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Advances In Infection Surveillance and Clinical Decision Support With Fuzzy Sets and Fuzzy Logic

Walter Koller[a], Jeroen S. de Bruin[b], Andrea Rappelsberger[b], Klaus-Peter Adlassnig[b,c]

[a] *Clinical Institute of Hospital Hygiene, Medical University of Vienna and Vienna General Hospital, Austria*
[b] *Section for Medical Expert and Knowledge-Based Systems, CeMSIIS, Medical University of Vienna, Austria*
[c] *Medexter Healthcare GmbH, Vienna, Austria*

Abstract

By the use of extended intelligent information technology tools for fully automated healthcare-associated infection (HAI) surveillance, clinicians can be informed and alerted about the emergence of infection-related conditions in their patients. Moni—a system for monitoring nosocomial infections in intensive care units for adult and neonatal patients—employs knowledge bases that were written with extensive use of fuzzy sets and fuzzy logic, allowing the inherent un-sharpness of clinical terms and the inherent uncertainty of clinical conclusions to be a part of Moni's output. Thus, linguistic as well as propositional uncertainty became a part of Moni, which can now report retrospectively on HAIs according to traditional crisp HAI surveillance definitions, as well as support clinical bedside work by more complex crisp and fuzzy alerts and reminders. This improved approach can bridge the gap between classical retrospective surveillance of HAIs and ongoing prospective clinical-decision-oriented HAI support.

Keywords:
Healthcare-associated infections; Automated surveillance and monitoring; Clinical alerts; Fuzzy sets and fuzzy logic; Moni.

Introduction

During the last two decades, healthcare-associated infection (HAI) surveillance evolved from rather limited research projects to widespread mandatory quality management (QM). Since HAI surveillance depends on clinical data collected by experienced healthcare workers and infection control practitioners (ICPs), it requires human resources that are usually not continuously available or interfere with other equally important healthcare requirements.

Provided that relevant data can be automatically collected and analyzed by intelligent software, fewer human resources are required to make surveillance data available for infection prevention and control (IP&C), adverse event monitoring, and other fields of patient safety and clinical QM.

Now that systems for IP&C have been established and become more sophisticated, we seem to have reached a point where the actual benefit of these measures is questionable and needs to be assessed [1]. Although HAI surveillance and control have a strong ethical background, the demand for evaluating IP&C in terms of its cost-effectiveness and its relevance in health economy is justified.

This infers a higher level of complexity, calling for new methodological measures to deal with the system appropriately and economically. Here information technology (IT) will play a significant role. With the transformation and results of the Moni system for IT-backed clinical HAI monitoring, we show the potential of this new approach.

Moni was initially designed as a bacteria and antimicrobial resistance monitoring tool. Later it was expanded to clinical data acquisition and was attached to a complex knowledge-processing rule engine, allowing for the interpretation and aggregation of clinical and laboratory findings in patient records. It was intended for automated detection and surveillance of HAIs and their retrospective reporting [2].

From our clinical colleagues we learned that the generally accepted international HAI definitions are of limited value in routine bedside work. Using almost the same dataset, they prefer sensing changes in their patients' clinical condition in a prospective patient-specific manner. This implied extension of terms and definitions in the existing surveillance systems. In particular, uncertainties in definitions and propositions must be considered when trying to assess borderline cases. To address these aspects, fuzzy-set- and fuzzy-logic-based technology was implemented for data and rule processing in Moni. This fundamentally new approach opened new perspectives.

Methods

Moni IT system

Moni is a system for automated nosocomial infection monitoring and surveys, alerts, and reports. This large-scale IT system is in operation at the Vienna General Hospital (VGH), the main teaching hospital of the Medical University of Vienna, with approximately 2,100 beds and 14 intensive care units (ICUs).

The system provides two separate clinical applications: Moni-ICU for adult patients and Moni-NICU for neonates. Moni's main characteristics are fully automated data transfer from electronic sources, the implementation of medical knowledge bases, and the use of specific processing algorithms that rely on these knowledge bases and evaluate, aggregate, and interpret clinical data in a stepwise manner until patient data can be mapped to the included HAI definitions.

