Automated, fuzzy-based monitoring of healthcare-associated infections—fundamentals and demonstration

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Clinical cooperation

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- Univ.-Prof. Dr. Angelika Berger
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plus

clinical users
- Department of Laboratory Medicine, Division of Clinical Virology
- Department of Medicine I, Clinical Division of Infection and Tropical Medicine
Computers in clinical medicine—steps of natural progression

• step 1: patient administration
  • admission, transfer, discharge, and billing

• step 2: documentation of patients’ medical data
  • electronic health record: all media, distributed, life-long

• step 3: patient and hospital analytics
  • data warehouses, quality measures, reporting and research databases, patient recruitment
    ... population-specific

• step 4: clinical decision support
  • safety net, quality assurance, evidence-based
    ... patient-specific
Clinical decision support and quality assurance (in general)

patients’ structured medical data

<table>
<thead>
<tr>
<th>diagnostic support</th>
<th>therapy advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>• clinical alerts, reminders, calculations</td>
<td>• drug alerts, reminders, calculations</td>
</tr>
<tr>
<td>• data interpretation, (tele)monitoring</td>
<td>– indication, contraindications, redundant medications, substitutions</td>
</tr>
<tr>
<td>• differential diagnostic consultation</td>
<td>– adverse drug events, interactions, dosage calculations, consequent orders</td>
</tr>
<tr>
<td>– rare diseases, rare syndromes</td>
<td>• management of antimicrobial therapies, resistance</td>
</tr>
<tr>
<td>– further or redundant investigations</td>
<td>• (open-loop) control systems</td>
</tr>
<tr>
<td>– pathological signs accounted for</td>
<td></td>
</tr>
<tr>
<td>• consensus-criteria-based evaluation</td>
<td></td>
</tr>
<tr>
<td>– definitions</td>
<td></td>
</tr>
<tr>
<td>– classification criteria</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>prognostic prediction</th>
<th>patient management guidelines &amp; quality assurance</th>
</tr>
</thead>
<tbody>
<tr>
<td>• illness severity scores, prediction rules</td>
<td>• evidence-based reminders and processes</td>
</tr>
<tr>
<td>• trend detection and visualization</td>
<td>• computerized clinical guidelines, protocols, SOPs</td>
</tr>
<tr>
<td></td>
<td>• healthcare-associated infection surveillance</td>
</tr>
</tbody>
</table>
ESBL – extended-spectrum beta-lactamase-producing bacteria

VRE – vancomycin-resistant enterococcus

MRSA – methicillin-resistant Staphylococcus aureus

MDR-TB – multidrug-resistant tuberculosis

increased disposition by low immunity

exposure to pathogens

entry sites
Background

Fact
Healthcare authorities demand—for good reasons—installation and regular application of healthcare-acquired infection (HAI) surveillance as part of quality management.

Dilemma
HAI surveillance is a time-consuming task for highly trained experts; unavailability of a suitable workforce meets increasing financial constraints.

Challenge
Obtaining reliable surveillance results without urging or relying on doctor’s or nurse’s time resources for retrieving and documenting surveillance data.
Specific characteristics of intensive care units

Electronic patient data management systems (PDMSs):

- are installed and in use in many ICUs
- receive continuous automated input from monitoring devices (vital parameters) and from laboratories (usually without microbiology)
- ICU caregivers are familiar with the documentation of patient-related clinical information into PDMSs
  - PDMSs thus hold structured clinical data relevant for infection surveillance; in addition, microbiological data have to be accessed (through the respective laboratory information system (LIS))
Target
Development and implementation of intelligent, knowledge-based software able to extract and analyze healthcare-associated infection (HAI)-related surveillance information from structured clinical and laboratory data held in PDMSs and LISs

Moni-ICU and Moni-NICU
Monitoring (for surveillance and alerts) of HAIs in ICUs with adult patients and in NICUs with neonatal patients

Characteristics
(1) PDMSs and LISs as electronic data sources provide structured medical data
(2) medical knowledge bases with computerized knowledge of all included clinical entities
(3) processing algorithms evaluate, aggregate, and interpret clinical data in a stepwise manner until raw data can be mapped into the given HAI definitions
Monitoring of nosocomial infections

- Artificial intelligence
- Fuzzy theories
- Knowledge-based systems
- Fuzzy sets and logic
- ICU clinical data
- Microbiology: data on microorganisms
- Natural-language definitions of nosocomial infections
- ICU patient-specific alerts
- ICU cockpit surveillance at ward
- Infection control: cockpit surveillance remote
- Medicine

