Knowledge-based detection and monitoring of healthcare-associated infections in intensive care patients

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### Clinical decision support systems

- **Diagnostic support**
  - clinical alerts, reminders, calculations
  - data interpretation, (tele)monitoring
  - differential diagnostic consultation
    - rare diseases, rare syndromes
    - further or redundant investigations
    - pathological signs accounted for
  - consensus-criteria-based evaluation
    - definitions
    - classification criteria

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

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

- **Patient management guidelines**
  - guideline-based reminders
  - computerized clinical guidelines, protocols, SOPs
  - high-level patient and hospital analytics
Medical information and knowledge-based systems

patient’s medical data

- symptoms
- signs
- test results
- clinical findings
- biosignals
- images
- diagnoses
- therapies
- nursing data

standardization
- telecommunication
- chip cards

physician’s medical knowledge

- anatomy
- biochemistry
- physiology
- pathophysiology
- pathology
- nosology
- therapeutic knowledge
- disease management

subjective experience
- intuition

knowledge-based systems

information systems

- telemedicine

integration

medical statistics
- clustering & classification
- data & knowledge mining
- machine learning

induction

many patients
- general knowledge

clinical decision support
- medical expert systems

deduction

single patient
- general knowledge

diagnosis
- therapy
- prognosis
- management

medical knowledge acquisition
- by clinicians
+ knowledge engineers

telemedicine integration
Nosocomial, or hospital-acquired, infections
increased disposition by low immunity

exposure to pathogens

ESBL - extended spectrum beta-lactamase

VRE - vancomycin-resistant enterococcus

MRSA - methicillin-resistant Staphylococcus aureus

MDR-TB - multidrug-resistant tuberculosis

entry sites
Potential for reducing the rate of hospital-acquired infections

<table>
<thead>
<tr>
<th>hospital-acquired (nosocomial) infections</th>
<th>% reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>wound infections</td>
<td>35</td>
</tr>
<tr>
<td>urinary tract infections</td>
<td>31</td>
</tr>
<tr>
<td>pneumonias</td>
<td>28</td>
</tr>
<tr>
<td>bloodstream infections</td>
<td>35</td>
</tr>
</tbody>
</table>

through continuous surveillance

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)
Moni-ICU and -NICU/Surveillance

knowledge-based identification and automated monitoring of hospital-acquired infections in adult and neonatal patients in intensive care units
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
- Infection control
- ICU patient-specific alerts
- ICU cockpit surveillance at ward
- ICU cockpit surveillance remote

Medicine
**INFECTION SITE:** Symptomatic urinary tract infection

**CODE:** UTI-SUTI

**DEFINITION:** A symptomatic urinary tract infection must meet at least one of the following criteria:

**Criterion 1:** Patient has at least one of the following signs or symptoms with no other recognized cause: fever (≥38°C), urgency, frequency, dysuria, or suprapubic tenderness and patient has a positive urine culture, that is, ≥10⁵ microorganisms per cm³ of urine with no more than two species of microorganisms.

**Criterion 2:** Patient has at least two of the following signs or symptoms with no other recognized cause: fever (≥38°C), urgency, frequency, dysuria, or suprapubic tenderness and at least one of the following:

a. positive dipstick for leukocyte esterase and/or nitrate

b. pyuria (urine specimen with ≥10 wbc/mm³ or ≥3 wbc/high power field of unspun urine)

c. organisms seen on Gram stain of unspun urine

d. at least two urine cultures with repeated isolation of the same uropathogen (gram-negative bacteria or *S. saprophyticus*) with ≥10⁵ colonies/ml in nonvoided specimens

e. ≤10⁵ colonies/ml of a single uropathogen (gram-negative bacteria or *S. saprophyticus*) in a patient being treated with an effective antimicrobial agent for a urinary tract infection

f. physician diagnosis of a urinary tract infection

g. physician institutes appropriate therapy for a urinary tract infection.

**Criterion 3:** Patient ≤1 year of age has at least one of the following signs or symptoms with no other recognized cause: fever (≥38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting and patient has a positive urine culture, that is, ≥10⁵ microorganisms per cm³ of urine with no more than two species of microorganisms.

Patient ≤1 year of age has at least one of the following signs or symptoms with no other recognized cause: fever (≥38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting and at least one of the following:

a. positive dipstick for leukocyte esterase and/or nitrate

b. pyuria (urine specimen with ≥10 wbc/mm³ or ≥3 wbc/high power field of unspun urine)

c. organisms seen on gram stain or unspun urine

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g. physician institutes appropriate therapy for a urinary tract infection.

**COMMENTS:**

- A positive culture of a urinary catheter tip is not an acceptable laboratory test to diagnose a urinary tract infection.

- Urine cultures must be obtained using appropriate technique, such as clean catch collection or catheterization.

- In infants, a urine culture should be obtained by bladder catheterization or suprapubic aspiration; a positive urine culture from a bag specimen is unreliable and should be confirmed by a specimen aseptically obtained by catheterization or suprapubic aspiration.