Data sources

Moni's data sources are the ICU's patient data management systems (PDMSs), which include administrative and clinical patient data as well as data from the central medical-chemical laboratory information system (LIS). In addition, microbiology data are derived from a separate LIS. All data are sent through a communication interface to Moni's data warehouse, which is the starting point of all subsequent data processing steps.

HAI surveillance and alert definitions

Moni's surveillance is based on the criteria and textual definitions issued by CDC/NHSN, Atlanta [3], ECDC, Stockholm [4], and the KISS criteria issued by the German National Reference Center for Surveillance of Nosocomial Infections, Berlin [5]. Moni's alert criteria are based on established surveillance rules, but were adapted to clinical needs. For instance, parameter definitions of clinical concepts were changed to avoid over-alerting [6].

Arden Syntax

The HAI surveillance and alert definitions were translated into Arden Syntax, version 2.7 [7], by a small team of clinical informaticians and experienced infection control specialists and clinicians. Arden Syntax is a medical knowledge representation and processing scheme for the development of clinical decision support systems. The syntax is maintained by Health Level Seven International [8], and new versions are regularly approved by the American National Standards Institute. A recent report on the Arden Syntax software (compiler, engine, server, database connector) embedded into state-of-the-art service-oriented software architecture can be found in [9].

Data and knowledge processing

Administrative, clinical, laboratory, and microbiological patient data from the PDMSs and the LISs are processed in a stepwise pipeline of aggregation, interpretation, and evaluation [10]. The first steps are pre-processing (checking for missing data and plausibility) and feature extraction (e.g., calculation of means and scores). This is followed by interpretation and intermediate to high-level clinical concept evaluation, for which a package of hierarchically interwoven medical logic modules (MLMs)—the building blocks of Arden-Syntax-based knowledge representation—was established. The topmost clinical concepts are the HAI surveillance and alert definitions to be evaluated. Many of the encoded clinical entities are modeled as fuzzy sets and the inference steps are performed by applying fuzzy logic.

The result of this automated processing is a list of HAIs whose definitions are either fulfilled or fulfilled to a certain degree. This evaluation is based on all available patient data, not only of the selected day but dating back to seven days. HAIs whose definitions are not fulfilled are not displayed.

Fuzzy terms and fuzzy logic

When trying to model uncertainty in clinical medicine, a distinction must be made between linguistic and propositional uncertainty.

Most clinical entities, such as fever or leukopenia, are linguistic concepts with gradual or fuzzy transitions between normal and pathological states—this is known as linguistic uncertainty. Such entities are formally modeled by fuzzy sets introducing a borderline range or transition zone between neighboring concepts.

Propositional uncertainty, in contrast, refers to uncertainty in medical conclusions. This is modeled by truth values between zero and one. One example is a patient in intensive care whose body temperature is in the normal range, but the patient is on external thermoregulation. He/She needs external cooling to decrease his/her body temperature and reduce risk. Since we have a strong but indirect hint towards "fever", the proposition "if thermoregulation then fever" is assigned a truth value smaller than 1.0 (here we assigned 0.8).

Table 1 shows the thresholds of the clinical concepts *increased body temperature, increased C-reactive protein, leukopenia,* and *leukocytosis*. The column "pathological range" contains thresholds as defined in the HAI surveillance definitions published by CDC/NHSN [3], ECDC [4], and KISS [5]. Data assigned to this column are constitutive elements of the surveillance results of these HAIs—provided the other relevant clinical concepts for this infection also fall into this definite pathological range.

The column "borderline range" is an additional range for borderline values and for assigning fuzzy degrees to the respective concept under consideration. By doing so, a body temperature of 37.9 °C signifies increased body temperature to the degree of 0.8. This column will include those patient days for which the clinical concept evaluation yields a near-pathological value, but misses the crisp thresholds defined for classical surveillance.

In classical surveillance, all data in the "normal range" and under the "borderline range" will be regarded as non-pathological and not concurring with the respective HAI surveillance definition. They are cut by a crisp threshold into "black and white". In contrast, the HAI alert criteria are furnished with borderline ranges to recognize tendencies and sense clinically important developments in the patient's state.