Processing layers

layer n (goal)
- linguistic HAI definitions
  - y inference steps

layer n-y
- intermediate concepts: pathophysiological states
  - x inference steps

layer n-x-y
- basic concepts: symptoms, signs, test results, clinical findings

layer n-x-y-1
- abstraction: rules, type-1 & type-2 fuzzy sets, temporal abstraction

layer 2
- feature extraction: mean values, scores, ...

layer 1
- preprocessing: missing data, plausibility, ...

layer 0 (start)
- ICU, NICU, and microbiology patient data bases

reasoning

symbols

data-to-symbol conversion

raw data

CDC, ECDC, KISS
Arden Syntax and Health Level Seven (HL7)

- A standard language for writing situation-action rules that can trigger alerts based on abnormal clinical events detected by a clinical information system.

- Each module, referred to as a Medical Logic Module (MLM), contains sufficient knowledge to make a single decision.
  - extended by packages of MLMs for complex clinical decision support

- The Health Level Seven Arden Syntax for Medical Logic Systems, Version 2.9— including fuzzy methodologies—was approved by the American National Standards Institute (ANSI) and by Health Level Seven International (HL7) on 14 March 2013.
General MLM Layout
- Maintenance Category
- Library Category
- Knowledge Category
- Resources Category

Identify an MLM

Data Types

Operators
- Basic Operators
- Curly Braces
- List Operators
- Logical Operators
- Comparison Operators
- String Operators
- Arithmetic Operators
- Other Operators

Control Statements

Call/Write Statements and Trigger
Sample MLM (excerpt)

logic:
result := new bmiResult; // create an empty result object

weight := latest of weights; // get the latest weight from the list

size := call mlmForReadSize with patientID; // get the size of the patient calculated by another MLM

result.bmi := weight / (size ** 2); // calculation of BMI
age := currenttime - birth; // calculation of AGE

// classification - the classification is only valid for patients older than 19
if the age is less than 19 years then result.classification := null;
elseif the result.bmi is less than 18.5 then result.classification := localized 'under';
elseif the result.bmi is less than 25 then result.classification := null;
else let the result.classification be localized 'over';
endif;

result.bmi := result.bmi formatted with localized 'msg'; // construct the localized message

if (time of weight) is before (currenttime - 6 months) then
 conclude false; //no bmi calculation if the latest measure was 6 months ago
else
 conclude result.classification is present ; // if there is a classification, execute the action slot
endif;

::
Translation of HAI definitions into IT terminology—example: bloodstream infections (BSIs)

HELICS-protocol HAI in ICU, version 6.1, Sep. 2004

**Recognized pathogen**

**BSI-A:** Patient has at least one of the following signs or symptoms: fever (>38°C), chills, or hypotension and 2 positive blood cultures for a common skin contaminant from two separate blood samples drawn within 48 hours.

- **skin contaminants = coagulase-negative staphylococci, Micrococcus sp., Propionibacterium acnes, Bacillus sp., Corynebacterium sp.**

**BSI-B:** Patient has at least one of the following signs or symptoms: fever (>38°C), chills, or hypotension.

And either

- 1 positive blood culture with a skin contaminant in patient with an intravascular line in place and in whom the physician instituted appropriate antimicrobial therapy.

*Or*

- positive blood Antigen test (e.g. *H.influenzae, S.pneumoniae, N meningitidis* or Group B *Streptococcus*)

**Comment:** BSI-A is the definition used by the majority of NI surveillance networks in Europe. BSI-B extends this definition to the CDC definition of laboratory-confirmed bloodstream infection. Networks should specify in the network data (table icu.net, see 6.3.1) whether only BSI A or both BSI B and BSI A are included in the surveillance (i.e. networks using CDC definition of laboratory confirmed bloodstream infection [CDC.com/BSI-A+B]). If this is the case, then BSI A and BSI B categories should be specified in the data collection.

**OR clinical signs AND growth of same skin contaminant from two separate blood samples**

**OR clinical signs AND growth of same skin contaminant from blood AND intravascular line**

**OR clinical signs AND positive antigen test from blood**
A bloodstream infection—with clinical signs and growth of same skin contaminant from two separate blood samples

- Patient has at least one of the following signs or symptoms: fever (>38°C), chills, or hypotension and 2 positive blood cultures for a common skin contaminant (from 2 separate blood samples drawn within 48 hours).

skin contaminants = coagulase-negative staphylococci, Micrococcus sp., Propionibacterium acnes, Bacillus sp., Corynebacterium sp.

