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

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Clinical decision support for patient safety and quality assurance

patients’ structured medical data (HIS, LIS, PDMS, Web, documentation)

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**diagnostic support**
- alerts, reminders, to-do lists
- clinical interpretation, (tele)monitoring
- differential diagnostics
  - rare diseases, rare syndromes
  - further or redundant examinations
  - diagnostic completeness (multi-morbidity)
- consensus-criteria-based evaluations
  - disease classification and surveillance criteria

**prognostic prediction**
- illness severity scores, prediction rules
- trend detection and visualization

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**therapy advice**
- drug alerts, reminders, calculations
  - indication, contraindications, redundant medications, substitutions
  - adverse drug events, interactions, dosage calculations, consequent orders
- management of antimicrobial therapies, resistance
- (open-loop) control systems

**hospital management and quality benchmarking**
- evidence-based reminders and processes
- computerized clinical guidelines, protocols, SOPs
- healthcare-associated infection surveillance

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**highly-structured medical knowledge (rules, tables, trees, guidelines)**
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 containing computerized knowledge of every clinical entities involved
3. Processing algorithms evaluate, aggregate, and interpret clinical data stepwise 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 patient-specific alerts

ICU cockpit surveillance at ward

Infection control cockpit surveillance remote

MICU clinical data

Microbiology data on microorganisms

Natural-language definitions of nosocomial infections

Medicine

linguistic HAI definitions

animal concepts:
symptoms, signs, test results, clinical findings

intermediate concepts:
pathophysiological states

abstraction:
rules, type-1 & type-2 fuzzy sets, temporal abstraction

feature extraction:
mean values, scores, …

preprocessing:
missing data, plausibility, …

ICU, NICU, and microbiology patient data bases

inference steps reasoning

symbols

data-to-symbol conversion

raw data

patient-specific cockpit & legal reporting & quality benchmarking
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

• Version 2.10—including ArdenML, an XML-based representation of Arden Syntax MLMs—was approved on 6 May 2014
  ➢ continuous development since 1989
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
Translation of HAI definitions into IT terminology—example: bloodstream infections (BSIs)

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

IT statement in free language

Recognized pathogen

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 <=
clinical_signs_of_BSI (t-1d, t, t+1d)
^ same_ski_contaminant_from_two_separate_blood_samples
Decomposition—clinical signs

clinical_signs_of_BSI (t-1d, t, t+1d)[yesterday, today, tomorrow]  
=  
clinical_signs_of_BSI (t-1d)  
=  
feverT (t-1d)  
∨  
hypotension (t-1d)  
∨  
leucopenia (t-1d)  
∨  
leucocytosis (t-1d)  
∨  
CRP increased (t-1d)  
∨  
clinical_signs_of_BSI (t)  
=  
feverT (t)  
∨  
hypotension (t)  
∨  
leucopenia (t)  
∨  
leucocytosis (t)  
∨  
CRP increased (t)  
∨  
clinical_signs_of_BSI (t+1d)  
=  
feverT (t+1d)  
∨  
hypotension (t+1d)  
∨  
leucopenia (t+1d)  
∨  
leucocytosis (t+1d)  
∨  
CRP increased (t+1d)
Linguistic uncertainty defined by fuzzy sets—example: fever

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

\[
\text{feverT (t)} \iff \lor
\]

\[
\text{thermoregulation applied } \ldots
\]

\[
\text{feverT (t+1d)} \iff \ldots
\]

\[
\text{data import}
\]

\[
\text{intensive care unit}
\]

\[
\text{maximum value of the day e.g., } 38.5 \, ^\circ\text{C}
\]

[Graph showing a fuzzy set for fever temperature with threshold at 38.5 °C]
Decomposition—skin contaminant

first blood culture
- coagulase-negative staphylococci
- Micrococcus sp.
- Propionibacterium acnes
- Bacillus sp.
- Corynebacterium sp.

second blood culture
- coagulase-negative staphylococci
- Micrococcus sp.
- Propionibacterium acnes
- Bacillus sp.
- Corynebacterium sp.

\[ \text{same skin contaminant from two separate blood samples} \iff \text{(within 48 hours)} \]

Data import

microbiology

\[ \text{\{first blood culture, second blood culture\}} \]
Fuzzy Arden Syntax: Modelling uncertainty in medicine

- **linguistic uncertainty**
  - due to the unsharpness (fuzziness) of boundaries of linguistic concepts; gradual transition from one concept to another
  - modeled by fuzzy sets, e.g., fever, increased glucose level

- **propositional uncertainty**
  - due to the uncertainty (or incompleteness) of medical conclusions; includes definitional and causal, statistical and subjective relationships
  - modeled by truth values between zero and one, e.g., usually, almost confirming
Two different hyperglycemia definitions