Table 1 – Four clinical concepts and their definition by fuzzy sets in the Moni-ICU knowledge base

Clinical Concept (Unit)	**Fuzzy Set**		
	Normal Range	**Borderline Range**	**Pathological Range**
Increased body temperature (fever) (°C)	< 37.5	37.5 – 38.0 [1)]	> 38.0 [2)]
Increased C-reactive protein (CRP) (mg/dl)	< 1.0	1.0 – 6.0 [3)]	> 6.0 [3)]
Leukopenia (WBC/mm^3)	> 5,000	4,000 – 5,000 [4)]	< 4,000 [2)]
Leukocytosis (WBC/mm^3)	< 11,000	11,000 – 12,000 [4)]	> 12,000 [2)]

[1)] as defined by clinicians
[2)] as defined by CDC/NHSN [3], ECDC [4], and KISS [5] for retrospective surveillance purposes
[3)] as defined by clinicians; CRP is an early phase protein, useful as an "infection radar" for prospective purposes
[4)] as defined by clinicians; white blood cell count (WBC) is a slowly reacting indicator, important for surveillance purposes

Study on fuzzy terms and fuzzy logic

In a retrospective study encompassing data for the whole of the year 2011, we analyzed all patient stays in ten ICUs for adult patients of the VGH. All patients aged 18 years or older were included, except admissions for less than 48 hours and the first 48 hours of longer admissions [4]. All clinical concepts and all included HAI surveillance definitions were established according to [4]. However, the borderline ranges were defined by clinical experts from the VGH in our group, referred to as clinicians.

The aim of the study was to determine the extent of borderline pathological states and borderline HAI results in the population under investigation, as a result of applying fuzzy terms and fuzzy logic.

For the analysis, data filtering and cleaning were done in both Python and Microsoft Excel 2007.

Results

Moni's routine operation

At present Moni is established at the VGH for ten ICUs with 87 beds for adults, and four neonatal ICUs with 51 positions. The ICUs and the microbiology department provide about 30,000 relevant data items for Moni-ICU and Moni-NICU every day. For each of the 138 patients, the available knowledge packages containing 72 MLMs for Moni-ICU and 160 MLMs for Moni-NICU are invoked automatically. Clinical concepts, higher-level intermediate clinical concepts, and the topmost HAI definitions are evaluated.

Results of fuzzy terms and fuzzy logic study

During the study period, 2,105 patients stayed at one or more of the selected ICUs; 1,253 patients were male (59.5%) and 844 female (40.1%); gender was not recorded for eight patients. The patients' ages ranged from 18 to 98 years (median 61 years; inter-quartile range 22). In total, 2,429 patient stays were recorded, amounting to 24,487 patient days. The duration of the stay ranged from 2 to 135 days (median 6 days; inter-quartile range 8). Of the 24,487 patient days, 162 were unaccounted for due to export and registration problems, which left 24,325 for data analysis.

For the analysis, we considered the definitions of bloodstream infection (BSI), general central-venous-catheter-associated infection (CRI2), microbiologically confirmed symptomatic urinary tract infection (UTI-A), and not microbiologically confirmed symptomatic urinary tract infection (UTI-B) [4]. Pneumonia was omitted because radiology findings are not yet part of the automated data importation into Moni-ICU. We also did not include local central-venous-catheter-associated infection (CRI1) because its definition in the knowledge base did not contain any fuzzy sets or fuzzy rules.

Table 2 (the first four lines) shows that a significant number of patient data fall into the established borderline ranges (11,474 of 97,300 = 11.8%). This is a relatively high number and indicates a possible near miss in case of HAI surveillance, but a clinically useful indication for HAI alerting.

As shown in Table 2 (last line), in 12.5% of the patient days, at least one of the definitions of the included HAIs (BSI or CRI2 or UTI-A or UTI-B) was fulfilled; a further 2.5% yielded a borderline result, i.e., fulfilled to a certain degree. Notably, in the case of several fulfilled HAI definitions only one was counted, where "present" superseded "borderline" and "borderline" superseded "absent". Moreover, in 606 patient days these data constellations obviously yielded an HAI borderline result. These borderline HAI results are shown, the data are explained fully, and clinicians have the option to explore and judge these results.