BSI-A2

\[
1 \Leftarrow \text{clinical_signs_of_BSI (t-1d, t, t+1d)} \land \text{same_skin_contaminant_from_two_separate_blood_samples}
\]
Decomposition—clinical signs

clinical_signs_of_BSI (t-1d, t, t+1d)[yesterday, today, tomorrow]

= feverT (t-1d)
  ∨ hypotension (t-1d)
  ∨ leucopenia (t-1d)
  ∨ leucocytosis (t-1d)
  ∨ CRP increased (t-1d)

  \[ \begin{align*}
  \text{clinical_signs_of_BSI (t-1d)} &= \left\{ 
  \quad \text{feverT (t-1d)} \\
  \quad \text{hypotension (t-1d)} \\
  \quad \text{leucopenia (t-1d)} \\
  \quad \text{leucocytosis (t-1d)} \\
  \quad \text{CRP increased (t-1d)}
  \end{align*} \right\} \\
  \text{clinical_signs_of_BSI (t)} &= \left\{ 
  \quad \text{feverT (t)} \\
  \quad \text{hypotension (t)} \\
  \quad \text{leucopenia (t)} \\
  \quad \text{leucocytosis (t)} \\
  \quad \text{CRP increased (t)}
  \end{align*} \right\} \\
  \text{clinical_signs_of_BSI (t+1d)} &= \left\{ 
  \quad \text{feverT (t+1d)} \\
  \quad \text{hypotension (t+1d)} \\
  \quad \text{leucopenia (t+1d)} \\
  \quad \text{leucocytosis (t+1d)} \\
  \quad \text{CRP increased (t+1d)}
  \end{align*} \right\} 
\]
Linguistic uncertainty defined by fuzzy sets—example: fever

\[
\text{fever}_T(t-1d) \iff \ldots
\]

\[
\text{fever}_T(t) \iff \bigvee
\]

thermoregulation applied \ldots

\[
\text{fever}_T(t+1d) \iff \ldots
\]
Decomposition—skin contaminant

same_skin_contaminant_from_two_separate_blood_samples \iff

\begin{align*}
\text{first blood culture} & \land \\
\text{- coagulate-negative staphylococci} & \land \\
\text{- Micrococcus sp.} & \land \\
\text{- Propionibacterium acnes} & \land \\
\text{- Bacillus sp.} & \land \\
\text{- Corynebacterium sp.} & \land \\
\text{second blood culture} & \land \\
\text{- coagulate-negative staphylococci} & \land \\
\text{- Micrococcus sp.} & \land \\
\text{- Propionibacterium acnes} & \land \\
\text{- Bacillus sp.} & \land \\
\text{- Corynebacterium sp.} & \land \\
\text{(within 48 hours)} & \land
\end{align*}

data import microbiology
Uncertainty in medicine

- **imprecision** (=fuzziness) of medical concepts
  - due to the unsharpness of boundaries of linguistic concepts; gradual transition from one concept to another
  - modeled by fuzzy sets

- **uncertainty** of medical conclusions
  - due to the uncertainty of the occurrence and co-occurrence of imprecise medical concepts
  - modeled by SigmaCounts (unconditioned and conditioned frequencies of fuzzy sets)

- **incompleteness** of medical data and medical theory
  - due to only partially known data and partially known explanations for medical phenomena
  - modeled by fuzzy intervals
Crisp sets vs. fuzzy sets

yes/no decision

\[ U = [0, 120] \]
\[ Y \subseteq U \text{ with } Y = \{ (\chi_Y(x)/x) \mid x \in U \} \]
\[ \chi_Y: U \rightarrow \{0, 1\} \]
\[ \chi_Y(x) = \begin{cases} 
0 & x > \text{threshold} \\
1 & x \leq \text{threshold} 
\end{cases} \quad \forall x \in U \]

gradual transition

\[ U = [0, 120] \]
\[ Y \subseteq U \text{ with } Y = \{ (\mu_Y(x)/x) \mid x \in U \} \]
\[ \mu_Y: U \rightarrow [0, 1] \]
\[ \mu_Y(x) = \begin{cases} 
\frac{1}{1 + (0.04 x)^2} & x > \text{threshold} \\
1 & x \leq \text{threshold} 
\end{cases} \quad \forall x \in U \]
Clinical concept “fever”—Arden vs. Fuzzy Arden Syntax