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Hospital-acquired infections as defined by HELICS

4.2 Case definition of ICU-acquired pneumonia

**CODE:** PN

Two or more serial chest X-rays or CT-scans with a suggestive image of pneumonia for patients with underlying cardiac or pulmonary disease. In patients without underlying cardiac or pulmonary disease one definitive chest X-ray or CT-scan is sufficient.

and at least one of the following

- Fever > 38 °C with no other cause
- Leukopenia (<4000 WBC/mm³) or leucocytosis (≥ 12 000 WBC/mm³)

and at least one of the following
(or at least two if clinical pneumonia only = PN 4 and PN 5)

- New onset of purulent sputum, or change in character of sputum (color, odor, quantity, consistency)
- Cough or dyspnea or tachypnea
- Suggestive auscultation (rales or bronchial breath sounds), ronchi, wheezing
- Worsening gas exchange (e.g., O₂ desaturation or increased oxygen requirements or increased ventilation demand)
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

\[
\text{clinical}_{\text{signs of BSI}} \ (t-1d, t, t+1d) \\
\wedge \\
\text{same}_{\text{skin contaminant from two separate blood samples}}
\]
Deamination—clinical signs

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

clinical_signs_of_BSI (t-1d) = 

\lor

clinical_signs_of_BSI (t) = 

\lor

clinical_signs_of_BSI (t+1d) = 

fever (t-1d) 
\lor
hypotension (t-1d) 
\lor
leucopenia (t-1d) 
\lor
leucocytosis (t-1d) 
\lor
CRP increased (t-1d) 
\lor
fever (t) 
\lor
hypotension (t) 
\lor
leucopenia (t) 
\lor
leucocytosis (t) 
\lor
CRP increased (t) 
\lor
fever (t+1d) 
\lor
hypotension (t+1d) 
\lor
leucopenia (t+1d) 
\lor
leucocytosis (t+1d) 
\lor
CRP increased (t+1d)
Clinical signs—fever

fever (t-1d) ← ...

\[
\begin{align*}
\text{fever (t)} & \leftarrow \begin{cases} 
\text{body temperature } & \uparrow \\
\text{thermoregulation applied} & \ldots
\end{cases} \\
\text{fever (t+1d)} & \leftarrow \ldots
\end{align*}
\]

data import
intensive care unit

maximum value of the day
e.g., 38.5 °C

0 37 37.5 38 38.5 °C

1
Decomposition—skin contaminant

\[
\text{same}\_\text{skin}\_\text{contaminant}\_\text{from}\_\text{two}\_\text{separate}\_\text{blood}\_\text{samples} \iff \begin{cases} 
\text{first blood culture} \\
- \text{coagulase-negative staphylococci} \\
- \text{Micrococcus sp.} \\
- \text{Propionibacterium acnes} \\
- \text{Bacillus sp.} \\
- \text{Corynebacterium sp.} \\
\end{cases} \\
\wedge (\text{within 48 hours}) \\
\begin{cases} 
\text{second blood culture} \\
- \text{coagulase-negative staphylococci} \\
- \text{Micrococcus sp.} \\
- \text{Propionibacterium acnes} \\
- \text{Bacillus sp.} \\
- \text{Corynebacterium sp.} \\
\end{cases}
\]
**Processing layers**

```
layer n (goal)
layers n-y
layers n-x-y
layers n-x-y-1
layer 2
layer 1
layer 0 (start)

CDC, ECDC, KISS

linguistic HAI definitions

intermediate concepts:
pathophysiological states

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

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

reasoning

symbols

data-to-symbol conversion

raw data
```
Data sources and integration

HIS: hospital information system (here: HIS of the City of Vienna)
PDMS: patient data management systems (here: CareVue by Philips)
CDA: clinical data archive
ISM: information support mart
LIS: laboratory information system of the microbiology (here: HIS of the City of Vienna)
HIS DB: relational data base of medical data
Results with Moni-ICU

• **standard ward reporting:**
  Surveillance results of ICUs in tables and graphs for periodic epidemiology reporting to the Clinical Institute of Hospital Hygiene of our hospital, as well as separately for each ICU; optional format for requested institutional reporting

• **advanced cockpit reporting:**
  Graphical user interface displays daily “infection patterns”; and allows for deep insight at the level of vital parameters and basic clinical indicators for the particular patient

• Option: **automated reminders (alerts)** for conditions related to hospital-acquired infections
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)
Advanced cockpit surveillance