Furthermore, the majority of HAI surveillance definitions require microbiology test results. If not available (no specimen for culture taken), classical surveillance would record the respective patient day with "no HAI" despite the presence of clinical signs of infection. Applying "weaker" definitions of HAI surveillance definitions, many of those patient days will fall into the "borderline" category.

Validation of fuzzy sets

Whether the definitions of the fuzzy sets for clinical concepts were adequately chosen to capture those borderline values that rightly generate borderline HAI surveillance results were tested and reported on in a previous study [11]. This investigation was based on central-venous-catheter-associated infections (CRIs) and confirmed, in statistical terms, that most of the expert-defined fuzzy sets and logical constructs currently included in the knowledge base of Moni-ICU are an accurate representation of the CRI borderline patient population.

Clinical studies

Studies addressing the aspect of efficacy have shown the excellent conformance of Moni-ICU with an established clinical reference standard, as well as Moni-ICU's superiority in minimizing time demands on the infection control team with respect to electronically supported versus purely human surveillance. The results can be found in [12, 13].

Table 2 – Frequency distribution of the results of four clinical concepts modeled by fuzzy sets, as well as the topmost HAI definitions (based on a total of 24,325 patient days)

Clinical Concept	Absent n (%)	Borderline n (%)	Present n (%)
Increased body temperature (fever)	16,074 (66.1)	3,421 (14.0)	4,830 (19.9)
Increased C-reactive protein (CRP)	4,383 (18.0)	5,841 (24.0)	14,101 (58.0)
Leukopenia	22,991 (94.5)	668 (2.8)	666 (2.7)
Leukocytosis	15,169 (62.4)	1,544 (6.3)	7,612 (31.3)
BSI or[1)] CRI2 or UTI-A or UTI-B	20,687 (85.0)	606 (2.5)	3,032 (12.5)

[1)] inclusive disjunction with precedence of "present" over "borderline" over "absent"

Table 3 – 3x3 contingency tables for four clinical concepts and the topmost HAI definitions

Clinical Concept		**BSI or[1)] CRI2 or UTI-A or UTI-B**		
		Absent	**Borderline**	**Present**
Increased body temperature (fever)	*Absent*	13,911 (57.2)	484 (2.0)	1,679 (6.9)
	Borderline	2,855 (11.7)	122 (0.5)	444 (1.8)
	Present	3,921 (16.1)	0	909 (3.7)
Increased C-reactive protein (CRP)	*Absent*	4,130 (17.0)	152 (0.6)	101 (0.4)
	Borderline	4,890 (20.1)	453 (1.9)	498 (2.0)
	Present	11,667 (48.0)	1 (0.0)	2,433 (10.0)
Leukopenia	*Absent*	19,578 (80.5)	564 (2.3)	2,849 (11.7)
	Borderline	569 (2.3)	42 (0.2)	57 (0.2)
	Present	540 (2.2)	0	126 (0.5)
Leukocytosis	*Absent*	13,201 (54.3)	551 (2.3)	1,417 (5.8)
	Borderline	1,306 (5.4)	54 (0.2)	184 (0.8)
	Present	6,180 (25.4)	1 (0.0)	1,431 (5.9)

[1)] inclusive disjunction

Discussion

"Crisp" and "fuzzy" definitions

Surveillance as well as benchmarking count on unambiguous consensus definitions, which can easily be shared in networks, but are often compromises negotiated in long expert discussions. Clinicians and intensive care specialists dislike stolid definitions; they prefer a more flexible interpretation of patient data with focus on transition from normal to pathological states, and on borderline situations.

The Moni IT system provides retrospective population-specific infection surveillance related to classical infection surveillance, as well as prospective patient-specific high-level data aggregation for clinical support in early detection of infection. Here, fuzzy logic revealed its potential and aroused the interest as well as cooperation of intensive care specialists.

Benefit of borderline

It should be noted that our analysis counted patient days in which HAI criteria were present and not HAI episodes, each of which usually lasts for several days. International networks report their rates in numbers of HAI episodes per, such as 1,000 patient days or device days (which means days under specific exposure).