- crisp boundary
  - borderline cases are not detected
  - result is 0[false] or 1[true]

- fuzzified boundary
  - borderline cases are detected
  - result is 0[false], between 0 and 1[true to a certain degree], or 1[true]
Different results—Arden vs. Fuzzy Arden Syntax

**Arden Syntax**

```plaintext
fever_boundary := 38;

temperature := 37.9;

message := "patient has no fever";
IF temperature > fever_boundary THEN
    message := "patient has fever";
END IF
```

- result: “patient has no fever”

**Fuzzy Arden Syntax**

```plaintext
fever_boundary := 38 fuzzified by 0.5;

temperature := 37.9;

message := "patient has no fever";
IF temperature > fever_boundary THEN
    message := "patient has fever";
END IF
```

- result: “patient has fever” (with applicability 0.8)
Linguistic variable

- Construct to represent a linguistic concept and its sub-concepts
- Subsumes the sub-concepts of a concept under one term
- Definition of a linguistic variable

  ```
  data:
  simpleBMI := LINGUISTIC VARIABLE [underweight,normal,overweight];
  logic:
  BMI := new simpleBMI ;
  BMI.underweight := FUZZY SET (18.5,1), (19.5,0);
  BMI.normal := FUZZY SET (18.5,0), (19.5,1), (24,1), (25,0);
  BMI.overweight := FUZZY SET (24,0), (25,1);
  ```
If-Then

Source

```
maintenance: [...]
knowledge: [...]
logic:
    //define BMI as above
    ...
myBMI := 24.8;
x := myBMI <= BMI.overweight;
if x then
    // this branch is executed
    // with applicability 0.8
    <then_block>
else
    // this branch is executed
    // with applicability 0.2
    <else_block>
endif;
[...]
end:
```
Arden Syntax server and software components

- Arden Syntax integrated development and test environment (IDE) including
  - Medical logic module (MLM) editor and authoring tool
  - Arden Syntax compiler (syntax versions 2.1, 2.5, 2.6, 2.7, 2.8, and 2.9)
  - Arden Syntax engine
  - MLM test environment
  - MLM export component
- command-line Arden Syntax compiler
- web-services-based Arden Syntax server including
  - Arden Syntax engine
  - MLM manager
  - XML-protocol-based interfaces, e.g., SOAP, REST, and HL7
  - a project-specific data and knowledge services center may be hosted
- Java libraries
  - Arden Syntax compiler
  - Arden Syntax engine
### Present state of Moni at the Vienna General Hospital (I)

<table>
<thead>
<tr>
<th></th>
<th>10 ICUs with 87 beds</th>
<th>2 NICUs and 2 NIMCs with 51 beds</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>knowledge base</strong></td>
<td>• 72 Arden Syntax MLMs (1 control, 70 clinical rules, 1 storage) for 24 ECDC (+ 15 ITS-KISS) definitions</td>
<td>• 161 Arden Syntax MLMs (1 control, 159 clinical rules, 1 storage) for 9 NEO-KISS definitions</td>
</tr>
<tr>
<td></td>
<td>• 72 Arden Syntax MLMs (1 control, 70 clinical rules, 1 storage) for 24 ECDC (+ 15 ITS-KISS) definitions</td>
<td>• 161 Arden Syntax MLMs (1 control, 159 clinical rules, 1 storage) for 9 NEO-KISS definitions</td>
</tr>
<tr>
<td></td>
<td>• data items</td>
<td>• data items</td>
</tr>
<tr>
<td></td>
<td>• 156 (+ 170) parameters</td>
<td>• 281 parameters</td>
</tr>
</tbody>
</table>
### Present state of Moni at the Vienna General Hospital (II)

<table>
<thead>
<tr>
<th>Data Input (approx. 15 minutes)</th>
<th>Data Input (approx. 2 minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• clinic: 17–19,000 data items per day from Philips ICCA</td>
<td>• clinic: about 30,000 data items per day from Philips ICCA</td>
</tr>
<tr>
<td>• microbiology: 21–25 relevant findings per day</td>
<td>• microbiology: about 80 relevant findings (pos and neg) per day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Processing (approx. 15 minutes)</th>
<th>Processing (approx. 12 minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 110–125 compliance evaluations with all definitions each day</td>
<td>• 45 compliance evaluations with all definitions each day</td>
</tr>
<tr>
<td>• 7,920–9,000 MLMs processed each day (maximum)</td>
<td>• about 7,000 MLMs processed each day</td>
</tr>
<tr>
<td>• 10–35 MLMs per second</td>
<td>• about 38 MLMs per second</td>
</tr>
</tbody>
</table>
Moni output