Each line in graph shows one patient stay

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

One patient stay selected at ward

Underlying clinical, lab, and RX findings

One day exploded

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
<table>
<thead>
<tr>
<th>Stationen/Patienten</th>
<th>BSI-1 (KISS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>2008-05-01</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Messwerte</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Interpretationen und Diagnosen</strong></td>
</tr>
<tr>
<td></td>
<td>lab: Interleukin 8: Min. 262 mg/dl</td>
</tr>
<tr>
<td></td>
<td>lab: Glucose: Max. 226 mg/dl</td>
</tr>
<tr>
<td></td>
<td><strong>BSI-1 (KISS)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>MIND 2</strong></td>
</tr>
<tr>
<td></td>
<td>path. Körpertemp. 100 %</td>
</tr>
<tr>
<td></td>
<td>path. Herzfrequenz (Definition) 100 %</td>
</tr>
<tr>
<td></td>
<td>metabolische Azidose (KISS) 100 %</td>
</tr>
<tr>
<td></td>
<td>neue Hyperglykämie (KISS) 100 %</td>
</tr>
<tr>
<td></td>
<td>laborchem. Zeichen für Entzündung (KISS) 100 %</td>
</tr>
<tr>
<td></td>
<td><strong>Interleukin 8 erhöht</strong></td>
</tr>
<tr>
<td></td>
<td>lab: Interleukin 8: Min. 262 mg/dl</td>
</tr>
<tr>
<td></td>
<td>lab: Interleukin 6 262 mg/dl</td>
</tr>
<tr>
<td></td>
<td>lab: Interleukin 8 262 mg/dl</td>
</tr>
<tr>
<td></td>
<td>lab: Interleukin 8 262 mg/dl</td>
</tr>
<tr>
<td>----------</td>
<td>------------</td>
</tr>
<tr>
<td>17:00</td>
<td>189</td>
</tr>
<tr>
<td>19:00</td>
<td>190</td>
</tr>
<tr>
<td>21:00</td>
<td>191</td>
</tr>
<tr>
<td>23:00</td>
<td>170</td>
</tr>
<tr>
<td>01:00</td>
<td>172</td>
</tr>
<tr>
<td>03:00</td>
<td>167</td>
</tr>
<tr>
<td>05:00</td>
<td>172</td>
</tr>
<tr>
<td>07:00</td>
<td>166</td>
</tr>
</tbody>
</table>
HAI episodes correctly / falsely identified or missed by Moni-ICU

<table>
<thead>
<tr>
<th></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>
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></td>
</tr>
<tr>
<td>- 156 + 170 parameters</td>
<td></td>
</tr>
<tr>
<td>• 161 Arden Syntax MLMs (1 control, 159 clinical rules, 1 storage) for 9 NEO-KISS definitions</td>
<td></td>
</tr>
<tr>
<td>- 7 bloodstream infections</td>
<td></td>
</tr>
<tr>
<td>- 2 ICU-acquired pneumonias (suspicion)</td>
<td></td>
</tr>
<tr>
<td>• data items</td>
<td></td>
</tr>
<tr>
<td>- 281 parameters</td>
<td></td>
</tr>
</tbody>
</table>
**Present state of Moni at the Vienna General Hospital (II)**

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

<table>
<thead>
<tr>
<th>Processing (about 15 minutes)</th>
<th>Processing (about 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>
Reasons for Moni’s success: clinical benefit

• 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 microbiology
  – support by medical administration
  – several lead users
Some notes on the generality of medical knowledge

Delta_k = given

Delta_I \rightarrow \text{as small as possible (by standardization)}

knowledge in MKPs

adaptation to institution

Delta_k = given

knowledge options: selection; configuration; confirmation

personalization of medical knowledge (sex, age, context)

data selection: preprocessing; feature selection

individual patient at institution
Arden Syntax—medical knowledge representation and processing
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

- Contraindication alerts, management suggestions, data interpretations, treatment protocols, and diagnosis scores are examples of the health knowledge that can be represented using MLMs.

  extended by single and differential diagnostic support, temporal monitoring, control systems, computerized processing of clinical pathways and management guidelines

- The first draft of the Arden Syntax was prepared at the Arden Homestead, New York, in 1989.

- The Health Level Seven Arden Syntax for Medical Logic Systems, Version 2.8, was approved by the American National Standards Institute (ANSI) and by Health Level Seven International (HL7) on 13 March 2012.
- **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**
Arden-Syntax-based, service-oriented clinical decision support
Arden Syntax, Arden Syntax server, and health care information systems

**Operational:**
- harmonized input data
- Arden Syntax MLMs
- collected reasoning data

**Exploratory:**
- rule learning/tuning
- data and concept mining

**Integration**
- HIS, MIS, PDMS, LIS,
- medical practice SW,
- web-based EHR,
- telemedicine applications,
- health portals,
- ...

**Functionality**
- reminders and alerts,
- monitoring,
- surveillance,
- diagnostic and therapeutic decision support,
- ...

*Data & Knowledge Services Center*

![Diagram of Arden Syntax server and health care information systems]
Computers in clinical medicine

Steps of natural progression

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>HIS 1.0</th>
<th>HIS 2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>patient administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ADT and billing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>medical data</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- electronic health record</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>medical data retrieval and analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- research databases, studies, quality management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>knowledge-based systems for clinical decision support</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- safety net, patient-centered quality assurance</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>... for the individual patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>... and the physician</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>... and the medical institution</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>