 474-478.
- [11] Zahlmann, G., Scherf, M. & Wegner, A. (1997), A neuro-fuzzy classifier for a knowledge-based glaucoma monitor, *Proc. AIME'97*, (E. Keravnou et al., eds.), *Lecture Notes in Artificial Intelligence* **1211**, Springer-Verlag: Berlin, pp. 273-284.
- [12] Liu, J. and Shiffman, R., (1997). Operationalization of clinical practice guidelines using fuzzy logic, *Proceedings of AMIA Ann. Fall Symp.*, 283-287.
- [13] Warren, J., Beliakov, G., Noone, J. & Frankel, H. (1999). Chronic disease coordinated care planning: flexible, task-centered decision support, *HICSS-32*.
- [14] Leape, L. (1990). Practice guidelines and standards: an overview, *Quarterly Review Bulletin '90* **16**, 42-49.
- [15] Grimshaw, J. & Russel, I. (1993). Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations, *Lancet* **324**, 1317-1322.
- [16] Agency for Health Care Policy and Research, URL: text.nlm.nih.gov.
- [17] Canadian Medical Association, URL: www.cma.ca/cpgs/.
- [18] Lam, S. (1994). Implementation and evaluation of practice guidelines, *JAMIA, Symp. suppl.*, 253-263.
- [19] Liem, E., Obeid, J., Shareck, E., Sato, L. & Greenes, R. (1995). Representation of clinical practice guidelines through an interactive World-Wide-Web interface, *JAMIA, Symp. suppl.*, 223-227.
- [20] Barnes, M. & Barnett, G. (1995). An architecture for a distributed guideline server, *JAMIA, Symp. suppl.*, 233-237.
- [21] Jenders, R., et al. (1995). Medical decision support: experience with implementing the Arden syntax at the Columbia-Presbyterian medical center, *JAMIA, Symp. suppl.*, 169-173.
- [22] Lobach, D. (1995). A model for adapting clinical guidelines for electronic implementation in primary care, *JAMIA, Symp. suppl.*, 581-585.
- [23] Liem, E., Obeid, J., Shareck, E., Sato, L. & Greenes, R. (1995). Representation of clinical practice guidelines through an interactive World-Wide-Web interface, *JAMIA, Symp. suppl.*, 223-227.
- [24] Ohno-Machado, L., et al. (1998). The GuideLine interchange format: a model for representing guidelines, *JAMIA* **5**, 357-372.
- [25] Shiffman, R. (1997). Representation of clinical practice guidelines in conventional and augmented decision tables, *JAMIA* **4**, 382-393.
- [26] Gordon, C., Johnson, P., Waite, C. and Veloso, M. (1997) Algorithm and Care Pathway: Clinical guidelines and healthcare process, *Proceedings of AIME Conf*, 66-69.
- [27] Klir, G. and Wierman, M., (1998) *Uncertainty-based information*, Physica-Verlag, Heidelberg.
- [28] Amaya Cruz, G.P. and Beliakov, G. (1995). Approximate reasoning and interpretation of laboratory tests in medical diagnostics, *Cybernetics and Systems* **26**, 713-729.
- [29] Beliakov, G. Aggregation operators as similarity relations, in (R. Yager, B. Bouchon-Meunier & L. Zadeh, eds.) *Information, Uncertainty, Fusion*. Kluwer, to appear.
- [30] Zimmermann, H.-J. (1996). *Fuzzy set theory - and its applications*, Kluwer, Boston.
- [31] Lopez de Mantaras, R (1990). *Approximate reasoning models*, Ellis Horwood, Chichester.
- [32] Klir, G. and Folger, T. (1992). *Fuzzy sets, uncertainty, and information*, Prentice Hall, Singapore.
- [33] Hisdal, E. (1998). *Logical structures for representation of knowledge and uncertainty*, Physica-Verlag, New York.