- **advanced cockpit surveillance**  
  graphical user interface displays daily “infection patterns”; and allows for deep insight at the level of vital parameters and basic clinical indicators for every patient

- **standard ward reporting**  
  provides surveillance results of ICUs in tables and graphs for periodic epidemiology reporting to our hospital’s Clinical Institute of Hospital Hygiene, as well as separately for each ICU

- **automated reminders (alerts)**  
  for conditions related to hospital-acquired infections (example: sepsis prediction)
Advanced cockpit surveillance

Each line in graph shows one patient stay.

One patient stay selected at ward.

One day exploded.

Colors indicate patient days with infection and % fuzzy degree of compliance with case definitions for healthcare-associated infections.

Underlying clinical, lab, and RX findings.

Healthcare-associated infection rules that have fired plus % fuzzy degree of compliance.
Moni output

Section of Moni screenshot for one ICU: Colors indicate patients with infection episodes
Standard ward reporting (I)

**Denominator data**

- admissions
- patient days
- mean length of stay (days)
Standard ward reporting (II)

Device use

- urine catheter days
- central venous catheter days
- respirator days
Standard ward reporting (III)

healthcare-associated infection by syndrome

catheter-related infection (CRI) by type

central-venous-catheter (CVC)-associated CRI rate (n/1000 device days)
Standard ward reporting (IV)

- Urinary tract infection (UTI) by type (k=with, nk=without catheter)
- Urine-catheter-associated UTI rate (n/1000 device days)
- Urine catheter use rate (n/1000 patient days)
- UTI incidence rate (n/1000 patient days)
First study:

⇒ 99 ICU patient admissions; 1007 patient days

<table>
<thead>
<tr>
<th>HAI episodes correctly / falsely identified or missed by Moni-ICU</th>
<th>episode present “gold standard” (n= 19)</th>
<th>episode absent “gold standard” (n= 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>episode present “Moni-ICU”</td>
<td>16 (84%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>episode absent “Moni-ICU”</td>
<td>3 (16%)</td>
<td>78 (100%)</td>
</tr>
</tbody>
</table>

Time expenditures for both surveillance techniques

<table>
<thead>
<tr>
<th></th>
<th>conventional surveillance</th>
<th>Moni-ICU surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>time spent</td>
<td>82.5 h (100%)</td>
<td>12.5 h (15.2%)</td>
</tr>
</tbody>
</table>

Second study:

⇒ 93 ICU patient admissions; 882 patient days

HAI episodes correctly / falsely identified or missed by Moni-ICU

<table>
<thead>
<tr>
<th></th>
<th>I+</th>
<th>I-</th>
</tr>
</thead>
<tbody>
<tr>
<td>I+</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>I-</td>
<td>4</td>
<td>75</td>
</tr>
</tbody>
</table>

\[\text{gold standard}\]

- sensitivity = 87%
  - missed 3 pneumonia + 1 CVC-related infection due to missing microbiology
- specificity = 99%
  - added 1 pneumonia + 1 CVC-related infection due to concomitant leukemia

Conclusions

- high specificity (= rare “false alarms”) with MONI surveillance

- 85% of doctors’ and nurses’ time saved with MONI compared to manual/conventional surveillance

- when PDMSs and LISs provide up-to-date clinical and denominator data, intelligent IT can provide valuable surveillance reports on demand and do it fast!

- MONI is also suited for day-to-day follow-up of infections and may support clinical decisions in ICUs and NICUs

- MONI enhances transparency of a hospital’s infection episodes and supports scientific work-up of unresolved questions
Combined reasons for Moni’s success

• clinical
  • no diagnoses, but graded compliance with definitions
  • no additional data entry
  • two-step reporting: (1) automated generation and (2) expert verification

• methodological
  • pure knowledge-based system with explanation component
  • consensual classification criteria
  • hierarchical layers of data and knowledge
  • fuzzy set theory and logic

• technical
  • separation of PDMS data collection, microbiology data collection, service-oriented rule engine server, knowledge packages, and web-based infection control cockpit
  • integration of different hospital IT systems (PDMS, LIS, CDSS server)

• administrative
  • digitized uniform PDMS data sources at the connected ICUs and data from microbiology
  • support by medical administration
  • several lead users