Patient days with fever, increased CRP, or leukocytosis were counted more often than days with fulfilled HAI definitions (see last column in Table 2). This can be explained by two facts: a) infection is only one of several conditions which trigger such pathologies, b) HAI definitions are composed of a number of pathologies, often including microbiological verification of the infective agent, all of which must be present. Since microbiological verification of the infective agent is a significant part of many HAI definitions, omission of specimens for microbiological investigations leads to underreporting of HAIs and might explain at least part of the borderline group in our analysis.

The borderline HAI group (2.5% of the totally tested 24,325 patient days) is not very large, but adds another fifth to the number of days with HAIs. It is—by the design of surveillance definitions—not relevant for retrospective surveillance. For the clinician, however (especially when he/she checks Moni's results at least once a day), it might serve as a "radar" for early detection of an incipient HAI. This is very valuable prospective information and a priceless benefit for the individual patient.

The absence of elevated body temperature in 6.9% of patient days, although the patients' data were fully compatible with one of the HAIs (Table 3, first line), might be explained by the frequent use of external thermoregulation for patients with fever (for instance with a cooling blanket). Hence, body temperature was considered normal in patients receiving external thermoregulation. The latter is captured by a separate fuzzy rule, which was not investigated in the present study.

Patient days with fever, increased CRP, leukopenia or leukocytosis fell either into the "absent" or the "present" class of the topmost HAI definitions, but never in the respective "borderline" class—except for one patient day with increased CRP and one with leukocytosis (Table 3, middle column). This can be explained by the following: a) a single clinical concept may or may not be part of a specific HAI definition, and b) a HAI definition is fulfilled when only one of a number of clinical concepts applies (i.e., when the rule defines that either A or B or C is present). We regard this as further proof of the previously reported [12] excellent precision of Moni's interpretation of infection-relevant clinical data.

The numbers and percentages in Table 3 in the borderline categories need further analysis, which will be the subject of another study. It may be stated here, however, that the numbers reflect the previously mentioned difference between clinical concepts as part of HAI definitions and the entire HAI definition itself, as well as different "constituents" of different HAI definitions.

Legal considerations

As long as Moni is applied for surveillance purpose—whether for in-hospital, national, or international quality benchmarking—it is not regarded as a medical device in accordance with the European Medical Device Directive 93/42/EEC. Even when the surveillance functionality of Moni is used by ward physicians at the patient's bedside to evaluate the patient's clinical condition (with potential impact on diagnosis and therapy), the intended use of Moni—as defined by the manufacturer—is strictly confined to surveillance.

Moni's alert component differs in this regard. The medical purpose here—as defined by the manufacturer—is to alert the attending physician, identify infection as early as possible, and incorporate the fact into the patient's treatment and care. Thus, the alert component is a medical device.

At present, the application of Moni's alert section is under clinical evaluation. It is being used and tested by several key clinical users who have received appropriate instructions.

Methodological perspectives

Moni-ICU was designed as a purely knowledge-based system with detailed explanatory capabilities. It does not rely on machine learning. The applied clinical knowledge for HAI surveillance is based on international consensus surveillance criteria, which are well known to the medical community. In addition, extended clinical experience is employed to establish useful alert criteria. The explanatory system clearly states what is included in the system and what is not, thus providing full transparency of any inferred clinical result. The approach of stepwise abstraction and aggregation is very similar to human reasoning in clinical medicine. Fuzzy set theory and logic avoid "jumps" in reasoning.

Conclusion

High precision of surveillance results, fully automated acquisition of relevant clinical and laboratory data, and significant time saving for ICPs have been prominent features of earlier versions of this electronic surveillance tool. Now, with broad application of fuzzy set theory and fuzzy logic, the scope of the system has been widened significantly. Comprehension of the inherent uncertainty of linguistic clinical terms and clinical or practice-based propositions, and thus straightforward "intelligent" processing of patients' borderline values, make it a powerful clinical extension of classical infection surveillance.

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Conflict of interest

Klaus-Peter Adlassnig is also co-founder, CEO, and Scientific Head of Medexter Healthcare GmbH, Vienna, Austria. Medexter Healthcare GmbH has been established to develop and disseminate decision support systems with confirmed applicability in the clinical setting.

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Address for correspondence

Professor Walter Koller, Martinstrasse 26, A-1180 Vienna, Austria.
walter.koller@meduniwien.ac.at