- Crisp threshold for surveillance
- Fuzzified threshold (gradual rise) for alert
Clinical concepts and relationships between them

\( (S_1 \land S_2) \lor \neg S_3 \rightarrow t \rightarrow \text{DoC} \)

truth value

DoC

\[ \text{fever} \]

\[ 37.5 \quad 38.0 \quad 37.9 \quad \text{°C} \]

DoC

1.0

0.8

0
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, 2.9, and 2.10)
  - 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>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><strong>knowledge base</strong></td>
</tr>
<tr>
<td>• 72 Arden Syntax MLMs (1 control, 70 clinical rules, 1 storage) for 24 ECDC (+ 15 ITS-KISS) definitions</td>
<td></td>
</tr>
<tr>
<td>- 3 (+ 2) bloodstream infections</td>
<td></td>
</tr>
<tr>
<td>- 9 (+ 6) ICU-acquired pneumonias</td>
<td></td>
</tr>
<tr>
<td>- 9 (+ 7) urinary tract infections</td>
<td></td>
</tr>
<tr>
<td>- 3 (+ 0) central venous catheter-related infections</td>
<td></td>
</tr>
<tr>
<td>• data items</td>
<td>• data items</td>
</tr>
<tr>
<td>- 156 (+ 170) parameters</td>
<td></td>
</tr>
</tbody>
</table>

- 161 Arden Syntax MLMs (1 control, 159 clinical rules, 1 storage) for 9 NEO-KISS definitions
  - 7 bloodstream infections
  - 2 ICU-acquired pneumonias (suspicion)

- 281 parameters
### 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)
BSI-3 (KISS) 100 %DoC
  klin. Anzeichen f. Pneumonie (KISS) 95 %DoC
  klin. Anzeichen f. Pneumonie (Alert) 95 %DoC
  2 klin. Anzeichen f. Sepsis (KISS) 100 %DoC
  2 klin. Anzeichen f. Sepsis (Alert) 100 %DoC
  laborchem. Zeichen für Pneumonie (Alert) 100 %DoC
  laborchem. Zeichen für Entzündung (Alert) 100 %DoC
  erhöhter Beatmungsaufwand (Alert) 95 %DoC
  erhöhtes CRP (abs. Alert) 100 %DoC
  allgemesenes Trachealsekret 100 %DoC
  imp.: kein Erreger in nicht-Blut ja
  imp.: nicht beatmet (KISS) ja
  imp.: Antinfektivum ja
  imp.: ZVK (Zentralvenenkath.) ja

neue Hyperglykämie (KISS) 100 %DoC
  UND

  Hyperglykämie (KISS) (t-1:d) 100 %DoC

  maximale Glukose 178 mg/dl
    imp.: Glukose 154 mg/dl
    imp.: Glukose 178 mg/dl
    imp.: Glukose 160 mg/dl
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

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

<table>
<thead>
<tr>
<th></th>
<th>episode present &quot;gold standard&quot; (n = 19)</th>
<th>episode absent &quot;gold standard&quot; (n = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>episode present &quot;Moni-ICU&quot;</td>
<td>16 (84%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>episode absent &quot;Moni-ICU&quot;</td>
<td>3 (16%)</td>
<td>78 (100%)</td>
</tr>
</tbody>
</table>

Time expenditure 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; 30 HAI episodes over complete or partial duration of stay; 76 stays with no HAI episodes

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

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

- **sensitivity = 87%**
  - 3 false-negative pneumonias + 1 false-negative CVC-related infection due to missing microbiology

- **specificity = 99%**
  - 1 false-positive CVC-related infection because of a present concomitant leukemia (with leukocytosis)

Significance of nosocomial infections

- 3 to 14% of patients admitted to acute care hospitals acquire one or more nosocomial infections
- in consequence, 5 to 7% of them die

Vienna General Hospital with 2,200 beds:

- patients admitted to wards: 94,715
- days of care: 688,619
- average length of stay: 6.1 days
- costs / patient / day: EUR 678.-

- nosocomial infections: 4,262 patients / year (rate of 4.5% assumed)
- 213 out of them die / year (5% mortality assumed)
- additional costs of EUR 14,448,180.- (5 days of prolonged stay, in average)

source: Prof. Dr. med. Ojan Assadian, Division of Hospital Hygiene, Medical University of Vienna (2002)
Combined reasons for Moni’s success

• clinical
  – no diagnoses, but graded compliance with definitions
  – no need for additional data entry
  – high-level monitoring cockpit
  – two-step reporting: (1) automated generation and (2) expert verification

• methodological
  – pure knowledge-based system with explanatory component
  – consensual surveillance 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
  – uniform digitized PDMS data sources at the connected ICUs and data from microbiology
  – support from medical administration
  – several lead users